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Drug allergy

Hypersensitivity to the diphtheria component in the Di-Te-Pol vaccine. A type I allergic reaction demonstrated by basophil histamine release

Pediatric Allergy and Immunology 1997

P S Skov, I Pelck, F Ebbesen, L K Poulsen

Link: https://pubmed.ncbi.nlm.nih.gov/9532258/

Abstract

We describe a two year-old multiallergic boy who developed generalized urticaria after the third Di-Te-Pol vaccination. A Type I reaction to the vaccine was demonstrated by performing basophil histamine release to the complete vaccine. Further, we found that the reaction could be exclusively ascribed to Diphtheria-Toxoid whereas no release was observed by the Polio and Tetanus component. The latter result was confirmed since no specific IgE to Tetanus Toxoid could be demonstrated.

Occupational rhinosinusitis due to etoposide, an antineoplastic agent

Scandinavian Journal of Work, Environment & Health 2010

Harald W Meyer, **Per Stahl Skov**

Link: https://pubmed.ncbi.nlm.nih.gov/20174772/

Abstract

Objective: This paper reports a rare case of an occupational hypersensitivity reaction to an antineoplastic agent.

Methods: This is a clinical case report of a 45-year-old nurse who developed throat irritation and chronic nasal congestion followed by sinusitis shortly after beginning work at an oncological out-patient clinic. The symptoms disappeared upon leaving the clinic two years later, but they returned when she resumed work at the oncology unit at Hillerød Hospital, Denmark, handling chemotherapy on a daily basis. We performed in vitro histamine release tests against nine suspected antineoplastic agents.

Results: The patient's histamine release test against the antineoplastic agent etoposide was positive; the other test results were negative. The histamine release test against etoposide using passive sensitization was also negative. Upon leaving the oncology department, the symptoms of the nurse disappeared once again. She was given a diagnosis of rhinosinusitis.

Conclusion: This case of a hypersensitivity reaction to etoposide was judged to be of occupational origin. It was not clear whether it was immunoglobulin E (IgE) or non-IgE mediated.

Anaphylaxis to Patent Blue V. II. A unique IgE-mediated reaction

Allergy 2010

S G O Johansson, **A Nopp**, **H Oman**, **P Stahl-Skov**, **A S Hunting**, **A B Guttormsen**

Link: https://pubmed.ncbi.nlm.nih.gov/19804438/

Abstract

Background: Patent Blue V (PBV) is injected in order to map sentinel nodes during cancer staging procedures. Anaphylactic reactions, allegedly IgE antibody mediated, have been reported. The aim of the study was to explore the immunological mechanism of anaphylaxis to PBV.

Methods: PBV allergen threshold basophil sensitivity, CD-sens, was performed on cells from nine patients diagnosed as having had adverse reactions to PBV. The mechanisms of the CD-sens were studied by immunological and immuno-chemical methods.

Results: Five of the nine patients had a positive CD-sens to PBV which was completely eliminated by washing the cells in phosphate buffered saline before allergen challenge. However, the positive CD-sens was completely reconstituted by incubating the cells in plasma or serum of that patient or the other PBV-anaphylactic patients for 15 min at room temperature. In some patients the factor mediating CD-sens was completely or partially destroyed by heating at +56 degrees C for 30 min or being exposed to the low pH used for elution from anti-Ig columns. A 1000-fold excess of monoclonal IgE blocked the reconstitution by approximately 50%.

Conclusion: Anaphylactic reactions to PBV are mediated by IgE antibodies giving a classical CD-sens reaction. However, the allergenic configuration seems to constitute a structure completely dependent on PBV, as a hapten, linked to a, so far, unknown carrier that seems to be unique for patients having experienced a PBV-induced reaction. Further studies are needed to characterize the postulated carrier.

