Oral Presentation 2

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OP-13

Influence of Thermal Processing on the Allergenicity of Walnut

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Background: Walnut (WN) is an emerging major allergen in Korea. As the WN used in diet comes from Juglans regia and Juglans nigra, the molecular characterization from both species including 3 superfamilies of proteins, namely the prolamin (Jug r 1, Jug n 1 and Jug r 3), cupin (Jug r 2, Jug n 2 and Jug r 4) and the profilin (Jug r 5). The consumption of WN is not only with a raw type but also with baked or boiled type in Korean children and this might contribute to the severity of allergic reactions in WN allergic patients. However, the influence of processing on the allergenicity of WN is not largely known so far.
Method: Crude extracts from raw, boiled (100°C, 10 minutes), and roasted (Frying pan 110°C, 8 minutes) WN were assessed by 2D PAGE for the comparison of protein profiles. IgE-binding proteins were studied using pooled sera from WN allergic children under 6 years of age. Proteins (peptides) profiles with or without thermal processing were analyzed using proteomic analysis (EIM, electrospray ionization mass).
Results: Multiple IgE-binding proteins were detected in the different WN preparations and many of which were dissemblance in 2D-blotting. Profiles of detectable proteins (peptides) of raw, roasted and boiled WN extracts were profoundly different in EMI analysis. Fifty seven of the 66 raw WN proteins were also recognized in the roasted WN. Meanwhile, only 4 of the 66 raw WN proteins were recognized in boiled WN. Four proteins which were stable to the all of thermal processing were identified, and those are prolamins (albumin seed storage protein, nonspecific lipid transfer protein) superoxide dismutase 3 and glyceraldehydes-3-phosphate dehydrogenase.
Conclusions: This study shows that protein profiling of boiled WN are significantly different from raw WN, however 4 proteins including prolamins are still identified after boiling or roasting. Further studies are needed to evaluatethe clinical relevance of these findings.

Key Words: Food allergy, Walnut, Allergenicity

OP-14

Oral allergy syndrome in pollen allergy in Korea : multicenter cross-sectional study

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Background: Oral allergy syndrome (OAS) is an IgE-mediated allergy caused by raw fruits and vegetables in patients with pollen allergy, which is known as the most common food allergy in adults. However, there has been no nation-wide study on oral allergy syndrome in Korea
Objective: To investigate the prevalence and clinical manifestations of OAS in Korea
Methods: Twenty two investigators from 19 hospitals and 2 private clinics participated in this study. The patients with allergic rhinoconjunctivitis and/or bronchial asthma with pollen allergy were enrolled to the survey. The questionnaires include demographics, a list of fruits and vegetables, and clinical manifestations of food allergy. Pollen allergies were diagnosed by positive results of one or more pollen allergens including birch, alder, hazel, beech, oak, willow, poplar, bermuda, meadow, orchard, rye, timothy, mugwort, ragweed, Hop japanese on allergy skin prick tests (A/H ratio ≥ 3+) and/or serum specific IgE levels using Multiple Allergen Simultaneous tests (MAST ≥ 2+) or immunoCAP (≥ 1+).
Results: A total of 673 pollen allergy patients answered the questionnaires. The prevalence of OAS was 41.7% (n=277). The OAS patients have allergic rhinitis (96.0%), allergic conjunctivitis (55.2%), and asthma (43.7%). The OAS patients was accompanied by cutaneous (42.2%), respiratory (19.9%), cadiovascular (10.8%), or neurologic symptoms (5.0%) in addition to oropharyngeal symptoms. Anaphylaxis was noted in 9% of OAS patients. Seventy kinds of fruits and vegetables were suggested as causes of OAS: peach (48.3%), apple (46.2%), kiwi (30.7%), peanut (17.0%), plum (16.3%), chestnut(14.4%), pineapple(14.1%), walnut(13.7%), Korean melon (12.6%), tomato(12.3%), melon(11.6%), apricot(11.2%), etc. in order of prevalences. There were also taro stems (9.0%), ginseng (7.9%), perilla leaf (5.0%), bellflower root (4.3%), crown daisy (3.3%), Deodeok (3.25%), kudzu root (2.9%), and lotus root (2.9%), which represents Korean eating habits.
Conclusion: This is the first nation-wide study for OAS in Korea. The prevalence of OAS in Korea was 41.7%, in which substantial proportion had anaphylaxis. These results will provide useful information for clinicians to apply in clinical practice.

