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Body Mass Index (BMI) and Immediate (“STAT”) Dose of Epinephrine im (EPI IM) Needed to Treat Subcutaneous Allergen Immunotherapy (SCIT) Systemic Reactions (SRs)
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Background: The purpose of this study is to document the number of SRs occurring in SCIT subjects. No significant association was found between BMI and the WAO Grade severity (P = 0.13 by Fisher’s exact test) and BMI and total epi IM dose given (P = 0.82 by Kruskal-Wallis test). BMI should not influence risk assessment of SCIT or IM epi administered for SR.

Methods: Ten patients with anaphylaxis to Ranitidine were enrolled from Ajou University Hospital and Seoul National University Bundang Hospital. Skin prick test (SPT) using Ranitidine extract were performed in 7 patients. Serum specific IgE and G1 antibodies were detected by ELISA using Ranitidine-HSA conjugate. The study subjects were divided into 2 groups according to the presence of serum specific IgE antibody to Ranitidine-HSA conjugate: 3 subjects had high serum specific IgE (Group I) and 7 subjects showed negative results (Group II), when positive cut off value was determined from mean + 3 SD of absorbance values of healthy controls.

Results: Six (60%) were female and 9 (90%) were atopics. 6 (86%) patients had positive responses to ranitidine on SPT, however, high serum specific IgE antibody to Ranitidine-HSA conjugate was detected in only 3 patients (30%), while serum specific IgG1 was undetectable in one patient (10%). There were no significant differences in clinical characteristics including age, sex, atopy and serum total IgE level between group I and II.

Conclusions: We confirmed the presence of serum specific IgE to Ranitidine-HSA conjugate by ELISA, suggesting that IgE mediated response is a major pathogenic mechanism of Ranitidine induced anaphylaxis. Further studies will be needed to investigate other immunologic and non-immunologic mechanisms and cross-reactivity among other H2 receptor antagonists.

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Muscle Relaxant Induced Allergic Reactions
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Background: There have been a few reports of hypersensitivity reactions to muscle relaxants, but the pathogenic mechanisms of H2 receptor antagonist induced hypersensitivity reactions are not understood. The purpose of this study was to observe the clinical characteristics of the patients with Ranitidine anaphylaxis and investigate the pathogenic mechanisms with detection of serum specific IgE antibody to Ranitidine-HSA conjugate.

Methods: Ten patients with anaphylaxis to oral muscle relaxants were included from 2 hospitals (2010 – 2011). Serum specific IgE antibody to Ranitidine-HSA conjugate was tested for antibiotics (Penicillin G and V, Ampicillin and amoxicillin) and local anesthetics.

Results: We report 3 allergic reactions caused by oral muscle relaxants that might be mediated by non-IgE-mediated responses. As muscle relaxant, eperisone and aloqualone act by relaxing both skeletal muscles and vascular smooth muscles to improve circulation and suppress pain reflex. These drugs are usually prescribed combined with non-steroid anti-inflammatory drugs (NSAIDs) as pain killers. Although there have been no reports on serious adverse reactions to muscle relaxant, this is the first report of 3 anaphylactic reactions caused by eperisone and aloqualone.

Conclusions: We report 3 allergic reactions caused by oral muscle relaxants that might be mediated by non-IgE-mediated responses. As muscle relaxant, eperisone and aloqualone, commonly prescribed drugs for chronic muscle pain, can induce severe allergic reactions therefore we should prescribe them carefully.

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Features of 51 Patients With Perioperative Anaphylaxis History
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Background: To evaluate the prevalence and the etiology of perioperative anaphylaxis (APEO) referred to an outpatient clinic specialized in adverse drug reactions.

Methods: We evaluated 806 patients throw the questionnaire “European Network for Drug Allergy” (ENDA) in the period from October 2006 to June 2011. Patients with a history of APEO were selected. The diagnostic criteria for anaphylaxis were based on the World Allergy Organization. Etiological investigation was made with skin tests for latex, neuromuscular blockers (NMBs), antibiotics, hypnotics, opioids and local anesthetics. Provocation tests for antibiotics, NSAIDs, local anesthetics and latex were also done. Specific IgE was tested for antibiotics (Penicillin G and V, Ampicillin and amoxicillin) and latex.
Results: We identified 51 (6%) patients with a history of APEO. Among them, 16 patients (31%) had hypersensitivity reactions with positive cutaneous test, 14 patients (27%) abandoned the investigation and 8 patients (16%) completed the investigation with all tests negative. Currently 12 patients (23%) are being investigated and one of them (2%) performed tests to drugs to use in the next surgery. The main cause of APEO was latex allergy (22%), followed by NMB hypersensitivity (6%). Three patients had positive tests for 2 different agents.

Conclusions: Latex allergy is the main cause of APEO in this study. The importance of testing all the possible agents involved was demonstrated by the occurrence of 3 cases with positive test for 2 agents.

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Drug Induced Anaphylaxis in a University Hospital in Sao Paulo, Brazil
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Background: Adverse drug reactions (ADRs) are common in clinical practice, most of them presented only with mucocutaneous symptoms. Drug induced anaphylaxis is rare, but it is responsible for most deaths due to ADRs. The aim of this study was to evaluate drug induced anaphylaxis treated in an Allergy Outpatient Clinic of a University Hospital.

