BOLETÍN BIBLIOGRÁFICO
DE INMUNOTERAPIA

Enero 2023

1

La ITA potencia la protección frente a virus en pacientes asmáticos.

Allergen Immunotherapy Enhances Airway Epithelial Antiviral Immunity in Patients with Allergic Asthma (VITAL Study): A Double Blind Randomized Controlled Trial T.

Woehlk C, Ramu S, Sverrild A, Nieto-Fontarigo JJ, Vázquez-Mera S

Am J Respir Crit Care Med. 2023 Jan 26. doi: 10.1164/rccm.202209-1708OC. Epub ahead of print. PMID: 36701676.

ARTÍCULO DESTACADO

INTRODUCTION
Allergic asthma is linked to impaired bronchial epithelial secretion of interferons (IFNs) which may be causally linked with the increased risk of viral exacerbations. We have previously shown that allergen immunotherapy (AIT) effectively reduces asthma exacerbations and prevents respiratory infections requiring antibiotics; however, whether AIT alters antiviral immunity is still unknown.

AIMS AND OBJECTIVES
To investigate the effect of house dust mite sublingual allergen immunotherapy (HDM-SLIT) on the bronchial epithelial antiviral and inflammatory responses in patients with allergic asthma.

METHODS
In this double blind randomized controlled trial (VITAL), adult patients with HDM allergic asthma received HDM-SLIT 12-SQ or placebo for 24-weeks. Bronchoscopy was performed at baseline and at week-24 which included sampling for human bronchial epithelial cells (HBECs). HBECs were cultured at baseline and at week-24 and stimulated with the viral mimic poly(I:C). mRNA expression was quantified by RT-qPCR and protein levels were measured by multiplex ELISA.

RESULTS
Thirty-nine patients were randomized to HDM-SLIT (n=20) or placebo (n=19). HDM-SLIT resulted in increased poly(I:C)-induced expression of IFN-β, both at gene (p=.009) and protein (p=0.02) level. IFN-λ gene expression was also increased (p=0.03), whereas IL-33 tended to be decreased (p=0.09). On the other hand, pro-inflammatory cytokines IL-6 (p=.009) and TNF-α (p=0.08) increased compared with baseline in HDM-SLIT group. There was no significant change in TSLP, IL-4, IL-13, and IL-10.

CONCLUSION
HDM-SLIT improves bronchial epithelial antiviral resistance to viral infection. These results potentially explain the efficacy of HDM SLIT reducing exacerbations in allergic asthma.

2

Esperanza para los jóvenes alérgicos: la ITA de pólenes mejora su calidad de vida.

Treatment with pollen allergen immunotherapy improves health-related quality of life in children and adolescents: a threeyear follow-up-study.

Agenäs H, Brorsson AL, Kull I, Lindholm-Olinder A

Allergy Asthma Clin Immunol. 2023;19(1):4. Published 2023 Jan 17. doi:10.1186/s13223-023-00756-9.

BACKGROUND
The immunological effect of allergen-specific immunotherapy is well documented, but few studies have examined the long-term effects of pollen subcutaneous immunotherapy (SCIT) on health-related quality of life (HRQoL) in children and adolescents. Therefore, the aims of this study were to evaluate the effect of pollen SCIT on HRQoL and to assess the association between HRQoL and symptoms among children and adolescents with allergic rhinoconjunctivitisin a 3 year follow-up.

METHODS
A prospective cohort study was conducted at a paediatric clinic in Sweden, including 158 children (5-16 years) on SCIT (birch and/or grass). Health-related quality of life, measured with DISABKIDS, symptom scores and allergen-specific IgE and IgG4 antibodies (blood test), were assessed at start, and after 1, 2 and 3 years of treatment. ANOVA and t-test were used to analyse differences over time, between groups and linear mixed model for the association between HRQoL and influencing factors.

RESULTS
After 1 year of pollen SCIT, HRQoL improved from 79.5 to 85.1 ($p < 0.001$), and the improvements were maintained (mean 1 years, 84.8, 3 years 87.2). Symptom scores decreased after 1 year, mean 19.9 to 11.5 ($p < 0.001$) and were maintained for year two (11.9) and year three (10.3). The proportion of children with severe or very severe symptoms decreased from 35.6% to 4.5% after 1 year of SCIT. Health related quality of life was associated with symptoms at all measured timepoints ($p = 0.001$-0.031); higher symptom scores were associated with lower perceived HRQoL. Allergen-specific IgE antibodies decreased, birch from 151.0 to 76.8 kU/L ($p < 0.001$), and IgG4 antibodies increased, birch from 2.2 to 17.6 g/L ($p < 0.001$), grass from 0.5 to 14.3 g/L ($p < 0.001$), during the study period.

CONCLUSION
After 1 year of pollen SCIT, HRQoL improved, and symptoms decreased; these changes were maintained during the study period. The proportion of severe and very severe symptoms significantly decreased.

3

ITA sublingual: cambios inmunológicos prometedores en niños con rinitis.

Changes in type 2 innate lymphoid cells and serum cytokines in sublingual immunotherapy in pediatric patients with allergic rhinitis.

Wang X, Shen Y, Hong S, Kang H, Ke X

BMC Pediatr. 2023 Jan 9;23(1):13. doi: 10.1186/s12887-022-03788-z. PMID: 36624390; PMCID: PMC9827662.

BACKGROUND

Type 2 innate lymphoid cells (ILC2) are upregulated in childhood allergic rhinitis (AR) and are associated with AR severity. This study aimed to investigate changes in the ILC2 milieu in pediatric patients with AR after sublingual immunotherapy (SLIT).

METHODS

Forty- pediatric patients with AR received house dust mite (HDM) allergen extract for SLIT group and thirty pediatric patients received placebo in the study, respectively. The levels of ILC2, ILC2-related cytokines (IL-5/IL-13) and their transcription factors (GATA binding protein 3, retinoic acid-related orphan receptor α) in the circulation were assessed after 1- and 2-year SLIT. Moreover, peripheral blood mononuclear cells (PBMCs) in patients were prepared and stimulated by recombinant thymic stromal lymphopoietin, IL-25, and IL-33 after 2-year SLIT. Subsequently, the levels of ILC2, IL-5, and IL-13 were tested.

RESULTS

The frequency of ILC2 and the levels of their transcription factors in the circulation were significantly decreased after SLIT in the SLIT group. The levels of ILC2-related cytokines in the SLIT group showed the same trend. The frequency of ILC2 was positively correlated with transcription factors and cytokines after SLIT. SLIT was observed to reduce the ability of HDM sensitization to generate the ILC2 milieu in PBMCs.

CONCLUSIONS

Changes in the ILC2 milieu may be correlated with the curative effect and immune regulation function of SLIT. Our results suggested that the regulatory effect on ILC2 is part of the therapeutic mechanism of SLIT.

4

Nuevo biomarcador que podría predecir la eficacia de la ITA.

Serum exosomal miR-146a-3p associates with disease severity and efficacy of sublingual immunotherapy in allergic rhinitis [published online ahead of print, 2023 Jan 28].

Zhang Y, Zhu K, Lv H, et al.

Int Immunopharmacol. 2023;116:109777. doi:10.1016/j.intimp.2023.109777.

BACKGROUND

Sublingual immunotherapy (SLIT) is an effective treatment for allergic rhinitis (AR), but its efficacy is variable among individuals. This study aimed to characterize serum exosome-derived microRNAs (miRNAs) and evaluate their abilities in predicting the efficacy of SLIT in AR.

METHODS

RNA sequencing was performed to explore differentially expressed exosomal miRNAs in serum exosomes between AR patients and healthy controls (HCs). Sequencing analysis results were verified in an independent cohort, and the correlations between the levels of exosome-derived miRNAs and disease severity were evaluated. The most promising miRNAs were further tested in two AR cohorts treated with SLIT to assess their abilities in predicting short and long term efficacy, respectively.

RESULTS

The exosome-derived miRNAs profiling in the AR group was significantly different from the HC group, and differentially expressed genes were enriched and clustered in pathways such as PI3K-Akt and ErbB signalling pathways. The top three most significant miRNAs were verified by reverse transcription polymerase chain reaction (qRT-PCR), and results showed that miR-146a-3p levels were significantly elevated in the AR group and correlated with the total and specific gE levels, the visual analogue scale of the total nasal symptom score (all $p < 0.05$). Further data in the first validation cohort suggested that miR-146a-3p levels were significantly downregulated in the effective group, and logistic regression showed that miR-146a-3p levels were associated with the short-term efficacy of SLIT($p < 0.05$). The receiver operating characteristic (ROC) curve showed that miR-146a-3p could early predict SLIT efficacy (AUC = 0.669, $p = 0.047$). In the second validation cohort, miR-146a-3p levels were also decreased in the effective group and the ROC curve further confirmed its reliable accuracy in predicting the long-term efficacy of SLIT in AR patients (AUC = 0.749, $p < 0.001$).

CONCLUSION

Serum exosome-derived miRNAs may be involved in the development of AR and associated with its disease severity. Serum exosome-derived miR-146a-3p seems to be a novel biomarker for predicting the short and long-term efficacies of SLIT in AR patients.

5

Factores predictores de éxito de la ITA en niños alérgicos a ácaros.

Effects of subcutaneous immunotherapy in allergic rhinitis children sensitive to dust mites.

Lin Y, Liu J, He J, Wu L, Li S

Allergol Immunopathol (Madr). 2023 Jan 1;51(1):84-91. doi: 10.15586/aei.v51i1.666. PMID: 36617826.

BACKGROUND

Subcutaneous immunotherapy (SCIT) is now the only treatment that can modify the natural course of allergic rhinitis (AR). However, not all children with AR benefit from SCIT.

OBJECTIVE

To evaluate the efficacy of SCIT in dust-mites-induced AR children and explore correlative factors predicting treatment response to SCIT.

METHODS

225 children aged 4-17 years old with AR were recruited from January 2016 to September 2019, and monitored at baseline, 4, 12, and 24 months after the start of SCIT treatment. The visual-analogue-score (VAS) was used to assess the clinical symptoms. Multivariate binary logistic regression analyses and receiver operating characteristic curves were used to explore correlative factors in predicting the efficacy of SCIT.

RESULTS

The significant declines in VAS started after 4 months of SCIT and continued to improve throughout the study compared with baseline. An increase in children's age (OR=0.688, 95%CI: 0.479-0.988) and those with allergic history (OR=0.097, 95%CI: 0.009-1.095) were negatively associated with the risk of poor efficacy. Polysensitized children were more likely to suffer poor efficacy (OR=15.511 95%CI: 1.319 182.355). The clinical response at month 4 (r=0.707) and month 12 (r=0.925) was related to that at month 24. The area under the curve (AUC) for improvement at month 4 and month 12 was 0.746 and 0.860, respectively.

CONCLUSION

Our study confirmed the clinical efficacy of SCIT in AR children. Children with younger age, negative allergic history, and multiple allergens may predict a worse efficacy. The onset of action and the clinical response to SCIT in the second year can be predicted as early as by month 4.

6

Tendencias de la ITA en rinoconjuntivitis: análisis bibliométrico de los últimos 20 años.

Knowledge mapping of immunotherapy for allergic rhinoconjunctivitis: a bibliometric study (2002-2021).

Chen N, Zhang K, Li Y, Liu Y

Allergol Immunopathol (Madr). 2023 Jan 1;51(1):63-73. doi: 10.15586. PMID: 36617823.

BACKGROUND

Allergic rhinoconjunctivitis(ARC) is a common chronic inflammatory disease. Numerous studies on the treatment of ARC have been published. By contrast, there are few bibliometric studies on immunotherapy for ARC. The purpose of this article is to describe the current treatments for ARC and to identify the trends in immunotherapy for ARC.

METHODS

Publications were searched from the Web of Science (WOS) Core Collection on April 25, 2022. CiteSpace and Microsoft Excel software were used for further bibliometric analysis.

RESULTS

A total of 969 publications on immunotherapy for ARC in English were retrieved. The number of relevant publications has been continuously increasing over the past 20 years, with many of the publications coming from Germany and the United States of America. In terms of institutions, the ALK Company in Denmark, Imperial College London in United Kingdom, and Charite-Universitatsmedizin Berlin in Germany published the most articles on immunotherapy for ARC. Meanwhile, Allergy and Journal of Allergy and Clinical Immunology published the most number of studies, and Oliver Pfaar from Germany authored the most number of articles. "Subcutaneous immunotherapy," "international consensus," "allergen immunotherapy," and "recommendation" were the most popular subjects. Thus, directions in research can be predicted as studies regarding mechanisms of ARC, clinical trials, and extracts have reported high-quality results.

CONCLUSION

Over the past 20 years, the overall quality of research on immunotherapy for ARC has gradually improved, allowing the introduction of specific and targeted treatment. Currently, the main focus of ARC research is the novel routes of drug delivery and combined treatment with biological agents.

7

Anticuerpos neutralizantes en la ITO de cacahuete: base molecular y relevancia clínica. New Study Identifies Molecular Basis for Successful Food Allergy Treatment with Neutralizing Antibodies“ "Neutralizing Antibodies in Oral Immunotherapy for Peanut Allergies: Molecular Basis and Clinical Relevance"

Immunotherapy-induced neutralizing antibodies disrupt allergen binding and sustain allergen tolerance in peanut allergy.

LaHood NA, Min J, Keswani T, Richardson CM, Amoako K
J Clin Invest. 2023 Jan 17;133(2):e164501. doi: 10.1172/JCI164501. PMID: 36647835.

ABSTRACT

In IgE-mediated food allergies, exposure to the allergen activates systemic allergic responses. Oral immunotherapy (OIT) treats food allergies through incremental increases in oral allergen exposure. However, OIT only induces sustained clinical tolerance and decreased basophil sensitivity in a subset of individuals despite increases in circulating allergen-specific IgG in all treated individuals. Therefore, we examined the allergen-specific antibodies from 2 OIT cohorts of patients with sustained and transient responses. Here, we compared antibodies from individuals with sustained or transient responses and discovered specific tolerance-associated conformational epitopes of the immunodominant allergen Ara h 2 recognized by neutralizing antibodies. First, we identified what we believe to be previously unknown conformational, intrahelical epitopes using x-ray crystallography with recombinant antibodies. We then identified epitopes only recognized in sustained tolerance. Finally, antibodies recognizing toleranceassociated epitopes effectively neutralized allergen to suppress IgE-mediated effector cell activation. Our results demonstrate the molecular basis of antibody-mediated protection in IgE-mediated food allergy, by defining how these antibodies disrupt IgE-allergen interactions to prevent allergic reactions. Our approach to studying the structural and functional basis for neutralizing antibodies demonstrates the clinical relevance of specific antibody clones in antibody-mediated tolerance. We anticipate that our findings will form the foundation for treatments of peanut allergy using neutralizing antibodies and hypoallergens.

8

Factores de riesgo de reacciones adversas con ITA de ácaros.

A single center retrospective study of systemic reactions' distribution and risk factors to subcutaneous immunotherapy with dust mite extract in patients with allergic rhinitis and/ or asthma.

Zhang X, Liu J, Chen H, Guo B, Liu F, Wang X
Heliyon. 2023;9(1):e13100. Published 2023 Jan 20. doi:10.1016/j.heliyon.2023.e13100.

OBJECTIVES

To analyze various risk factors including causes that may lead to adverse reactions, especially systemic adverse reactions（SRs）, before and after mite allergen subcutaneous immunotherapy (SCIT), so as to provide real-world reference data for further improving the safety of mite allergen SCIT.

METHODS

The local adverse reactions（LRs）and SRs of 230 patients with allergic rhinitis and/or asthma who received SCIT in Weifang people's hospital were analyzed retrospectively. The data of patient characteristics, drug factors and environmental elements of adverse reactions were collected and statistically analyzed.

RESULTS

There were 28 cases (12.2%) of SRs in 230 patients. All the patients received a total of 7515 injections and 37 SRs (0.49%) were observed. 32.4% (12/37) of SRs could identify their external and subjective triggers. SRs patients had higher 2-year SCIT compliance than no-SRs patients (p = 0.026). The prevalence of SRs in SCIT patients with atopic dermatitis or simple allergic asthma are no statistical significance (P = 0.111).

CONCLUSION

The incidence of SRs in this study is within an ideal range. Through professional patient education and pre injection risk factor assessment, Compliance is still wellcontrolled and guaranteed although SRs occurred.

9

Relación entre la rinitis y el asma en niños y la importancia de la ITA.

Diagnosis and Management of Allergic Rhinitis in Asthmatic Children.

Tenero L, Vaia R, Ferrante G, Maule M, Venditto L, Piacentini G, Senna G, Caminati M
J Asthma Allergy. 2023 Jan 5;16:45-57. doi: 10.2147/JAA.S281439. PMID: 36636703.

ABSTRACT

Allergic rhinitis (AR) is a common upper airways inflammatory condition especially in paediatric population; its burden potentially impacts on quality of life, quality of sleep and daily performance, which can be difficult to perceive but not less relevant in the middle-long term. The present review aims to provide an updated overview on AR epidemiology, diagnosis and with a special focus on its connections with bronchial asthma. In fact, when considering asthmatic pediatricpopulation, AR is probably the most important risk factor for asthma onset and the most impactful extra bronchial determinant of asthma control. Under this perspective, allergen immunotherapy (AIT) should always be considered in the light of a precision medicine approach. In fact, AIT does represent a unique opportunity to specifically interfere with AR immunological background, improve both AR and bronchial asthma control and prevent allergic disease evolution. Verifying the patient's eligibility to that option should be considered as a priority for every physician managing children suffering from AR, especially when associated with bronchial asthma.

10

¿Cuánto saben los médicos sobre inmunoterapia? Pregunta y analiza

Analysis of factors influencing the determination of indications for allergen-specific immunotherapy.

Ding B, Gao S, Huang J, Gong S, Lin J

Allergol Immunopathol (Madr). 2023 Jan 1;51(1):168-176. doi: 10.15586/aei.v51i1.756. PMID: 36617837.

OBJECTIVE

To develop a questionnaire and a scoring system for evaluating physicians' knowledge of allergen immunotherapy (AIT).

METHODS

Questionnaire was designed using the Questionnaire Star tool. A total of 1024 physicians were assessed, and based on the score divided into accurate judgment and inaccurate judgment groups. Statistical analysis was done, and counting data were expressed as frequencies and percentage values. Chi-square test and multi-factor logistic analysis were used to determine influencing factors on the indications for AIT.

RESULTS

Physician's age, grade of the hospital, and pediatric specialty influenced the accurate judgment of AIT indication after adjustment for independent variables ($P < 0.05$). In all, 80.5% physicians exercised accurate assessment for allergic rhinitis. Allergic conjunctivitis was judged accurately by 47.0% physicians. Bronchial asthma was judged accurately by 71.0% physicians, and atopic dermatitis by 61.3% physicians, with a higher accuracy rate for pediatricians than nonpediatriciansfor all the mentioned conditions ($P < 0.05$). There was no significant difference in the accuracy of judgment between pediatricians and non-pediatricians in terms of AIT for food allergy and dust mite sensitization ($P > 0.05$).

CONCLUSION

The results of our study demonstrated a high accuracy judgment rate among clinicians for rhinitis, asthma, and dermatitis, and a low accuracy rate for desensitization of healthy people with allergic conjunctivitis, food allergies, and allergen sensitization.

BOLETÍN BIBLIOGRÁFICO
DE INMUNOTERAPIA

Febrero 2023

1

¡Última hora en ITA frente a ácaros!

Current advances in house dust mite allergen immunotherapy (AIT): Routes of administration, biomarkers and molecular allergen profiling.

Thierry Batard, Walter G. Canonica, Oliver Pfaar, Mohamed H. Shamji, Robyn E. O'Hehir, Menno C. van Zelm, Laurent Mascarell

Mol Immunol. 2023 Mar;155:124-134.doi: 10.1016/j.molimm.2023.02.004. Epub 2023 Feb 16.

ARTÍCULO DESTACADO

ABSTRACT

Allergy to house dust mites (HDM) is a perennial respiratory disease that affect more than half a billion people worldwide. Dermatophagoides pteronyssinus and D. farinae, two HDM species, are major sources of indoor allergens triggering allergic inflammation. Although symptomatic drugs are widely used to block the allergic reaction, allergen immunotherapy is the only curative treatment of IgE-mediated type I respiratory allergies. In this article, we review recent advances in various routes of allergen immunotherapy. We particularly focus on subcutaneous (SCIT) and sublingual (SLIT) immunotherapy, used as a reference therapy since they have transformed allergic treatments by improving symptoms (asthma and rhinitis) as well as the quality of life of patients. We also highlight recent data in more exploratory routes (i.e., oral, intralymphatic, epicutaneous and intradermal) and discuss respective advantages of various route, as well as their foreseen modes of action. Finally, we provide an update on biomarkers as well as on the relevance of the molecular profiling of allergic individuals related to treatment efficacy or asthma prediction.

2

¿Cuánto dura el efecto de la ITSL frente a cacahuete tras finalizarla?

Open-label study of the efficacy, safety, and durability of peanut sublingual immunotherapy in peanut-allergic children.

Edwin H Kim, MD MS, Corinne A Keet, MD PhD, Yamini V Virkud, MD MPH, Stacy Chin, MD, Ping Ye, PhD, Anusha Penumarti, PhD, Johanna Smeekens, PhD, Rishu Guo, MD PhD, Xiaohong Yue, MS DDS, Quefeng Li, PhD, Michael R Kosorok, PhD, Michael D Kulis, PhD, A Wesley Burks, MD

J Allergy Clin Immunol. 2023 Feb 22;S0091-6749(23)00218-X. doi: 10.1016/j.jaci.2023.01.036. Online ahead of print.

BACKGROUND

Studies are limited on the efficacy of peanut sublingual immunotherapy (SLIT). The durability of desensitization after SLIT has not been well described.

OBJECTIVE

To evaluate the efficacy and safety of 4 mg peanut SLIT and persistence of desensitization after SLIT discontinuation.

METHODS

Challenge proven peanut-allergic 1-11 year old children were treated with open-label 4 mg peanut SLIT for 48 months. Desensitization after peanut SLIT was assessed by 5000 mg double-blind, placebo-controlled food challenge (DBPCFC). A novel randomly assigned avoidance period between 1-17 weeks was followed by a DBPCFC. Skin prick testing (SPT), immunoglobulins, basophil activation testing (BAT), TH1, TH2, and IL-10 cytokines were measured longitudinally. Safety was assessed through patient-reported home diaries.

RESULTS

Fifty-four participants were enrolled and 47 (87%) completed peanut SLIT and the 48- month DBPCFC per protocol. Mean successfully consumed dose (SCD) during DBPCFC increased from 48 mg to 2723 mg peanut protein after SLIT (p800 mg) and 36% full desensitization (SCD = 5000 mg). Modeled median time to loss of clinically significant desensitization was 22 weeks. Peanut SPT; peanut-specific IgE, IgG4, IgG4/IgE ratio; and peanut-stimulated BAT, IL-4, IL-5, IL-13, IFNgamma, and IL-10 changed significantly compared to baseline with changes seen as early as 6 months. Median rate of reaction per dose was 0.5% with transient oropharyngeal itching most common and no dosing symptoms requiring epinephrine.

CONCLUSION

In this open-label, prospective study, peanut SLIT was safe and induced clinically significant desensitization in the majority of children lasting more than 17 weeks after discontinuation of therapy.

3

Los niños que se vacunan necesitan menos medicación sintomática.

Real-world study: drug reduction in children with allergic rhinitis and asthma receiving immunotherapy.

Jorge Sanchez, Leidy Alvarez, Elizabeth García

Immunotherapy. 2023 Mar;15(4):253-266. doi: 10.2217/imt-2022-0215. Epub 2023 Feb 15.

BACKGROUND

The reduction of pharmacological treatment after allergen immunotherapy (AIT) for house dust mites (HDMs) has been little studied in children.

OBJECTIVE

To evaluate the reduction of pharmacological treatment comparing children that receive HDM immunotherapy (AIT group) versus only pharmacotherapy.

METHODS

A historic cohort of children with rhinitis or asthma was assessed. The main outcome was the frequency of complete drug discontinuation.

RESULTS

100% drug reduction was higher for rhinitis (4-year cumulative incidence: 30 vs 10.7%) and asthma (24.1 vs 10.5%) in the AIT group (n = 987) than in the pharmacotherapy group (n = 2012).

CONCLUSION

Immunotherapy is associated with a significant reduction of pharmacotherapy in children. This is a marker of clinical control and could be associated with positive economic impact.

4

¿En qué debemos fijarnos antes de iniciar una ITO? Busquemos un acuerdo de mínimos antes de iniciar ITO con alimentos.

Oral immunotherapy for food allergy: Translation from studies to clinical practice?

Guillaume Pouessel, Guillaume Lezmi

World Allergy Organ J . 2023 Feb 3;16(2):100747. doi: 10.1016/j.waojou.2023.100747. eCollection 2023 Feb.

ABSTRACT

Oral immunotherapy (OIT) is now recognized as an alternative active treatment to strict food avoidance in certain patients with IgE-mediated food allergy. Studies have confirmed the efficacy of OIT to desensitize children with allergy to cow's milk, eggs, and peanuts. The benefits, risks, and constraints of OIT are becoming increasingly well understood. However, there is no consensual criteria to select patients to whom OIT could be proposed, and many issues remain to address including the definitions of desensitization and long-term efficacy, the as sessment of patient's experience in real life, the optimization of buildup and maintenance protocols, and the utility of multiple food OIT. The recent authorization by medical agency concerning the first medicine for peanut OIT is a step forward towards higher standardization in the practice of OIT. This article summarizes in comprehensive narrative format data on efficacy, tolerance, impact on quality of life and adverse effects of OIT and discuss elements to consider in clinical practice before starting OIT.

5

La ITA no es inclusiva en USA: negros, hispanos y asiáticos salen perdiendo.

Racial and Ethnic Disparities in Allergen Immunotherapy Prescription for Allergic Rhinitis.

Sunjay Modi, Matthew R. Norris, Victoria Nguyen, Robert Bower, Timothy J. Craig, Taha Al-Shaikhly

J Allergy Clin Immunol Pract. 2023 Feb 1;S2213-2198(23)00120-4. doi: 10.1016/j.jaip.2023.01.034.

BACKGROUND

Racial and ethnic differences exist in the severity of various atopic diseases including allergic rhinitis (AR). Patients of under represented races and ethnicities may be subjected to disparate subcutaneous allergen immunotherapy (SCIT) prescription practices.

OBJECTIVE

To explore the racial and ethnic disparities in the use of SCIT among patients with AR.

METHODS

In this retrospective matched cohort study, we used the TriNetX US Collaborative Network, a multicenter electronic health record-based database to identify patients with AR 18 years and older. Patients were grouped according to their racial and ethnic identification. Study groups were matched for baseline demographics, atopic comorbidities, heart diseases and utilization of β blockers, and angiotensin-converting enzyme inhibitors. The proportion of patients of under-represented racial and ethnic groups started on SCIT was contrasted to the non-Hispanic White cohort.