Key Words: Oral allergy syndrome, Pollen, Food

OP-15

Accurate Assessment of Alpha-gal Syndrome using Cetuximab and Bovine Thyroglobulin-specific IgE

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Scope: IgE against galactose-α-1,3-galactose (α-Gal) cause alpha-gal syndrome. Bovine thyroglobulin (BTG) and cetuximab share this epitope. We aimed to determine the utility of specific IgE (sIgE) against cetuximab as compared to BTG for discriminating alpha-gal syndrome.
Methods and results: Twelve patients with alpha-gal syndrome, 11 patients with immediate beef or pork allergy, 18 asymptomatic individuals with meat sensitivity, and 10 non-atopic subjects were enrolled. We checked the levels of sIgE against BTG and cetuximab using the streptavidin CAP assay. Additionally, IgE reactivity to BTG and cetuximab was assessed by immunoblotting. All alpha-gal syndrome patients had a high sIgE concentration against BTG, and cetuximab. In contrast to alpha-gal syndrome, patients with immediate allergic reactions to meat consumption and those with asymptomatic sensitization had significantly lower concentration of BTG and cetuximab sIgE, and a high prevalence of sIgE against bovine or porcine serum albumin. Although the concentration of sIgE against alpha-gal was lower in individuals with asymptomatic sensitization, IgE immunoblotting showed the presence of sIgE against α-Gal in this group.
Conclusion: Differentiation of alpha-gal syndrome from patients with immediate allergy to meat consumption or asymptomatic sensitization requires quantification of cetuximab- or BTG-induced sIgE via detection of IgE for α-gal.

Key Words: Alpha-gal syndrome; Bovine thyroglobulin-specific IgE; Cetuximab-specific IgE

OP-16

Airborne Formaldehyde Exacerbates Skin Barrier Dysfunction In Atopic Dermatitis

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Formaldehyde (HCHO), an indoor air pollutant emitted from building materials, has been known to aggravate the symptoms of atopic dermatitis (AD). However, it remains controversial how airborne HCHO affects the skin of AD.
In this study, we investigated the effects of airborne HCHO exposure on the skin barrier in AD using the atopic-prone NC/Nga mice.
Four-week-old female NC/Nga mice were divided into 4 groups: (1) negative control group, (2) house dust mite (HDM) group in which HDM was topically applied on the skin, (3) HDM plus 2 ppm HCHO-exposed group and (4) HDM plus 5 ppm HCHO-exposed group. After 1 week of acclimation, mice were topically treated with 100 mg of HDM on dorsal skin twice a week. One day after the first application of HDM, mice were exposed to airborne HCHO (2 and 5 ppm) in a chamber for 4 hours a day for 5 days.
Two days after the last HCHO exposure, the dorsal skin of mice was collected to estimate the clinical, histological and immunological alterations. The clinical severity of AD-like skin lesions in mice was measured by using a modified SCORAD (SCORing of Atopic Dermatitis) index. Expression of skin barrier proteins, such as filaggrin and sodium hydrogen exchanger 1 (NHE1) were evaluated by western blot analysis.
Topical application of HDM increased epidermal thickness, the number of degranulated mast cell, and the severity of skin lesions. In HDM plus HCHO-exposed group, epidermal thickness, the severity scores and mast cell degranulation was significantly increased than in HDM group. The exposure to airborne HCHO at 2 ppm caused abnormal processing of profilaggrin to filaggrin, and also reduced the expression level of NHE1, a regulator of pH in skin.
Our results suggest that airborne HCHO exposure to the skin in AD might aggravate skin barrier dysfunction by activating mast cells and altering the expression of filaggrin and NHE1.

