2017 KAAACI-WPAS-INTERASMA Joint Congress

Poster

P-01

Synchronization of seasonal rhino- and influenza- virus epidemic and burden of asthma exacerbation across all age groups

Shinhae Lee[2], Seung Won Lee[1], Youn Ho Sheen[3], Eun Kyo Ha[2], Sun Hee Choi[4], Min-Suk Yang[5], Sohyun Hwang[6], Sung Soon Kim[7], Jang-Hoon Choi[7], Man Yong Han[2]*

[1]CHA University School of Medicine, [2]Department of Pediatrics, CHA University School of Medicine, Seongnam, [3]Department of Pediatrics, CHA Gangnam Medical Center, CHA University School of Medicine, Seoul, [4]Department of Pediatrics, Kyung Hee University Hospital at Gangdong, Kyung Hee University School of Medicine, Seoul, [5]Department of Internal Medicine, SMG-SNU Boramae Medical Center, Seoul, [6]Department of Biomedical Science, CHA University School of Medicine, Seongnam; [7]Division of Respiratory Viruses Center for Infectious Diseases, National Institutes of Health, Korea Centers for Disease Control and Prevention, Cheongju-si, Chungcheongbuk-do, Korea

Background: Seasonal variation of asthma exacerbation (AE) is associated with virus spread and the returning to school after vacation.
Objective: This study aims to elucidate the period, phase and amplitude of seasonal cycles of asthma exacerbation across all age groups and regard to rhino- and influenza-virus epidemic in Korea.
Methods: The number of daily Emergency Department (ED) visits with AE across of all age groups and nationwide weekly incidence of rhino- and influenza- virus were obtained, during the 2008-2012. Fourier model for rhythmicity and Cosinor method for the amplitude and phase of cycle in five age groups (infant, preschool, school, adult and elderly) was applied. Cross-correlation function (CCF) was performed between the AE and rhino- and influenza-virus epidemic.
Results: The cohort consists of 157,559 events (0.62 event/1,000 population/1 years) of AE during study period. Bimodal peak of AE in spring and fall is observed in children and adult, whereas only one peak in winter is observed in the elderly. The amplitude of peak asthma exacerbation in infant was higher in spring than in fall (9.16 vs 3.04, $P < 0.01$), and the peak appeared approximately a month later in infant than in school age (Oct ,11 vs Nov 13, $P < 0.01$). Associations between the incidence of AE and rhinovirus has a peak in the school children (CCF rho=0.331), and influenza virus was a old aged (rho=0.682).
Conclusions: Rhythmicity, amplitude and phase of cycle of AE different with age group. Virus-dependent variations in asthma exacerbation were observed.

Key Words: Asthma exacerbation, Age, Respiratory virus, Rhythmicity, Cycle, Amplitude

P-02

Small airway bronchodilator response to different doses of salbutamol in 7-year-old children

Dong Keon Yon, Hye Mi Jee, Eun Gyo Ha, Jae Woo An, Seung Jin Lee, Young-Ho Jung, Gyong Suk Lee, Man Yong Han*

Department of Pediatrics, CHA Bundang Medical Center, CHA University School of Medicine, Seongnam, Korea

Background: The Global Initiative for Asthma (GINA) guidelines do not specify a bronchodilator range for BDR testing, and simply recommend a salbutamol dose of 200 to 400 μg.
Purpose: In this study, we determined the oscillometric BDR results of children given low-dose (2 puffs, 200 μg) and standard-dose (4 puffs, 400 μg) salbutamol to compare the small airway responses of healthy controls and exclusion subjects.
Method: We prospectively recruited 248 Korean children who were 7 years-old (167 boys, 81 girls) who participated in the atopy prevention project in the Seongnam Atopy Prevention program between January 2016 and December 2016. Each subject was given salbutamol (2 or 4 puffs), using a randomized and physician-blinded method, prior to IOS BRD testing. Subjects were categorized as having received 2 puffs (83 healthy controls and 41 exclusion subjects) or 4 puffs (85 healthy controls and 39 exclusion subjects) of salbutamol.
Results: Comparison of the oscillometric BDR data of healthy subjects in the low-dose and standard-dose groups indicated no significant absolute or relative differences in reactance at 5 Hz (Xrs5), and 10 Hz (Xrs10), resistance at 5 Hz (Rrs5), and 10 Hz (Rrs10), reactance area (AX), and difference of Rrs5 and Rrs20 (Rrs20-5). The exclusion subjects in the low-dose and standard-dose groups had significant differences in relative Xrs5 (baseline: -19.4 ± 14.4% versus -26.0 ± 12.6, $p = 0.032$), Xrs10 (baseline: -26.7 ± 50.6% versus -47.1 ± 15.4, $p = 0.017$), and AX (baseline: -28.4 ± 36.8% versus -43.7 ± 12.2, $p = 0.015$) and in absolute XRs10 (0.06 versus 0.08, $p = 0.043$).
Conclusion: The oscillometric response to salbutamol is significantly associated with small airway ysfunction in exclusion children. For further examination of reactance, we suggest use of the standard dose of salbutamol for oscillometric BDR testing. It is also necessary for the GINA guidelines to specify the amount of salbutamol inhaler to be used for BDR testing.

Key Words: Salbutamol, Small airway bronchodilator response, Children

P-03

Seasonal cycle and relationship of seasonal rhino- and influenza virus epidemics with episodes of asthma exacerbation in different age groups

Seung Won Lee[1], Shinhae Lee[2], Youn Ho Sheen[3], Eun Kyo Ha[2], Sun Hee Choi[4], Min-Suk Yang[5], Sohyun Hwang[6], Sung Soon Kim[7], Jang-Hoon Choi[7], Man Yong Han[2]*

[1]CHA University School of Medicine, [2]Department of Pediatrics, CHA University School of Medicine, Seongnam, [3]Department of Pediatrics, CHA Gangnam Medical Center, CHA University School of Medicine, Seoul, [4]Department of Pediatrics, Kyung Hee University Hospital at Gangdong, Kyung Hee University School of Medicine, Seoul, Korea, [5]Department of Internal Medicine, SMG-SNU Boramae Medical Center, Seoul, [6]Department of Biomedical Science, CHA University School of Medicine, Seongnam, [7]Division of Respiratory Viruses Center for Infectious Diseases, National Institutes of Health, Korea Centers for Disease Control and Prevention, Cheongju-si, Chungcheongbuk-do, Korea

Background: Seasonal variations of asthma exacerbation (AE) are associated with respiratory virus outbreaks and the return of children to school after vacation.
Objective: This study aims to elucidate the period, phase, and amplitude of seasonal cycles of AE in 5 age groups with regard to rhino- and influenza virus epidemics in Korea.
Methods: The number of daily emergency department (ED) visits for AE in all age groups of Korea and the nationwide weekly incidence of rhino- and influenza virus, were obtained for 2008-2012. Fourier regression was used to model rhythmicity, and the Cosinor method was used to determine the amplitude and phase of the cycles in each age group. The cross-correlation function (CCF) between AE and the rhino- and influenza virus epidemics was also calculated.
Results: There were 157,559 events of AE (0.62 events/1,000 people/year) during the study period. There were spring and fall peaks of AE in children and adults, but only 1 winter peak in the elderly. The amplitude of the AE peak in infants was higher in spring than in fall (9.16 vs. 3.04, $P < 0.01$), and the fall peak was approximately 1 month later in infants than in school children (Oct 11 vs. Nov 13, $P < 0.01$). The association between AE and rhinovirus was greatest in school children (CCF rho = 0.331), and the association between AE and influenza virus was greatest in those older than 60 years-old (CCF rho = 0.682).
Conclusions: The rhythmicity, amplitude, and phase of the annual cycle of AE differed among different age groups. The patterns of AE were related to the annual rhino- and influenza virus epidemics.

Key Words: Asthma exacerbation, Seasonal cycle, Virus epidemics

P-04

Clinical features of adult asthmatic patients according to the frequency of severe asthma exacerbation

Ga-Young Ban[1], Hyun Young Lee[2], Young-Min Ye[1], Yoo Seob Shin[1], Hae-Sim Park[1]*

[1]Department of Allergy and Clinical Immunology, Ajou University School of Medicine, [2]Department of Statistics, Clinical Trial Center, Ajou University Medical Center, Suwon, Korea

Background: The long-term goals of asthma management are to achieve good symptom control, and to minimize future risk of exacerbations. Identification of risk factors is important for reducing asthma exacerbation. The majority of researches that assessed predictors associated with asthma exacerbation are studied on the basis of controlled study design. In the present study, we investigated the predictors for asthma exacerbation in long term follow up management with analyzing big data of electronic medical records (EMR).
Methods: Subjects diagnosed as asthma from Jan., 1995 to Nov., 2014 with J45 code in EMR of Ajou University Hospital and treated for more than 1 year were enrolled. From cumulative EMR big data, systemic steroid prescription history was extracted. Extracted EMR data was condensed depending on the history of systemic steroid burst (SSB, prednisone-equivalent dose $\geq$45mg/3days in a 1 year).
Results: A total of 10,759 patients were enrolled. Of total study subjects, 311 (2.9%) subjects experienced severe asthma exacerbation ($\geq$2 SSB) during initial 2 years of asthma treatments. The number of SSB episode was significantly elevated in the patients with older age of initial diagnosis of asthma (OR=1.021, $P<0.001$) and low lung functions (OR=0.986, $P<0.001$ in FEV1 and OR=0.978, $P<0.001$ in FEV1/FVC). The number of SSB episode in total follow up period was significantly affected by that of SSB during initial 2 years of asthma treatment (number of SSB during initial 2 years $\geq$4, OR=15.101, $P<0.001$; 2-3, OR = 9.253, $P<0.001$ compared to those with 0-1 episode). Furthermore, number of SSB during initial 2 years significantly influenced the lung function declining tendency including FEV1 and FEV1/FVC ($P<0.001$ for all).
Conclusion: Asthmatics with lower lung function at initial assessment should be carefully monitored for predicting future risk of severe asthma exacerbation. Further studies regarding biomarkers predicting future asthma exacerbation are needed.

Key Words: Asthma, Severe asthma exacerbation, FEV1

P-05

Effect of pregnancy on quantitative medication-use and their relation with exacerbations in asthma

Yunsun Kim[1], So-My Koo[2], Chorong Park[1], Gun Woo Park[3], MoonGyu Lee[3], Sungho Won[3], Hyeon-Jong Yang[1]*

[1]SCH Biomedical Informatics Research Unit, Soonchunhyang University Seoul Hospital, Seoul, Korea. Pediatric Allergy and Respiratory Center, Department of Pediatrics, Soonchunhyang University Seoul Hospital, Soonchunhyang University College of Medicine, [2]Division of Allergy and Respiratory Medicine, Department of Internal Medicine, Soonchunhyang University Seoul Hospital, Soonchunhyang University College of Medicine, [3]Department of public health science, Graduate School of Public Health, Seoul National University, Seoul, Korea. Interdisciplinary Program of Bioinformatics, Seoul National University, Seoul, Korea. Institute of Health and Environment, Seoul National University, Seoul, Korea

Background: Pregnant women tend to stop or reduce asthma treatment during pregnancy. Few studies have assessed the asthma symptoms followed by the changes in maintenance of therapy during pregnancy.
Methods: We conducted a nationwide, retrospective asthmatic pregnant women cohort study using the data from Health Insurance Review and Assessment Service in South Korea. All of asthma-medications were categorized as 1 to 4 of rank according to the guideline-based stepwise approach. We assessed the daily rank-sums of asthma-medications and their association with asthma-exacerbations during three phases based on the dates of delivery; before, during, and after pregnancy.
Results: The study cohort included 115,169 asthmatic pregnant women who gave a birth between 2011 and 2013.They were clustered into four groups according to the rank-sum of asthma-medication. Overall asthma-medications were rapidly reduced in the beginning of pregnancy, and then slowly increased after the delivery. However, reduced ranks of asthma- medications were not related with asthma-exacerbations.
Conclusions: The Korean asthmatic pregnant women tended to stop or reduce asthma-medications during pregnancy. That caused more asthma-exacerbation in only part of population, but others were not affected. Further study is needed to determine whether the reduced asthma-medications cause exacerbations during pregnancy in real practice.
Funding source: This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (grant number : HC15C1302)

Key Words: Asthma, Insurance claim review, pregnancy

P-06

Trend of aero inhalant-allergen and Dermatophagoides pteronissus sensitization ratio over the past three decades in Korea

Eun Kyo Ha[1], Min Sun Na[1], Hyeong Yun Kim[1], Keong Suk Lee[1], Young-Ho Jung[1], Mi Ae Kim[2], Hye Mi Jee[1], Youn Ho Sheen[3], Man Yong Han[1]*

[1]Department of Pediatrics, CHA Bundang Medical Center, CHA University, Seongnam, [2]Department of Medicine, CHA Bundang Medical Center, CHA University School of Medicine, Seongnam, [3]Department of Pediatrics, CHA Gangnam Medical Center, CHA University, Seoul, Korea

Background: Prevalence of allergic diseases is known to be closely linked to aero-allergen sensitization and may be associated with recent climate changes. The aim of this study is to investigate trends of relative sensitization rates of aeroallergens compared to that of Dermatophagoides pteronyssinus (Der p.) of the national population in Korea over the past three decades.
Method: Previous studies with data on skin prick tests of house dust mites (Der p.) along with other aeroallergens published between 1982 and 2014 were reviewed by searching websites of institutes and libraries of medicine in Korea. We calculated the relative sensitization ratio of inhalant allergens to Der p. To explore the trend of the sensitization ratio of aeroallergens to Der p during the study period, we used the generalized linear regression model after adjustment for the subject number, gender, age group (children and adults), region (mainland of Korea and Jeju island), and type of study (epidemiologic study or hospital-based study).
Results: Fifty-three articles were included and a total of 70,773 subjects were analyzed during the study period. Increasing trends in common pollen to Der p sensitization ratio such as birch/Der p ($B=1.183$, $SE=0.01$, $P < 0.025$) and oak/Der p ($B=0.579$, $SE=0.246$, $P = 0.019$) were observed. A similar trend was observed in grass sensitization such as timothy/Der p ($B=0.734$, $SE=0.3378$, $P = 0.030$). Trends of sensitization ratio for weeds did not change significantly over the study period. However, alternaria/Der p ($B=-0.280$, $SE = 0.1370$, $P = 0.041$) and Cockroach/Der p ($B=-1.073$, $SE=0.3612$, $P = 0.003$) significantly decreased during the study period. Sensitization ratio of animals such as cat ($B=-1.832$, $SE =0.3759$, $P < 0.001$) and dog ($B=-0.983$, $SE=0.2590$, $P < 0.001$) also decreased significantly.
Conclusion: An increase in sensitizations ratio of pollen to Der p was observed for pollens (e.g. birch and aak), whereas mold (e.g alternaria), cockroach, and pet danders (e

Key Words: Sensitization, Trend, 30 years

P-07

A Delphi approach to development of standard questionnaire to investigate asthma in Korean children

Jae Woo An, Eun Kyo Ha, Dong Keon Yon, Kyung Suk Lee, Man Yong Han*

Department of Pediatrics, CHA Bundang Medical Center, CHA University, Seongnam

Purpose: Nowadays, the prevalence and disease burden of asthma have increased. So the need for early diagnosis and appropriate management of asthma is emerging. However, it is difficult to identify the diagnosis, symptoms and the prevalence of asthma due to lack of reliable investigating items. The purpose of this study is development of survey and manual in order to assess prevalence of pediatric asthma in Korea.
Experimental design: We investigated surveys and related information that are utilized to assess asthma diagnosis and prevalence by Systematic Review. After then, delphi survey was conducted on 20 Korean pediatric allergists in order to develop a standardized survey and manual in Korea. The process consisted of 3 serial rounds across 3 age groups (less than 5 years old, greater than or equal to 5 years old). Each subsequent round narrowed investigating items for the decision of standard set about asthma prevalence, current asthma, and asthma aggravation.
Results: Lifetime asthma was defined "ever doctor-diagnosed asthma" in all age groups. Current asthma was defined "treatment for asthma during the past 12 months" in all age groups, and "doctor-diagnosed asthma during the past 12 months" was added on greater than or equal to 5 years old group. 'Wheezing, ever" was defined "wheezing at any time in the past?" and Current wheeze was defined "wheezing in the last 12 months" Asthma aggravation was defined "visited emergency room or admission due to asthma attack within the last 12 months" in all age groups.
Conclusion: We could conclude applicable nationwide definition of "lifetime asthma", "current asthma" and "asthma aggravation" in Korean children by the Delphi survey

Acknowledgement: This research was supported by fund 2015-P66002-00 by Research of Korea Centers for Disease Control and Prevention.

Key Words: Asthma, questionnaire, Delphi

P-08

Risk factors predicting acute exacerbations in elderly asthma cohort in Korea

Kyoung-Hee Sohn[1], Ha-Kyeong Won[1], Sung-Yoon Kang[1], Byung-Keun Kim[4], Woo-Jung Song[1], Jong-Suk Park[5], Hye-Ryun Kang[1], Tae-Bum Kim[6], Heung-Woo Park[1], Choon-Sik Park[5], Sang-Heon Cho[1]*

[1]Division of Allergy and Clinical Immunology, Department of Internal Medicine, Seoul National University College of Medicine, Seoul, [2]Institute of Allergy and Clinical Immunology, Seoul National University Medical Research Center, Seoul National University College of Medicine, Seoul, [3]Department of Public Health andMedical Service, Seoul National University College of Medicine, Seoul, [4]Department of Internal Medicine, Korea University Medical Center Anam Hospital, Seoul, [5]Division of Allergy and Respiratory Medicine, Soonchunhyang University Bucheon Hospital, Bucheon, [6]Department of Allergy and Clinical Immunology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

Introduction: Asthma in the elderly (age ≥ 65 year-old)is increasing and poses a great socioeconomic burden on the health care system.So far, little has been known on the risk factors associated acute exacerbations in elderly asthma patients.
Methods: Three existing adult asthma cohorts in Korea merged into one elderly asthma cohort with a unified protocol and database.We selected a total of 598 patients from the merged cohort to evaluate risk factors predicting acute exacerbation during one year prior to the enrollment. They were divided into two sets; recovery and validation set.Using the recovery set, we searched clinical characteristics associated with acute exacerbation. Then we tested whether these results were replicated in the validation set.
Results: A total of 334 patients were assigned to the recovery set and the rest in the validation set. Duration of symptom, smoking, baseline FEV1, FVC, FEV1/FVC ratio and fixed airway obstruction (defined as a state when predictive value of post bronchodilator FEV1 is less than 80% after 6 months of treatment) showed significant associations with acute exacerbations in the recovery set, which was replicated in the validation set. Among risk factors for acute exacerbations, fixed airway obstruction was the most significant one in both sets.
Conclusion: In this study we identified fixed airway obstruction as the most important factor predicting acute exacerbations in the elderly asthma patients.

(This research was supported by a fund(code: HD16A1150) by Research of Korea Centers for Disease Control and Prevention.)

Key Words: Asthma, elderly, cohort studies

P-09

Integrative Information Theoretic Network Analysis for Genome-Wide Association Study of Aspirin Exacerbated Respiratory Disease in a Korean Population

Sehee Wang[1], Kyung-Ah Sohn[1], Kyubum Wee[1], Hae-Sim Park[2], Seung-Hyun Kim[2]*

[1]Department of Software and Computer Engineering, Ajou University, [2]Department of Allergy and Rheumatology, School of Medicine, Ajou University

Aspirin Exacerbated Respiratory Disease (AERD) is a chronic medical condition that encompasses asthma, nasal polyposis, and hypersensitivity to aspirin and other non-steroidal anti-inflammatory drugs. Several previous studies have shown that part of the genetic effects of the disease may be induced by the interaction of multiple genetic variants. However, heavy computational cost as well as the complexity of the underlying biological mechanism has prevented a thorough investigation of epistatic interactions and thus most previous studies have typically considered only a small number of genetic variants at a time.

In this study, we propose a gene network based analysis framework to identify genetic risk factors from a genome-wide association study dataset. We first derive multiple single nucleotide polymorphisms (SNP)-based epistasis networks that consider marginal and epistatic effects by using different information theoretic measures. Each SNP epistasis network is converted into a gene-gene interaction network, and the resulting gene networks are combined as one for downstream analysis. The integrated network is validated on existing knowledgebase of DisGeNET for known gene-disease associations and GeneMANIA for biological function prediction.

We demonstrated our proposed method on a Korean GWAS dataset, which has genotype information of 440,094 SNPs for 188 cases and 247 controls. The topological properties of the generated networks are examined for scale-freeness, and we further performed various statistical analyses in the Allege and Asthma Portal (AAP) using the selected genes from our integrated network. Our result reveals that there are several gene modules in the network that are of biological significance and have evidence for controlling susceptibility and being related to the treatment of AERD.

Key Words: Aspirin Exacerbated Respiratory Disease, Genome-Wide Association Study, Epistasis

P-10

Additive effect between socioeconomic status and meat diet pattern on current symptoms of allergic diseases in school children : A cross-sectional study

Hyeok Kwon[1], So-Yeon Lee[2], Hyo Bin Kim[3], Hea Young Oh[1], Jisun Yoon[2], Ho-Jang Kwon[4], Se-Young Oh[5], Soo Jong Hong[2]*

[1]Research Center for Standardization of Allergic Diseases, Asan Institute for Life Sciences, University of Ulsan College of Medicine, Seoul, [2]Department of Pediatrics, Childhood Asthma and Atopy Center, Environmental Health CenterAsan Medical Center, University of Ulsan College of Medicine, [3]Department of Pediatrics, Inje University Sanggye Paik Hospital, Seoul, [4]Department of Preventive Medicine, College of Medicine, Dankook University, Cheonan, [5]Department of Food & Nutrition, Research Center for Human Ecology, College of Human Ecology, Kyung Hee University, Seoul, Korea

Background: Socioeconomic status(SES) influences the lifestyle, such as diet pattern, which may affect the development of allergic diseases.
Objective: We investigated the association between SES and allergic diseases mediated by diet pattern in elementary schoolchildren.
Methods: We included 4,086 children (mean age:7.7) with food frequency questionnaire(FFQ) data from the Children's HEalth and Environmental Research. We evaluated on household income, parental education, allergic diseases and children\'s FFQ. Factor analysis through the FFQ showed dietary pattern was classified into traditional, convenient and meaty patterns. Logistic regression analysis was used to examine the association between allergic diseases, SES and dietary patterns.
Results: The high SES was significantly associated with the lifetime prevalence of atopic dermatitis (AD) diagnosis (income: aOR 1.386, 95%CI 1.191-1.613, education: aOR 1.233, 95%CI 1.056-1.440) and allergic rhinitis (AR) diagnosis (income: aOR 1.504, 95%CI 1.271-1.778, education: aOR 1.656, 95%CI 1.402-1.956). The higher SES was associated with the higher score of meat diet pattern. Meat diet pattern was associated with current symptoms and treatment of AD (aOR 1.226, 95%CI 1.005-1.495, aOR 1.337, 95%CI 1.074-1.665) and AR (aOR 1.203, 95%CI 1.009-1.433, aOR1.182, 95%CI 0.958-1.459). Current symptoms of AD and AR were significantly increased in children with high maternal education level and high meat diet pattern (aOR 1,549, 95%CI 1.235-1.944, aOR 1.293, 95%CI 1.003-1.667). Current treatment of AR is also increased (aOR 1.803, 95%CI 1.362-2.387).
Conclusion: Current symptoms of AR and AD were related with SES and diet pattern. Therefore, SES may affect current status of allergic diseases by lifestyle, such as diet.
Funding: This research was supported by Basic Science Research Program through the National Research Foundation of Korea(NRF) funded by the Ministry of Science, ICT and future Planning(NRF-2014R1A2A1A10050687)

Key Words: Socioeconomic status, diet, allergic diseases

P-11

Demographic and clinical characteristics of adult patients with severe refractory asthma: the Korean Academy of Asthma, Allergy and Clinical Immunology, Severe Asthma Work Group Registry

Min-Hye Kim[1], Sang-Heon Kim[2], Hye-Ryun Kang[9], Jong-Sook Park[10], Tae-Bum Kim[3], Heung-Woo Park[9], Kwang-Ha Yoo[11], Yeon-Mok Oh[3], Young-Il Koh[12], An-Soo Jang[10], Byung-Jae Lee[13], Ho Joo Yoon[2], So-Young Park[3], Young-Joo Cho[1], Sang-Heon Cho[9], Hae-sim Park[4], Choon-Sik Park[10], Ga-Young Ban[4], Joo-Hee Kim[5], Jae-Woo Jung[6], Ji Yong Moon[2], Hyouk-Soo Kwon[3], Jae-Woo Kwon[7], Jae Hyun Lee[8], You Sook Cho[3]*

[1]Department of Internal Medicine, Ewha Womans University School of Medicine, [2]Department of Internal Medicine, Soonchunhyang University College of Medicine, [3]Department of Internal Medicine, Konkuk University College of Medicine, [4]Department of Internal Medicine, Chonnam National University Medical School & Hospital, [5]Department of Medicine, Sungkyunkwan University School of Medicine, [6]Department of Internal Medicine, Hanyang University College of Medicine, [7]Department of Internal Medicine, University of Ulsan College of Medicine, [8]Department of Allergy and Clinical Immunology, Ajou University School of Medicine, [9]Department of Internal Medicine, Hallym University College of Medicine, [10]Department of Internal Medicine, Chung-Ang University College of Medicine, [11]Department of Internal Medicine, Kangwon National University School of Medicine, [12]Department of Internal Medicine, Yonsei University College of Medicine, [13]Department of Internal Medicine, Seoul National University College of Medicine

Background: Although severe asthma accounts for only 5-10% of total asthmatics, the morbidity and mortality is much higher than mild to moderate asthma. To understand the characteristics and the pathomechanisms of severe asthma, we registered the patients with severe refractory asthma in the Korean Academy of Asthma, Allergy and Clinical Immunology, Severe Asthma Work Group Registry.
Methods: We have enrolled the patients with severe asthma from the 15 hospitals nationwide in Korea since 2010. Severe asthma was defined as followings: patients who do not consistently reach a well-controlled state even after GINA treatment step 4, or who have reached a well-controlled state, but have more than one urgent care visit a year or need to use more than 3 times of steroid burst or exacerbate when oral or inhaled corticosteroids (ICS) reduced 25% or have a near-fatal-asthma attack anytime in the past. Information for demographics, medical history, pulmonary function test, and skin prick test were collected.
Results: A total of 494 patients were enrolled with a mean age of 62 years and 45% men. The most common comorbidities were allergic rhinitis (52.0%) and hypertension (30.0%). Aspirin hypersensitivity was observed in 11.3% and non-smokers were 53.4%. In terms of asthma medications, ICS + long-acting β-agonists were prescribed dominantly (95.3%), followed by leukotriene antagonists (70.0%), methylxanthines (56.3%), and short-acting β-agonist (37.2%). Systemic steroids and anti-IgE antibody had been used in 58.5% and 1.8% of patients, respectively. The mean FVC, FEV1, and FEV1/FVC were 78.8%, 67.6% of predicted value, and 68.1%, respectively. Bronchodilator response was proven in 34.1% and skin test was positive in 50.2% of patients.
Conclusions: The characteristics of severe asthma patients were analyzed through the Severe Asthma Work Group Registry. Based on this cohort, more prospective studies will be done to evaluate and manage severe asthma in the future.

Key Words: Asthma; Severe asthma; Registry; Population Characteristics

P-12

Laboratory Animal Allergy and Pet Allergy among Korean Laboratory Animal Researchers

Sang Min Lee, Jeong Woo Shim, Hong Seok Park, Sang Pyo Lee*

Gachon University Gil Medical Center

Background: Prevalence of laboratory animal allergy (LAA) and pet allergy (PA) among laboratory animal researchers, especially in Korea, is not fully investigated yet.
Methods: Korean laboratory researchers who attended 2016 annual symposium of Korean Association of Laboratory Animal Science were asked to answer the questionnaires regarding animal allergy and to undergo skin prick test for animal allergens including mouse, rat, cat, dog, rabbit, hamster, guinea pig, cow, pig, horse, and chicken.
Results: A total of 135 out of 618 attendants were enrolled. Among them, seventy three (11.8% of attendants) complained of allergic symptom while they contacted with laboratory or pet animals (29 with mouse, 15 with rat, 11 with cat, 8 with dog, 7 with rabbit, 1 with hamster, 1 with pig, and 1 with hedgehog). In these subjects with animal allergy, allergic conjunctivitis was more prevalent (17.8% vs. 1.6%, $P=0.002$), and sensitization to animal allergen including mouse, rat, dog, cat, guinea pig, hamster, and horse was more frequent ($P<0.05$ for each allergen) than in those without animal allergy. Furthermore, they were also sensitized to various animal allergens other than their causal animal allergen. Meanwhile, they contacted less diverse kinds of animals (3.6 ± 2.8 species vs. 4.6 ± 3.1 species, $P=0.051$) in their lives, especially in terms of dog, hamster, chicken, monkey and sheep ($P<0.05$ for each animal). In them, symptoms of rhinitis were most frequently complained of (76.7%), followed by those of skin (42.5%), conjunctivitis (41.1%), and lower respiratory tract (19.2%).
Conclusion: More than 10 percent of laboratory animal researchers experienced LAA or PA, and sensitized to various animal allergens, however they had contacted with less variety of animals in their lives compared to those without animal allergy.

Acknowledgement: This research was supported by BSRP through the NRF funded by the Ministry of Science, ICT & Future Planning (NRF-2015R1D1A1A02061943).

Key Words: Laboratory animal, Pet, Allergy

P-13

Analysis of airway and gut microbiome in IL-13 rich chronic asthma model

Bo-Ram Bae[1], Sung-Mi Choi[2], Kyoung-Hee Sohn[4], Hyun-Seung Lee[1], Woo-Jung Song[3], Hana Yi[5], Heung-Woo Park[3], Sang-Heon Cho[3], Hye-Ryun Kang[3]*

[1]Institute of Allergy and Clinical Immunology, Seoul National University Medical Research Center, Seoul National University College of Medicine, Seoul, [2]Department of Public Health Sciences, Graduate School, Korea University, Seoul, [3]Division of Allergy and Clinical Immunology, Department of Internal Medicine, Seoul National University College of Medicine, Seoul, [4]Department of Public Health and Medical Service, [5]School of Biosystem and Biomedical Science, Korea University, Seoul, Korea

Background: The potential role of microbial colonization in the inception of chronic airway diseases is increasingly evident with recent studies. However, it is not clear whether their association is a result of co-phenomenon or mutual interaction and the impact of airway microbial dysbiosis can induce alteration of microbiota in gut.
Objective: We investigated to characterize airway microbiome in IL-13 over-expressing mice and the related alteration of gut microbiota.
Methods: Bronchalveolar lavage fluid (BAL), lung tissue, and stool were obtained for microbiome analysis from 10 week old normal C57BL/6 mice (n = 30) and IL-13 over-expressing mice (n = 30). After extracting the metagenome using Mobio\'s FastDNA™ SPIN Kit for Soil DNA, amplify the V3-V4 of 16s rRNA using the Nextera XT Index Kit according to the 16S Metagenomic Sequencing Library Preparation Manual of Illumina.
Results: In BAL samples, 2 major bacterial phyla, Cyanobacteria, Proteobacteria, were present in higher proportions in IL-13 over-expressing mice compared control mice. At the species level, the OTU analysis was conducted through the eztaxon database to identify the most similar species and a total of 22 OTUs showed differences between normal and IL-13 over-expressing mice. In stool samples, 3 major bacterial phyla, Bacteroidetes, TM-7, and Verrucomicrobia, were increased while Firmicutes were decreased in mice with lung-specific IL-13 overexpression. The Shannon index and Simpson index showed that the lung-specific IL-13 over-expression mice had slightly reduced microbial diversity composition compared to the normal mice. Composition of bacterial community also differed in their relative abundance in BAL and stool samples between IL-13 over-expressing mice and normal mice.
Conclusion: IL-13 over-expressing mice showed alteration of diversity and compostion of airway and gut microbiome.These data suggest that lung microenvironmental changes by IL-13 can induce dysbiosis of airway and gut micr

Key Words: Asthma, Microbiome, IL13

P-14

Genetic Effects on Production of Arachidonic acid metabolites and their Clinical Implication

Ga-Young Ban[1], Hyun Young Lee[2], Su Chin kim[2], Seung-Hyun Kim[2], Yoo-Seob Shin[1], Young-Min Ye[1], Hae-Sim Park[1]*

[1]Department of Allergy and Clinical Immunology, Ajou University School of Medicine, [2]Department of Statistics, Clinical Trial Center, Ajou University Medical Center, Suwon, Korea

Background: It is widely known that several arachidonic acid metabolites play important roles in airway inflammation in asthma. However, there are few studies investigating genetic effects on production of these arachidonic acid metabolites.
Objectives: To investigate the genetic effects on production of arachidonic acid metabolites related with asthma pathogenesis.
Subjects and Method: A total of 95 aspirin-exacerbated respiratory disease (AERD) and 94 aspirin tolerant asthma (ATA) patients were enrolled. The metabolites of LTE4, 15-HETE and eoxin C4 were analyzed using the UHPLC/Q-ToF MS system. HLA-DPB1 high-resolution genotyping was obtained from direct sequencing method and polymorphisms of CysLTR1 -634C>T, LTC4S -444A>C, ALOX15 -272C>A and ALOX15 -427 G>A were genotyped using SNaP shot ddNTP primer extension kit.
Results: The levels of urine LTE4 were significantly higher in patients carrying HLA-DPB1*0301 and TT genotype at CYSLTR1 -634C>T (P = 0.041 and 0.015, respectively), while no differences were found in serum LTE4. The levels of urine and serum LTE4, eoxin C4, and 15-HETE were not significantly different according to the genotype of LTC4S and ALOX15 polymorphisms. The levels of serum eoxin C4 in AERD patients with the AA genotype at LTC4S -444A>C were significantly increased after Lys-ASA BPT, while the AERD patients with AC/CC genotype showed no significant changes. The interaction between the TT genotype at CYSLTR1 -634C>T and urine LTE4 levels had a significant effect on the % fall of FEV1 after Lys-ASA BPT (P <0.001, OR= 1.756). AERD patients with TT genotype at CYSLTR1 -634C>T showed lower levels of FEV1 and FEV1/FVC than those with CT/TT genotype in long term follow up period (P =0.034, OR= 0.603 and P=0.031,OR=0.796).
Conclusion: HLA-DPB1*0301 and genetic polymorphisms of CysLTR1 -634C>T affect LTE4 overproduction which can contribute to promote the airway inflammation in AERD.

Key Words: Leukotriene E4, Asthma, Gene

P-15

The comparison of gene expression profiling in lungs of high fat diet-induced obesity and allergic airway inflammation in mice

Yoon Hee Park, Misuk Yang, Eun Yi Oh, Kyung Hee Park, Jae-Hyun Lee, Jung Won Park*

Department of Internal Medicine, Institute of Allergy, Yonsei University College of Medicine, Seoul 03722, Korea

Background: Obese asthma patients respond poorly to conventional asthma medications, resulting in severe symptoms and poor prognosis. To investigate the comparison of gene expression levels among obesity, asthma and obese asthma, we performed the microarray analysis in murine model.
Methods: We fed C57BL/6J mice a normal diet (ND) or high-fat diet (HFD) for 3 months with or without ovalbumin (OVA) sensitization and challenge. We designed four groups (Naive ND, OVA ND, Naive HFD and OVA HFD). Airway hyper-responsiveness (AHR), bronchoalveolar lavage fluid (BALF) and microarray analysis of the lungs in mice were analyzed.
Results: OVA ND group, Naive HFD group and OVA HFD group showed significant AHR compared to Naive ND group. Although OVA ND group and OVA HFD group increased the cell proliferation in bronchoalveolar fluid (BALF), naive HFD group did not affect that. We evaluated the different gene expression levels in four groups.
Conclusion: In this study, we suggested that HFD group induced AHR through the different mechanism in contrast with OVA group. Therefore, the functional implication of up- and down-regulated genes on HFD group should be studied more in detail.

Key Words: Airway Inflammation, Asthma, Obesity, Microarray

P-16

Role of Transforming Growth Factor-β1 in Workers Exposed to Toluene Diisocyanate

Ji-Ho Lee, Hoang Kim Tu Trinh, Chang-Gyu Jung, Youngwoo Choi, Eun-Mi Yang, Batsetseg Ulambayar, Hae-Sim Park*

Department of Allergy and Clinical Immunology, Ajou University School of Medicine, Suwon, Korea

Background: Although, toluene diisocyanate (TDI) is one of the leading cause of occupational asthma (OA), its pathogenic mechanism has not been fully recognized. Neutrophil activation and increased expression of TGF-β1(a representing cytokine of airway remodeling) were noted in airway mucosa of TDI-induced OA patients. This study investigated the role of TGF-β1 in the development of TDI-induced OA.
Methods: Enzyme-linked immunosorbent assay was used to measure serum level of TGF-β1. In vitro test, human airway epithelial cells (HAECs), A549 cells, was treated with TDI-human serum albumin conjugate (TDI-HSA) to find inflammatory cytokine including IL-8, a key chemokine for neutrophil recruitment, by which TDI affects on airway inflammation. Peripheral blood neutrophils were isolated from healthy control for co-culture with HAECs.
Results: Eighty eight TDI-OA, 125 asymptomatic exposed controls (AECs) and 159 unexposed healthy normal controls (NCs) were enrolled. Serum level of TGF-β1 was significantly higher in TDI-exposed subjects including TDI-OA and AECs than in NCs (all $P<0.001$). TDI-exposed subjects was well discriminated from NCs with cut-off value of 34.5 ng/ml of TGF-β1 (AUC=0.833, $P<0.001$). TGF-β1 and IL-8 production were measured in HAECs after treating with TDI-HSA. Both levels were increased by TDI in dose-dependent manners and positively correlated ($r=0.501$, $P<0.001$). Co-culture with peripheral blood neutrophils also increased TGF-β1 production from HAECs.
Conclusion: Airway epithelial cells can be activated and release TGF-β1, which might be involved in airway remodeling in TDI-OA, either by TDI directly or neutrophil recruitment indirectly.