RESULTS

We identified 1,038,000 patients with AR; the mean age (±standard deviation) at the index was 49.7 (±16.1) years, and 64.6% were female. Ethnicity information was available from 87.3% of patients, and the majority (92.3%) were non-Hispanic. Over a 3-year observation period, fewer Black patients (relative risk [RR], 0.40; 95% confidence interval [CI], 0.33-0.48) and Hispanic patients (RR, 0.80; 95% CI, 0.64-0.99) were started on SCIT compared with non-Hispanic White patients. The proportions of Asian patients who were initiated on SCIT tended to be lower when compared with non-Hispanic White patients (RR, 0.69; 95% CI, 0.47-1.009).

CONCLUSIONS

In the United States, differences in SCIT prescription exist between Black and Hispanic patients relative to White patients. Barriers to treatment should be explored and mitigated.

6

ITA nasal vehiculizada en hidrogel, ¿será la solución?

ITA nasal vehiculizada en hidrogel, ¿será la solución?

Yiwei Zhong, Caixia Su, Shuting Wu, Chunhui Miao, Bin Wang

Int Immunopharmacol. 2023 Feb 2;116:109718.doi: 10.1016/j.intimp.2023.109718. Online ahead of print.

ABSTRACT

Asthma poses a significant threat to public health, with an estimated burden of over 334 million people worldwide. Available treatments are often inadequate. We developed a thermo-sensitive hydrogel vaccine containing allergen and FK506 that induced immune tolerance via intranasal administration to treat experimental allergic asthma. The hydrogel delivery system was formulated based on Poloxamer 407 (P407), Carbopol 974P NF, and Polyoxyl 15 hydroxystearate (Kolliphor HS15, HS15). It flowed freely at room temperature and rapidly formed a hydrogel in the nasal cavity once the temperature rose over 33 °C. Ovalbumin and FK506 were slowly released from the hydrogel form and their mucosal residence time was significantly prolonged compared to the liquid formulation. In both an OVA-induced asthma model and an HDM-induced asthma model, the vaccines formulated in hydrogel gave lower levels of eosinophilic inflammation, and airway remodeling. The reduction of lung function was ameliorated, and Foxp3-expressing CD4 + Treg cells were significantly higher. The frequency of Foxp3 + Tregs in lung-draining lymph nodes (dLNs) was correlated with the amelioration. Depletion of Foxp3 + Treg cells abolished the beneficial effects of the allergen/FK506 hydrogel vaccinations. Thus, the allergen/FK506 hydrogel formulation has the potential to be a delivery system for therapeutic allergy vaccines to induce immune tolerance.

7

La ansiedad que genera la ITO varía con la edad del paciente y el género. Tengámoslo en cuenta.

Validated anxiety assessments among pediatric patients with peanut allergy on oral immunotherapy.

Kelsey Kaman, Meera Dhodapkar, Veronika Shabanova, Sarah McCollum, Jeffrey Factor, Stephanie Leeds

Int Immunopharmacol. 2023 Feb 2;116:109718.doi: 10.1016/j.intimp.2023.109718. Online ahead of print.

BACKGROUND

While efficacy, safety, and quality of life measures associated with peanut oral immunotherapy (OIT) have been studied, the relationship between peanut OIT and clinical anxiety has not yet been assessed. The latter is important to help providers and families have an improved shared medical decision discussion around the benefits of initiating OIT.

OBJECTIVE

We aimed to investigate the relationship between undergoing OIT and anxiety in patients with peanut allergy.

METHODS

In this prospective cross-sectional cohort study, using validated and age appropriate anxiety scales administered with electronic survey questionnaires, we used generalized linear regressions to compare anxiety between patients undergoing OIT and similar patients with peanut allergy but not on OIT (controls).

RESULTS

In the younger cohort (< 7 years, n=80), there was generally a low prevalence of diagnosable anxiety across patients on OIT and controls. In the older cohort (> 7 years, n=125), there was a higher prevalence of anxiety but no clinically meaningful difference between anxiety scores of patients on OIT and controls. In the older cohort, patients with asthma were more likely to have higher mean anxiety scores (p=0.04), as were female patients compared to male patients (p=0.004).

8

Nunca fue necesario esperar 3 años: la respuesta a la ITA con ácaros se prevé en los primeros meses.

Clinical response to subcutaneous immunotherapy at 3 years in allergic rhinitis patients is predicted by short-term treatment effectiveness.

Dong Liu, Jingyun Li, Yunbo Gao, Feifei Cao, Wei Xiong, Chengshuo Wang, Yuan Zhang, Luo Zhang

Clin Transl Allergy. 2023 Feb;13(2):e12223. doi: 10.1002/clt2.12223.

ABSTRACT

No disponible. Carta al editor.

9

Nuestra respuesta inmune a la ITA marca la mejoría clínica. Fenotipemos y triunfaremos.

Deciphering Differential Behavior of Immune Responses as the Foundation for Precision Dosing in Allergen Immunotherapy.

Antoine Magnan, Jean-François Nicolas, Davide Caimmi, Marc Vocanson, Thierry Haddad, Luc Colas, Silvia Scurati, Laurent Mascarell, Mohamed H. Shamji

J Pers Med. 2023 Feb 13;13(2):324.doi: 10.3390/jpm13020324.

ABSTRACT

Like in many fields of medicine, the concept of precision dosing has re emerged in routine practice in allergology. Only one retrospective study on French physicians' practice has addressed this topic so far and generated preliminary data supporting dose adaptation, mainly based on experience, patient profile understanding and response to treatment. Both intrinsic and extrinsic factors shape the individual immune system response to allergen immunotherapy (AIT). Herein, we focus on key immune cells (i.e., dendritic cells, innate lymphoid cells, B and T cells, basophils and mast cells) involved in allergic disease and its resolution to further understand the effect of AIT on the phenotype, frequency or polarization of these cells. We strive to discriminate differences in immune responses between responders and non-responders to AIT, and discuss the eligibility of a non/low-responder subset for dose adaptation. A differential behavior in immune cells is clearly observed in responders, highlighting the importance of conducting clinical trials with large cohorts of well-characterized subjects to decipher the immune mechanism of AIT. We conclude that there is a need for designing new clinical and mechanistic studies to support the scientific rationale of dose adaptation in the interest of patients who do not properly respond to AIT.

10

La efectividad de la ITO con leche mejora si añadimos probióticos.

La efectividad de la ITO con leche mejora si añadimos probióticos.

K. Yamamoto-Hanada, M. Sato, K. Toyokuni, M. Irahara, E. Hiraide-Kotaki, N. Harima-Mizusawa, H. Morita, K. Matsumoto, Y. Ohya

ABSTRACT

Safer and more effective cow milk (CM)-oral immunotherapy that does not induce allergic reactions has not yet been standardised. We sought to explore the efficacy and feasibility of a combination of heat-killed Lactiplantibacillus plantarum YIT 0132 (LP0132) and oral immunotherapy for treating IgE-mediated cow milk allergy (CMA). We conducted a 24-week, double-blind, randomised (1:1), two-arm, parallel-group, placebo-controlled, phase 2 trial of LP0132 intervention for treating IgE-mediated CMA in children aged 1-18 years (n=60) from January 29, 2018 to July 12, 2019 in Tokyo, Japan. Participants were randomly assigned to the LP0132 group receiving citrus juice fermented with LP0132 or to the control group receiving citrus juice without. Both groups received low-dose slow oral immunotherapy with CM. The primary outcome was improved tolerance to CM, proven by the CM challenge test at 24 weeks. Secondary outcomes were changes in serum biomarkers of serum-specific β-lactoglobulin-IgE (sIgE) and β-lactoglobulin-IgG4 (sIgG4). Exploratory outcomes included changes in serum cytokine levels and gut microbiota composition. A total of 61 participants were included. Finally, 31 children were assigned to the LP0132 group and 30 to the control group, respectively. After the intervention, 41.4 and 37.9% of the participants in the LP0132 and control groups, respectively, showed improved tolerance to CM. In serum biomarkers after the intervention, the sIgG4 level was significantly higher, and interleukin (IL)-5 and IL-9 were significantly lower, in the LP0132 group than in the control group. In the gut microbiome, the α-diversity and Lachnospiraceae increased significantly in the LP0132 group, and Lachnospiraceae after the intervention was significantly higher in the LP0132 group than in the control group. In conclusion, low-dose oral immunotherapy with modulating gut microbiota might be a safer and more effective approach for treating cow's milk allergy.

BBI BOLETÍN BIBLIOGRÁFICO DE INMUNOTERAPIA

Marzo 2023

1

La efectividad de la ITA, ¿cómo es en la vida real?

Real-world, long-term effectiveness of allergy immunotherapy in allergic rhinitis: Subgroup analyses of the REACT study.

Contoli M, Porsbjerg C, Buchs S, Larsen JR, Freemantle N, Fritzsching B

J Allergy Clin Immunol. 2023 Mar 3:S0091-6749(23)00284-1. doi: 10.1016/j.jaci.2023.02.024. Epub ahead of print. PMID: 36871918.

ARTÍCULO DESTACADO

BACKGROUND

Randomized controlled trials have demonstrated the efficacy of allergy immunotherapy (AIT) in allergic rhinitis (AR) and the disease-modifying effects of the SQ grass sublingual immunotherapy (SLIT) tablet.

OBJECTIVE

We sought to assess real-world, long-term effectiveness and safety across AIT subgroups: route of administration, therapeutic allergen, persistence to AIT, and SQ grass SLIT tablet.

METHODS

The primary outcome of AR prescriptions from a retrospective cohort study (REAl-world effeCtiveness in allergy immunoTherapy; 2007-2017) was assessed across prespecified AIT subgroups in subjects with AR with and without AIT prescriptions (controls). Safety was assessed as anaphylaxis for 2 days or less of the first AIT prescription. Subgroup follow-up continued until samples were fewer than 200 subjects.

RESULTS

Subcutaneous immunotherapy (SCIT) and SLIT tablets showed similarly greater reductions in AR prescriptions than controls (SCIT vs SLIT tablets: year 3, P = .15; year 5, P = .43). Comparably greater reductions in AR prescriptions were observed for grass- and house dust mite-specific AIT than for controls, but significantly smaller reductions were observed for tree-specific AIT (tree vs house dust mite, and vs grass: years 3 and 5, P < .0001). Persistence to AIT was associated with greater reductions in AR prescriptions versus nonpersistence (persistence vs nonpersistence: year 3, P = .09; year 5, P = .006). SQ grass SLIT tablet showed sustained reductions versuscontrols for up to 7 years (year 3, P = .002; year 5, P = .03). Rates of anaphylactic shock were low (0.000%-0.092%), with no events for SQ SLIT tablets.

CONCLUSIONS

These results demonstrate real-world, long-term effectiveness of AIT, complement disease-modifying effects observed in SQ grass SLIT-tablet randomized controlled trials, and highlight the importance of using newer evidence-based AIT products for tree pollen AR.

2

¡Por fin una comparativa de SCIT frente a SLIT!

Comparison of rush-subcutaneous and sublingual immunotherapy with house dust mite extract for pediatric allergic rhinitis: A prospective cohort study.

Hamada M, Saeki K, Tanaka I

Allergol Int. 2023 Mar 12:S1323-8930(23)00011-4. doi: 10.1016/j.alit.2023.02.007. Epub ahead of print. PMID: 36918306.

BACKGROUND

We aimed to compare the effectiveness and safety of subcutaneous immunotherapy (SCIT) and sublingual immunotherapy (SLIT) with standardized house dust mite (HDM) extract for allergic rhinitis.

METHODS

Participants with allergic rhinitis selected their treatment between HDM SCIT or HDM SLIT, according to their wishes. We prospectively followed symptoms of allergic rhinitis using the alergic rhinitis symptom medication score (ARSMS), along with adverse reactions, during the dose escalation and maintenance phases for two years. We compared the outcomes between propensity scorematched groups to adjust the confounding factors.

CONCLUSIONS

After propensity score matching, 88 patients in the HDM SCIT(n = 44) and HDM SLIT groups (n = 44) remained for analysis. The HDM SCIT group showed significantly earlier effectiveness than the HDM SLIT group (median time to decrease in ARSMS [≥2 points]: 5.5 vs. 18.0 months, p < 0.001). The incidence of systemic reactions was not significantly different between the two groups in the dose escalation phase (68.2% vs. 56.8%, p = 0.379). In the maintenance phase, the incidence of systemic reactions was higher in the HDM SCIT group than in the HDM SLIT group (18.2% vs. 0%, p < 0.006). All 44 patients in the HDM SCIT group completed two years of treatment, while nine patients in the HDM SLIT group discontinued treatment.

3

Veamos los cambios inmunológicos que explican quién responde mejor a la IT con cacahuete.

Immune Response Evolution in Peanut Epicutaneous Immunotherapy for Peanut-Allergic Children.

Bastin M, Carr WW, Davis CM, Fleischer DM, Lieberman JA, Mustafa SS, Helleputte T, Bois T, Campbell DE, Green TD, Greenhawt M

Allergy. 2023 Mar 14. doi: 10.1111/all.15709. Epub ahead of print. PMID: 36916639.

BACKGROUND

Epicutaneous immunotherapy (EPIT) with investigational Viaskin™ Peanut 250 μg (DBV712) has demonstrated statistically superior desensitization versus placebo in peanut-allergic children in clinical trials. It is unclear if serologic biomarkers predict response.

METHODS

Serum-specific IgG4 and IgE (whole peanut and components) from subjects enrolled in the phase 3 PEPITES study were examined by exploratory univariate and multivariate analyses to determine trajectories and predictors of treatment response, based upon peanut protein eliciting dose (ED) at Month (M) 12 double-blind placebo-controlled food challenge.

RESULTS

Among Viaskin Peanut-treated subjects, peanut sIgG4 significantly increased from baseline through M12 and peanut sIgE peaked at M3 and fell below baseline by M12, with sIgG4 and sIgE peanut components mirroring these trajectories. Placebo subjects had no significant changes. By univariate analysis, M12 peanut sIgG4/sIgE was higher in treatment responders ($P < 0.001$) and had highest area under the curve (AUC) for predicting ED ≥300 mg and ≥1000 mg (AUC 69.5% and 69.9%, respectively). M12 peanut sIgG4/sIgE >20.1 predicted M12 ED ≥300 mg (80% positive predictive value). The best performing component was Ara h 1 sIgE <15.7 kUA /L (AUC 66.5%). A multivariate model combining Ara h 1 and peanut sIgG4/sIgE had an AUC of 68.2% (ED ≥300 mg) and 67.8% (ED ≥1000 mg).

CONCLUSIONS

Peanut sIgG4 rise most clearly differentiated Viaskin Peanut versus placebo subjects. sIgG4/sIgE ratios >20.1 and the combination of Ara h 1 and peanut sIgG4/sIgE had moderate ability to predict treatment response and could potentially be useful for clinical monitoring. Additional data are needed to confirm these relationships.

4

El efecto a largo plazo de la ITA... ¿es mejor en niños o en adultos?

Long-term efficacy of HDM-SCIT in pediatric and adult patients with allergic rhinitis.

Ren L, Wang C, Xi L, Gao Y, Zhang Y, Zhang L

Allergy Asthma Clin Immunol. 2023 Mar 11;19(1):20. doi: 10.1186/s13223-023-00781-8. PMID: 36906588; PMCID: PMC10007655.

BACKGROUND

Subcutaneous immunotherapy (SCIT) is a well-validated and effective disease modification treatment for house dust mites (HDM)-induced allergic rhinitis (AR). Long-term post-treatment comparisons in children and adults treated with SCIT have rarely been published. This study aimed to evaluate the long-term efficacy of HDM SCIT administered under a cluster schedule in children compared to adults.

METHODS

This was an open-design, observational, long-term clinical follow-up study on children and adults with perennial AR treated with HDM-SCIT. The follow-up consisted of a three-year treatment duration plus a post-treatment follow-up of over three years.

RESULTS

Patients in the pediatric ($n = 58$) and adult ($n = 103$) groups completed a post-SCIT follow-up of over three years. The total nasal symptom score (TNSS), combined symptom medication score (CSMS), and rhinoconjunctivitis quality-of-life questionnaire (RQLQ) score decreased significantly at T1 (three-year SCIT completed) and T2 (follow-up completed) in the pediatric and adult groups. In both groups, the improvement rate of TNSS (T0-T1) was moderately correlated with the baseline TNSS ($r = 0.681$, $p < 0.001$ and $r = 0.477$, $p < 0.001$ for children and adults, respectively). Only in the pediatric group, TNSS was significantly lower at T2 compared with that right after SCIT cessation (T1) ($p = 0.030$).

CONCLUSIONS

Children and adults with HDM-induced perennial AR could achieve a sustainable post-treatment efficacy for over three years (up to 13 years) following a three-year SCIT. Patients with relatively severe nasal symptoms at baseline may benefit more from SCIT. Children who have completed an adequate course of SCIT may gain further improvement in nasal symptoms after SCIT cessation.

5

Polisensibilización en alergia a himenópteros: combinar el diagnóstico molecular y la inhibición con CCD nos dará la solución.

Molecular diagnostics and inhibition of cross-reactive carbohydrate determinants in Hymenoptera venom allergy.

Jovanovic D, Peric-Popadic A, Djuric V, Stojanovic M, Lekic B, Milicevic O, Bonaci-Nikolic B
Clin Transl Allergy. 2023 Mar;13(3):e12230. doi: 10.1002/clt2.12230. PMID: 36973962; PMCID: PMC9993137.

BACKGROUND

The composition of venom extracts, cross-reactive carbohydrate determinants (CCD) and the component-resolved diagnostics (CRD) are important fields of investigation. IgE-reactivity to CCD complicates the interpretation of IgE to Hymenoptera venoms, especially in patients with multiple-positivity. We analyzed the clinical importance of CRD and CCD-inhibition for selection of allergens for venom immunotherapy (VIT).

METHODS

In 71 patients, we measured specific IgE (sIgE) to honeybee venom (HBV), wasp venom (WV), hornet venom (HV), CCD, and recombinant allergens: phospholipase A2 (rApi m 1), hyaluronidase (rApi m 2), icarapin (rApi m 10), antigen 5 (rVes v 5), and phospholipase A1 (Immunoblot). In 29/71 HBV/WV/HV/CCD-positive patients CCD-inhibition was performed. According to CRD and CCDinhibition, we identified true sensitization and defined groups of multiple-positive patients who needed CCD-inhibition before starting VIT.

RESULTS

sIgE-rApi m 1, sIgE-rApi m 2, and sIgE-rApi m 10 were detected in 65.7%, 68.4%, and 58%, respectively. In HBV allergic patients, CRD sensitivity was 86.8%. In WV allergic patients, sensitivity of sIgE rVes v 5 was 94%. True multiple-sensitization was found in 44.8% of HBV/WV/HV/CCD-positive patients after CCD-inhibition. Patients with multiple venom- and CCD-positivity had more frequent severe allergic reactions ($p < 0.001$). CCD-inhibition was helpful in HBV/WV/HV/CCD-positive patients who were negative to all tested recombinant honeybee allergens. Persistence of HBV-positivity after CCD-inhibition requires CRD to other honeybee recombinant allergens.

CONCLUSION

CRD, using a profile of five most important recombinant allergens and CCD, has a high sensitivity for the diagnosis of venom allergy, especially in patients positive to several venom extracts. CRD and CCD-inhibition are helpful to reveal the clinically relevant, true sensitization and improve the selection of venoms for long-lasting VIT.

6

Uno de cada cuatro pacientes está mal diagnosticado si no hacemos estudio molecular.

Molecular allergy diagnosis is sensitive and avoids misdiagnosis in patients sensitized to seasonal allergens.

Koch L, Laipold K, Arzt-Gradwohl L, Sturm EM, Aberer W, Aumayr M, Hemmer W, Čerpes U, Sturm GJ
Clin Transl Allergy. 2023 Mar;13(3):e12231. doi: 10.1002/clt2.12231. PMID: 36973961; PMCID: PMC10011670.

BACKGROUND

The specificity of extract-based pollen allergy diagnosis is decreased due to cross-reactivity via cross-reactive carbohydrate determinants (CCDs) or panallergens such as profilins or polcalcins. This study aimed to explore the prevalence of sensitization to seasonal extracts, CCDs, profilin and polcalcin and investigate the sensitivity and specificity of seasonal molecular allergy diagnosis (MAD) using commercially available test methods.

METHODS

2948 patients were screened for specific immunoglobulin E to ash, birch, mugwort, ragweed and timothy grass pollen extracts and grouped according to the number of positive tests (1-5). 100 patients from each group and a control group were randomly selected to calculate the prevalence of CCD and panallergen sensitization. With 742 patients, sensitivity and specificity of MAD (Alt a 1, Fra/Ole e 1, Bet v 1, Phl p 1, Art v 1, and Amb a 1) was determined.

RESULTS

1627 patients (55.2%) were positive to at least one, and 1002 patients (34.0%) were positive to multiple of the five pollen allergens investigated; 18.5% of the pollen-sensitized patients had sensitization to CCDs or panallergens. Specifically, sensitization to CCDs, profilins, and polcalcins was observed in 8.7%, 10.9%, nd 2.9% of these patients, respectively. The sensitivity of MAD was high, with sensitivities between 96.2% and 100% using ImmunoCAP and 91.5% and 100% using ALEX2. Specificity was 100% for both assays.

CONCLUSIONS

Due to cross-reactivity, about one-fifth of pollen-sensitized patients is at risk of misdiagnosis. However, MAD is sensitive, specific and helps to avoid misdiagnosis and select primary allergen sources for immunotherapy.

7

Si tiene asma, no lo dudes: ¡vacuna!

Allergic asthma: An indication for allergen immunotherapy.

Ankermann T, Brehler R

Allergol Select. 2023 Mar 1;7:33-38. doi: 10.5414/ALX02332E. PMID: 36925993; PMCID: PMC10012881.

ABSTRACT

Allergen immunotherapy (AIT) as a validated, disease-modifying treatment is nowadays a widely recommended therapy option for allergic rhinitis and allergic asthma. The registration of allergen extracts used for AIT is based on allergen standardization, dose finding trials, and phase 3 trials proving their efficacy in high-quality, statistically significant randomized clinical trials. Real-world evidence (RWE) studies confirm the clinical relevance of these findings. The most data are available for the treatment of patients suffering from allergic rhinitis. Due to the similar inflammatory mechanisms, allergic rhinitis is often associated with allergic asthma. AIT, which induces tolerance against individual allergens, is the approach to treat the underlying mechanisms of these two interrelated respiratory diseases. Some trials have been published focusing primarily on the effect of AIT on parameters of allergic asthma. Here we give a summary of the evidence for the efficacy of AIT in the indication of allergic asthma.

8

Recomendaciones (y censuras) de la guía internacional de consenso 2023 para rinitis.

International consensus statement on allergy and rhinology: Allergic rhinitis - 2023. Knowledge mapping of immunotherapy for allergic rhinoconjunctivitis: a bibliometric study (2002-2021).

Wise SK, Damask C, Roland LT, Ebert C, Levy JM

Int Forum Allergy Rhinol. 2023 Apr;13(4):293-859. doi: 10.1002/alr.23090. Epub 2023 Mar 6. PMID: 36878860.

BACKGROUND

In the 5 years that have passed since the publication of the 2018 International Consensus Statement on Allergy and Rhinology: Allergic Rhinitis (ICAR-Allergic Rhinitis 2018), the literature has expanded substantially. The ICAR-Allergic Rhinitis 2023 update presents 144 individual topics on allergic rhinitis (AR), expanded by over 40 topics from the 2018 document. Originally presented topics from 2018 have also been reviewed and updated. The executive summary highlights key evidence-based findings and recommendation from the full document.

METHODS

ICAR-Allergic Rhinitis 2023 employed established evidence based review with recommendation (EBRR) methodology to individually evaluate each topic. Stepwise iterative peer review and consensus was performed for each topic. The final document was then collated and includes the results of this work.

RESULTS

ICAR-Allergic Rhinitis 2023 includes 10 major content areas and 144 individual topics related to AR. For a substantial proportion of topics included, an aggregate grade of evidence is presented, which is determined by collating the levels of evidence for each available study identified in the literature. For topics in which a diagnostic or therapeutic intervention is considered, a recommendation summary is presented, which considers the aggregate grade of evidence, benefit, harm, and cost.

CONCLUSION

The ICAR-Allergic Rhinitis 2023 update provides a comprehensive evaluation of AR and the currently available evidence. It is this evidence that contributes to our current knowledge base and recommendations for patient evaluation and treatment.

9

¿Y si vacunásemos frente a “todo” independientemente de la causa del problema?

Randomized Double Blind Pilot Study of Universal, Species Abundant, Multi-Allergen Subcutaneous Immunotherapy for ModerateSevere Allergic Rhinitis.

Tversky J, Patel P, Sowho M, Natarajan R, Chung T, Whelton A, Azar A

Ann Allergy Asthma Immunol. 2023 Mar 27:S1081-1206(23)00204-1. doi: 10.1016/j.anai.2023.03.022. Epub ahead of print. PMID: 36990203.

BACKGROUND

Allergic rhinitis affects approximately 10-20% of people living in industrialized nations leading to significant morbidity and large health care expenditures. Individualized high-dose, single species allergen immunotherapy has been shown to be effective in treating allergic rhinitis but can be associated with significant risks including anaphylaxis. Few studies have examined the safety and efficacy of universal low-dose multi-allergen immunotherapy.

OBJECTIVE

To determine the efficacy and safety of a universal, multi allergen immunotherapy formula for the treatment of allergic rhinitis.

METHODS

Patients with moderate-severe perennial and seasonal allergic rhinitis were randomized in a double-blind, placebo-controlled fashion to receive a novel, subcutaneous multi-allergen immunotherapy (MAIT) regimen containing a unique mixture of more than 150 aeroallergens, including several cross-reactive species. All patients received the exact same universal immunotherapy formula regardless of which specific skin tests were positive. Primary outcome measures at 8 and 12 weeks of therapy included validated clinical assessments; TNSS and mini-RQLQ, and the use of rescue medications.

RESULTS

Thirty-one subjects (n=31) were randomized to receive multi allergen immunotherapy (MAIT) versus placebo. By week twelve, MAIT resulted in a -4.6 (-58%) decrease in the combined TNSS and rescue medication score (DCS) compared to -1.5 (-20%) for placebo (P = 0.037). Likewise, MAIT resulted in a mini-RQLQ decrease of -34.9 (-68%) compared to -17 (-42%) for placebo (P = 0.039). Mild adverse events were uncommon and with similar frequency among the groups.

CONCLUSION

A novel and universal, high species abundance, multi-allergen immunotherapy formula was well-tolerated and resulted in significant improvement in symptoms of moderate-severe allergic rhinitis. The results of this pilot study should be considered preliminary, pending further randomized clinical trials.

10

Éxito de ITO = pauta + ÉTICA individualizada.

Viewing Pediatric Food Oral Immunotherapy Through an Ethical Lens-A Narrative Systematic Review.