Inhibition of polyethylene glycol–induced histamine release by monomeric ethylene and diethylene glycol: A case of probable polyethylene glycol allergy

Journal of Allergy and Clinical Immunology 2013

Emily Cathrine Wenande, Per Stahl Skov, Holger Mosbech, Lars K Poulsen, Lene H Garvey

Link: https://pubmed.ncbi.nlm.nih.gov/23228247/

No abstract available

Standardized testing with chlorhexidine in perioperative allergy – a large single-centre evaluation

Allergy 2014

M S Opstrup, H-J Malling, M Krøigaard, H Mosbech, P S Skov, L K Poulsen, L H Garvey

Link: https://pubmed.ncbi.nlm.nih.gov/24957973/

Abstract

Background: Perioperative allergic reactions to chlorhexidine are often severe and easily overlooked. Although rare, the prevalence remains unknown. Correct diagnosis is crucial, but no validated provocation model exists, and other diagnostic tests have never been evaluated. The aims were to estimate (i) the prevalence of chlorhexidine allergy in perioperative allergy and (ii) the specificity and sensitivity for diagnostic tests for chlorhexidine allergy.

Methods: We included all patients investigated for suspected perioperative allergic reactions in the Danish Anaesthesia Allergy Centre during 2004-2012. The following tests were performed: specific IgE (Immunocap® ; Phadia AB, Sweden), histamine release test (HR) (RefLab ApS, Denmark), skin prick test (SPT) and intradermal test (IDT). Positivity criteria were as follows: specific IgE >0.35 kUA/l; HR class 1-12; SPT mean wheal diameter ≥3 mm; IDT mean wheal diameter ≥ twice the diameter of negative control. Chlorhexidine allergy was post hoc defined as a relevant clinical reaction to chlorhexidine combined with two or more positive tests. Based on this definition, sensitivity and specificity were estimated for each test.

Results: In total, 22 of 228 patients (9.6%) met the definition of allergy to chlorhexidine. Estimated sensitivity and specificity were as follows: specific IgE (sensitivity 100% and specificity 97%), HR (sensitivity 55% and specificity 99%), SPT (sensitivity 95% and specificity 97%) and IDT (sensitivity 68% and specificity 100%).

Conclusions: In patients investigated for suspected perioperative allergic reactions, 9.6% were diagnosed with allergy to chlorhexidine. Using our definition of chlorhexidine allergy, the highest combined estimated sensitivity and specificity was found for specific IgE and SPT.

Role of Histamine Release Test for the Evaluation of Patients with Immediate Hypersensitivity Reactions to Clavulanic Acid

International Archives of Allergy and Immunology 2015

Fernando Pineda, Adriana Ariza, Cristobalina Mayorga, Francisca Arribas, Rosario González-Mendiola, Natalia Blanca-López, Galicia Davila, Nieves Cabañes, Gabriela Canto, José Julio Laguna, Carlos Senent, Per Stahl-Skov, Ricardo Palacios, Miguel Blanca, María José Torres

Link: https://pubmed.ncbi.nlm.nih.gov/26894754/

Abstract

Background: Immediate hypersensitivity reactions to clavulanic acid (CLV) seem to be on the increase. Diagnosis is mainly based on skin testing and the drug provocation test (DPT), procedures that are not risk free. The aim of this study was to evaluate whether the histamine release test (HRT) could help evaluate patients with selective hypersensitivity to CLV.

Methods: Eighteen patients with immediate selective hypersensitivity reactions to CLV (positive skin tests to CLV but negative to the major and minor determinants of benzylpenicillin and amoxicillin; negative DPT to benzylpenicillin and amoxicillin) and 21 controls with tolerance to CLV were included. Direct and passive HRT, using patient whole blood or 'IgE-stripped' donor blood sensitized by patient serum, respectively, were performed by stimulating the blood with CLV, and basophil histamine release was detected by fluorometric determination.

Results: The clinical symptoms were anaphylaxis (n = 6), urticaria (n = 9) and urticaria-angioedema (n = 3). The median time interval between the reaction and the study was 225 days (interquartile range, IQR: 120-387.5) and between drug intake and the development of symptoms 30 min (IQR: 6.25-30). We obtained similar data for both the direct and passive HRT, with a sensitivity and specificity of 55 and 85%, respectively, a positive predictive value of 76% and a negative predictive value of 69%.

Conclusions: The sensitivity of both the direct and passive HRT for diagnosing patients with immediate allergy to CLV is less than 60%. However, the passive HRT has the advantage that it is based on the testing of serum samples that can be handled more easily than fresh blood samples.