Key Words: Formaldehyde, Filaggrin, Atopic Dermatitis

OP-17

TLR3-Agonist Primed Mesenchymal Stem Cells Decreased T Helper 2 and 17 Immune Responses in Skin Draining Lymph Node of Atopic Dermatitis Model Induced by Aspergillus fumigatus

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Purpose: Atopic dermatitis (AD) is a chronic and relapsing inflammatory skin disease. Mesenchymal stem cells (MSC) have an immunomodulatory effect. Enhancement of immunomodulatory effect of MSC is needed to apply to the treatment of atopic dermatitis, although MSC were known to have a therapeutic effect on the atopic dermatitis in a clinical trial and in vivo models. We investigated whether TLR3 agonist enhances the therapeutic effect of human umbilical cord derived MSC (UC-MSC) for AD using a murine model.
Methods: We applied Aspergillus fumigatus (Af) extract (40 μg) to the dorsal skin of BALB/c mice 5 times a week repeatedly with an interval of 2weeks to induce AD-like skin lesions. UC-MSC (2x107/mL) and UC-MSC treated with TLR3 agonist, poly (I:C) (UC-MSC poly I:C) were injected subcutaneously at the last day of Af application. Clinical score and transepidermal water loss (TEWL) were assessed and histology was examined at 5 days after injection of UC-MSC and UC-MSC poly I:C. The levels of interferon (IFN)-γ, IL-13, IL-10 or IL-17 were measured in skin draining lymph node (LN) stimulated with CD3/CD28.
Results: The clinical score and TEWL were decreased after subcutaneous injection of both UC-MSC and UC-MSC poly I:C without a significant difference between two UC-MSCs. However, UC-MSC poly I:C inhibited inflammatory infiltrate in skin lesions compared with UC-MSC. Moreover, the levels of IL-13 and IL-17 were decreased in LN of UC-MSC poly I:C, compared to LN of UC-MSC.
Conclusion: UC-MSC poly I:C alleviated skin inflammation and decreased T helper 2 and 17 immune response in a murine model, which suggest that therapeutic effect of UC-MSC can be enhanced by poly (I:C) through the modulation of Th2 and Th17 immune response.

Key Words: Atopic dermatitis, Mesenchymal stem cells, Aspergillus fumigatus

OP-18

Perturbations of the colonizing gut microbiome and their functions in early life affect the development of Atopic Dermatitis

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Background: Perturbations of the developing gut microbiota in early life can shape the development of immune system and directly associated with the risk of allergic diseases. Therefore, the analysis of gut microbiome in infancy is important to understand the development of allergic disease.
Methods: In this study, we analyzed the gut microbiota in collected fecal samples from 129 infants (6-month age), including 66 healthy infants (control) and 63 infants with atopic dermatitis (AD). The composition and functional profile of gut microbiome were analyzed by pyrosequencing based on 16S rRNA genes and whole metagenome sequencing. In addition, the quantity of total bacteria in feces were determined by real-time PCR.
Results: The compositions and colonized cell amounts of 6-month infant gut microbiota were differently developed mainly by feeding type. Bifidobacterium dominated microbiota and Escehrichia/Veillonella dominated microbiota were found in each feeding type. The bacterial cell amounts in gut microbiota were lower in infants with AD than that in controls. Although the specific taxa related to AD was not found, the difference of functional genes related to immune development was found in whole metagenome analysis. Diverse microbes and mucin-degrading bacteria (Akkermansia muciniphila and other bacteria) were highly contributed to metabolisms of NOD-like receptor signaling pathway, and antigen processing and presentation in control group compared to AD group ($P < 0.05$).
Conclusion: The dysbiosis of immune development by differently colonizing gut microbiome at 6-month infant may be associated with the development atopic dermatitis, mediated by innate immune and antigen presentation pathway.