Bjelac J, Shaker M, Greenhawt M, Kodish E

J Allergy Clin Immunol Pract. 2023 Mar 23:S2213-2198(23)00308-2. doi: 10.1016/j.jaip.2023.03.024. Epub ahead of print. PMID: 36965706.

BACKGROUND

Food allergy remains a common problem and a lifelong condition for many children. In recent years food allergy management has increasingly involved conversations about food oral immunotherapy. While ethical considerations of autonomy, beneficence, non-maleficence, and justice implicitly inform these conversations, applying these principles can be complex, particularly in young children. Families of young children assume a role of surrogate decision maker and must balance immediate risks with the hope of longer-term benefits.

OBJECTIVE

To explore implementation of oral immunotherapy in children through an ethical lens.

METHODS

To evaluate OIT through an ethical lens, a literature search was conducted to explore currently published frameworks in this arena.

RESULTS

Evaluation of the harm principle, the basic interest principle, and the best interest principle of parental decision making can be informative. Shared decision making continues to be central to the process of engaging with patient-family units to individualize the best care, at the right time, and minimize decisional discord. Whie OIT is well positioned to promote health and well-being, challenges to equity, sustainability, and organizational support must be considered to improve access for appropriate patients.

CONCLUSION

While approaches to food OIT may be tailored to the individual context of each patient-family unit, ethical principles must guide decisions to initiate and continue therapy. Traditional ethical principles of autonomy, beneficence, non-maleficence, and justice remain cornerstones when considering the ethical context of OIT.

BBI BOLETÍN BIBLIOGRÁFICO DE INMUNOTERAPIA

Abril 2023

1 Apps para no enMASKcarar la efectividad de la ITA.

Patient-centred digital biomarkers for allergic respiratory diseases and asthma: the ARIA-EAACI approach.

Jean Bousquet, Mohamed H Shamji, Josep Manto, Holger J Schünemann, G Walter Canonica, Marek Jutel et al

Allergy. 2023 Apr 11. doi: 10.1111/all.15740. Online ahead of print.

ARTÍCULO DESTACADO

Biomarkers for the diagnosis, treatment and follow-up of patients with rhinitis and/or asthma are urgently needed. Although some biologic biomarkers exist in specialist care for asthma, they cannot be largely used in primary care. There are no validated biomarkers in rhinitis or allergen immunotherapy (AIT) that can be used in clinical practice. The digital transformation of health and health care (including mHealth) places the patient at the centre of the health system and is likely to optimise the practice of allergy. ARIA (Allergic Rhinitis and its Impact on Asthma) and EAACI (European Academy of Allergy and Clinical Immunology) developed a Task Force aimed at proposing patient-reported outcome measures (PROMs) as digital biomarkers that can be easily used for different purposes in rhinitis and asthma. It first defined control digital biomarkers that should make a bridge between clinical practice, randomised controlled trials, observational real-life studies and allergen challenges. Using the MASK air app as a model, a daily electronic combined symptom-medication score for allergic diseases (CSMS) or for asthma (e-DASTHMA), combined with a monthly control questionnaire, were embedded in a strategy similar to the diabetes approach for disease control. To mimic real-life, it secondly proposed quality-of-life digital biomarkers including daily EQ-5D visual analogue scales and the bi-weekly RhinAsthma Patient Perspective (RAAP). The potential implications for the management of allergic respiratory diseases were proposed.

2 ITA y omalizumab, ¿mejor juntos que separados?

Adding a biologic to allergen immunotherapy increases treatment efficacy.

Andrzej Bożek, Andreas Fischer, Agnieszka Bogacz-Piaseczynska, Giorgio Walter Canonica

ERJ Open Res. 2023 Apr 17;9(2):00639-2022. doi: 10.1183/23120541.00639-2022. eCollection 2023 Mar.

BACKGROUND

The application of allergen immunotherapy (AIT) in combination with biological agents has been found to increase both the safety and efficacy of the desensitisation procedure in patients with food and insect venom allergy. The aim of our study was to compare the effectiveness of AIT in patients with house dust mite (HDM)-driven asthma treated with and without omalizumab.

MATERIALS AND METHODS

The study was a placebo-controlled, three-armed, randomised, parallel group, multicentre trial that included 52 patients with HDMdriven asthma. Only patients with monosensitisation to HDM were included. The study compared three patterns of therapy: omalizumab alone, HDM subcutaneous immunotherapy (SCIT-HDM)+ omalizumab, and SCIT alone. The main outcomes were evaluate the Asthma Control Questionnaire (ACQ) score, number of asthma exacerbations and reduction in the daily dose of inhaled steroids during 12 months of observation.

RESULTS

All variants of therapy led to significantly improved ACQ scores and reduction of asthma exacerbations in all study groups after 12 months of treatment. A statistically significant reduction in the daily doses of inhaled corticosteroids in the group with omalizumab alone (650±150 µg versus 500±50 µg for p=0.003) or SCIT-HDM+omalizumab (550±250 µg versus 375±75 µg for p=0.001) was observed, favouring the latter group.

CONCLUSION

The efficacy of AIT for HDM-driven asthma is significantly increased by the combination of allergen vaccine with omalizumab.

3 Receta con los ingredientes para manejar con éxito la alergia a alimentos.

An update on recent developments and highlights in food allergy.

Arielle Locke, Lisa Hung, Julia E M Upton, Liam O'Mahony, Jennifer Hoang, Thomas Eiwegger

Allergy. 2023 Apr 23. doi: 10.1111/all.15749. Online ahead of print.

ABSTRACT

While both the incidence and general awareness of food allergies is increasing, the variety and clinical availability of therapeutics remain limited. Therefore, investigations into the potential factors contributing to the development of food allergy and the mechanisms of natural tolerance or induced desensitization are required. In addition, a detailed understanding of the pathophysiology of food allergies is needed to generate compelling, enduring, and safe treatment options. New findings regarding the contribution of barrier function, the effect of emollient interventions, mechanisms of allergen recognition, and the contributions of specific immune cell subsets through rodent models and human clinical studies provide novel insights. With the first approved treatment for peanut allergy, the clinical management of food allergy is evolving towards less intensive, alternative approaches involving fixed doses, lower maintenance dose targets, coadministration of biologicals, adjuvants, and tolerance-inducing formulations. The ultimate goal is to improve immunotherapy and develop precision-based medicine via risk phenotyping allowing optimal treatment for each food-allergic patient.

4

Confirmado (tras meta-análisis): la IT intralinfática en rinitis es efectiva, segura y mejora el cumplimiento.

Evaluation of Safety, Efficacy, and Compliance of Intralymphatic Immunotherapy for Allergic Rhinoconjunctivitis: A Systematic Review and Meta-Analysis

Wenping Wang, Xiaoyan Wang, Hongtian Wang, Xueyan Wang

Int Arch Allergy Immunol. 2023 Apr 27;1-13. doi: 10.1159/000529025. Online ahead of print.

INTRODUCTION

Intralymphatic immunotherapy (ILIT) is an emerging type of allergen immunotherapy with fewer injections and shorter course for allergic rhinoconjunctivitis (ARC). The efficacy and safety have not been confirmed by informative and powerful evidence yet.

METHODS

A systematic review and meta-analysis were conducted through electronic searching with PubMed, Web of Science, Embase, Scopus, and China National Knowledge Infrastructure (CNKI). The safety (incidence of adverse events [AEs]), compliance (percent of patients completing treatment), and clinical efficacy of ILIT were evaluated. Clinical efficacy could be assessed by improvement of subjective symptom and rescue medication use or the nasal tolerance to specific allergen. This study is registered with PROSPERO (CRD42022353562)

RESULTS

12 randomized controlled trials (RCTs) comparing ILIT with placebo and 3 trials (2 RCTs and one case-control study) comparing ILIT and SCIT were included in this review. Totally, 582 patients diagnosed as AR or ARC were enrolled. Almost all the AEs were mild-to-moderate reactions except 2 patients developed anaphylactic reactions at the intralymphatic injection dose 5,000 SQ-U in one study. ILIT got higher incidence of local AEs than placebo, but their incidence of systemic AEs was similar. ILIT was safer than SCIT ($p < 0.05$). Almost all the patients could complete ILIT treatment, and the most common reason for discontinuation of ILIT was AEs. The compliance of patients receiving ILIT seemed higher than patients receiving SCIT. ILIT could significantly ameliorate subjective allergic symptoms, especially for seasonal ARC, and increase nasal tolerance, similar to SCIT.

CONCLUSION

ILIT was a safe and effective treatment for ARC and could achieve comparable clinical improvement with SCIT with shorter duration and higher compliance. Moreover, ILIT was safer than SCIT.

5

ITA vs monoclonal: efectos opuestos sobre la actividad del basófilo.

Differences in allergen-specific basophil activation and T cell proliferation in atopic dermatitis patients with comorbid allergic rhinoconjunctivitis treated with a monoclonal anti-IL-4Rα antibody or allergen-specific immunotherapy.

Anne-Sophie Layritz , Jorge Galicia-Carreón, Said Benfadal, Natalija Novak

Immun Inflamm Dis. 2023 Apr;11(4):e808.doi: 10.1002/iid3.808.

BACKGROUND

Atopic dermatitis (AD), a chronic inflammatory disorder, is often accompanied by allergic rhinoconjunctivitis (ARC) as a co morbidity. The use of a monoclonal anti-IL-4Rα antibody has been effective in controlling moderate to severe AD symptoms. Allergen-specific immunotherapy (AIT) is widely used for the treatment of ARC and asthma. The effects of AIT on basophil reactivity/effector functions have already been examined and used as indicators of the treatment efficacy. However, it is unclear, how an anti-IL-4Rα antibody can influence allergen-specific immune responses of basophils and T cells of AD patients with comorbid ARC.

OBJECTIVE

To investigate the effect of a monoclonal anti-IL-4Rα antibody on the in vitro allergic responses of basophils and T cells deriving from AD patients with comorbid ARC.

METHODS

Blood samples of 32 AD patients were obtained before, after 4 and 16 weeks of an anti-IL-4Rα antibody therapy (300 mg subcutaneously/2 weeks; n = 21) or AIT (daily sublingual application; n = 11). Patients treated with an anti-IL-4Rα antibody were grouped according to their serum specific immunoglobulin E levels and ARC symptoms, while patients receiving an AIT were additionally grouped according to the allergen specificity of their AIT. Basophil activation test and T cell proliferation assays were undertaken after an in vitro allergen stimulation.

RESULTS

A significant reduction of the immunoglobulin E levels and the allergen specific T cell proliferation was observed in AD patients treated with an anti-IL4Rα -antibody, while the allergen-specific basophil activation/sensitivity were found to be significantly increased. In patients receiving an AIT, the in vitro allergenspecific basophil activation and the T cell proliferation were found to be significantly decreased in response to seasonal allergens.

CONCLUSIONS

An IL-4Rα blockade induced by a monoclonal anti-IL-4Rα antibody leads to an increased activity/sensitivity of early effector cells (such as basophils), in contrast to a decreasing reactivity observed under an AIT. The late-phase T cell reaction to allergens did not differ between the herein assessed treatments.

6

No randomizar un estudio equivale a mayor riesgo de sesgo.

Comparison of evidence of treatment effects in randomized and nonrandomized studies on allergen immunotherapy.

Danilo Di Bona, Palma Carlucci, Federico Spataro, Giovanni Paoletti, Enrico Heffler, Jaakko Pulkanen

Clin Exp Allergy. 2023 Apr 3. doi: 10.1111/cea.14311. Online ahead of print.

ABSTRACT

Nonrandomized studies (NRS) on allergen immunotherapy (AIT) particularly lend themselves to evaluate outcomes that are insufficiently addressed in randomized controlled studies (RCTs). However, NRS are prone to several sources of bias, which limit their validity. We aimed at comparing AIT effects between RCTs and NRS and evaluate the reasons for discrepancies in study results. In this analysis, we compared NRS on AIT (including subcutaneous and sublingual immunotherapy, SCIT and SLIT, respectively) with SLIT and SCIT RCTs from published meta-analyses, assessing the Risk of Bias (RoB) for each study and the certainty of evidence from NRS and RCTs using the GRADE approach. We found: (1) very serious RoB in the 7 NRS included in the meta analysis showing a large difference between AIT and controls (standardized mean difference [SMD] for symptom score [SS], -1.77; 95% CI, -2.30, -1.24; p < .001; I2 = 95%) with very low certainty evidence; (2) serious RoB in the 13 SCIT-RCTs reporting a moderate-to-high difference between SCIT and controls (SMD for SS, -0.81; 95% CI, - 1.12, -0.49; p < .001; I2 = 88%) with moderate certainty evidence; (3) low RoB in the 13 SLIT-RCTs reporting a small benefit (SMD for SS, -0.28; 95% CI, -0.37, - 0.19; p < .001; I2 = 54.2%) with high certainty evidence. Similar results were reported for medication score. Our evidence is sufficient to conclude that the magnitude of effect estimates of NRS and RCTs directly correlate with the degree of RoB and inversely with the overall evidence certainty. NRS, which are more affected than RCTs by bias resulting in low certainty evidence, showed the largest effect size. Sound NRS are needed to complement RCTs.

7

ITA intralinfática en rinitis: 3 dosis y persistencia de mejoría tras 2 años.

Intralymphatic immunotherapy with birch and grass pollen extracts. A randomized double-blind placebo-controlled clinical trial.

Lars Ahlbeck, Emelie Ahlberg, Linn Stuivers, Janne Björkander, Ulla Nyström, Pavlos Retsas

Clin Exp Allergy. 2023 Apr 4.doi: 10.1111/cea.14307. Online ahead of print.

INTRODUCTION

There is a need to evaluate the safety and efficacy of intralymphatic immunotherapy (ILIT) for inducing tolerance in patients with allergic rhinitis.

METHODS

Thirty-seven patients with seasonal allergic symptoms to birch and grass pollen and skin prick test >3 mm and/or IgE to birch and timothy >0.35 kU/L were randomized to either ILIT, with three doses of 0.1 mL of birch pollen and 5-grass pollen allergen extracts on aluminium hydroxide (10,000 SQ-U/ml; ALKAbelló) or placebo using ultrasound-guided intralymphatic injections at monthly intervals. Daily combined symptom medical score and rhinoconjunctivitis total symptom score were recorded during the peak pollen seasons the year before and after treatment. Rhinoconjunctivitis total symptom score, medication score and rhinoconjunctivitis quality of life questionnaire were recorded annually starting 2 years after treatment. Circulating proportions of T helper cell subsets and allergen-induced cytokine and chemokine production were analysed using flow cytometry and ELISA.

RESULTS

There were no differences between the groups related to daily combined symptom medical score the year before and after treatment. Two years after ILIT (after unblinding), the actively treated group reported significantly fewer symptoms, lower medication use and improved quality of life than did the placebo group. After the pollen seasons the year after ILIT, T regulatory cell frequencies and grass-induced IFN-γ levels increased only in the actively treated group.

CONCLUSION

In this randomized controlled trial, ILIT with birch and grass pollen extract was safe and accompanied by immunological changes. Further studies are required to confirm or refute the efficacy of the treatment.

8

Acerca de optimizar el diagnóstico en alergia a venenos.

Venom anaphylaxis: Decision points for a more aggressive workup.

Patrizia Bonadonna, Peter Korosec, Francesca Nalin, David Bk Golden

J Allergy Clin Immunol Pract . 2023 Apr 27;S2213-2198(23)00456-7. doi: 10.1016/j.jaip.2023.04.016. Online ahead of print.

ABSTRACT

Diagnostic testing of patients who present for evaluation of insect venom allergy can involve many levels of investigation. A detailed initial history is critical for diagnosis and prognosis. The severity of previous sting reactions and the presence or absence of urticaria or hypotension predict severe future sting reactions and underlying mast cell disorders. Venom skin tests and specific IgE measurement can confirm the diagnosis but have limited positive predictive value for the frequency and severity of future sting reactions. Testing for serum IgE to recombinant venom component allergens can distinguish true allergy from crossreactivity to honey bee and yellowjacket venoms. Basophil activation tests can improve detection of venom allergy, and predict severity of reactions and the efficacy of venom immunotherapy, but are limited in availability. Elevated basal serum tryptase level is an important marker for severe sting anaphylaxis and underlying mast cell disorders (eg, hereditary alpha-tryptasemia and clonal mast cell disease). When there is high suspicion (eg, using the REMA score), bone marrow biopsy is the definitive tool to characterize the mast cell disorders that are associated with the most severe outcomes in patients with insect sting allergy.

9

ITO a huevo...¿mejor con dosis bajas o altas?

Efficacy and safety of low- and high-dose slow oral egg immunotherapy for hen's egg allergy: Single-center non-inferiority randomized trial.

Yuri Takaoka, Yoichi M Ito, Junko Kumon, Tomohiro Yamaguchi, Rumi Ueno, Yuki Tsurinaga

Asian Pac J Allergy Immunol . 2023 Apr 17. doi: 10.12932/AP-130722-1411. Online ahead of print.

BACKGROUND

Low-dose oral immunotherapy (OIT) is a safe treatment for hen's egg allergy; however, comparison of its therapeutic effects with those of highdose OIT has not been reported.

OBJECTIVE

To compare the efficacy of low- and high-dose boiled egg-white (EW) OIT for hen's egg allergy.

METHODS

Patients with hen's egg allergy were randomly assigned to two groups: OIT using hard-boiled EW with a maximum maintenance dose of 2 and 20 g in the low-dose (L-D) and high-dose (H-D) groups, respectively. The intake dose was ingested twice a week, increased by approximately 20% per week until reaching the target maintenance dose (2 or 20 g hard-boiled EW), and maintained thereafter according to the schedule. The threshold was confirmed via oral food challenge (OFC) after 6 months, and the difference in the proportion of subjects passing the exit OFC between groups was evaluated.

RESULTS

Fifty-two patients (L-D, n = 23; H-D, n = 29) were enrolled. Thirty-three patients (L-D, n = 17; H-D, n = 16) completed the 6-month OIT and underwent an exit OFC. In total, three (L-D, 3/17; H-D, 3/16) patients in each group tested negative for an exit OFC with a 20-g reactive dose (p = 1.000). EW-specific IgE levels in both groups decreased significantly after OIT (L-D, p < 0.001; H-D, p = 0.002).

CONCLUSIONS

A threshold-elevating effect was observed in the L-D group, not inferior to that in the H-D group. Low-dose OIT may be appropriate to treat hen's egg allergy for the first 6 months.

10

¿ITO con varios alimentos a la vez?... menos cuentos chinos.

Double-blind, placebo-controlled study of E-B-FAHF-2 in combination with omalizumab-facilitated multi-allergen oral immunotherapy.

Julie Wang, Robert A Wood, Samantha Raymond, Mayte Suárez-Fariñas, Nan Yang, Scott H Sicherer

J Allergy Clin Immunol Pract. 2023 Apr 20;S2213-2198(23)00406-3. doi: 10.1016/j.jaip.2023.03.051. Online ahead of print.

BACKGROUND

Oral immunotherapy (OIT) is limited by adverse events, and most patients require continued treatment to maintain their increased threshold. Adjunctive treatments have been explored to increase the safety and efficacy of OIT.

OBJECTIVE

This study aimed to determine the safety and efficacy of E-B-FAHF-2 for inducing remission in subjects undergoing omalizumab-facilitated multiallergen OIT.

METHODS

In this double-blind, placebo-controlled clinical trial, subjects were randomized 1:1 to receive either E-B-FAHF-2 or placebo, starting 2 months before OIT and continuing throughout OIT. All subjects received a 4-month course of omalizumab, starting 2 months before OIT through the 2-month OIT build-up phase. Following 24 months of multi-OIT (maintenance dose of 1000 mg of each allergen), desensitization and remission were assessed. The primary objective was to determine if subjects in the E-B-FAHF-2 group (EOIT) were more likely than the placebo group (OIT) to develop remission to all 3 allergens treated with multi-OIT, as defined by the absence of dose-limiting symptoms to a cumulative dose of 4,444 mg protein after discontinuing treatment for 3 months.

RESULTS

Thirty-three subjects were randomized. 63.6% were desensitized to 4444mg protein for each allergen at 26 months, and 24.2% met the primary outcome of remission at 29 months, with no difference between treatment groups. There was good adherence (>85%) with study medications, with no difference between treatment groups. There was no difference in reported overall adverse events between treatment groups.

CONCLUSION

Omalizumab facilitated multi-food OIT was safe and effective, and emission was achieved in about a quarter of subjects. However, utcomes were not improved by addition of E-B-FAHF-2.

BOLETÍN BIBLIOGRÁFICO DE INMUNOTERAPIA

Mayo 2023

1

Espaldarazo definitivo a la ITO con cacahuete en niños.

Phase 3 Trial of Epicutaneous Immunotherapy in Toddlers with Peanut Allergy.

Greenhawt M, Sindher SB, Wang J, O'Sullivan M, du Toit G et al.

N Engl J Med. 2023 May 11;388(19):1755-1766. doi: 10.1056/NEJMoa2212895. PMID: 37163622.

ARTÍCULO DESTACADO

BACKGROUND

No approved treatment for peanut allergy exists for children younger than 4 years of age, and the efficacy and safety of epicutaneous immunotherapy with a peanut patch in toddlers with peanut allergy are unknown.

METHODS

We conducted this phase 3, multicenter, double-blind, randomized, placebo-controlled trial involving children 1 to 3 years of age with peanut allergy confirmed by a double-blind, placebo controlled food challenge. Patients who had an eliciting dose (the dose necessary to elicit an allergic reaction) of 300 mg or less of peanut protein were assigned in a 2:1 ratio to receive epicutaneous immunotherapy delivered by means of a peanut patch (intervention group) or to receive placebo administered daily for 12 months. The primary end point was a treatment response as measured by the eliciting dose of peanut protein at 12 months. Safety was assessed according to the occurrence of adverse events during the use of the peanut patch or placebo.

RESULTS

Of the 362 patients who underwent randomization, 84.8% completed the trial. The primary efficacy end point result was observed in 67.0% of children in the intervention group as compared with 33.5% of those in the placebo group (risk difference, 33.4 percentage points; 95% confidence interval, 22.4 to 44.5; P<0.001). Adverse events that occurred during the use of the intervention or placebo, irrespective of relatedness, were observed in 100% of the patients in the intervention group and 99.2% in the placebo group. Serious adverse events occurred in 8.6% of the patients in the intervention group and 2.5% of those in the placebo group; anaphylaxis occurred in 7.8% and 3.4%, respectively. Serious treatment-related adverse events occurred in 0.4% of patients in the intervention group and none in the placebo group. Treatment-related anaphylaxis occurred in 1.6% in the intervention group and none in the placebo group.

CONCLUSIONS

In this trial involving children 1 to 3 years of age with peanut allergy, epicutaneous immunotherapy for 12 months was superior to placebo in desensitizing children to peanuts and increasing the peanut dose that triggered allergic symptoms.

2

¡Aquí verás el resumen de todo lo que hay sobre ITA intralinfática!

Evaluation of Intralymphatic Immunotherapy in Allergic Rhinitis Patients: A Systematic Review and Meta-analysis.

Jiang S, Xie S, Tang Q, Zhang H, Xie Z, Zhang J, Jiang W

Mediators Inflamm. 2023 May 8;2023:9377518. doi: 10.1155/2023/9377518.

BACKGROUND

Intralymphatic immunotherapy (ILIT) is short-course administration of allergen-specific immunotherapy (AIT). This study is aimed at assessing the clinical efficacy and safety of ILIT in patients with allergic rhinitis (AR).

METHODS

MEDLINE, PUBMED, and Cochrane Library were used to conduct electronic searches for clinical trials comparing ILIT and placebo in patients with AR. The final search took place on August 24, 2022. Cochrane Handbook for Systematic Reviews of Interventions was used to assess the risk of bias in the included studies. The outcomes included combined symptom and medication scores (CSMS), visual analog scale (VAS), allergic rhinoconjunctivitis quality of life (RQLQ), Skin-prick test (SPT), and adverse events (AEs). Data were synthesized as mean difference (MD)/standard mean difference (SMD) or risk difference (RD) and 95% confidence interval (CI).

RESULTS

Thirteen studies (454 participants) were included in this study. The ILIT group had better clinical improvement on the CSMS (random effects model, SMD-0.85, 95% CI [-1.58, -0.11], P = 0.02) and RQLQ (fixed-effects model, MD-0.42, 95% CI [0.69, 0.15], P = 0.003) than the placebo group. The booster injection was beneficial for CSMS (P < 0.0001), and the 4-week injection interval was superior to the 2-week injection period for improving VAS (P < 0.0001). Local swelling or erythema was the main AE following injection (random effects model, RD 0.16, 95% CI [0.05, 0.27], P = 0.005).

DISCUSSION

For individuals with AR, ILIT is safe and effective. ILIT alleviates clinical symptoms and reduces pharmaceutical consumption without causing severe AEs. However, the validity of this study is compromised by the substantial heterogeneity and risk of bias in the included researches.

3

Evidencia de la vacuna de melocotón, de principio a fin.

Immunotherapy with Pru p 3 for food allergy to peach and non-specific lipid transfer protein: a systematic review.

Rossi CM, Lenti MV, Merli S, Licari A, Marseglia GL, Di Sabatino A
Clin Mol Allergy. 2023 May 31;21(1):3. doi: 10.1186/s12948-023-00184-5.

BACKGROUND

Non-specific lipid-transfer protein (nsLTP) is a pan-allergen in the plant world, and a cause of significant concern as food allergen in the Mediterranean area, due to its general heat- and acid resistance and hence the risk of severe allergic reactions. Pru p 3, the peach nsLTP, is considered the primary sensitizer to this allergen family and this allergy is usually persistent. Allergen-free diet and acute treatment of manifestations are the main recognized management goals in food allergy.

MAIN TEXT

The role of immunotherapy for treating food allergy in adult patients is controversial, but immunotherapy for Pru p 3 could potentially represent a relevant therapeutic strategy. We systematically searched databases for studies assessing the role of immunotherapy Pru p 3 in food allergy. Overall, nine studies were included. Immunotherapy with Pru p 3 appears to be effective and with a good safety profile in both peach and LTP allergy for some foods, such as peanut, in both RCT and real-life studies.

CONCLUSIONS

Immunotherapy with Pru p 3 is a possible treatment option for food allergy to the peach LTP in the Mediterranean area, although at present have not reached routinary clinical practice. Larger studies are needed to confirm these findings and identify predictive biomarkers.

4

¿Y si la ITA disminuye la gravedad de la infección por COVID-19?

Aeroallergen immunotherapy associated with reduced risk of severe COVID-19 in 1095 allergic patients.

Larenas-Linnemann D, Morfin-Maciel BM, Bedolla-Barajas M, López-Bago A, Navarrete Rodríguez EM et al
World Allergy Organ J. 2023 May;16(5):100779. doi: 10.1016/j.waojou.2023.100779. Epub 2023 May 3.