Key Words: Transforming growth factor-β1, toluene diisocyanate, occupational asthma

P-17

Eosinophilic Biomarkers for Predicting the Phenotypes of Severe Asthma

Youngsoo Lee, Ji-Ho Lee, Eun-Mi Yang, Chang-Gyu Jung, Su-Chin Kim, Young-Min Ye, Yoo Seob Shin, Hae-Sim Park*

Department of Allergy & Clinical Immunology, Ajou University School of Medicine, Suwon, Korea

Background: Severe asthma accounts for only 5-10% of total asthma patients, however, it is responsible for > 50% of total medical expenses for asthma patients. Severe asthma patients are suffering from frequent asthma exacerbations, in which ICS is a key anti-inflammatory agent to control eosinophilic inflammation to prevent asthma exacerbation.
Objective: We determined to compare clinical characteristics and serum levels of eosinophilic biomarkers between severe and non-severe asthma (mild to moderate) patients to evaluate whether they may predict the phenotypes of severe asthma.
Methods: A retrospective analysis of electrical medical record was performed. Severe (n=235) and non-severe (n=898) asthma patients were recruited from Ajou University Hospital. Asthma-related clinical parameters were collected. We measured eosinophilic cationic protein (ECP), serum eotaxin-1/2, eosinophil-derived neurotoxin (EDN), and periostin in sera of study subjects using ImmunoCAP (TheromoFisher, Sweden) and ELISA.
Results: Severe asthmatics had more smoking history (P=0.043), higher prevalences of chronic rhinosinusitis (P=0.008)/nasal polyps (P=0.007), higher serum ECP levels (P=0.001), lower FEV1% (P<0.001) and PC20 methacholine values (P=0.017) compared to non-severe asthmatics. Eosinophilic inflammatory markers such as eotaxin-2 (P=0.024), EDN (P=0.012), soluble P-selectin (P<0.001) and periostin (P=0.001) were significantly higher in severe asthmatics than in non-severe asthmatics. EDN showed positive correlations with peripheral eosinophil count (r=0.380, P=0.008), and soluble P-selectin (r=0.329, P=0.003) and periostin (r=0.354, P=0.001) in severe asthmatics.
Conclusion: Elevated levels of eosinophilic biomarkers reflect activation of ongoing eosinophilic inflammatory pathways leading to development of severe asthma. Additional research for these biomarkers will be a great value for improvement of severe asthma management by application of medicines targeting them.

Key Words: Severe asthma; Biomarkers; Eosinophil

P-18

Role of folliculin in aspirin-exacerbated respiratory disease

Trinh Hoang Kim Tu[1], Le Duy Pham[2], Young-Woo Choi[1], Dong-Hyun Lee[2], Seung-Hyun Kim[1], Hae-Sim Park[2]*

[1]Department of Allergy & Clinical Immunology, [2]Department of Biomedical Sciences, The Graduate School, Ajou University School of Medicine, Suwon, Korea

Introduction: The role of folliculin (FLCN), an intracellular protein of epithelial cells, in asthma and aspirin-exacerbated respiratory disease (AERD) is under-investigated.
Objectives: To elucidate the role of FLCN in AERD compared to aspirin-tolerant asthma (ATA) groups.
Material & Methods: We enrolled 178 patients with AERD, 276 patients with ATA and 71 normal healthy controls (NCs) from the Ajou University Medical Center. Commercial ELISA kits were used to measure levels of FLCN (Cusabio, Wuhan, China) and interleukin (IL)-8 (Endogen, MA, USA) in sera from AERD and ATA groups and cell-free supernatants were measured by ELISA. Peripheral blood eosinophils (PBEs) isolated from asthmatic patients were co-cultured with airway epithelial cells (AECs), A549 cells or human small airway epithelial cells (SAEC) with additions of cysteinyl leukotriene (LT) E4, dexamethasone or montelukast.
Results: Serum level of FLCN was significantly higher in patients with AERD than in ATA, as well as to NCs (P<0.001 for each). AERD patients with chronic rhinosinusitis or chronic urticaria showed increased serum FLCN level than those without them (P<0.05 for each). Subjects with serum FLCN level higher than 56.6 pg/mL were classified as "FLCN-high" phenotype. "FLCN-high phenotype" had significantly lower PC20 methacholine level (P=0.015). Serum FLCN level discriminated AERD from ATA with 84.4% specificity and 33.7% sensitivity (AUC=0.619; P<0.001). Upregulation of FLCN was noted in AECs stimulated by LTE4 in dose-dependent manners. Coculture of AECs with eosinophils enhanced release of FLCN and IL-8 (P<0.05 for each), which were attenuated by dexamethasone but not by montelukast. A significant correlation was found between FLCN and IL-8 production (r=0.3896, P=0.044).
Conclusions: These findings suggest that the airway eosinophilia and elevated LTE4 level may induce production of FLCN, thereby amplifying epithelial cell dysfunction and contributing to AERD pathogenesis.

Key Words: Aspirin-exacerbated respiratory disease, folliculin, epithelial cell

P-19

Imaging Assessment of Airway Hyperresponsiveness to specific and non-specific stimuli in murine asthma model

Jae-Woo Jung[2], Jung Suk Oh[3], Boram Bae[1], Hyun Seung Lee[1], Jiwoong Choi[4], Chang Hyun Lee[4], Hye-Ryun Kang[5]*

[1]Institute of Allergy and Clinical Immunology, Seoul National University Medical Research Center, [2]Department of Internal Medicine, Chung-Ang University College of Medicine, [3]Department of Radiology, Catholic University, Seoul St. Mary's Hospital, [4]Department of Radiology and Institute of Radiation, Seoul National University College of Medicine, [5]Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Korea

The development of airway hyper-responsiveness (AHR), a cardinal feature of asthma, its mechanism and related dynamic changes of airway is not clearly understood. In clinics, methacholine, a non-specific stimulating agents, is widely used for the measurement of AHR but it is not unknown that pathophysiologic response to methacholine is similar to those by allergen stimuli. The purpose of this study was to investigate difference of in vivo changes of airway hyperresponsiveness in airway and lung parenchyma by allergens and methacholine challenge in murine asthma model using serial CT images. A 128-multidetector computed tomography (MDCT) scan providing 1,024 x 1,024 matrix (Ingenuity, Philips Healthcare) was performed after challenge of either methacholine or OVA on Balb/c mice sensitized and challenged with OVA. AHR was analyzed using non-invasive lung function measurements (All Medicus). The peribronchial inflammation and airway lumen was assessed by the consensus of two radiologists. While methacholine challenge showed no visible parenchymal changes in the lungs, OVA challenge induced significant immediate changes of peribronchial ground glass opacity or consolidation. After methacholine challenge, normal control mice showed compensatory increase of proximal airways but these compensatory changes were obliterated in response to OVA as well as methacholine. When Penh was monitored after OVA challenge for 10 hours, the compensatory dilatation of proximal airways were well correlated with airway constriction and air trapping. In conclusion, Airway and parenchymal changes by methacholine challenge are different from those by allergens challenge in murine asthma model.

Key Words: Asthma, Bronchial hyperresponsiveness, Imaging

P-20

Effects of a small molecule inhibitor of NLRP3 inflammasome, MCC950 on OVA-induced asthma

Yong Chul Lee*, So Ri Kim, Jong Hwan Woo, Jae Jun Heo, Dong Im Kim, Hae Jin Park, Jae Seok Jeong, Yeong Hun Choe, Seung Yong Park

Division of Respiratory Medicine and Allergy, Department of Internal Medicine, Chonbuk National University Medical School, Jeonju, South Korea

Recent studies have demonstrated that NLRP3 inflammasome activation plays a critical role in various pulmonary disorders. However, to date, the role of NLRP3 inflammasome is controversial in the pathogenesis of allergic asthma. In this study, to evaluate the role of NLRP3 inflammsome in the pathogenesis of Th2 high allergen induced asthma, we used ovalbumin (OVA)-sensitized and challenged mice and a small molecule inhibitor for NLRP3 assembly/activation, MCC950. OVA-inhaled mice showed typical features of bronchial asthma; increased airway inflammatory cells, the histologic changes, the increased levels of Th2 cytokines in lungs of fungal allergen-inhaled mice, and increased bronchial hyper-responsiveness. Interestingly, the NLRP3 inflammasome activation indicators, NLRP3, caspase-1, and IL-1β were dramatically increased in lung tissues of mice. When dexamethasone was administered to OVA-inhaled mice, mice showed the dramatic improvement of all asthmatic features including NLRP3 inflammasome activation. However, the administration of MCC950 did not affect the airway inflammation, histologic changes, bronchial hyper-responsiveness in OVA-inhaled mice although MCC950 decreased the level of IL-1β in lung tissues. These findings suggest that NLRP3 inflammasome assembly is not a major component in the pathogenesis of OVA-induced asthma, though NLRP3 inflammasome may assist the induction/maintenance of OVA-induced asthma.

Key Words: Th2 high asthma, MCC950, inflammasome

P-21

Interaction between PKR activation and ER stress is associated with bronchial epithelial cell activation in acute exacerbated neutrophilc severe asthma

So Ri Kim*, Yong Chul Lee, Dong Im Kim, Jae Jun Heo, Hae Jin Park, Yeong Hun Choe, Seung Yong Park, Jae Seok Jeong

Division of Respiratory Medicine and Allergy, Department of Internal Medicine, Chonbuk National University Medical School, Jeonju, South Korea

Bronchial epithelial cells play an important role in the induction of asthma and its aggravation by many factors including viral infection. The double-stranded RNA (dsRNA)-activated serine/threonine kinase R (PKR) is well characterized as an essential component of the innate antiviral response. Endoplasmic reticulum (ER) stress activates PKR which stimulates various inflammatory signaling pathways. However, to date, there is little information on its role in severe neutrophilic asthma, especially in epithelial cell activation. In this study, we investigated whether PKR activation is involved in the pathogenic features of severe asthma and its acute exacerbation induced by poly (I:C) focusing on the interaction between PKR pathway and ER stress in bronchial epithelium. We found that PKR inhibition using 2-AP decreased severe asthmatic features; the number of airway inflammatory cells in bronchoalveolar lavage (BAL) fluids, airway hyperresponsiveness, and the expression of Th2 cytokines, IL-17, KC and IFN-γ in lung tissues. Interestingly, the expression of PKR, ER stress markers including p-eIF2α, and epithelial derived cytokines IL-25, -33, TSLP was increased in lung tissues from mice sensitized with ovalbumin (OVA) and lipopolysaccharide (LPS) and challenged with OVA (OVALPS-OVA mice). Moreover, the expression of PKR and ER stress markers in LPS-stimulated normal human bronchial epithelial (NHBE) cells. These findings were attenuated significantly by the treatment with 2-AP. In addition,the exacerbated asthmatic features by poly (I:C) were suppressed by the administaration of 2-AP. This study indicates that PKR activation plays an important role the induction/maintenance of severe neutrophilic asthma and its acute exacerbation, highlighting the potential of PKR inhibitor as a potent controller of bronchial epithelial cell activation in severe asthma and its acute exacerbation.

Key Words: PKR, severe asthma, bronchial epithelial cells

P-22

HDM-induced epithelial cell-derived cytokines is controlled by PI3K-δ signaling pathway independently of inflammasome activation

So Ri Kim*, Yong Chul Lee, Kyung Bae Lee, Hae Jin Park, Jae Jun Heo, Yeong Hun Choe, Seung Yong Park, Jae Seok Jeong

Division of Respiratory Medicine and Allergy, Department of Internal Medicine, Chonbuk National University Medical School, Jeonju, South Korea

House dust mite (HDM) is one of the commonest aeroallergens in the world. Bronchial epithelial cells induce Th2 immunity to inhaled allergens via the release of innate pro-Th2 cytokines that include TSLP, IL-25 and IL-33. Although several related receoptors and their downstreams are now actively being defined in the process of HDM-induced activation of bronchial epithleial cells, there are still considerable unrevealed molecular mechanisms for the regulation of IL-25, -33, and TSLP. In this study, we aimed to investigate the role of PI3K-δ signaling in HDM-induced bronchial epithelial cell activation focusing on the relastionship with NLRP3 inflammasome, one of pattern recognition receptor-induced protein complex in epithelial cells. Our data showed that primary cultured tracheal epithelial cells from HDM-inhaled mice showed significant increase in the expression of epithelial cell-derived cytokines, IL-25, -33, and TSLP, which were dramatically reduced by the treatment with IC87114, PI3K-δ inhibitor. As expected, NLRP3 inflammaosome activation was noted in primary cultured tracheal epithelial cells from HDM-inhaled mice, interestingly, the treatment with MCC950, NLRP3 inflammasome inhibitor did not significantly affect the protein expression levels of IL-25, IL-33, and TSLP. These findings were consistent in lung tissues from HDM-inhaled wild type mice and PI3K-δ knock out (KO) mice or siRNA treated mice revealing no definitive increase of the protein levels of IL-25, -33, and TSLP. However, the treatment with MCC950 into HDM-inhaled mice showed the attenuation of asthmatic features despite no significant effect on epithelial cell cytokines, IL-25, 33, and TSLP. Taken together, we suggest that NLRP3 inflammasome assembly is not a major component in the HDM-induced epithelial cell cytokine production which seems to be regulated by PI3K-δ isofrom, although NLRP3 inflammasome may contribute to the induction/maintenance of HDM-induced asthma.

Key Words: House dust mite, Epithelial cytokines, NLRP3 inflammasome

P-23

Association of genetic variants on NLRP4 with asthma exacerbation in smoker

Jong-Uk Lee[1], Chang An Jung[1], Hun Soo Chang[1], Soo Taek Uh[3], Jong-Sook Park[2], Choon-Sik Park[2]*

[1]Department of Interdisciplinary Program in Biomedical Science Major, Soonchunhyang Graduate School, Bucheon, [2]Genome Research Center and Division of Allergy and Respiratory Medicine, Soonchunhyang University Bucheon Hospital, [3]Division of Respiratory and Allergy Medicine, Department of Internal Medicine, Soonchunhyang University Seoul Hospital, Seoul, Korea

Background: Despite the long-continued therapy with inhaled and/or systemic corticosteroids (ICSs), patients with refractory asthma (RA) frequently suffer from severe asthma manifestations: exacerbation and persistent airway Obstruction. Furthermore, smoking is related with more severe symptoms in asthma. Recently, NLRP4 negatively regulates type I IFN signaling in response to dsDNA and dsRNA generated by viral infections Suppress NF-kappa B induction by the cytokines TNFA and IL1B in the innate immune response. These factors are related with exacerbation of asthma. Therefore, alterations of NLRP4 gene function may lead to different courses in patients with asthma.
Method: We genotyped 16 SNPs in *NLRP4* in 2597 patients with BA (Exa<2 in 1st year; n=2469 vs. Exa ≥ 2 in 1st year; n=128, and non-smoking; n=1908 vs. smoking; n=689). The data were managed and analyzed using SAS version 9.1 and SPSS version 12.0. For correction of P-values, the effective number of independent markers in *NLRP4* was calculated using the software SNPSpD (http://genepi.qimr.edu.au/general/daleN/SNPSpD)
Result: Polymorphisms of NLRP4 gene were analyzed for the association the number of acute exacerbation. Two or more acute exacerbation per year deeply related with SNP *rs441827* and *rs1696718* after correction of multiple comparisons (p-value and p corrected <0.05). In addition, ht1, which were composed with minor alleles of *rs441827* and *rs1696718*, showed significant association with acute exacerbation (p<0.05). In non-smoking patient with BA, rs16986718 and ht1 associated with the number of exacerbation, however, they were not significant after correcting multiple comparison. In contrast, rs16986718 and ht1 showed significant association with the number of exacerbation in smoker group (p-value and p corrected <0.05).
Conclusion: NLRP4 polymorphisms may affect frequency of exacerbation under interaction with smoking status.

Funding: The DNA samples were provided by a BioBank at Soonchunhyang University Hospital, and funded 2016- ER7402-00

Key Words: Asthma, *NLRP4*, Polymorphisms

P-24

Role of Eosinophil Extracellular Traps(EETs) in Eosinophilic Asthma

Dong-Hyun Lee, Youngwoo Choi, Duy Le Pham, Tu Hoang Kim Trinh, Seung-Hyun Kim, Hae-Sim Park*

Department of Allergy and Clinical Immunology, Ajou University Medical Center

Background: EETs are known to be involved in innate immune responses as well as Th2 responses in multiple infectious, allergic, and eosinophilic diseases. EETs are composed of DNA fibers and granule proteins, such as MBP, ECP and EPO. However, the exact role of EETs in the airway inflammation of asthma is unknown.
Objective: To understand the role of EETs in eosinophilic airway inflammation.
Methods: EETs released(%) from peripheral eosinophils were compared between patients with severe (n=6) and those with non-severe asthma (n=13) using a confocal microscope stained with anti-EPO/DNA dye after the stimulation of purified eosinophils. To evaluate their pro-inflammatory effects, EETs were co-cultured with airway epithelial cells(A549), and mice were treated with EETs via intranasal administration.
Results: EET% were significantly higher in patients with severe asthma compared to that of non-severe asthma (P<0.05). Isolated EETs from peripheral eosinophils of asthmatic patients were found to contain DNA fibers and diverse granule proteins such as MBP, ECP, and EPO. When EETs were co-cultured with A549 cells, IL-8/IL-6 productions increased significantly (P<0.05, respectively). Mice that treated with EETs for 5 days showed decreased body mass and increased IL-33 level in bronchoalvelar lavage fluid along with increased airway hyper-responsiveness to methacholine.
Conclusion: These findings suggest EETs derived from activated eosinophils may contribute to enhance eosinophilic inflammation in the asthmatic airway. Further studies will be needed to investigate EET-mediated pathways and new therapeutic targets.

Key Words: EET, Asthma

P-25

Role of surfactant protein D in relation with eosinophils in AERD

Youngwoo Choi, Dong-Hyun Lee, Duy Le Pham, Tu Hoang Kim Trinh, Seung-Hyun Kim, Hae-Sim Park*

Department of Allergy and Clinical Immunology, Ajou University Medical Center, Suwon, Korea

Background: Surfactant protein D (SPD) is a member of the collectin family that has an important role against lung infection and asthma. Moreover, SPD dysfunction is related with several pulmonary diseases as it regulates inflammation. However, the function of SPD in the pathogenesis of aspirin-exacerbated respiratory disease (AERD) is still unclear.
Objective: To understand the role of SPD in airway mechanisms of AERD.
Methods: SPD concentrations were measured by human SPD enzyme-linked immunosorbent assay (ELISA) in serum samples collected from patients with AERD (n=78), aspirin-tolerant asthma (ATA, n=191) and healthy control subjects (HC, n=55). To analyze SPD polymorphisms, target SNP genotyping was performed by the primer extension method.
Results: Serum SPD levels were significantly lower in patients with AERD compared to those of ATA (P<.001). Moreover, AERD patients carrying the CC genotype at 2538C>T were significantly higher than ATA patients (P=0.026) and serum SPD levels were significantly different according to this genetic polymorphism..
Conclusion: These findings suggest that decreased level of SPD may contribute to promote airway inflammation in the pathogenic mechanism of AERD.

Key Words: Asthma, AERD, Surfactant protein D

P-26

Asthmatics Have More Innate Lymphoid Cells in Induced Sputum, Affecting the Polarization of Macrophages and Endotypes of Asthma

Jihyun Kim[1], Boram Bae[4], Hyun Seung Lee[4], Kyoung-hee Sohn[5], Hye-Ryun Kang[5], Hye Young Kim[2]*

[1]Department of Biomedical Sciences, Seoul National University College of Medicine, [2]Department of Biomedical Sciences and Medical Science, Seoul National University College of Medicine, [3]Biomedical Science Project (BK21PLUS), Seoul National University College of Medicine, [4]Institute of Allergy and Clinical Immunology, Seoul National University Medical Research Center, [5]Department of Internal Medicine, Seoul National University Hospital, Seoul, Korea

Asthma is one of chronic respiratory disease that has various endotypes triggered by heterogeneous factors. It is well known that Th2 cells produce type 2 cytokines, such as IL-5 and IL-13, enhancing allergic inflammation. In addition to T cells, recent studies using mouse model suggest that innate lymphoid cells play an important role in development of asthma. Type 2 ILC produces type 2 cytokines, like Th2 cells, that promote allergic inflammation in lung. Also, type 3 ILC releases IL-17 and IL-22 in non-allergic asthma model. In human, several studies show that ILC2s are increased in blood, broncho-alveolar fluid and induced sputum of asthma patients. However, it remains unclear that whether and how ILCs are involved in development of asthma in patients. In this study, we analyzed ILCs using induced sputum from asthmatics. Total numbers of ILCs are increased in the induced sputum of asthma patients compared with healthy controls. Because ILCs produce various cytokines that affect other immune cells, we also evaluate subtypes of macrophages, one of major immune cells in induced sputum. Asthma patients have more classically activated macrophages (M1 macrophages) and alternatively activated macrophages (M2 macrophages) than healthy controls. In atopic asthma patients, they have more ILC2 and M2 macrophages but less M1 macrophages than non-atopic asthmatics. Moreover, the percentage of ILC2 and M2 macrophages in induced sputum show positive correlation, and the percentage of ILC1 or ILC3 are also positively correlated with the percentage of M1 macrophages. Taken together, our data suggest that ILCs contribute to the development of asthma by regulating the polarization of macrophages in human.

Key Words: Asthma, Innate lymphoid cells, macrophages

P-27

Comparison of upper airway hyperresponsiveness between histamine and methacholine in suspected asthmatics

Jin-Won Kim, Inseon S. Choi*

Division of Allergy, Chonnam National University Hospital

Background: Only a part of patients with allergic rhinitis develop asthma because aeroallergens enter the lung through nose. The airway muscles from allergen-sensitized animals in vitro show a higher response to histamine, but not to carbachol, and we previously reported that mild asthma patients responded more easily to histamine than to methacholine. The purpose of this study was to determine whether the upper airway is more sensitive to histamine than methacholine or not.
Methods: The medical records of young male patients, who required a medical certificate for asthma in order to be exempted from obligatory military service and received the bronchial challenge tests with both methacholine and histamine, were reviewed retrospectively.
Results: The geometric mean value for PC25-MIF50 to histamine was lower than that to methacholine, without statistical significance (1.33 vs. 1.85 mg/mL, p=0.534). The response expressed as the reactivity indices to the stimuli was similar, probably due to too small subjects (the data for only 13 of 19 subjects were comparable). The post-challenge MIF50 values to histamine or methacholine significantly improved after bronchodilator therapy (histamine: 44.2±9.7%, methacholine: 38.0±9.1%)
Conclusion: There was only a trend of increased sensitivity of upper airway to histamine than to methacholine. Greater data are needed to confirm. The induced upper airway obstruction was responsive to bronchodilator therapy.

Key Words: Upper airway; Asthma; Hyperresponsiveness

P-28

Function of miR-21 and effect of anti-miR-21 antagomir in a chronic asthma model with airway remodeling

Ji Young Kang*, Jung Hur, Hwa Young Lee, Chin Kook Rhee, Sook Young Lee, Young Kyoon Kim, Soon Seog Kwon

Division of Pulmonology, Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, Korea

Background: Previously we observed that inhibition of mir-21 shows the effect on airway inflammation and hyperresponsiveness (AHR) in an acute asthma of murine model. The present study was to investigate the role of mir-21 on a chronic asthma with airway remodeling and verify anti-miR-21 antagomir as a therapeutic drug.
Methods: 6-month-aged female BALB/c were sensitized and challenged with ovalbumin (OVA) about for three months. Ant-mir-21 antagomir of 50 ug was administered via intranasal route before OVA challenge. We measured inflammatory profiles in bronchoalveolar lavage fluid and AHR. Parameters of airway remodeling and the expression of PTEN in the lung tissue were assessed.
Results: Airway resistance decreased significantly after the administration with anti-miR-21 antagomir in the OVA Eosinophil counts and Th2 cytokines such as IL-4 and IL-5 also improved by the anti-miR-21 antagomir. The expression of IL-12p35, a target of miR-21, increased after the antagomir- treated group than the OVA group. Goblet cell hyperplasia and smooth muscle hypertrophy ameliorated by the anti-mir-21 antagomir. PTEN expression in the lung showed further decreased in the treated group than the OVA group.
Conclusion: This study shows that blocking miR-21 by antagomir could have the effect on not only airway inflammation and AHR, but also remodeling. Further research is needed to find out the underlying mechanism of anti-miR-21 antagomir on airway remodeling in a chronic asthma.

Key Words: Mir-21, airway remodeling, asthma

P-29

Pulmonary fibrosis is exacerbated by obesity through TGF-β signaling in mice

Misuk Yang, YoonHee Park, Eun-Yi Oh, Jae-Hyun Lee, DaWoon Sim, KyungHee Park, Jung-Won Park*

Department of Internal Medicine, Institute of Allergy, Yonsei University College of Medicine, Seoul 03722, Korea

Background: Obese patients with asthma have severe symptoms and poor prognosis and respond poorly to conventional asthma medication. Some studies reported that the baseline level of transforming growth factor β (TGF-β) was elevated in high-fat diet fed mice. TGF-β was also known to induce subepithelial fibrosis in asthmatic airways remodeling. The aim of this study is to evaluate the effects of TGF-β on obesity in a murine model.
Methods: We generated diet-induced obesity (DIO) models by high fat feeding during three month. Then DIO and DIO-OVA mice were treated with TGF-β neutralizing antibody as a TGF-β blockade through the tail vein. Glucose tolerance test (ITT) and insulin tolerance test (ITT) was performed. Airway hyperresponsiveness (AHR), airway inflammatory cells from bronchoalveolar lavage fluid (BALF) were measured. T cell analysis on lung homogenates of mice were also performed by flow cytometry.
Results: DIO mice and DIO-OVA mice induced insulin intolerance and glucose intolerance. AHR and lung fibrosis were increased in DIO and DIO-OVA mice compared to normal diet mice. While DIO and normal diet mice did not affect the inflammatory cells in BALF, OVA and DIO-OVA mice increased that. Lung fibrosis and T cell pupulation on DIO mice were attenuated by anti-TGF-β antibody.
Conclusion: These results suggest that TGF-β may play an important role in development of lung fibrosis and AHR by DIO in the murine model.

Key Words: Airway hyper-responsiveness, Obesity, Fibrosis, TGF-β

P-30

PI3K-δ p110 protein is localized to mitochondria in blood and BAL cells of LPS-instilled mice

So Ri Kim, Hee Jung Kim, Yeong Hun Choe, Seung Yong Park, Jae Seok Jeong, Yong Chul Lee*

Division of Respiratory Medicine and Allergy, Department of Internal Medicine, Chonbuk National University Medical School, Jeonju, Korea

With new concept of mitochondrial biological roles, mitochondrial abnormalities appear to be implicated in the pathogenesis of various pulmonary disorders. In addition, phosphoinositide 3-kinase (PI3K)-δ-pathway is associated with severe respiratory diseases. In asthmatic murine model, PI3K-δ inhibition significantly reduced mitochondrial reactive oxygen species linked to inflammatory responses. However, their relationship between PI3K-δ signaling and mitochondria remains unclear, more specifically in the physical interaction. In this study, we aimed to observe the changes of distribution and expression of PI3K-δ isoform proteins, i.e., p110 catalytic subunit and p85 regulatory subunit focusing on mitochondria in various cells from blood and bronchoalveolar lavage (BAL) cells of LPS-instilled mice. LPS-instilled mice showed the significant neutrophilia, pulmonary infiltration with inflammatory cells and increased vascular leakage. Interestingly, electron-microscopic analysis with gold immune staining for PI3K-δ proteins revealed that swelling and friable mitochondria were increased in each cell of blood and BAL cells from LPS-stilled mice compared to control healthy mice. In addition, the number of immunostaining dots for PI3K-δ proteins was increased per each cell and the dot distribution pattern showed the tendency of localization in mitochondria in case of LPS-instilled mice compare with those of control healthy mice. We also observed that the formation of extracellular vesicle structures secreted from the cells and they included the fragmented or friable mitochondria with immunostaining of PI3K-δ proteins in LPS-instilled mice. These findings suggest that in LPS-induced inflammatory state PI3K-δ proteins are more expressed in cells specifically in mitochondria than those in stable state and that mitochondria targeting therapeutic approach can work via PI3K-δ signaling and PI3K-δ can be a candidate as a biomarker for therapeutic monitoring.

Key Words: PI3K-δ protein, biomarker, mitochondria

P-31

Endoplasmic Reticulum Stress in Pathogenesis of Allergic March Murine Model

Mi-Jin Kang[1], Seung-Hwa Lee[1], So-Yeon Lee[2], Soo-Jong Hong[3]*

[1]Asan Institute for Life Sciences, University of Ulsan College of Medicine, [2]Department of Pediatrics, Childhood Asthma and Atopy Center, Asan Medical Center, [3]Department of Pediatrics, Childhood Asthma and Atopy Center, Environmental Health Center, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

Background and aim: Allergic march (AM) is the progression of allergic diseases from atopic dermatitis in infants to asthma in children. However, the mechanism of AM has remained unclear. The present study was to identify the AM-related protein marker and mechanism of AM.
Materials and Methods: Lung and skin samples from ovalbumin (OVA)-induced AM and control mice were used to generate two-dimensional electrophoresis gels. 4-PBA (4-phenylbutyric acid, Inhibitor of ER stress) was administrated to AM mice before sensitization and after challenge, respectively. We evaluated the clinical score, transepidermal water loss (TEWL) of mouse skin, bronchial hyperresponsiveness (BHR), total IgE, OVA-specific IgE, and histology of skin and lung. Immunohistochemistry was carried out to detect expression of TSLP and IL-17.
Results: Expression of GRP78 was up-regulated in skin and lung of AM group compared to control group. Clinical score of skin and TEWL significantly reduced at 3rd sensitization in mice with 4-PBA administration before sensitization compared to AM mice, but not in mice with 4-PBA administration after challenge. BHR, serum total IgE level, and inflammation in skin and lung significantly reduced in 4-PBA administrated mice before sensitization and after challenge compared to AM mice. The expression of TSLP and IL-17 were increased in skin and lungs of AM and they were decreased in skin by 4-PBA administration before sensitization and in lung by 4-PBA administration before sensitization and after challenge.
Conclusion: These results indicate that ER stress might be important in the pathogenesis of AM via regulation of the expression of TSLP and IL-17. Blocking ER stress is capable to inhibit the phenotypes of AD and asthma, thus further study need to prevent the progression of AM.

This research was supported by Basic Science Research Program through the National Research Foundation of Korea(NRF) funded by the Ministry of Education(2016R1A6A3A11933044)

Key Words: Allergic march, Endoplasmic Reticulum Stress, Pathogenesis

P-32

Impulse oscillometry system and spirometry exhibit different clinical features in bronchodilator response test

Youn Ho Sheen[1], Hye Mi Jee[2], Eun Kyo Ha[2], Ho Min Jang[2], Seung Jin Lee[2], Shinhae Lee[2], Kyung Suk Lee[2], Yong Ho Jung[2], Sun Hee Choi[3], Myung Hyun Sohn[4], Man Yong Han[2]*

[1]Department of Pediatrics, CHA Gangnam Medical Center, CHA University, Seoul; [2]Department of Pediatrics, CHA Bundang Medical Center, CHA University, Seongnam, [3]Department of Pediatrics, Kyung Hee University College of Medicine, Seoul, [4]Department of Pediatrics, Severance Hospital, Institute of Allergy, Brain Korea 21 PLUS Project for Medical Science, Yonsei University College of Medicine, Seoul, Korea.

Purpose: Bronchodilator response (BDR) measurements from impulse oscillometry (IOS) are not interchangeable with those from spirometry. Our purpose is to identify the characteristic features of children with small airway hyperresponsiveness, and to determine whether BDR data from IOS provides an important supplement to BDR data from spirometry.
Materials and Methods: The records of 592 consecutive children (median age: 6.4 years, age range: 5.1-9.3 years) with asthma or suspected asthma who underwent spirometric and oscillometric BDR tests at our institution were retrospectively reviewed. Oscillometric BDR was defined as positive when relative or absolute changes of Rrs5 or Xrs5 were beyond 2 standard deviations. Based on spirometric and IOS BDR results, subjects were classified as FEV1+IOS+, FEV1+IOS-, FEV1-IOS+, or FEV1-IOS-.
Results: The BDR results indicated 101 (17.6%) subjects were FEV1+IOS-, 49 (8.5%) were FEV1-IOS+, 48 (8.3%) were FEV1+IOS+, and 377 (65.6%) were FEV1-IOS-. The agreement between spirometric and oscillometric BDR results was poor (kappa=0.234, 95% CI: 0.144-0.324, $P<0.001$). Baseline FEV1, Rrs5, and Xrs5 values strongly influenced the values measured in the BDR. Subjects who were FEV1-IOS+ were younger than those who were FEV1+IOS- ($P<0.001$). Subjects who were FEV1+IOS+ were more likely to have physician-diagnosed asthma, atopic dermatitis, wheezing apart from cold, and decreased baseline lung function relative to those who were FEV1+IOS-or FEV1-IOS+ ($P<0.001$).
Conclusions: There was a low concordance between spirometric and oscillometric BDR results. Use of IOS to detect small airway hyperresponsiveness helps to characterize the specific clinical characteristics of asthma.

Key Words: asthma, bronchodilator response test (BDR test), impulse oscillometry system

P-33

Comparison on the profiles of the two dyspnea score during an induced bronchoconstriction in children with clinical asthma

You Sun Kim, Jeongmin Shin, Minjung Kim, Bo Ra Lee, Dong In Suh, Young Yull Koh, Yun Jung Choi*

Department of Pediatrics, Seoul National University College of Medicine, Seoul, Korea

Purpose: Dyspnea is the critical manifestation of asthma. Although modified Borg (mBorg) scale has been settled successfully in evaluating dyspnea in adult asthma, it is difficult to apply with ease to childhood asthma. Recently, pediatric dyspnea scale (PDS) was introduced and used spread wide. This study aims to compare two dyspnea scales to assess degree of dyspnea triggered by induced-bronchoconstriction in childhood asthma model.
Methods: Total 73 patients were participated in this study. Individual 'fractional exhaled nitric oxide (FeNO)' was measured. Forced expiratory volume in 1 sec (FEV1), mBorg, PDS were notated during methacoline provocation test.
Result: Canonical plot analysis showed overall similarity between two scales with evident different. While mBorg scale described more diverse scores in low-grade dyspnea, PDS elicited more one in medium-grade dyspnea. A perception score of dyspnea at the point of 20% decline of FEV1 (PS20) of each scale was distributed in wide and biphasic manner. PS20 scores expressed by two scales were statistically significant by Spearman correlation (Rs=0.903, P<0.001) as well as by Bland-Altman analysis. Although PS20 of mBorg score was statistically negative (Rs=0.224, P=0.154) with the concentration of methacholine at 20% decline in FEV1 (PC20), that of PDS score was weak-positive (Rs=0.29, P=0063). There was no relevance between PS20 and FeNO.
Conclusions: Comparability of PDS and mBorg scale in evaluating childhood dyspnea suggested the usefulness of PDS. Two scales could be utilized complementarily each other.

Key Words: Asthma, Dyspnea, Bronchial Provocation Tests

P-34

Comparison of steroid responsiveness between two fungal allergen induced asthma models

Yong Chul Lee*, So Ri Kim, Kyung Bae Lee, Hae Jin Park, Jong Hwan Woo, Yeong Hun Choe, Seung Yong Park, Jae Seok Jeong

Division of Respiratory Medicine and Allergy, Department of Internal Medicine, Chonbuk National University Medical School, Jeonju, South Korea

Severe asthma has significant disease burden and results in high healthcare costs. While existing therapies are effective for the majority of asthma patients, treatments for individuals with severe asthma are often ineffective. In addition, Sensitization to fungi and long term or uncontrolled fungal infection are associated with poor control of asthma, the likelihood of more severe disease and complications such as bronchiectasis and chronic pulmonary aspergillosis. As nowadays the interest of fungal allergy in asthma, especially severe asthma has been increased by clinicians, the needs for animal models representing the asthma with fungal sensitization become also increased to define the role of fungal allergy and the related mechanisms in the pathogenesis of asthma with various severity. In this study, we have established asthma murine models using two types of fungal allergens, Aspergillus fumigatus(Af) and Alternaria Alternata(Aa) and compared the pathophysiologic characteristics between two models. Current data revealed that two types of fungal allergen-induced asthma models were established under same protocol for 2 weeks and both of them showed typical asthmatic airway inflammation and hyper-responsiveness. Interestingly, Af-induced asthmatic features did not respond to the treatement with oral dexamethasone, while Aa-indcued asthmatic inflammation and hyper-responsiveness were well controlled by the treatment with dexamethasone. More interestingly, fungal allergen-exposed mouse models for 3 weeks showed also typical asthmatic features and in the case of using 3 week-exposed protocol, both of them, Af-exposed mice and Aa-exposed mice exhibited the refractoriness to treatment with oral dexamethasone for asthmatic features. These findings suggest that there are differences between fungal allergens in induction/maintenance of bronchial asthma and therapeutic response or severity and also provide some applicable fungal asthma animal models.