Key Words: Gut microbiome, dysbiosis, atopic dermatitis

OP-19

Carbonic anhydrase inhibitors-induced Severe Cutaneous Adverse Reactions: Analysis of Korean SCAR Registry Database 2010-2015

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Background: Severe Cutaneous Adverse Reactions (SCARs) including Stevens-Johnson syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) by carbonic anhydrase inhibitors (CAIs) have been reported in patients of Asian descent. The aim of study was to describe clinical characteristics and outcomes of CAIs-induced SCARs.
Methods: SCAR cases between 2010 and 2015 were retrospectively analyzed using a web-based Korean SCAR Registry database. SCARs caused by CAIs were compared with other drug-induced SCARs.
Results: Of the 783 patients with SCARs, 15 (1.9%) cases were reported CAIs including methazolamide and acetazolamide as major culprit drugs. They all developed SJS or TEN, but no Drug Reaction with Eosinophilia and Systemic Symptoms. More than half the CAIs-induced SCAR cases developed TEN (n=8, 53.5%), followed by SJS/TEN overlap (n=4, 26.7%) and SJS (n=3, 20%). The period of hospitalization was 24.5±14.1 days, which was longer than SJS/TEN cases caused by other drugs. The mean duration of exposure and latent period was 9.1±8.0 days and 11.3±5.7 days. CAIs-induced SJS/TEN cases had higher than average rate of complications (20% vs. 8.4%).
Conclusion: SCAR cases related with CAIs showed the most severe manifestations and poor prognosis despite the relatively short period of drug exposure.

Key Words: Carbonic anhydrase inhibitor, Severe cutaneous adverse reactions, Registry

OP-20

Clinical Efficacy of Prescreening Intradermal Skin Tests with Cephalosporin Antibiotics: A multicenter retrospective study in Korea

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Introduction: Prescreening intradermal skin test before using intravenous antibiotics is common practice in Korea. However, the clinical efficacy of prescreening skin test is not validated.
Objective: To assess the clinical efficacy of prescreening skin test with cephalosporin antibiotics
Methods: A retrospective review of medical records was conducted between January 1st, 2013 and December 31st, 2015 in 12 Korean hospitals. During study period, 8 hospitals (study groups) provided prescreening intradermal skin tests to all patients before using intravenous cephalosporin antibiotics and 4 hospitals (control groups) did not. Primary outcome was the difference in the incidence of anaphylaxis between 2 groups. Twenty one kinds of cephalosporin antibiotics were included in the analysis. The information of total usage of cephalosporin antibiotics and the cases of anaphylaxis related with dose medication was provided from each hospital. The unit of analysis was a treatment course which was defined as maintenance of one cephalosporin antibiotic on a continuous basis without interruption.
Result: Total treatment courses used in all 12 hospitals were 1,140,354 (605,851 for study and 534,503 control groups). A total of 21 anaphylaxis consisted of three 1st generation, nine 2nd generation, six 3rd generation, and three 4th generation cephalosporin antibiotics were included in the analysis. There were at least one case of anaphylaxis after using 12 out of 21 antibiotics. However, the numbers of anaphylaxis were not significantly different between two groups (32 for the study group and 44 for the control group, 0.01% vs. 0.008%, $p = 0.0554$). When analyzed for each antibiotic frequently used in both groups, there was no difference in the incidence of anaphylaxis according to the prescreening of antibiotics pretest.
Conclusion: The prescreening skin test with cephalosporin antibiotics showed no significant clinical efficacy for the prevention of anaphylaxis.