INTRODUCTION

Allergen immunotherapy (AIT) brings along changes in the immune system, restoring dendritic cell function, reducing T2 inflammation and augmenting the regulatory cell activation. Coronavirus disease (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections, interferes with the immune system causing immune suppression during the first phase and over-activation in more advanced disease. We decided to explore the interaction of both in a real-world observational trial.

METHODS

We registered COVID-19 outcomes in patients with allergic disorders in Latin America, treated with and without AIT. The registry was conducted during the first 1.3 years of the pandemic, with most of the data collected before COVID-19 vaccination was concluded in most countries. Data collection was anonymous via a web based instrument. Ten countries participated.

RESULTS

630/1095 (57.6%) of the included patients received AIT. Compared to patients without AIT, those treated with AIT had a reduced risk ratio (RR) for COVID-19 lower respiratory symptoms (RR 0.78, 95% CI: 0.6703-0.9024; p = 0.001662) and need for oxygen therapy (RR 0.65, 95% CI: 0.4217-0.9992; p = 0.048). In adherent patients on maintenance sublingual immunotherapy/subcutaneous immunotherapy (SLIT/SCIT) the RR reduction was larger [RR = 0.6136 (95% CI 0.4623 0.8143; p < 0.001) and RR: 0.3495 (95% CI 0.1822-0.6701; p < 0.005), respectively]. SLIT was slightly more effective (NS). We excluded age, comorbidities, level of health care attendance, and type of allergic disorder as confounders, although asthma was related to a higher frequency of severe disease. When analyzing patients with allergic asthma (n = 503) the RR reduction favoring AIT was more pronounced with 30% for lower respiratory symptoms or worse (RR 0.6914, 95% CI 0.5264 to 0.9081, p = 0.0087) and 51% for need of oxygen therapy or worse (RR 0.4868, 95% CI 0.2829-0.8376, p = 0.0082). Among severe allergic patients treated with biologics (n = 24) only 2/24 needed oxygen therapy. There were no critical cases among them.

CONCLUSION

In our registry AIT was associated with reduced COVID-19 severity.

5

ITA en EEUU vs UE: similitudes y diferencias.

Comparison of allergen immunotherapy practice patterns in inhalant allergies in the United States of America and Europe: Similarities and differences 2023.

Pfaar O, Becker S, Calabria C, Hartenstein D, Jung J, Zimmer J, Ponda P
World Allergy Organ J. 2023 May 24;16(5):100766. doi: 10.1016/j.waojou.2023.100766.

ABSTRACT

IgE-mediated atopic diseases such as allergic rhinitis and rhinoconjunctivitis are common chronic diseases in the western world. Allergen immunotherapy (AIT) plays a fundamental role in the treatment of allergic patients by modulating the underlying immune mechanisms. Though this treatment is integrated in practice-patterns globally, many differences are found in the application of AIT on the national or international level due to heterogeneous methods, and clinical recommendations are given in different parts of the world. This review from authors in Europe and the United States highlights differences and similarities in important aspects of AIT application in the 2 global regions. First, the regulatory situation differs regarding marketing authorization and licensing. Secondly, differences are elaborated in manufacturing practices, marketing distribution and formulations of AIT products. Thirdly, clinical administration patterns in the current guidelines show similarities in indications and contraindications of AIT, but also are divergent in some practical aspects. Informing the readership on similarities, as well as differences of standards in AIT in the United States and Europe, the authors highlight the unmet need of thorough harmonization of standards of AIT, as it is the only disease modifying treatment option available for patients with allergic rhinitis and rhinoconjunctivitis.

6

Claves para el éxito con la ITO a cacahuete.

Peanut allergy: risk factors, immune mechanisms, and best practices for oral immunotherapy success.

Tirumalasetty J, Barshow S, Kost L, Morales L, Sharma R, Lazarte C, Nadeau KC
Expert Rev Clin Immunol. 2023 May 5:1-11. doi: 10.1080/1744666X.2023.2209318. Epub ahead of print. PMID: 37129440.

INTRODUCTION

Peanut oral immunotherapy (pOIT) is the only FDA-approved treatment for food allergy and its adoption amongst allergist immunologists and their patients is growing. pOIT is the subject of numerous clinical trials, however, the focus is often on treatment efficacy, safety, and tolerability, rather than identifying patients most likely to benefit from pOIT. Here, we review existing data on the clinical and immunological outcomes of pOIT that inform best practices for pOIT candidate selection.

AREAS COVERED

In this review, we describe the natural history of peanut allergy, summarize immunological and clinical outcomes of pOIT at different ages, discuss the optimization of pOIT in key age groups, and finally suggest an ideal age range at which to initiate pOIT for best outcomes.

EXPERT OPINION

pOIT is currently underutilized by patients and allergist immunologists. Developing guidelines for selecting appropriate patients and optimizing treatment may help to increase access to pOIT. Many aspects of pOIT need additional study to further our understanding of the optimal timing to start pOIT, with careful consideration to clinical, immunological, and quality of life outcomes.

7

¿El paciente con asma ocupacional “nace o se hace”?

Mechanistic and Therapeutic Approaches to Occupational Exposure-Associated Allergic and Non-Allergic Asthmatic Disease.

Schwab A, Poole JA
Curr Allergy Asthma Rep. 2023 May 8. doi: 10.1007/s11882-023-01079-w. Epub ahead of print.

PURPOSE OF REVIEW

Occupational lung disease, including asthma, is a significant cause of disability worldwide. The dose, exposure frequency, and nature of the causal agent influence the inflammatory pathomechanisms that inform asthma disease phenotype and progression. While surveillance, systems engineering, and exposure mitigation strategies are essential preventative considerations, no targeted medical therapies are currently available to ameliorate lung injury post-exposure and prevent chronic airway disease development.

RECENT FINDINGS

This article reviews contemporary understanding of allergic and non-allergic occupational asthma mechanisms. In addition, we discuss the available therapeutic options, patient-specific susceptibility and prevention measures, and recent scientific advances in post-exposure treatment conception. The course of occupational lung disease that follows exposure is informed by individual predisposition, immunobiologic response, agent identity, overall environmental risk, and preventative workplace practices. When protective strategies fail, knowledge of underlying disease mechanisms is necessary to inform targeted therapy development to lessen occupational asthma disease severity and occurrence.

8

Retos en la rinitis alérgica local.

Challenges in Local Allergic Rhinitis Diagnosis, Management, and Research: Current Concepts and Future Perspectives.

Mortada MM, Kurowski M

Medicina (Kaunas). 2023 May 11;59(5):929. doi: 10.3390/medicina59050929.

ABSTRACT

Local allergic rhinitis (LAR) is diagnosed based on the presence of clinical symptoms such as rhinorrhea, sneezing, and nasal itching using negative skin prick testing and serum IgE assessment. Several novel studies have shown that it is possible to use the assessment of nasal sIgE (specific immunoglobulin E) secretion as an additional diagnostic criterion for local allergic rhinitis. Additionally, allergen immunotherapy is a promising-albeit still not fully assessed and evaluated-future method of managing patients with LAR. In this review, the historical background, epidemiology, and main pathophysiological mechanisms of LAR shall be presented. Additionally, we address the current state of knowledge based on selected articles regarding the assessment of the local mucosal IgE presence in response to exposure to such allergens as mites, pollen, molds, and others. The impact of LAR on quality of life as well as the possible options of management (including allergen immunotherapy (AIT), which showed promising results) will then be presented.

9

Evidencia en rinitis alérgica, de la A a la Z.

Allergic Rhinitis: Rapid Evidence Review..

Weaver-Agostoni J, Kosak Z, Bartlett S

Am Fam Physician. 2023 May;107(5):466-473.

ABSTRACT

Allergic rhinitis, the fifth most common chronic disease in the United States, is an immunoglobulin E-mediated process. A family history of allergic rhinitis, asthma, or atopic dermatitis increases a patient's risk of being diagnosed with allergic rhinitis. People in the United States are commonly sensitized to grass, dust mites, and ragweed allergens. Dust mite-proof mattress covers do not prevent allergic rhinitis in children two years and younger. Diagnosis is clinical and based on history, physical examination, and at least one symptom of nasal congestion, runny or itchy nose, or sneezing. History should include whether the symptoms are seasonal or perennial, symptom triggers, and severity. Common examination findings are clear rhinorrhea, pale nasal mucosa, swollen nasal turbinates, watery eye discharge, conjunctival swelling, and allergic shiners (i.e., dark circles under the eyes). Serum or skin testing for specific allergens should be performed when there is inadequate response to empiric treatment, if diagnosis is uncertain, or to guide initiation or titration of therapy. Intranasal corticosteroids are first-line treatment for allergic rhinitis. Second-line therapies include antihistamines and leukotriene receptor antagonists and neither shows superiority. If allergy testing is performed, trigger-directed immunotherapy can be effectively delivered subcutaneously or sublingually. High-efficiency particulate air (HEPA) filters are not effective at decreasing allergy symptoms. Approximately 1 in 10 patients with allergic rhinitis will develop asthma.

10

La dentición como co-factor en la ITO.

Eruption of Permanent Teeth As Risk Factor for Allergic Reactions During Oral Immunotherapy.

Mori F, Pessina B, Giovannini M, Liccioli G, Sarti L, Paladini E, Tomei L, Barni S

Pediatr Allergy Immunol Pulmonol. 2023 May 9. doi: 10.1089/ped.2023.0018. Epub ahead of print.

BACKGROUND

Oral immunotherapy (OIT) increases the threshold of reaction in children older than 4 years with food allergy. The risk for severe allergic reactions (ARs) during OIT has been reported in several studies, often in the presence of concomitant cofactors such as physical exercise, empty stomach, medications, poorly controlled asthma, menses, and alcohol consumption. Cases Presentation: We describe a case series of 5 scholar age patients undergoing OIT who showed ARs to a known, previously tolerated dose of allergen during permanent tooth eruption, in which other known cofactors were excluded. Conclusions: Patients may be exposed to cofactors due to behavioral habits not only in the second and third decades of life, but also in the first decade of life, due to the timing of mixed dentition. More studies are needed to estimate the frequency and entity of tooth eruption as cofactor, as well as to know the correct management of children undergoing dentition during OIT.

BBI BOLETÍN BIBLIOGRÁFICO DE INMUNOTERAPIA

Junio 2023

1

Lo breve, si bueno, dos veces bueno.

Short-course subcutaneous treatment with PQ Grass strongly improves symptom and medication scores in grass allergy.

J. de Kam , S. Zielen, J. A. Bernstein, U. Berger, M. Berger, M. Cuevas et al

Allergy. 2023 Jun 27. doi: 10.1111/all.15788. Online ahead of print.

ARTÍCULO DESTACADO

BACKGROUND

A modified grass allergen subcutaneous immunotherapy (SCIT) product with MicroCrystalline Tyrosine and monophosphoryl lipid-A as an adjuvant system (Grass MATA MPL [PQ Grass]) is being developed as short-course treatment of grass-pollen allergic rhinitis (SAR) and/or rhinoconjunctivitis. We sought to evaluate the combined symptom and medication score (CSMS) of the optimized cumulative dose of 27,600 standardized units (SU) PQ Grass in a field setting prior to embarking on a pivotal Phase III trial.

METHODS

In this exploratory, randomized, double-blind, placebo-controlled trial subjects were enrolled across 14 sites (Germany and the United States of America). Six pre-seasonal subcutaneous injections of PQ Grass (using conventional or extended regimens) or placebo were administered to 119 subjects (aged 18-65 years) with moderate-to-severe SAR with or without asthma that was well-controlled. The primary efficacy endpoint was CSMS during peak grass pollen season (GPS). Secondary endpoints included Rhinoconjunctivitis Quality of Life Questionnaire standardized (RQLQ-S) and allergen-specific IgG4 response.

RESULTS

The mean CSMS compared to placebo was 33.1% (p = .0325) and 39.5% (p = .0112) for the conventional and extended regimens, respectively. An increase in IgG4 was shown for both regimens (p .01) as well as an improvement in total RQLQ-S for the extended regimen (mean change -0.72, p = .02). Both regimens were well-tolerated.

CONCLUSIONS

This trial demonstrated a clinically relevant and statistically significant efficacy response to PQ Grass. Unprecedented effect sizes were reached for grass allergy of up to ≈40% compared to placebo for CSMS after only six PQ Grass injections. Both PQ Grass regimens were considered equally safe and well-tolerated. Based on enhanced efficacy profile extended regime will be progressed to the pivotal Phase III trial.

2

¿Vacunar a nuestro hijo es seguro?

Adverse events in children and adolescents undergoing allergen immunotherapy for respiratory allergies-Report from the Allergen Immunotherapy Adverse Events Registry (ADER), a European Academy of Allergy and Clinical Immunology taskforce.

Julijana Asllani, Dimitrios Mitsias, George Konstantinou, Eris Mesonjesi, Fatmira Xhixha, Esmeralda Shehu et al

Clin Transl Allergy. 2023 Jun;13(6):e12250. doi: 10.1002/clt2.12250.

BACKGROUND

Although it has been shown that allergen immunotherapy (AIT) is well-tolerated in children, systematic and prospective surveillance of AIT safety in real life settings is needed.

METHODS

The multinational Allergen Immunotherapy Adverse Events Registry (ADER) was designed to address AIT safety in real life clinical practice. Data on children ≤18 years old with respiratory allergies undergoing AIT were retrieved. Patient- and AIT-related features were collected and analyzed. The characteristics of adverse events (AE) and risk factors were evaluated.

RESULTS

A total of 851 patients, 11.3 ± 3.4 years old, with rhinitis only (47.6%); asthma and rhinitis (44.5%); asthma (7.9%), receiving 998 AIT courses were analyzed. Sublingual immunotherapy (SLIT) accounted for 51% of the courses. In 84.5% of patients only one AIT treatment was prescribed. Pollen was the most frequent sensitizer (57.1%), followed by mites (53.4%), molds (18.2%) and epithelia (16.7%). Local and systemic AEs were reported in 85 patients (9.9%). Most AEs (83.1%) were mild and occurred in <30 min (87%). Respiratory and cutaneous symptoms were more frequent. Only 4 patients (0.47%) had severe AE (none after 6 weeks of maintenance). The risk of AE was higher in patients undergoing SCIT.

CONCLUSIONS

AIT is safe and well tolerated in children and adolescents with respiratory allergies in real-life clinical practice. Though SCIT is more prone to AE compared to SLIT, overall severe reactions are rare and occur during build-up and early maintenance.

3

Alergia a mariscos... ¿la siguiente ITO disponible?

IgE-Mediated Shellfish Allergy in Children.

Mattia Giovannini, Burcin Beken, Betul Buyuktiryaki, Simona Barni, Giulia Liccioli, Lucrezia Sarti et al

Nutrients. 2023 Jun 11;15(12):2714. doi: 10.3390/nu15122714.

ABSTRACT

Shellfish, including various species of mollusks (e.g., mussels, clams, and oysters) and crustaceans (e.g., shrimp, prawn, lobster, and crab), have been a keystone of healthy dietary recommendations due to their valuable protein content. In parallel with their consumption, allergic reactions related to shellfish may be increasing. Adverse reactions to shellfish are classified into different groups: (1) Immunological reactions, including IgE and non-IgE allergic reactions; (2) non-immunological reactions, including toxic reactions and food intolerance. The IgE-mediated reactions occur within about two hours after ingestion of the shellfish and range from urticaria, angioedema, nausea, and vomiting to respiratory signs and symptoms such as bronchospasm, laryngeal oedema, and anaphylaxis. The most common allergenic proteins involved in IgE-mediated allergic reactions to shellfish include tropomyosin, arginine kinase, myosin light chain, sarcoplasmic calcium-binding protein, troponin c, and triosephosphate isomerase. Over the past decades, the knowledge gained on the identification of the molecular features of different shellfish allergens improved the diagnosis and the potential design of allergen immunotherapy for shellfish allergy. Unfortunately, immunotherapeutic studies and some diagnostic tools are still restricted in a research context and need to be validated before being implemented into clinical practice. However, they seem promising for improving management strategies for shellfish allergy. In this review, epidemiology, pathogenesis, clinical features, diagnosis, and management of shellfish allergies in children are presented. The cross reactivity among different forms of shellfish and immunotherapeutic approaches, including unmodified allergens, hypoallergens, peptide based, and DNA-based vaccines, are also addressed.

4

Vitamina D, un adyuvante por explorar en ITA.

Vitamin D Role in Childhood Mite Allergy and Allergen Immunotherapy (AIT)

Claudia Petrarca, Davide Viola

Biomedicines. 2023 Jun 13;11(6):1700. doi: 10.3390/biomedicines11061700.

ABSTRACT

The post hoc analysis presented here aimed to address the influence of endogenous vitamin D in the immunological mechanism underlying effective mite allergoid immunotherapy (AIT). Previously, we have shown that in allergic children, after 12 months of this immunoactive treatment, functionally potentiated memory regulatory T cells are identified. Indeed, AIT is the only known treatment that is able to reshape the detrimental immune response against the allergen into a non-noxious one. Besides, VD is widely considered an immunoregulatory molecule that is endogenously produced and exogenously provided by foods and supplements that might interact with the AIT mechanism, thus affecting its outcome. Therefore, a post hoc analysis of the clinical and immunological data from three different cohorts of allergic patients was performed. One cohort (N = 70) was on a standard symptom-controlling pharmacological treatment, while the other to (N = 60 and N = 35) were treated with AIT for 12 months. In the first cohort, a lower mean endogenous VD level (<22 ng/mL) was observed along with worse symptoms and a greater use of medications. Remarkably, the comparison between two sub-cohorts of patients with a serum VD level above (N = 32) or below (N = 28) a cut-off value set at the mean value (27 ng/mL) revealed that optimal improvement of all clinical and immune parameters was achieved (as expected from effective AIT), irrespective of the VD level. Notably, the third analysis, carried out on one cohort of AIT patients that were also concomitantly taking VD3 as a food supplement (N = 19), was distinguished by an uppermost overall treatment outcome (the amelioration of symptoms, the lowest medication requirements, and a reduction in the total and allergen-specific IgE levels), as well as an increase in the allergen-specific tolerogenic memory T regulatory cells. These findings suggest that the endogenous VD level affects the allergy severity and allergen immunotherapy effectiveness. In addition, VD3 might be investigated as an add-on supplement to obtain the best out of immunotherapy in VD-deficient/-insufficient allergic patients. The immunogenic, but low-allergenic, mite allergoid used as the bioactive agent might have contributed to minimizing the allergic response and highlighting the immunological effects described here.

5

Citoquinas predictoras de efectividad en IT con venenos.

Time-dependent cytokines changes in ultra-rush wasp venom immunotherapy.

W. Urbańska, L. Szymański, M. Ciepelak3, A. Cios , W. Stankiewicz, E. Klimaszewska et al

ABSTRACT

Venom immunotherapy (VIT) represents a potential therapeutic approach for the management of venom allergies, aiming to modify the immune response to venom allergens and enhance its precision. Previous studies have demonstrated that VIT induces a shift in T helper cell responses from Th2 to Th1, characterized by the production of IL-2 and interferon gamma by CD4+ and CD8+ cells. In order to explore long-term pathways following VIT treatment and verify potential new outcomes, the serum concentrations of 30 cytokines were assessed in a cohort of 61 patients (18 control, 43 study group) exhibiting hypersensitivity to wasp venom. Cytokine levels were measured at 0, 2, 6, and 24 weeks after the initiation phase of VIT in the study group. The present study found no significant alterations in the levels of IL-2 and IFN-γ in the peripheral blood following VIT. However, a noteworthy finding was the substantial increase in the concentration of IL-12, a cytokine capable of promoting the differentiation of Th0 cells into Th1 cells. This observation supports the involvement of the Th1 pathway in the desensitization process induced by VIT. Additionally, the study revealed a significant rise in the levels of IL-9 and TGF-β after VIT. These cytokines may play a role in the generation of inducible regulatory T (Treg) cells, indicating their potential importance in the immune response to venom allergens and the desensitization process associated with VIT. Nevertheless, further investigations are required to comprehend the underlying mechanisms driving the VIT process comprehensively.

6

La afinidad de union de IgE y la IgG4 orientan a la evolución en la ITO con huevo.

The Combination of Binding Avidity of Ovomucoid-Specific IgE Antibody and Specific IgG4 Antibody Can Predict Positive Outcomes of Oral Food Challenges during Stepwise Slow Oral Immunotherapy in Children with Hen's Egg Allergy.

Shoichiro Taniuchi, Rika Sakai, Takahiro Nishida, Meguru Goma, Masatoshi Mitomori, Aya Imaide et al

Nutrients. 2023 Jun 16;15(12):2770. doi: 10.3390/nu15122770.

ABSTRACT

To increase the prediction accuracy of positive oral food challenge (OFC) outcomes during stepwise slow oral immunotherapy (SS-OIT) in children with a hen's egg (HE) allergy, we evaluated the predictive value of the combination of antigen-specific IgE (sIgE) with antigen binding avidity and sIgG4 values. Sixty-three children with HE allergy undergoing SS-OIT were subjected to repeated OFCs with HE. We measured the ovomucoid (OVM)-sIgE by ImmunoCAP or densely carboxylated protein (DCP) microarray, sIgG4 by DCP microarray, and the binding avidity of OVM sIgE defined as the level of 1/IC50 (nM) measured by competitive binding inhibition assays. The OFC was positive in 37 (59%) patients undergoing SSOIT. Significant differences in DCP-OVM-sIgE, CAP-OVM-sIgE, I/IC50, DCP-OVM-sIgG4, the multiplication products of DCP-OVM-sIgE, and the binding avidity of DCP-OVM-sIgE (DCP-OVM-sIgE/IC50) and DCP OVM-sIgE/sIgG4 were compared between the negative and positive groups ($p < 0.01$). Among them, the variable with the greatest area under the receiver operating characteristic curve was DCP-OVM-sIgE/IC50 (0.84), followed by DCP-OVM-sIgE/sIgG4 (0.81). DCP-OVM-sIgE/IC50 and DCP-OVM sIgE/sIgG4 are potentially useful markers for the prediction of positive OFCs during HE-SS-OIT and may allow proper evaluation of the current allergic status in the healing process during HE-SS-OIT.

7

Biomateriales a utilizar en IT transdérmica para aumentar su efectividad.

Biomaterial-based delivery platforms for transdermal immunotherapy.

Mohammad Dahri, Nima Beheshtizadeh, Nasrin Seyedpour, Amin Nakhostin-Ansari, Faezeh Aghajani, Simin Seyedpour et al

Biomed Pharmacother. 2023 Jun 27;165:115048. doi: 10.1016/j.biopha.2023.115048. Online ahead of print.

ABSTRACT

Nowadays, immunotherapy is one of the most essential treatments for various diseases and a broad spectrum of disorders are assumed to be treated by altering the function of the immune system. For this reason, immunotherapy has attracted a great deal of attention and numerous studies on different approaches for immunotherapies have been investigated, using multiple biomaterials and carriers, from nanoparticles (NPs) to microneedles (MNs). In this review, the immunotherapy strategies, biomaterials, devices, and diseases supposed to be treated by immunotherapeutic strategies are reviewed. Several transdermal therapeutic methods, including semisolids, skin patches, chemical, and physical skin penetration enhancers, are discussed. MNs are the most frequent devices implemented in transdermal immunotherapy of cancers (e.g., melanoma, squamous cell carcinoma, cervical, and breast cancer), infectious (e.g., COVID-19), allergic and autoimmune disorders (e.g., Duchenne's muscular dystrophy and Pollinosis). The biomaterials used in transdermal immunotherapy vary in shape, size, and sensitivity to external stimuli (e.g., magnetic field, photo, redox, pH, thermal, and even multi stimuli-responsive) were reported. Correspondingly, vesicle-based NPs, including niosomes, transferosomes, ethosomes, microemulsions, transfersomes, and exosomes, are also discussed. In addition, transdermal immunotherapy using vaccines has been reviewed for Ebola, Neisseria gonorrhoeae, Hepatitis B virus, Influenza virus, respiratory syncytial virus, Hand-foot-and-mouth disease, and Tetanus.

8

Manejo de la rinitis alérgica 3.0.

Updates in the diagnosis and practical management of allergic rhinitis.

Chiara Trincianti, Maria Angela Tosca, Giorgio Ciprandi

Expert Rev Clin Pharmacol. 2023 Jun 16;1-8. doi: 10.1080/17512433.2023.2225770. Online ahead of print.

INTRODUCTION

Allergic rhinitis (AR) is a widespread disease that can be associated with other conditions, including conjunctivitis, rhinosinusitis, asthma, food allergy, and atopic dermatitis. Diagnosis is based on the history and documentation of sensitization, such as the production of allergenspecific IgE, preferably using molecular diagnostics. Treatments are based on patient education, non-pharmacological and pharmacological remedies, allergen-specific immunotherapy (AIT), and surgery. Symptomatic treatments mainly concern intranasal/oral antihistamines and/or nasal corticosteroids.

AREAS COVERED

This review discusses current and emerging management strategies for AR, covering pharmacological and non-pharmacological remedies, AIT, and biologics in selected cases with associated severe asthma. However, AIT presently remains the unique causal treatment for AR.

EXPERT OPINION

The management of allergic rhinitis could include new straegies. In this regard, particular interest should be considered in the fixed association between intranasal antihistamines and corticosteroids, probiotics and other natural substances, and new formulations (tablets) of AIT.

9

Ensayos clínicos o de "vida real" en IT: mejor juntos que separados.

Moving forward with allergen immunotherapy: The significance of real-world studies.

Roy Gerth van Wijk, Paul van Daele

J Allergy Clin Immunol. 2023 Jun 3;S0091-6749(23)00710-8.

ABSTRACT

The efficacy of allergen immunotherapy (AIT) has been demostrated in numerous randomized clinical trials (RCT) with optimal conditions and strong evidence. In recent years, numerous real-life studies have been developed to minimize the limitations of the of RCTs (highly selected patiens, expensive, usual duration of 1-2 years and not suitable for assesing adherence and persistence), and they have provided valuable information that complements the information obtained in RCTs such as evidence of the effectiveness of AIT over an extended period of time and in a larger number of patients. To minimize limitations of this kind of studies (prone to confounding bias, generally retrospective, data sources of variable quality and study heterogeneity), some tools have been developed by both scientific and regulatory societies. Both types of studies should complement each other in order to advance the knowledge of AIT.

10

¿La edad (avanzada) es una limitación para la ITA?

Clinical outcomes of AIT in the elderly population.

Andrzej Bożek

Curr Opin Allergy Clin Immunol. 2023 Jun 20.doi: 10.1097/ACI.0000000000000925. Online ahead of print.

PURPOSE OF REVIEW

This review aims to present the current knowledge on the effectiveness and safety of allergen immunotherapy (AIT) in patients over 60 years of age with inhalant allergies.

