Oral Presentation 6

· **Date:** May 13, Saturday 2017

· **Chairs:** Jong Myung Lee (Kyungpook Nat'l Univ.), Man Yong Han (CHA Univ.)

OP-61

Alteration in hysteresis-dependency of spirometric measurements by controller asthma treatments in acute asthma

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Background: We previously demonstrated that the hysteresis effect of FVC maneuver primarily depends on spontaneous airflow limitation, but not on lung function change induced by methacholine or beta agonist in asthma. This study was performed to investigate whether alteration of spontaneous airflow limitation by asthma treatment affect on the hysteresis in acute asthma.
Methods: Fifteen among 76 patients hospitalized due to acute asthma to Chonnam National University Hospital between March 2006 and Ferburary 2007, whose airflow limitations were significantly improved with controller treatment, were included in this study. The flow-volume loops obtained from tidal breathing as well TLC during FVC maneuver and the flow at 40% FVC from TLC (T) was compared to the flow at isovolume from partial FV loop (P).
Results: The duration of hospitalization was 10.9±6.2 days. The FEV1 significantly increased from 45.1±17.1% to 60.8±23.2% ($p<0.001$) and the T/P ratio also significantly increased from 0.71±0.17 to 0.96±0.31 ($p=0.033$). The morning FEV1 significantly decreased from 55.8±24.0% of the afternoon FEV1 to 51.6±22.6% ($p=0.013$) and the T/P ratio also significantly decreased from 1.05±0.31 to 0.84±0.29 ($p=0.026$).
Conclusion: The controller asthma treatment improving lung function seems to increase the T/P ratio probably due to restoring the interdependence between the airways and lung parenchyma in acute asthma. The spontaneous airflow limitation in the morning also seems to relate to increased parenchymal hysteresis with airway inflammation.

Key Words: Asthma; Hysteresis; Treatment

OP-62

Environmental compound-induced lung inflammation can be improved by an indole derivative

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There is evidence on the implication of various environmental compounds in fatal lung injury. Mitochondria are crucial organelles in many lung diseases. Recently, we developed novel necrosis inhibitors, NecroX compound (NecroX), which preserve mitochondrial functionalities. We aim to evaluate therapeutic potential and related action mechanisms of NecroXs in environmental compound-induced lung injury. We investigated therapeutic effects of NecroXs on lung injury associated with polyhexamethylene guanidine (PHMG) and bleomycin in mice, focusing on functionalities of mitochondria and endoplasmic reticulum (ER). Moreover, we checked the expression of an ER stress marker in human lung tissues with fatal injury. Respiratory exposure to PHMG and bleomycin led to lung injury manifesting inflammation followed by fibrosis in the lung parenchyma, which were further verified by histopathologic and radiologic measurements. Exposure to these compounds impacted on mitochondria in regard to biogenesis, mitochondrial DNA (mtDNA) integrity, and generation of mitochondrial reactive oxygen species (mtROS) in various cells of the lung. Notably, NecroXs improved pathobiologic features of environmental compound-induced lung injury through regulation of mitochondrial functionalities including biogenesis, mtDNA integrity, and generation of mtROS. Additionally, ER stress was implicated in fatal lung injury of mice and human, and NecroXs improved lung injury partly via regulation of ER stress.