Key Words: Prescreening intradermal skin test, Cephalosporin, Efficacy

OP-21

Genome-wide association study (GWAS) using two different control groups identified novel genetic variations in drug hypersensitivity

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Drug hypersensitivity accounts for about 5 to 15% of all adverse drug reactions (ADRs) and it is unpredictable. To date, the mechanism of drug hypersensitivity has not been clearly elucidated, but the most relevant mechanism is known as the genetic factors. However, most studies have focused on specific phenotypes or drugs. Thus, we planned to perform a genome-wide association (GWAS) study to discover the common genetic markers associated with both in immediate and delayed drug hypersensitivity reactions.
We studied 190 patients who were diagnosed with drug hypersensitivity at an Asan Medical Center. We extracted genomic DNA from peripheral blood lymphocytes and genotyped with the Affymetrix Axiom Asian chip. The control subjects were selected by calculated principal component score (PC score) from Korean Association Resource (KARE) data (Affymetrix 5.0) and Cohort of rural (Illumina exome chip) respectively (Three times the number of subjects to be analyzed). The analysis was performed in three ways; immediate and delayed reactions were compared to the control group, the total hypersensitivity was compared to the control group, and three groups were independently compared.
First, significant top 3 SNPs were obtained as compared with the KARE control group in an analysis of all the various methods performed. The top 3 SNPs were rs6448057, rs270928, and rs79185118. We then analyzed the Cohort of rural as a control and obtained the significant top 3 SNPs in all of the various analyses, which were rs6448057, rs2579824, and rs11920283. In the both comparisons, the most significant and identical SNP was rs6448057, which is a SNP of the Kv channel in interacting protein 4 (KCNIP4) gene on chromosome 4.
Genetic variants of the KCNIP4 gene might be significant genetic markers of drug hypersensitivity reactions. Replication analysis with other subjects and functional studies are needed to validate the potential involvement of KCNIP4 in modulating drug hypersensitivity.

Key Words: Drug hypersensitivity, Genome-wide association study (GWAS), Adverse drug reaction (ADR)

OP-22

Characteristics of Severe Cutaneous Adverse Reactions induced by Nonsteroidal anti-inflammatory drugs: an experience from the Korean SCAR registry

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Background: We aimed to investigate the characteristics of SCAR induced by NSAIDs through the Korean SCAR registry.
Methods: A total of 34 university hospitals joined the Korean SCARs registry to collect cases with SCAR which occurred from 2010 to 2015. We analyzed 170 registered cases where NSAIDs were responsible for the cause of SCAR.
Results: Among 170 cases of SCARs induced by NSAID, 50.0% (85 cases) of them were Stevens-Johnson syndrome (SJS), 18.8% (32 cases) were Toxic Epidermal Necrosis (TEN), 10.0% (17 cases) were SJS-TEN overlap syndrome, and 21.2% (36 cases) were Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS). SJS was common (60.5%) in acetaminophen-induced SCAR, whereas DRESS was more common (62.5%) than SJS or TEN in coxib-induced SCAR. During the clinical course of SCAR, 133 patients were fully recovered, 26 patients were complicated, and 7 patient expired. The clinical outcome did not differ according to the pharmaceutical classification. Logistic regression analysis revealed that risk factors for complication or death were associated with TEN (OR=35.0, 95% CI, 4.0-305.3, p=0.001) as the manifestation of SCAR, the presence of fever (OR=1.2, 95% CI, 1.0-5.1, p=0.001), and large extent of skin involvement (OR=2.8, 95% CI, 1.1-7.2, p=0.027). While the elevation of serum creatinine level and liver function test were not associated with complication or death, the former was associated with an increase in incidence of ICU admission (OR=7.064, 95% CI, 1.3-37.7, p=0.022) and the latter was associated with an increase in disease duration, admission duration, and extent of skin involvement.
Conclusion: The most common type and causative agent of NSAID-induced SCARs were SJS and acetaminophen in the Korean SCARs registry. The pharmaceutical classification of causative agent was associated with type of SCARs, but not clinical outcome. Risk factors for complication or death were TEN, fever, and extensive skin involvement.