RECENT FINDINGS

Over the last 10 years, the problem of immunoglobulin E allergy in seniors has been noticed by many authors. At the same time, in the 1990s, trials of desensitization to selected inhalant allergens were started, obtaining evidence of the effectiveness of AIT, both with the use of sublingual immunotherapy (SLIT) and injection immunotherapy (SCIT), in patients over 60 years of age with allergic rhinitis. Such data have been confirmed for AITs for grasses, birch, and house dust mites. Currently, these patients are being monitored to assess the long-term effect of AIT. All available observations confirm the high safety of AIT in seniors.

SUMMARY

Seniors with allergic rhinitis or asthma may qualify for IT if they do not have contraindications. These patients can experience a sustained clinical benefit even after completing AIT treatment. Studies indicate that injectable and sublingual routes of administration may be effective in this age group, provided the suspect allergen is accurately diagnosed.

BOLETÍN BIBLIOGRÁFICO
DE INMUNOTERAPIA

Julio 2023

1

La ITO tiene riesgo, pero cura.

Efficacy and safety of oral immunotherapy for peanut, cow's milk, and hen's egg allergy: A systematic review of randomized controlled trials.

Lodge CJ, Waidyatillake N, Peters RL, Netting M, Dai X

Clin Transl Allergy. 2023 Jul;13(7):e12268. doi: 10.1002.

ARTÍCULO DESTACADO

BACKGROUND

Oral immunotherapy (OIT) is a promising treatment for food allergies; however, safety is a concern. We synthesized evidence from the best randomized controlled trials (RCTs) on efficacy/safety of OIT for desensitization (DS) and remission (sustained unresponsiveness (SU)) in IgE mediated allergy to peanut, hen's eggs, and cow's milk. BODY: We searched Pubmed, EMBASE, and Cochrane databases (Until Oct 22) identifying 16 eligible RCTs published in English measuring food allergy by food challenge at the beginning and at the end of the study. The Cochrane Risk of Bias tool was used to assess study quality. We found 18 eligible studies. There was evidence of efficacy for DS for all allergens: peanut (RR 11.32; 95% CI 5.93, 21.60, I2 49%, 8 studies); hen's egg (RR 4.67; 2.66, 8.21, I2 0%, 5 studies); cow's milk (RR 13.98; 3.51, 55.65, I2 0%, 4 studies) and evidence for SU for peanut (RR 7.74; 2.90, 20.69, I2 0%, 3 studies) and hen's egg (RR 6.91; 1.67, 28.57, I2 0%, 2 studies). Allergic events were increased with intervention, and risk of adrenaline use increased for peanut RR 2.96; 1.63, 5.35, I2 0%, 8 studies; egg RR 1.71; 0.42, 6.92, I2 0%, 6 studies; and milk RR 8.45; 2.02, 35.27, I2 0%, 4 studies.

CONCLUSION

We found strong evidence that peanut, hen's egg, and cow's milk OIT can induce DS and some evidence for remission. There was a high risk of allergic reactions. Generalizability to the entire food allergic population is not known.

2

¿Qué hace la ITA? La respuesta está en la nariz.

Nasal and blood transcriptomic pathways underpinning the clinical response to grass pollen immunotherapy.

Altman MC, Segnitz RM, Larson D, Jayavelu ND, Smith M

J Allergy Clin Immunol. 2023 Jul 15:S0091-6749(23)00890-4. doi: 10.1016.

BACKGROUND

Allergen immunotherapy (AIT) is a well-established disease modifying therapy for allergic rhinitis, yet the fundamental mechanisms underlying its clinical effect remain inadequately understood.

OBJECTIVE

The GRASS study was a randomized, double-blind, placebo controlled trial of timothy grass allergic individuals who received 2 years of placebo (n=30), subcutaneous (SCIT) (n=27), or sublingual immunotherapy (SLIT) (n=27) and were then followed for 1 additional year. Here we used yearly biospecimens from the GRASS study to identify molecular mechanisms of response.

METHODS

We utilized longitudinal transcriptomic profiling of nasal brush and peripheral blood mononuclear cell (PBMC) samples after allergen provocation to uncover airway and systemic expression pathways mediating responsiveness to AIT.

RESULTS

SCIT and SLIT demonstrated similar changes in gene module expression over time. In nasal samples, alterations included downregulation of pathways of mucus hypersecretion, leukocyte migration/activation, and endoplasmic reticulum stress (log2 fold changes (logFC) -0.133 to -0.640, FDRs <0.05). Interestingly, we observed upregulation of modules related to epithelial development, junction formation, and lipid metabolism (logFC 0.104 to 0.393, FDRs <0.05). In PBMCs, modules related to cellular stress response and type 2 cytokine signaling were reduced by immunotherapy (logFC -0.611 to -0.828, FDRs <0.05). Expression of these modules was also significantly associated with both Total Nasal Symptom Score and Peak Nasal Inspiratory Flow responses, indicating important links among treatment, module expression, and allergen response.

CONCLUSION

Our results identify specific molecular responses of the nasal airway impacting barrier function, leukocyte migration activation, and mucus secretion, that are affected by both SCIT and SLIT, offering potential targets to guide novel strategies for AIT.

3

¿Qué nos lleva a ELEGIR una ITA?

CHOICE Survey Team. CHOICE international survey: Clusters of allergen immunotherapy prescription from French and Spanish cohorts.

Rodriguez Del Rio P, Caimmi D, Rico Nieto P, Vidal C, Moreno C

World Allergy Organ J. 2023 Jul 1;16(6):100791. doi: 10.1016.

BACKGROUND

There is no description of the drivers of prescription for allergen immunotherapy (AIT) for respiratory allergic diseases.

METHODS

A prospective, multicentre, observational, non-interventional real-life study was performed in France and Spain for 20 months. Data were gathered using 2 different questionnaires, anonymously collected in an online platform. No names of AIT products were recorded. Multivariate analysis and unsupervised cluster analysis were performed.

RESULTS

One hundred and three physicians (50.5% from Spain and 49.5% from France) reported 1735 patients (433 in France and 1302 in Spain), 47.9% males, 64.8% adults with a mean age 26.2 years old. They suffered from allergic rhinitis (99%), allergic conjunctivitis (70.4%), allergic asthma (51.8%), atopic dermatitis (13.9%), and food allergy (9.9%). A clustering analysis based on 13 predefined relevant variables for AIT-prescription identified 5 different clusters, each of them including information regarding doctor's profile and patient demographics, baseline disease characteristics, and main AIT indication: 1) Looking at the future: focusing on asthma prevention (n = 355), 2) Efficacy after discontinuation of AIT (n = 293), 3) Fighting severe allergic disease (n = 322), 4) Looking at the present, facing current symptoms (n = 265) and 5) Doctor's own clinical experience (n = 500). Each one of these clusters have specific patients' and doctors' characteristics, representing distinctive AIT prescription drivers.

CONCLUSION

Using data-driven analysis, we identified for the first time some reasons and patterns of AIT prescriptions in real-life clinical settings. There is no uniform indication for prescribing AIT, which varies amongst patients and doctors with multiple but specific drivers, taking into account several relevant parameters.

4

ITA con péptidos hipoalergénicos para mejorar la efectividad.

Peptide immunotherapy for aeroallergens.

Midoro-Horiuti T, Schein CH

Allergy Asthma Proc. 2023 Jul 1;44(4):237-243. doi: 10.2500.

BACKGROUND

Allergen specific immunotherapy (SIT) has been used for more than a century. Researchers have been working to improve efficacy and reduce the side effects.

OBJECTIVE

We have reviewed the literature about peptides immunotherapy for inhaled allergens. The mechanism of SIT is to induce regulatory T (Treg) cells and to reduce T helper (Th)2 cells to induce class switching from IgE to IgG and induce blocking antibodies to inhibit allergen binding of IgE.

METHODS

The relevant published literatures on the peptide SIT for aeroallergens have been searched on the medline.

RESULTS

Modification of allergens and routes of treatment has been performed. Among them, many researchers were interested in peptide immunotherapy. T-cell epitope peptide has no IgE epitope, that is able to bind IgE, but rather induces Treg and reduces Th2 cells, which was considered an ideal therapy. Results from cellular and animal model studies have been successful. However, in clinical studies, T-cell peptide immunotherapy has failed to show efficacy and caused side effects, because of the high effective rate of placebo and the development of IgE against T-cell epitope peptides. Currently, the modifications of IgE-allergen binding by blocking antibodies are considered for successful allergen immunotherapy.

CONCLUSION

Newly developed hypoallergenic B cell epitope peptides and computational identification methods hold great potential to develop new peptide immunotherapies.

5

ITO + ejercicio = mala combinación.

Exercise-Induced Allergic Reactions in Children Desensitized to Hen's Eggs and Cow's Milk by Oral Immunotherapy.

Tsuji G, Matsui T, Takasato Y, Kitamura K, Kubota S, Sugiura S, Ito K

J Allergy Clin Immunol Pract. 2023 Jul 7:S2213-2198(23)00727-4. doi: 10.101.

BACKGROUND

Exercise-induced allergic reactions on desensitization (EIARDs) after successful in-hospital rush oral immunotherapy (OIT) for wheat allergy have been reported. However, the incidence rates of EIARDs after rush OIT for egg allergy and milk allergy have not been determined.

OBJECTIVE

To determine the frequency of EIARDs and risk factors associated with rush OIT for egg and milk allergy.

METHODS

This retrospective chart review, conducted in January 2020, enrolled 64 and 43 patients who underwent rush OIT for egg and milk allergy, respectively (in 2010 to 2014). In particular, 48 and 32 desensitized patients underwent exercise-provocation tests (Ex-P) after allergen administration (4,400 mg boiled egg white and 6,600 mg cow's milk protein, respectively). The EIARDs were determined by Ex-P or a suspicious event even after passing the Ex-P. Specific IgE levels to egg white, cow's milk, ovomucoid, casein, α-lactalbumin, and β-lactoglobulin were analyzed using ImmunoCAP.

RESULTS

At least one episode of EIARD was observed in 10 and 17 patients with egg and milk allergy (21% and 53%), respectively, which persisted for more than 5 years in one patient with egg allergy (2.1%) and 11 patients with milk allergy (34.4%) as of January 2020. We could not find background differences between the EIARD-positive and EIARD-negative groups, except that the egg white-specific IgE/total IgE ratio before rush OIT was significantly higher in patients with egg allergy with EIARD than in those without it.

CONCLUSIONS

Exercise-induced allergic reactions on desensitization were more frequent and common in patients with milk allergy.

6

En la expresividad de tus genes está la respuesta a la ITA.

Identification of key genes and the pathophysiology associated with allergen-specific immunotherapy for allergic rhinitis.

Fan K, Zhou S, Jin L, Tan S, Lai J

BMC Immunol. 2023 Jul 10;24(1):19. doi: 10.1186.

BACKGROUND

Allergen-specific immunotherapy (AIT) is a causative treatment in allergic rhinitis (AR), comprising long-term allergen administration and over three years of treatment. This study is carried out for revealing the mechanisms and key genes of AIT in AR.

METHODS

The present study utilized online Gene ExpressionOmnibus (GEO) microarray expression profiling dataset GSE37157 and GSE29521 to analyze the hub genes changes related to AIT in AR. Based on limma package, differential expression analysis for the two groups (samples of allergic patients prior to AIT and samples of allergic patients undergoing AIT) was performed to obtain differentially expressed genes (DEGs). Gene Ontology (GO) analysis and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis of DEGs were conducted using DAVID database. A Protein-Protein Interaction network (PPI) was built and a significant network module was acquired by using Cytoscape software (Cytoscape, 3.7.2). Utilizing the miRWalk database, we identified potential gene biomarkers, constructed interaction networks of target genes and microRNAs (miRNAs) using Cytoscape software, and explore the cell type-specific expression patterns of these genes in peripheral blood using publicly available single-cell RNA sequencing data (GSE200107). Finally, we are using PCR to detect changes in the hub genes that are screened using the above method in peripheral blood before and after AIT treatment.

RESULTS

GSE37157 and GSE29521 included 28 and 13 samples, respectively. A total of 119 significantly co-upregulated DEGs and 33 codownregulated DEGs were obtained from two datasets. The GO and KEGG analyses demonstrated that protein transport, positive regulation of apoptotic process, Natural killer cell mediated cytotoxicity, T cell receptor signaling pathway, TNF signaling pathway, B cell receptor signaling pathway and Apoptosis may be potential candidate therapeutic targets for AIT of AR. From the PPI network, 20 hub genes were obtained. Among them, the PPI sub-networks of CASP3, FOXO3, PIK3R1, PIK3R3, ATF4, and POLD3 screened out from our study have been identified as reliable predictors of AIT in AR, especially the PIK3R1.

CONCLUSION

Our analysis has identified novel gene signatures, thereby contributing to a more comprehensive understanding of the molecular mechanisms underlying AIT in the treatment of AR.

7

Tengamos las guías como referencia. Pero ... ¿todas las guías son de calidad?

Evaluation of the quality of guidelines for sublingual immunotherapy of allergic rhinitis.

Wang Q, Zhu R, Ning Y, Feng Y, Feng Y, Han S

Eur Arch Otorhinolaryngol. 2023 Jul 6. doi: 10.1007.

BACKGROUND

Guidelines are intended to facilitate evidence-based clinical decision-making and knowledge translation; however, the quality and rigor of the guidelines are different. This study was conducted to assess the quality of sublingual immunotherapy guidelines for allergic rhinitis, in order to provide a reference for evidence-based clinical treatment and management of sublingual immunotherapy.

METHODS

Using both Chinese and English search methods, articles were obtained from PubMed, Cochrane, Web of Science, CNKI, CBM, WanFang Data, VIP, and other databases from the construction of the database to September 2020. The AGREE II instrument was used by two researchers to independently evaluate the quality of the extracted articles, and the consistency of the researchers was evaluated using the inter-group correlation coefficient.

RESULTS

Ten articles were included in this study, of which two articles ranked A level, six articles ranked B level, and two articles ranked C level. The six sections of AGREE II included scope and aim, clarity, participant, applicability, rigor, and editorial independence, with standardized scores of 78.06%, 45.83%, 42.81%, 77.50%, 50.42%, and 46.25%, respectively.

CONCLUSION

The quality of the current guidelines for sublingual immunotherapy is average. The formulation methodology and reporting standards of these guidelines must be developed. By standardizing the treatment of sublingual immunotherapy properly, it is recommended that guideline makers refer to the AGREE II to formulate high-quality guidelines and promote their wide application.

8

"PROMs" como biomarcador de cabecera.

Patient-centered digital biomarkers for allergic respiratory diseases and asthma: The ARIA-EAACI approach - ARIA-EAACI Task Force Report.

Bousquet J, Shamji MH, Anto JM, Schünemann HJ, Canonica GW

Allergy. 2023 Jul;78(7):1758-1776. doi: 10.1111.

ABSTRACT

Biomarkers for the diagnosis, treatment and follow-up of patients with rhinitis and/or asthma are urgently needed. Although some biologic biomarkers exist in specialist care for asthma, they cannot be largely used in primary care. There are no validated biomarkers in rhinitis or allergen immunotherapy (AIT) that can be used in clinical practice. The digital transformation of health and health care (including mHealth) places the patient at the center of the health system and is likely to optimize the practice of allergy. Allergic Rhinitis and its Impact on Asthma (ARIA) and EAACI (European Academy of Allergy and Clinical Immunology) developed a Task Force aimed at proposing patient-reported outcome measures (PROMs) as digital biomarkers that can be easily used for different purposes in rhinitis and asthma. It first defined control digital biomarkers that should make a bridge between clinical practice, randomized controlled trials, observational real-life studies and allergen challenges. Using the MASK air app as a model, a daily electronic combined symptommedication score for allergic diseases (CSMS) or for asthma (e-DASTHMA), combined with a monthly control questionnaire, was embedded in a strategy similar to the diabetes approach for disease control. To mimic real-life, it secondly proposed quality-of-life digital biomarkers including daily EQ-5D visual analogue scales and the bi weekly RhinAsthma Patient Perspective (RAAP). The potential implications for the management of allergic respiratory diseases were proposed.

9

Coste-efectivad de ITA subcutánea vs intralinfática.

Potential Cost Savings by Switching from Subcutaneousto Intralymphatic Insect Venom Immunotherapy.

Chabot A, Lang C, Kündig TM, Schmid-Grendelmeier P, Johansen P

Int Arch Allergy Immunol. 2023 Jul 19:1-9. doi: 10.1159.

INTRODUCTION

IgE-mediated bee venom allergy can be treated with allergen-specific immunotherapy (AIT). Subcutaneous immunotherapy (SCIT) is time and cost intensive due to the repeated consultations, but the costs are justified by the high risk of potentially lifethreatening allergic reactions, including anaphylaxis. However, intralymphatic immunotherapy (ILIT) offers potential to reduce treatment costs due to a significant reduction in injections and a shorter duration of therapy. Therefore, we calculated the cost savings that arise when switching from SCIT to ILIT.

METHODS

Treatment protocols for ILIT were based on previous ILIT studies. Treatment protocols for SCIT were based on routine treatment at the University Hospital Zurich (USZ). The treatment costs were calculated based on the internal hospital information system (KISIM).

RESULTS

The calculations revealed a potential two-fold reduction in treatment costs if ILIT is used instead of SCIT in patients with bee venom allergy. The costs could be reduced from EUR 11,612.59 with SCIT to EUR 5,942.15 with ILIT over 5 years.

CONCLUSIONS

This study shows that bee venom ILIT has a cost-benefit potential for health insurances and patients, which should encourage further ILIT studies and which should be taken into account when considering future implementation of ILIT in the standard care of venom allergy.

10

Dónde estamos en la ITA frente a cucaracha.

Current practices and future trends in cockroach allergen immunotherapy.

Reginald K, Chew FT
Mol Immunol. 2023 Jul 20;161:11-24. doi: 10.1016.

PURPOSE OF REVIEW

This review evaluates the current modes of allergen specific immunotherapy for cockroach allergens, in terms of clinical outcomes and explores future trends in the research and development needed for a more targeted cockroach immunotherapy approach with the best efficacy and minimum adverse effects.

SUMMARY

Cockroach allergy is an important risk factor for allergic rhinitis in the tropics, that disproportionately affects children and young adults and those living in poor socio-economic environments. Immunotherapy would provide long-lasting improvement in quality of life, with reduced medication intake. However, the present treatment regime is long and has a risk of adverse effects. In addition, cockroach does not seem to have an immuno-dominant allergen, that has been traditionally used to treat allergies from other sources. Future trends of cockroach immunotherapy involve precision diagnosis, to correctly identify the offending allergen. Next, precision immunotherapy with standardized allergens, which have been processed in a way that maintains an immunological response without allergic reactions. This approach can be coupled with modern adjuvants and delivery systems that promote a Th1/Treg environment, thereby modulating the immune response away from the allergenic response.

BBI BOLETÍN BIBLIOGRÁFICO DE INMUNOTERAPIA

Agosto 2023

1

¿3 pinchazos ó 36? ... y otras características de la IT intralinfática.

Intra-cervical lymphatic immunotherapy for dust mite-induced allergic rhinoconjunctivitis in children: a 3-year prospective randomized controlled trial.

Qixing Wang, Kai Wang, Yang Qin, Weijun Huang, Yin Li, Qingqing Yu, Yu Xiong et al

Front Immunol. 2023 Aug 1;14:1144813.doi: 10.3389/fimmu.2023.1144813. eCollection 2023.

ARTÍCULO DESTACADO

BACKGROUND

Pediatric allergic rhinoconjunctivitis has become a public concern with an increasing incidence year by year. Conventional subcutaneous immunotherapy (SCIT) has long treatment time, high cost and poor compliance. The novel immunotherapy significantly shortens the course of treatment by directly injecting allergens into cervical lymph nodes, which can perform faster clinical benefits to children.

OBJECTIVE

By comparing with SCIT, this study aimed to evaluate the long term efficacy and safety of intra-cervical lymphatic immunotherapy (ICLIT).

METHODS

This is a prospective randomized controlled study. A total of 50 allergic rhinoconjunctivitis children with dust mite allergy was randomly divided into ICLIT group and SCIT group, receiving three cervical intralymphatic injections of dust mite allergen or three years of subcutaneous injection, separately. Primary outcomes included total nasal symptom scores (TNSS), total ocular symptom scores (TOSS), total symptom scores (TSS), total medication scores (TMS), and total quality of life score. Secondary outcomes included pain perception and adverse reactions during treatment. Other secondary outcome was change in Dermatophagoides pteronyssinus (Derp) and Dermatophagoides farina (Derf) -specific IgE level.

RESULTS

Both groups had significantly decreased TNSS, TOSS, TSS, TMS, and total quality of life score after 36 months of treatment ($p<0.0001$). Compared with SCIT, ICLIT could rapidly improve allergic symptoms ($p<0.0001$). The short-term efficacy was consistent between the two groups ($p=0.07$), while the long-term efficacy was better in SCIT group ($p<0.0001$). The pain perception in ICLIT group was lower than that in SCIT group ($p<0.0001$). ICLIT group was safer. Specifically, the children had only 3 mild local adverse reactions without systemic adverse reactions. The SCIT group had 14 systemic adverse reactions. At last, the serum Derp and Derf-specific IgE levels in ICLIT and SCIT groups decreased 3 years later ($p<0.0001$).

CONCLUSION

ICLIT could ameliorate significantly the allergic symptoms in pediatric patients with an advantage in effectiveness and safety, besides an improved life quality including shortened period of treatment, frequency of drug use and pain perception.

2

Vía sublingual, sí. Pero también estudios de más calidad.

Efficacy of Sublingual Immunotherapy in Allergic Rhinitis Patients with Asthma: A Systematic Review and MetaAnalysis.

Dijiang Ma, Qiling Zheng, Jianing Sun, Shenjun Tang, Wudan He

Am J Rhinol Allergy. 2023 Aug 9;19458924231193528. doi: 10.1177/19458924231193528.

OBJECTIVE

Sublingual immunotherapy (SLIT) has been widely applied to treat patients with allergic rhinitis (AR). However, meta-analyses on the efficacy of SLIT in AR patients with asthma are still limited.

METHODS

Literature without language limitation published before October 28, 2022, were retrieved from PubMed, EMBASE, and Cochrane Library. STATA 16.0 software was used for the meta-analysis of the extracted data. The results reported were symptom scores, drug scores, adverse effects rates, and cost of treatment.

RESULTS

Ten studies involving 1722 patients met the inclusion criteria. The total rhinitis score (TRSS) (weighted mean difference [WMD] = -1.23, 95% CI: -1.39--1.06, P < .001) and total asthma symptom score (TASS) (WMD = -1.00, 95% CI: -1.12-0.89, P < .001) were significantly lower in the SLIT group than the placebo group. The SLIT group had higher rates of treatment-related adverse events (relative risk [RR] = 2.82, 95% CI: 1.77 4.48, P < .001) and total costs of treatment (standardized mean difference [SMD] = 0.71, 95% CI: 0.45-0.97, P < .001). There was no significant difference in inhaled corticosteroids (ICS) dose (P = .195), fractional exhaled nitric oxide (FeNO) (P = .158), forced expiratory volume in 1 s (FEV1) (P = .237), and direct costs of treatment (P = .630) between the SLIT and placebo groups.

CONCLUSION

SLIT may be a therapeutic method for improving rhinitis symptoms and asthma symptoms in AR patients with asthma. However, as there was significant heterogeneity in results, more high-quality and well designed studies are needed in the future to elucidate the efficacy of SLIT.

3

Éxito ITA en asmáticos = correcto diagnóstico + adecuada selección paciente.

How can we improve our use of allergen immunotherapy as a treatment option for asthma and severe asthma?

Désirée Larenas-Linnemann, Blanca María Morfin Maciel

Expert Rev Respir Med. 2023 Aug 29;1-9. doi: 10.1080/17476348.2023.2251403.

INTRODUCTION

In patients suffering from allergic asthma, especially in the pediatric age-group, allergen immunotherapy (AIT) could be of benefit and has the potential of long-term disease modification.

AREAS COVERED

We reviewed the evidence for a beneficial effect of AIT in allergic asthma. A correct selection of the possible candidates for AIT is crucial. We define the comprehensive allergic asthma diagnosis: confirming asthma, confirming allergic sensitization and having symptoms on exposure to the relevant allergens.We analyze why the first trials on AIT for asthma were contradictory; we consider the results of systematic reviews and discuss the high degree of heterogeneity often found in meta-analysis. We assess recent, double-blind, placebo-controlled trials in sublingual AIT that provide robust evidence for a reduction in acute asthma exacerbations and a decrease in the use of inhaled corticosteroids. Further, we demonstrate how real-world trials and large pharmacy data-based analyses confirm these findings for SLIT and SCIT. Finally, we explore the option of AIT in severe asthma patients, once well-controlled on biologic therapy.

EXPERT OPINION

Clear indications for AIT in asthma guidelines would benefit allergic asthmatics. AIT is a therapeutic option in appropriately selected asthmatics. Three years treatment has the potential for long-term tolerance, with persisting benefits years after discontinuation.

4

En la alergia a leche el fenotipo importa.

Identification of cow milk epitopes to characterize and quantify disease-specific T cells in allergic children.

Sloan A Lewis, Aaron Sutherland, Ferran Soldevila, Luise Westernberg, Minori Aoki, April Frazier et al

J Allergy Clin Immunol. 2023 Aug 19;S0091-6749(23)01061-8. doi: 10.1016/j.jaci.2023.07.020.

BACKGROUND

Cow milk (CM) allergy is the most prevalent food allergy in young children in the US and Great Britain. Current diagnostic tests are either unreliable (IgE, skin prick test), or resource-intensive with risks (food challenges).

OBJECTIVE

Here we set out to determine if allergen-specific T cells in cow milk allergic (CMA) patients have a distinct quality and/or quantity that could potentially be used as a diagnostic marker.

METHODS

Using PBMC from 147 pediatric food allergic subjects, we mapped T cell responses to a set of reactive epitopes in cow milk that we compiled in a peptide pool. This pool induced cytokine responses in in vitro cultured cells distinguishing CMA from non-CMA subjects. We further used the pool to isolate and characterize antigen specific CD4 memory T cells using flow cytometry and scRNA/TCR-Seq assays.

RESULTS

We detected significant changes in the transcriptional program and clonality of cow milk antigen-specific (CM+) T cells elicited by the pool in CMA vs. non-CMA subjects ex vivo. CM+ T cells from CMA subjects had increased percentages of FOXP3+ over FOXP3- cells. FOXP3+ cells are often equated with regulatory T cells (Tregs) that have suppressive activity, but CM+ FOXP3+ cells from CMA subjects showed significant expression of interferon-responsive genes and dysregulated chemokine receptor expression compared to non-CMA subjects, suggesting that these are not conventional Tregs. The CM+ FOXP3+ cells were also more clonally expanded than the FOXP3- population. We were further able to utilize surface markers (CD25, CD127, CCR7) in combination with our peptide pool stimulation to quantify these CM+ FOXP3+ cells by a simple flow cytometry assay. We show increased percentages of CM+ CD127 CD25+ cells from CMA subjects in an independent cohort, which could be used for diagnostic purposes. Looking specifically for Th2 cells normally associated with allergic diseases, we found a small population of clonally expanded CM+ cells that were significantly increased in CMA subjects and that had high expression of Th2 cytokines and pathogenic Th2/Tfh markers.