Key Words: polyhexamethylene guanidine, mitochondira, reactive oxygen species

OP-63

Effect of Omalizumab on Severe Asthma: A Real World Study in Korea

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Background: Omalizumab, anti-IgE monoclonal antibody, has proven to be effective for the treatment of severe persistent asthma. This is the first real-world study to evaluate the effect of Omalizumab in Korean adult patients suffering from severe asthma.
Patients and methods: A retrospective analysis of electrical medical record was performed on severe persistent asthma patients treated with Omalizumab (ranged from 150mg to 450mg, group A) for more than 6 months between 10 March 2008 to 23 February 2016 at Ajou University Hospital. Propensity score matching was applied to define the control group who had been treated with standardized pharmacologic treatment except Omalizumab (group B). Changes in asthma exacerbations (AEs), systemic steroid requirements, hospitalization and FEV1% were compared between group A and B, and analyzed before and after Omalizumab treatment in group A. The aim of this study was to evaluate the real world effectiveness of Omalizumab in severe asthma patients and to find parameters for predicting favorable responders (having >50% reduction in AE and/or systemic steroid requirement during study period).
Results: Sixty two patients of group A (mean age: 44.5 years, 36 female) and group B (mean age: 46.3 years, 27 female) were enrolled. Favorable responders were significantly higher in group A than in group B (67.7%. vs 41.9%, P =0.007). Significant differences were noted in reduction of AE (P =0.006), hospitalization (P =0.009), hospitalization days (P =0.006), dose of systemic corticosteroid (P =0.027) and sputum eosinophil counts (P =0.031) between group A B after the treatment. No significant associations were found in atopic status, aspirin intolerance, asthma duration, FEV1%, serum total IgE level, and blood eosinophil counts between favorable and unfavorable responders in group A.
Conclusion: We confirmed that Omalizumab can reduce AE/hospitalization/systemic steroid burst in severe asthma patients in real-world practice in Korea.

Key Words: Omalizumab, severe asthma, asthma exacerbation

OP-64

Effects of Immunoglobulin Replacement on Asthma Exacerbation in Adult Asthmatics with IgG Subclass Deficiency

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Purpose: Recurrent respiratory tract infection is a common manifestation of primary immunodeficiency disease, and respiratory viruses or bacteria are important triggers of asthma exacerbations. Asthma often coexists with humoral immunodeficiency in adults and some asthmatics with immunoglobulin (Ig) G subclass deficiency (IgGSCD) suffer from recurrent exacerbations. Although some studies suggest a benefit from Ig replacement, others have failed to support its use. This study aimed to assess the effect of Ig replacement on asthma exacerbation caused by respiratory infection in, as well as the asthma control status of, adult asthmatics with IgGSCD.
Methods: This was a multi-center, open-label study of adult asthmatics with IgGSCD. All patients received monthly intravenous immunoglobulin (IVIG) for 6 months and were evaluated regarding asthma exacerbation related to infection, asthma control status, quality of life, and lung function pre- and post- IVIG infusion.
Results: A total of 30 patients were enrolled, and 24 completed the study. Most of the patients had a moderate degree of asthma severity with partly (52%) or uncontrolled (41%) status at baseline. IVIG significantly reduced the proportion of patients with asthma exacerbations, the number of respiratory infections, and asthma control status, compared to the baseline values ($p<0.001$). The mean asthma-specific quality of life and asthma control test scores improved significantly ($p=0.009$ and $p=0.053$), however, there were no significant changes in lung function.
Conclusions: IVIG reduced the frequency of asthma exacerbations and improved asthma control status in adult asthmatics with IgGSCD, suggesting that IVIG could be an effective treatment option in this population.

Key Words: Asthma, Exacerbation, Immunodeficiency, Immunoglobulins, Intravenous

OP-65

Response of FeNO, small airway dysfunction and lung heterogeneity in montelukast with 2 week short term treatment with asthma

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Background: Leukotriene receptor antagonist (LTRA) is known to reduce airway obstruction, small airway dysfunction, lung heterogeneity, airway inflammation and airway hyperresponsiveness.
Purpose: This study aims to identify markers to prove rapid improvement of lung function, airway inflammation and bronchodilator response after 2-week LTRA administration.
Methods: Thirty-two children aged 3-12 years with mild, well-controlled, persistent asthma were randomized into a double-blind, placebo-controlled, cross-over study to receive montelukast 4 - 5 mg or placebo daily for 2 weeks. Airway inflammation with exhaled NO (FeNO), small airway dysfunction with an impulse oscillation system (IOS), lung heterogeneity with multiple breath washout test (MBW) and forced expiratory volume in 1 second (FEV1) with spirometry before and after 4 puff salbutamol.
Results: Eight subjects (25%) showed symptom aggravation while on medication, 7 (87.5%) of which were on placebo. There was significant difference in resistance at 5 hz on IOS between the subjects with symptom aggravation and the rest (z score 0.18 vs. 0.94, P = 0.006). FeNO improved in LTRA administered patients at 2 weeks compared with those treated with placebo, while small airway dysfunction, FEV1 and lung heterogeneity did not show significant difference after 2-week treatment. Moreover, airway hyperresponsiveness showed no statistical difference.
Conclusion: Airway inflammation was the earliest responding marker, and small airway dysfuction was a predictor of symptom aggravation in asthmatic patients after 2-week montelukast treatment.