Key Words: Animal model, Fungal allergen, Steroid resistance

P-35

Alteration of airway proteome profile in asthma by transforming growth factorbeta1 expression

Kyung-Min Ahn[1], Boram Bae[1], Hyun Seung Lee[1], KyungCho Cho[2], Min Jueng Kang[2], Eugene C. Yi[2], Hye-Ryun Kang[1]*

[1]Institute of Allergy and Clinical Immunology, Seoul National University Medical Research Center, [2]Department of Molecular Medicine and Biopharmaceutical Sciences, Seoul National University College of Medicine and Pharmacy, [3]Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Korea

Background: Transforming growth factor beta 1 (TGF-β1) has dual roles in the pathogenesis of inflammatory lung diseases. In the previous study with murine asthma model, TGF-β1expression by low dose doxycycline (0.05 mg/mL) resulted in alteration of macrophage population as well as improvement of asthma phenotype such as lung inflammation and airway hyperresponsiveness. Therefore, proteomic alterations by TGF-β1 expression can be used to discover a biomarker or therapeutic target of asthma.
Objective: The aim of this study is to trace a biosignature of TGF-β1 transgene expression showing anti-asthmatic effect in asthmatic airway by using proteomic analysis for screening potential therapeutic candidates.
Methods: Six week-old TGF-β1 transgenic C57BL/6 mice and wild type mice were sensitized and challenged with ovalbumin (OVA). TGF-β1 transgene was turned on by low dose doxycycline water (0.05 mg/ml) for 4 weeks. Proteins from pooled bronchoalveolar lavage fluid (BAL) cells were resolved by two-dimensional gel electrophoresis and identified by Hybrid Quadrupole-orbitrap mass spectrometer. SEQUEST algorithm program was used for protein identification.
Results: About 3,000 proteins were identified in BAL cells and those could be classified into 5 clusters according to expression pattern. In the OVA-induced asthma group, 621 kinds of proteins showed huge increase compared to the control group but 96 of them were significantly reversed by TGF-β1 expression. AHNAK, FGG, LGALS1, and ROCK1 were representative of those proteins and commonly up-regulated by a transcription activator SMARCA4.This alteration by TGF-β1was also observed in PBS group regardless of OVA treatment.
Conclusion: Proteins such as AHNAK, FGG, LGALS1, and ROCK1 might be related with anti-asthmatic effect of low level TGF-β1 expression.

Key Words: Asthma, TGF-β1, Proteome

P-36

Zanthoxylum schinifolium seed oil can attenuate bronchial asthmatic features and inhibit LPS-induced epithelial cell activation

So Ri Kim*, Yong Chul Lee, Dong Im Kim, Hae Jin Park, Jae Jun Heo, Jong Hwan Woo, Yeong Hun Choe, Seung Yong Park, Jae Seok Jeong

Division of Respiratory Medicine and Allergy, Department of Internal Medicine, Chonbuk National University Medical School, Jeonju, South Korea

Zanthoxylum schinifolium is one of traditional oriental herbal medications as well as spices for food. Previous reports have demonstrated their medical properties including anticancer activity, anti-platelet aggregation, and anti-inflammatory activity. Bronchial asthma is a heterogeneous airway inflammatory disorders characterized by airflow obstruction and hyper-responsiveness. To date, there are little studies and information regarding the effects of Zanthoxylum schinifolium on asthmatic features and airway inflammation. In this study, we evaluated the effects of Zanthoxylum schinifolium on ovalbumin (OVA)-induced asthmatic features including airway inflammation and hyper-responsiveness and on LPS-induced activation of epithelial cells in vitro using Zanthoxylum schinifolium seed oil extracted by expeller- pressed method. OVA-inhaled mice showed the typical features of eosinophilic asthma; increased airway inflammatory cells, the pathologic changes, the increased levels of Th2 cytokines (IL-4, IL-5, and IL-13), and increased airway hyper-responsiveness in lungs of OVA-inhaled mice. Interestingly, we found that in OVA-inhaled mice, treatment with Zanthoxylum schinifolium seed oil remarkably attenuated the increases in inflammatory airway cells and cytokines, airway hyper-responsiveness, and pathologic changes. In addition, in vitro data revealed that the pre-treatment with Zanthoxylum schinifolium seed oil reduced the increased expression levels of various cytokines including IL-5, IL-25, IL-33, and TSLP in LPS-stimulated primary tracheal epithelial cells of mice and A549 cells. These findings indicate that Zanthoxylum schinifolium seed oil attenuates OVA-induced asthmatic features effectively at least in part via the regulation of epithelial cell activation and that Zanthoxylum schinifolium seed oil can be one of candidate materials for novel therapeutic agents of bronchial asthma.

Key Words: Zanthoxylum schinifolium, Asthma, Therapeutic effects

P-37

Effects of anti-IL-5 antibody on severe asthma with fungal sensitization

Yong Chul Lee, Hae Jin Park, Jong Hwan Woo, Jae Jun Heo, Yeong Hun Choe, Seung Yong Park, Jae Seok Jeong, So Ri Kim*

Division of Respiratory Medicine and Allergy, Department of Internal Medicine, Chonbuk National University Medical School, Jeonju, South Korea

Recently, a subphenotype of severe asthma with fungal sensitization (SAFS) has been described in adults and is associated with reduced lung function and increased morbidity. In fact, in adults fungal sensitization is associated with increased asthma severity, morbidity, and mortality, including higher rates of hospital and intensive care unit admission. In children with persistent symptoms, asthma with fungal sensitization was associated with worse disease severity, increased bronchial reactivity, increased airway eosinophilic inflammation, and more exacerbations. Anti-IL-5 antibody has been approved as a therapeutic agent for patients with severe eosinophilic asthma. In this study, we evaluated the molecular mechanisms associated with severe asthma with fungal sensitization focusing on the role of IL-5. The mice sensitized and challenged with Aspergillus fumigatus (Af-inhaled mice) showed the typical features of bronchial asthma; increased airway inflammatory cells, the pathologic changes, the increased levels of Th2 cytokines in lungs of Af-inhaled mice, and increased bronchial hyper-responsiveness. These asthmatic features were refractory to the treatment with oral dexamethasone. Interestingly, airway inflammatory cells including eosinophils, peribronchial and perivascular inflammation, the expression of IL-5 in lung tissues and airway hyperresponsiveness were reduced markedly by the administration of anti-IL-5 antibody intraperitoneally. However, the expression of other Th2 cytokines, IL-4 and IL-13 did not affected significantly by the treatment with anti-IL-5 antibody. These findings suggest that IL-5 plays more critical roles in SAFS than other Th2 cytokines and that anti-IL-5 antibody can control its own expression of IL-5 in lung tissues maybe partly due to the reduction of source cells of IL-5.

Key Words: Anti-IL-5 antibody, severe asthma with fungal sensitization

P-38

Effect of Paquinimod on Neutrophilic Inflammation of Murine Asthma Model

Ji Ae Jun[1], Hun Soo Chang[1], Jong Sook Park[2], Tae-Hyeong Lee[1], Choon-Sik Park[3]*

[1]Department of Interdisciplinary Program in Biomedical Science Major, Soonchunhyang Graduate School, Bucheon, [2]Genome Research Center and Division of Allergy and Respiratory Medicine, Soonchunhyang University Bucheon Hospital, Bucheon, [3]Division of Allergy and Respiratory Medicine, Department of Internal Medicine, Soonchunhyang University Bucheon Hospital, 1174, Jung-Dong, Wonmi-Ku, Bucheon, Kyeonggi-Do, 420-767, Korea

Background: S100 calcium binding protein A9 (S100A9) is known to exert pro-inflammatory effects in various chronic inflammatory disorders. We previously demonstrated the elevation of S100A9 in the sputum of neutrophilic inflammation in severe uncontrolled asthma and in the neutrophilc airway of murine asthma model. The purpose of this study was to evaluate the effect of Paquinimod on the neutrophilic inflammation of murine asthma model.
Materials and Methods: For neutrophilic inflammation model, mice were intraperitoneally sensitized with OVA/CFA and challenged by intranasal OVA (OVA/CFA) and various concentrations of paquinimod (0.1, 1, 10, 25mg/kg/day) were fed with drinking water. Bronchoalveolar lavage and histological assessment on inflammation were performed immediately after the measurement of Airway resistance using a flexiVent. Lung tissue sections were stained with periodic acid-Schiff (PAS) staining to count goblet cell. Levels of S100A9, Caspase-1, IL-1beta, MPO, IL-17, IFN-gamma, TNF-alpha and IL-13 were measured in the lung using western blotting assay. S100A9 and neutrophil elastase expression in the bronchus cells was assessed by using confocal microscopy.
Result: Total cell and neutrophil number were significantly increased in the OVA/CFA mice and paquinimod significantly suppressed the cell numbers in a dose dependent model. Concomitantly, the enhanced airway resistance of the OVA/CFA mice was significantly attenuated. In histology, inflammation index and proportion of goblet cells in bronchus were markedly decreased by the treatment with paquinimod. On western blot, Paquinimod treatment significantly decreased the enhanced expression of S100A9, Caspase-1, IL-1beta, MPO, IL-17,IFN-gamma and TNF-alpha in CFA/OVA mice.
Conclusion: Paquinimod may be an effective inhibitor on neutrophilic asthma of murine model via inhibition of inflammatory mediators and IL-17.

Funding: 2017-R1A2B40126

Key Words: Asthma, Neutrophilic inflammation, Pauqinimod

P-39

Delivery of phosphoinositide 3-kinase-δ targenting siRNA into the lung successfully attenuates HDM-induced asthmatic features

So Ri Kim*, Yong Chul Lee, Dong Im Kim, Kyung Bae Lee, Hae Jin Park, Jae Jun Heo, Yeong Hun Choe, Seung Yong Park, Jae Seok Jeong

Division of Respiratory Medicine and Allergy, Department of Internal Medicine, Chonbuk National University Medical School, Jeonju, Korea

RNA interference (RNAi) is an almost standard method for the knockdown of any target gene of interest in vitro, exploring a naturally occurring catalytic mechanism. The downregulation of pathologically relevant genes in various disorders will offer novel therapeutic approaches. RNAi is mediated by small interfering RNAs (siRNA), and thus siRNA delivery in vivo is of critical importance for its implementation. In addition, phosphoinositide 3-kinase (PI3K)-δ-dependent Akt activation is associated with the pathogenesis of severe respiratory diseases partly through the induction of steroid resistance. In this study, we aimed to investigate the effects of in vivo delivery of siRNA targeting PI3K-δ isoform on house dust mite (HDM)-induced asthmatic features and its therapeutic potential. We found that HDM inhalation induced the typical asthmatic features in mice including increased airway inflammatory cells, airway hyperresponsiveness, and Th2 cytokine expression in lung of mice. Moreover, the significant increased PI3K-Akt pathway activation in lung tissues of mice with PI3K-δ isoform expression. PI3K-δ knockdown by intratracheal delivery of siRNA into the murine lung decreased HDM-induced typical allergic asthmatic features and in vitro transfection of siRNA targeting PI3K-δ showed the decrese in PI3K-δ mRNA expression in primary cultured tracheal epithelial cells from mice. This study indicates the therapeutic potential of pulmonanry delivery in vivo of siRNA targeting PI3K-δ in allergic airway inflammation.

Key Words: siRNA, pulmonary delivery, PI3K-δ

P-40

Nanoparticles increased airway hyperresponsiveness and inflammation though transient receptor potential vanilloid 1 (TRPV1) signal pathway in a mouse model of asthma

Sun-Hye Lee[1], Um Sodari[2], Choon-Sik Park[1], Moh Moh Myint Aung[3], Khine Thandar Moe[4], Nyein Yu Han[4], Ae-Rin Baek[1], Jong-Sook Park[1], June-Hyuk Lee[1], Sung-Woo Park[1], Do-Jin Kim[1], An-Soo Jang[1]*

[1]Department of Internal Medicine, Soonchunhyang University Bucheon Hospital, [2]Ly Srey VyNa Clinic in Cambodia, [3]University of Medicine Myanmar, [4]North Okkalapa General Hospital Myanmar

Background: The interaction between chronic inflammation and neural dysfunction points to an involvement linking the nervous and the immune system in the airways. In particular, environmental exposure to nanoparticles (defined as particulate matter having one dimension <100 nm), has been associated with an enhanced risk of childhood and adult asthma. But the impact of nanoparticles on neurogenic asthma remains to be determined.
Objective: The aim of this study was to identify the impact of nanoparticles on nuro modulation such as TRPV1 in a mouse model of allergic asthma.
Methods: Using mice sensitized with ovalbumin (OVA) and OVA challenged (OVA sensitized/challenged mice) as well as mice treated with saline and challenged with air, and mice exposed to nanoparticles 200 ug/m3 on days 21-23. The effect of nanoparticles on TRPV1 was estimated using ELISA, immunoblotting, and immunohistochemical stain.
Results: Nanoparticles exposure more increased in airway inflammation, and airway obstruction in OVA mice, and those were augumented in nanoparticles exposed mice. TRPV1 protein increased in OVA and nanoparticles exposed mice lung tissue. Substance P, ATP, and CGRP increased in OVA mice lung, and augumented in nanoparticles exposed mice lung. Bradykinin, ATP, and CGRP were increased in nanoparticles exposed NHBE cells.
Conclusion: These results indicate that TRPV1 might be involved in the pathogenesis of bronchial asthma, and nanoparticles can exacerbate asthma through neurogenic mechanism.

Key Words: Bronchial asthma, Neurogenic, TRPV1

P-41

Efficacy of air cleaners for the removal of house dust mites and dog allergens

Da Woon Sim[2], Chang Gyu Woo[3], Hak-Joon Kim[3], Bangwoo Han[3], Yong-Jin Kim[3], Jong Sun Lee[1], Kyung Hee Park[1], Kyoung Yong Jeong[1], Jae-Hyun Lee[1], Jung-Won Park[1]*

[1]Division of Allergy and Immunology, Department of Internal Medicine, Institute of Allergy, Yonsei University College of Medicine, Seoul, [2]Department of Internal Medicine, Chonnam National University Hospital, Gwangju, [3]Environmental & Energy System Research Division, Korea Institute of Machinery & Materials, 156, Gajeongbuk-ro, Yuseong-gu, Daejeon, Korea

Background: Allergens derived from house dust mites (HDM) and pets are a common cause of respiratory allergic disease, and an air cleaner may be an effective tool for control of the allergens in indoor air. The aim of this study was to evaluate the efficacy of an air cleaner for the removal of HDM and dog dander allergens.
Materials and methods: Samples obtained for allergen detection were composed of dust collected from homes inhabited by dogs and dried HDM culture medium that contained mite body particles and excretions. The sample dust was dispersed in a 30 m3 chamber equipped with an air cleaner (LG Electronics). The number of airborne particles was recorded continuously by a dust spectrometer for 60 minutes, and airborne particles were collected on a sampling filter at four different collection start times (0, 5, 10, and 20 minutes following dust dispersion). Der f 1 and Can f 1 concentration in the extract of the sampling filters were measured by 2-site enzyme-linked immunosorbent assay (ELISA).
Results: The concentrations of Can f 1 and Der f 1 in the dispersed dust were 53.5 ng/g and 367.4 μg/g, respectively. Approximately 63% of the fine particulate matter (PM2.5) in the sample dust dispersed in the chamber remained after 60 minutes. Allergen concentrations of airborne Can f 1 and Der f 1 decreased to 54.6% and 58.4%, respectively, of the initial value measured 5 min after dispersion of sample dust. The air cleaner efficiently removed fine particulate matter (PM2.5) by nearly 99% during 30 minutes after being turned on. In the same duration, the air cleaner decreased the concentration of Der f 1 and Can f 1 by 95.8% and 95.3%, respectively.
Conclusions: Significant amounts of PM2.5, HDM, and dog dander allergen are airborne even at 20 min after dust dispersion. An air cleaner can remove airborne PM2.5, HDM, and dog allergens effectively.

Key Words: Chamber study, house dust mite, dog dander

P-42

The effects of ambient particulate matter on the symptoms of atopic dermatitis are influenced by weather type

Young-Min Kim, Jihyun Kim, Kangmo Ahn*

Environmental Health Center for Atopic Diseases, Samsung Medical Center; Department of Pediatrics, Samsung Medical Center, Sungkyunkwan University School of Medicine

Introduction: It has been reported that atopic dermatitis (AD) flares are affected by weather and air pollution. This study aimed to investigate how the effects of particulate matters on AD symptoms are influenced by weather type.
Methods: A total of 127 young children with AD under 6 years of age living in Seoul, Korea, were enrolled as a panel and followed for 17 months between August 2013 and December 2014. AD symptoms including itching, sleep disturbance, erythema, dry skin, oozing, and edema were recorded on a daily basis. Daily weather was classified into 6 categories according to Spatial Synoptic Classification (SSC): dry moderate (DM), dry polar (DP), dry tropical (DT), moist moderate (MM), moist polar (MP), and moist tropical (MT). Exposure to particulate matter with a diameter less than 10 μm (PM10) in each individual was estimated with time-weighted average of concentrations considering outdoor and indoor level of PM10 and time activity of each individual. To analyze the effects of PM10 on AD symptoms, a generalized linear mixed model (GLMM) was used controlling for ambient temperature and humidity, age, sex, SCORAD at enrollment, fever, and topical steroid treatment.
Results: A total of 22,221 person-days of records were collected. Among 6 weather types, the presence of AD symptom was higher on DP days (45.0%, $P < .0001$) and lower on MT days (36.2%, $P < .0001$). Overall, the risk of AD symptoms increased by the exposure to PM10 [adjusted odds ratio (aOR) = 5.39; 95% confidence interval (CI), 3.33-7.50 per 10 μg/m3 of PM10]. Interestingly, the increased risk of AD symptoms by the exposure to PM10 was the highest on MP days (aOR = 26.35; 95%, 21.53-30.66), whereas the adverse effect of PM10 was not significant on DP days.
Conclusion: The harmful effects of PM10 on AD symptoms vary by weather type. Both weather type and air pollution should be considered for the proper management of AD.

Key Words: Particulate matter, Weather type, Atopic dermatitis

P-43

Could air pollution, respiratory viral epidemic, weather condition and aero-allergen bridge the gap between the differences in risk factors for asthma exacerbations in relation to age

Seung Won Lee[1], Eun Kyo Ha[2], Shin Hye Lee[2], Jung Won Yoon[3], Hey Sung Baek[4], Sun Hee Choi[5], Youn Ho Sheen[6], Jae-Won Oh[7], Man Yong Han[2]*

[1]CHA University School of Medicine, [2]Department of Pediatrics, CHA Bundang Medical Center, CHA University School of Medicine, Seongnam, [3]Department of Pediatrics, Myongji Hospital, Seonm University, Goyang, [4]Department of Pediatrics, Kangdong Sacred Heart Hospital, Hallym University, Seoul, [5]Department of Pediatrics, Kyung Hee University School of Medicine, Seoul, [6]Department of Pediatrics; CHA Gangnam Medical Center, CHA University School of Medicine, Seoul, [7]Department of Pediatrics, College of Medicine Hanyang University, Seoul, Korea

Background: Asthma exacerbation is known to be affected by respiratory virus infection (e.g. rhinovirus), air pollutants, aeroallergen sensitization, and/or weather change. This study aims to discriminate the risk factors for asthma exacerbation in different age groups.
Methods: The number of emergency department (ED) visits for asthma attack was obtained in Seoul, Korea over five years (2008-2012), along with daily weather condition (diurnal temperature range (DTR), humidity, and solar irradiation), level of air pollutants (PM10, NO2, SO2, O3, and CO), respiratory virus epidemics (rhinovirus and respiraotory syncytial virus) and aeroallergen pollen (tree, grass, and weed) count. Subjects were classified into five groups by age: <2, 2-5, 6-19, 20-59, and >60. For the time-series analysis, Poisson generalized linear model with distributed lag non-linear model was used for the relative risk evaluation of lag-time effect after adjustment for confounding factors.
Results: A total of 59,375 ED visits for asthma exacerbation were identified during the study period. The subjects in the age group <2 years were most significantly affected by PM10 (RR = 1.365, 95% CI 1.068 - 1.744), NO2 (RR = 1.426, 95% CI 1.103 - 1.843) and DTR (RR 1.355, 95% CI 1.053 - 1.743). School-aged children were mostly likely influenced by rhinovirus infection (RR 1.247, 95% CI 1.073-1.449), weed pollen count (RR 2.084, 95% CI 1.260 - 3.447), and O3 (RR, 1.558 95% CI 1.207 - 2.011). Tree aeroallergen (RR 1.547, 95% CI 1.260 - 1.900), and CO (RR 1.183, 95% CI 1.085 - 1.291) in adults and SO2 (RR 1.192, 95% CI 1.073 - 1.324) in the elderly of >60 years were found to be risk factors associated with asthma ED visits.
Conclusions: Asthma exacerbation leading to ED visits had different risk factors in relation to age. Our results showed that different environmental modification strategies may be needed to prevent asthma aggravation with regard to age.

Key Words: asthma exacerbation, age, risk factor

P-44

Associations of urine phthalate level with small airway dysfunction and bronchial hyperresponsiveness in 6 year-old children

Mi-Ae Kim[1], Hye Mi Jee[2], Gyong Suk Lee[2], Young-Ho Jung[2], Seung Jin Lee[2], Eun Gyo Ha[2], Man Young Han[2]*

[1]Department of Pulmonology, Allergy and Critical Care Medicine, CHA Bundang Medical Center, CHA University, Seongnam, [2]Department of Pediatrics, CHA Bundang Medical Center, CHA University School of Medicine, Seongnam, Korea

We investigated the clinical implications of urine phthalate levels in lung function, especially focusing on small airway.
A population-based cross-sectional study was conducted in the Seongnam Atopy Project in the year of 2016 (SAP 2016). Demographic data, such as age, sex, height, and weight were collected and questionnaires were completed by their parents. Skin prick test to common inhalant and food allergen was conducted and spirometry and impulse oscillation system (IOS) was performed. Three metabolite of phthalate, mono-(iso-butyl) phthalate (MiBP), mono-(2-ethyl-5-oxohexyl) phthalate (MEOHP), and mono-(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP) were measured using liquid chromatography with triple quadrupole tandem mass spectrometry method in urine samples of children.
A total of 131 children, first graders at an elementary school, were included in the study. Mean age was 7.1 years old and male consisted 59.5%. Mean BMI was 16.6 kg/m2 and BMI scores were transformed into z-score. Mean urine MiBP, MEOHP, and MEHHP levels were 114.9 μg/L, 9.4 μg/L, and 25.4 μg/L, respectively. Thirty (22.9%) children experienced wheezing previously and 13 (9.9%) were diagnosed as asthma.
Uine MiBP level was correlated with resistance at 5 Hz (Rrs5) and reactance at 5 Hz (Xrs5) (r=0.197, P=0.028; r=-0.352, P<0.001) and higher in children with ever wheeze than those without it (204.9 ±421.3 μg/L vs 88.1±94.7 μg/L, P=0.013). MEOHP and MEHHP were also correlated with Rrs5 (r=0.158, P=0.078; r=0.200, P=0.025) and Xrs5 (r=-0.178, P=0.047; r=-0.233, P=0.009) and urine MEOPH level was higher in children with ever wheeze (11.0±10.1 μg/L vs 8.9±8.5 μg/L, P=0.046).
In conclusion, urine phthalate metabolites were correlated with IOS parameters, which reflecting small airway dysfunction, and significantly higher in children with ever wheeze.

Key Words: Phthalate,small airway dysfunction, Bronchial hyperresponsiveness

P-45

Association between maternal phthalate exposure and respiratory infection in infancy

Nam Goung Sun Ju[1], So-Yeon Lee[2], Jisun Yoon[2], Sungsu Jung[2], Hyun-Ju Cho[2], Ju-Hee Seo[3], Dong In Suh[4], Youn Ho Shin[5], Kyung Won Kim[6], Kangmo Ahn[7], Soo-Jong Hong[2]*

[1]Asan medical Center Environmental Health Center Asan, Seoul, [2]Department of Pediatrics, Asan Medical Center, Ulsan University College of Medicine, Seoul, [3]Department of Pediatrics, Dankook University Hospital, [4]Department of Pediatrics, Seoul National University College of Medicine, Seoul, [5]Department of Pediatrics, Gangnam CHA Medical Center, CHA University School of Medicine, Seoul, [6]Department of Pediatrics, Yonsei University College of Medicine, Seoul, [7]Department of Pediatrics, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

Background: There is growing concern that maternal exposure to phthalates, which are widely used in consumer products, might affect susceptibility to infections and the development of allergic diseases in children. But there was currently few prospective study.
Object: We investigated the effect of maternal phthalate exposure on infant respiratory infection of offspring according to phthalate exposure dose.
Method: We measured phthalate MEHHP, MEOHP, MnBP in urine samples collected 604 pregnant women during the third trimester participating in the COCOA birth cohort study. The occurrence of lower respiratory tract infections (Tracheobronchitis, pneumonia, bronchiolitis) and upper respiratory tract infections (common cold, sinusitis, otitis media and croup) in infants was assessed at age 6 months and 1 years through doctor diagnosis.
Result: Higher maternal urinary MnBP concentrations were associated with an increased risk of lower respiratory tract infections(OR, 4.91;95% CI 1.6-15.08) and bronchiolitis(OR, 4.54;95% CI 1.46-14.19) at 6 month-old. We found no statistically association of other phthalate metabolites with respiratory infections.
Conclusion: Prenatal exposure to phthalate, especially MnBP, may affect the susceptibility lower respiratory infection in infancy.

Key Words: Phthalate, Lower respiratory tract infections, Upper respiratory tract infections

P-46

Early life PM10 exposure increase airway hyperresposiveness and incident asthma in schoolchildren

Song-I Yang[1], So-Yeon Lee[2], Hyeon Jong Yang[3], Hyo-Bin Kim[4], Ju-Hee Seo[5], Young-Ho Kim[6], Eun Lee[7], Hyun-Ju Cho[2], Jisun Yoon[2], Young-Ho Jung[8], Soo-Jong Hong[2]*

[1]Department of Pediatrics, Hallym University Sacred Heart Hospital, Hallym University College of Medicine, Anyang, [2]Department of Pediatrics, Childhood Asthma Atopy Center, Environmental Health Center, Asan Medical Center, University of Ulsan College of Medicine, Seoul, [3]Department of Pediatrics, Soonchunhyang University College of Medicine, Seoul, [4]Department of Pediatrics, Inje University Sanggye Paik Hospital, Inje University College of Medicine, Seoul, [5]Department of Pediatrics, Dangook University Hospital, Cheonan, [6]Department of Pediatrics, Gyeongsang National University Changwon Hospital, Changwon, [7]Department of Pediatrics, Chonnam National University Hospital, Gwangju, [8]Department of Pediatrics, Bundang CHA Hospital, College of Medicine, CHA University, Seongnam, Korea

Background: The most relevant time of PM10 exposure for airway hyperresponsiveness (AHR) and asthma in schoolchildren are unclear.
Objective: To investigate the relevant time of PM10 exposure on the development of AHR and asthma in schoolchildren.
Methods: From 2005, 3,570 elementary schoolchildren were enrolled to a prospective 4-year follow-up survey. Individual annual PM10 exposure was estimated by using an ordinary kriging method from the prenatal period to 7 years of age. Information on asthma was collected by questionnaire. AHR was defined as methacholine PC20 $\leq$ 8mg/dL.
Results: The effect of PM10 on AHR was the highest at 1 year of age (aOR, 1.750; 95% CI, 1.343-2.282). Higher PM10 during pregnancy was associated with new development of asthma diagnosis and symptoms (aOR, 2.056; 95% CI, 1.240-3.409 and aOR, 1.643; 95% CI, 1.097-2.460, respectively). The risk of new development of asthma diagnosis and symptoms with AHR were more increased by higher PM10 during pregnancy (aOR, 5.774; 95% CI, 1.317-25.309 and aOR, 4.647; 95% CI, 1.632-13.234, respectively).
Conclusion: Early life PM10 exposure was relevant for AHR and new development of asthma. The avoidance of exposure to PM10 in early life could prevent future development of asthma.

Key Words: Particulate matter, Early life, Asthma

P-47

Phthalate enhances the inflammatory cytokine and chemokine secretion induced by human rhinovirus in BEAS2B cell

Jin Hee Kim, Sae-Hoon Kim, Junghyun Kim, Yoon-Seok Chang*

Department of Internal Medicine, Seoul National University Bundang Hospital, Seongnam-si, Gyeonggi-do, 13620, Korea

Background: Di-(2-butyl)- phthalate (DBHP) is a ubiquitous chemical used in consumer products, and is known to cause endocrine disruption in humans and animals, as well as enhance airway inflammation. Recently it has been reported that inflammatory cytokines produced by bronchial epithelial cells after exposure to phthalates contributed to airway remodeling, and that ginger may reverse phthalate-induced airway remodeling. Human rhinovirus (RV) is a cause of common cold and considered to be involved in the pathogenesis and the exacerbation of asthma. We evaluated the effect of DBHP on the inflammatory response induced by RV in bronchial epithelial cell.
Methods: BEAS2B cells were treated with DBHP (5 μM) and RV. After 6 and 24hours, the cells and cell media were harvested for quantitative real-time polymerase chain reaction and enzyme-linked immunosorbent assays for IFN-β, TNF-α, Thymic stromal lymphopoietin (TSLP), RANTES, IL-8, IL-25, and IL-33.
Results: The mRNA expression of IFN-β, TSLP, and TNF-α were increased significantly in the 24-h DBHP+RV-treated group compared with those in the RV-only-treated group. The protein expressions of IFN-β, RNATES, TNF-α, and IL-33 were also increased significantly in the 24-h DBHP+RV-treated group compared with those in the RV-only-treated group.
Conclusion: Phthalate enhances the inflammatory cytokine and chemokine secretion induced by human rhinovirus in BEAS2B cell.

Key Words: Bronchial epithelial cell, Human rhinovirus (RV), Di-(2-butyl)- phthalate (DBHP)

P-48

Proteomics responses of human lung microvascular endothelial cells exposed to titanium dioxide nanoparticles

Byeong-Gon Kim[1], Um Sodari[2], Choon-Sik Park[1], Moh Moh Myint Aung[3], Khine Thandar Moe[3], Nyein Yu Han[4], Ae-Rin Baek[1], Jong-Sook Park[1], Junehyuck Lee[1], Sung-Woo Park[1], Do-Jin Kim[1], An-Soo Jang[1]*

[1]Department of Internal Medicine, Soonchunhyang University Bucheon Hospital, [2]Ly Srey VyNa Clinic in Cambodia, [3]Department of Medicine, University of Medicine, Myanmar, [4]North Okkalapa General Hospital, Myanmar

Background: Nanoparticles (NPs) have at least one dimension less than 100 nm with unique characteristics compared to their corresponding bulk materials. Titanium dioxide (TiO2) nanoparticles as one of air pollutants exacerbates chronic airway disease such as asthma and COPD. But underlying mechanism remains unresolved. Although many studies have reported the adverse effects of NPs on humans, little is known about the effects on respiratory systems or the related mechanisms.
Objective: The aim of study was to identify protein expression in human lung microvascular endothelial cells (HMVEC-L) exposed to titanium dioxide nanoparticles. Methods: A proteomic approach using 2DE and nano-LC-MS/MS was used to determine the different expression of proteins at 8h and 24h after treatment of TiO2 NPs 20 μM and 40 μM to HLMVEC-L.
Results: Treatment of HMVEC-L with titanium dioxide nanoparticles 20 μM altered 10 protein spots. These proteins included calcium regulation, transport, cytoskeleton, and muscle contraction. The proteins were classified into three groups according to the time course of their expression patterns such as continually increasing, transient increasing, and continually decreasing. Treatment of HMVEC-L with TiO2 NPs 40 μM altered 5 protein spots. These proteins included cytoskeleton, myosin regulation, action modulating, and GDP and GTP regulation. The proteins were classified into three groups according to the time course of their expression patterns such as transient increasing, transient decreasing, and continually decreasing. For validation immunohistochemical staining and Western blotting was perfomed on lung tissues from TiO2 NPs exposed mice. Profilin-1 and Cofilin-1 were expressed in endothelium, epithelium, and inflammatory cells and decreased in lung tissues of TiO2 NPs exposed mice compared with sham treated mice.
Conclusion: These results indicate that some of proteins may be an important role for airway disease caused by TiO2 NPs exposure.

Key Words: Titanium dioxide, Proteome, Endothelial cells

P-49

The optimal conditions for the long term storage of the extracts from pollens of allergenic importance in Korea

Ji Eun Yuk, Jongsun Lee, Kyoung Yong Jeong, Kyung Hee Park, Jung-Won Park*

Department of Internal Medicine, Institute of Allergy, Yonsei University College of Medicine, Seoul 03722, Korea

Background: Sawtooth oak, Japanese hop, ragweed, and mugwort pollens are important causes of seasonal allergic rhinitis in Korea. Precise diagnosis and effective treatment by pollen extracts are greatly dependent on the stability of the extract.
Methods: The lyophilized allergen extracts were reconstituted in various buffer (normal saline, 0.3% phenol saline, and 50% glycerol with saline) and stored at room temperature (18-26°C) or refrigerated (4°C). Subsequently, protein concentration and allergen content in the extracts were examined by Bradford assay and two-site ELISA.
Results: The lyophilized allergen extracts were reconstituted in various buffer (normal saline, 0.3% phenol saline, and 50% glycerol with saline) and stored at room temperature (RT, 18-26°C) or refrigerated (4°C). Subsequently, protein concentration and allergen content in the extracts were examined over one year. At least 62.6% of the original protein concentration in all four extracts examined was detected when 50% glycerol was added and refrigerated over one year, whereas 16.2 to 37.7% remained in the extracts at RT. Without 50% glycerol, 23.6 to 86.2% of protein was detected in the refrigerated extracts whereas 3.7 to 33.0% remained at RT. As for Japanese hop and mugwort, reconstitution in 0.3% phenol and 50% glycerol showed best preservation of protein content (97.2% and 72.6%), while 50% glycerol was found to be the best constituent for the storage of oak (65.9% of protein remained). Amb a 1, a major allergen of ragweed, was almost completely degraded in week 9 at RT when reconstituted in a buffer without 50% glycerol. However, more than 50% of Amb a 1 was detected after one year of incubation at RT when 50% glycerol was added. No loss of Amb a 1 was observed when refrigerated.
Conclusions: Addition of 50% glycerol as well as refrigeration was found to be the important to increase the shelf-life of allergen extracts from pollens of allergenic importance.

Key Words: Allergen, Pollen, Stability

P-50

Clustering of the food- and aero- allergen and change of the sensitization over age in allergic disease patients

WonKyung Cho[1], Jaewoo An[2], Wonki Lee[1], Eun Kyo Ha[2], Mi Ae Kim[3], Chang Ho Lee[4], SoHyun Hwang[5], Youn Ho Sheen[6], Young-Ho Jung[2], Hye mee Jee[2], Man Yong Han[2]*

[1]School of Medicine, CHA University, Seongnam, [2]Department of Pediatrics, CHA Bundang Medical Center, CHA University, Seongnam, [3]Department of Allergy & Clinical Immunology, CHA Bundng Medical Center, CHA University, Seongnam, [4]Department of Otorhinolaryngology-Head and Neck Surgery, CHA Bundang Medical Center, CHA University, Seongnam, [5]Department of Pathology, CHA Bundang Medical Center, and Department of Biomedical Science, CHA University, Seongnam, [6]Department of Pediatrics, CHA Gangnam Medical Center, CHA University School, Seoul, Korea

Background: There is a lack of comprehensive study outlining the change of food-, and aero- allergen sensitization over the whole course of life. Our study aims to looks at cross reactivity of comprehensive allergen and the allergen sensitization change over a lifetime through a cross-sectional study.
Methods: This study enrolled 13,326 allergic or suspected allergy patients with sIgE tests (males, 56.9%, median age; 6.0 years) from January 2013 to June 2016 at CHA University hospital in Korea. We measured allergen sIgE using Polycheck Allergy (Biocheck GmbH, Munster, Germany) (from Jan, 2013 to May 2015, n=9,071) and Advansure (LG Life Science, Seoul, Korea) (from June 2015 to June 2016, n=4,255). We considered a test positive if the class score was greater than class 1. Total eosinophil count and Total IgE were also measured for change over age. We used the default clustering of heatmap.2 function in R for hierarchical clustering of the 61 antigens.
Result: Allergens were separated into two clusters. Cluster 1 included outdoor allergen and Type II food allergen while Cluster 2 consisted of indoor allergen and Type I food allergen. Ratio of sensitization to Cluster 1 increased during middle childhood, especially in 11-to-15 year olds and continued to middle age. On the other hand, sensitization to Cluster 2 begins in toddlers, especially in 1-to-2 year olds. Total eosinophil count is the highest in 0-to-2 year olds and shows no significant change until 20 years when it begins to decrease. Contrarily, total IgE parallels the change seen in Cluster 1.
Conclusion: When food- and aero-allergen is clustered into two entities, an age prevalence is seen. Moreover, age-dependent trend seen in Cluster 1 parallels that of total IgE and Cluster 2 with total eosinophil count. An age prevalence in allergen sensitization will provide a helicopter view on the choice of treatment and diagnostic tool for allergy.

Key Words: Cross-reactivity, Age-dependent change, Allergy

P-51

Allergenic Characterization of Que m 1, a major allergen from Mongolian oak, Quercus mongolica

Kyoung Yong Jeong, June Yong Lee, Misuk Yang, Da Woon Sim, Kyung Hee Park, Jae-Hyun Lee, Jung-Won Park*

Department of Internal Medicine, Institute of Allergy, Yonsei University College of Medicine

Background: Oak is the most common tree in Korean forest, and Mongolian oak, Quercus mongolica is the dominant species. However, no allergen has been characterized from Mongolian oak. In this study, we tried to characterize a major allergen from Mongolian oak.
Methods: A molecule homologous to pathogenesis-related protein 10, Que m 1, was cloned by RT-PCR and its recombinant protein along with Que a 1, an allergen from white oak (Q. alba) was also produced for comparison. Allergenicity and diagnostic value of recombinant Que m 1, Que a 1 and Bet v 1 proteins were compared by ELISA using sera from oak sensitized subjects. Basophil activation test was also performed using CD63 expression as an activation marker.
Results: Que m 1 sequence shares 57.5 to 96.2% amino acid sequence identity (96.2%) with PR-10-like allergens from various plants. Specific IgE to recombinant Que m 1, Que a 1, and Bet v 1 were detected in 90.0%, 78.0%, and 94.0% of 50 serum samples from Korean tree pollinosis patients. Recombinant Que m 1 was able to inhibit IgE reactivity to Que a 1 and Bet v 1, indicating its strong cross-reactivity. Activation pattern of basophils from five patients was similar in terms of CD63 expression and protein concentration of challenged Bet v 1 and Que m 1.
Conclusions: A major allergen, Que m 1, was cloned, and its recombinant protein was produced from Mongolian oak which is a dominant species in Korea. Recombinant Que m 1 is potentially useful for the diagnosis and treatment of tree pollinosis in Korea.