CONCLUSION

Overall, these findings suggest that there are several differences in the phenotype of CM+ T cells with CM allergy and that the increase in CM+ FOXP3+ cells is a potential diagnostic marker of an allergic state. Such markers have promising applications in monitoring natural disease outgrowth and/or the efficacy of immunotherapy that will need to be validated in future studies.

5

¿"Deconstruir" un alimento es la solución para disminuir su alergenicidad?

Food Allergens: When Friends Become Foes-Caveats and Opportunities for Oral Immunotherapy Based on Deactivation Methods.

M Victoria Gil, Nuria Fernández-Rivera, Carlos Pastor-Vargas, Pedro Cintas

Nutrients. 2023 Aug 20;15(16):3650. doi: 10.3390/nu15163650.

ABSTRACT

Food allergies represent a serious health concern and, since the 1990s, they have risen gradually in high-income countries. Unfortunately, the problem is complex because genetic, epigenetic, and environmental factors may be collectively involved. Prevention and diagnoses have not yet evolved into efficacious therapies. Identification and control of allergens present in edible substances hold promise for multi-purpose biomedical approaches, including oral immunotherapy. This review highlights recent studies and methods to modify the otherwise innocuous native proteins in most subjects, and how oral treatments targeting immune responses could help cancel out the potential risks in hypersensitive individuals, especially children. We have focused on some physical methods that can easily be conducted, along with chemo-enzymatic modifications of allergens by means of peptides and phytochemicals in particular. The latter, accessible from naturally-occurring substances, provide an added value to hypoallergenic matrices employing vegetal wastes, a point where food chemistry meets sustainable goals as well.

6

Si estás con ITSL y te infectas con SARS-CoV-2, tendrás menos síntomas.

The relationship between sublingual immunotherapy for allergic rhinitis and the risk of symptoms in patients with COVID-19 infection.

Shipeng Zhang, Chenxin Liu, Qiqi Liu, Xingyi He, Qinwei Fu, Xi Chen et al

Hum Vaccin Immunother. 2023 Aug 1;19(2):2236538.doi: 10.1080/21645515.2023.2236538.

ABSTRACT

To evaluated the risk ratio of Allergic rhinitis (AR) people on the symptoms after COVID-19 infection, and explored the relationship between AR and the symptoms after COVID-19 infection. An observational study was performed of people from outpatient department of the Hospital of Chengdu University of Chinese Medicine. Participants completed an electronic survey and between January 10 to January 20, 2023. We divided the participants into three groups according to the disease information of the population: non-AR people group (AR-N), AR patients with sublingual immunotherapy group (AR-S), and AR patients with conventional therapy group (AR-C). A total of 1116 participants were included in the study, with an average age of 21.76 ± 8.713, women accounted for 62.5%, men accounted for 37.5%. The final results showed that the risk of most symptoms after AR-C infection was not different from that of AR-N, except for sore throat, dry and itchy, chest distress, shortness of breath, and dyspnea. AR-S could effectively reduce the risk of post-infection symptoms including: dry and itchy (OR = 0.484, 95%CI: 0.335-0.698), pain (OR = 0.513, 95%CI:0.362-0.728), cough (OR = 0.506, 95% CI:0.341-0.749), expectoration (OR = 0.349, 95% CI:0.244-0.498), fever (OR = 0.569, 95% CI:0.379- 0.853), head and body pain (OR = 0.456, 95% CI:0.323-0.644), fatigue (OR = 0.256, 95% CI:0.177-0.371), cold limbs (OR = 0.325, 95%CI:0.227-0.465), diarrhea (OR = 0.246, 95% CI:0.132-0.457), constipation (OR = 0.227, 95%CI:0.100-0.513), hyposmia (OR = 0.456, 95% CI:0.296-0.701), hypogeusia (OR = 0.397, 95% CI:0.259-0.607), chest distress (OR = 0.534, 95% CI:0.343-0.829), shortness of breath (OR = 0.622, 95% CI:0.398- 0.974), palpitations (OR = 0.355, 95% CI:0.206-0.613). The risk of symptoms after COVID-19 infection in allergic rhinitis population receiving sublingual immunotherapy is lower.

7

Uso de proteómica para detectar biomarcadores de efectividad (temprana) en la ITSL.

Serum proteomics identifies S100A11 and MMP9 as novel biomarkers for predicting the early efficacy of sublingual immunotherapy in allergic rhinitis.

Yongquan Zhang, Jian Shui, Lu Wang, Fengjun Wang

Int Immunopharmacol. 2023 Aug 28;124(Pt A):110857. doi: 10.1016/j.intimp.2023.110857.

BACKGROUND

Allergic rhinitis (AR) is a chronic inflammatory disorder, and sublingual immunotherapy (SLIT) is an important therapy. However, SLIT exhibits a wide range of fluctuations and lacks objective monitoring indicators. Therefore, exploring biomarkers for early prediction of the efficacy of SLIT is urgently needed.

METHODS

We recruited two independent cohorts. In the discovery cohort, house dust mite (HDM) -induced AR patients underwent SLIT for at least 1 year, and were categorized into response and no response groups based on early efficacy. Serum proteomics was conducted to detect variations in protein expression levels between the two groups. The candidate proteins were confirmed in the validation cohort with enzyme-linked immunosorbent assay (ELISA), and their predictive values and levels of change before and after treatment were evaluated.

RESULTS

Serum proteomics identified a total of 113 differential proteins between the two groups, including 41 proteins upregulated and 72 downregulated in the no response group than the response group. The top 5 up- and down-regulated proteins were selected for further validation, and ELISA results revealed that serum CCL14, LTA4H, S100A11 and MMP9 levels were significantly elevated, and TGFBI and MASP1 were decreased in the response group than those in the no response group($P < 0.05$). Moreover, receiver operating characteristic curves revealed that serum S100A11 and MMP9 exhibited greater ability in predicting the early effectiveness of SLIT (AUC > 0.7, $P < 0.05$). Furthermore, these two biomarkers exhibited significant reductions 1 year after SLIT, particularly in those patients who responded positively to the treatment ($P < 0.05$).

CONCLUSION

Serum S100A11 and MMP9 have the potential to serve as iomarkers for early prediction of the effectiveness of SLIT and monitoring the therapeutic effects. The circulating proteomic alterations might contribute to guiding treatment and understanding the mechanism of SLIT in AR patients.

8

“Ábrete, sésamo”: entremos y conozcamos los detalles de la alergia a esta semilla.

Sesame eliciting and safe doses in a large sesame allergic population.

Liat Nachshon, Joost Westerhout, W Marty Blom, Benjamin Remington, Michael B Levy, Michael R Goldberg

Allergy. 2023 Aug 22. doi: 10.1111/all.15863.

BACKGROUND

Sesame is a significant food allergen causing severe and even fatal reactions. Given its increasing prevalence in western diet, sesame is listed as an allergenic food requiring labeling in the United States and EU. However, data on the population reaction doses to sesame are limited.

METHODS

All sesame oral food challenges (OFCs), performed either for diagnosis or for threshold identification before the beginning of sesame oral immunotherapy (OIT) between November 2011 and July 2021 in Shamir medical center were analyzed for reaction threshold distribution. Safe dose challenges with 90-120 min intervals were also analyzed.

RESULTS

Two hundred and fifty patients underwent 338 positive OFCs, and additional 158 safe-dose OFCs were performed. The discrete and cumulative protein amounts estimated to elicit an objective reaction in 1% (ED01) of the entire cohort (n = 250) were 0.8 mg (range 0.3-6.3) and 0.7mg (range 0.1-7.1), respectively, and those for 5% of the population (ED05) were 3.4 mg (range 1.2-20.6) and 4.5 mg (range 1.2-28.8), respectively. Safe-dose OFCs showed similar values of ED01 (0.8, 0.4-7.5 mg) and ED05 (3.4, 1.2-22.9 mg). While doses of ≤1 mg sesame protein elicited oral pruritus in 11.6% of the patients, no objective reaction was documented to this amount in any of the challenges, including safe dose OFCs.

CONCLUSIONS

This study provides data on sesame reaction threshold distribution in the largest population of allergic patients studied, with no right or left censored data, and with validation using a safe-dose OFC. It further supports the current methods for ED determination as appropriate for establishing safety precautions for the food industry.

9

Repasemos la historia para mejorar la tolerancia a la ITA.

Safety and adverse reactions in subcutaneous allergen immunotherapy: a review.

Cristoforo Incorvaia, Carlo Cavaliere, Jan W Schroeder, Gualtiero Leo, Francesca Nicoletta, Alessandro Barone et al

Acta Biomed. 2023 Aug 3;94(4):e2023172.doi: 10.23750/abm.v94i4.14239.

BACKGROUND

Allergen immunotherapy (AIT) is the only treatment which acts on the causes of allergic diseases by modifying their natural history. In the eighties subcutaneous immunotherapy (SCIT) with high biological power allergen extracts caused a number of severe systemic reactions and also fatalities in the UK and the US, resulting in its limitation and in the introduction of other routes of administration. A decisive advance for SCIT safety was understanding that the major cause of mortality was injecting the allergen extract to patients with uncontrolled asthma at the time of injection.

AREAS COVERED

This awareness resulted in a significant decrease in fatalities, but not in their abolition. In 2019, an increase in SCIT-related mortality was observed, suggesting to continue the research for still unidentified factors favoring severe reactions, such as the administration of a wrong extract or of allergen doses higher than listed, unintentional intravenous administration, and missed dose reduction after protracted interruption. Moreover, in the context of the improving of the safety, the role played in tolerance-promoting by adjuvants such as CpG oligodeoxynucleotides has to be taken into account, as well as the potential preventive effect performed by the monoclonal anti-IgE antibody omalizumab against the exacerbation of severe reactions during SCIT.

CONCLUSION

The safety of SCIT is good, but the research to improve it further must continue. In particular, the pathophysiological mechanisms related to AIT for inhalants and for Hymenoptera venom should be studied, based on the evident diversity demonstrated by the complete absence of fatal reactions to Hymenoptera venom immunotherapy from its introduction in comparison with the history of serious and fatal offenses examined in this review.

10

La ITO la sufren los niños... y sus padres: tengámoslo en cuenta.

Development of an Oral Immunotherapy-Related Parental Burden Scale.

Akihiro Maeta, Yuri Takaoka, Masaaki Hamada, Atsuko Nakano, Shinichi Sumimoto, Kaori Anzai, Yuki et al

Int Arch Allergy Immunol. 2023 Aug 30;1-13.doi: 10.1159/000533332.

INTRODUCTION

Oral immunotherapy (OIT) imposes a burden on parents and their children with food allergies (FAs). We already developed a questionnaire for OIT-related Parental Burden (OIT-PB) scale. However, the previous questionnaire had some problems. This study modified OIT PB and verified its reliability and validity.

METHODS

A 20-item draft covering the physical and mental burdens caused by OIT was prepared jointly with multiple allergists. The Food Allergy Quality of Life Questionnaire-Parental Burden (FAQLQ-PB) and Stress Response Scale-18 (SRS-18) were used to verify concurrent validity. A questionnaire survey was administered during treatment to parents of FA children who had started OIT for the first time. An additional OIT-PB survey was performed at one specific institution 1 week after the posttreatment survey.

RESULTS

The responses of 64 of the 76 recruited parents were analyzed. Of the 20 questions, 1 item was excluded owing to the floor effect, 1 was excluded because its commonality was less than 0.2, and 2 were excluded because their factor loading values were less than 0.4. Factor analysis was used to classify the OIT-PB into the following 4 subscales: "burden caused by adherence to treatment plan," "anxiety about symptom induced risk," "burden due to patient's eating behavior," and "anxiety about treatment effect." The Cronbach's α for all 16 items of the OIT-PB was 0.893; Cronbach's α for each subscale was 0.876, 0.898, 0.874, and 0.717. The re-test reliability coefficient was 0.864 (95% confidence interval [CI]: 0.720-0.937, $p < 0.001$). A significant positive correlation was found between the OIT-PB and FAQLQ-PB ($R = 0.610$ [95% CI: 0.422-0.747], $p < 0.001$) and the SRS-18 ($R = 0.522$ [95% CI: 0.306-0.687], $p < 0.001$). A significant negative correlation was found between the rate of increase in OIT food intake and the "anxiety about treatment effect" score ($R = -0.355$ [95% CI: -0.558-0.112], $p < 0.001$). Parents of children on the hen's egg OIT treatment scored higher on the "burden due to patient's eating behavior" subscale than did parents of children on the milk and wheat OIT treatment.

CONCLUSION

The burden of OIT experienced by parents can be broadly classified into four categories. The modified OIT-PB was able to evaluate them individually and was shown to have reliability and validity. This scale is expected to be useful in the development of OIT that considers not only therapeutic effect but also the burden experienced by FA children and their parents.

BOLETÍN BIBLIOGRÁFICO DE INMUNOTERAPIA

Septiembre 2023

1

El futuro de la ITA en 7 preguntas.

Future directions of Allergen Immunotherapy (AIT) for allergic rhinitis: an experts' perspective.

Pfaar O, Portnoy J, Nolte H, Chaker AM, Luna-Pech JA, Patterson A, Pandya A, Larenas-Linnemann D

J Allergy Clin Immunol Pract. 2023 Sep 14:S2213-2198(23)01015-2. doi: 10.1016/j.jaip.2023.08.047. Epub ahead of print. PMID: 37716529.

ARTÍCULO DESTACADO

BACKGROUND

Allergen Immunotherapy (AIT) is broadly used all over the world as the only available disease-modifying treatment option. The aim of this experts' perspective is to address seven important unmet needs for the further direction of AIT and to provide the readership with the authors' positions on these topics.

METHODS

An international group of experts in the field of AIT have formulated seven important aspects for the future position of AIT, performed a current literature review and proposed a consented position on these topics.

RESULTS

The aspects discussed and consented by the authors include i) alternative routes of allergen application in AIT, ii) the potential of recombinant vaccines, iii) the role of allergy diagnosis based on component-resolved diagnosis for AIT composition, iv) the impact of COVID-19 vaccination for further innovations in AIT, v) potential of combining biologics to AIT, vi) future innovations in high-risk children/adolescents and vii) the future regulatory position on AIT.

CONCLUSION

Important unmet needs and topics for AIT have been addressed in this expert review. The authors' views and personal position on these seven aspects have also been elaborated.

2

SARS-CoV-2 y asma, no hay mal que por bien no venga.

The SARS-CoV-2 Pandemic and Asthma: What We Have Learned and What is still Unknown.

McPhee C, Yevdokimova K, Rogers L, Kraft M

J Allergy Clin Immunol. 2023 Sep 20:S0091-6749(23)01184-3. doi: 10.1016/j.jaci.2023.09.005. Epub ahead of print. PMID: 37739069.

ABSTRACT

The SARS-CoV-2 pandemic has brought new insights into the immunological intricacies of asthma. In this review, we discuss the epidemiology of asthma in patients infected with SARS-CoV-2 and the risk of severe infection. Type 2 inflammation had an overall protective effect against SARS-CoV-2 infection by various mechanisms summarized in this review. Asthma, intranasal, and inhaled corticosteroids decreased the ACE2 receptor, an important receptor for SARS-CoV-2 entry into host cells. We summarize the nuances of treatment of type 2 inflammation despite its underlying protective effects. Research to date has shown that patients on various allergen immunotherapies and biologics do benefit from being vaccinated.

3

Evidencia de los comprimidos de ácaros de 300 IR tras su puesta de largo.

Safety and effectiveness of a 300 IR house dust mite sublingual tablet: descriptive 4-year final analysis of a post-marketing surveillance in Japan.

Okamoto Y, Kato M, Ishii K, Sato Y, Hata T, Asaka Y

Immunotherapy. 2023 Sep 20. doi: 10.2217/imt-2023-0100.

BACKGROUND

Data are limited for clinical outcomes with house dust mite (HDM) allergen immunotherapy beyond 2 years' observation.

MATERIALS AND METHODS

A post-marketing drug-use survey assessed the safety and effectiveness of the 300 index of reactivity (IR) HDM tablet during use for up to 4 years in Japan.

RESULTS

538 patients were evaluable for safety and 383 for effectiveness. Most adverse drug reactions (ADRs) occurred early and were local reactions; 5.6% of 249 total events were reported during years 2 to 4 as new ADRs after the interim analysis. The CAP-RAST score was identified as a potential risk factor for ADRs. The proportion of evaluable patients with severe allergic rhinitis symptoms decreased from 46.4% at baseline (n = 317) to 1.0% at 4 years (n = 104). Patients (n = 16) who discontinued 300 IR HDM tablet due to symptomatic improvement had sustained improvement relative to baseline 1 to 2 years later.

CONCLUSION

Long-term use of the 300 IR HDM tablet is safe and effective.

4

ITA y biológicos, la pareja perfecta.

Combination of omalizumab with allergen immunotherapy versus immunotherapy alone for allergic diseases: A meta-analysis of randomized controlled trials.

Zhang YY, Zhang M, Zhang JQ, Li QQ, Lu MP, Cheng L

Int Forum Allergy Rhinol. 2023 Sep 16. doi: 10.1002/alr.23268. Epub ahead of print. PMID: 37715592.

BACKGROUND

Allergen immunotherapy (AIT)-associated adverse events (AEs) limit its usage in the management of allergic diseases. The monoclonal anti-IgE antibody (omalizumab) and AIT have complementary actions. However, no consensus has been reached on whether their combination could exert superior efficacy and safety.

OBJECTIVE

To evaluate whether the combination of AIT with omalizumab is superior to AIT alone in treating allergic diseases.

METHODS

The MEDLINE/PubMed, Embase, Scopus and Cochrane Library databases were searched to identify randomized control trials (RCTs) reporting the outcomes of omalizumab combined with AIT (omalizumab + AIT) versus AIT alone. A random-effect model was established to estimate outcomes with a 95% confidence interval (CI).

RESULTS

A total of 11 eligible RCTs (involving 901 patients) were screened out for the meta-analysis. According to a pooled analysis, omalizumab + AIT significantly increased the number of patients achieving the target maintenance dose (TMD) and sustained unresponsiveness (SU) to allergens (odds ratio [OR] = 2.43; 95% CI: 1.33-4.44; p = 0.004; I2 = 35%, and OR = 6.77; 95% CI: 2.10-21.80; p = 0.001; I2 = 36%, respectively). Similarly, individuals receiving the combination therapy reported significantly fewer episodes of severe systemic AEs than AIT alone (OR = 0.32; 95% CI: 0.18-0.59; p = 0.0003; I2 = 0%). Meanwhile, the improvements in symptom severity score (mean difference [MD] = -0.26), rescue medication daily means score (MD = -0.14), and number of patients consuming epinephrine in AIT (OR = 0.20) were all more evident than those in AIT alone.

CONCLUSION

Omalizumab + AIT can significantly enhance the efficacy and safety of AIT by increasing TMD and SU to allergens, while decreasing severe systemic Aes.

5

Tener controlada mi alergia me beneficia en el caso de tener COVID-19.

COVID-19 and Its Impact on Common Diseases in the Allergy Clinics.

Kocatürk E, Abrams EM, Maurer M, Mitri J, Oppenheimer J, Vestergaard C, Zein J

J Allergy Clin Immunol Pract. 2023 Sep 1:S2213-2198(23)00962-5. doi: 10.1016/j.jaip.2023.08.038. Epub ahead of print. PMID: 37660731.

ABSTRACT

Coronavirus disease 2019 (COVID-19) is a highly contagious viral disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It has various effects on asthma, allergic rhinitis, atopic dermatitis, and urticaria and may change the course of the disease depending on the severity of the infection and control status of the disease. Conversely, these diseases may also impact the course of COVID-19. Patients with chronic urticaria and atopic dermatitis may have COVID-19-induced disease exacerbations and biological treatments reduce the risk of exacerbations. Poor asthma control is linked to severe COVID-19 while allergic asthma is associated with lower risk of death and a lower rate of hospitalization due to COVID-19 compared with nonallergic asthma. The use of intranasal corticosteroids is associated with lower rates of hospitalization due to COVID-19 in patients with allergic rhinitis, whereas the effect of inhaled corticosteroids is confounded by asthma severity. These observations reinforce the importance of keeping allergic diseases under control during pandemics. The use of biologicals during COVID-19 is generally regarded as safe, but more evidence is needed. The pandemic substantially changed the management of allergic disorders such as home implementation of various biologicals, allergen immunotherapy, food introduction, and increased use of telemedicine and even home management of anaphylaxis to reduce emergency department burden and reduce risk of infection. Physicians need to be aware of the potential impact of COVID-19 on allergic diseases and educate their patients on the importance of continuing prescribed medications and adhering to their treatment plans to maintain optimal control of their disease.

6

Conoce los tratamientos que están a punto de llegar para la rinitis alérgica.

Promising New Diagnostic and Treatment Modalities for Allergic Rhinitis: What's Coming Next?

Barrett TF, Roland LT

Otolaryngol Clin North Am. 2023 Sep 16:S0030-6665(23)00155-X. doi: 10.1016/j.otc.2023.08.008. Epub ahead of print. PMID: 37722952.

ABSTRACT

Novel diagnostic tests may help diagnose patients with local allergic rhinitis (AR) when systemic testing is negative or inconclusive. Surgical approaches including septoplasty, inferior turbinate reduction, nasal swell body reduction, and posterior nasal nerve ablation may improve symptoms in patients whose symptoms are refractory to medical therapy, though high-quality evidence is lacking in the AR population. Intralymphatic and epicutaneous immunotherapy have the potential to improve adherence to allergen immunotherapy, though comparisons with current gold standard treatments are lacking and studies reporting long-term outcomes are needed. Immunomodulatory agents in combination with subcutaneous immunotherapy (SCIT) may improve tolerance of SCIT but reports to date do not demonstrate a clear benefit in symptom alleviation. Future work in these areas may support these options as beneficial for testing and treatment of AR.

7

¿Podemos identificar entre los alérgicos a alimentos a los pacientes de riesgo?

Can we identify patients at risk of severe reactions to food?

Anagnostou A, Muraro A

Expert Rev Clin Immunol. 2023 Sep 27. doi: 10.1080/1744666X.2023.2265069. Epub ahead of print. PMID: 37753864.

INTRODUCTION

The burden of food allergy is multifaceted, including dietary, social limitations, financial burden and a significant psychological impact resulting in decreased quality of life for food-allergic Individuals. Patients and families live in fear of accidental exposures resulting in severe allergic reactions and negative outcomes, including fatalities. The perception of this last risk is often overinflated compared with the actual risk, but since it is difficult to identify with certainty patients who are most at risk, families often live in constant fear. A variety of severity scores exists for allergic reaction grading. Multiple studies have attempted to pinpoint risk factors for severe allergic reactions that are food-induced, with sometimes controversial results, and the search is ongoing.

8

“¡No quiero que me pinchen!” Buscando estrategias de distracción.

Evaluation of pain-alleviating strategies during allergy shots (subcutaneous immunotherapy): a randomized controlled pilot study.

Pfieffer J, Wehmeier K, Gee K, DeSanto T, Yousef E

Eur Ann Allergy Clin Immunol. 2023 Sep 6. doi: 10.23822/EurAnnACI.1764-1489.312. Epub ahead of print. PMID: 37671862.

BACKGROUND

Subcutaneous immunotherapy (SCIT) is a potential disease-modifying therapy effective for treatment of various allergic disorders. Pain and fear are common concerns of children, which can pose stress and result in negative experiences. The purpose of this study was to evaluate and compare the effectiveness of three marketed distraction devices and ethyl chloride spray (a routinely used topical anesthetic agent for painful procedures), the current clinical standard of care in reducing the perception of needle pain during SCIT administration in children.

METHODS

40 children, aged 4-17 years, receiving SCIT with use of one of three alternative pain therapies or with standard practice were enrolled. Participants were randomly assigned to one of the pain modifying interventions. The three interventional groups were ShotBlocker® (Bionix, Toledo, OH, USA), Buzzy® I (Pain Care Labs, Atlanta, GA, USA) (vibration only), and Buzzy® II (vibration with ice). Control group was ethyl chloride spray. The study consisted of two visits during SCIT administration process.

RESULTS

Of these 40 children, 12 received the ShotBlocker, 8 received the Buzzy I, 11 received the Buzzy II, and 9 received ethyl chloride spray (control group).

CONCLUSIONS

There were no significant differences found between each of the distraction devices and between the control group. Type II error/false negative finding cannot be ruled out because of a small sample. Therefore, we cannot conclude that no true difference exists between each distraction device and the control group simply because of occurrence of a non-significant P-value in our study.

9

¿El tamaño del prick importa?

Does skin prick test response intensity predict symptom severity and efficacy of subcutaneous immunotherapy in allergic rhinitis?

Yuan X, Xie S, Meng L, Zhong W, Zhang H, Wang F, Fan R, Jiang W, Xie Z

Eur Arch Otorhinolaryngol. 2023 Sep 16. doi: 10.1007/s00405-023-08220-5. Epub ahead of print. PMID: 37715808.

OBJECTIVES

To investigate the effect of response intensity of allergen skin prick test (SPT) on symptom severity and long-term efficacy of dust mite subcutaneous immunotherapy (SCIT) in allergic rhinitis (AR).

METHODS

AR Patients diagnosed with dust mite allergy and completed 3 years of SCIT were collected and classified into three groups: grade 2 (SPT of + +), grade 3 (SPT of + + +) and grade 4 (SPT of + + + +). Comparisons between groups were performed to examine the associations of SPT categories and symptom severity and the long-term efficacy of SCIT in AR.

RESULTS

181 AR patients were included. There was no significant difference in the baseline TNSS, SMS, RQLQ and VAS, and particularly to symptom severity grading among three SPT grade groups ($P > 0.05$). The moderate-severe AR was more likely to be smoking and accompany with asthma and had higher prevalence of sensitization to cockroach, mixed grass and tree pollen than mild AR ($P < 0.05$). Prevalence of sensitization to cockroach, mixed grass, ragweed and animal dander was increased in AR patients with asthma and allergic conjunctivitis ($P < 0.05$). Furthermore, after 3 years of SCIT, no statistical differences in TNSS, SMS, RQLQ, VAS and long-term efficacy were observed among the three SPT grade groups ($P > 0.05$). Similarly, long-term outcomes of patients with different SPT grades did not differ among different clinical characteristics and different efficacy determination criteria ($P > 0.05$).

CONCLUSIONS

The SPT response intensity cannot be used as an objective evaluation index for symptom severity and the long-term efficacy of SCIT in AR patients.

BOLETÍN BIBLIOGRÁFICO
DE INMUNOTERAPIA

Octubre 2023

1

La ITA consigue “prevenir además de curar”.

PREVENTION IS BETTER THAN CURE: IMPACT OF ALLERGEN IMMUNOTHERAPY ON THE PROGRESSION OF AIRWAY DISEASE.

