Barry Kay Award winning Abstracts

Presented at the 2017 Annual Meeting

of the

British Society for Allergy and Clinical Immunology

Category: Adult Clinical

O.005

Basophil histamine release assay predicts response and time of response to omalizumab in severe chronic spontaneous urticaria

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Objectives

Omalizumab (anti-IgE) is a licensed add-on therapy for chronic spontaneous urticaria (CSU) non-responsive to H_1-antihistamines. There are no validated biomarkers to predict response and time of response to omalizumab. Basophil histamine release assay (BHRA) detects serum histamine-releasing IgG autoantibodies to high affinity receptor for IgE (FcεRI) or cell-bound IgE.

Method

In our centre BHRA is routinely performed in all severe CSU patients before starting omalizumab or immunosuppressants. A retrospective case review of patients treated with 300mg omalizumab every 4 weeks was undertaken to assess if BHRA result predicted the likelihood of response and time of response to omalizumab. Urticaria activity score 7 (UAS7) was used to monitor response, which was defined as reduction (UAS7<16) or complete resolution of symptoms (UAS7=0). Fast response occurred within the first week of treatment.

Results

113 patients (75 female; mean age 44) were treated with omalizumab from November 2015 to March 2017. 104(92.0%) patients responded: 97(93.3%) were BHRA-negative and 7(6.7%) were BHRA-positive. Average pre-treatment UAS7 was 37 in the BHRA-negative group and 38 in BHRA-positive group. In the BHRA-negative group, 52(53.6%) patients responded within a week, 17 between 1-4weeks, 11 between 5-8weeks, 13 between 9-12weeks and 4 between 13-16weeks. In the BHRA-positive group, 2 patients responded within a week, 2 between 5-8weeks, 2 between 9-12weeks and 1 between 13-16weeks. Median time to response in BHRA-negative patients was within 1 week whereas in BHRA-positive patients it was 6.5 weeks. The response rate in BHRA-negative was 96.0% (97/101) and in BHRA-positive was 58.3% (7/12). The response rate ratio was 1.646 (95% CI: 1.02-2.66; p=0.0417). Of 9 omalizumab non-responders, 4 (44.4%) were BHRA-negative and 5(55.6%) were BHRA-positive.

Conclusions

BHRA-negative patients appear to be more likely to respond and be fast responders to omalizumab than BHRA-positive patients. These findings suggest that BHRA could be a useful marker to gauge response to omalizumab.

Category: Paediatric Clinical

O.009

Gene-environment interaction between filaggrin and hard water associated with increased risk of atopic eczema

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Objectives

We performed a longitudinal analysis in the Enquiring About Tolerance (EAT) cohort to examine whether domestic water hardness was associated with an increased atopic eczema risk after 3 months of age and to assess the role of common filaggrin (FLG) loss-of-function mutations.

Method

All EAT study children aged 3 to 36 months without atopic eczema by 3 months were selected from a cohort of 1,303 children participating in the EAT study. Water hardness exposure was defined as the domestic water calcium carbonate concentration supplied to the child's main residence. The primary outcome was the development of 'any eczema', a composite of visible eczema or parent-reported eczema, between 3-36 months of age.

Results

A Cox proportional hazards model was fitted with adjustment for key confounders, including ethnicity, home location (urban versus rural) and the presence of a domestic water softener. 958/1,303 (74%) infants were included in the analysis. Of these, 351 (37%) developed eczema by 36 months of age. There was no overall statistically significant association between exposure to harder (>255 mg/L CaCO3) versus softer (≤255 mg/L CaCO3) water: crude HR 0.98 (95% CI 0.80, 1.21). However, stratification by FLG mutation status showed a significant interaction with water hardness: HR 2.94 (1.90, 4.53) compared to the reference group with wild-type FLG living in softer water areas. The relationship remained significant [HR 2.75 (95% CI 1.76, 4.28)] following adjustment for confounders.

Conclusions

These data provide evidence of a gene-environment interaction between water hardness and common loss-of-function mutations in the FLG gene. We are planning an intervention study with a water softening device installed around the time of birth to further test the effect of water hardness on skin barrier function and atopic eczema risk in early life.

Category: Basic Science

P.097

Identification of allergens from *Trichoderma viride*: an important biofungicide

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Objectives

Immuno-proteomic study was performed aiming for determination of the allergenicity of *Trichoderma viride*, one of the prevalent airborne fungi in India as well as a well-known biofungicide, and also identification of allergenic components by mass spectrometry based analysis.

Method

Allergenic potential of *Trichoderma viride* was tested by Skin Prick Test. Sera were collected from SPT positive patients with their written consent. To confirm allergenicity, individual sera were used for in vitro tests like IgE ELISA and Total Histamine Assay. Total protein of *Trichoderma viride* was resolved in 12% SDS-PAGE and 2-Dimensional gel electrophoresis. To detect allergens, 1D and 2D Immunoblot were performed by using individual and pooled sera respectively. Periodic Acid Schiff's staining was done to detect the presence of glycoproteins in the allergen profile. Mass spectrometry based identification of allergens from IgE reactive spots was done by MALDI-TOF-TOF. Major allergen was partially purified by ion exchange chromatography.

Results

Individual sera with positive responses in SPT elevated specific IgE level against *Trichoderma viride* extract in ELISA and also induced a significant amount of total histamine. Seven IgE reactive proteins were detected as allergens from Immunoblot. Periodic Acid Schiff's staining showed negative results for allergens. 56% of *Trichoderma viride* allergic patients were sensitized to a predicted protein (54 kDa) by IgE immunoblot, which was identified as major allergen by MALDI-TOF-TOF. This major allergen (pI 5.214) was partially purified by ion exchange chromatography and showed its IgE reactivity by 1D immunoblot confirming successful partial purification of this allergen.