Key Words: Oak, Pollinosis, PR-10

P-52

Prevalence of asthma and allergic diseases and associated school absenteeism in Korean school-aged children

Jung-Hyun Kim[3], Kyounghee Sohn[2], Sung-Yoon Kang[1], Byung-Keun Kim[1], Yoon-Seok Chang[3], Sang-Heon Cho[1], Sae-Hoon Kim[3]*

[1]Department of Internal Medicine, Seoul National University College of Medicine, Seoul, [2]Institute of Allergy and Clinical Immunology, Seoul National University Medical Research Center, Seoul, [3]Department of Internal Medicine, Seoul National University Bundang Hospital, Seongnam, Korea

Background: Asthma and allergic diseases account for school absenteeism and may limit academic and social opportunities for a substantial number of students, as they are common, chronic disorders affecting school-aged children. We evaluated the prevalence of asthma and allergic diseases in Korean children, as well as associated school absenteeism.
Methods: We administered a questionnaire survey in 148 asthma-friendly schools from 14 counties or cities in Gyeonggi province in South Korea. The questionnaire was modified from the ISSAC questionnaire, which consists of 13 questions regarding prevalence of asthma, allergic rhinitis, and atopic dermatitis, and the impact of these conditions on school attendance.
Results: A total of 41,062 subjects were enrolled in this study. The overall lifetime prevalence of asthma, allergic rhinitis, and atopic dermatitis was 5.3%, 38.4%, and 25.0%, respectively. Among subjects who had ever been diagnosed with asthma, 9.1% missed school due to asthma. Many subjects with allergic rhinitis (3.2%) or atopic dermatitis (1.8%) also responded that they had missed school because of their diseases. Subjects with current symptoms or having undergone recent treatment of allergic rhinitis had a significantly increased risk of missing school due to asthma. Similarly, current symptoms or recent treatment of atopic dermatitis were also significantly associated with missing school due to asthma.
Conclusion: Asthma and allergic diseases present a substantial health and socio-economic burden, as demonstrated by the prevalence and related school absenteeism observed in this study among school-aged children in Korea. Co-existing symptomatic allergic rhinitis and atopic dermatitis are associated with increased risk of school absenteeism due to asthma.

Key Words: Asthma, Allergy, School absenteeism

P-53

Baicalin inhibits IL-1β-Stimulated Extracellular Matrix Production in Nasal Fibroblasts

Jae-Min Shin[1], Ju-Hyung Kang[2], Seung-Ae Lee[3], Il-Ho Park[1], Heung-Man Lee[1]*

[1]Department of Otorhinolaryngology-Head and Neck Surgery; [2]Division of Brain Korea 21 Program for Biomedical Science; [3]Research-Driven Hospital, Korea University Guro Hospital; Korea University College of Medicine, Seoul, Korea

Purpose: Baicalin, a Chinese herbal medicine, has anti-fibrotic and anti-inflammatory effects. The aims of present study were to investigate the effects of baicalin on the myofibroblast differentiation, extracellular matrix production, migration, and collagen contraction of interleukin (IL)-1β-stimulated nasal fibroblasts and to determine the molecular mechanism of baicalin in nasal fibroblasts.
Methods: Nasal fibroblasts were isolated from the inferior turbinate of patients. Baicalin was used to treat IL-1β- stimulated nasal fibroblasts. To evaluate cytotoxicity, a 3-(4,5-dimethylthiazol-2yl)-2,5-diphenyl-tetrazolium bromide assay was used. The expression levels of α-smooth muscle actin (SMA), fibronectin, phospho-mitogen-activated protein kinase (p-MAPK), p-Akt, p-p50, p-p65, and p-IκBα were measured by western blotting, reverse transcription-polymerase chain reaction (RT-PCR),or immunofluorescence staining. Fibroblast migration was analyzed with scratch assays and transwell migration assays. Total collagen was evaluated with the Sircol collagen assay. Contractile activity was measured with a collagen gel contraction assay.
Results: Baicalin (0-50 μM) had no significant cytotoxic effects in nasal fibroblasts. The expression of α-SMA and fibronectin were significantly down-regulated in baicalin-treated nasal fibroblasts. Migration, collagen production, and contraction of IL-1β-stimulated nasal fibroblasts were significantly inhibited by baicalin treatment. Baicalin also significantly down-regulated p-MAPK, p-Akt, p-p50, p-p65, and p-IκBα in IL-1β-stimulated nasal fibroblasts.
Conclusions: We showed that baicalin down-regulated myofibroblast differentiation, extracellular matrix production, migration, and collagen contraction via the MAPK and Akt/ NF-κB pathways in IL-1β-stimulated nasal fibroblasts.

Key Words: Baicalin, Extracellular matrix production, Nasal fibroblasts

P-54

Effect of Diesel Exhaust Particles on MUC4 Expression in NCI-H292 Cells and Nasal Epithelial Cells

Jae-Min Shin[1], Ju-Hyung Kang[2], Seung-Ae Lee[3], Il-Ho Park[1], Heung-Man Lee[1]*

[1]Department of Otorhinolaryngology-Head and Neck Surgery; [2]Division of Brain Korea 21 Program for Biomedical Science; [3]Research-Driven Hospital, Korea University Guro Hospital; Korea University College of Medicine, Seoul, Korea

Purpose: Diesel exhaust particles (DEPs), the major contributors to air pollution, induce inflammatory responses in the nasal epithelium. Overproduction of airway mucins is an important pathogenic finding in inflammatory airway diseases. The aims of the present study were to determine the effect of DEPs on the expression of the mucin gene MUC4 and to investigate the underlying mechanism of DEP-induced MUC4 expression in NCI-H292 cells and primary nasal epithelial cells (PNECs).
Methods: NCI-H292 cells were stimulated for 24 h with DEPs. Messenger RNA (mRNA) and protein expression of MUC4 was determined by real-time reverse transcription (RT) polymerase chain reaction (PCR) and Western blotting. NCI-H292 cells were exposed to 3 mitogen-activated protein kinase inhibitors (U0126, SB203580, and SP600125) and a CREB (cAMP response element-binding protein) inhibitor prior to stimulation with DEPs, and MUC4 expression was examined by RT-PCR and Western blotting. PNECs were pretreated with a p38 inhibitor and CREB inhibitor prior to stimulation with DEPs, and MUC4 expression was then determined by RT-PCR and/or Western blotting.
Results: DEPs significantly increased the expression of MUC4 mRNA and protein. MUC4 mRNA and protein expression was inhibited by pretreatment with p38 and CREB inhibitors in NCI-H292 stimulated with DEPs. p38 and CREB inhibitors also blocked the expression of MUC4 mRNA and protein in DEP-stimulated PNECs.
Conclusions: We demonstrated that DEPs stimulated the expression of MUC4 via the p38/CREB pathway in NCI-H292 cells and PNECs. The results of the present study pave the way for further studies on the role of MUC4 in DEP-induced hypersecretion in airway epithelium.

Key Words: Diesel exhaust particles, MUC4, Nasal epithelial cells

P-55

Activation of phosphoinositide 3-kinase delta may define an important eosinophilic sub-phenotype of nasal polyp in chronic rhinosinusitis patients

Jae Seok Jeong[1], Jong Seung Kim[2], Kyung Bae Lee[1], So Ri Kim[1], Heung Bum Lee[1], Seoung Ju Park[1], Seung Yong Park[1], Yeong Hun Choe[1], Sam Hyun Kwon[2], Yong Chul Lee[1]*

[1]Department of Internal Medicine, Research Center for Pulmonary Disorders, Chonbuk National University Medical School, [2]Department of Otorhinolaryngology-Head and Neck Surgery, Chonbuk National University Medical School

Phosphoinositide 3-kinases (PI3Ks) are lipid signaling kinases that phosphorylate inositol lipids at the cell membrane. Biological consequences of PI3K pathway are largely determined by isoforms of activation, given their uneven distribution throughout diverse cell types. Among them, expression of PI3K-δ, consisting of a catalytic p110 subunit (p110δ) in association with a regulatory subunit, is restricted to circulating leukocytes, and that it plays a pivotal role in leukocyte activation and trafficking including eosinophils. In chronic rhinosinusitis (CRS), local Eosinophilic inflammation in sinonasal cavity has been thought as a result from systemic deregulation of eosinophils and patients with eosinophilic CRS suffer from severe disease burden and impaired quality of life. In this study, we investigated whether PI3K-δ activation could identify a particular phenotype of CRS having distinct clinical behavior. We subdivided total 33 CRS patients having NP into NP with higher p110δ expression (NP p110δ hi)/NP with lower p110δ expression (NP p110δ lo) according to the extent of p110δ expression. Data showed that increased expression of eosinophil cationic protein (ECP), a marker protein for eosinophils, was observed in NP p110δ hi compared to that in NP p110δ lo. Similarly, blood counts of eosinophils in patients with NP p110δ hi were significantly increased compared to those in NP p110δ lo. Tissue levels of IL-5 protein, a major regulator of maturation and survival of eosinophils, were also notably increased in NP p110δ hi, however, there was no significant difference in the levels of serum total Ig E levels between two groups. Furthermore, CRS patients possessing NP p110δ hi displayed more severe radiologic, endoscopic, and symptomatic features of the disease compared to patients possessing NP p110δ hi. These data suggest that assessing the extent of PI3K-δ activation may be used as a promising biomarker for identifying clinically important subgroup of CRS.

Key Words: Phosphoinositide 3-kinases, Chronic rhinosinusitis, Eosinophilic polyp

P-56

Chronic Rhinosinusitis and Nasal Polyp and Its Relationships with Asthma and Lower Airway Obstruction in the General Adult Population

Ha-Kyeong Won[1], Jisu Shim[1], Yoon-Seok Chang[5], Sang-Heon Cho[1], Soo Jie Chung[1], Sung-Yoon Kang[1], Jung-Hyun Kim[5], Min-Gyu Kang[3], Min-Hye Kim[4], Min-Suk Yang[6], Sae-Hoon Kim[5], Heung-Woo Park[1], Woo-Jung Song[1]*

[1]Department of Internal Medicine, Seoul National University College of Medicine, Seoul, [2]Institute of Allergy and Clinical Immunology, Seoul National University Medical Research Center, Seoul, [3]Department of Internal Medicine, Chung-Buk National University Hospital, Cheong-Ju, [4]Department of Internal Medicine, Ewha Woman's University School of Medicine, Seoul, [5]Division of Allergy and Clinical Immunology, Department of Internal Medicine, Seoul National University Bundang Hospital, Seongnam, [6]Department of Internal Medicine, SMG-SNU Boramae Medical Center, Seoul, Korea

Background: Chronic rhinosinusitis (CRS) is a major disease condition with a high degree of morbidity, and may influence lower airway function and disease status in adults. However, its associations with adult asthma onset and activity have rarely been reported in nationwide population surveys.
Objective: To investigate the relationships of CRS with asthma onset and lower airway conditions.
Methods: A cross-sectional dataset from 17,506 adult participants (age≥18 years) in the Korean National Health and Nutrition Examination Survey 2010-2012 was analyzed. CRS was defined using structured questionnaires according to the international guideline, and comorbid nasal polyps were objectively defined using nasal endoscope. Asthma onset and activity were asked by structured questionnaires. Lower airway obstruction was defined positive if FEV1/FVC ratio was lower than 0.70 in pulmonary function tests.
Results: CRS was significantly related with asthma in adults, but the relationships were distinct according to CRS and asthma status. In particular, CRS with nasal polyps (CRSwNP) showed significant associations with late-onset asthma (onset after 40 years), whereas CRS without nasal polyps (CRSsNP) were only related to early-onset asthma (onset before 40 years) in adults. In terms of asthma activity, both forms of CRS showed significant associations with current asthma, but not with past asthma. In non-asthmatic population, CRSwNP, but not CRSsNP, showed associations with lower airway obstruction. These relationships remained statistically significant in multivariate analyses.
Conclusions: This cross-sectional analysis based on a nationwide population survey supports for the notion that CRSwNP plays a major role in the pathophysiology of late-onset adult asthma. Also, its relationships with lower airway obstruction in non-asthmatic population could suggest its effects on lower airways.

Key Words: Chronic Rhinosinusitis, Nasal Polyp, Asthma

P-57

Risk factors and comorbidities of allergic rhinitis phenotype according to ARIA classification in children

Sungsu Jung[1], Jisun Yoon[1], Sung-Il Woo[8], You-Sook Youn[9], Kang Seo Park[10], Hwa Jin Cho[11], Myung-Hee Kook[12], Hye Ryoung Yi[12], Hai Lee Chung[13], Ja Hyung Kim[14], Hyung Young Kim[15], Jin A Jung[16], Hyun-Ju Cho[1], Hyang-Ok Woo[17], So-Yeon Lee[1], Yeongho Kim[2], Dong In Suh[3], Song-I Yang[4], Ji-won Kwon[5], Gwang Cheon Jang[6], Yong Han Sun[7], Soo-Jong Hong[1]*

[1]Department of Pediatrics, Childhood Asthma Atopy Center, Environmental Health Center, Asan Medical Center, University of Ulsan College of Medicine, Seoul, [2]Department of Pediatrics, Presbyterian Medical Center, Jeonju, [3]Department of Pediatrics, Chonnam National University Hospital, Chonnam National University Medical School, Gwangju, [4]Department of Pediatrics, Gwangju Veterans Hospital, Gwangju, [5]Department of Pediatrics, Catholic University of Daegu School of Medicine, Deagu, [6]Department of Pediatrics, Ulsan University Hospital, Ulsan, [7]Department of Pediatrics, Pusan National University Yangsan Hospital, Yangsa, [8]Department of Pediatrics, Anatomy, College of Medicine, Dong-A University, Busan, [9]Department of Pediatrics, Gyeongsang National University College of Medicine, Jinju, [10]Department of Pediatrics, Gyeongsang National University Changwon Hospital, Changwon, [11]Department of Pediatrics, Seoul National University College of Medicine, Seoul, [12]Department of Pediatrics, Hallym University Sacred Heart Hospital, Hallym University College of Medicine, Anyang, [13]Department of Pediatrics, Seoul National University Bundang Hospital, Seongnam, [14]Department of Pediatrics, National Health Insurance Service Ilsan Hospital, Ilsan, [15]Department of Pediatrics, Gachon University Gil Medical Center, Incheon, [16]Department of Pediatrics, College of Medicine, Chungbuk National University, Cheongju, [17]Department of Pediatrics, College of Medicine, The Catholic University of Korea, Seoul, Korea

Allergic rhinitis (AR) is increasing in Korean children since last 20 years. Investigation on risk factors of AR according to clinical phenotype by ARIA classification is important. Therefore, we aimed to investigate risk factors and comorbidities of AR according to ARIA classification from Panel Study of Korean Children (PSKC). Methods: The PSKC study is a general population based birth cohort study which recruited 2,150 mother-baby dyads by using 2-step stratified random sampling at 2008. 1,577 children were followed at 2015 from PSKC study. 642 children visited the hospital to be performed allergic evaluations. Among children with nasal symptoms within the last 12 months, the subtype of AR was classified by pediatricians according to ARIA guideline. Results: Prevalence of mild and moderate to severe AR was 37.2% and 8.8%. AR was highly associated with history of asthma diagnosis and family history. The risk factors of AR were similar in each phenotype, whereas those of mild-persistent AR included recent use of analgesics or pyretics (aOR, 2.32; 95% CI, 1.03-5.24) and current cat ownership (aOR, 10.18; 95% CI, 1.46-71.23). Associated positive sensitizations on skin prick tests with moderate to severe-persistent AR were Der P (aOR, 2.75; 95% CI, 1.18-6.38), Japanese Hop (aOR, 5.16; 95% CI, 1.51-17.59) and Cat (aOR, 5.28; 95% CI, 1.17-23.63), and mild-persistent AR was associated with Alternaria (aOR, 6.81; 95% CI, 1.03-45.03). The rate of comorbidities of AR were high in moderate to severe AR (asthma 19.6%, PC20 $\leq$ 4mg/ml 17.0%). Conclusion: Prevalence of mild and moderate to severe AR was 37.2% and 8.8% at age 7 years. Moderate to severe-persistent AR were associated with sensitization of Der P, Japanese Hop and Cat, whereas mild-persistent AR was associated with that of Alternaria. The comorbidities of asthma and BHR were high in moderate to severe AR. These findings suggest that AR phenotype may be distinct and helpful to care patients.

Key Words: Allergic rhinitis, Risk factor, Comorbidity

P-58

Total IgE and Mannose Binding Lectin levels in serum with respiratory allergic Mongolian adults

Enkhbayar Bazarsad[1], Narantsetseg Logii[2], Bayar-Ulzii Batmunkh[3], Tuvshintur Naidansuren[4], Munkhbayarlakh Sonomjamts[4]*

[1]Department of Physiology and Molecular Biology, Ach Medical University, Ulaanbaatar, Mongolia, [2]Department of Biochemistry and Laboratory, School of Pharmacy and Bio-Medicine, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia, [3]Effect Allergy and Asthma clinic, Ulaanbaatar, Mongolia, [4]School of Medicine, Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia

Objectives: Total serum IgE measurement and skin prick tests (SPT) are the most common tools for allergy diagnosis. Mannose-binding lectin (MBL) is a vital protein of an innate immune system. The serum level of MBL is associated with an increased susceptibility to infection with a high risk of allergic and autoimmune diseases. This study was conducted to evaluate total serum IgE and SPT relationships in Mongolian atopic adults with respiratory allergy. We determined the profile of serum levels of MBL in atopic and healthy Mongolian subjects.
Methods: Serum samples were collected from 219 healthy adult blood donors and 216 atopic subjects. SPT were performed in allergic subjects, using standardized aeroallergenic extracts. We analyzed the total serum IgE levels were measured by ELISA and MBL level in each serum by using the double-antibody sandwich ELISA method.
Results: All subjects with atopic diseases had positive results on SPT. Common allergens were mugwort, brome grass and dust mites. The mean serum level of IgE was 4321.5 ± 1730.7 ng/ml in atopic subjects. MBL level in serum was 3088.28 ± 669.8 ng/ml in atopic subjects and 2165.07 ± 708.5 ng/ml in healthy subjects. In male, the MBL mean serum level of atopic subjects was 3012.8 ± 783.16 ng/ml and healthy group was 2073.33 ± 678.26 ng/ml. The MBL mean serum level of female atopic subjects was 3138.22 ± 580.6 ng/ml and in the healthy group was 2263.61 ± 733.1 ng/ml. Low association and significant differences were observed between MBL levels of atopic and healthy subjects. There were not significant differences of serum levels of IgE between age groups.
Conclusion: The serum level of MBL in atopic subjects was comparatively higher than in healthy group and there was not statistically significant association between the level of total IgE and MBL levels in serum of Mongolian adults with respiratory allergy.

P-59

Immunomodulatory effects of autologous total IgG in patients with atopic dermatitis

Dong-Ho Nahm*, Su-Mi Cho, Myoung-Eun Kim, Byul Kwon

Department of Allergy and Clinical Immunology, Ajou University School of Medicine

Background: Idiotype network theory proposes that antigen-binding portion (idiotype) of the autologous immunoglobulin is immunogenic enough to induce active immune response to itself. We hypothesized that intramuscular administrations of autologous total IgG could produce immunomodulatory effects in patients with allergic diseases.
Method: This study aimed to evaluate the immunomodulatory effects of intramuscular administration of autologous total IgG on hypersensitivity reaction in patients with atopic dermatitis (AD). Sixteen adult patients with AD received intramuscular injections of 50 mg autologous total IgG twice a week for 4 weeks (from 0 to 4 weeks). The serum concentrations of interleukin (IL)-4, IL-10, IL-12, and interferon gamma (IFN-γ) were measured using enzyme-linked immunosorbent assay at -4, 0 (baseline), 4, 8, and 12 weeks.
Results: The serum concentrations of IL-10 and IFN-γ significantly increased at 4, 8, and 12 weeks compared to baseline ($P < 0.05$). There were no significant changes in serum concentrations of IL-4 and IL-12 at 4, 8, and 12 weeks compared to baseline ($P > 0.05$). There were no significant changes in serum concentrations of IL-4, IL-10, IL-12, and IFN-γ between -4 week and baseline ($P > 0.05$).
Conclusion: Intramuscular administrations of autologous total IgG significantly increased the serum concentrations of IL-10 and INF-γ in patients with AD. Further studies are required to investigate the clinical significance and detailed mechanism of these immunomodulatory effects.

Key Words: Atopic dermatitis; Immunoglobulins; Immunomodulation; Hypersensitivity

P-60

Current Management of moderate-to-severe Atopic Dermatitis: A Survey of physicians in Korea

HyunHee Kim[1], HyeYung Yum[1], HyungJung Kim[2], WooKyung Kim[3], SoYeon Lee[4], GapSuk Lee[5], DongHun Lee[6]*

[1]Department of Pediatrics, Seoul Medical Center, Seoul, [2]Department of Dermatology, Seoul Medical Center, Seoul, [3]Department of Pediatrics, Inje University School of Medicine, Seoul, [4]Department of Pediatrics, Hallym University College of Medicine, Anyang, [5]Department of Dermatology, Choongang University College of Medicine, Seoul, [6]Department of Dermatology, Seoul National University College of Medicine, Seoul, Korea

Purpose: There is lack of evidence for treatment of moderate-to-severe atopic dermatitis, resulting in variation in strategies in patient management. We collect data on current practice as reported by allergist, pediatricians, and dermatologist in Korea.
Methods: This survey was conducted in physician members of Korean Academy of Asthma and Allergy, Korean Academy of Pediatric Allergy and Respiratory Disease, and Korean Academy of Atopic Dermatitis.
Results: A total of 93 physicians participated in the study. Sixty five percent were pediatricians and 31% were dermatologists. The major patients' age group was less than 5 years for 89.8% of pediatrician and 6-12 year-olds for 38% of dermatologists. The proportion of moderate-to-severe AD was higher in dermatologists and allergists compared to pediatricians. The respondents agreed the necessity of education including demonstration of basic skin care and applying topical medicines, psychological, and nutritional support in 88.2%, 75.3%, and 83.9% respectively. Less than half of physicians conducted education and counseling in real practice. There were distinct differences in choosing first-line treatments according specialty. The order of preferred systemic treatment was wet wrap therapy, systemic corticosteroid, cyclosporin in pediatrician. Dermatologists ranked cyclosporin, phototherapy, and systemic corticosteroid as the first-line regimen. The major factors quoted as barrier for proper management were steroid phobia, unproven complement-alternative medicine, lack of education, and unreasonable insurance system.
Conclusion: Our findings suggested distinct differences in moderate-to-severe AD treatment exist among physician's specialty. There is still an unmet need for personalized, evidence-based, and multi-disciplinary approach including therapeutic patient education in real practice. Consensus in approach of management should be implemented for the best outcomes based further randomized controlled trials.

Key Words: Atopic dermatitis; Management; Questionnaire

P-61

Influence of infection and antibiotic exposure on the development of atopic dermatitis: a nationwide population-based case-control study

Chong Won Choi[1], Bo Ram Yang[2], Dong In Suh[3], Jungyoon Ohn[1], Joongyub Lee[2], Kyu Han Kim[1]*

[1]Department of Dermatology, Seoul National University College of Medicine, [2]Division of Clinical Epidemiology, Medical Research Collaborating Center, Biomedical Research Institution, Seoul National University Hospital, [3]Department of Pediatrics, Seoul National University Children's Hospital

Background: Hygiene hypothesis suggested the association between atopic dermatitis and exposure to microorganisms and antibiotics. Studies on the association between atopic dermatitis and infection and antibiotic exposure have limitations and the sole influence of each on the development of atopic dermatitis was elusive.

Methods: We conducted a nationwide population-based case-control study. A total of 244,805 children with AD from among 2,283,601 children born between January 2010 and December 2014 and equal number of sex and age-matched healthy children as controls. Patients were diagnosed with AD if they visited medical institutions more than twice during a 6-month period, with a principal diagnostic code of AD. Conditional logistic regression analysis was used to evaluate the association between AD and infection or antibiotic exposure and to estimate adjusted odds ratio (OR) for the independent effect of infection or antibiotic exposure on AD.

Results: Infections and antibiotic exposure increased the risk for AD (OR 1.604, 95% confidence interval (CI) 1.579–1.630 for infections and OR 1.11, 95% CI 1.094–1.129 for antibiotic exposure, respectively). A dose-dependent relationship was observed between risk for AD and number of infectious episodes and duration of antibiotic exposure. On further analysis using a conditional logistic model, infection with or without the use of antibiotics and antibiotic exposure when uninfected increased the risk for AD. Risk for AD was the lowest when infections were treated with antibiotics. Additionally, risk for AD decreased when infections treated with antibiotics lasted for < 7 days.

Conclusion: Infections and antibiotic exposure increased the risk for AD. However, the risk varied depending on duration of infection and antibiotic use. Severity of infection and antibiotic use have to be considered when analysing the effect of microorganisms or infection on development of AD.

Key Words: Atopic dermatitis, Infection, Antibiotics

P-62

Additive effect of maternal meat and fish diet and maternal pre-pregnancy underweight on the risk of infant atopic dermatitis

Hea Young Oh[1], So-Yeon Lee[1], Kyeong Ok Koo[7], Se-Young Oh[7], Jisun Yoon[1], Sungsu Jung[1], Hyun-Ju Cho[1], Ju-Hee Seo[2], Dong In Suh[3], Youn Ho Shin[4], Kyung Won Kim[5], Kangmo Ahn[6], Soo-Jong Hong[1]*

[1]Department of Pediatrics, Childhood Asthma Atopy Center, Asan Medical Center, University of Ulsan College of Medicine, [2]Department of Pediatrics, Dankook University Hospital, [3]Department of Pediatrics, Seoul National University College of Medicine, [4]Department of Pediatrics, CHA Medical Center, CHA University College of Medicine, [5]Department of Pediatrics, Yonsei University College of Medicine, [6]Department of Pediatirics, Samsung Medical Center, Sungkyunkwan University School of Medicine, Environmental Health for Atopic Disease, Samsung Medical Center, [7]Department of Food and Nutrition, Kyunghee University

Background: The aim of this study was to identify the association between maternal diet during pregnancy and the risk of atopic dermatitis (AD) in infant and evaluate the association according to pre-pregnancy BMI.
Methods: The Cohort for Childhood of Asthma and Allergic Diseases (COCOA) was selected from the general Korean population. A pediatric allergist assessed 1061 infants for the presence of AD at 6 months, 1 and 2 years of age. This study included 927 infants with AD (n=246) or without AD (n=681) during 2 years. Dietary pattern was investigated using principle factor analysis and multivariable logistic regression analysis was performed to assess odds ratio (OR) and 95% confidence interval (CI) of infant AD.
Results: Three maternal dietary patterns were identified; vegetable and fruit diet, sugar and confectionary diet, and meat and fish diet. High score group of meat and fish diet, characterized by a high intake of calorie and fat, had a higher risk of infant AD at 6 months (aOR, 1.35; 95% CI, 0.95-1.94), 1 year (1.49; 1.03-2.16), and 2 years (1.39; 1.00-1.91) of age, compared to low score group for that. When stratified by pre-pregnancy BMI, the underweight alone showed a significant association of meat and fish diet and infant AD at 6 months (aOR, 2.01; 95% CI, 0.86-4.66), 1 year (2.49; 1.02-6.08) and 2 years (2.89; 1.29-6.51) of age. Combination of high score group of meat and fish diet and pre-pregnancy underweight had a higher risk of infant AD at 6 months (1.84; 1.02-3.69), 1 year (2.00; 1.04-3.86), and 2 years (1.86; 1.02-3.38) of age, compared to combination of low score group of that and pre-pregnancy normal weight.
Conclusion: This study demonstrated that maternal meat and fish diet, characterized by a high intake of calorie and fat, has a higher risk of infant AD. In addition, we found an additive effect on the risk of infant AD between this maternal meat and fish diet and pre-pregnancy underweight.

Key Words: Maternal diet, Atopic dermatitis, Body mass index

P-63

Maternal dietary intakes of vitamin A, D and retinol during pregnancy are associated with atopic dermatitis in infant

Si Hyeon Lee[1], So Yeon Lee[2], Hyo Jeong Hwang[8], kyeong ok Koo[9], Se-Young Oh[9], Jisun Yoon[2], Sungsu Jung[2], Hyun-Ju Cho[2], Dong In Suh[3], Youn Ho Shin[4], Kyung Won Kim[5], Kangmo Ahn[6], Sung Ok Kwon[7], Soo-Jong Hong[2]*

[1]Asan Institute for Life Science, Asan Medical Center, University of Ulsan College of Medicine, Seoul, [2]Department of Pediatrics, Asan Medical Center, Ulsan University College of Medicine, Seoul, [3]Department of Pediatrics, Seoul National University College of Medicine, Seoul, [4]Department of Pediatrics, Gangnam CHA Medical Center, CHA University School of Medicine, Seoul, [5]Department of Pediatrics, Yonsei University College of Medicine, Seoul, [6]Department of Pediatrics, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, [7]Department of Food and Nutrition, Hallym University, [8]Biomaterials Research Institute, Sahmyook University, Seoul, [9]Department of Food and Nutrition, Research Institute of Human Ecology, Kyung Hee University, Seoul, Korea

Background: Maternal nutrient intake during pregnancy potentially influences the allergic diseases of offspring. This study examined the association between maternal intake of antioxidants during pregnancy and the risk of atopic dermatitis in infant.
Methods: This study population was derived from Cohort for Childhood Origin of Asthma and Allergic Diseases (COCOA) birth cohort study, prenatal maternal diet was assessed by administering a food frequency questionnaire (FFQ). A total of 1160 children, who completed questionnaire, were included in the analysis. We conducted logistic regression to assess the potential association between maternal intake of antioxidants and atopic dermatitis. Maternal intake of antioxidants levels were categorized in tertiles, and the highest tertile was used as the reference category.
Results: Lower retinol and vitamin D intake during pregnancy were associated an increased risk of AD at age 1 year. (aOR [95% CI]; respectively 2.45 [1.36-4.43], 1.75 [1.03-2.96]), whereas adjusted ORs for vitamin E, vitamin C and vitamin B in infancy remained elevated but not statistically significant. Lower maternal dietary retinol and vitamin D, vitamin A intake was significantly associated with the persistence of AD at 1 year old. (aOR [95% CI];respectively 3.48 [1.12-10.82], 3.94 [1.31-6.81], 3.59 [1.06-12.16]).
Conclusions: Lower dietary vitamin A, D and retinol intakes during pregnancy may be associated with AD in infancy and persistent AD at 1-year-old. Retinol and vitamin D intake during pregnancy might decrease the risk of AD in early childhood.

Funding sources: This research was supported by a fund (2008-E33030-00, 2009-E33033-00, 2011-E33021-00, 2012-E33012-00, 2013-E51003-00, 2014-E51004-00, 2014-E51004-01, 2014-E51004-02) by Research of Korea Centers for Disease Control and Prevention.

Key Words: Atopic dermatitis, Maternal, Vitamin, Nutrient

P-64

Epigenetic gene methylation by cord blood 25-hydroxyvitammin D deficiency contributes to the development of atopic dermatitis in offspring mediated by oxidative stress

Youn Ho Sheen[1], Hyun-Ju Cho[2], Kyung Won Kim[8], Yoon Hee Kim[8], Dong In Seo[9], Mi-Jin Kang[3], Seung-Hwa Lee[3], So Yeon Lee[2], Ji-Sun Yoon[2], Yeongho Kim[4], Song-I Yang[5], Eun Lee[6], Kangmo Ahn[7], Soo-Jong Hong[2]*

[1]Department of Pediatrics, CHA Medical Center, CHA University College of Medicine, Seoul, [2]Department of Pediatrics, Childhood Asthma Atopy Center, Environmental Health Center, Asan Medical Center, University of Ulsan College of Medicine, Seoul, [3]Asan Institute for Life Science, University of Ulsan College of Medicine, Seoul, [4]Department of Pediatrics, Gyeongsang National University Changwon Hospital, Changwon, [5]Department of Pediatrics, Hallym University Secred Heart Hospital, Hallym University College of Medicine, Seoul, [6]Department of Pediatrics, Chonnam National University Hospital, Chonnam National University College of Medicine, Gwangju, [7]Department of Pediatrics, Samsung Medical Center, Sungkyunkwan University School of Medicine, Environmental Health Center for Atopic Disease, Samsung Medical Center, Seoul, [8]Department of Pediatrics, Yonsei University College of Medicine, Seoul, [9]Department of Pediatrics, Seoul National University College of Medicine, Seoul, Korea

Purpose: We showed that cord blood (CB) 25-hydroxyvitamin D affects the development of AD in infancy; however, the mechanism is unknown. We determined whether deficient CB 25-hydroxyvitamin D induces CB DNA methylation of leukocytes and AD in offspring within six months of age.
Methods: The subjects were stratified as 1) CB vitamin D sufficiency (≥30.0 ng/mL) and normal skin, 2) CB vitamin D sufficiency and AD, 3) CB vitamin D deficiency (<10.0 ng/mL) and normal skin, and 4) CB vitamin D deficiency and AD. Gene expression for MICAL3 and OGG1 were performed using rt-PCR.
Results: Microarry analysis showed that MICAL3 was hypomethylated in children of deficient CB vitamin D. Children of CB vitamin D deficiency and AD were 3.15 times more likely to have hypomethylated MICAL3 and 5.22 times more likely to have hypomethylated OGG1 compared with controls. A correlation was found between CB vitamin D and MICAL3 and a trend between CB vitamin D and OGG1. The AD severity was positively associated with MICAL3 and OGG1.
Conclusion: Hypomethylation of MICAL3 of CB leukocytes by CB 25-hydroxyvitamin D deficiency is associated with the development of AD in infancy mediated by ROS.

Key Words: 25-hydroxyvitamin D, Atopic dermatitis, Cord blood, Cohort

P-65

Alterations in the composition and functional gene profiles of the gut S.mitis may affect the persistence of AD in infancy

park yoon mee[1], Mi Jin Kang[1], So-Yeon Lee[2], JiSun Yoon[2], Hyun-Ju Cho[2], Eun Lee[3], Dong In Suh[4], Youn Ho Shin[5], Kyung Won Kim[6], Kang Mo Ahn[7], Soo-Jong Hong[2]*

[1]University of Ulsan College of Medicine, Seoul, [2]Department of Pediatrics, Childhood Asthma Atopy Center, Environmental Health Center Asan Medical Center, University of Ulsan College of Medicine, Seoul, [3]Department of Pediatrics, Chonnam National University Hospital, Gwangju, [4]Department of Pediatrics, Seoul National University College of Medicine, Seoul, [5]Department of Pediatrics, CHA Gangnam Medical Center, CHA University School of Medicine, Seoul, [6]Department of Pediatrics, Yonsei University College of Medicine, Seoul, [7]Department of Pediatrics, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

Background: Alteration of gut microbiota in early life was important to understand the development of atopic dermatitis (AD). A recent study shows that the metabolism by gut microbiota may effect to development AD, however, the association with the development of AD and gut microbiota still remains unclear.
Objective: To investigate the association between S. mitis in gut and AD, to compare genes that function of gut microbiome.
Methods: AD phenotype was characterized by non-persistence of AD symptom and persistence of AD symptom over 1year of age. We analyzed the gut microbiota in 72 healthy controls, 44 non-persistence AD and 26 persistence AD, and the metagenome shotgun in 20 healthy controls and 18 persistence AD by using fecal samples at 6 months of age. Differences in potential functional genes profiles were identified using Genomes (KEGG; Kyoto Encyclopedia of Genes and Genomes) database among the three groups which obtained from metagenome sequencing. Total IgE, specific IgE to egg and milk, and percentage of blood eosinophils were measured at 1 year of age.
Results: S. mitis species were increased in both AD phenotypes including non-persistence AD ($P = 0.029$) and persistence AD ($P = 0.023$), compared to healthy infants. The relative abundance of S. mitis in gut was positive correlated with total IgE and egg or milk-specific IgE ($P < 0.001$) in AD groups, but not in healthy control. Differences in gene profiles of functional genes among the three groups resulted from different microbiome compositions ($P < 0.1$). S. mitis was associated with Cyanoamino acid metabolism which affects inflammation.
Conclusion: Alterations in the composition and functional gene profiles of the S. mitis in gut may affect the development or persistence of AD in infancy, mediated by Cyanomino acid metabolism pathway related inflammation.

Key Words: Streptococcus mitis, Atopic Dermatitis, Microbiome, metagenome shotgun

P-66

Effects of kestose on gut mucosal immunity in an atopic dermatitis mouse model

Seung-Hwa Lee[1], Ha-Jung Kim[2], Han-Na Go[1], Jae-Rin Ahn[1], Hye-Jung Kim[3], Mi-Jin Kang[1], Jisn Yoon[4], So-Yeon Lee[4], Soo-Jong Hong[5]*

[1]Asan Institute for Life Sciences, College of Medicine, University of Ulsan, Seoul, [2]Department of Veterinary Internal Medicine, College of Veterinary Medicine, Chonnam National University, Gwangju, [3]Food R&D center, Samyang Corp, Seongnam 13488, [4]Department of Pediatrics, Childhood Asthma Atopy Center, Asan Medical Center, Seoul, [5]Department of Pediatrics, Childhood Asthma Atopy Center, Asan Medical Center, Environmental Health Center, College of Medicine, University of Ulsan, Seoul, Korea

Background: The probiotics, is a predominant component of the intestinal microbiota in infants and is believed to provide beneficial effects pertaining to the prevention of atopic dermatitis (AD). Kestose, a prebiotic fructo-oligosaccharide, is defined as functional food ingredients that stimulate the growth and activity of probiotics in the intestines, thereby improving AD symptoms and host health. However, the clinical effects and mechanism of kestose are still not clearly understood.
Objective: The aim of this study was to investigate the effects of kestose as prebiotics on atopic dermatitis in mice.
Methods: An AD mouse model was developed by (ovalbumin) epidermal sensitization using BALB/c mice. Kestose (1%, 5%, and 10%) or fructooligosaccharide (5%, FOS, positive control) was orally administered throughout the study. AD phenotypes and systemic immune response were estimated and also evaluated gut immune responses and metabolites.
Results: In comparison with the control AD mice, transepidermal water loss(TEWL), clinical score, and skin inflammation on histopathology were significantly decreased by the oral administration of kestose. Total immunoglobulin(Ig)E production and mRNA expression of thymic stromal lymphopoietin(TSLP) and interleukin(IL)-4 in skin were also suppressed by this administration. In addition, the population of CD4+Foxp3+ cells in mesenteric lymph nodes (MLNs) and acetate concentrations in feces were significantly increased by kestose treatment.
Conclusions: Kestose can significantly improve clinical symptoms and Th2- allergic inflammation in the skin by increasing CD4+Foxp3+Treg cells in MLNs in the AD mouse model. These findings suggest that the mechanism involves stimulating the growth of beneficial intestinal microbes that generate SCFAs in feces to increase CD4+Foxp3+Treg cells in MLNs.