Key Words: Montelukast, FeNO, IOS, Spirometry, MBW, Bronchodilator response

OP-66

New Education Method for Asthma Control in Patients with Well or Partly Controlled Asthma

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Background: Education on inhaler technique is critical for asthma treatment. However, traditionally used face-to-face education is a time-consuming, costly, and often effort-wasting method.
Objective: To evaluate the efficacy of a newly developed method of video-based education on inhaler technique.
Methods: A total 184 subjects with well- or partly controlled asthma were enrolled from 12 hospitals in South Korea from November 30, 2015 to June 1, 2016. Subjects were randomly divided into two groups in a 1:1 ratio: the control group, which received face-to-face education, and the study group, which received video education. All subjects received fluticasone propionate plus salmeterol xinafoate (Fluterol® 250/50 inhalation capsules) for 12 weeks.
Results: The forced expiratory volume in 1 second (FEV1) was significantly improved at 12 weeks in both control and study groups, but FEV1 improvement was not significantly different between the two groups after adjustment. Secondary outcome measures, including change in FEV1 at 4 weeks, asthma control test, and various parameters concerning inhaler technique and satisfaction at 4 and 12 weeks, were not significantly different between the two groups. Subgroup analysis of elderly subjects and subjects with well-controlled asthma showed that FEV1 was significantly improved at 12 weeks in the study group, but not in the control group.
Conclusion: This study showed that newly developed video education can be suitable to substitute the face to face education to educate well or partly controlled asthma patients for inhaler technique, especially in old patients and well controlled asthma patients.

Key Words: Asthma, inhaler, education

OP-67

Development of a monoclonal antibody-based sandwich ELISA for quantification of buckwheat allergen Fag e 3

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Background: Buckwheat is a major cause of anaphylaxis, and Fag e 3 is the key major allergen in buckwheat. However, an immunoassay system for the quantification of Fag e 3 has yet to be developed.
Methods: We developed a two-site ELISA using monoclonal antibodies produced against recombinant Fag e 3. We applied this ELISA to quantify native Fag e 3 in total buckwheat extract.
Results: Four clones of monoclonal antibodies were produced, and all recognized vicilin allergens not only from buckwheat, but also from peanut and walnut. However, the ELISA using these antibodies was only able to quantify Fag e 3 in the total extract after addition of 1% SDS and heating, which facilitated dissociation of the allergen. The detection limit of the developed two-site ELISA was 0.8 μg/mL. The measurement of Fag e 3 in the total extract of buckwheat showed that approximately 12% of protein in total buckwheat extract was Fag e 3.
Conclusions: We have developed an ELISA system for the quantification of the group 3 buckwheat allergen, Fag e 3, specifically. This assay will be useful for standardization of buckwheat allergens and monitoring of buckwheat contamination in foods.

Key Words: Buckwheat, Fag e 3, vicilin

OP-68

Comparison of Korean made inhalant Skin Prick Test Reagents with Commercial Skin Prick Test Reagents using in vivo and in vitro Methods