Basophil Histamine Release Induced by Amoxicilloyl-poly-L-lysine Compared With Amoxicillin in Patients With IgE-Mediated Allergic Reactions to Amoxicillin

Journal of Investigational Allergology and Clinical Immunology 2017

F Arribas, S Falkencrone, J Sola, M P Gomez-Serranillos, J J Laguna, M I Montañez, T D Fernandez, D Rodríguez, F Pineda, P S Skov, C Mayorga, M J Torres

Link: https://pubmed.ncbi.nlm.nih.gov/28628008/

Abstract
Background: Amoxicillin (AX) is the ß-lactam most often involved in IgE-mediated reactions. Diagnosis is based mainly on skin testing, although sensitivity is not optimal. We produced a new AX derivative, amoxicilloyl-poly-L-lysine (APL), and analyzed its recognition of IgE using the passive histamine release test (pHRT).

Methods: The study population comprised patients (n=19) with confirmed AX allergy and specific IgE to AX and controls (n=10) with good tolerance to AX. pHRT was performed using "IgE-stripped" blood from a single donor that was sensitized in vitro by patient sera and incubated with AX or APL. Histamine release was determined and expressed as nanograms of histamine released per milliliter of blood.

Results: The clinical symptoms were anaphylaxis (n=9), urticaria (n=7), erythema (n=2), and nondefined immediate reactions (n=1). The median (IQR) time interval between reaction and study was 90 (60-240) days and between drug intake and development of symptoms 24 (10-60) minutes. The median sIgE level was 3.37 (0.95-5.89) kUA/L. The sensitivity of pHRT to APL was 79% and the specificity 100%, which were higher than data obtained with pHRT to AX (63% sensitivity and 90% specificity). There was a positive correlation between maximal histamine release levels obtained with AX and APL (r=0.63).

Conclusions: In patients with immediate hypersensitivity reactions to AX, APL showed higher sensitivity and specificity than the culprit drug, AX, when tested in vitro by pHRT. This indicates that APL can improve the in vitro diagnostic accuracy of allergic reactions to AX. Further assessment of skin testing is necessary.

Sugammadex hypersensitivity and underlying mechanisms: a randomized study of healthy non-anaesthetised volunteers

British Journal of Anaesthesia 2018

P-J de Kam, H Nolte, S Good, M Yunan, D E Williams-Herman, J Burggraaf, C Kluft, N F Adkinson, C Cullen, P S Skov, J H Levy, D J van den Dobbelsteen, E L G M van Heumen, F C M van Meel, D Glassner, T Woo, K C Min, P A M Peeters

Link: https://pubmed.ncbi.nlm.nih.gov/30236238/

Abstract
Background: We investigated potential for hypersensitivity reactions after repeated sugammadex administration and explored the mechanism of hypersensitivity.

Methods: In this double-blind, placebo-controlled study (NCT00988065), 448 healthy volunteers were randomised to one of three arms to receive three repeat i.v. administrations of either sugammadex 4 mg kg^{-1}, 16 mg kg^{-1}, or placebo. Primary endpoint was percentage of subjects with hypersensitivity (assessed by an independent adjudication committee). Secondary endpoint of anaphylaxis was classified per Sampson and Brighton criteria. Exploratory endpoints included skin testing, serum tryptase, anti-sugammadex antibodies [immunoglobulin (Ig) E/IgG], and other immunologic parameters.

Results: Hypersensitivity was adjudicated for 1/148 (0.7%), 7/150 (4.7%), and 0/150 (0.0%) subjects after sugammadex 4 mg kg^{-1}, 16 mg kg^{-1}, and placebo, respectively. After sugammadex 16 mg kg^{-1}, one subject met Sampson criterion 1 and Brighton level 1 (highest certainty) anaphylaxis criteria; two met Brighton level

2 criteria. After database lock it was determined that certain protocol deviations could have introduced bias in the reporting of hypersensitivity signs/symptoms in a subject subset. Objective laboratory investigations indicated that potential underlying hypersensitivity mechanisms were unlikely to have been activated; the results suggest that most of the observed hypersensitivity reactions were unlikely IgE/IgG-mediated.

Conclusion: Dose-dependent hypersensitivity or anaphylaxis reactions to sugammadex were observed when administered without prior neuromuscular blocking agent. Laboratory investigations do not suggest prevalent allergen-specific IgE/IgG-mediated immunologic hypersensitivity. Because it could not be fully excluded that estimates of hypersensitivity/anaphylaxis incidence were unbiased, an additional study was conducted to characterise the potential for hypersensitivity reactions and is described in a companion report.