Key Words: Atopic dermatitis, Kestose, Prebiotics

P-67

Maternal dietary pattern during pregnancy affect the development of offspring's atopic dermatitis by gut microbiota

So-Yeon Lee[1], Sung-Ok Kwon[2], Youn Ho Sheen[9], Dong In Seo[10], Mi-Jin Kang[3], Yoon Mee Park[3], Ji-Sun Yoon[1], Kangjin Kim[4], Sungho Won[5], Bong-Soo Kim[6], Kangmo Ahn[7], Kyung Won Kim[8], Soo-Jong Hong[1]*

[1]Department of Pediatrics, Childhood Asthma Atopy Center, Environmental Health Center, Asan Medical Center, University of Ulsan College of Medicine, Seoul, [2]Department of Pediatrics, Seoul National University College of Medicine, Seoul, [3]School of Medicine Kanwon National University, Chuncheon, Gangwon-do, [4]Asan Institute for Life Science, University of Ulsan College of Medicine, Seoul, [5]Department of Public Health Science, Seoul National University, Seoul, [6]Graduate School of Public Health, Seoul National University, Seoul, [7]Department of Life Sciences, Hallym University, Chuncheon, Gangwon-do, [8]Department of Pediatrics, Samsung Medical Center, Sungkyunkwan University School of Medicine, Environmental Health Center for Atopic Disease, Samsung Medical Center, Seoul, [9]Department of Pediatrics, Yonsei University College of Medicine, Seoul, [10]Department of Pediatrics, CHA Medical Center, CHA University College of Medicine, Seoul, Korea

Background: There were no consistent link maternal dietary intake during pregnancy and atopic outcomes in their children despite many studies. Most studies have focused on the effects of individual nutrients and foods rather than dietary patterns. In addition, further investigations are still required to understand mechanisms how diet affects allergic diseases.
Objective: This prospective study examined the relationship between maternal dietary pattern during pregnancy and the risk of atopic dermatitis (AD) in offspring aged 6, 12 months and whether the mechanism is mediated by gut microbiota.
Methods: Subjects were 1,335 mother-child pairs from Cohort for Childhood Origin of Asthma and Allergic Diseases (COCOA). Data on maternal intake during pregnancy were assessed with a validated food frequency questionnaire and constructed three dietary patterns such as "traditional healthy", "meat food" and "sweets/fast food" diets. Fecal samples were collected at 1 month of age from infants who were breastfeed. Microbiota characterization was performed using 16s rRNA pyroseuencing on a Roche/454 GS junior system according to the manufacturer's instructions and difference among groups analyzed the byt Mann-Whitney U test.
Results: Mothers took higher intake of meat diet during pregnancy and breastfeed have higher risk of offspring's atopic dermatitis at 6 and 12 months.(OR 2.14 95% CI 1.05-4.37 ; OR 2.18, 95% CI 1.05-4.53) This association was not observed in nonbreast-fed offspring. Chryseobacterium was significantly increased in infants whose mother had meat diet pattern than traditional healthy diet pattern and also increased in infants with AD whose mother had meat diet pattern than in infants without AD whose mother had traditional healthy diet patten.
Conclusion: Higher maternal meat intake during pregnancy may increase the risk of atopic dermatitis in their offspring who breastfed. Maternal meat dietary pattern might affect the development of offspring's AD by gut microbiota.This research was supported by a fund (2008-E33030-00, 2009-E33033-00, 2011-E33021-00, 2012-E33012-00, 2013-E51003-00, 2014-E51004-00, 2014-E51004-01, 2014-E51004-02) by Research of Korea Centers for Disease Control and Prevention. This research was supported by Basic Science Research Program through the National Research Foundation of Korea(NRF) funded by the Ministry of Education(NRF-2015R1D1A1A01059599).

Key Words: Atopic dermatitis, Pregnancy, Gut microbiome, Diet pattern

P-68

The psychological impact of pediatric anaphylaxis on their parents; using BDI-II, BAI, and IES-R

Gwang Cheon Jang[1]*, Jihyun Kim[2], Meeyong Shin[11], Hye Yung Yum[12], You Hoon Jeon[10], Kyung Won Kim[13], Kyunguk Jeong[3], Kangmo Ahn[2], Bok Yang Pyun[4], KAPARD Study Group on Food Allergy and Atopic Derm[14], KAAACI Work Group on Urticaria/Angioedema/Anaphyla[15], Sooyoung Lee[3], Taek Ki Min[4], Tae Won Song[5], Woo Kyung Kim[6], Sun Hee Choi[7], Jeong Hee Kim[8], Yong Ju Lee[9], So-Yeon Lee[10]

[1]Department of Pediatrics, National Health Insurance Service, Ilsan Hospital, Goyang, [2]Department of Pediatrics, Hallym University College of Medicine, Seoul, [3]Department of Pediatrics, Soonchunhyang University College of Medicine, Bucheon, [4]Department of Pediatrics, Seoul Medical Center, Seoul, [5]Department of Pediatrics, Yonsei University College of Medicine, Seoul, [6]Korean Academy of Pediatric Allegy and Respiratory Disease, [7]The Korean Academy of Asthma, Allergy and Clincal Immunology, [8]Department of Pediatrics, Environmental Health Center for Atopic Diseases, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, [9]Department of Pediatrics, Ajou University School of Medicine, Suwon, [10]Pediatric Allergy and Respiratory Center, Department of Pediatrics, Soonchunhyang University Hospital, Seoul, [11]Department of Pediatrics, Ilsan Paik Hospital, Inje University College of Medicine, Goyang, [12]Department of Pediatrics, Inje University College of Medicine, Seoul, [13]Department of Pediatrics, Kyung Hee University Hospital at Gangdong, Kyung Hee University School of Medicine, Seoul, [14]Department of Pediatrics, Inha University College of Medicine, Seoul, [15]Department of Pediatrics, Hallym University Kangnam Sacred Heart Hospital, Seoul, Korea

Background: Anaphylaxis is a life-threatening disorder. Having a child with anaphylaxis can have a significant long-term psychological impact on parents and this anxiety may in some cases be transferred from parents onto their children. The aim of this study was to investigate the post traumatic stress disorder (PTSD) in parents of pediatric anaphylaxis patients.
Methods: To investigate the PTSD for parents of child with anaphylaxis, we had been using the Korean Beck Depression Inventory II (BDI-II), Korean Beck Anxiety Inventory (BAI), and of Impact of Event Scale-Revised Korean version (IES-R-K) scale in 13 hospitals between Oct. 1, 2016 and Mar. 31, 2017.
Results: Total 100 parents who had children having experienced anaphylaxis, were participated in this study. Response rate of BDI-II was 99%, mean score was 16.38 (S.D.; 13.09), 42.4% was scored 17 or above (depression), and Cronbach's alpha was 0.939. Response rate of BAI was 91%, mean score was 13.73 (S.D.; 14.02), 16.5% was scored 22 or above (anxiety), and Cronbach's alpha was 0.969. Response rate of IES-R was 88%, mean score was 30.39 (S.D.; 22.25), 56.8% was scored 25 or above (impact), and Cronbach's alpha was 0.963.
Conclusion: We found that 42.4% (BDI-II), 16.5% (BAI), and 56.8% (IES-R) of all parents who had experienced a traumatic event were classified as having a high risk of PTSD, and this proportion is higher than that of other groups (e.g., firefighters). This finding indicates that PTSD-related interventions and management are needed for parents of children with anaphylaxis.

Key Words: Post-Traumatic Stress Disorder, Anaphylaxis

P-69

Perioperative anaphylaxis in a single tertiary hospital

Sang Mi Chung, Ju Whan Choi, Jee Youn Oh, Young Seok Lee, Kyung Hoon Min, Sung Yong Lee, Jae Jeong Shim, Kyung Ho Kang, Gyu Young Hur*

Department of Internal Medicine, Korea University College of Medicine, Seoul, Korea

Introduction: Anaphylactic reactions during the perioperative period are non common but life threatening events. But data on its incidence and causative agents vary in different studies.
Objectives: We purposed to investigate the incidence of the perioperative anaphylaxis in a hospital with the clinical data. We conducted a retrospective chart review and identify 12 anaphylaxis cases that had possible anaphylaxis related with anesthesia between 2011 January to 2016 December. We reviewed the clinical, demographic data and the results of skin tests.
Results: Among them, 8 patients were identified as having the perioperative anaphylaxis. Overall incidence anaphylaxis during 6 years was 6.84 per 100,000 (8 out of 117,044 anesthesia). Half of the patients (4 of 8) were female, and mean age was 44.38 ± 17.85 (from 24 to 69 years). Half of the patients (4 of 8) had atopic tendency, and 3 patients had history of allergic rhinitis. According to anaphylaxis grading, 1 (12.5%) was grade A with respiratory symptoms, 6 (75.0%) were grade B with life-threatening cardiovascular and/or respiratory derangement, 1 (12.5%) was grade C with cardiac arrest. The causative drugs were identified in 6 of 8 using intradermal and prick testing. Among them, 66.7% (4 of 6) were caused by antibiotics (1 vancomycin, and 3 3rd generation cephalosporin), and 33.3% (2 of 6) were caused by neuromuscular blocking agent (1 rocuronium, and 1 both rocuronium and cisatracurium)
Conclusions: Antibiotics was the most common cause of perioperative anaphylaxis in our instituite. To identify culprit agent, appropriate skin testing with standardized protocol should be performed to reduce the recurrence of life-threatening events.

Key Words: Anaphylaxis, Perioperative, Skin test

P-70

Beta-lactams induced anaphylaxis in hospitalized patients

Chan Sun Park[1], DoungYoon Kang[2], Su Jung Kim[3], Young-Hee Nam[4], So Young Park[5], Hye Jung Park[7], Jae-Woo Jung[7], Min-Suk Yang[8], Hye-Ryun Kang[10], Hye-Kyung Park[9]*

[1]Department of Internal Medicine,Inje University haeundae Paik Hospital, Busan, [2]Department of Internal Medicine, Seoul National University Medical Research Center, Seoul National University College of Medicine, Seoul, [3]Regional Pharmacovigilance Center, Seoul National University Hospital, Seoul, [4]Department of Internal Medicine, Kyungpook National University Hospital, Daegu, [5]Department of Internal Medicine, Dong-A University College of Medicine, Busan, [6]Department of Internal Medicine, Eulji General Hospital, Eulji University School of Medicine, [7]Department of Internal Medicine, Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, [8]Department of Internal Medicine, Chung-Ang University College of Medicine, Seoul, [9]Department of Internal Medicine, SMG-SNU Boramae Medical Center, Seoul, [10]Department of Internal Medicine, Pusan National University Hospital, Busan, Korea. and Korean Academy of Asthma, Allergy and Clinical Immunology Work Group on drug allergy

Background: Beta-lactams(BLs) are the most commonly used antibiotics and can cause a wide range of allergic reactions from mild cutaneous reaction to life-threatening anaphylaxis.
Objective: We evaluated clinical manifestations and major culprit drugs, the status of skin test in patients with anaphylaxis to BLs. We also assessed the contributing factors for the development of BLs induced anaphylaxis.
Methods: We enrolled 74 patients who developed anaphylaxis to intravenous BLs during hospitalization. We evaluated whether the skin test was properly conducted. Also, to figure out the risk factors for the BLs induced anaphylaxis, we compared various clinical parameters between patients with BLs-tolerable controls, matched by age, sex, matched by age, sex, causative drug, and the purpose of antibiotics usage.
Results: Mean age was 42.7 ± 18 years. Mean duration of symptom onset after drug administration was 13.6 minutes. The major eliciting drugs were ceftriaxone (N = 12), piperacillin (N = 8), cefazedone (N = 8), cefbuperazone (N=7), ceftizoxime (N = 5), amoxicillin (N=4), cefotetan (N=4). In the remaining 26 cases, different beta-lactams were involved. The most common manifestations were cutaneous reactions (74.3%), followed by respiratory (67.6%), cardiovascular (62.2%), and gastrointestinal reactions (29.7%). Skin tests were performed in 83% of all patients. Only 42% of skin tests were performed using appropriate concentration. Concurrent administration of angiotensin enzyme inhibitors(ACEIs) and the history of drug allergy were significantly increased in the anaphylaxis group.
Conclusion: However, the procedure of skin test was not adequate in considerable cases. It is necessary to encourage the skin test to be carried out according to the guideline. Administration of angiotensin enzyme inhibitors and a history of drug allergy were identified as contributing factors of anaphylaxis to beta-lactams.

Key Words: Anaphylaxis, Beta-lactams, Skin test

P-71

Epidemiology of Ananphylaxis in Korea: study of community-based hospital

Hyunseok Cho[1], Dohyun Kim[2], Youngkwang Choo[3], Jungseok Park[4], Jangwon Choi[5], Dongwhan Jang[6], Taekwon Kim[7], Jae-Woo Kwon[8]*

[1]Department of Pediatrics, Hwacheon Health Center and County Hospital, Hwacheon, [2]Department of Pediatrics, Gangneung Medical Center, Gangneung, [3]Department of Pediatrics, Samcheok Medical Center, Samcheok, [4]Department of Internal Medicine, Sunchang Health Center and County Hospital, Sunchang, [5]Department of Internal Medicine, Uljingun Medical Center, Uljin, [6]Department of Neurosurgery, Korea Workers' Compensation and Welfare Service Jeongseon Medical Center, Jeongseon, [7]Department of Emergency Medicine, Cheongsong Health Center and County Hospital, Cheongsong, [8]Division of Allergy and Clinical Immunology, Department of Internal Medicine, Kangwon National University School of Medicine, Chuncheon, Korea

Background: To prevent anaphylaxis and associated mortality, the prevalence and monthly causes of anaphylaxis in the community were investigated. There are few community-based epidemiologic studies of anaphylaxis other than university hospitals
Methods: We retrospectively reviewed the medical records of patients diagnosed with anaphylaxis at seven community-based hospitals during the period from 2012 to 2016 to investigate monthly age-specific causes, prevalence rates, recurrence rates, and serious consequences of anaphylaxis. Anaphylaxis was identified on physician-certified diagnoses using the ICD-10 codes (T780, T782, T805, T886). In addition, Patients who received epinephrine were included in the study if their medical records were consistent with anaphylaxis diagnosis criteria.
Results: A total of 1,021 cases of anaphylaxis were reported (65% male, 51.5 ± 16 years). The prevalence rate for 5 years was 0.045%, and it's trend was increasing. The most common causes were insect bites (55.9%), food (21.3%), medicines (13.2%) and unknown causes (6.7%). More affected age was 50-59 years. Anaphylaxis occurred in summer (47.9%). Autumn (28,2%), spring (12.3%) and winter (11.6%). The month with the highest incidence of anaphylaxis was August. The recurrence rate of anaphylaxis was 12.8%. The most common cause of recurrence was insect bites (44.3%), food (22.9%), drugs (14.5%) and unknown causes (14.5%). No single Epinephrine automatic injector was prescribed. There were no deaths associated with anaphylaxis
Conclusions: In communities, the main causes of anaphylaxis were insect bites, food and drugs. Summer, especially in August, the incidence of anaphylaxis is high and needs attention.

Key Words: Anaphylaxis, Epidemiology, Community based

P-72

Fructose induced anaphylaxis

Chang-Gyu Jung, Eun-Mi Yang, Ji-Ho Lee, Seung-Hyun Kim, Hae-Sim Park, Yoo Seob Shin*

Department of Allergy and Clinical Immunology, Ajou University School of Medicine, Suwon, Korea

Fructose is a component of sucrose, a disaccharide composed of 1 molecule of glucose and fructose each, mainly exists in fruits as natural sugar. To date, no case of immediate hypersensitivity reaction caused by fructose has been reported.
We report on a 20-year-old girl who had no past history of allergic diseases but developed anaphylaxis after the drinking a fructose containing food. She had the first episode of angioedema, urticaria, dyspnea, and fainting after eating several foods including coke in November 2015. After then she experienced six episodes of anaphylaxis with loss of consciousness after ingesting a variety of foods containing sugar.
Skin prick tests and intradermal tests were performed with fructose and glucose. Intradermal tests with fructose (1 mg/mL) and the highest concentration (10 mg/mL) of glucose showed a positive reaction. In single-blind, placebo-controlled, oral challenge test with various kinds of food containing monosaccharides and disaccharides including cola and wheat flour were performed. Generalized urticaria and angioedema were observed by taking 200 mL of Cola, 18.56 g of sugar and fructose, respectively, which all contain fructose. In basophil activation test by flow cytometry, high concentrations of fructose markedly enhanced expression of CD203c from the patient, not those from two healthy adult controls.
We first report a case of anaphylaxis caused by fructose. From oral provocation test, skin test, and in vitro tests, we concluded that the anaphylaxis observed in this patient was probably mediated by type I hypersensitivity against fructose.

Key Words: Anaphylaxis; Food allergy; Fructose; Sugar

P-73

A Case of Piperacillin induced anaphylaxis cross-reacting with Amoxicillin

Eun-Mi Yang, Bastsetseg Ulambyar, Seung-Hyun Kim, Young- Min Ye*

Department of Allergy and Clinical immunology, Ajou University School of Medicine, Suwon, Korea

Piperacillin-tazobactam is a combination of an extended-spectrum β-lactam antibiotic with a β-lactamase inhibitor (tazobactam) that commonly is used for treatment of critically ill patients. Beta-lactam antibiotics have been well known to induce IgE-mediated immediate hypersensitivity. A 25-yr-old female patient with atopic dermatitis has been working at intensive care unit of a university hospital since a year ago. As her eczematous lesions got worse, she experienced chest tightness, dizziness, generalized urticaria, and diarrhea right after spilling a bottle of piperacillin-tazobactam on her hands. Skin test with piperacillin was strongly positive, but not with tazobactam. We detected a significantly higher level of piperacillin-specific IgE in the sera from the patient as compared with those from 10 non-atopic healthy controls. The binding of piperacillin-specific IgE was significantly inhibited by free piperacillin and piperacillin-HSA conjugated. But, it did not affected by other beta-lactams including ampicillin and cefaclor, whereas a 57% of inhibition was shown upon addition of free amoxicillin. We confirmed an increased level of serum specific IgE to amoxicillin 0.39kU/l by ImmunoCAP in her sera. These results suggested that piperacillin can cause IgE-mediated anaphylaxis only by topical exposure. Moreover, it can cause a cross-reaction with other betalactams and need to be educated to avoid these drugs together.

Key Words: Anaphylaxis; piperacillin; Cross-reactivity; IgE; Immune CAP

P-74

Assessment of allergenicity of novel proteins (Avhppd03, Hppdpfw336) in genetically modified soybean

Jinyoung Lee[2], Jeongok Lee[2], Jae-Hwan Kim[3], Hae-Yeong Kim [3], Woo-Jung Song[4], Jihyun Kim[5], Kangmo Ahn[5]*

[1]Samsung Biomedical Research Institute, Seoul, [2]Environmental Health Center for Atopic Diseases, Samsung Medical Center, Seoul, [3]Institute of Life Sciences & Resources and Graduate School of Biotechnology, Kyung Hee University, Yongin, [4]Department of Internal Medicine, Seoul National University College of Medicine, Seoul, [5]Department of Pediatrics, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

Background: Allergic reactions to proteins expressed in genetically modified (GM) crops have been regarded as one of the health risks among the consumers, although they were initially developed to tolerate herbicides and resist disease and insects. The purpose of this study was to evaluate the potential allergenicity of newly expressed proteins (Avhppd03 and Hppdpfw336) in GM soybean (SYHT0H2 and FG72, respectively) by using sera from children with allergic disease.
Methods: Sera were obtained from 40 allergic children who are sensitized with soybean. Specific IgE was measured by ImmunoCAP (ThermoFischer, Uppsala, Sweden), and positivity was determined when its level was > 0.35 kU/L. Newly inserted gene, avhppd03 in SYHT0H2 and hppdpfw336 in FG72 were sequenced and cloned. These proteins (Avhppd03, Hppdpfw336) were expressed and purified for the serum screening test. The allergenicity of purified-recombinant proteins was assessed by using SDS-PAGE and immunoblotting.
Results: Sera from 40 allergic patients sensitized to soybean (29 boys and 11 girls) were obtained. Their age ranged between 0 and 13 years (mean age 3.3 years). The soybean-specific IgE level of the patients was 11.4 kU/L on average. The immunoblotting between patients\' sera and proteins from traditional soybeans showed positive IgE reactivity. Serum screening test between patients' sera and purified-recombinant proteins (Avhppd03, Hppdpfw336) in GM soybean was done. Hppdpfw336 did not show any reactivity by immunoblotting. Out of 40 sera, 20 were found to exhibit strong IgE reactivity against Avhppd03, and this reaction was inhibited by inhibition ELISA test. However, avhppd03 was easily degraded by pepsin digestion.
Conclusion: Our results suggest that proteins encoded by newly inserted gene in GM soybean (Avhppd03, Hppdpfw336) are not likely to cause allergic reactions.

Key Words: Allergenicity, Genetically Modified food

P-75

Assessment of allergenicity of novel proteins (CspB, eCry3.1Ab, EPSPS GRG23ACE5) in genetically modified maize

jinyoung lee[2], Jeongok Lee[2], Jae-Hwan Kim[3], Hae-Yeong Kim[3], Woo-Jung Song[4], Jihyun Kim[5], Kangmo Ahn[2]*

[1]Samsung Biomedical Research Institute, Seoul, [2]Environmental Health Center for Atopic Diseases, Samsung Medical Center, Seoul, [3]Institute of Life Sciences & Resources and Graduate School of Biotechnology, [†]Kyung Hee University, Yongin, [4]Department of Internal Medicine, Seoul National University College of Medicine, Seoul, [5]Department of Pediatrics, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul

Background: An assessment of the potential allergenicity of the proteins expressed by the genes introduced into genetically modified(GM) food is essential when determining the safety of a GM food. The purpose of this study was to evaluate the potential allergenicity of newly expressed proteins CspB, eCry3.1Ab and EPSPS GRG23ACE5 in GM maize (Mon87460, 5307 and VCO-01981-5, respectively) by using sera from children with allergic disease.
Methods: The recombinant proteins (CspB, eCry3.1Ab, EPSPS GRG23ACE5) were expressed and purified for the serum screening test. Sera were obtained from allergic children who are sensitized with maize. The level of serum specific IgE was measured by the ImmunoCAP system and considered as positive when they were 0.35 kU/L or higher. The allergenicity of purified-recombinant proteins was evaluated by immunoblot analysis using sera from allergic children.
Results: Sera from 40 allergic patients sensitized with maize were obtained to evaluate the allergenicity of CspB. The maize-specific IgE level of the patients was 5.1 kU/L on average. The immunoblot analysis showed positive IgE reactivity between maize-sensitized patients' sera and proteins from traditional maize. However, CspB did not show any reactivity by immunoblot analysis. Sera from 40 allergic patients sensitized with maize were obtained to evaluate the allergenicity of eCry3.1Ab and EPSPS GRG23ACE5. The level of specific IgE against maize was 4.0 kU/L on average. Serum screening test was done using patients' sera and newly inserted proteins(eCry3.1Ab, EPSPS GRG23ACE5) in GM maize. The immunoblot analysis showed positive IgE reactivity between patients' sera and proteins from traditional maize. However eCry3.1Ab, EPSPS GRG23ACE5 did not show any reactivity.
Conclusion: The results of this study suggest that proteins (CspB, eCry3.1Ab, EPSPS GRG23ACE5) encoded by newly inserted gene in GM maize are not likely to cause allergic reactions.

Key Words: Allergenicity, Genetically modified food

P-76

Oral allergy syndrome in birch pollen sensitized patients in Korea: Results of a Retrospective Chart Review

Jung-Hyun Kim[3], Woo-Jung Song[1], Sung-Yoon Kang[1], Sae-Hoon Kim[3], Heung-Woo Park[1], Sang-Heon Cho[1], Yoon-Seok Chang[3]*

[1]Department of Internal Medicine, Seoul National University College of Medicine, Seoul, [2]Institute of Allergy and Clinical Immunology, Seoul National University Medical Research Center, Seoul, [3]Department of Internal Medicine, Seoul National University Bundang Hospital, Seongnam, Korea

Background: Oral allergy syndrome (OAS), also known as pollen-food syndrome, is a form of a contact allergic reaction that mainly occurs when the mouth and throat comes in contact with raw fruit, vegetables or nuts. It is caused by cross-reacting allergens found in both pollens and food and the most common type of pollen-fruit cross-reaction is the birch pollen-related food allergy. Although OAS is a common form of food allergy in adults, there have been few epidemiologic studies of OAS in Korea.
Material and method: To evaluate the prevalence and triggers of birch pollen-related food allergy, a retrospective chart review was conducted on 125 patients who visited the allergy clinic in Seoul National University Bundang Hospital and showed positive skin prick test to birch pollen from January 2011 to December 2016.
Results: Of the 125 birch pollen sensitive patients, only 3 patients were birch pollen-monosensitive and the others showed mult-sensitivity to trees, grasses, weeds or house dust mite(HDM) allergens. Birch pollen multisensitive patients were also sensitized to Beech(71.2%), Alder(68.0%) in tree pollens, Velvet(22.4%) in grass pollens, Mugwort(32.8%) and Japanese Hop(32.8%) in weed pollens. Patients sensitized to HDM accounted for 58.4%. In total, 20%(n=26) of the study population experienced food allergy and the OAS was the main clinical manifestation(n=25). Apple(n=17), peach(n=12) and persimmon(n=6) were identified as the most frequent triggers. The incidence of OAS was 17.4%(n=12) in males and 23.2%(n=13) in females. There was no significant difference between the groups with and without OAS in age , serum eosinophil counts or serum total IgE levels. 72%(n=18) of patients with OAS had rhinitis, 20%(n=5) had asthma and 12%(n=3) had chronic urticaria as comorbid diseases.
Conclusions: Although we discovered some difference in the prevalence with previous reports, OAS was still common to atopy patients who were sensitized to birch pollen.

Key Words: Oral allergy syndrome, Birch

P-77

An Unusual Case Of Seizures With Anaphylaxis To Wheat

Kok Wee Chong[1]*, Simon Ling[2], Wenyin Loh[1]

[1]Allergy Service, [2]Neurology Service, Department of Paediatric Medicine, KK Women's and Children's Hospital, Singapore

Introduction: Wheat allergy is one of the most common food allergies in childhood and it typically presents with IgE mediated reactions, including anaphylaxis. Seizures are not typically reported to be a manifestation of anaphylaxis, though it can occur secondary to hypoxia following significant haemodynamic compromise.
Case Report: We describe a case of a previously well infant, who presented with anaphylactic shock to wheat, whom responded well to the initial management, but subsequently developed a cluster of brief generalised tonic clonic seizures without any ongoing haemodynamic instability. The tryptase level that was performed at 4-5 hours post reaction was significantly raised at 49.1 μg/L. Skin prick test to wheat, wheat specific IgE, the omega-5 gliadin IgE were positive. Extensive work-up was performed to look for an underlying cause of seizures and all returned negative.
Conclusion: To our knowledge, this is the first case report describing an unusual presentation of multiple seizures in a young infant, in association with an anaphylactic episode. In the absence of any other seizure provoking factor and underlying cause, we believe the association is more likely causative than coincidental.

P-78

Cause and clinical features of food allergy in adult Food Allergy patients: Single tertial care hospital experience

Sang Chul Lee[1], Sunyoung Kim[1], Jinyoung Choi[1], Nasil Kong[1], Kyung Hee Park[1], Jae-Hyun Lee[1], Jung-Won Park*

[1]Division of Allergy and Immunology, Department of Internal Medicine, Yonsei University College of Medicine, Seoul, [2]Institute of Allergy, Yonsei University College of Medicine, Seoul, Korea

Introduction: Food allergy is quite different in clinical features and culprit allergen between adult and children, Clinical manifestation vary from urticaria, angioedema to anaphylaxis. The aim of this study was to investigate the clinical features and culprit allergen of food allergy in Korean adult patients.
Methods: Between 2015.1.1 and 2017.4.11, 440 adult patients who suspected as having food allergy visit our Allergy-Asthma center, and finally 98 patients were diagnosed as food allergy. We diagnosed food allergy by compatible temporal relation, clinical features, and identification of IgE to suspected food allergen by ImmunoCAP or Skin prick test (SPT).
Results: In addition to classical food allergy (n=74), oral allergy syndrome (OAS, n=14), wheat dependent exercise induced anaphylaxis (WDEIA, n=4), classical anaphylaxis (n=11), and red meat allergies (n=6) were frequently diagnosed. Most frequent culprit allergens were shrimp (n=33), crab (n=21), fruit (apple, peach: n=25), wheat (n=20), peanut (n=6), pork (n=5), beef (n=4).
Conclusion: Compared with children, culprit food of food allergy in adults is very different. Shrimp, crab, wheat, fruits (apple, peach) are the important allergens in adult food allergy. Spectrum of disease is also variable, such as OAS, WDEIA, red-meat allergy, and anaphylaxis. The proportion of patients with severe systemic symptoms is higher that of children.

Key Words: Food allergy, specific IgE test, Anaphylaxis

P-79

Food allergy in school-aged children with atopic dermatitis

Sung-Yoon Kang[1], Hyeon-Ji Woo[2], Sung-Ug An[2], Gun-Woo Kim[3], Ji-Won Kwon[4], Jung-Im Na[5], Woo-Jung Song[1], Sae-Hoon Kim[2], Sang-Heon Cho[1], Yoon-Seok Chang[2]*

[1]Division of Allergy and Clinical Immunology, Department of Internal Medicine, Seoul National University College of Medicine, Seoul, [2]Department of Internal Medicine, Seoul National University Bundang Hospital, Seongnam, [3]Department of Internal Medicine, St.Carollo Hospital, Suncheon, [4]Departments of Pediatrics, Seoul National University Bundang Hospital, Seongnam, [5]Departments of Dermatology, Seoul National University Bundang Hospital, Seongnam, Korea

Background: Food allergy could be a trigger in atopic dermatitis. We aimed to investigate the prevalence and clinical manifestations of food allergy in children with atopic dermatitis from five elementary schools.
Methods: We enrolled 240 children of atopic dermatitis whose diagnoses were confirmed by ISAAC questionnaire survey and physical examination. Self-reported food allergy symptoms were surveyed with a questionnaire. Allergen-specific IgE to that food were measured in those who experienced any symptom after food ingestion. Serum total IgE was also measured. Positive allergen-specific IgE was defined as higher than 0.35 kU/L.
Results: Self-reported food allergy symptoms occurred in 35.4 % (n=85). The symptoms were pruritus (35.8%), hive or rash (32.1%), and the exacerbation of eczematous lesions (21.6 %). Among them, thirty children (35.3%) showed positive allergen-specific IgE to the possible causative foods. The most commonly sensitized food allergen was cow's milk (10.6 %), followed by walnut, peanut, wheat, and egg white. Those with positive allergen-specific IgE had higher SCORing Atopic Dermatitis index (34.0 vs. 20.6, p=0.003) and log-transformed serum total IgE levels (3.1 vs. 2.3 kU/L, p=0.001). Self-reported food allergy symptoms and positive allergen-specific IgE was associated with high levels of serum total IgE (adjusted odds ratio [aOR], 39.607; 95% confidence interval [CI], 4.645-337.690), severity of atopic dermatitis (aOR, 1.090; 95% CI, 1.004-1.184), and age (aOR, 0.570; 95% CI, 0.331-0.981).
Conclusion: Food such as cow's milk can induce various symptoms in a portion of atopic dermatitis. Food allergy symptoms with allergen-specific IgE could be associated with severe atopic dermatitis.

Key Words: Atopic dermatitis, Food allergy, Children

P-80

Drug-induced cough: Analysis of Nationwide Spontaneous Reports in Korea over ten years (2006-2015)

Gun Woo Koo, Yeonkyung Park, Ji-Hee Min, Tai Sun Park, Dong Won Park, Ji-Yong Moon, Sang-Heon Kim, Tae-Hyung Kim, Jang Won Sohn, Ho Joo Yoon*

Department of Internal Medicine, Hanyang University College of Medicine, Seoul, Korea

Purpose: Many drugs can cause cough by various mechanisms. While angiotensin-converting enzyme (ACE) inhibitors are known as the most common cause of cough, the number of cough-inducing drugs are increasing with the introduction of new drugs into the market. The study aimed to assess the causative drugs of cough and the characteristics of the subjects with drug-induced cough using nationwide spontaneous reports in Korea.
Methods: Cases of drug-induced cough were recruited from the spontaneously reported pharmacovigilance data, which has been recorded in the Korea Institute of Drug Safety & Risk Management-Korea Adverse Event Reporting System database (KIDS-KAERS database) over recent 10 years (from Jan 2006 to Dec 2015). The ingredients of drugs were classified according to Anatomical Therapeutic Chemical code (ATC code). Adverse drug reactions were defined using WHO-Adverse Reaction Terminology (WHO-ART) indicative of cough.
Results: From 856,524 cases of spontaneously reported adverse drug event cases, a total of 9,003 cases (4.5%) were identified as drug-induced cough. Most cases occurred in adults (93.4% of the subjects) and females were more common than males (54.9% vs. 45.1%). Regarding severity, only 629 cases (7.0%) were classified as serious based on WHO criteria. The most common causative drug category was antineoplastic and immunomodulating agents (24.8%), followed by cardiovascular drugs (24.2%). The most common causative drugs were ACE inhibitors including perindopril and ramipril.
Conclusions: In the nationwide spontaneous reports of adverse drug events, many cases of drug-induced cough have been reported so far. Much attention is needed to find new causative drugs of cough in the future.

Key Words: Adverse drug event, Cough, KIDS KAERS database

P-81

A Fatal Case of Allopurinol induced Drug Reaction with Eosinophilia and Systemic Symptoms combined with Cytomegalovirus Ulcer

Heesun Park, Ha Kyung Won, Sung Yoon Kang, Woo Jung Song, Heung Woo Park, Sang-Heon Cho, Hye-Ryun Kang*

Department of Internal Medicine, Seoul National University Hospital

Drug Reaction with Eosinophilia and systemic symptoms (DRESS) is one of the severe cutaneous adverse drug reaction. Allopurinol is the most frequently reported causative agent of DRESS in Korea. Reactivation of latent virus such as herpes virus 6, Epstein Bar virus, cytometalovirus (CMV) is commonly observed in DRESS but its clinical importance is still under investigation. We recently experienced severe refractory CMV ulcer in patient with allopurinol induced DRESS which resulted in mortality. Viral infection is critical factor on patient's survival, who was diagnosed as DRESS. A 89-year-old Korean male presented with generalized maculopapular eruption on trunk and extremities and fever of 39°C. He was treated with allopurinol for 6 months. Blood test showed a leukocyte count of 10,660/mm3 with 9% eosinophil and marked elevation of alanine aminotransferase (101 IU/L). He was diagnosed with DRESS related with allopurinol. HLA typing was underwent and showed HLA-A*30:31/33:03, B*13:02/58:01, Cw*03:02/06:02. Despite high dose systemic steroid (equivalent to prednisolone 1 mg/kg), his skin lesion showed multiple flare-ups and there were multiple major bleeding from gastric ulcer bleeding intractable to continuous infusion of proton pump inhibitor. CMV antigen was detected in gastric ulcer. After repeated bleeding episodes, the patient eventually succumbed to death. We report a case of DRESS with a reactivation of CMV and a development of fatal CMV gastric ulcers confirmed with as immunohistochemical stain. Gastrointestinal bleeding related with CMV ulcer can be severe and take a fatal course. Therefore, early detection of CMV reactivation and appropriate treatment with antiviral is required for the management of DRESS showing prolonged grave clinical course.

Key Words: DRESS, CMV ulcer, Allopurinol

P-82

Outcomes and Prognosis of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis based on the Korean SCAR Registry Data 2010-2015

Joo-Hee Kim[1], Sang-Min Lee[2], Gyu-Young Hur[3], Dong Yoon Kang[4], Min Gyu Kang[5], Sujeong Kim[6], Young Min Ye[7], Sae Hoon Kim[8], Hye-Kyung Park[9], Jung-Won Park[10], Hye-Ryun Kang[4]*

[1]Department of Internal Medicine, Hallym Sacred Heart Hospital, Hallym University College of Medicine, Anyang, [2]Department of Internal Medicine, Yonsei University College of Medicine, Seoul, [3]Department of Internal Medicine, Gachon University Gil Medical Center, Incheon, [4]Department of Internal Medicine, Korea University College of Medicine, Seoul, [5]Seoul National University Regional Pharmacovigilance Center, Seoul, [6]Department of Internal Medicine, Chungbuk National University Hospital, Cheongju, [7]Department of Internal Medicine, Kyungpook National University Hospital, Daegu, [8]Department of Internal Medicine, Ajou University School of Medicine, Suwon, [9]Department of Internal Medicine, Seoul National University Bundang Hospital, Seongnam, [10]Department of Internal Medicine, Pusan National University Hospital, Busan, Korea

Background: Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are a rare but fatal condition characterized by cutaneous exfoliation of the epithermal layers and mucosal surfaces. Extensive skin detachment has been associated with increased mortality.
Objective: This study aims to analyze SCORTEN and other related factors that affect mortality in patients with SJS, TEN or overlap in Korea.
Method: Data from a nationwide multicenter registry of severe cutaneous adverse reactions (SCARs) were used, which included clinical data of SCARs during the period of 2010-2015 in 35 hospitals in Korea.
Results: A total of 408 (284 SJS, 84 TEN, and 40 overlaps) cases were collected during the study period. Overall morality in this population was 8.82%; 50% in TEN, 33.3% in SJS and 16.7% in the overlap. The most common causative drug was NSAIDs (29.7%), followed by beta-lactam antibiotics (23.3%), anticonvulsant (18.4%), and allopurinol (13.5%). Age, skin detachment, heart rate and BUN on day 1, heart rate, BUN, bicarbonate on day 7, the peak creatinine, the lowest platelet count, and the peak alanine aminotransferase level did differ between survivors and non-survivors. Total score of SCORTEN was significant different between the two groups, however, of the seven individual SCORTEN parameters, only associate heart rate and serum urea level on day 1 were statistically significant on mortality using multivariate analysis. Renal dysfunction such as increased baseline serum creatinine or peak creatinine levels was associated with mortality.
Conclusion: The SCORTEN score is effective to discriminate mortality, of which heart rate and serum urea level on day 1 are significant predictors. In our study, we determine renal insufficiency and failure to be a marker for predicting a poor outcome.