Methods: Retrospective analysis of medical records from patients who seek assistance because of ADR. We looked for clinical criteria for diagnosing anaphylaxis, as recommended in WAO Guidelines. Criteria were classified in numbers 1 to 3:1) Acute onset of an illness (minutes to several hours) with involvement of the skin-mucosal tissue and respiratory and/or cardiovascular compromise; 2) Two or more of the following that occur rapidly after exposure to a likely allergen: involvement of skin-mucosal tissue, respiratory, cardiovascular and/or gastrointestinal compromise; 3) Reduced blood pressure after exposure to known allergen for that patient. We analyzed patients gender and age, drugs involved in reactions and administration of epinephrin.

Results: We studied 306 patients with history of ADR, of whom 123 (15.3%) presented clinical criteria of anaphylaxis (mean age 39.0 year old, female 19%). The first clinical criteria was found in 60.2% and the second one in 38.2%. Epinephrin was injected in only 42 patients (34.1%), Non-steroidal anti-inflammatory drugs (NSAIDs) were most commonly suspected culprit drugs involved in anaphylactic reactions, with 59 patients (47.9%), followed by 40 patients with perioperative anaphylaxis (32.5%), 6 cases due to local anesthetics (4.9%) and 4 to antibiotics (3.2%). Between perioperative anaphylaxis, latex was involved in 10 reactions and neuromuscular blocking agents in 3.

Conclusions: We found a high prevalence of anaphylaxis, probably because patients with severe ADRs tend to be followed in university hospitals. Nevertheless, anaphylaxis is underdiagnosed in emergency departments, as we observed less than 35% of patients with drug induced anaphylaxis were treated with epinephrin. NSAIDs are still the most common drugs involved in ADRs in Brazil, including severe reactions, as anaphylaxis. In our country, latex still is an important agent incriminated in perioperative anaphylaxis, but anaphylaxis due to antibiotics are less common than in other countries.

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Analysis of Anaphylactic Reactions to Biological Agents Reported to the Italian Pharmacovigilance Database
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Background: Spontaneous reporting of adverse drug reactions (ADR) to biological agents used for cancer and immuno-mediated disease treatment is important for furthering knowledge regarding the safety of these new drugs. An analysis was carried out in Italy on reports of anaphylaxis caused by biological agents.

Methods: Data were extracted from the national Spontaneous Reporting Database. Since biological drugs refer to different ATC (Anatomical Therapeutic Classification) codes, in this study they have been extracted by the presence of “mab” and/or “cept” suffixes. Cases were defined as following: A) reports with the string “anaph” in the description of the event or in the WHO-ART (Adverse Reactions Terminology) coded preferred terms; B) reports with adverse reactions referring at least 2 of selected System Organ Classes (skin, respiratory, cardiovascular and gastrointestinal disorders) with an onset within 24 hours after administration. All selected cases were reviewed and the case definition from the “Second Symposium on the Definition and Management of Anaphylaxis” was applied to evaluate the reports (JACI 2005;115(3):584–591).

Results: The Italian database up to March 2011 contains 3820 reports related to biologicals. According to selection criteria, a total of 334 reports were extracted: 65 for group A and 269 for group B. By application of the anaphylaxis case definition, 2 cases belonging to group A and 139 to group B were excluded after individual review. Out of 193 reports meeting the case definition, 8 (4.1%) were reported in children and adolescents up to 18 years of age. The most reported responsible drugs were infliximab with 83 (43%) cases, followed by cetuximab (41–21%) and rituximab (28–14%); other 11 different biologicals were associated with the remaining 32 cases (22%), with up to 8 reports each.

Conclusions: Spontaneous reporting is an important source to provide further knowledge on the reactogenicity of biological agents. Three-fourths of Italian reports of anaphylaxis concern 3 chimeric antibodies containing a murine component. In our study, the best identification of cases of anaphylactic reactions came out of the combination of selected reported terms, application of case definition and expert review of individual reports.

ATOPIC DERMATITIS

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Contribution of IL-33 and Nuocyte to Experimental Allergic Dermatitis
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Background: IL-33 is a member of the IL-1 family cytokines and the ligand of ST2 (IL-33R alpha chain). IL-33 stimulates Th2 cells, basophils, mast cells, and nuocytes, a recently discovered new lymphocyte, to produce various cytokines. We have previously shown that the serum level of IL-33 is significantly elevated in patients with Japanese cedar pollinosis3 and IL-33 has the potential to induce Th2 cytokine-mediated allergic conjunctivitis4. As these results suggest that IL-33 may also have some relations to allergic dermatitis, we now examined the pathological role of IL-33 in dermatitis. First, we investigated an immediate reaction of skin by challenging BALB/c mice with DNFB repeatedly. We also tested the involvement of natural killer cells (nuocyte) in dermatitis of NC/Nga mice.

Methods: (1) Wild-type BALB/c mice or ST2 KO mice were sensitized and repeatedly challenged with DNFB on the left ear at 1 week intervals. When they are challenged 4 or 5 times, the ear shows biphasic (bimodal) responses which consist of an immediate phase and a delayed-type reaction. (2) When NC/Nga mice are raised in conventional (non-SPF) circumstances, skin