

First-year Results of the Multicenter Prospective Web-based Anaphylaxis Registry in Korea

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Purpose: We have developed the first multicenter prospective web-based registry of anaphylaxis in Korea to collect precise and standardized data including all ages. Here we report the first-year results from the registry.

Methods: The case report form was developed by experienced allergists, and the web-based registry was established in cooperation with a professional medical software team. Twenty-two departments from 16 hospitals took part during the first year (Nov 2016 – Oct 2017).

Results: During the first-year, 358 cases of anaphylaxis were registered. The age ranged from 2 months to 83 years, and 66% were less than 18 years old. In children, foods (85.7%) were the most common cause of anaphylaxis followed by drugs (6.8%). In adults, drugs (54.5%) were more common than foods (31.4%). The most common food triggers were eggs (27.1%), milk (15.8%), and walnut (7.9%) in children, and shrimps (21.1%), wheat (15.8%), and crab (7.9%) in adults. Antibiotics (50.0%) were the most common cause among drug-induced anaphylaxis in adults, followed by NSAIDs (16.7%), and H2-blockers (13.6%). In about half of the cases, the onset time was ≤ 10 minutes. In children, home was the most common place of occurrence, whereas adults experienced anaphylaxis in out-of-home settings more often than children. Among the 289 cases registered via the emergency department, epinephrine was administered in 66.8% (62.5% in adults, 69.8% in children) and the number of epinephrine administration was single in 83%, twice in 13.5%, and more than thrice in 3.5%. The epinephrine autoinjector was prescribed in 54% of children and 63% of adults.

Conclusion: This multicenter prospective registry would provide a better understanding of anaphylaxis, and provide visionary modalities to improve the management and prevention of anaphylaxis in future.

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Key Words: Anaphylaxis, Registry, Prospective

Linguistic validation of Urticaria Severity Score (USS) questionnaire translated into Tagalog language for Adolescent Filipino with Chronic Urticaria

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Objective: To conduct a linguistic validation of Urticaria Severity Score to the Tagalog language

Methodology: Ethics Review board approval and informed consent were secured. This was a validation study based on the cultural and linguistic validation standard by the World Health Organization and International Society for Pharmacoeconomics and Outcomes Research (ISPOR). The study was conducted from January 1, 2017 to December 31, 2017 at the Allergy-Immunology Unit of Fe Del Mundo, Barangay Tatalon Quezon City and Sinagtala Elementary School. After content and format revisions, the final questionnaire was validated to 30 adolescent patients with chronic urticaria. The questionnaire was again answered by 30 patients to determine the reliability of the questionnaire by measuring internal consistency and the test re-test reliability.

Results: The translated questionnaire had a good content validity with all the content validity index score at 1.00. Each expert panel also gave an excellent congruency percentage of 100% for the questionnaire. The questionnaire had excellent internal consistency with an overall Cronbach's alpha of only 0.904577 (95% lower confidence limit = 0.856564). Test retest reliability showed a high correlation and ICC coefficient with correlation of 1. The overall correlation of the total score for each subject was also very high at 0.98 for both test retest and ICC coefficient.

Conclusion: The translated Tagalog version USS, "Palatanungan hinggil sa antas ng kalubhaan ng Urticaria" was a sensitive, reliable, and valid instrument for monitoring disease severity, quality of life, and treatment efficacy in adolescent patients with chronic urticaria.

Common causes of emergency department visits for anaphylaxis in Korean community

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Background: Anaphylaxis is a severe, life-threatening generalized hypersensitivity reaction. It is important to know about the triggers of anaphylaxis to avoid anaphylaxis. We investigated the triggers of anaphylaxis in regional community in Korean.

Objective: To evaluate the triggers of anaphylaxis in emergency department (ED) of community hospitals in Korea.