Key Words: Stevens-Johnson syndrome, Toxic epidermal necrolysis, SCORTEN, Prognosis

P-83

Clinical characteristics of severe cutaneous adverse reactions by Anti- tuberculosis medication based on Korean SCAR Registry Database 2010-2015

Hyun Jung Jin[1]*, Hye-Kyung Park[2], Gyu-Young Hur[10], Jun-Gyu Lee[11], Jeong Hee Choi[12], Min-Hye Kim[13], Young-Il Koh[14], Sae Hoon Kim[3], Dong Yoon Kang[4], Hye-Ryun Kang[4], Sujeong Kim[5], Young Min Ye[6], Young Hee Nam[7], Min Seok Yang[8], Cheol-Woo Kim[9]

[1]Department of Internal Medicine, Yeungnam University Hospital, Daegu, [2]Department of Internal Medicine, Korea University College of Medicine, Seoul, [3]Department of Internal Medicine, Dongguk University Ilsan Hospital, Goyang, [4]Department of Internal Medicine, Hallym University Dongtan Sacred Heart Hospital, Hwaseing, [5]Ewha Womans University Hospital, Seoul, [6]Chonnam National University Hospital, Gwangju, [7]Department of Internal Medicine, Pusan National University Hospital, Busan, [8]Department of Internal Medicine, Seoul National University Bundang Hospital, [9]Seoul National University Regional Pharmacovigilance Center, [10]Department of Internal Medicine, Kyungpook National University Hospital, Daegu, [11]Department of Internal Medicine, Ajou University School of Medicine, Suwon, [12]Department of Internal Medicine, College of Medicine, Dong-A University, Busan, [13]Department of Internal Medicine, SMG-SNU Boramae Medical Center, Seoul, [14]Department of Internal Medicine, Inha University School of Medicine, Seoul, Korea

Background: Severe Cutaneous Adverse Reactions (SCARs) including Stevens-Johnson syndrome (SJS), Toxic Epidermal Necrolysis (TEN) and Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) by anti-tuberculosis medication have been reported. The aim of this study was to describe the clinical characteristics and outcomes of anti- tuberculosis medications-induced SCARs.
Methods: We analyzed SCAR cases to anti- tuberculosis medications between 2010-2015 using a web-based Korean SCAR Registry Database.
Results: Of the 783 patients with SCARs, 52 (6.6%) cases were reported anti- tuberculosis medication including isoniazid, rifampicin, ethambutol, pyrazinamide, para-aminosalicylic acid, cycloserine, prothionamide as major culprit drugs. There were 25 male and 27 female patients. The age group range from 21 to 86 years. The mean onset time and length of hospital stay was 35.19 ± 32.45 days and 24.77 ± 19.24 days. Six patients (11.5%) were admitted to intensive care unit (ICU). SJS/TEN cases were 11 (20.7%) and DRESS cases were 41 (79.3%). In DRESS group, the patients were younger (50.29± 17.49 years vs. 71.27±12.00 years, p =0.001) and the mean duration of latent periods was shorter (27.49±23.63 days vs. 63.91 ± 44.55 days, p =0.002). There was no difference in the duration of hospitalization, however, ICU admission rate and morality were higher in SJS/TEN group. (36.4% vs 6.1%, p =0.011, 27.3% vs 2.5%. p = 0.01, respectively).
Conclusion: Although SJS/TEN to anti-tuberculosis medication are not common, more attentions and intensive treatment are needed because of their poor prognosis.

Key Words: Drug hypersensitivity, Severe Cutaneous Adverse Reactions, Anti-tuberculosis medication

P-84

Severe cutaneous adverse reactions to antiepileptic drugs in Korea based on a nationwide registry

Chan Sun Park[1], Dongyoon Kang[2], Jae-Woo Jung[11], Young-Koo Jee[12], Jung-Won Park[13], Yeong-Min Ye[14], Su Jung Kim[15], Young-Hee Nam[16], Sae-Hoon Kim[17], Young-il Koh[18], Hye-Ryun Kang[19], Jae-Chun Lee[3], Min-Gyu Kang[4], Sang-Hoen Kim[5], Seoung Ju Park[6], Young-Eun Kwon[7], Min-Suk Yang[8], Hye-Kyung Park[9], Mi-Young Kim[10], Jeong-Hee Choi[20]*

[1]Department of Internal Medicine, Inje University Haeundae Paik Hospital, Busan, [2]Department of Internal Medicine, Inje University Pusan Paik hospital, Busan, [3]Department of Internal Medicine, Chung-Ang University College of Medicine, Seoul, [4]Department of Internal Medicine, Dankook University College of Medicine, Cheonan, [5]Department of Internal Medicine, Yonsei University College of Medicine, Seoul, [6]Department of Internal Medicine, Ajou University School of Medicine, Suwon, [7]Department of Internal Medicine, Kyungpook National University Hospital, Daegu, [8]Department of Internal Medicine, Dong-A University College of Medicine, Busan, [9]Department of Internal Medicine, Seoul National University Bundang Hospital, Seongnam, [10]Department of Internal Medicine, Chonnam National University Hospital, Gwangju, [11]Regional Pharmacovigilance Center, Department of Internal Medicine, Seoul National University Hospital, Seoul, [12]Regional Pharmacovigilance Center, Seoul National University Hospital, Seoul, [13]Department of Internal Medicine, Hallym University Dongtan Sacred Heart Hospital, Gyeonggi-do, [14]Department of Internal Medicine, Jeju National University Hospital, Jeju, [15]Department of Internal Medicine, Chungbuk National University Hospital, Cheongju, [16]Department of Internal Medicine, Hanyang University College of Medicine, Seoul, [17]Department of Internal Medicine, Chonbuk National University Medical School, Jeonju, [18]Department of Internal Medicine, Chosun University College of Medicine, Gwangju, [19]Department of Internal Medicine, SMG-SNU Boramae Medical Center, Seoul, [20]Department of Internal Medicine, Pusan National University Hospital, Busan, Korea

Background: Severe cutaneous adverse reactions(SCARs) including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug-induced hypersensitivity syndrome (DIHS)/drug reaction with eosinophilia and systemic symptoms (DRESS) to antiepileptic drugs(AEDs) are rare but have significant morbidity and mortality.
Objective: We investigated the characteristics, culprit drugs, managements and outcomes for AED-induced SCARs using a nationwide registry.
Methods: A total 166 patients with AED-induced SCARs reported from 28 hospitals were analyzed. Clinical characteristics, causative AEDs, organ involvements, treatments, and outcomes were evaluated. We compared various clinical and laboratory parameters between SJS/TEN and DRESS.
Results: Carbamazepine and lamotrigine were the most common causative AEDs for SJS/TEN (65%) and DRESS (71%), respectively. The liver was the most frequently involved internal organ in AED-DRESS. Other organ involvements including fever, lymphadenopathy, and kidney injury were also more common in AED-DRESS. Whereas, mucosal involvement was commonly seen in AED-SJS/TEN. Mortality rates of SJS/TEN and DRESS were 5.4% and 2.2%, respectively. Both intravenous immunoglobulin and glucocorticoid administrations were significantly increased in AED-SJS/TEN. There were no significant differences in disease duration, latent period, hospitalization period.
Conclusion: Carbamazepine and lamotrigine were the major causative AEDs for SCARs in Korea. Clinical features and outcomes of SCARs were similar to those reported previously. SJS/TEN and DRESS showed different clinical and laboratory findings as well as treatment options.

Key Words: Antiepileptic drugs Hypersensitivity reactions, Stevens-Johnson syndrome, Toxic epidermal necrolysis

P-85

The clinical utility of basophil activation test for the diagnosis of cefaclor induced IgE-mediate hypersensitivity

Joo-Hee Kim[1]*, Jeong-Hee Choi[2], Young-Suk Jang[1], Ji Young Park[1], Yong Il Hwang[1], Sunghoon Park[1], Seung-Hun Jang[1], Ki-Suck Jung[1]

[1]Division of Pulmonary, Allergy, and Critical Care Medicine, Department of Medicine Hallym University Medical Center, Hallym University College of Medicine, Anyang, [2]Division of Pulmonary, Allergy, and Critical Care Medicine, Department of Medicine Hallym University Dongtan Sacred Heart Hospital, Hallym University College of Medicine, Hwaseong, Korea

Background: Cefaclor is a common antibiotic to cause IgE-mediated hypersensitivity reactions. For the diagnosis of cefaclor induced drug allergy, skin test and immunoCAP assay for cefaclor have been used, however, in some cases, there are false negative results. The aim of the study is to evaluate a basophil activation test (BAT) in patients with IgE-mediate hypersensitivity due to cefaclor.
Methods: We evaluated 19 patients with confirmed IgE-mediate hypersensitivity caused by cefaclor. For validation, 9 individuals were included as controls. Those with anaphylaxis were considered allergic by clinical history, once other possible causes were ruled out, and those with positive responses by drug provocation. ImmunoCAP assay, skin test, and BAT with cefaclor were performed.
Results: The most common clinical manifestation was anaphylaxis (16/19, 84.2%), generalized urticaria (2/19, 10.5%), and angioedema (1/19, 5.2%). Skin tests showed positive results in 10 cases (52.6%) and immunoCAP assay in 11 cases (57.8%). With BAT, 14 cases were positive responses (73.6%). In patients showing negative to immunoCAP assay, skin tests were positive in four cases and BAT in six cases. For controls, skin test showed a false positive in one case and immunoCAP assay was all negative. However, BAT was positive 6 cases, showing 73.6% of sensitivity and 33.3% of specificity.
Conclusion: In this study, we found that the BAT is a less specific for confirming cefaclor induced immediate hypersensitivity. However, in cases of convincing history but negative to immunoCAP assay, the BAT could be useful and complementary to a skin test.

Key Words: Drug allergy, Basophil activation test, Cefaclor

P-86

Is Selective COX-2 inhibitor (Celecoxib) really safe? : Understanding clinical aspects and possible mechanisms of Adverse Drug Reactions (ADRs) to celecoxib

Sunyoung Kim, Kyunghee Park, Jaehyun Lee, Sang Chul Lee, Jinyoung Choi, Nasil Kong, Jungwon Park*

Division of Allergy and Immunology, Department of Internal Medicine, Yonsei University College of Medicine

Background: Background: As the prescription of selective COX-2 inhibitor is increasing in conjunction with the need for safer nonsteroidal anti-inflammatory drugs (NSAIDs), the incidence of adverse drug reactions (ADRs) to celecoxib is also growing in numbers. However, little is known about its clinical aspects.
Methods: Celecoxib-related pharmacovigilance data of Severance hospital was reviewed from January 2005 to December 2016. ADRs with causal relationship were selected. Medical records of the patients were thoroughly reviewed. Clinical manifestations, onset time of symptoms, medication history, and provocation test results were analyzed.
Results: During 12 years, 169 cases of celecoxib related ADRs were reported. The most common clinical manifestation was cutaneous (67, 76.1%) followed by systemic (13, 15.3%), pulmonary (5, 5.88%), and neurologic reactions (3, 3.53%). No serious adverse events such as anaphylactic shock happened. Among 169 cases, 59(34.9%) were due to immunologic reactions. The majority of immunologic ADRs to celecoxib did not show any cross-reactivity with other medications (35 cases, 67.3%). The next frequent manifestation was cross-reaction with other NSAIDs (16, 30.8%). On the contrary to most believed concept that celecoxib and so-called "sulfa-ring" containing drug has cross-reactivity, only 1(1.92%) had possible cross-reaction with sulfonamide-containing medication.
Conclusion: Although physicians routinely consider celecoxib as the safe alternative choice of NSAIDs, celecoxib can also cause various ADRs. Moreover, ADRs to only celecoxib and no cross-reactivity with other NSAIDs comprise the major part of the reported immunologic ADRs. Therefore, physicians should keep in mind that information and warnings of possible ADRs must be given to patients before prescribing celecoxib.

Key Words: Celecoxib, Classification, Drug allergy

P-87

Clinical Characteristics of Iodine CT radiocontrast media induced hypersensitivity in a Single University Hospital

Hee-Kyoo Kim[1]*, Gil-Soon Choi[1], Min-Hee Park[1], Ye-Jin Yu[1], Eun-Kee Park[2]

[1]Department of Internal medicine, Kosin University College of Medicine, [2]Medical Humanities and Social Medicine, Kosin University College of Medicine

Background: CT contrast media is highly concentrated iodine compounds and is commonly used in radiologic images required for enhancement of contrast enhancement. By introduction of low ionic contrast medium, the rates of radiocontrast induced adverse reaction were decreased compared to the past, but is still reported.
Aims: This study is purposed to investigate the frequency and clinical characteristics of hypersensitivity responses according to the products of iodine CT contrast media.
Methods: Total 459 cases considered as hypersensitivity response from documented immediate adverse reaction records in the Gospel Hospital CT room were collected and analyzed. Used products were Ultravist, Optiray, Iomeron, Pamiray, Xenetix, Optisure, Scanlux, Omnihexol and Vispaque.
Results: The rate of documented hypersensitivity responses from total cases was 0.4%. The mean ages were 56 years old, the ratio of females was 57%. The most common comorbid disease was malignancy(58.6%) and the portion of the CT examination site was the highest in the abdominal region with 62.1 %. According to product, Iomeron (1.1 %), Optiray (0.78 %), and Omnihexol (0.67 %). In pattern of hypersensitivity, the ratio of skin reaction was 60.1% of total, gastrointestinal 29.4%, neurologic 6.5%, respiratory 5.2%, and cardiovascular 2.6%, respectively. 41.9% of total cases were treated with medication after event. Among them, the Omnihexol group was 43.2%. As for 2 or more treated medications, the Scanlux group was highest with 24.1%.
Conclusion: There was a different in hypersensitivity rates depending on low ionic contrast medium. We need to pay attention to use radiocontrast media with highly possible hypersensitivity responses.

Key Words: Hypersensitivity, Contrast media, CT

P-88

Drug hypersensitivity reactions among Adverse Drug Events in patients visiting Emergency Department: A retrospective Observational Study in Three University Hospital

Jae-Woo Jung[1], Min-Gyu Kang[2], Ju-Yeun Lee[3], Tae-Ho Lim[4], Byoung Whui Choi[1], Chan-Woong Kim[5], Baegeum Kim[3], Ho Joo Yoon[6], Sang-Heon Kim[6]*

[1]Department of Internal Medicine, Chung-Ang University College of Medicine, Seoul, [2]Department of Internal Medicine, Chungbuk National University College of Medicine, Cheongju, [3]College of Pharmacy, Institute of Pharmaceutical Science and Technology, Hanyang University, Ansan, [4]Department of Emergency Medicine, Hanyang University College of Medicine, Seoul, [5]Department of Emergency Medicine, Chung-Ang University College of Medicine, Seoul, [6]Department of Internal Medicine, Hanyang University College of Medicine, Seoul, Korea

Background: Adverse drug events (ADE) has been recognized as an important cause of serious morbidity and mortality. Severe cases of ADE requires immediate medical treatment including Emergency Department (ED) visits. However, the study about the proportion or difference of drug hypersensitivity reactions (DHRs) among these ADEs is not well studied in Korea. We aimed to estimate the prevalence and features of DHRs leading to ED visits.
Methods: In this retrospective observational study, we reviewed all the cases of ED visits for six months, from July 2014 to December 2014, in three university hospitals in South Korea. By reviewing all the medical records including National Emergency Department Information System Database, we identified cases of ADEs and DHRs and assessed the causative drugs, severity, types and preventability.
Results: Among 29,428 patients in the emergency room, ADEs were 3,093 (3.5%) and DHRs was 343 (0.6% of total ED visits, 16.3% of ADEs). Distribution of DHRs was 47.2% for urticaria and angioedema, 36.5% for drug eruption and 11.3% for anaphylaxis. The DHRs group showed younger age (37.16 ± 21.76 vs. 53.97 ± 23.73, P <0.001) and higher proportion of female (59.5% vs. 66.5%, P = 0.016) when compared with ADEs without DHRs. In DHR groups, the duration of ED stay was shorter (365.07 ± 1114.76 minutes vs. 660.42 ± 3879.39 minutes, P = 0.008) and hospital admission rate was lower (7.6% vs. 33.2%, P = 0.001) than that in ADEs without DHRs. In DHRs cases, study for evaluation of the causative agent was done only 10 cases and DHRs recurred in 17 cases.
Conclusion: The prevalence of DHRs has a meaningful weight in ED visits with ADEs in Korea. Patients who visited the ED with DHRs were relatively less severe than the other ADR patients. However, they are likely to recur if they are re-exposed to the same drug, and clinicians need to avoid re-exposure of these patients by evaluation of the causative agents.

Key Words: Adverse drug events, Emergency Department, Drug hypersensitivity reactions

P-89

Beta-lactam antibiotic-induced severe cutaneous adverse reactions: a nationwide multicenter registry in Korea

Seoung Ju Park[1]*, Chin Ho Rhee[2], Min-Gyu Kang[3], Young-Koo Jee[4], Young-Il Koh[5], Su-Jeong Kim[6], Jung-Won Park[7], Young-Hee Nam[8], Young-Min Ye[9], Sae Hoon Kim[10], Hye-Kyung Park[11], Jae Woo Jung[12], Min Seok Yang[13], Sang Heon Kim[14], Jun-Gyu Lee[15], Cheol-Woo Kim[16], Gyu-Young Hur[17], Joo Hee Kim[18], Yong Eun Kwon[19], Mi-Yeong Kim[20], Hyen O La[21], Sang Hyun Kim[22], Myung Goo Lee[23], Min-Hye Kim[24], Chan sun Park[25], Jae Won Jeong[26], Hee-Kyoo Kim[27], Yi Yeong Jeong[28], Dong Yoon Kang[29], Hye-Ryun Kang[29], Korean Registry of Severe Cutaneous Adverse Reactions Consortium

[1]Regional Pharmacovigilance Center, Chonbuk National University Medical School, Jeonju, [2]Presbyterian Medical Center, Jeonju, [3]Chungbuk National University College of Medicine, Cheongju, [4]Dankook University College of Medicine, Cheonan, [5]Chonnam National University Medical School, Gwangju, [6]Kyungpook National University School of Medicine, Daegu, [7]Yonsei University College of Medicine, Seoul, [8]Dong-A University College of Medicine, Busan, [9]Ajou University School of Medicine, Suwon, [10]Seoul National University Bundang Hospital, Seongnam, [11]Pusan National University Hospital, Busan, [12]Chung-Ang University College of Medicine, Seoul, [13]SMG-SNU Boramae Medical Center, Seoul, [14]Hanyang University College of Medicine, Seoul, [15]Dongguk University Ilsan Hospital, Goyang, [16]Inha University School of Medicine, Seoul, [17]Korea University College of Medicine, Seoul, [18]Hallym University College of Medicine, Seoul, [19]Chosun University Hospital, Gwangju, [20]Inje University Pusan Paik Hospital, Busan, [21]Catholic University of Korea, College of Medicine, Seoul, [22]Keimyung University Dongsan Medical Center, Daegu, [23]Hallym University Chuncheon Sacred Heart Hospital, Chuncheon, [24]Ewha Womans University Hospital, Seoul, [25]Inje University Haeundae Paik Hospital, Busan, [26]Inje University Ilsan Paik Hospital, Goyang, [27]Kosin University College of Medicine, Busan, [28]Gyeongsang National University School of Medicine, Jinju, 29Seoul National University College of Medicine, Seoul

Severe cutaneous adverse reactions (SCARs) are rare but can result in a significant morbidity and mortality. Beta-lactam antibiotics, most widely used drugs to treat infectious diseases, can also cause SCARs. We investigated the clinical characteristics and outcomes of beta-lactam antibiotic-induced SCARs from the data of a nationwide multicenter registry in Korea. A total of 34 university hospitals joined the multicenter registry of SCARs and provided cases occurred from 2010 to 2015.
In total, 138 cases with beta-lactam antibiotic-induced SCARs were reported. Drug reaction with eosinophilia and systemic symptoms (DRESS) was the most frequent presentation (45.7%), followed by Stevens-Johnson syndrome (SJS) (37.0%), toxic epidermal necrolysis (TEN) (12.3%), and SJS-TEN overlap (5.1%). The mean age was 51.2 years and 78 patients (56.5%) were male. The most frequently involved beta-lactam antibiotics were cephalosporins (30.4%), followed by beta-lactam/beta-lactamase inhibitors (18.9%) and penicillins (8.9%). Among cephalosporins, the most common cause was ceftriaxone (13.0%). The mean value of skin involvement was 71.8% of body surface area and mucosal involvement occurred in 65 cases (47.1%). Average time to reaction was 10.0 days and disease duration was 24.8 days. While most cases (115 cases, 83.3%) fully recovered, 9 patients (6.5%) died of SCARs and carbapenem showed the highest mortality rate of 40.0%.
DRESS is the most frequent presentation in SCARs related with beta-lactam antibiotics and 3rd generation cephalosporins are the most common culprit drugs. Although the overall recovery rate of beta-lactam antibiotics-induced SCARs is 83.3%, 40% of carbapenem-related SCARs deceased eventually.

Key Words: Beta-lactam antibiotic, severe cutaneous adverse reactions

P-90

CD8+ T-cell activation by methazolamide causes methazolamide-induced Stevens-Johnson syndrome and toxic epidermal necrolysis

Seung-Hyun Kim[1]*, Young-Koo Jee[2], Sujeong Kim[3], Jong-Myung Lee[3], Hae-Sim Park[1]

[1]Department of Allergy & Clinical Immunology, Ajou University School of Medicine, [2]Department of Internal Medicine, Dankook University College of Medicine, [3]Department of Internal Medicine, Kyungpook National University School of Medicine

Background: Methazolamide (MZ), a carbonic anhydrase inhibitor, occasionally causes Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN). Susceptibility to MZ-induced SJS/TEN is strongly associated with HLA-B*59:01.
Objective: To characterize the T-cell response against MZ in patients with MZ-induced SJS/TEN,
Methods: We enrolled four patients with MZ-induced SJS/TEN, performed lymphocyte transformation tests, generated MZ-specific T-cell clones, and evaluated the cytotoxic activities of these clones. Subsequently, we analyzed the human leukocyte antigen (HLA)-restricted T-cell response.
Results: Strong proliferative response to MZ was evident, whereas mild proliferative response to acetazolamide was also apparent. MZ-specific T-cell clones (CD8+ T-cells) were generated from the patient. These clones proliferated and secreted granzyme B upon MZ stimulation; MZ also increased the expression level of CD107a and granzyme B. Cell proliferation and granzyme B secretion stimulated by MZ were blocked by anti-HLA class I antibodies.
Conclusions: This is the first demonstration of the immunologic mechanism by which MZ -induces SJS/TEN.

*This research was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIP) (grant number: 2015R1C1A2A01053492) and the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI) grant funded by the Ministry of Health & Welfare, Republic of Korea (grant number : HI16C0992).

Key Words: Methazolamide, Stevens-Johnson syndrome, Toxic epidermal necrolysis

P–91

Levofloxacin-induced seizure in a patient with NSAIDs anaphylaxis

Young-Hee Nam[1], Hee-Joo Nam[3], Soo-Keol Lee[1]*

[1]Department of Internal Medicine, College of Medicine, Dong-A University, Busan, [2]Dong-A University Hospital Regional Pharmacovigilance Center, [3]Department of Pharmacy, Dong-A University Hospital, Korea

Fluoroquinolones are extensively prescribed based on its safety and tolerability. Central nervous system disturbances are the second most commonly reported adverse event after gastrointestinal disorders, with an overall incidence of about 1-2%. Symptoms like headache, dizziness, insomnia and agitation usually occur on the first day of therapy and resolve after discontinuation. Even more infrequent, but of serious concern, is the occasional appearance of convulsions. Seizures related to levofloaxin have been more observed in patients taking antidepressants. It may be related to potential drug-drug interactions with inhibition of cytochrome P450 (CYP) 1A2.
A 20-year-old female was admitted to evaluate drug allergy. She had several history of urticaria and dyspnea after medication for the common cold. She had no prior psychiatric history, seizure episodes, or neurological problems. We suspected NSAIDs or antibiotics hypersensitivity, and planned to provocation test. There were no adverse reactions during oral provocation test to celecoxib, acetaminophen, clarithromycin and moxifloxacin. The last dose of levofloxacin with graded dose escalation of levofloxacin was given, she presented localized erythematous rash 3 hours later. She developed dyspnea followed by seizures consisting of approximately 30s of tonic-clonic contractions without loss of consciousness. She was fully recovered after 10 minutes with only conservative treatment. Laboratory test results were in the normal range, and neurological examination did not detect any abnormalities. Two days later, oral provocation test with aspirin was performed. The final dose of aspirin (500mg) was given one hour later, she developed facial swelling, rash, nasal congestion, hypoxemia. She was treated with epinephrine and corticosteroids.

Acknowledgement: This research was supported by a grant from Ministry of Food and Drug Safety to operation of the regional pharmacovigilance center in 2017.

Key Words: Levofloxacin; Seizure

P–92

Fatal allopurinol-induced DRESS syndrome with necrotizing pancreatitis and hemoperitoneum

Young-Hee Nam[1], Hee-Joo Nam[3], Soo-Keol Lee[1]*

[1]Department of Internal Medicine, College of Medicine, Dong-A University, Busan, [2]Dong-A University Hospital Regional Pharmacovigilance Center, [3]Department of Pharmacy, Dong-A University Hospital, Korea

Allopurinol is a xanthine oxidase inhibitor widely used in clinical practice for the treatment of hyperuricemia and gout. However, allopurinol has been reported one of the most common causative drugs of DRESS syndrome. Hepatitis and pneumonitis are the most frequent visceral manifestations. DRESS syndrome can result in multiorgan failure and, which is responsible for a high mortality rate of about 10%. Pancreatitis associated to hypersensitivity syndrome has been reported in few cases, however, most cases were fatal. The use of corticosteroids is controversial as they are effective against the immune response, but they may be detrimental when virus reactivation exceeds host's immunity. Although the role of human herpes virus-6 (HHV-6) in the physiopathology of DRESS syndrome is not fully understood, the intensity of HHV-6 replication seems to be correlated with the severity of DRESS syndrome.
A 63-year-old female presented with a diffuse erythematous rash and fever which developed 3 weeks after starting allopurinol therapy for gout. Allopurinol hypersensitivity was suspected and the drug was withdrawn. She was treated with antibiotics and conservation without systemic corticosteroids. However, she developed oliguria, pneumonia and decreased mentality, and continuous renal replacement therapy and systemic corticosteroids started. She experienced frequent cutaneous symptoms worsening during attempts at corticosteroid tapering, and cyclosporine therapy was added. She experienced frequent cutaneous symptoms worsening during attempts at corticosteroid tapering, and cyclosporine therapy was added. She continued regular hemodialysis with corticosteroids and antibiotics treatment, but he died by septic shock on day 115.

Acknowledgement: This research was supported by a grant from Ministry of Food and Drug Safety to operation of the regional pharmacovigilance center in 2017.

Key Words: Allopurinol; Drug hypersensitivity; Pancreatitis

P-93

Autoimmune thyroiditis developed after recovery from DRESS syndrome

Young-Hee Nam[1], Hee-Joo Nam[3], Soo-Keol Lee[1]*

[1]Department of Internal Medicine, College of Medicine, Dong-A University, Busan, [2]Dong-A University Hospital Regional Pharmacovigilance Center, [3]Department of Pharmacy, Dong-A University Hospital, Korea

Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is a rare and severe drug-induced hypersensitivity syndrome characterized by hematological abnormalities and multiorgan involvement. The long-term outcomes of DRESS after complete resolution of the disease are unclear, because of a lack of long-term follow-up and the potential development of sequelae after a disease-free period of several months to years. Despite the complete recovery form DRESS, autoimmune sequelae such as autoimmune thyroiditis, sclerodermoid lesions, type 1 diabetes mellitus, and lupus erythematosus has been reported. The development of autoimmune diseases, along with the presence of autoantibodies, were observed in the noncorticosteroid treatment group in DRESS.
A 62-year-old female with hypertension and diabetes mellitus developed diffuse erythematous rash and fever after administration of isotretinoin and dapsone for 4 weeks due to rosacea. Peripheral blood examination revealed leukocytosis and atypical lymphocyte without eosinophilia. Elevation of liver enzymes and mild proteinuria were observed. She was diagnosed with DRESS syndrome. She was treated with systemic corticosteroid. However, her cutaneous symptoms were deteriorated, and cyclosporine therapy was added. She improved gradually and corticosteroid and cyclosporine were tapered slowly over 4 months. One week later, she complained of weakness, decreased oral intake and weight loss. There was no evidence of adrenal insufficiency. She developed autoimmune hyperthyroidism (Hashimoto thyroiditis) with markedly elevated thyroid peroxidase antibody titers in the thyrotoxic phase, and was treated with propranolol for 2 weeks. Five months after drug exposure, the patient had not developed signs or symptoms of autoimmune thyroiditis and completely recovered from DRESS.

Acknowledgement: This research was supported by a grant from Ministry of Food and Drug Safety to operation of the regional pharmacovigilance center in 2017.

Key Words: Autoimmune; Drug hypersensitivity; Thyroiditis

P-94

Evaluation of drug-induced liver injury based on EHR in a single hospital

Yewon Kang[1], Bomi Seo[1], Bo Young Park[2], So-Young Park[1], Oh Young Kwon[1], Hyouk-Soo Kwon[1], You Sook Cho[1], Hee-Bom Moon[1], Tae-Bum Kim[1]*

[1]Department of Allergy and Clinical Immunology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, [2]Pharmacovigilance center, Asan Medical Center, Seoul, Korea

Background: Drug-induced liver injury (DILI) has been increasing. However, there are few algorhythms to accurately find it through EHR (Electronic Healthcare Record), and it is difficult to investigate the exact incidence and characteristics of DILI. We aimed to identify and evaluate DILI with an appropriate screening protocol.
Materials and Methods: Between June 2015 to May 2016, the data were collected from ABLE (Asan Biomedical Research Environment), EHR-based large data retrieval program at Asan Medical Center. Among patients with ALT $\leq$120 IU/L and total bilirubin less than 2.4 mg/dL in the blood test within 48 hours of admission and no other illness related to liver disease at discharge, we retrospectively reviewed the EHR to evaluate the incidence of DILI, and estimate the causative drugs. We developed our own in-house criteria for defining DILI.
Result: Approximately one-third of the screened patients were identified as DILI. It was more common in male and the 60s, and most were hepatocellular type liver injury. The common causes were piperacillin-tazobactam, methotrexate and total parenteral nutrition. Overall, antibiotics were the most common, followed by chemotherapy agent. Patients excluded from DILI were often associated with ischemic liver injury due to septic shock, heart failure and postoperative status as well as graft versus host disease after hematopoietic stem cell transplantation.
Conclusion: Antibiotics are the most common culprit drugs for DILI. Modified criteria for detection of DILI should be developed to evaluate DILI more accurately based on EHR in the hospitals.

*This research was supported by a grant from Korea Institute of Drug Safety and Risk Management in 2016.

Key Words: Drug-induced liver injury, EHR (Electronic Healthcare Record)

P-95

Immune-mediated thrombocytopenia induced by ciprofloxacin; no cross-reactivity with gemifloxacin

Da Woon Sim, Jiung Jeong, Ji Eun Yu, Young-Il Koh*

Division of Allergy, Asthma and Clinical Immunology, Department of Internal Medicine, Chonnam National University Medical School, Gwangju, Korea

Drug-induced immune-mediated thrombocytopenia (DITP) is mediated by antibody-mediated platelet destruction. Although a few cases of fluoroquinolones-induced DITP have been published, there is no reports on cross-reactivity between the different fluoroquinolones. Here, we describe a case of ciprofloxacin-induced DITP of showing no cross-reactivity with gemifloxacin.
A 77-year-old woman was admitted for pneumonia. Bronchoalveolar lavage examination revealed quinolone-susceptible Pseudomonas aeruginosa. After two doses of ciprofloxacin, her blood platelets were decreased rapidly. However, the ciprofloxacin treatments had been continued. After 4-day treatments with ciprofloxacin, the pneumonia improved but the platelet counts remained to be very lower. The administration of ciprofloxacin was stopped due to a possibility of ciprofloxacin-associated thrombocytopenia. Shortly after the discontinuation, the platelets were increased to normal ranges. Later, she received again other fluoroquinolones, gemifloxacin. At those times, no thrombocytopenia was detected. Being reviewed retrospectively, she had a past history of thrombocytopenia following the use of ciprofloxacin at local hospital. Taken together, she assumed to have ciprofloxacin-induced DITP and did not react to gemifloxacin, which may suggest no cross-reactivity between ciprofloxacin and gemifloxacin in terms of DITP.

Key Words: Drug-induced immune-mediated thrombocytopenia, Ciprofloxacin, Gemifloxacin

P-96

Associations between genetic variants of costimulatory molecules and antituberculosis drugs-induced maculopapular eruption

Sang-Heon Kim[1,2], Ji-Yong Moon[1], Jang Won Sohn[1], Ho Joo Yoon[1], Young-Koo Jee[3]*

[1]Department of Internal Medicine, Hanyang University College of Medicine, Seoul, [2]Department of Internal Medicine, Eulji University School of Medicine, Seoul, [3]Department of Internal Medicine, Dankook University College of Medicine, Cheonan, Korea

Maculopapular eruption (MPE) induced by antituberculosis drugs (ATD) is the most frequent adverse reactions requiring the discontinuation of the scheduled treatment. Genetic susceptibility to ATD-induced MPE is not well determined yet, although CYP2C19 and CYP2C9 genetic polymorphisms were reported to be significantly associated with the risk of developing ATD-induced MPE. Since costimulatory molecules play crucial roles in the activation of lymphocytes, we examined if the polymorphisms in costimulatory molecules (CD28, CTLA-4, CD40 and CD40L) are associated with ATD-induced MPE. We enrolled 72 patients with ATD-induced MPE and 238 ATD-tolerant subjects who were treated with the first line ATDs including isoniazid, rifampicin, ethambutol and pyrazinamide. After enrollment, DNA was isolated from whole blood of the subjects and genotyped for the single nucleotide polymorphisms (SNPs) in CD28, CTLA4, CD40 and CD40LG. Genotype frequencies of SNPs and haplotypes were compared between patients with ATD-induced MPE and ATD-tolerant patients. In the comparisons of genotype frequencies of SNPs of CD28 (rs3116496), CTLA4 (rs5742909, rs231775, rs3087243, rs17268364), CD40 (rs1800686, rs1883832) and CD40LG (rs3092952), there was no significant difference between the patients with ATD-induced asthma and ATD-tolerant controls. Next, the haplotypes frequencies of CTLA4 and CD40LG genes were not different between case and control groups. Genetic polymorphisms of costimulatory molecules (CD28, CTLA-4, CD40 and CD40L) were not associated with ATD-induced MPE. These findings suggest that genetic variations of costimulatory molecules do not confer susceptibility to ATD-induced MPE.

Key Words: Costimulatory molecules, Maculopapular eruption, Antituberculosis drugs

P-97

Proper Cutoff Levels of Serum Specific IgE to Cefaclor for Patients with Cefaclor Allergy

Young-Hee Nam[1], So-Hee Lee[2], Chang-Gyu Jung[2], Ji-Ho Lee[2], Ga-Young Ban[2], Yoo-Seob Shin[2], Soo-Keol Lee[1], Hae-Sim Park[2], Young-Min Ye[2]*

[1]Department of Internal Medicine, College of Medicine, Dong-A University, Busan, [2]Department of Allergy and Clinical Immunology, Ajou University School of Medicine, Suwon, Korea

Background: Cefaclor, a second-generation oral cephalosporin has been known to cause IgE-mediated hypersensitivity, particularly anaphylaxis is most commonly reported. Assays of serum specific IgE (sIgE) to cefaclor are commercially available using CAP system. Serum levels of sIgE >0.35 kU/L were considered positive, whereas some patients with cefaclor allergy had low serum IgE.
Objective: To evaluate the proper cutoff levels of sIgE in the diagnosis of immediate hypersensitivity to cefaclor.
Methods: A total of 269 patients with drug allergy history who performed sIgE to cefaclor assay were collected retrospectively at Ajou University hospital and Dong-A University Hospital. One hundred ninety-three patients were cefaclor-induced immediate hypersensitivity with certain or probable of adverse drug reaction causality according to WHO-UMC algorithm, and 76 controls were delayed hypersensitivity reactions to non-antibiotics.
Results: One hundred twenty-six (65.3%) were anaphylaxis, they had higher serum IgE levels than patients with immediate hypersensitivity except anaphylaxis (6.36±12.39 kU/L vs 3.35±11.58 kU/L, P<0.001). The best cutoff values for cefaclor-induced immediate hypersensitivity was 0.105 kU/L with sensitivity 80.2% and specificity 81.6%. The cutoff value of 0.44 kU/L in differentiating anaphylaxis from immediate hypersensitivity showed the best sensitivity (75.4%) and specificity (65.7%).
Conclusion: Patients with cefaclor anaphylaxis had high serum IgE levels, and a cutoff value of sIgE of 0.105kU/l is proper for identifying patients with cefaclor allergy and 0.44 kU/L may be useful to diagnose anaphylaxis.