Key Words: Drug Hypersensitivity Syndrome; Anti-Inflammatory Agents, Non-Steroidal; Stevens-Johnson Syndrome

OP-23

Sublingual immunotherapy in elderly rhinitis patient sensitized to house dust mites: a multicenter trial for 12 months

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Background/Aims: Allergic rhinitis(AR) in elderly is increasing with extension of life expectancy. Although immunotherapy in AR patients was proved by various previous reports in efficacy and safety, In this study, we were to find characteristics of elderly AR sensitized to house dust mites (HDMs) and evaluate the safety and efficacy of SLIT with HDMs .
Methods: Total 40 patients older than 60 years-old with HDM sensitized AR (either >3+ A/H ratio on skin prick test and/or >0.35 IU/L by ImmunoCAP to D.farinae and D.pteronyssinus) were enrolled from 4 University Hospitals in South Korea. All patients had taken medications according to their symptoms. To evaluate the additional effects of SLIT with HDMs, they were randomized to either SLIT-treated group with LAIS® Mites Sublingual tablets (Lofarma, Milano, Italy, 2 tablets/week) or observation group with standardized pharmacological treatment. RTSSs/adverse reactions/RQLQ/ACT scores in cases of AR with asthma, were monitored at every 3 months for 2 intervals (V3, V4)) and 6 months interval (V5.)
Results: Of 40 patients, 30 (75.0%) patients were in the treated group, and 10 (25.0%) patients were in the observation group. Mean age was 67.02 years ranged from 60 to 81 years, and male/female ratio was 1.5(24/16). There were no significant differences in demographics, TRSS, skin reactivity to HDMs, and total/ specific IgE levels to HDMs (P>0.05, respectively). Compared to baseline level, significant reductions of TRSS were noted at visit (V)3 (P=0.001) and V5 (P=0.001) in the treated group, and in RQLQ between V3(P=0.015) and V5 (P=0.043). No significant changes were noted in the observation group. ACT score and rhinitis control score did not show differences with clinical significance. Adverse reactions were observed in both groups, but no serious adverse reactions were noted.
Conclusions: Sublingual immunotherapy in the elderly rhinitis patients sensitized to HDM may be a option to control nasal symptoms.

Key Words: Allergic rhinitis, elderly rhinitis, sublingual immunotherapy

OP-24

Changes in basophil activation during subcutaneous allergen immunotherapy with house dust mite and mugwort in patients with allergic rhinitis

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Background: The basophil activation test (BAT) is a promising tool for monitoring allergen-specific immunotherapy responses. Here, we aimed to investigate the changes in basophil activation in response to the inhalant allergens of house dust mite (HDM) and mugwort pollen during immunotherapy in patients with allergic rhinitis.
Methods: We enrolled patients with allergic rhinitis who were to receive subcutaneous immunotherapy for the inhalant allergens HDM or mugwort. A BAT was performed to assess CD63 upregulation in response to allergen stimulation using peripheral blood collected from the patients prior to immunotherapy and at 3, 6, 12, and 24 months after beginning immunotherapy. Rhinitis symptoms were evaluated using the rhinitis quality of life questionnaire (RQLQ) at one-year intervals.
Results: Seventeen patients (10 with HDM sensitivity, 3 with mugwort sensitivity, and 4 with sensitivity to both HDM and mugwort) were enrolled in the study. Basophil reactivity to HDM did not change significantly during 24 months of immunotherapy. However, a significant reduction in basophil reactivity to mugwort was observed at 24-month follow-up. There was no significant association between the change in clinical symptoms by RQLQ and the change in basophil reactivity to either allergen. The change in allergen-specific basophil reactivity to HDM was well correlated with the change in non-specific basophil activation induced by anti-Fc ε RI antibody, although basophil reactivity to anti-Fc ε RI antibody was not significantly reduced during immunotherapy.
Conclusion: Suppression of CD63 upregulation in the BAT was only observed with mugwort at 2-year follow-up. However, the basophil response did not reflect the clinical response to immunotherapy.

Key Words: Rhinitis, Allergic, Basophils, Immunotherapy