Methods: Patients who visited the ED for anaphylaxis in seven community hospitals January 1, 2012, to December 31, 2016 were enrolled. Anaphylaxis was defined according to the WAO anaphylaxis criteria through a thorough review of medical records. Medical records were reviewed by one pediatrician for patients who diagnosed as anaphylaxis (ICD-10 codes: T780, T782, T805, T886) at ED or who were administered epinephrine at ED. Triggers of anaphylaxis were also evaluated by review of medical records.

Results: We identified 1,021 cases of ED visit for anaphylaxis (65% male, 51.5 ± 16 years). There were no deaths associated with anaphylaxis. For five years, the incidence of patients treated with anaphylaxis in ED was 0.08%. The triggers were bee venom (55.0%), food (21.3%), drug (13.2%) and unidentified triggers (9.6%). It occurred mostly in summer (47.9%) and autumn (28.2%). Anaphylaxis was most common in August and bee venom anaphylaxis accounted for 80% of anaphylaxis ED visits in August. Epinephrine auto-injector was not prescribed in any case. Food-induced anaphylaxis were more common in winter but the profile of causative food was not different among season.

Conclusions: The incidence of anaphylaxis ED visits showed pronounced seasonal change with peak in summer in Korea. Bee sting was the most common trigger and also closely related with seasonal variations in Korean community. Prevention and education program for anaphylaxis should be different according to target community and needs their own epidemiologic studies for target area over whole year to cover possible seasonal variations.

Key Words: anaphylaxis, community, trigger

Smartphone-based patient centered drug allergy preventive system

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Backgrounds: Patients who had experienced drug allergy are continuously having the risk to re-experience similar catastrophic allergic events. To date, drug safety card that described the adverse events and culprit drug is considered the best way to prevent drug allergy. However, drug safety card has some limitations such as no standardized format or difficulties to provide appropriate information.

Objective: We aimed to develop the patient-oriented drug utilization review (DUR) smartphone application, and so construct personalized drug allergy prevention system.

Methods and results: The smartphone application called Smart-DUR app is designed to work according to the individualized information of drug allergy. The allergy specialist registered each patient's information on the web-based system such as culprit drug, potentially cross-reactive drug groups, and tolerable similar efficacy drug groups. The patient with drug allergy can see information about their drug allergy and easily provide the drug allergy action plan to other healthcare providers. Patients can check whether a specific drug is dangerous to themselves or not. In addition, Smart DUR app. will identify automatically if a prescription contains a hazardous drug by simple scanning QR or 2D bar-code on prescription. Now, we are conducting a pilot study with 40 patients with drug allergy to test usefulness and feasibility of our application.

Conclusion: We developed the smartphone-based drug allergy prevention systems. By using Smart DUR app, patients with drug allergy can easily prevent re-exposure to dangerous drugs.

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Key Words: Adverse drug reactions, prevention, smartphone

Bee venom allergy due to bee venom acupuncture point injection in China: clinical features and risk factors

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Purpose: Bee venom acupuncture point injection (BVAPI) has been used to treat chronic inflammatory diseases for hundreds of years in Asia. The prevalence of large localized and systemic reactions to Hymenoptera stings in the general population is 20% and 1-5%, respectively. Systemic reaction incidence to Hymenoptera stings in beekeepers is as high as 14-43%. However, there is few study investigated bee venom allergy (BVA) due to BVAPI.

Methods: A multicenter cross-sectional study on the patients with BVAPI was performed from December 2017 to January 2018 in three hospitals - Shijiazhuang Dazheng Apitherapy Hospital (in North China), First Hospital Affiliated to Guangzhou University of Chinese Medicine and Shenzhen Traditional Chinese Medicine Hospital (in South China). Clinical manifestations post BVAPI were reviewed. Positive result of skin prick test(SPT) to honeybee venom can confirm the bee venom allergy diagnosis.