Key Words: Anaphylaxis; Cefaclor; Drug hypersensitivity; Specific IgE

P-98

An optimal prophylactic strategy to prevent the recurrence of iodinated contrast media hypersensitivity: a retrospective cohort study of patients experiencing mild immediate reaction

Hye-Ryun Kang[1]*, Sae-Jin Park[2], Dong-Yoon Kang[3], Kyoung-Hee Sohn[4], Soon-Ho Yoon[2], Whal Lee[2], Young-Hoon Choi[2], Sang Heon Cho[3]

[1]Department of Internal Medicine, Seoul National University College of Medicine, [2]Department of Radiology, Seoul National University College of Medicine, Seoul, [3]Drug Safety Monitoring Center, Seoul National University Hospital, Seoul, [4]Institute ofAllergy and Clinical Immunology, Seoul National University Medical Research Center, Seoul, [5]Department of Internal Medicine, Seoul National University Hospital, Seoul, Korea

Background: Purpose: Although premedication with antihistamine and multi-dose corticosteroid has been recommended for the prevention of hypersensitivity reactions (HSR) to iodinated contrast media (ICM) in high-risk patients, an optimal strategy for those who experienced mild HSR has not been established.
Materials and Methods: The outcomes of a cohort of high-risk patients with mild HSR to ICM who subsequently underwent enhanced computed tomography (CT) between 2008 and 2015 were analyzed using the database of an institutional real-time monitoring system. Approval of the Institutional Review Board and an informed consent waiver were obtained. Student's t-test and logistic regression analysis were used to compare the groups.
Results: A total of 1,241 patients with mild immediate HSR were re-exposed to ICM 3,896 times. When re-exposed to the culprit ICM without premedication, the recurrence rate was 31.1%; most recurrent cases were mild; only 1.2% was moderate in severity. While antihistamine premedication lowered the recurrence rate to 24.7% ($p < 0.001$), steroid premedication did not convey any additional protective effect compared to antihistamine premedication. Re-administration of the culprit ICM is a major risk factor for the recurrence of HSR to ICM; the recurrence rate decreased to 12% by changing the culprit ICM (odds ratio 0.303; 95% confidence interval 0.218 - 0.420; $p < 0.001$). When a change in ICM was combined with antihistamine premedication, the recurrence rate decreased to 7.6%.
Conclusions: Changing the culprit ICM and antihistamine premedication could be an optimal preventive strategy in patients with mild HSR to ICM.

Key Words: Contrast media, Hypersensitivity, Mild immediate reaction, Prevention

P–99

Clinical application of HLA typing for the prediction of carbamazepine hypersensitivity reactions in Koreans: A retrospective exploratory study

Young-Chan Kim[1], Ha Kyung Won[1], Sung Yoon Kang[1], Woo Jung Song[1], Heung Woo Park[1], Sang-Heon Cho[1], Hye-Ryun Kang[1]*

[1]Department of Internal Medicine, Seoul National University College of Medicine, [2]Institute of Allergy and Clinical Immunology, Seoul National University Medical Research Center, Seoul National University College of Medicine, [3]Seoul National University Regional Pharmacovigilance Center

Background: Hypersensitivity reaction is common adverse reaction of carbamazepine, from mild maculopapular rash to severe cutaneous adverse reaction (SCAR) such as Stevens-Johnson syndrome, toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms. Previous reports presented ethnically different association of a couple of HLA types with carbamazepine-related SCARs. However, the usefulness of HLA screening was proved only in Han Chinese population.
Methods: We assessed incidence and the risk for the development of hypersensitivity reaction among patients taking carbamazepine or oxcarbazepine according to HLA types in Koreans. For subjects who underwent HLA typing and were ever prescribed with carbamazepine at Seoul National University Hospital from 2000. Jan to 2017. Apr, a history of hypersensitivity reaction related with use of carbamazepine was retrospectively reviewed.
Results: A total of 187 subjects were studied for the incidence of hypersensitivity reactions and the frequency of hypersensitivity reactions was 2.14% (4/187) but no SCARs occurred. All four hypersensitivity reactions reported maculopapular eruption and one of them had fever. HLA types did not show any significant association with carbamazepine-related hypersensitivity reaction. Among subject with serotype B75 (n=2) comprised of B*15:02 and B*15:11 in Koreans, no one had hypersensitivity reaction to carbamazepine. A31 (5.88%) showed marginal association with carbamazepine-related hypersensitivity reactions (p-value = 0.06) but its positive predictive value was only 5.56%. B51 (6.90%) and B44 (6.45%) serotypes showed relatively higher incidence of carbamazepine hypersensitivity but statistical significance was not observed.
Conclusion: Our study suggests that A31 is a potential serotype as a marker of carbamazepine-related hypersensitivity reactions in Korean population but its routine screening seems not to be reasonable considering its low positive predictive value.

Key Words: Drug hypersensitivity; HLA Antigens; carbamazepine

P–100

Outcomes of a New Desensitization Protocol without Dilution for Chemotherapy-related Infusion Reactions

Young-Chan Kim[1], Ha Kyung Won[1], Sung Yoon Kang[1], Woo Jung Song[1], Tae Min Kim[1], Heung Woo Park[1], Sang-Heon Cho[1], Hye-Ryun Kang[1]*

[1]Department of Internal Medicine, Seoul National University College of Medicine, [2]Institute of Allergy and Clinical Immunology, Seoul National University Medical Research Center, Seoul National University College of Medicine, [3]Seoul National University Regional Pharmacovigilance Center

Background: Taxanes and rituximab are known to frequently cause infusion reactions. To reduce infusion reactions, several desensitization protocols have been used with some success but most of them need multiple dilution steps. Here we present outcomes of a new 1-bag desensitization protocol without dilution for the patients with infusion reactions to taxane or rituximab.
Methods: We performed an observational study with 22 patients who experienced infusion reactions to taxane or rituximab and underwent a new 1-bag desensitization protocol for their re-exposure to culprit drugs at Seoul National University Hospital from 2015. Nov - 2017. Apr. The occurrence and severity of breakthrough reaction (BTR) during the desensitization were evaluated.
Results: A total of 22 subjects (paclitaxel = 9, docetaxel = 6, rituximab = 7) were included and 85 cases of desensitization were performed (paclitaxel = 40, docetaxel = 13, rituximab = 32). Except for two cases of docetaxel desensitization interrupted due to the shelf life, all 83 cases (100%) completed by the last step. Among 85 desensitization cases, BTR occurred in 20 cases (23.5%). The frequency of hypersensitivity reactions of each drug was 20% for paclitaxel, 53.8% for docetaxel, and 12.5% for rituximab, respectively. However, grade 3 BTR was only 5% including one anaphylactic reaction requiring epinephrine injection and desensitization was resumed in all of those cases. Among cases with BTRs, 55% occurred at the later steps (10th or after) during desensitization. All BTRs occurred during the first three desensitization cycles.
Conclusion: The new 1-bag desensitization protocol is safe and useful for preventing infusion reactions related with taxanes and rituximab.

Key Words: Drug hypersensitivity; Desensitization, immunologic; Drug-Related Side Effects and Adverse Reactions

P-101

Incidence and Risk of Oxaliplatin-induced Hypersensitivity in Patients with Asymptomatic Remote Exposure: A Prospective Observational Study in Korea

Kyoung-Hee Sohn[1], Dong Yoon Kang[3], Ju-Young Kim[4], Suh Young Lee[5], Kyung Hun Lee[6], Sae Won Han[6], Hye-Ryun Kang[1]*

[1]Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Korea, [2]Institute of Allergy and Clinical Immunology, Seoul National University Medical Research Center, Seoul National University College of Medicine, Seoul, Korea, [3]Institute of Allergy and Clinical Immunology, Seoul National University Medical Research Center, Seoul National University College of Medicine, Seoul, Korea, [4]Department of Internal Medicine, Gyeongsang National University College of Medicine, Jinju-si, Korea, [5]Division of Pulmonary, Allergy and Critical Care Medicine, Kangdong Sacred Heart Hospital, Seoul, Korea, [6]Cancer Research Institute, Seoul National University, Seoul, Korea

Background: Oxaliplatin-related hypersensitivity reactions (HSR) raise a dilemma on the use of chemotherapy agent due to the concern of severe life-threatening reactions. As repeated exposures increase the risk of sensitization, risk-stratified care is needed in patients with a history of remote asymptomatic exposure. The aim of this study was to elucidate the incidence and risk of the development of oxaliplatin HSR in patients with a history of asymptomatic remote exposure.
Methods: We performed a prospective observational study on patients who completed oxaliplatin-based chemotherapy between March 2013 and January 2015. Prior exposure to oxaliplatin, oxaliplatin free-interval, the severity, eosinophil counts, and premedication were reviewed in order to assess the risk factors.
Results: A total of 793 patients were enrolled and 148 patients (18.7%) experienced HSR. Incidence of HSR was 15.2% in oxaliplatin naïve patients while it rose to 30.4% in those with a history of asymptomatic exposure and 75.0% in those with a history of oxaliplatin HSR in the previous exposure despite preventive prophylaxis (P for trend$<$ 0.001). The median onset cycle of HSR was earliest in the previous HSR group followed by previous exposure group and non-exposure group (2.18 $\pm$ 2.72, 2.71 $\pm$ 1.90, 4.72 $\pm$ 2.73 cycle, respectively, P $<$ 0.001). The severity of HSR were also different according to the history of previous exposure and HSR (CTCAE grade 1.7 $\pm$ 0.1, 2.2 $\pm$ 0.1, 2.9 $\pm$ 0.7, P $<$ 0.001). In multivariate analysis, prior exposure to oxaliplatin (Hazard ratio (HR), 3.78; 95% Confidence interval (CI), 2.46-5.17), longer oxaliplatin-free interval ($\geq$36 months; HR, 4.85; 95% CI, 1.60- 14.37) are independent risk factors for the development of HSR.
Conclusions: Previous exposure to oxaliplatin is a risk factor of earlier onset, more severe and frequent HSR even if it was tolerated without symptoms.

Key Words: Oxaliplatin, Drug hypersensitivity, Prospective studies

P-102

Outcomes of re-exposure to iodinated contrast media in patients with moderate to severe iodinated contrast media hypersensitivity reactions

Dong Yoon Kang[1], Se-Jin Park[2], Ji Young koh[1], Young Hoon Choi[2], Whal Lee[2], Sang-Heon Cho[3], Hye-Ryun Kang[3]*

[1]Drug Safety Monitoring Center, Seoul National University Hospital, Seoul, Korea, [2]Department of Radiology, Seoul National University College of Medicine, Seoul, Korea, [3]Department of Internal Medicine, Seoul National University Hospital, Seoul, Korea

Background: Although pre-medication has been widely used to prevent recurrence of iodinated contrast media (ICM) hypersensitivity reactions (HSR) in high-risk patients, preventive effect and optimal combination of ICM changes for those who ever experience moderate to severe ICM HSR has not been established.
Methods: We retrospectively reviewed the history of ICM HSR in all patients who underwent computed tomography scan from October 2012 to April 2017. Each use of ICM from the first occurrence to the recent was investigated in patients with moderate to severe HSR history. The kind of ICM, type of pre-medication, occurrence and type of HSR, symptoms, treatment, prognosis, and combination of ICM change were evaluated.
Results: A total of 537 patients with a history of moderate to severe HSR to ICM were identified during the study period. Of these, 266 (49.5%) patients were re-exposed to ICM after HSR. There were 940 cases of ICM re-exposure, 90% of them were asymptomatic or had mild HSR while 7.4% had moderate, and 2.6% had severe recurrence of HSR. Depending on the preventive method, HSR recurred in 43.0% of patients who received premedication without ICM change, 18.1% of the patients who changed ICM without premedication, and 14.3% of the patients who had premedication with ICM change. There was a difference in recurrence rate according to the combination of changing ICM after HSR. Among the various combinations of ICM changes, the combination of iohexol-iopamidol and iopromide-iomeprol showed a significantly higher recurrence rate of 27.0% and 23.1% compared to the mean outcomes of ICM change.
Conclusion: The incidence of recurrence was 10% in patients with a history of moderate to severe ICM HSR. In order to prevent recurrence of HSR, changing ICM is important as well as appropriate pre-medication.

Key Words: contrast media, hypersensitvity, recurrence prevention

P-103

Incidence of teicoplanin hypersensitivity in patients with vancomycin adverse drug reaction

Byung-Keun Kim[1], Ga-Young Oh[2], Kyounghee Sohn[3], Sung-Yoon Kang[3], Min-Suk Yang[5], Woo-Jung Song[3], Hye-Ryun Kang[3], Heung-Woo Park[3], Yoon-Seok Chang[2], Sang-Heon Cho[3], Sae-Hoon Kim[2]*

[1]Department of Internal Medicine, Korea University Medical Center Anam Hospital, [2]Department of Internal Medicine, Seoul National University Bundang Hospital, [3]Department of Internal Medicine, Seoul National University College of Medicine, [4]Institute of Allergy and Clinical Immunology, Seoul National University Medical Research Center, [5]Department of Internal Medicine, Boramae Medical Center, Seoul National University College of Medicine

Background: Vancomycin has a reliable antibacterial activity and is recommended as the first-line treatment for infections caused by MRSA, MRCNS, ampicillin-resistant Enterococcus. However, it may elicit various adverse drug reactions (ADRs) including hypersensitivity reactions. Teicoplanin is an glycopeptide antibiotic which can be used as an alternative in case of vancomycin ADR. However, there is not enough data regarding the incidence of teicoplanin hypersensitivity in patients with vancomycin ADR.
Method: We analyzed the incidence of teicoplanin hypersensitivity retrospectively with electric medical record. All patients who were administered teicoplanin between January 2006 and December 2015 at Seoul National University Bundang Hospital were included.
Results: A total of 304 patients were enrolled. Mean duration of teicoplanin use is 12.2 days and mean daily dose was 372.6mg. Fifty-eight (19.1%) patients experienced hypersensitivity reaction after teicoplanin use. The duration of teicoplanin use and history of drug allergy were risk factors of teicoplanin hypersensitivity ($p=0.031$, $p=0.015$, respectively). Among them, 238 (78.3%) patients experienced vancomycin ADR before teicoplanin use and their incidence of teicoplanin hypersensitivity was 23.1%. Among patients with vancomycin hypersensitivity (except acute kidney injury) incidence of teicoplanin hypersensitivity was 25.5% and it was significantly higher than that of patients without vancomycin hypersensitivity (5.2%) ($p<0.001$). Classified with type of vancomycin ADRs, previous experience of skin reaction, drug fever and neutropenia after vancomycin use were significantly associated with incidence of teicoplanin hypersensitivity reaction.
Conclusion: This is the largest study regarding the incidence of teicoplanin hypersensitivity reaction in patients with vancomycin ADR. In case of vancomycin ADR, teicoplanin administration should be used with caution and clinicians must consider the risk of cross-reactivity

Key Words: Vancomycin, Teicoplanin, Adverse drug reaction, Hypersensitivity

P-104

Validation of the prescreening intradermal skin test for predicting hypersensitivity of Iodinated Contrast Media : a prospective study with contrast media challenge

Oh Young Kwon, Bomi Seo, So-Young Park, Hyouk-Soo Kwon, You Sook Cho, Hee-Bom Moon, Tae-Bum Kim*

Department of Allergy and Clinical Immunology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

Background: Recently, as the use of iodine-based radiocontrast media (RCM) increases, related hypersensitivity is rapid growing. These hypersensitivity reactions are unpredictable and often lead to severe reactions such as anaphylaxis. This study was performed to investigate the clinical value of prescreening iodinated contrast media (ICM) skin testing for predict hypersensitivity reactions.
Methods: We recruited patients who scheduled enhanced Computed tomography (CT) at the Asan medical hospital from September 2015 to April 2017 ($n=1194$). Then we prospectively conducted intradermal skin test (IDT) with one to seven kinds of ICM; iopromide, iohexol, iopamidol, ioversol, iobitridol, iomeprol, and iodixanol. After the skin test of the ICM, whatever the results, CT exam was performed with the scheduled ICM.
Results: As a result of skin test, total 8 patients (8/1194, 0.6%) were positive to iohexol ($n=7$) and iopamidol ($n=1$) which are scheduled to be administered for CT. However, none of them had hypersensitivity reactions after administration of the ICM, even though positive in the skin test. Only 5 patients who underwent CT showed hypersensitivity reaction, all of them showed the negative results of skin test. As a result, the IDT for ICM had a sensitivity of 0%, a specificity of 99.3%, a negative predictive value (NPV) of 99.6%, and a positive predictive value (PPV) of 0%.
Conclusion: Routine skin testing with ICM before CT examination is not useful for predicting hypersensitivity reactions because of low sensitivity and low PPV.

Key Words: Contrast media; intradermal tests; predictive value

P-105

Differences in clinical features according to the causative drugs in patients with DRESS syndrome

Da Woon Sim[1], Jiung Jeong[1], Min Seok Yang[9], Young-Koo Jee[10], Min Gyu Kang[11], Sang Heon Kim[12], Cheol-Woo Kim[13], Mi-Yeong Kim[14], Joo Hee Kim[15], Gyu-Young Hur[16], Jaechun Lee[17], Jun-Gyu Lee[18], Ji Eun Yu[1], Sang Hyun Kim[19], Hyen O La[20], Hyun Jung Jin[21], Jeong Hee Choi[22], Seong Ju Park[23], Hee-Kyoo Kim[24], Yong Eun Kwon[25], Hye-Ryun Kang[26], Dong Yoon Kang[26], Chan Sun Park[27], Jae Woo Jung[2], Suh-Young Lee[28], Sujeong Kim[3], Young Min Ye[4], Sae Hoon Kim[5], Hye-Kyung Park[6], Jung-Won Park[7], Young Hee Nam[8], Young-Il Koh[1]*

[1]Division of Allergy, Asthma and Clinical Immunology, Department of Internal Medicine, Chonnam National University Medical School, Gwangju, [2]Department of Internal Medicine, Dankook University College of Medicine, Cheonan, [3]Department of Internal Medicine, Chungbuk National University Hospital, Cheongju, [4]Department of Internal Medicine, Hanyang University College of Medicine, Seoul, [5]Department of Internal Medicine, Inha University School of Medicine, Seoul, [6]Department of Internal Medicine, Inje University Pusan Paik Hospital, [7]Department of Medicine, Hallym University Sacred Heart Hospital, Anyang, [8]Department of Internal Medicine, Korea University College of Medicine, Seoul, [9]Department of Internal Medicine, Jeju National University Hospital, Jeju, [10]Department of Internal Medicine, Dongguk University Ilsan Hospital, Goyang, [11]Department of Internal Medicine, Keimyung University Dongsan Medical Center, Daegu, [12]Department of Internal Medicine, Chung-Ang University College of Medicine, Seoul, [13]Department of Pharmacology, Catholic University of Korea, College of Medicine, Seoul, [14]Department of Internal Medicine, Yeungnam University College of Medicine, Daegu, [15]Department of Internal Medicine, Hallym University Dongtan Sacred Heart Hospital, Hwaseing, [16]Department of Internal Medicine, Chonbuk National University Hospital, Jeonju, [17]Department of Internal Medicine, Kosin University College of Medicine, Busan, [18]Department of Internal Medicine, Chosun University Hospital, kwang-ju, [19]Seoul National University Regional Pharmacovigilance Center, Seoul, [20]Department of Internal Medicine, Haeundae Paik Hospital, Inje University, Pusan, [21]Department of Internal Medicine, Hallym University Sacred Heart Hospital, Seoul, [22]Korean Severe Cutaneous Adverse Reactions Consortium, [23]Department of Internal Medicine, Kyungpook National University Hospital, Daegu, [24]Department of Internal Medicine, Ajou University School of Medicine, Suwon, [25]Department of Internal Medicine, Seoul National University Bundang Hospital, Seongnam, [26]Department of Internal Medicine, Pusan National University Hospital, Busan, [27]Department of Internal Medicine, Yonsei University College of Medicine, Seoul, [28]Department of Internal Medicine, College of Medicine, Dong-A University, Busan, [29]Department of Internal Medicine, SMG-SNU Boramae Medical Center, Seoul

Backgrounds: Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome is characterized by serious involvements of various systemic organs and long-term treatments caused by various drugs. It is important to recognize the diverse clinical manifestations according to the culprit drugs in order to provide appropriate clinical management. Here, we analyzed the clinical feature in patients with DRESS syndrome according to the causative drugs.
Methods: Data on 375 patients with symptoms pertaining to DRESS syndrome reported in the Korea Severe Cutaneous Adverse Reactions registry during January 2009 to May 2016 were obtained. To improve the accuracy of our analysis, 160 patients with DRESS syndrome above a certain RegiSCAR degree (probable, definite) were recruited. Culprit drugs were categorized into allopurinol, carbamazepine, anti-tuberculosis drugs, vancomycin, cephalosporins, dapsone, and nonsteroidal anti-inflammatory drugs (NSAIDs).
Results: Significant differences among various drugs were observed with regard to hepatitis ($p = 0.007$), renal dysfunction ($p < 0.001$), lymphadenopathy ($p = 0.005$), and atypical lymphocytosis ($p = 0.004$). Allopurinol induced both hepatic and renal impairments. Carbamazepine and dapsone were associated with hepatitis and atypical lymphocytosis. Anti-tuberculosis drugs and cephalosporins caused mostly hepatic dysfunction. Vancomycin involved more frequently kidney than liver. NSAIDs revealed all the abnormalities evenly. Following further analyses, DRESS syndrome caused by cephalosporin, NSAIDs and vancomycin showed shorter latent period than DRESS syndrome caused by other drugs. In addition, DRESS syndrome caused by anti-tuberculosis drugs and vancomycin revealed longer treatment duration than DRESS syndrome caused by other drugs.
Conclusions: Clinical manifestations and outcomes may differ according to the culprit drugs, which may provide useful information to assess causality and treat the patients with DRESS syndrome

Key Words: DRESS syndrome, difference, causative drugs

P-106

Incidences and risk factors of adverse drug reactions of gadolinium-based contrast media

Kyung Hee Park, Sunyoung Kim, Sang Chul Lee, Jinyoung Choi, Nasil Kong, Jae-Hyun Lee, Jung-Won Park*

Division of Allergy and Immunology, Department of Internal Medicine, Yonsei University College of Medicine

Introduction: As the use of Gadolinium-based contrast media (GBCM) increases, the adverse drug reactions (ADRs) are also increasing. However, the clinical manifestations and risk factors of GBCM related ADR are still not fully-understood.
Objectives: To compare the incidence rates of ADR by type of GBCM agents and reveal the risk factors of GBCM ADRs. Methods: GBCM-related pharmacovigilance data from 2007 to 2015 were reviewed. ADRs with causal relationships were selected, and clinical manifestations, outcomes, and drug-related information were assessed.
Results: During 9 years, total of 276,799 GBCM injections were performed at Severance hospital. Among them, 357 patients experienced GBCM releated ADRs. The ADR incidence among the GBCMs was the lowest with gadodiamide (6.16%) and gadobutrol had the highest rate (42.58%) ($p < 0.001$). The clinical manifestations of ADR were as follows: cutaneous (72.5%), gastro-enteric (27.4%), cardiologic (3.08%), respiratory (2.24%), neurologic (3.64%). Among 357 patients, 101 patients (30.81%) were re-exposed to any kinds of GBCM. The incidence of ADR in these patients with repeated exposure was significantly higher compared to first exposure (5.45%, $p < 0.001$). To analyze the risk factors of GBCM induced ADRs, we compared with age-matched 357 patients as control group. The rate of ADR was significantly higher in patients with malignancies ($p < 0.001$) and in patients who had previous allergic reaction to iodine contrast media for computed tomography (CT) ($p < 0.001$).
Conclusions: The ADR incidences among GBCMs differed significantly ($p < 0.001$) as follows, gadopentetic acid, gadoteric acid, gadodoamide, gadobutrol, and gadoxetic acid. There was no significant difference in clinical presentations of ADR among compared GBCMs. Patients with re-exposure who were previously allergic to GBCMs, patients with malignancies and previous allergic reaction to iodine contrast media for CT had higher risk of ADR.

Key Words: gadolinium contrast media, adverse drug reactions

P-107

Comparison of Hypersensitivity Reaction Rate According to The Type of Radiocontrast Media

Hye Jung Park[1]*, Chul Hwan Park[2], Hye Sun Lee[3], Sinae Kim[3], Sung Ryeol Kim[4], Jung-Won Park[4]

[1]Department of Internal Medicine, Yong-in Severance Hospital, Severance Hospital, Yonsei University College of Medicine, Gyeonggido, Korea, [2]Departmet of Radiology, Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Korea, [3]Biostatistics Collaboration Unit, Yonsei University College of Medicine, Seoul, Korea, [4]Division of Allergy and Immunology, Department of Internal Medicine, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea

Purpose: Various types of radiocontrast media (RCM), which can be substituted for each other, are used in clinical settings. However, data on comparisons of hypersensitivity reactions (HSR) based on types of RCM are lacking. Therefore, we aimed to compare adverse drug reaction (ADR) rates to facilitate the choice of appropriate RCM types in clinics.
Methods: From January 2011 to December 2015, we retrospectively reviewed 209,027 clinical events involving seven different RCM in Gangnam Severance Hospital. We analyzed HSR events using an internally developed ADR reporting system. Furthermore, we defined risk factors for HSR, including RCM type.
Results: During the 5-year study period, 209,027 RCM usage occurred in 97,374 patients. During that period, 108 HSR happened in 88 patients (0.05%). The HSR rate for iodixanol (0.16%) was the highest, followed by that for iopamidol (0.08%), iopromide (0.04%), iobitridol (0.04%), ioversol (0.02%), ioxitalamic acid (0.01%), and iohexol (0.01%). Multivariate generalized estimating equation analysis showed age (odds ratio [OR], 0.980; 95% confidence interval [CI], 0.969-0.990; $P < 0.001$), urticaria (OR, 1.936; 95% CI, 1.003-3.737; $P = 0.049$), drug allergy (OR, 9.212; 95% CI, 5.353-15.853; $P < 0.001$), iopamidol use (OR, 8.327; 95% CI, 1.129-61.401; $P = 0.038$, compared to iohexol), iodixanol use (OR, 18.780; 95% CI, 2.564-137.560; $P = 0.004$, compared to iohexol), and use in 2014-2015 (OR, 2.704; 95% CI, 1.780-4.108; $P < 0.001$) were significant HSR-associated risk factors.
Conclusions: Among the RCMs, iodixanol (iso-osmolar RCM) and iopamidol (low-osmolar RCM) showed a significantly higher risk for HSR than did other agents.

Key Words: radiocontrast media, hypersensitivity reaction

P-108

A Nationwide Survey for Adverse Drug Reactions Related to Cephalosporins in Korea

Bomi Seo, Bo Young Park, So-Young Park, Oh Young Kwon, Hyouk-Soo Kwon, You Sook Cho, Hee-Bom Moon, Tae-Bum Kim*

[1]Department of Allergy and Clinical Immunology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

Background: As the prescriptions of cephalosporins have increased, the prevalence of the adverse drug reactions (ADRs) also appears to be on an increasing trend. To identify the ADRs of cephalosporins in Korea, we analyzed the spontaneous ADR reporting system (KAERS) of Korea Institute of Drug Safety and Risk Management (KIDS).
Materials and Methods: Data were collected and analyzed from KAERS system of KIDS from January 2012 to December 2015. We picked out and analyzed ADR cases and matters related to cephalosporins. "A matters" was defined as one symptom matched to one culprit drug include in an ADR case.
Results: In total, 23146 cases of ADRs associated with cephalosporins were identified after excluding cases for duplication and cases assessed as unlikely, unclassified, and unassessable. Total 33607 matters found from 23146 ADRs for were analyzed. Third generation cephalosporin (17671, 52.5%) is the most common causative generation. In each generation, cefazolin (2692, 65.5%) was the most common in the first generation, cefaclor (3778, 39.1%) was the most common in the second generation, ceftriaxone (9724, 55.0% and 28.3%) was the most common in the third generation and all the cephalosporin, and cefepime (2063, 94.2%) was the most common in the fourth generation. Ceftriaxone was the most common causative cephalosporin of the serious ADRs. The most common clinical manifestation of ADRs related to cephalosporins was skin disorders, followed by gastrointestinal disorders.
Conclusions: There are differences in prevalence of ADRs among cephalosoporins. We need to be cautious when we use the cephalosporins showing more prevalent ADRs.

*This research was supported by a grant from Korea Institute of Drug Safety and Risk Management in 2017.´

Key Words: cephalosporins, adverse drug reactions

P-109

Validation of the Korean version of urticaria control test and it's correlation with salivary cortisol

Young-Min Ye[1]*, Su-Chin Kim[2], Hyun-Young Lee[2], Ga-Young Ban[1], Yoo-Seob Shin[1], Hae-Sim Park[1]

[1]Department of Allergy and Clinical Immunology, Ajou University School of Medicine
[2]Clinical Trial Center, Ajou University Medical School

Objectives: Chronic urticaria (CU) exalts psychological stress and reversely stress can also be a trigger of CU. To explore the potential of salivary cortisol to be a biomarker of urticaria control, we investigated the responsiveness to change of the Korean version of UCT (K-UCT) for assessing CU and it's relation with salivary cortisol.
Methods: A linguistically validated translation of the German UCT into the Korean (K-UCT) was validated in 80 Korean CU patients before and after 4-week treatment. Correlations between K-UCT and Physicians' assessment of urticaria severity and control status, and general assessment of symptom scores by patients were analyzed by a generalized estimating equations model adjusted for age, sex and treatment step. Salivary cortisol was measured by ELISA.
Results: Strong correlations between the K-UCT and disease severity including UAS (OR 0.54, P <0.001), physicians' global assessment of urticaria control (OR 101.8, P <0.001) and patients' assessment of symptom severity (OR 0.008, P <0.001), and CU-specific quality of life (OR 53.64, P <0.001). Excellent internal consistency and intra-class reliability were obtained. K-UCT score of ≥12 (sensitivity 91.7% and specificity 61.7%, AUC on ROC analysis 0.824) was found to be optimal for determining well-controlled CU. Perceived stress scale was significantly correlated with K-UCT (0.47, P <0.001).Salivary cortisol levels were significantly correlated with K-UCT scores as well as were significantly different according to the control status determined by K-UCT score of ≥12 (3.55±4.39 vs 2.21±2.16, P=0.011).
Conclusions: This study demonstrates the clinical utility of the K-UCT to assess control status of CU and to detect clinical response to treatment in the Korean patients. Urticaria severity and control status impact significantly on individual perceived stress and salivary cortisol levels in patients with CU.

This study was supported by a grant from IIS Program of Norvatis Korea.

Key Words: Chronic urticaria, Urticaria Control Test, Salivary Cortisol

P-110

Clinical features of hereditary angioedema in Korean patients: A nationwide multicenter study

Jae Woo Jung, Hye-Ryun Kang*

Korea Hereditary Angioedema Network

Background: Hereditary angioedema (HAE) is a genetically heterogenous autosomal dominant disorder characterized by recurrent episodes of non-pruritic, non-pitting, edema increasing after puberty. It can be fatal due to laryngeal or gastrointestinal (GI) involvement varied and changing frequency of mortality according to the literature from Western countries. Epidemiologic and clinical data on of HAE in Asian countries are sparse.
Objective: To examine clinical characteristics of HAE patients present in Koreans.
Methods: A survey on HAE was sent to allergy specialists in Korea. Medical records of patients diagnosed with HAE were retrospectively reviewed.
Results: A total of 65 patients diagnosed with HAE by 2016 were identified. The prevalence of HAE was estimated to be 1.3/1,000,000 in Korea. Of the 65 patients, 21 (32.3%) were males. A total of 59 (90.8%) patients had type I HAE while the remaining 6 (9.2%) patients had type II HAE. The first symptom developed after 20 years in 73.8% of patients with a mean age 28.4±14.1 years. The age at diagnosis were 36.5±15.8 years with a mean time delay of 7.8 ± 10.5 years. While the involvement of face (82.3%) and extremities (upper 71.0%, lower 62.9%) were the most frequent, GI involvement was found in 40.5% of Korean HAE patients. Prophylaxis was maintained in 62.5% of patients. There was no reported case of death from HAE so far.
Conclusion: The clinical manifestation and severity of HAE might be different according to ethnicity. HAE is more infrequent and less likely to have GI involvement in Korea compared to Western countries.

Key Words: Herediditary Angioedema tyes I and II, Koreans, mortality

P-111

The Role of Translationally Controlled Tumor Protein in Chronic Spontaneous Urticaria

Bastsetseg Ulambayar[1], Hee-Won Lee[2], Eun-Mi Yang[1], Hae-Sim Park[1], Kyunglim Lee[2], Young-Min Ye[1]*

[1]Departlment of Allergy and Clinical Immunology, Ajou University School of Medicine
[2]Graduate School of Pharmaceutical Sciences, College of Pharmacy, Ewha Womans University

Objectives: Translationally controlled tumor protein (TCTP) also known as histamine releasing factor (HRF) as it has ability to activate mast cells. However, cytokine-like activity of TCTP is dependent on the dimerization. To investigate the role of TCTP in the pathogenesis of CSU, we measured TCTP levels and basophil activation test with TCTP. Methods: TCTP level was measured by ELISA and IgG autoantibody against FcεRIα level was measured by rapid dot-blot immunoassay in the sera from 116 CSU patients and 40 healthy controls (NCs). Basophil activation test (BAT) was done by measuring CD203c expression upon to recombinant monomer and dimer TCTP protein.
Results: No difference was observed in serum TCTP levels between CSU patients and NCs. TCTP levels were significantly higher in patients with severe CSU (51.1±31.6 vs 44.6±45.6 ng/ml, P=0.049) and a positive IgG to FceRIa (60.4±49.8 vs 42.5±37.6 ng/ml, P=0.038). A significant positive correlation was observed between TCTP and eosinophil cationic protein (ECP) levels in CSU patients (Spearman's rho 0.341, P=0.001). CD203c expression on peripheral blood basophils was significantly increased after stimulation with dimerized TCTP (P<0.01), but not with monomeric one.
Conclusion: We confirmed that the dimerized TCTP is essencial for activating peripheral basophils in CSU patients. Significant associations of serum TCTP levels with urticaria severity, increased ECP and the presence of IgG to FcεRIα in CSU patients indicated that autoimmune mechanisms can be involved in the dimerization of TCTP and influence histamine release and cytokine-like activity.

Key Words: Chronic urticaria, Translationally controlled tumor protein, Basophil activation

P-112

Rush Immunotherapy using IFN-gamma for Aspirin in Acute Coronary Syndrome: Case Report

Geunwoong Noh[1]*, Seung Ho Kang[1], Kyutaek Lee[1], Woo Jin Kim[1], Chi Wha Han[1], Ihl Bohng Choi[1], Chang Won Ha[1], Hyeryeon Noh[2]

[1]Cheju Halla General Hospital, [2]Central Valley Specialty Hostpial

Introduction: Aspirin desensitization involves slowly increasing exposure to oral aspirin. Several desensitization protocols have been described. IFN-gamma was reported to have allergen-specific tolerogenic effects and introduced for a patient who failed by classic desensitization, in an urgent and inevitable situation.
Cases: Case 1. Rush immunotherapy without IFN-gamma
A 82 year-old male patient who had stenosis of proximal left circumflex artery was admitted. PTCI was indicated but patients had aspirin hypersensitivity. Patients received oral desensitization for aspirin successful up to the dose of 300mg for 3 hours. Case 2. Rush immunotherapy using IFN-gamma
A 62 year-old male patient who had stenosis in proximal left anterior descending artery showed angioedema and generalized urticarial after taking aspirin for PTCI. Desensitization was started and showed allergic reactions to aspirin at the dose of 50mg at the twice consecutively with more aggravated allergic reactions at the second challenge. Desensitization was failed and was stopped. IFN-gamma was introduced and patient did not show allergic reaction to 50mg again. Desensitization was proceeded and successfully finished. Signed consent forms were obtained from the patients. This treatment was approved by the Institutional Review Board (IRB) of Cheju Halla General Hostpial, Jeju-si, Korea.
Discussion: Hypersensitivity to aspirin constitutes a serious problem for patients with coronary artery disease. The issue of desensitization for aspirin in coronary artery disease is the time consuming and success of desensitization. Limitation of aspirin desensitization is that in patients who failed the desensitization protocol, a new attempt to desensitize was absent in a recent report. In this report, desensitization of aspirin using IFN-gamma was successful as the new therapeutic protocol for the failed desensitization case. IFN-gamma may be effective for desensitization of drug allergy.

Key Words: Aspirin allergy, Desensitization, IFN-gamma

P-113

Treating Multiple Food Allergy of different types in Atopic Dermatitis : Specific Oral Immunotherapy using IFN-gamma for Anaphylactic IgE-mediated and Non-IgE-mediated Food Allergy, Case Report

Geunwoong Noh*, Kyutaek Lee

Cheju Halla General Hospital

Introduction: Food allergy was revealed as an important cause of atopic dermatitis (AD). Specific oral tolerance induction (SOTI) was the only modality to solve this problem. IFN-gamma has been used more than 17 years for SOTI for anaphylactic and non-IgE-mediated food allergy in AD.
Cases: Case 1. A 8 year-old boy visited Cheju Halla General Hospital in 2016 because of AD and food allergy. Patients received oral food challenge tests and had multiple food allergy of different types; anaphylactic food allergy for eggs, wheat, yellow croaker, anchovy, abalone, mushroom, walnut and sesame, and non-IgE-mediated food allergy for pork, chicken, beef and soybean. Patients received SOTI using IFN-gamma for anaphylactic food allergy of eggs and wheat and non-IgE-mediated food allergy of pork, chicken, beef, soybean which provoke atopic dermatitis,. He is taking treated food freely and clinical symptoms and signs of AD are free until now.
Case 2. A 4 year-old male patient was visited Cheju Halla General Hostpital due to AD and food allergy in 2016. Patient received oral food challenge and had multiple food allergy of different types; anaphylactic IgE-mediated food allergy for wheat and shrimp, IgE-mediated allergy for mackerel and non-IgE-mediated allergy for eggs, milk, pork, chicken, s curd, abalone and shellfish. He received SOTI using IFN-gamma for eggs, milk, pork, chicken, s curd, and wheat successfully and is taking treated foods freely in his daily living. AD was much improved without any other treatment.
Discussion: Food allergy is an important issue in allergic fields. Food allergy is an important cause of AD, even with multiple food allergy of various type; anaphylactic IgE-mediated, non-IgE-mediated eczematous type or both. SOTI for food allergy using IFN-gamma in AD is performed effectively as a causative diagnosis and treatment of food allergy.