Conclusions

In the present study, seven allergens were identified from *Trichoderma viride* for the first time. Immuno-proteomic identification of all IgE reactive proteins is helpful for proper diagnosis and immunotherapy of atopic diseases.

Category: Allied Health

O.019

An audit of the prescription and use of adrenaline auto injector devices in adults and children

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Objectives

There is discrepant national advice on how many Adrenaline auto injector devices (AAIs) should be prescribed. There has been no large audit to date which has looked at whether patients comply with recommended guidelines. This audit sought to clarify both prescribing and patient behaviours for the use of AAIs.
Are AAIs prescribed appropriately?
Is the number of AAIs being carried in line with national recommendations and are patients and parents taking full responsibility for their devices?
Is AAI training being provided when a device is prescribed?
Are Personal Allergy Action plans being issued?

Method

The BSACI nurses' committee developed an audit proposal, circulated to all BSACI nurse members. Data collection in each centre took place over a four month period including all patients or parents of children attending an Allergy Clinic prescribed an AAI either previously or during their appointment. A standard questionnaire developed by the Nurses' Committee was used for data collection.

Results

7 allergy centres participated. (Data collection is ongoing). Preliminary results at Bristol Children's Hospital identified 29 children prescribed an AAI. 3 patients had used their device; 1 was administered unnecessarily by nursery staff. No patient received a second dose. Patients carried between 2 and 9 devices but only 8(47%) had their device with them. 7 devices were out of date or the incorrect dose. 1 patient was carrying a new, unfamiliar AAI. No patient prescribed an AAI in primary care had an Action Plan or had received any training.

Conclusions

Preliminary data suggests that many patients possess an excessive number of AAIs but frequently do not carry their device. Possession of expired devices was common. Prescriptions from primary care were often not supported by training or an Action Plan. No patient using their AAI required a second dose of adrenaline.

Category: Primary Care

P.114

Non-specialist management and referral pathways in allergy

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Objectives

The demand for Allergy Services is increasing and there is a growing need for the training and education of General Practitioners and other Allied Health Care Professionals in managing allergic disease in the Primary Care setting. Some patients with mild to moderate allergic disease such as seasonal rhinitis, or with urticaria/ACE-Inhibitor related angioedema, can be treated successfully by Primary Care Physicians without the need for specialist Allergy Clinic review. Furthermore, introducing these pathways will hopefully allow for the more immediate management of these patients who may have otherwise experienced a delay in their treatment commencing, whilst awaiting an appointment in the Allergy clinic. Our objective was to develop Primary Care referral pathways for Allergic Rhinitis and Urticaria and Angioedema to assist General Practitioners in the initial assessment, management and onward referral to the Allergy Clinic for these conditions.

Method

Referral and management pathways for Rhinitis and Urticaria and Angioedema were developed by the Sheffield Clinical Immunology and Allergy Unit with input and review by the Sheffield Clinical Reference Group (consisting of General Practitioners, Public Health Specialists and other Allied Health Care Professionals).

Results

We describe two General Practice Allergy referral and management pathways for Rhinitis and Urticaria and Angioedema.

Conclusions

These referral pathways aim to educate and support Primary Care Health Professionals with the symptomatic management of mild allergic disease, to provide closer working links between Primary Care and Specialist Allergy centres and ultimately, to improve patient experience and outcomes. Also, there is a potential cost saving for General Practitioners who may refer fewer patients to the Allergy clinic as a result of using these pathways. This is in line with the Next Steps Five year forward view of enhanced primary care and developing closer links with specialists to reduce the need for referrals when certain patients can be managed within primary care.

Category: Undergraduate

P.059

Optimal mode of delivery for using probiotics or prebiotics to prevent eczema: a systematic review and meta-analysis

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Objectives

To undertake a systematic review and meta-analysis to assess the relationship between diet during pregnancy, lactation and the first year of life and future risk of allergic or autoimmune disease, or allergic sensitisation.

Method

In this systematic review, searches were made to produce a library of trials from January 1946 to February 2017 from MEDLINE, EMBASE, Web of Science, CENTRAL and LILACS. This systematic review includes randomised controlled trials, systematic reviews and meta-analyses which explore the relationship between diet during pregnancy, lactation or an infant's first year of life and risk of allergic disease or sensitisation. Two authors independently selected eligible studies, extracted data and assessed the quality of evidence using the Cochrane Risk of Bias tool. The certainty of evidence was assessed using GRADE. A senior consultant also independently checked all findings to ensure rigor and accuracy during data extraction and analysis. Statistical analysis was later performed and results analysed comprehensively.

Results

Overall the quality of evidence was moderate - there was a low or unclear risk of bias in most studies. Probiotics reduced AD risk at age ≤4 years (RR: 0.78; [0.68, 0.90]) with high statistical heterogeneity (I^2 = 60%). Subgroup analyses showed some evidence that postnatal administration to mother during lactation is more effective than infant supplementation alone during the postnatal period (p=0.005) – high statistical heterogeneity remained in this subgroup analysis. Other subgroup analyses showed no clear evidence that one subgroup had different efficacy to another. This effect did not persist in 5-14 year olds.

Conclusions

These findings suggest that further trials are needed to investigate the use of probiotics during pregnancy for the prevention of allergic rhinitis, wheeze and food allergy.