Results: Gender ration male: female was 39:88; mean age 50.6±16.5 years old. 29%(36/124) patients who had adverse reactions post BVAPI were confirmed the diagnosis by positive SPT. The prevalence of large localized and systemic reactions post BVAPI is 17.7% and 11.3%, respectively. The highest prevalence of BVA was found in healthy subgroup (6/8, 75.0%). 35.7%(5/14) patients with systemic reaction presented with large localized reactions before onset of system symptoms post BVAPI. Logistic regression analysis showed that the higher BVAPI frequency, the lower risk of bee venom allergy (P=0.838, 95% CI 0.708-0.991).

Conclusions: Bee venom allergy is common during BVAPI and cannot be ignored. For the subjects at high risk, such as healthy person or having large localized reactions post BVAPI, closer observations after BVAPI and equipped with an emergency kit including epinephrine will be necessary. Regular BVAPI without unexpected suspend also can contribute to avoid bee venom allergy.

Risk factors for mortality of the patient with severe cutaneous adverse reactions in Korea based on nationwide registry

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Background: Severe cutaneous adverse reactions (SCARs) are life-threatening delayed hypersensitivity induced by various drugs. Despite the seriousness of these conditions, epidemiologic and clinical information is still not sufficient due to their sporadic occurrence.

Methods: The Korean SCARs registry was built based on the network of 34 tertiary referral university hospitals. SCAR cases occurred from 2010 to 2015 were retrospectively registered and demographic information, culprit agents, causality, and clinical outcomes were assessed.

Results: A total of 745 SCAR cases were enrolled; 384 cases of SJS or TEN and 361 cases of DRESS. The overall mortality rate was 8.9% in SJS/TEN patients while 4.2% in DRESS. In patients with SJS/TEN, age older than 40 years (odds ratio (OR)=3.18, 95% confidence interval (CI)=1.09-9.27), SCAR occurrence during admission (OR=6.06, 95% CI=2.58-14.25), fever (OR=3.81, 95% CI=1.61-9.01), Nikolsky sign (OR=4.60, 95% CI=1.46-14.46), leukopenia (OR=3.37, 95% CI=1.30-8.73), thrombocytopenia (OR=12.02, 95% CI=4.04-35.77), alanine aminotransferase above 200 IU/L (OR=4.50, 95% CI=1.86-10.86), serum creatinine increase 30% from baseline (OR=2.64, 95% CI=1.05-6.64) and specific underlying disease (hypertension, chronic renal failure, ongoing infection, asthma, allergic rhinitis) were significant risk factors for mortality. However, only leukopenia (OR=5.08, 95% CI=1.27-20.31), and thrombocytopenia (OR=8.21, 95% CI=1.81-37.22) were significantly related to mortality in patients with DRESS. Components of SCORTEN scores such as heart rate over 120/min and blood urea nitrogen (BUN) over 27 mg/dL were significantly different according to the prognosis of DRESS patients.

Conclusion: Diverse clinical feature other than SCORTEN score is associated with mortality of SJS/TEN patients. Hematologic parameters such as leukopenia and thrombocytopenia and SCORTEN score components such as heart rate and BUN were related to mortality in DRESS patients.

Key Words: severe cutaneous adverse reaction, risk factors for mortality

Diagnostic Strategy for Fish Allergy in Asian Children

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Purpose: Data on fish allergy in Asia is limited. This study investigated the epidemiology of fish allergy in Hong Kong, the diagnostic utility of component-resolved diagnosis on IgE-mediated fish allergy, and cross-reactivity of major allergen parvalbumin amongst a selected panel of fish species.

Methods: Forty-two children with convincing history of immediate-type fish allergy were included. Subjects' serum samples were tested for specific IgE (sIgE) against six seawater fishes, two freshwater fishes and two component fish allergens. Serological IgE reactivity to these allergens was measured by ImmunoCaP and ELISA. Cross-reactivity between parvalbumins from freshwater fish *Ctenopharyngodon idella* and seawater fish *Larimichthys crocea* with cod was elucidated by competitive inhibition ELISA.