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Aims & Background: Several commercial skin prick test (SPT) reagents are available. However, each manufacturer utilizes its own potency unit and quality control programs. Also, they made their own raw allergen materials which may not reflect regional allergen distribution in each country.
We developed new inhalant allergens SPT reagent that reflects the environmental characteristics of Korea and compare its efficacy and potency with available commercial SPT reagents in Korea. Allergenicity of our 8 important inhalant allergens (D. farinae, D. pteronyssinus, pollens of oak, ragweed, mugwort, and Japanese Hop, cat dander, dog dander) were compared with 3 different commercial products.
Methods: For comparison of in vitro properties, Bradford assay, SDS-PAGE, 2-site ELISA, inhibition assay with ImmunoCAP® and Western-blot were used. For in vivo comparison, 94 allergic patients were enrolled for SPT. Analysis of SPT positivity and concordance rates with ImmunoCAP® results were compared.
Results: Positivity and concordance rate with results of ImmunoCAP® were varies significantly among SPT reagents in each allergen. In concordance rate of allergens to ImmunoCAP® results, kappa showed variable results of 0.209 to 0.849 (fair to moderate). Especially, Yonsei products showed non-inferior results at the concordance rate with ImmunoCAP compared with other products. Significant differences in the concentration of major allergen of house dust mite, pet animals were found among the 4 different products. The results of 50% inhibition concentration, which directly reflects allergenicity of SPT reagents, were also showed significant differences. Allergen potencies vary among commercial SPT reagents.
Conclusions: Korean made inhalant SPT reagents were not inferior compared to commercial SPT Reagents. However, there were some differences in concordance rate with ImmunoCAP and clinicians should consider properties of each SPT reagents when they prescribe SPT.

Key Words: Skin prick test (SPT), inhalant allergens, Allergy diagnosis

OP-69

Comparative analysis between Provocholine and mannitol bronchial provocation test in the diagnosis of asthma in patients with chronic cough or symptoms suggestive of asthma

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Background: Bronchial provocation test (BPT) with methacholine has been used to measure airway responsiveness with a concern of safety profile. Provocholine, an FDA-approved methacholine formulation, was replaced industrial methacholine by law since September 2015 in Korea. The efficacy and safety of mannitol was demonstrated and mannitol BPT has a high specificity for diagnosis of asthma.
Objective: The aim of this study is to compare the results of BPT with between Provocholine and mannitol in patients with chronic cough.
Methods: A total of 545 patients with chronic cough or symptoms suggestive of asthma underwent BPT with either Provocholine (n=321) or mannitol (n=224) at Dong-A university hospital from January 2015 to December 2016.
Results: The patients in Provocholine group were younger than patients in mannitol group (43.16±17.55 years vs 47.13±16.82 years, P=0.008). Of the total patients, 15.9% and 24.6% had airway hyperresponsiveness to Provocholine and mannitol, respectively. Bronchial asthma was 24.3% and 48.2% in each group, and 59% and 47.2% had airway hyperresponsiveness of them. Among asthmatics, the proportion of patients previously treated with bronchial asthma was higher in mannitol group (16.7% vs 34.3%, P=0.008). The sensitivity Provocholine and mannitol for the diagnosis of asthma was 59% and 47.2%, specificity 97.9% vs 96.6%, positive predictive value 90.2% vs 92.7%, and negative predictive value 88.1% vs 66.3%, respectively.
Conclusion: BPT with Provocholine showed better sensitivity and specificity than mannitol in the diagnosis of asthma.

Key Words: Asthma; mannitol; Provocholine

OP-70

Implication of inspiratory and expiratory resistance and reactance in pediatric asthma

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Background: Impulse Oscillometry (IOS) is an easy-performing tool to evaluate lung function by measuring respiratory resistance and reactance using tidal breaths. Respiratory resistance and reactance can be measured separately during inspiration and expiration (inspiratory-expiratory analysis).
Objectives: We investigated the differences of inspiratory-expiratory measurements obtained by IOS between children with asthma and control subjects.
Methods: We analyzed 827 children aged 4 to 18 years including asthmatic children (n = 608) and controls (n = 219). Asthma was diagnosed in accordance with ATS/ERS guideline. Spirometry and IOS were performed in all subjects.
Results: In whole-breath analysis, children with asthma have higher resistance at 5 Hz (R5) and reactance area (AX) and lower reactance at 5 Hz (X5) than those of controls. In inspiratory-expiratory analysis, asthmatic children showed increased expiratory R5 and AX and decreased expiratory X5 compared with control group. The changes in R5, X5 and AX between inspiration and expiration showed a greater absolute value in children with asthma than control (0.138 ± 0.195 vs. 0.102 ± 0.162, P=0.014; -0.106 ± 0.200 vs. -0.086 ± 0.434, P<0.001; 0.460 ± 11.63 vs. 0.398 ± 2.88, P=0.002, respectively).
Conclusion: Inspiratory-expiratory IOS analysis differentiated asthmatic children from the control subjects, reflecting airway narrowing on expiration in pediatric asthma. The changes in R5, X5 and AX between inspiration and expiration can be useful index to diagnose asthma in children without assessment response to bronchodilator.