Hasan Arshad, Gideon Lack, Stephen R Durham, Martin Penagos, Désireé Larenas-Linneman, Susanne Halken

J Allergy Clin Immunol Pract. 2023 Oct 14:S2213-2198(23)01130-3.

ARTÍCULO DESTACADO

ABSTRACT

Allergen immunotherapy is highly effective for seasonal pollinosis. 3 years treatment results in long-term efficacy. This disease modification is accompanied by downregulation of allergen-specific Th2 responses and the induction of persistent specific IgG and IgA- associated IgE-blocking activity. In children with seasonal rhinitis, both subcutaneous and sublingual pollen immunotherapy have been shown to reduce development of asthma symptoms and asthma medication requirements. House dust mite tablet allergen immunotherapy has been shown to be effective for perennial mite-driven rhinitis in adults and children and may suppress asthma exacerbations, whereas its long-term efficacy has yet to be explored. The success of primary prevention of peanut allergy in childhood by introduction of peanut into the diet during infancy provides a strong rationale to explore whether primary prevention of inhalant allergies and asthma may also be possible. House dust mite allergy is a major risk factor for developing asthma. Preliminary data in at-risk children suggests that sublingual house dust mite immunotherapy initiated during infancy could reduce onset of multiple allergen sensitisations and prevent development of asthma at age 6 years. This possibility should now be explored in an adequately powered prospective randomised controlled trial.

2

Cada vez tenemos más opciones en la ITA con alimentos.

New Approaches to Food Allergy Immunotherapy.

Jennifer A Dantzer, Edwin H Kim

J Allergy Clin Immunol Pract . 2023 Oct 16:S2213-2198(23)01135.

ABSTRACT

Food allergy is an increasing public health problem in children and adults. In addition to the risk of potentially severe reactions, food allergy can have a significant burden on quality of life, nutrition, cost of living, and social activities. Traditionally, treatment has primarily included strict food allergen avoidance and use of emergency medications to treat an allergic reaction. However, in recent years, there have been significant strides in the advancement of food allergy treatment, including the approval of the first and only approved therapy (peanut oral immunotherapy) for food allergy in 2020. Clinical trials have primarily focused on food allergen immunotherapy (oral, epicutaneous, sublingual). Building off of a foundation of promising data supporting the efficacy of food oral immunotherapy and our greater understanding of the underlying mechanism of immunotherapy, newer approaches, including alternative routes of delivery, adjuncts to therapy, modified allergens, and utilization in younger patients, aim to provide safer and more effective treatment approaches to the millions of patients burdened by food allergy.

3

Los adyuvantes potentes (VLP) y la presencia de RNA son clave para conseguir inmunogenicidad en la vacuna a cacahuete.

Influence of antigen density and TLR ligands on preclinical efficacy of a VLP-based vaccine against peanut allergy.

Pascal S Krenger, Romano Josi, Jan Sobczak, Thalia L C Velazquez, Ina Balke, Murray A Skinner, et al
Allergy. 2023 Oct 10.doi: 10.1111/all.15897.

BACKGROUND

Virus-like particle (VLP) Peanut is a novel immunotherapeutic vaccine candidate for the treatment of peanut allergy. The active pharmaceutical ingredient represents cucumber mosaic VLPs (CuMVTT -VLPs) that are genetically fused with one of the major peanut allergens, Ara h 2 (CuMVTT - Ara h 2). We previously demonstrated the immunogenicity and the protective capacity of VLP Peanut-based immunization in a murine model for peanut allergy. Moreover, a Phase I clinical trial has bee initiated using VLP Peanut material manufactured following a GMP compliant manufacturing process. Key product characterization studies were undertaken here to understand the role and contribution of critical quality attributes that translate as predictive markers of immunogenicity and protective efficacy for clinical vaccine development.

METHOD

The role of prokaryotic RNA encapsulated within VLP Peanut on vaccine immunogenicity was assessed by producing a VLP Peanut batch with a reduced RNA content (VLP Peanut low RNA). Immunogenicity and peanut allergen challenge studies were conducted with VLP Peanut low RNA, as well as with VLP Peanut in WT and TLR 7 KO mice. Furthermore, mass spectrometry and SDS-PAGE based methods were used to determine Ara h 2 antigen density on the surface of VLP Peanut particles. This methodology was subsequently applied to investigate the relationship between Ara h 2 antigen density and immunogenicity of VLP Peanut.

RESULTS

A TLR 7 dependent formation of Ara h 2 specific high-avidity IgG antibodies, as well as a TLR 7 dependent change in the dominant IgG subclass, was observed following VLP Peanut vaccination, while total allergen-specific IgG remained relatively unaffected. Consistently, a missing TLR 7 signal caused only a weak decrease in allergen tolerability after vaccination. In contrast, a reduced RNA content for VLP Peanut resulted in diminished total Ara h 2 specific IgG responses, followed by a significant impairment in peanut allergen tolerability. The discrepant effect on allergen tolerance caused by an absent TLR 7 signal versus a reduced RNA content is explained by the observation that VLP Peanut-derived RNA not only stimulates TLR 7 but also TLR 3. Additionally, a strong correlation was observed between the number of Ara h 2 antigens displayed on the surface of VLP Peanut particles and the vaccine's immunogenicity and protective capacity.

CONCLUSIONS

Our findings demonstrate that prokaryotic RNA encapsulated within VLP Peanut, including antigen density of Ara h 2 on viral particles, are key contributors to the immunogenicity and protective capacity of the vaccine. Thus, antigenicity and RNA content are two critical quality attributes that need to be determined at the stage of manufacturing, providing robust information regarding the immunogenicity and protective capacity of VLP Peanut in the mouse which has translational relevance to the human setting.

4

ITA intra-amígdala, nueva vía efectiva y que mejora el cumplimiento.

Efficacy and Safety of Intratonsillar Immunotherapy for Allergic Rhinitis: A Randomized, Double-blind, PlaceboControlled Clinical Trial.

Junyan Zhang, Xiaobin Yang, Guangui Chen, Jintao Hu, Ying He, Jinxiang Ma, et al
Ann Allergy Asthma Immunol . 2023 Oct 30:S1081-1206(23)01392-3.

BACKGROUND

A lower adherence rate existed in patients received allergen specific immunotherapy (AIT) due to its lengthy period and side effects even though it is the only curative treatment for IgE-mediated allergies. Therefore, exploring innovative AIT routes are necessary.

OBJECTIVE

This study was designed to explore the efficacy and safety of the intratonsillar injection of house dust mite (HDM) extract in patients with HDM-induced allergic rhinitis.

METHODS

A randomized double-blind placebo-controlled clinical trial was conducted. Eighty patients with HDM-induced AR were randomized to receive 6 intratonsillar injections with HDM extract or placebo over 3 months. The total nasal symptom score (TNSS), Visual Analogue Scale (VAS) of nasal symptoms, combined symptom and medication score (CSMS), Mini Rhinoconjunctivitis Quality of Life Questionnaire (MiniRQLQ), and serum allergen-specific IgG4 to D. pteronyssinus were all monitored at baseline, 3, 6, and 12 months after the treatment finished. The intent to-treat (ITT) and per protocol set (PPS) are both analyzed.

RESULTS

The primary endpoints TNSS and ΔTNSS were improved significantly at 3 months after AR patients finished a 3-month 6 injection intratonsillar immunotherapy (ITIT) by comparing to the placebo treatment in both ITT and PPS. VAS, CSMS and MiniRQLQ were also improved significantly at 3 months after treatment in PPS. However, the improvement effect of ITIT at 6 and 12 months was limited and uncertain based on the data. The increase of serum Der p IgG4 in the active group was significantly higher than that in the placebo group at 3, 6, and 12 months after the treatment finished. Adverse events were monitored, and no systemic adverse reactions were observed.

CONCLUSION

The clinical trial showed that intratonsillar injection with HDM extract was safe and effective in patients with AR. Optimizing the protocol and allergen formulations is expected to increase and maintain the efficacy of this novel approach.

5

Veamos cuál es la efectividad de la IT intralinfática a largo plazo.

A 5-Year Open-Label Follow-up of a Randomized Double-Blind Placebo-Controlled Trial of Intralymphatic Immunotherapy for Birch and Grass Allergy Reveals Long-term Beneficial Effects.

Hjalmarsson E, Hellkvist, Karlsson A, Winquist O, Kumlien Georén S, Westin U, Cardell LO

J Investig Allergol Clin Immunol . 2023 Oct;33(5):362-372.

BACKGROUND

Intralymphatic immunotherapy (ILIT) is a novel, faster alternative to conventional allergen immunotherapy (AIT). Few previous studies have evaluated its long-term effects. The objective of the present study was to complete a 5-year follow-up of a randomized double-blind placebocontrolled trial of ILIT for a combination of birch and grass allergens.

METHODS

Fifty-eight patients with allergic rhinitis were treated with either placebo or a combination of ALK Alutard Birch and Grass 1000 SQ-U administered in 3 intralymphatic injections at 1-month intervals. A year after the vaccination, the symptoms induced by nasal provocation were significantly reduced. After 5-6 years, 20 out of 26 actively treated patients were followed up with a nasal provocation test (NPT) and seasonal registration of the combined symptom and medications score (CSMS), IgE and IgG4 levels in blood, and immunological markers in blood and lymph nodes and compared with 13 unvaccinated controls.

RESULTS

The reduction in the NPT response with ILIT at year 1 could not be convincingly reproduced at year 5. The new CSMS scores were markedly lower among the previously treated patients than among the control group. Furthermore, grass-specific IgG4 was increased, grass specific IgE decreased, FcεR1 on basophils was reduced, and the fraction of memory T-cells in lymph nodes increased.

CONCLUSION

The combination of seasonal clinical data and immunological parameters supports the notion of a long-lasting effect of ILIT. These data support the concept of ILIT as a good alternative to traditional AIT in pollen-induced allergic rhinitis.

6

ITA con extracto despigmentado-polimerizado: si trato 3 años es efectiva 10.

House dust mite subcutaneous immunotherapy has sustained long-term effectiveness on allergic rhinitis and asthma: A 10-year follow-up.

Elena Rodriguez-Plata, Ariel Callero Viera, Monica Ruiz-Garcia, Aida Gomez-Cardenosa, Eva Nieto, Jose Carlos García-Robaina

Immun Inflamm Dis . 2023 Oct;11(10):e1004.

BACKGROUND

Maintenance doses for allergen immunotherapy (AIT) have been recommended for at least 3 years but little data on long-term efficacy is available depending on AIT duration. To show sustained efficacy 10 years after completion of treatment with depigmented-polymerized house dust mite (dpg-pol HDM) allergen extract in adults with asthma and/or rhinoconjunctivitis.

METHODS

Patients included in a double-blind placebo-controlled AIT study with dpg-pol HDM allergen extract were reviewed at completion of the perennial treatment and 10-year follow-up (10y-FU). Change in symptom and rescue medication score was the primary objective. Visual analog scale (VAS), asthma control test (ACT), and degree of disease control were the secondary objectives. A comparative analysis between patients who underwent AIT treatment for <3 years and ≥3 years was performed.

RESULTS

Data from 31 patients (mean age 38 years) were available at 10y-FU. All had asthma and 29 had rhinoconjunctivitis at baseline. Twentythree patients were treated ≥3 years and 8 for <3 years. Seventeen (55%) patients were asymptomatic at completion of AIT, with significant differences for nasal, conjunctival, and bronchial symptoms ($p < .0001$) compared with baseline only in those patients treated ≥3 years. Nine (52.9%) patients remained completely asymptomatic at 10y-FU, all were treated for ≥3 years. Moreover, significant reduction in the number of patients with rhinitis ($p = .0117$), conjunctivitis ($p < .0001$), and bronchial ($p = .0005$) sym ptoms was observed at 10y-FU compared with baseline only in the ≥3 years treated. Ten (32.3%) patients did not require any rescue medication at 10y-FU, all had been treated for ≥3 years. ACT at 10y-FU showed a good control of asthma (median 23.5; 95% IC[22.0, 25.0]). No significant differences were observed between VAS at end of treatment compared with VAS at 10y-FU.

CONCLUSIONS

Sustained clinical efficacy is achieved 10 years after completion of depigmented-polymerized HDM, however, these findings were observed only if patients are treated for at least 3 years.

7

¿Y si vacunando frente a un alérgeno consigo (también) modificar la respuesta immune frente otro alérgeno diferente?

Decreased Basophil Activation against House Dust Mite after Japanese Cedar Pollen Subcutaneous Immunotherapy: A Retrospective Study.

Chisato Inuo, Hitoshi Ando, Kenichi Tanaka, Yoichi Nakajima, Ikuya Tsuge, Atsuo Urisu

Int Arch Allergy Immunol . 2023 Oct 18:1-6.

BACKGROUND

Allergen-specific immunotherapy (AIT), an established treatment for allergic diseases, prevents the development of other allergic manifestations. Although the mechanisms remain unclear, AIT has been shown to reduce basophil activation (BA) against nontarget allergens.

OBJECTIVES

The aim of this study was to assess immunological changes in Dermatophagoides farinae (Der f) after Japanese cedar pollen (JCP)- based subcutaneous immunotherapy (SCIT) monotherapy.

METHOD

The data of 16 patients (age: 6-37 years) with JCP-induced allergic rhinitis who were sensitive to Der f (serum Der f-specificimmunoglobulin E [IgE] level >0.34 kUA/L) and received JCP-based SCIT for 5 years were reviewed retrospectively. BA by Der f and JCP extracts and serum-specific IgE and immunoglobulin G4 (IgG4) levels against these allergens were evaluated before and after completing 5 years of JCPbased SCIT monotherapy.

RESULTS

The areas under the dose-response curves of BA by Der f and JCP extracts were significantly reduced ($p = 0.02$ and $p = 0.002$, respectively). JCP-specific IgE levels decreased and JCP-specific IgG4 levels increased significantly ($p < 0.001$ for both), whereas Der f-specific IgE and IgG4 levels did not change significantly.

CONCLUSIONS

JCP-based SCIT monotherapy reduced Der f-specific BA. These findings suggest that JCP-based SCIT has the potential to modulate immune response toward nontarget allergens.

8

Receptores TAM como biomarcadores de gravedad y de respuesta.

Soluble TAM Receptor Tyrosine Kinases Correlate with Disease Severity and Predict the Early Responsiveness of Sublingual Immunotherapy in Allergic Rhinitis.

Yandan Zhou, Zhili Feng, Jie Wen, Chi Yang, Qiancheng Jing

J Inflamm Res. 2023 Oct 25:16:4845-4855.

BACKGROUND

Allergic rhinitis (AR) is a common allergic disease, and SLT has shown effectiveness as a treatment method. This study focuses on the evaluation of serum TAM receptor tyrosine kinases (TYRO3, AXL, and MER) levels as potential indicators of disease severity and predictive markers for sublingual immunotherapy (SLIT) responsiveness in AR patients.

METHODS

A total of 160 AR subjects, including 40 mild AR (MAR) and 120 moderate-severe AR (MSAR) patients, and 40 healthy controls (HC) were recruited. Serum concentrations of TYRO3, AXL, and MER were measured and their relationships with disease severity were examined. In the MSAR group, 102 patients underwent SLIT, and the early efficacy was evaluated. The correlations between the baseline serum concentrations of TYRO3, AXL, and MER and the early responsiveness of SLIT were analyzed.

RESULTS

Serum concentrations of TYRO3, AXL, and MER were significantly reduced in AR patients, particularly in those MSAR subjects. Correlation analysis results indicated that serum TYRO3 and MER levels were negatively correlated with the visual analog scale (VAS) and the total nasal symptom score (TNSS). After one year of follow-up, 80 AR patients completed the treatment and were divided into effective and ineffective groups. Serum baseline levels of TYRO3 and MER were found to be lower in the effective group compared to the ineffective group. Additionally, there was a significant increase in serum TYRO3 and MER levels compared to baseline levels. Receiver operating characteristic (ROC) analysis revealed that circulating TYRO3 and MER had potential values for reflecting AR severity and predicting early SLIT responsiveness.

CONCLUSION

Serum TYRO3 and MER concentrations were decreased in AR patients and negatively associated with disease severity. Circulating TYRO3 and MER seem to be promising indicators for monitoring the efficacy of SLIT in AR patients.

9

Además de la clínica...¿qué nivel de IgE sérica considero como "relevante"?

Back to basics: likelihood ratios for olive and grass pollen specific IgE in seasonal allergic rhinitis.

Bárbara Manzanares, Rafael González, Pilar Serrano, Ana Navas, Corona Alonso, Lourdes Fernandez et al

Front Allergy. 2023 Oct 4:4:1241650.

INTRODUCTION

Specific IgE (sIgE) is merely a sensitization marker that cannot be used for allergy diagnosis if there are no associated clinical symptoms. As of 2023, there is still no evidence regarding the quantity of sIgE necessary to confirm or exclude clinical disease. Therefore, this study aimed to calculate cut-offs for sIgE, allowing us to effectively diagnose olive or grass pollen allergy and select allergenic immunotherapy (AIT) candidate patients in a region under high olive and grass allergenic pressure.

METHODS

An observational retrospective study consisting of the review of electronic medical records from 1,172 patients diagnosed with seasonal rhino-conjunctivitis and suspected allergy to olive or grass pollen. Symptoms correlated with sIgE to Poaceae and Oleaceae whole extracts and sIgE to genuine allergenic components were evaluated. Optimal cut-off values were calculated using receiver operating characteristic curves. Relevant clinical symptoms and AIT indications were taken into consideration when determining the clinical allergy diagnosis.

RESULTS

sIgE to Lolium showed the best area under the curve (AUC) for both diagnosis (0.957) and an indication of AIT (0.872). The optimal cut-off values for grass diagnosis and AIT indication were 1.79 kUA/L and 8.83 kUA/L, respectively. A value of 5.62 kUA/L was associated with a positive likelihood ratio (LR) of 10.08 set for grass allergy. Olea sIgE showed the best AUC for the diagnosis (0.950). The optimal cut-off for diagnosis was 2.41 kUA/L. A value of 6.49 kUA/L was associated with a positive LR of 9.98 to confirm olive pollen allergy. In regard to immunotherapy, Ole e 1 sIgE showed the best AUC (0.860). The optimal cut-off was 14.05 kUA/L. Ole e 1 sIgE value of 4.8 kUA/L was associated with a 0.09 negative LR to exclude olive AIT indication.

CONCLUSIONS

The sIgE cut-offs found in this population under high olive and grass allergenic pressure reduce the gap between sensitization and clinical allergy, providing a new tool for the diagnosis of seasonal allergic rhinitis/asthma and helping to discriminate patients who will benefit from AIT.

10

Modelos experimentales para encontrar alternativas a la ITO en la alergia a alimentos.

Preclinical evaluation of alternatives to oral immunotherapy for food allergies

Brandi T Johnson-Weaver

Front Allergy. 2023 Oct 3:4:1275373.

ABSTRACT

The increasing food allergy incidence has led to significant interest in developing therapies for allergic diseases. Oral allergen-specific immunotherapy (OIT) is a recently FDA-approved therapeutic to treat peanut allergies. OIT utilizes daily allergen dosing to reduce allergic reactions to peanuts. However, there is diminished enthusiasm for daily OIT, potentially due to the strict regimen required to induce desensitization and the risks of severe adverse events. Thus, there remains a need for safe and effective food allergy treatments that are well-received by allergic individuals. Preclinical research studies investigate methods to induce allergen desensitization in animals and support clinical studies that address the limitations of current food allergy OIT. Because allergic reactions are triggered by allergen doses above an individual's activation threshold, immunotherapy regimens that induce allergen desensitization with lower allergen doses or without the requirement of daily administrations may expand the use of food allergy immunotherapy. Administering allergen immunotherapy by alternative routes is a strategy to induce desensitization using lower allergen doses than OIT. Several animal models have evaluated oral, sublingual, epicutaneous, and intranasal immunotherapy routes to treat food allergies. Each immunotherapy route may require different allergen doses, formulations, and treatment schedules to induce desensitization. This article will discuss scientific findings from food allergy immunotherapy animal studies that utilize various immunotherapy routes to induce allergen desensitization to support future clinical studies that enhance the safety and efficacy of allergen immunotherapy to treat food allergies.

BBI BOLETÍN BIBLIOGRÁFICO DE INMUNOTERAPIA

Noviembre 2023

1

ITA, más de 100 años y un gran futuro.

Hot topics in allergen immunotherapy, 2023: Current status and future perspective. Allergy. 2023 Nov 20. doi: 10.1111/all.15945. Epub ahead of print. PMID: 37984449.

Zemelka-Wiacek M, Agache I, Akdis CA, Akdis M, Casale TB et al

Allergy . 2023 Nov 20. doi: 10.1111/all.15945. Online ahead of print.

ARTÍCULO DESTACADO

ABSTRACT

The importance of allergen immunotherapy (AIT) is multifaceted, encompassing both clinical and quality-of-life improvements and costeffectiveness in the long term. Key mechanisms of allergen tolerance induced by AIT include changes in memory type allergen specific Tand B-cell responses towards a regulatory phenotype with decreased Type 2 responses, suppression of allergen-specific IgE and increased IgG1 and IgG4 , decreased mast cell and eosinophil numbers in allergic tissues and increased activation thresholds. The potential of novel patient enrolment strategies for AIT is taking into account recent advances in biomarkers discoveries, molecular allergy diagnostics and mobile health applications contributing to a personalized approach enhancement that can increase AIT efficacy and compliance. Artificial intelligence can help manage and interpret complex and heterogeneous data, including big data from omics and non-omics research, potentially predict disease subtypes, identify biomarkers and monitor patient responses to AIT. Novel AIT preparations, such as synthetic compounds, innovative carrier systems and adjuvants, are also of great promise. Advances in clinical trial models, including adaptive, complex and hybrid designs as well as real-world evidence, allow more flexibility and cost reduction. The analyses of AIT costeffectiveness show a clear long-term advantage compared to pharmacotherapy. Important research questions, such as defining clinical endpoints, biomarkers of patient selection and efficacy, mechanisms and the modulation of the placebo effect and alternatives to conventional field trials, including allergen exposure chamber studies are still to be elucidated. This review demonstrates that AIT is still in its growth phase and shows immense development prospects.

2

Evolución natural de la rinitis alérgica.

Natural course of pollen-induced allergic rhinitis from childhood to adulthood: A 20-year follow up.

Lindqvist M, Leth-Møller KB, Linneberg A, Kull I, Bergström A et al

Allergy . 2023 Nov 2. doi: 10.1111/all.15927. Online ahead of print.

BACKGROUND

Allergic rhinitis (AR) is one of the most common chronic diseases worldwide. There are limited prospective long-term data regarding persistency and remission of AR. The objective of this study was to investigate the natural course of pollen induced AR (pollenAR) over 20 years, from childhood into early adulthood.

METHODS

Data from 1137 subjects in the Barn/Children Allergi/Allergy Milieu Stockholm Epidemiologic birth cohort (BAMSE) with a completed questionnaire regarding symptoms, asthma, treatment with allergen immunotherapy (AIT) and results of allergen-specific IgE for inhalant allergens at 4, 8, 16 and 24 years were analyzed. Pollen-AR was defined as sneezing, runny, itchy or blocked nose; and itchy or watery eyes when exposed to birch and/or grass pollen in combination with allergen-specific IgE ≥0.35kUA /L to birch and/or grass.

RESULTS

Approximately 75% of children with pollen-AR at 4 or 8 years had persistent disease up to 24 years, and 30% developed asthma. The probability of persistency was high already at low levels of pollen-specific IgE. The highest rate of remission from pollen-AR was seen between 16 and 24 years (21.5%); however, the majority remained sensitized. This period was also when pollen specific IgE-levels stopped increasing and the average estimated annual incidence of pollen-AR decreased from 1.5% to 0.8% per year.

CONCLUSION

Children with pollen-AR are at high risk of persistent disease for at least 20 years. Childhood up to adolescence seems to be the most dynamic period of AR progression. Our findings underline the close cross-sectional and longitudinal relationship between sensitization, AR and asthma.

3

Mejor el MAT cuando no basta con el BAT.

LAD2 mast cell activation test associates with the reaction severity and diagnoses BAT nonresponders in Hymenoptera venom allergy.

Koren A, Dejanovic L, Kopac P, Erzen R, Bajrovic N, Zidarn M, Korosec P

J Investig Allergol Clin Immunol. 2023 Nov 7:0. doi: 10.18176/jiaci.0969. Epub ahead of print. PMID: 37937714.

BACKGROUND AND OBJECTIVE

The usefulness of the mast cell activation test (MAT) in diagnosing patients with uninterpretable basophil activation test (BAT) caused by nonresponding basophils has not yet been addressed. It should be further evaluated if the results of MAT are associated with the severity of the allergic reaction.

METHODS

We recruited 39 Hymenoptera venom allergic (HVA) patients, 22 non-sensitized controls, and 37 BAT nonresponding HVA patients. Specific IgE levels for honey bee venom (HBV), yellow jacket venom (YJV) and total IgEs were quantified using the Immulite system. BAT and MAT with LAD2 cells in response to HBV and YJV were performed.

RESULTS

We first optimized the susceptibility of LAD2 cells to IgE-mediated degranulation in HVA and showed that prestimulation with IL33 and IL-6 significantly increased the LAD2 cells´responsiveness to allergen stimulation ($P<0.01$). LAD2 MAT results correlated with BAT results, and patients with severe sting reactions (Mueller grades IV or III) had a median 2-fold higher LAD2 MAT than the patients with nonsevere sting reactions (Mueller grades II, I or LLR) ($P<0.05$). Further, LAD2 MAT provided conclusive results in 54.1% (20 of 37) of HVA patients with nonresponding basophils in the BAT.

CONCLUSION

The LAD2 MAT represents a new diagnostic tool for HVA patients with nonresponding basophils. Further, LAD2 MAT can identify patients at risk of severe sting reactions and thus can help guide recommendations for venom immunotherapy and improve the management of patients with HVA.

4

¡¡Se buscan candidatos a biomarcador predictivo para la ITA!!

Mechanisms and predictive biomarkers of allergen immunotherapy in the clinic.

Layhadi JA, Lalioti A, Palmer E, van Zelm MC, Wambre E, Shamji MH

J Allergy Clin Immunol Pract . 2023 Nov 22:S2213-2198(23)01296-5. doi: 10.1016/j.jaip.2023.11.027. Online ahead of print.

ABSTRACT

Allergen-specific immunotherapy (AIT) remains the only disease-modifying treatment for IgE-mediated allergic diseases such as allergic rhinitis (AR). It can provide long-term clinical benefits when given for three years or longer. Mechanisms of immune tolerance induction by AIT are underscored by the modulation of several compartments within the immune system. These include repair of disruption in epithelial barrier integrity, modulation of the innate immune compartment that includes regulatory dendritic cells (DCreg) and innate lymphoid cells (ILCreg), and adaptive immune compartments such as induction of regulatory T and B cells. Altogether, these are also associated with dampening allergen-specific Th2 (Th2A) and T follicular helper cell responses and subsequent generation of blocking antibodies. Whilst AIT is effective in modifying the immune response, there is a lack of validated and clinically relevant biomarkers that can be used to monitor desensitization, efficacy, and the likelihood of response, all of which can contribute to accelerating personalized medication and increasing patient care. Candidate biomarkers comprise humoral, cellular, metabolic and in vivo biomarkers; however, these are primarily studied in small trials and require further validation. In this review, we evaluate the current candidates of biomarkers of AIT and how we can implement changes in future studies to help us identify clinically relevant biomarkers of safety, compliance and efficacy.