Results: The average age of first fish-allergic reaction was 8.2 months old, freshwater fish was reported as the cause in 68% patients, and 69% of patients were able to tolerate at least one fish species despite being allergic to other species. Thirty-eight subjects (90%) were positive to at least one fish allergen. The highest mean sIgE was to freshwater fish component, rCyp c 1, and all seawater fishes except herring had significantly lower sIgEs compared to catfish and tilapia. The sensitivity of fish allergy diagnosis using catfish and tilapia was 82.1% and 79.1% respectively, which were higher than the mean of 62.5%. Competitive inhibition ELISA revealed that *C. idella* parvalbumin inhibited >85% of IgE binding to both *L. crocea* and cod parvalbumin, while reciprocally only inhibition of 60% and 50% could be achieved respectively.

Conclusions: This study highlights the importance of including locally important fish species for fish allergy diagnosis. Specific IgE to freshwater fishes, particularly freshwater component allergen, has improved sensitivity and usefulness in assessing IgE-mediated fish allergy in Hong Kong children.

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Selective strategies based on skin test for prevention of recurrent hypersensitivity reactions to radiocontrast media

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Background: Recently, there have been a lot of studies about the hypersensitivity reactions and intradermal skin test (IDT) of radiocontrast media (RCM). This study aimed to evaluate the skin test as a tool for preventing patients from recurrent hypersensitivity reactions to RCM who already had hyperactivity to RCM.

Methods: The patients who were contacted with the allergist about hypersensitivity reactions to RCM were enrolled. 75 subjects were recruited from 2015 to 2017. Except in cases of delayed type hypersensitivity and difficulty in identifying the causative agent, total of 54 subjects were included. In this study, we evaluated IDT of the 7 kinds of RCMs and recommended safe RCM according to the results of IDT. All patients were instructed to administer the RCM with the premedication (steroids and antihistamine) in the following exam using RCM and the response was investigated.

Results: 27 of the 54 subjects were positive for IDT in the previously culprit RCM and 27 were negative. Twelve of the 27 subjects who were positive IDT of culprit RCM were re-administered RCM after skin test. Six of the 12 patients used the RCM of IDT positive. Five of the six patients were pretreated, but hypersensitivity reactions occurred. In 27 patients with negative IDT in the culprit RCM, 15 patients re-administered RCM after skin test. And only 1 subject showed hypersensitivity reaction among 15 patients.

Conclusions: Depending on the results of the IDT about culprit RCM, the strategy for selecting next RCM can be changed. If the test is negative, premedication may be more important than the choice of RCM to prevent hypersensitivity reaction of the next RCM. If positive, choosing the RCM of negative for IDT is important for preventing hypersensitivity reactions of RCM.

Key Words: hypersensitivity, radiocontrast media, intradermal skin test

Three year follow-up after a low-dose oral food challenge for cow's milk allergy

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Purpose: We previously reported that low-dose (LD) oral food challenges (OFCs) enable half children with cow's milk (CM) allergies to partially consume CM and avoid complete elimination of CM. However, long-term prognoses after LD-OFCs are not well described. The aim of our study was to clarify the 3-year prognosis after LD-OFCs.

Method: We performed a retrospective chart review of subjects with immediate-type CM allergy symptoms who had undergone their first LD-OFC before 7 years of age between 2012 and 2014. Subjects who had passed the first LD-OFC were defined as LD-tolerant; subjects who had failed were defined as LD-intolerant. We compared the ratios of subjects who acquired tolerance to 3, 25, and 200 mL of CM 3 years after the first LD-OFC between the LD-tolerant and LD-intolerant groups, using Kaplan-Meier analysis with log-rank tests and Cox hazard analysis.