Key Words: Food allergy,atopic dermatitis, specific oral tolerance induction

P-114

Efficacy of subcutaneous immunotherapy including Fagales pollen on patients with oral allergy syndrome and their allergic rhino-conjunctivitis

Nasil Kong, Kyunghee Park, Jaehyun Lee, Sang Chul Lee, Sunyoung Kim, Jinyoung Choi, Jungwon Park*

Division of Allergy & Clinical immunology, Department of Internal Medicine, Severance Hospital, Yonsei University College of Medicine

Background: The oral allergy syndrome (OAS) is the most common food allergy-related manifestation in adult and is due to the cross-reactivity between tree pollen and fruits or vegetables in Korea. .
Objective: The purpose of this retrospective study was to investigate whether specific immunotherapy with tree pollens can modify the prognosis of OAS.
Methods: Thirty-five patients with OAS were included. Nineteen subjects were treated with SIT with Fagales pollen and sixteen were not. Baseline OAS and clinical characteristics were assessed by questionnaire and patient medical records. To assess the effect of specific immunotherapy, allergic rhino-conjunctivitis symptoms were also measured before and after treatment.
Results: After the SIT, Nine out of 19 subjects (47.37%) reported decreased OAS symptoms by more than 50% ($p = 0.007$). In contrast, only one out of 16 patients (6.25%) without SIT reported their OAS symptoms reduced by 50% or more. Fourteen of 18 (77.78%) SIT-treated patients reported their allergic rhino-conjunctivitis symptoms improved more than 50% after treatment, whereas only one of 16 (6.25%) individuals without SIT ware improved their allergic rhino-conjunctivitis symptoms more than 50% ($p = 0.001$).
Conclusion: This study suggests that SITs with Fagales pollen-containing extracts may reduce OAS as well as improve allergic rhino-conjunctivitis symptoms.

Key Words: oral allergy syndrome, allergic rhino-conjunctivitis, specific immunotherapy

P-115

Sublingual immunotherapy in mite-sensitized children with atopic dermatitis: a randomized, open, parallel-group study

MinJu Kim[1], Eun Lee[2], Jisun Yoon[3], Sungsu Jung[3], Jinho Yu[3]*

[1]Department of Nursing, Asan Medical Center, Seoul, [2]Department of Pediatrics, Chonnam National University Hospital, Gwangju, [3]Department of Pediatrics, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

Purpose: Allergen immunotherapy with house dust mite (HDM) preparation has recently been shown to improve eczema in patients with atopic dermatitis (AD). But there is less data regarding efficacy and safety of sublingual immunotherapy (SLIT) in children with AD. The aim of this study is to evaluate the effect of SLIT with HDM allergen extracts preparation in mite-sensitized children with AD
Methods: In this single center, randomized, open, parallel group trial, 26 children (aged 5-17 years) with a chronic course of AD (Scoring Atopic Dermatitis [SCORAD]> 8) and sensitization to HDM were randomized to receive (n=14) or not to receive (n=12) SLIT. SCORAD, Visual analogue scale (VAS) scores, Investigator global Assessment (IGA) were compared respectively between two groups at different time points, and specific IgE and IgG4 to HDM were measured at baseline and 12 months after treatment.
Results: The SLIT group had significantly reduced SCORAD and IGA compared with the baseline after 12 months, while the control group did not show significance. No significant difference could be detected in VAS scores of both groups after 12-month treatment. Meanwhile, specific IgE to HDM was not decreased, whereas IgG4 to HDM increased significantly only in SLIT group. No subjects experienced serious adverse events during SLIT. Five patients (36%) showed transient oral itching and swelling among SLIT group.
Conclusion: SLIT for 1 year with HDM preparation improved AD in HDM-sensitized children. It suggests that SLIT may be a treatment option in children with AD who are sensitized to HDM.

Key Words: Atopic dermatitis, House dust mites, Sublingual immunotherapy

P-116

Incidence and prevalence of respiratory virus for 10 years in children

Seung Jin Lee[1], Eun Kyo Ha[1], Hye mee Jee[1], Young-Ho Jung[1], Shinhae Lee[1], Kyung Suk Lee[1], Youn Ho Sheen[2], Myongsoon Sung[3], Man Yong Han[1]*

[1]Department of Pediatrics, Bundang CHA medical center, CHA University School of Medicine
[2]Department of Pediatrics, CHA Gangnam medical center, CHA University School of Medicine
[3]Department of Pediatrics, CHA Gumi medical center, CHA University School of Medicine

Background and objective: It is well known that respiratory viral infection has epidemiological characteristics including seasonality. This study was aim to investigate the patterns of prevalence of common respiratory viruses during 10 years with regard to age, sex, and seasons in Korean children.
Methods: From June 2006 to November 2016, we obtained 11,798 specimens from patients who were admitted with lower respiratory infections, aged less than 18 years. Ten respiratory viruses were detected using multiplex RT PCR.
Results: Of 11,798 specimens, at least one viruse was detected in 4,271 (36.2%) specimens.. HRV (14.8%) was the most common virus detected, followed by RSV (10.1%), ADV (9.5%), and HBoV (7.4%). The ratio of HRV detection was higher in male subjects (male 15.8% vs female 13.6%, P = 0.004), but other viruses had no significant differences with regard to sex. The subjects who were tested positive for HCoV were the youngest (median, 13 months, IQR 4.5-25 month), followed by HRV (median, 14 months), PIV (median, 15 months) and MNV (median, 16 months).
Conclusion: We investigated the characteristics of the prevalence of respiratory virus in Korean children for 10 years, which was different with regard to age, sex, and seasons. Further research collected from different part of the world is warranted to infer clinical implication of our results.

Key Words: respiratory viruses, seasonality, children

P-117

Maternal Fetal Attachment During Pregnancy Affects Respiratory Tract Infection in offspring: the COCOA study

Mi-Young Lee[1], Si-Hyeon Lee[1], Kyung-Sook Lee[8], Yee-Jin Shin[9], Ji-sun Yoon[2], Sung-su Jung[2], So-Yeon Lee[2], Dong- In Suh[3], Youn-Ho Shin[4], Kyung-Won Kim[5], Kang-mo Ahn[6], Hyoung-Yoon Chang[7], Soo-Jong Hong[2]*

[1]Asan Institute for Life Science, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea, [2]Department of Pediatrics, Childhood Asthma Atopy Center, Environmental Health Center, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea, [3]Department of Pediatrics, Seoul National University College of Medicine, Seoul, Korea, [4]Department of Pediatrics, Gangnam CHA Medical Center, CHA University School of Medicine, Seoul, Korea, [5]Department of Pediatrics, Yonsei University College of Medicine, Seoul, Korea, [6]Department of Pediatrics, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea, [7]Department of Psychiatry, Ajou University College of Medicine, Sunflower Center of Southern Gyeonggi for Women and Children Victims of Violence, [8]Department of Rehabilitation, Hanshin University, Osan, [9]Department of Psychiatry, Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Korea

Background: Little is known about the relationship between maternal fetal attachment during pregnancy and early immune development in their offspring. This study investigated the effect of maternal fetal attachment during pregnancy and respiratory tract infection (RTI) in offspring.
Methods: This study included1,827 mother-child dyads from the Cohort of Childhood Origin of Asthma and allergic diseases (COCOA) study. Maternal fetal attachment scales were evaluated using self-reported questionnaires by Maternal Fetal Attachment Scale (MFAS) on 36th weeks of pregnancy. Development of RTI in offspring was evaluated by the report of physician's diagnosis. RTI included acute nasopharyngitis, rhinosinusitis, otitis media, croup, tracheobronchitis, bronchiolitis, and pneumonia.
Results: Lower maternal fetal attachment (MFAS<93) significantly increased the offspring RTI at 6-month (aOR, 1.40, 95%, CI,1.10-1.78) and at 1-year-old (aOR 1.62, 95 % CI 1.14-2.30). Lower maternal fetal attachment also significantly associated with 1.78-fold greater likelihood of having cummulative RTI until 3-year-old (95% CI 1.18-2.69). It also significantly increased the offspring's LRTI at 6-month (aOR, 1.68, 95%, CI, 1.09-2.59), at 3-year-old (aOR 1.84, 95 % CI 1.01-3.33), and cummulative LRTI until 3-year-old (95% CI 1.10-1.88). Acute bronchiolitis at 6-month (aOR 1.82, 95%, CI, 1.15-2.89) and cummulative bronchiolitis until 3-year-old (aOR 1.44, 95% CI 1.06-1.94) were also significantly associated with low maternal fetal attachment.
Conclusion: Poor maternal fetal attachment influenced the development of their offspring's RTI at 6-month and 1-year-old. Improving fetal maternal attachment may reduce RTI in the offspring. The mechanism related to RTI needs to be investigated.

Key Words: Maternal Fetal Attachment, Pregnancy, Respiratory Tract Infection, Offspring

P-118

Common causes of blood eosinophilia depending on the degree of eosinophilia

Ji Eun Yu[1], Da Woon Sim[1], Ji-Ung Jeong[2], Young-Il Koh[1]*

[1]Division of Allergy, Department of Internal Medicine, Chonnam National University Hospital,
[2]Department of Internal Medicine, Chonnam National University Hospital

Backgrounds: Blood eosinophilia is defined as peripheral blood eosinophil ≥5% or 500/uL. The degree of eosinophilia can be categorized as mild (500 to 1500 eosinophils/uL), moderate (1500 to 5000 eosinophils/uL), or severe (>5000 eosinophils/uL). We would like to investigate the common causes of blood eosinophilia depending on the degree of eosinophilia.
Methods: We analyzed the cause and the extent of eosinophilia in 98 patients with blood eosinophilia who first visited the allergy department of Chonnam National University Hospital in 2016. The value of eosinophil at first visit was selected, and the highest value was selected for drug allergy.
Results: Blood eosinophilia was caused by allergic disease (49.0%), drug allergy (20.4%), parasitic infection (19.4%), HES (3.1%), CEP (3.1%), ABPA (2.0%) and CSS (1.0%), and mean values of eosinophil were 8.3%, 18.6%, 22.1%, 44.5%, 15.4%, 29.8% and 63.8%, respectively. Allergic disease includes asthma, allergic rhinitis, atopic dermatitis, chronic urticaria and contact dermatitis. And drug allergy includes drug-induced eosinophilia, drug rash, drug fever, DRESS syndrome and hypersensitivity vasculitis.
In the patients who visited for evaluation of incidentally discovered eosinophilia, allergic disease was 17.4%, drug allergy was 8.7% and parasitic infection was 73.9%.
In the patients with moderate eosinophilia, drug allergy was 42.3%, parasitic infection was 38.5%, CEP was 7.7%, ABPA was 3.8%, HES was 3.8%, and there was no allergic disease. In the patients with severe eosinophilia, drug allergy was 33.3% (All cases were DRESS syndrome), HES was 33.3%, ABPA was 16.7% and CSS was 16.7%.
Conclusions: Common causes of blood eosinophilia are allergic disease, drug allergy, and parasitic infection. It is necessary to evaluate causes other than allergic disease when moderate to severe eosinophilia is present.

Key Words: Eosinophilia

P-119

Clinical Validation of Point-of-Care Testing of IgG assay Compared with Laboratory Based Testing

Jinyoung Choi[1], Kyunghee Park[1], Jaehyun Lee[1], Dawoon Sim[2], Sang Chul Lee[1], Sunyoung Kim[1], Nasil Kong[1], Jungwon Park[1]*

[1]Division of Allergy and Immunology, Department of Internal Medicine, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea, [2]Department of Internal Medicine, Chonnam National University Hospital, Gwangju, Korea

Conventional immunoglobulin G (IgG) assay is time-consuming and requires a relatively large amount of specimen (1,500 μL). To overcome this limitation, Point-of-care testing (POCT) for IgG was newly developed which can detect rapidly, and requires small amount of specimen (5 μL). The aim of this study was to compare IgG results obtained by newly developed POCT and the conventional laboratory IgG levels in serum and whole blood.
The blood samples(both serum and whole blood) from 120 Korean patients were used to compare with ImmuneCheck IgG POCT kit (Proteomtec, Seoul) and conventional laboratory based Roche Cobas 6000, respectively. The IgG POCT result was read 3 times by naked eyes of one blind researcher.
The results of POCT were expressed semi-quantitatively by 0, 7.8, 31, 125, 250, 500, 750, 1000, 1500, 2000 and this numbers represented the value within the range of 70 ~ 140% of each number.
To compare the intra-rater and inter-test variability, Intraclass Correlation Coefficient (ICC) analysis was used. An acceptable level for reliability was defined as ICC > 0.7.
Total 120 adults (44 males and 76 females) were compared. Mean age was 48 years old (range: 18-89). The conventional laboratory serum IgG results by Roche Cobas 6000 ranged from 690.4 to 2756.4 mg/dL, and the mean was 1184.1 mg/dL. The serum IgG POCT results by ImmuneCheck ranged from 750 to 2000 mg/dL, and the median was 1500 mg/dL.
The intra-rater reliability was acceptable (serum ICC = 0.724, p <0.001; whole blood ICC = 0.843, p <0.001).
A statistically significant correlation was observed between IgG POCT results (median of the 3 readings) using the ImmuneCheck kit and the reference laboratory results (serum ICC = 0.805, p <0.001; whole blood ICC = 0.842, p <0.001).
Conclusively, the ImmuneCheck IgG POCT kit is reliable and easy to handle method for the rapid screening of abnormal total IgG level in patients.

Key Words: IgG, IgG POCT

P-120

A scoring system for primary immunodeficiency for treatment guideline of immunoglobulin replacement therapy

Chang-Gyu Jung, So-Hee Lee, Ga-Young Ban, Ji-Ho Lee, Young-Min Ye, Yoo Seob Shin, Hae-Sim Park*

Department of Allergy and Clinical Immunology, Ajou University School of Medicine, Suwon, Korea

Background and obejctive: Primary immunodeficiency diseases (PIDs) in adults are mostly derived from humoral immune dysfunction. Major clinical manifestations of PIDs are recurrent upper and lower respiratory infections, that are not closely correlated with laboratory abnormalities. The main treatment modality in PIDs is intravenous immunoglobulin (IVIG), which needs lifelong therapy, and there has been no standardized guideline to select who needs IVIG treatment in this country. Here, we propose to an Ajou-scoring system composing laboratory and clinical findings to recommend IVIG for PID patients.
Methods: Laboratory parameters included the values of total IgG and IgG subclass (IgG1-4). Clinical parameters included 1) modified ones from 10 warning signs by Jeffrey Modell Foundation, 2) pulmonary function abnormalities, and 3) evidence of bronchiectasis from radiologic findings. By using these parameters, we developed a two-step scoring system (laboratory and clinical) and applied in 20 patients with suspected PID symptoms.
Results: The mean age was 46.55 years (range, 20-69 years) and male/female ratio was 4/16. Based on our scoring system, 10(50%) of the study subjects were recommend IVIG therapy. Between recommended and not-recommend groups, there were no significant differences in the laboratory score. However, the clinical score including frequency of viral/sinus infections and IV antibiotics use within the past 1 year were significantly higher in the recommended group (P<0.05, respectively).
Conclusion: We suggest that clinical scoring is more critical to recommend IVIG therapy for PID patients. This new scoring system should be validated in a larger cohort of PID patients in this country.

Key Words: Primary immunodeficiency; Intravenous immunoglobulin; Scoring system

P-121

Two Cases of Familial IgG3 Subclass Deficiency

Ji-Ho Lee, Seung-Hyun Kim, Chang-Gyu Jung, Youngwoo Choi, Hae-Sim Park*

Department of Allergy and Clinical Immunology, Ajou University School of Medicine, Suwon, Korea

Primary immunodeficiency (PID) in adults has not been thoroughly investigated in Korea, therefore PID patients are thought to be underestimated/ undertreated. IgG subclass deficiency (IgGSD), a subtype of PID, defined as a deficiency at least among 4 subtype of IgG subclass, IgG1, IgG2, IgG3, and IgG4, affects humoral immune responses and results in recurrent infectious disease, in which IgG3SD is the most commonly found in adult asthmatic patients. Herein, we report 2 cases of familial IgGSD. In family 1, the mother aged 50 having underlying allergic rhinitis (AR) and asthma had recurrent upper respiratory infection (URI), otits media, urinary tract infection, gastroenteritis, and oral ulcer. Her two daughters aged 17 and 9 having AR had recurrent URI almost all the year round.
In family 2, the mother aged 39 having AR had recurrent URI and oral ulcer. Her son aged 16 and daughter aged 13 having underlying AR and asthma had recurrent URI, resulting in frequent asthma exacerbations.
In laboratory analysis, family 1 was shown to have IgA deficiency in mother and daughter aged 17: 63 mg/dl and 78 mg/dl (reference range of 93-365 mg/dl), respectively, and IgG3 deficiency in two daughters: 136mg/l and 136mg/l (138-1058 mg/l), respectively. The IgG3 level of mother was also of low normal: 197 mg/l (110-850 mg/l). Family 2 was found to be IgG3 deficiency in mother and son: 95mg/l (110-850 mg/l) and 127 mg/l (138-1058 mg/l), respectively and IgA deficiency in son: 75mg/dl (93-365 mg/dl). The IgG3 level of daughter was of low normal: 139 mg/l (138-1058 mg/l). We sought to find a genetic mutation involved in common in two familial IgGSD with or without IgA deficiency using exome sequencing, with analysis being still underway. In conclusion, we report two cases of familial IgGSD with genetic studies. Further extended studies will be needed to pursue genetic susceptibility factors in the development of PID in adults.

Key Words: Primary immunodeficiency, IgG subclass deficiency, asthma

P-122

Primary Immunodeficiency Cohort in Korean adult population (PICK)

Joo-Hee Kim[1], Ga-Young Ban[2], Hyun Jung Jin[9], Young-Min Ye[2], Mi-Ae Kim[3], Young-Hee Nam[4], Soo-Keol Lee[4], Jeong-Hee Choi[5], Gyu-Young Hur[6], You Sook Cho[7], Sang-Ha Kim[8], Hae-Sim Park[2]*

[1]Department of Medicine, Hallym University Sacred Heart Hospital, Hallym University College of Medicine, Anyang, Korea, [2]Department of Allergy & Clinical Immunology, Ajou University School of Medicine, Suwon, Korea, [3]Department of Allergy and Clinical Immunology, CHA Bundang Medical Center, CHA University, [4]Department of Internal Medicine, College of Medicine, Dong-A University, Busan, Korea, [5]Department of Medicine, Hallym University Dongtan Sacred Heart Hospital, Hallym University College of Medicine, Hwaseong, Korea, [6]Department of Internal Medicine, Korea University Guro Hospital, Seoul, Korea, [7]Department of Allergy and Clinical Immunology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea, [8]Department of Internal Medicine, Yonsei University Wonju College of Medicine, Wonju, Korea, [9]Department of Internal Medicine, Yeungnam University College of Medicine, Daegu, Korea

Background: Primary immune deficiencies (PIDs) is known to be a relatively rare disease, especially in adults. Once recognized, these rare disorders are preventable and treatable; however, undiagnosed or untreated PIDs are serious, or even fatal. Therefore, constructing registries of PIDs is necessary as it is a useful tool to assess clinical information of affected individuals, which can provide the provision of treatments.
Objective: The registry' goal is to register diagnosed PID patients in Korea and the long-term objective is to build a registry that provides clinical information to the medical community, and PID patients for the high-quality medical care in this field.
Method: This is a prospective and observational cohort study. This registry was initiated in September 2015 and comprises 10 medical centers with experience in the care of adults with PID. The web-based registry collects clinical and laboratory information on PID patients.
Results: Between September 2015 and Dec 2016, 64 patients were registered. Male to female ratio was 1:2.2 and the mean age was 53.1±14.4 years. All registered patients were diagnosed with 'predominantly antibody deficiencies'. Within this disease category, the most frequent diagnosis is 'immunoglobulin G subclass deficiency (84%), followed by total IgG deficiency (4%), thymoma with immunodeficiency (4%), and common variable immunodeficiency (2%). The most common manifestation was a recurrent viral infection (47.4%), sinus infection (16.6%), and need to intravenous antibiotics to clear infections (11.5%). Most patients received immunoglobulin replacement after diagnosis of PIDs.
Conclusion: In our PID cohort, 'predominantly antibody disorders' are the most frequent category. The registry will help to build up a network of expert physicians in Korea, allowing for productive medical and scientific collaboration with the goal of improvement of patient care.

Key Words: Primary Immunodeficiencies; Registry; Adults; Korea

P-123

Prevalence of primary immunodeficiency diseases in adult asthmatic patients

So-Hee Lee[1], Chang-Gyu Jung[1], Hyun-Young Lee[2], Ga-Young Ban[1], Su-Chin Kim[2], Ji-Ho Lee[1], Hae-Sim Park[1]*

[1]Department of Allergy and Clinical Immunology, Ajou University School of Medicine, Suwon, Korea
[2]Department of Statistics, Clinical Trial Center, Ajou University Medical Center, Suwon, Korea

Background and objective: Most adult-onset primary immunodeficiency diseases (PIDs) are derived from humoral immune deficiencies in which their cardinal manifestations are recurrent upper and lower respiratory infections. Among PID patients, asthma is the most prevalent comorbid condition and asthmatic patients with PID are suffering from frequent asthma exacerbations. The aim of this study is to evaluate the prevalence of PID in adult asthmatic patients in a single tertiary center.
Methods: We examined the medical records of 3293 asthmatic patients (≥19 years old) who had been treated for >2 years under the J45 code at Ajou University Hospital(Suwon, Korea) from April, 1994 to March, 2016. PID was defined as the subjects who had lower levels of serum IgG/M/A and/or IgG subclass with presenting recurrent infections. Levels of IgG/A/M and IgG subclass were measured using immunoturbidimetric methods and immunodiffusion assay, respectively.
Results: Two hundred five patients (6.23%) were found to have PID. The female/male ratio was 142:63 and their mean age was 45.42 years ranged from 9 to 78 years. Of the total PID patients, 110 (3.34%) had IgG subclass deficiency, in which an isolated IgG3 deficiency was the most common type, followed by an isolated IgG4 deficiency and both IgG1/IgG3 deficiency. Both IgG/IgG subclass deficiency was found in 48 patients (1.46%) and IgG/IgA/IgM deficiency was found in 47 patients (1.43%).
Conclusions: Prevalence of PID was estimated as 6.23% among adult asthmatic patients. Further studies will be followed to investigate their clinical characteristics.

Key Words: Primary immunodeficiency diseases; Asthma

P-124

B cell profiles in asthmatic patients with IgG subclass deficiency

Chang-Gyu Jung, Seung-Hyun Kim, So-Hee Lee, Ji-Ho Lee, Young-Min Ye, Hae-Sim Park*

Department of Allergy and Clinical Immunology, Ajou University School of Medicine, Suwon, Korea

Purpose: Immunoglobulin G subclass deficiency (IgGSCD) is the most common phenotype of primary immunodeficiency diseases (PIDs) in adult asthmatic patients. B cells and regulatory B (Breg) cells play a key role in balancing immune responses and controlling disease symptoms in asthma by producing immunoglobulin (Ig) or cytokine such as IL-10. However, the function of B cell in PID is not understood. The aims of this study were, 1) to investigate the pathogenic mechanisms of PID in asthmatic patients focusing on B cell dysfunctions, and 2) to evaluate their functional changes before and after intravenous immunoglobulin (IVIG) treatment.
Methods: One hundred ten adult asthmatic patients with or without PID and healthy normal controls (NCs) were enrolled at Ajou University Hospital in Korea, and the medical records including age, sex, atopic status, severity of asthma, and fraction of exhaled nitric oxide (FeNO) were reviewed. Heparinized peripheral blood mononuclear cells (PBMCs) were isolated from all the subjects and expression of B cell markers were analyzed by using FACS CantoTM II flow cytometer. In addition, the B cells were activated by PIB (phorbol 12-myristate 13-acetate, ionomycin, Brefeldin A) or CpG and re-analyzed.
Results: Breg cells were significant lower in patients with asthma than in NCs (7.6% vs. 13.6%, P<0.005). Among asthmatic patients, the patients with high FeNO had significantly lower B reg cell% than those with low FeNO with a negative correlation between these two parameters (R=-0.242, P=0.005). Both baseline and stimulated of Breg/IgG3-producing plasma B cells were significantly lower in asthmatic patients with PID than in NC, both of which did not change (increase) after > 6 months' IVIG treatment.
Conclusion: We demonstrated decreased IgG3-producing B cell count/Breg cell dysfunction in adult asthmatics with PID, which did not change after Ig replacement therapy.

Key Words: B cell; Regulatory B cell; Primary immunodeficiency

P-125

Two Rare Cases of Asthma Exacerbations with Eosinophilia

Bomi Seo, Hee-Bom Moon*

Department of Allergy and Clinical Immunology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

Background: Eosinophil is one of the important factors in asthma pathophysiology. Sputum or blood eosinophilia is an independent risk factor of exacerbations. We report herein two rare cases of asthma exacerbations with eosinophilia in sputum and blood.
Case 1: A 57-year-old female patient with history of asthma and allergic rhinitis was referred to our hospital. She had taken no asthma medication and the methacholine bronchial provocation test (MBPT) was negative. Six months later she was hospitalized for evaluation for a persistent cough. Laboratory tests revealed increased eosinophil in the blood (21%, 1050/μL) and sputum (78%). Forced expiratory volume in 1 second (FEV1) is 2.27 L (83%), which was decreased compared to her usual FEV1. MBPT was performed again and revealed positive (PC20 8.41 mg/ml). Her symptoms were improved after the treatment, including inhaled and oral corticosteroids. Case2: An 80-year-old male patient with asthma was hospitalized for evaluation for chest tightness at night that began two months ago. He had no asthma symptoms for more than 6 months and ICS/LABA combination inhaler was replaced by a tiotropium inhaler. In addition, the medication for anxiety was added because the cause of chest tightness was unclear in the examinations. During hospitalization, he complained of chest symptom only between 10 pm to 2 am. Laboratory tests revealed increased eosinophil in the blood (10.8%, 658/μL) and sputum (14%). Spirometry performed during daytime was normal. While he complained of chest symptom at night, the oxygen saturation was decreased to 84%, the respiratory rate was increased to 29/min with wheezing sounds in the whole lung. His peak expiratory flow rate was 130L/min. It was significantly decreased compared with 320L/min measured during no symptom. His symptoms were improved after restarting ICS/LABA inhaler. Discussion: Sputum or blood Eosinophilia may indicate asthma exacerbation when the symptoms or spirometry is not typical.

Key Words: Asthma, Exacerbations, Eosinophilia

P-126

Chronic cough, generalized skin rash and hypereosinophilia as presenting manifestations of follicular variant peripheral T-cell lymphoma with systemic infiltrations of eosinophils

Yu Jeong Lim[1], Jeong Eun Kim[2], Ji-Yong Moon[1], Sang-Heon Kim[1], Tae Hyung Kim[1], Jang Won Sohn[1], Kang Nyeong Lee[1], Byoung-Bae Park[1], Ji Eun Uhm[1], Yeonkyung Park[1], Ji-Hee Min[1], Gun woo Koo[1], Tai Sun Park[1], Dong Won Park[1], Ho Joo Yoon[1]*

[1]Department of Internal Medicine, Hanyang University College of Medicine, Seoul, Korea
[2]Department of Dermatology, Hanyang University College of Medicine, Seoul, Korea

Lymphoma has been known as a rare cause of incidentally detected peripheral blood eosinophilia. Sometimes, T-cell lymphoma can present as hypereosinophilic syndrome (HES) characterized by persistent eosinophilia, and multiple organ involvements. While most cases of pulmonary involvement of T-cell lymphoma related HES were eosinophilic infiltration of lung parenchyma, bronchial infiltration of eosinophils without parenchymal infiltrations has not been reported. Here we report a case of follicular variant peripheral T-cell lymphoma which presented as chronic cough in the form of chronic eosinophilic bronchitis, skin rash and peripheral blood hypereosinophilia.
A 62-year-old female visited allergy clinic for the evaluation of chronic cough and generalized skin erythematous papules which lasted for 18 months. Persistent peripheral blood eosinophilia, more than 3,000 cells/microliter, was noted from the initial lab tests at the primary clinic. Cervical and inguinal lymphadenopathies aggravated along with dermatologic symptom. Oral corticosteroid therapy temporarily relieved symptoms, but they recurred during tapering period. While simple radiography of the chest was normal, chest CT revealed bronchiolitis in the both lungs and mid esophageal thickening. Although spirometry, methacholine bronchial provocation test and exhaled nitrate oxide level were normal, induced sputum analysis showed an elevated fraction of eosinophils of 26%. Bone marrow aspiration demonstrated normal cellularity with normal myeloid series. Genetic tests like JAK2, CML Major/Minor, BCR/ABL, PDGFRA mutation were all negative. Pathologic evaluation of inguinal lymph node biopsy showed findings compatible with follicular variant peripheral T-cell lymphoma. After 6 cycles of CHOP chemotherapy, there was a resolution of cough, skin lesions, peripheral blood eosinophilia and the thickening of the bronchial tree, esophagus and lymph nodes.

Key Words: lymphoma, eosinophilia, chronic cough

P-127

A case of eosinophilic granulomatosis with polyangiitis presenting with acute polyneuropathy resembling Guillain–Barré syndrome

Jee Seon Kim, June Hong Ahn, Jin Hong Chung, Hyun Jung Jin*

Department of Internal Medicine, Yeungnam University College of Medicine, Daegu, Korea

Eosinophilic granulomatosis with polyangiitis (EGPA) is a rare systemic vasculitis which commonly affects the peripheral nervous system. But EGPA rarely presents with acute polyneuropathy resembling Guillain-Barré syndrome (GBS). A 51-year-old female with a history of asthma, suddenly developed bilateral lower extremity paresthesias that progressed to asymmetric ascending paralysis from 10 days ago. Nerve conduction studies were compatible with acute motor sensory axonal neuropathy, considering of GBS subtype. A clinical and a neurophysiological diagnosis were made and high-dose IV immunoglobulins were administered. However, patient's painful motor weakness was persistent. And she had newly developed skin lesions in her back, face and arms. Her blood test revealed marked eosinophilia (>60%). And anti-neutrophil cytoplasmic antibodies (ANCAs) were reported positive. A water's view image showed both maxillary sinusitis. Considering the history of asthma, we suspected EGPA-associated polyneuropathy and started steroid treatment. The patient's strength and eosinophilia improved rapidly and dramatically. EGPA can mimic GBS and should be differentiated, because of different treatment strategies. Early diagnosis and prompt treatment help to achieve good outcome.

Key Words: Eosinophilic granulomatosis with polyangiitis, polyneuropathy, Guillain-Barré syndrome

P-128

Correlation of HAMP gene polymorphisms and expression with the susceptibility and length of hospital stays in Taiwanese children with Kawasaki disease

HO-CHANG KUO

Kawasaki Disease Center and Department of Pediatrics, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Taiwan

Purpose: Kawasaki disease (KD) is a form of systemic vasculitis. Regarding its pathogenesis, HAMP gene encoding hepcidin, which is significant for iron metabolism, has a vital function.
Methods: In this study, we recruited a total of 381 KD patients for genotyping. Data from 997 subjects (500 subjects from cohort 1; 497 subjects from cohort 2) were used for analysis. Using TaqMan allelic discrimination, we determined five tag SNPs (rs916145, rs10421768, rs3817623, rs7251432, and rs2293689). Treatment outcome data related to such clinical phenotypes as coronary artery lesions (CAL), coronary artery aneurysms (CAA), and intravenous immunoglobulin (IVIG) effects were also collected. Furthermore, we measured plasma hepcidin levels with an enzyme-linked immunosorbent assay.
Results: We found that HAMP gene polymorphisms (rs7251432, and rs2293689) were significantly correlated with KD risk and that plasma hepcidin levels both before and after IVIG treatment had a significantly positive correlation with length of hospital stays ($R = 0.217$, $p = 0.046$ and $R = 0.381$, $p < 0.0001$, respectively). In contrast, plasma hepcidin levels has a negative correlation with KD patients' albumin levels ($R = -0.27$, $p < 0.001$) prior to IVIG treatment.
Conclusion: Our findings indicate that HAMP might have a role in the disease susceptibility, as well as its expressions correlated length of hospital stays, and albumin levels in Taiwanese children with KD.

P–129

Monogenic polyarteritis nodosa caused by deficiency of adenosine deaminase type 2 (DADA2): genotypes and phenotypes in 21 subjects

Sira Nanthapisal[1,2], Claire Murphy[1], Ebun Omoyinmi[1], Ariane Standing[1], Ying Hong[1], Sonia Melo Gomes[1], Nigel Klein[1], Despina Eleftheriou[1] and Paul A Brogan[1]

[1]Institute of Child Health, University College London, London United Kingdom, [2]Faculty of Medicine, Thammasat University, Pathumthani, Thailand

Background: Recessive mutations in Cat Eye syndrome Critical Region 1 (CECR1), the gene encoding adenosine deaminase 2 (ADA2) have been recently reported to cause deficiency of adenosine deaminase type 2 (DADA2) an autoinflammatory disease resembling polyarteritis nodosa (PAN) with highly varied clinical expression. ADA2 converts extracellular adenosine into inosine and also functions as monocyte growth factors. Clinical manifestations and immunological defects in DADA2 are still unclear.
Objective: 1) to use Sanger sequencing to identify mutations in CECR1 in a cohort of patients with childhood PAN and their family 2) to study the ADA2 enzyme activity and CECR1 mRNA expression in DADA2 subjects, childhood PAN and healthy controls 3) to study the immunological defects in the differentiation of monocytes into macrophages from isolated monocytes of DADA2 patients and healthy controls.
Methods: Sanger sequencing was performed in select paediatric cases of PAN. Inclusion criteria were: 1. Onset of PAN <age-10-years; 2. Suspected familial PAN; 3. Sporadic PAN particularly with neurological involvement; and 4. Clinical features resembling the recent description of deficiency of ADA2 (DADA2). CECR1 qPCR was done using whole blood samples from patients and healthy controls. ADA2 activity was tested using serum samples from patients as well as healthy and disease controls. Monocytes, isolated from whole blood samples of patients and healthy controls, were differentiated into macrophages and polarised toward either an M1 or M2 subtype.
Results: Loss of function mutations in CECR1 were identified 21 subjects; 8 were asymptomatic. The main clinical features were: cutaneous involvement (66.7%; livedo racemose, peripheral ischaemia), neurological involvement (52.4%; intracranial haemorrhage, stroke, peripheral nervous system involvement) and immunological involvement (33.3%; lymphopaenia, hypoglobulinaemia). Disease was well controlled in 11 patients using anti-TNF-α therapy. CECR1 mRNA expression and ADA2 enzyme activity in patients with DADA2 were significantly decreased compared to healthy controls. DADA2 affected the differentiation of monocytes into M1 and M2 macrophage in some patients.
Conclusions: The clinical severity of DADA2 is heterogeneous ranging from asymptomatic to full-blown systemic PAN. DADA2 affects the function and polarisation of macrophages and may be involved in the vaso-protective mechanism of endothelial cells. ADA2 enzyme activity and CECR1 mRNA expression may be used as a clinical screening test for DADA2, and/ or as a functional readout to confirm pathogenicity for patients identified to have CECR1 variants of unknown significance, or heterozygous mutations.

P–130

Cyclophosphamide as Successful Adjunct treatment in Patients with Adult Onset Immunodeficiency Disease associated with Interferon-gamma Autoantibodies

Wannada Laisuan, Chamard Wongsa, Porntip Intapiboon

Division of Allergy, Immunology and Rheumatology, Department of Medicine, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

Introduction: Interferon-gamma (IFN-g) autoantibodies have been reported to be associated with adult-onset immunodeficiency in patients from Southeast Asia. This syndrome has been strongly related to the opportunistic infections especially nontuberculous mycobacteria. More than half of the patients had persistent or relapsed infection, despite intensive antibiotic treatment. Rituximab was reported as the successful treatment in refractory cases, however, few patients can afford this regimen.
Objective: To study the efficacy of cyclophosphamide for treatment in patients with refractory to antibiotics with adult-onset immunodeficiency disease associated with IFN-g autoantibodies.
Results: Four patients who had refractory to antibiotics and/or relapsed infection associated with interferon-gamma autoantibodies were included in this study. All patients received intravenous cyclophosphamide therapy which classified into 2 protocol by the frequency of injection with average 5-12 mg/kg/dose. The clinical response and laboratory markers such as white blood cell count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and IFN-g autoantibodies titers were determined. The ratio of male: female is 1:1. All patients had disseminated non mycobacterium tuberculosis infection more than two episodes, and the most common clinical manifestation is lymphadenopathy, constitutional symptoms with Sweet's syndrome. Three of them had hearing-loss post amikacin treatment. Following the cyclophosphamide regimens, all patients achieved the clinical response and remission with significantly decrease in the level of white blood cell, CRP and ESR. One patient has been achieving the clinical remission without the antibiotics even though the cyclophosphamide was stopped for 6 months.
Conclusion: Cyclophosphamide should be considered as the adjunctive treatment in patient with adult-onset immunodeficiency disease associated with interferon-gamma autoantibodies who had persistent or recurrent infection and refractory to antibiotics.