Key Words: Asthma, impulse oscillation system, inspiratory-expiratory analysis

OP-71

Humidifier disinfectants increase the risk of childhood asthma

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Background: In South Korea, a cluster of humidifier disinfectant-induced lung injury (HDLI) cases developed between 2006 and 2011. However, the risk of humidifier disinfectants (HDs) on allergic airway diseases in children remains unknown. The purpose of this study was to investigate whether exposure to HDs in young children affect asthma development later in life.
Methods: This is a general population-based birth cohort multicenter study, Panel Study of Korean Children (PSKC) from 2008, HDs-related questionnaires were administered to 1577 subjects in 2015. Development of asthma in aged 5 to 7 years was evaluated by reporting of wheezing symptoms and asthma treatment during the last 12 months, and diagnosis ever in the lifetime from 2013 to 2015.
Results: There was no association between HDs exposure and asthma development in the whole study population. However, HDs exposure was associated with 2.25-fold greater likelihood of having asthma treatment during the last 12months (95% CI, 1.01-5.00) in children who had history of acute bronchiolitis before 3 years of age group. When we divided into four groups according to the HDs exposure and the history of acute bronchiolitis, the risk of asthma treatment during the last 12 months was higher for groups who exposed to HDs with acute bronchiolitis than those without exposed to HDs with acute bronchiolitis. (aOR 5.07, 95% CI 2.52-10.20 vs. aOR 2.20, 95% CI 1.07-4.52)
Conclusion: We propose a novel hypothesis that HD exposure exacerbate and/or induce asthma in a certain group who had a history of acute bronchiolitis before 3 years of age. These results are the first to link early-life HDs exposure to later development of asthma using a natural experiment in a birth cohort study.The mechanism related to allergic airway diseases needs to be investigated.
Funding: This study was supported by a fund (2015-ER6601-00) from the Research of KCDC, Environmental Health Center for Hazardous Chemical Exposure (2017), and KICCE

Key Words: Humidifier disinfectants, asthma, acute bronchiolitis

OP-72

Association between allergic disease and suicidal behaviors in Korean adolescents

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Background: There is growing literature focusing on psychosomatic aspects of allergic diseases. Obesity also has bidirectional association with psychosocial factors. However, no previous studies have explored psychological behaviors in adolescents with comorbid allergic disease and obesity.
Methods: This study included 427,895 participants aged 12 to 18 who completed the Korea Youth Risk Behavior Web-based Survey from 2011 to 2016. The subjects' reported diagnosis of allergic disease (atopic dermatitis(AD), allergic rhinitis(AR), bronchial asthma(BA)), height, weight and answers to questions about depressive symptoms and suicidal behaviors were examined. The relationships between the disease status and suicidal behaviors were analyzed using multiple logistic regression models.
Results: Youth with comorbid BA+obesity demonstrated significantly higher prevalence of suicidal ideation than those with obesity-only (OR (95%CI); 1.38 (1.10-1.64)) and BA-only (1.21 (1.03-1.42)). Suicidal planning was also found to be more frequent in BA+obesity group than obesity-only (1.93 (1.51-2.47)) and BA-only group (1.32 (1.07-1.63)). AR+obesity group also showed increased odds of suicidal ideation (1.27 (1.16-1.39)) and planning (1.33 (1.14-1.54)) compared to obesity-only group. Similar differences were noted in between AR+obesity group(1.10 (1.03-1.18)) and AR-only group (1.21 (1.09-1.34)). In AD+obesity group, there was increased odds of suicidal ideation (1.12 (1,00-1.26)) compared to obesity-only group, however, no differences were noted compared to AD-only group.
Conclusion: Youth with allergic disease+obesity was significantly more likely to have suicidal behaviors compared to those with obesity-only and allergic disease-only. Allergic disease and obesity could affect suicidal behaviors additively and negatively in Korean adolescents.

Key Words: allergic disease, suicidal behavior, youth, Korea Youth Risk Behavior Web-based Survey (KYRBWS)