Result: Of the 214 included subjects, the median age was 3.9 years, and the median specific immunoglobulin E (sIgE) level to CM was 22.9 UA/mL. Of them, 115 (54%) were LD-tolerant and 99 (46%) were LD-intolerant. The ratio of tolerance to 3 mL of CM 3 years after LD-OFCs was estimated as 30.8% in the LD-intolerant group; that to 25 mL was 78.7% in the LD-tolerant group and 11.9% in the LD-intolerant group ($p < 0.001$); and that to 200 mL was 31.7% and 2.8% ($p < 0.001$), respectively. Predictors of intolerance to 200 mL of CM over 3 years were: LD intolerance (hazard ratio [HR]: 6.99, $p = 0.012$), older age (HR: 1.68, $p = 0.008$), higher titer of CM sIgE (HR: 4.31, $p = 0.006$), and other food allergies (HR: 3.51, $p = 0.014$).

Conclusion: Patients who had reacted to the LD-OFC did not easily acquire tolerance over 3 years, especially among those who were older, with higher titers of CM sIgE and other food allergies.

Prediction of Cetuximab Hypersensitivity Reaction before Administration Using 4 Methods

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Background: Cetuximab (chimeric monoclonal antibody to human epidermal growth factor receptor) has been used as a treatment for colorectal and head and neck cancer. It is known that cetuximab can induce hypersensitivity even at the first administration due to cross-reactivity with galactose alpha-1, 3-galactose (alpha-gal). In this study, we aimed to establish a model to predict hypersensitivity reaction before administration of cetuximab.

Methods: Patients over 18 years of age who scheduled for cetuximab administration according to standard treatment guidelines were enrolled prospectively. Before first cetuximab administration, skin prick test was done with cetuximab. Specific IgE to cetuximab, alpha-gal and beef were measured using ImmunoCAP. Adverse drug reactions were monitored after cetuximab administration.

Results: Of the 36 patients who participated in this study, 2 patients (5.6%) experienced severe anaphylaxis after first administration of cetuximab. Only two patients with anaphylaxis showed positive skin reactions (P value = 0.003). Positive reaction with skin prick test, Cetuximab specific IgE titer was 20.3 ± 22.8 kUA/L in anaphylaxis group and 0.01 ± 0.03 kUA/L in the control group (P value = 0.003). The results of alpha-gal and beef sIgE were similar to those of cetuximab sIgE. Patients who did not experience hypersensitivity were negative in 4 tests. Therefore, 4 tests showed 100% of sensitivity, specificity, positive predictive value and negative predictive value.

Conclusions: Skin prick test and specific IgE detection of cetuximab can predict cetuximab-induced anaphylaxis before administration.

Key Words: Anaphylaxis, Cetuximab, Specific IgE

Food Sensitization in Young Thai Children with Atopic Dermatitis

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Background: Atopic dermatitis (AD) is the most common allergic skin disease in young children. Food allergen plays role as triggering factors of AD. There are few data about IgE-mediated food sensitization in Thai young children with AD.

Objective: To study the prevalence and factors associated with food sensitization among AD-children aged less than 5 years.

Methods: A cross-sectional study in children aged less than 5 years with AD at allergy clinic, Chiang Mai University hospital was performed. The participants were assessed for IgE-sensitization by parent-interview, skin prick test (SPT), serum specific IgE (SIgE; ImmunoCAP, Thermo Fisher).

Results: A total of 101 children were enrolled, median age 9.3 months (IQR: 6.1-17.1 months). The severity of AD were mild (37.6%), moderate (59.4%), and severe (3.0%). There were high over all rates of food sensitization (64.4%). The correlation of food sensitization results between SPT and SIgE was moderate ($\kappa=0.398$). The common food allergens were egg white (55.4%), cow's milk (34.7%), wheat (30.7%), peanut (17.8%), and soy (10.9%). House dust mite sensitized (20.7%) were found only in participants aged more than 1 year. The significant factors associated with food sensitization were personal history of other atopic disease, exclusive breast feeding > 6 months, and moderate to severe AD.

Conclusions: The prevalence of food sensitization in Thai children with AD aged less than 5 years is high. Further studies to evaluate clinical relevance of food IgE-sensitization, food allergies, and elimination diet treatment are required.

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