5

La efectividad es proporcional a la dosis (con polimerizado despigmentado)

A high-dose, depigmented polymerized birch pollen extract for subcutaneous allergen immunotherapy has a favourable efficacy/safety ratio.

Pfaar O, Sager A, Mösges R, Worm M

Clin Transl Allergy. 2023 Nov;13(11):e12315. doi: 10.1002.

BACKGROUND

Subcutaneous allergen immunotherapy (SCIT) with depigmented, polymerized (DPP) birch pollen extract has been marketed at doses of up to 1000 DPP units/mL since 2001. We sought to determine the dose-dependent efficacy of a DPP birch pollen extract formulation in patients suffering from birch-pollen induced allergic rhinitis or rhinoconjunctivitis with or without intermittent asthma.

METHODS

A titrated conjunctival provocation test (CPT) was applied as a surrogate marker. This Phase II randomized, double-blind, parallel-group, dose-ranging clinical trial was performed at 39 centres in Germany, Lithuania and Poland. After randomization to four dose-level groups (100, 1000, 5000 and 10,000 DPP units/mL) and up-dosing, participants received maintenance SCIT with five monthly subcutaneous injections. The primary endpoint was the proportion of patients in whom a higher concentration of birch pollen (vs. baseline) was needed to elicit a positive CPT.

RESULTS

Three hundred forty-three patients were included (mean (range) age: 42.6 (19-70)). The highest CPT responder rates were seen in the higher dose-level groups. In the intention-to-treat analysis, the difference between the 100 and 10,000 groups was statistically significant (p = 0.0118). Although the proportion of patients with ≥1 treatment-emergent adverse events increased with the dose, almost all these events were mild (65.6%) or moderate (18.5%).

CONCLUSION

Judging by the results of a CPT, the efficacy/safety ratio in SCIT appears to be favourable for a high-dose-level preparation of a DPP birch pollen extract.

6

¿Preferible empezar la ITO con cacahuete cuanto antes?

Early Peanut Immunotherapy in Children (EPIC) trial: protocol for a pragmatic randomised controlled trial of peanut oral immunotherapy in children under 5 years of age.

O'Sullivan MD, Bear N, Metcalfe J

BMJ Paediatr Open. 2023 Nov;7(1):e002294. doi: 10.1136.

INTRODUCTION

Food allergy is a major public health challenge in Australia. Despite widespread uptake of infant feeding and allergy prevention guidelines the incidence of peanut allergy in infants has not fallen, and prevalence of peanut allergy in school-aged children continues to rise. Therefore, effective and accessible treatments for peanut allergy are required. There is high-quality evidence for efficacy of oral immunotherapy in children aged 4-17 years old; however, few randomised trials have investigated peanut oral immunotherapy (OIT) in young children. Furthermore, the use of food products for OIT with doses prepared and administered by parents without requiring pharmacy compounding has the potential to reduce costs associated with the OIT product.

METHODS AND ANALYSIS

Early Peanut Immunotherapy in Children is an open-label randomised controlled trial of peanut OIT compared with standard care (avoidance) to induce desensitisation in children aged 1-4 years old with peanut allergy. n=50 participants will be randomised 1:1 to intervention (daily peanut OIT for 12 months) or control (peanut avoidance). The primary outcome is the proportion of children in each group with a peanut eliciting dose >600 mg peanut protein as assessed by open peanut challenge after 12 months, analysed b intention to treat. Secondary outcomes include safety as assessed by frequency and severity of treatment-related adverse events, quality of life measured using age appropriate food allergy-specific questionnaires and immunological changes during OIT.

ETHICS

The trial is approved by the Child and Adolescent Health Service Human Research Ethics Committee and prospectively registered with the Australia and New Zealand Clinical Trials Registry.

DISSEMINATION

Trial outcomes will be published in a peer review journal and presented and local and national scientific meetings.

7

Por esto pautamos omalizumab en las ITO.

Food oral immunotherapy: Any distinguishing factors predicting the need of anti-IgE?

Akarcan SE, Şenol HD, Gülen F, Demir E

Allergol Immunopathol (Madr). 2023 Nov 1;51(6):104-111. doi: 10.15586/aei.v51i6.907. PMID: 37968804.

ABSTRACT

Oral immunotherapy (OIT) has gained popularity recently for IgE-mediated food allergy. Omalizumab (OMZ) has been used in patients (10-20%) who have too severe/frequent allergic reactions (AR) to continue OIT, to reduce these reactions. In this study, it was aimed to compare two groups of patients who completed OIT with and without OMZ and to seek determinants predicting the need of this treatment. It was also aimed to share the clinical findings regarding the long-term use of OMZ and the withdrawal process. Forty-one patients were started OIT and 93% could be desensitized. Two groups were similar in means of demographic characteristics, and clinical and laboratory findings. The patients who needed OMZ during OIT had also lower reaction doses during oral challenge ($p = 0.037$). Higher AR rate in this group declined after starting OMZ ($p < 0.001$). The injection intervals of OMZ were gradually extended. Most patients were able to discontinue OMZ (81%). There were no severe reactions during drug withdrawal attempts. The low reaction thresholds during oral food challenge may give a clue about OMZ requirement during OIT. It may be an option to start the treatment before OIT if reaction was seen in the first few steps of the oral food challenge. For the sake of safety, extension of injection intervals should be preferred instead of abruptly stopping OMZ.

8

Resultados prometedores con ITA nasal con Bet v 1-galactomanano.

Local nasal immunotherapy with birch pollen-galactomannan conjugate-containing ointment in mice and humans.

Komatsuzaki K, Kageshima H, Sekino Y, Suzuki Y, Ugajin T, Tamaoka M, Hanazawa R, Hirakawa A, Miyazaki Y

Allergol Int . 2023 Nov 17:S1323-8930(23)00111-9. doi: 10.1016/j.alit.2023.10.007. Online ahead of print.

BACKGROUND

Allergen immunotherapy (AIT) is the only disease-modifying treatment for immunoglobulin (Ig) E mediated allergy. Owing to the high prevalence and early onset of hay fever and pollen-food allergy syndrome (PFAS), a safer and simpler treatment method than conventional AIT is needed. To develop a local nasal immunotherapy using an ointment containing hypoallergenic pollen and assess its efficacy in mice and healthy humans.

METHODS

Hypoallergenicity was achieved by combining pollen and galactomannan through the Maillard reaction to create birch pollengalactomannan conjugate (BP-GMC). The binding of galactomannan to Bet v 1 was confirmed using electrophoresis and Western blotting (WB). Binding of specific IgE antibodies to BP-GMC was verified using enzyme-linked immunosorbent assay (ELISA) and basophil activation test (BAT). The localization of BP-GMC absorption was confirmed using a BALB/c mouse model. BP-GMC mixed with white petrolatum was intranasally administered to 10 healthy individuals (active drugs, 8; placebo, 2) for 14 days.

RESULTS

In electrophoresis and WB, no 17-kDa band was observed. In ELISA and BAT, BP-GMC did not react to specific IgE but was bound to IgA and IgG. In the mouse model, BP-GMC was detected in nasopharyngeal-associated lymphoid tissues. In the active drug group, the salivary-specific IgA level significantly increased on day 15 ($p = 0.0299$), while the serum-specific IgG level significantly increased on day 85 ($p = 0.0006$).

CONCLUSIONS

The BP-GMC ointment rapidly produced antagonistic antibodies against IgE; it is safe and easy to use and might serve as a therapeutic antigen for hay fever and PFAS.

9

Objetivo: ITA personalizada (con péptidos)

In Silico Design of a New Epitope-Based Vaccine against Grass Group 1 Allergens.

Moten D, Batsalova T, Apostolova D, Mladenova T, Dzhambazov B, Teneva I

Adv Respir Med. 2023 Nov 8;91(6):486-503. doi: 10.3390/arm91060036.

ABSTRACT

Allergic diseases are a global public health problem that affects up to 30% of the population in industrialized societies. More than 40% of allergic patients suffer from grass pollen allergy. Grass pollen allergens of group 1 and group 5 are the major allergens, since they induce allergic reactions in patients at high rates. In this study, we used immunoinformatic approaches to design an effective epitope-based vaccine against the grass group 1 allergens. After the alignment of all known pollen T-cell and B-cell epitopes from pollen allergens available in the public databases, the epitope GTKSEVEDVIPEGWKADTSY was identified as the most suitable for further analyses. The target sequence was subjected to immunoinformatics analyses to predict antigenic T-cell and B-cell epitopes. Population coverage analysis was performed for CD8+ and CD4+ T cell epitopes. The selected T-cell epitopes (VEDVIPEGW and TKSEVEDVIPEGWKA) covered 78.87% and 98.20% of the global population and 84.57% and 99.86% of the population of Europe. Selected CD8+, CD4+ T-cell and B-cell epitopes have been validated by molecular docking analysis. CD8+ and CD4+ T-cell epitopes showed a very strong binding affinity to major histocompatibility complex (MHC) class I (MHC I) molecules and MHC class II (MHC II) molecules with global energy scores of -72.1 kcal/mol and -89.59 kcal/mol, respectively. The human IgE-Fc (PDB ID 4J4P) showed a lower affinity with B-cell epitope ($\Delta G = -34.4$ kcal/mol), while the Phl p 2-specific human IgE Fab (PDB ID 2VXQ) had the lowest binding with the B-cell epitope ($\Delta G = -29.9$ kcal/mol). Our immunoinformatics results demonstrated that the peptide GTKSEVEDVIPEGWKADTSY could stimulate the immune system and we performed ex vivo tests showed that the investigated epitope activates T cells isolated from patients with grass pollen allergy, but it is not recognized by IgE antibodies specific for grass pollen allergens. This confirms the importance of such studies to establish universal epitopes to serve as a basis for developing an effective vaccine against a particular group of allergens. Further in vivo studies are needed to validate the effectiveness of such a vaccine against grass pollen allergens.

10

ITA en tabletas, mejor sublingual que vestibular.

Tolerability of sublingual versus vestibular allergy immunotherapy tablet administration: A randomized pilot study.

Simard ML, Novak N, Drolet JP, Joly MC, Nolte H, Wuestenberg E, Gagnon R
Clin Exp Allergy. 2023 Nov 21. doi: 10.1111/cea.14427. Epub ahead of print. PMID: 37990117.

BACKGROUND

Local application site reactions are common with sublingual allergy immunotherapy (AIT)-tablets for the treatment of allergic rhinitis/conjunctivitis (AR/C) and occasionally lead to treatment discontinuation. Because of the lower mast cell density in the vestibular mucosa than the sublingual area, vestibular AIT tablet administration may result in fewer adverse events (AEs). This pilot study evaluated the tolerability of the vestibular administration route of AIT-tablets compared with the sublingual route in adult subjects with AR/C.

METHODS

Adults (n = 164) aged 18-65 years with AR/C treated with daily birch pollen, grass pollen, ragweed pollen or house dust mite AIT in tablet form were randomized 1:1 to vestibular or sublingual administration for 28 days, followed by 28 days of sublingual administration only. The primary endpoint was the severity (mild, moderate, severe) of local treatment related adverse events (TRAEs) during the first 28 days of treatment.

RESULTS

During the first 28 days, the percentage of subjects in the vestibular and sublingual groups reporting mild TRAEs were 55.6% versus 50.6%, respectively; moderate TRAEs were 27.2% versus 30.1%; and severe TRAEs were 12.3% versus 6.0% (p = .16). In the vestibular group, 95.1% of the subjects experienced at least one TRAE during the first period versus 81.9% in the sublingual group (p = .01) and discontinuation rates due to AEs were higher (12.3% vs. 3.6%).

CONCLUSION

The frequencies of subjects experiencing severe TRAEs, at least one TRAE, and discontinuations due to AEs at the initiation of AIT-tablets were numerically higher with vestibular administration than sublingual administration. Sublingual administration should remain the standard of care for subjects treated with AIT tablets for AR/C.

BOLETÍN BIBLIOGRÁFICO
DE INMUNOTERAPIA

Diciembre 2023

1

¡Lo más importante del año en alergia a alimentos!

Feast for Thought: A Comprehensive Review of Food Allergy 2021-2023.

Irene Bartha, MD, Noorah Almulhem, MD, Alexandra F. Santos, MD PhD

J Allergy Clin Immunol. 2023 Dec 12:S0091-6749(23)02414-4.

ARTÍCULO DESTACADO

ABSTRACT

This review covers the latest publications in food allergy over the last couple of years. Food allergy is a major public health concern, affecting about 8% of children and 10% of adults in developed countries. The food allergy prevalence varies around the world, with environmental factors mainly driving the increase, possibly together with genetical susceptibility to environmental changes. A precise diagnosis of food allergy is extremely important - both new tests (e.g. basophil activation test) and improved optimization of information provided by existing tests (e.g. skin prick test and specific IgE) can contribute to improving the accuracy and patients' comfort of food allergy diagnosis. Understanding the underlying immune mechanisms is fundamental to designing allergen-specific treatments that can be safe and effective in the long-term. New discoveries have emerged at various levels of the immune response to food allergens, including T cell and B cell responses. Novel therapeutic approaches are being trialed at various stages of development and will hopefully allow for more active intervention to treat food allergy. Prevention is key to reduce the increase in prevalence. Early introduction of allergenic foods seems to be the most effective intervention, but others are being studied, and will hopefully lead to modification of the epidemiological trajectory of food allergy over time.

2

ITA, cuanto antes mejor.

Quantifying the benefits of early sublingual allergen immunotherapy tablet initiation in children.

Eckard Hamelmann, Eva Hammerby, Katrine Skaarup Scharling, Mikkel Pedersen, Anna Okkels, Jochen Schmitt

Allergy . 2023 Dec 26. doi: 10.1111/all.15985.

BACKGROUND

Allergic rhinitis (AR) is a chronic inflammatory disease of the upper airway, which progresses into allergic asthma (AA) in up to 45% of children. This analysis aimed to investigate clinical and economic benefits of sublingual allergen immunotherapy (SLIT tablets) initiated early in childhood for the treatment of AR by quantifying the long-term reduction in new cases of AA.

METHODS

A Markov model was developed to estimate the long-term effects of SLIT tablets on the risk of developing asthma. Key parameters were primarily based on data from the GRAZAX® Asthma Prevention trial and included the age- and treatment-dependent risk of developing AA as well as annual probabilities of progression/remission in AR severity. Healthcare costs were estimated using data from the REACT study.

RESULTS

In a modelled cohort of children with moderate to-severe seasonal AR initiated on SLIT tablets at ages 7 and 12, 24% and 29%, respectively, develop AA during a 20-year period. In comparison, when initiated at age 5, 19% develop AA. Additionally, initiation of SLIT tablets at age 5 is associated with a total healthcare cost of EUR 20,429 per patient, whereas initiation at ages 7 and 12 is associated with, respectively, EUR 21,050 and EUR 22,379 per patient 20 years after AR diagnosis.

CONCLUSION

Initiation of SLIT tablets in early childhood is associated with a clinically meaningful and permanent reduction in new cases of AA and lower healthcare costs among children with AR. This finding supports the clinical relevance of initiating SLIT tablets early for children with AR to obtain long-term clinical benefits.

3

“Cara a cara” de ITSL vs. ILSC en niños.

Efficacy and safety of sublingual versus subcutaneous immunotherapy in children with allergic rhinitis: a systematic review and meta-analysis.

Jiumei Yang, Sihong Lei

Front Immunol. 2023 Dec 15:14:1274241. doi: 10.3389/fimmu.2023.1274241.

AIM

To systematically compare the efficacy and safety of subcutaneous immunotherapy (SCIT) and sublingual immunotherapy (SLIT) in children with allergic rhinitis (AR).

METHODS

PubMed, Embase, Cochrane Library, and Web of Science were searched from inception to March 2, 2023. Outcomes included symptom scores (SSs), medication scores (MSs), symptom and medication scores (SMSs), new sensitizations, development of asthma, improvement, and treatment-related adverse events (TRAEs). The quality of the included studies was assessed by the modified Jadad scale and Newcastle-Ottawa scale (NOS). Meta-regression was carried out to explore the source of heterogeneity. Subgroup analysis was further conducted in terms of study design [randomized controlled trials (RCTs), cohort studies], allergen [house dust mites (HDMs), grass pollen], treatment duration (≥ 24, 12-23 or < 12 months), allergen immunotherapy (AIT) modality (drops or tablets), and AIT protocol [continuous, pre-seasonal, co-seasonal, or after the grass pollen season (GPS)]. Sensitivity analysis was conducted for all outcomes. A Bayesian framework and a Monte Carlo Markov Chain (MCMC) model were developed for indirect comparison.

RESULTS

Totally 50 studies with 10813 AR children were included, with 4122 treated with SLIT, 1852 treated with SCIT, and 4839 treated with non-SLIT or nonSCIT therapy. For direct comparison, the SLIT group had a similar SS to the SCIT group [pooled standardized mean difference (SMD): 0.41, 95% confidence interval (CI): -0.46, 1.28, P = 0.353]. Comparable MSs were observed in the SLIT and SCIT groups (pooled SMD: 0.82, 95%CI: -0.88, 2.53, P = 0.344). For indirect comparison, no significant differences were found in SSs (pooled SMD: 1.20, 95% credibility interval (CrI): -1.70, 4.10), MSs (pooled SMD: 0.57, 95%CrI: -1.20, 2.30), SMSs (pooled SMD: 1.80, 95%CrI: -0.005, 3.60), new sensitizations [pooled relative risk (RR): 0.34, 95%CrI: 0.03, 3.58], and development of asthma (pooled RR: 0.68, 95%CrI: 0.01, 26.33) between the SLIT and SCIT groups; the SLIT group illustrated a significantly lower incidence of TRAEs than the SCIT group (pooled RR: 0.17, 95%CrI: 0.11, 0.26).

CONCLUSION

Considering both efficacy and safety, SLIT might be a more favorable AIT than SCIT in the treatment of pediatric AR, which may serve as a decision-making reference for clinician.

4

La ITA experimental con péptidos en alergia a cacahuete funciona.

Phase 1 trial supports safety and mechanism of action of peptide immunotherapy for peanut allergy.

Astrid L. Voskamp, Sugandhika Khosa, Tracy Phan, Hannah A. DeBerg, Judy Bingham, Mark Hew et al

Allergy. 2023 Dec 26. doi: 10.1111/all.15985.

BACKGROUND

Food allergy is a leading cause of anaphylaxis worldwide. Allergen-specific immunotherapy is the only treatment shown to modify the natural history of allergic disease, but application to food allergy has been hindered by risk of severe allergic reactions and short-lived efficacy. Allergen-derived peptides could provide a solution. PVX108 comprises seven short peptides representing immunodominant T-cell epitopes of major peanut allergens for treatment of peanut allergy.

METHODS

Pre-clinical safety of PVX108 was assessed using ex vivo basophil activation tests (n = 185). Clinical safety and tolerability of single and repeat PVX108 doses were evaluated in a first-in-human, randomized, double-blind, placebo-controlled trial in peanut-allergic adults (46 active, 21 placebo). The repeatdose cohort received six doses over 16 weeks with safety monitored to 21 weeks. Exploratory immunological analyses were performed at pre-dose, Week 21 and Month 18 after treatment.

RESULTS

PVX108 induced negligible activation of peanut sensitised basophils. PVX108 was safe and well tolerated in peanut-allergic adults. There were no treatment-related hypersensitivity events or AEs of clinical concern. The only events occurring more frequently in active than placebo were mild injection site reactions. Exploratory immunological analyses revealed a decrease in the ratio of ST2+ Th2A:CCR6+ Th17-like cells within the peanut-reactive Th pool which strengthened following treatment.

CONCLUSION

This study supports the concept that PVX108 could provide a safe alternative to whole peanut immunotherapies and provides evidence of durable peanut-specific T-cell modulation. Translation of these findings to clinical efficacy in ongoing Phase 2 trials would provide important proof-of-concept for using peptides to treat food allergy.

5

Se confirman los buenos resultados con los comprimidos de gramíneas 300 IR.

Clinical relevance of pre- and coseasonal sublingual immunotherapy with a 300 index of reactivity 5-grass SLIT tablet in allergic rhinoconjunctivitis.

Oliver Pfaar, Ulrich Wahn, Giorgio Walter Canonica, Farah Bahbah, Philippe Devillier

Clin Transl Allergy. 2023 Dec;13(12):e12321. doi: 10.1002/clt2.12321.

BACKGROUND

There is considerable interest in improving the scoring methods for evaluating the efficacy of allergen immunotherapy (AIT) and to show if this is associated with clinically meaningful results from the patient's perspective. We aimed to assess the efficacy and clinical relevance of a 300 index of reactivity (IR) 5-grass pollen sublingual immunotherapy (SLIT) tablet in children, adolescents and adults with moderate to severe grass-induced allergic rhinoconjunctivitis (ARC) with or without controlled asthma using the combined symptom and medication score CSMS0-36.

METHODS

The data of the European population that participated in 3 Phase III, international, randomized double blind placebo-controlled clinical trials were analyzed post hoc.

RESULTS

A total of 864 patients randomized to 300 IR 5 grass tablet or placebo were analyzed. Over the primary evaluation period, the difference in CSMS0-36 between the 300 IR and placebo groups was statistically significant (point estimates: -2.51, CI95% [-3.88; -1.14], $p < 0.0001$ in clinical trial1; -2.31, CI95%[-3.39; -1.23], $p < 0.0001$ in CT2; and -2.31, CI95% [-3.58; -1.03], $p = 0.0004$ in CT3). The relative differences between the 300 IR 5-grass tablet and placebo were - 29.7%, -33.8%, and -26.3%, respectively. The results based on CSMS0-36 were consistent with those obtained with the primary endpoints of the trials and support the consideration of the 2-point threshold of the CSMS0 36 for clinical relevance of AIT.

CONCLUSION

Post hoc analysis of 3 CTs with the 300 IR 5-grass SLIT tablet confirmed its significant and clinically relevant effect in the European population with grass pollen-induced ARC with or without controlled asthma.

6

Si tienes predisposición genética al asma y perfil inflamatorio T2, responderás mejor a la ITA.

Genetic and T2 biomarkers linked to the efficacy of HDM sublingual immunotherapy in asthma.

Ilka Hoof, Klaus Bønnelykke, Thomas Stranzl, Stephanie Brand, Xingnan Li, Mohamed H Shamji et al

Thorax . 2023 Dec 30:thorax-2023-220707. doi: 10.1136/thorax-2023-220707.

BACKGROUND

Hypersensitivity to house dust mite (HDM) allergens is a common cause of allergic asthma symptoms and can be effectively treated with allergy immunotherapy (AIT).

OBJECTIVE

To investigate whether genetic and type 2 (T2) inflammatory biomarkers correlate with disease severity in subjects with allergic asthma, and whether this can be modified by AIT.

METHODS

MITRA (NCT01433523) was a phase III, randomised, double-blind, placebo-controlled trial of HDM sublingual immunotherapy (SLIT)-tablets in adults with HDM allergic asthma. Post hoc analyses of the study population (N=742) evaluated associations between T2 inflammatory (blood eosinophils, eosinophil cationic protein (ECP), total IgE and tryptase) and genetic (single-nucleotide polymorphisms, SNP) biomarkers (n=582) for the primary study endpoint (time to first moderate/severe asthma exacerbation). SNP associations were verified in HDM-positive subgroup from an independent 3-year Severe Asthma Research Programme (SARP3) subject cohort.

RESULTS

An increased asthma exacerbation risk in subjects homozygous for SNP rs7216389 (chromosomal locus 17q12-21) was reduced ($p=0.037$) by treatment with HDM SLIT (HR=0.37 (95% CI 0.22 to 0.64), $p<0.001$). The associations between exacerbation risk and 17q12-21 SNPs were replicated in the SARP3 HDMpositive subgroup. High levels of T2 biomarkers were associated with increased risk of asthma exacerbations in the placebo group. HDM SLIT-tablet treatment reduced this risk (blood eosinophils: HR=0.50 (95% CI 0.30 to 0.85); ECP: HR=0.45 (95% CI 0.29 to 0.87); tryptase: HR=0.45 (95% CI 0.25 to 0.80)). The treatment effect was higher ($p=0.006$) for subjects with a higher number of elevated T2 biomarkers.

CONCLUSIONS

HDM SLIT-tablet AIT is efficacious in HDM sensitised asthma subjects with a genetic asthma predisposition and/or an underlying T2 endotype.

7

ITA y omalizumab, mejor juntos que separado.

Progressive clinical effects of the combination omalizumab and HDM – allergen immunotherapy in asthma.

Andrzej Bozek, Barbara Rogala, Martyna Miodonska, Giorgio Walter Canonica

J Asthma . 2023 Dec 8:1-7. doi: 10.1080/02770903.2023.2293057.

OBJECTIVE

The combination of allergen immunotherapy (AIT) and omalizumab is used to treat patients at risk of anaphylaxis. There is currently a very little evidence that this combination increases the effectiveness of AIT in patients with inhalant allergies. The study aimed to evaluate the effectiveness of HDM-SCIT therapy (injection immunotherapy for house dust mites) in combination with omalizumab in treating HDM-induced asthma.

METHODS

This study was a placebo-controlled, randomized, multicenter trial including 82 patients with HDM-driven mild to moderate asthma. Omalizumab alone (A), HDM SCIT + omalizumab (B), SCIT alone (C), or placebo (D) for 24 months were applied. All patients received asthma treatment in accordance with GINA recommendations. The treatment efficacy was defined by a reduction in the daily dose of inhaled steroids (ICS) and a reduction in the number of asthma exacerbations (AX).

RESULTS

After 24 months of therapy, a statistically significant reduction in the daily doses of ICS in groups A and B was observed ($p = 0.021$ and $p = 0.008$). Daily ICS reduction was considerably more significant in group B ($p = 0.01$). During 24 months of observation, the AX was significantly reduced in all study groups, with the greatest significant difference observed between groups A and B and groups C and D (placebo) as follows: 0.42 patient/per year vs. 0.39 vs. 0.84 vs. 0.91 ($p = 0.023$).

CONCLUSION

The combination of HDM SCIT and omalizumab is significantly and progressively reducing ICS use and AX in a 24-month study. The combination is significantly more effective than the single treatments or placebo.

8

La ITA es efectiva a largo plazo en niños mono- y polisensibilizados.

Long-Term Efficacy and Safety of Subcutaneous Immunotherapy in Monosensitized and Polysensitized Children With Allergic Rhinitis.

Xuan Yuan, Shaobing Xie, Hua Zhang, Junyi Zhang, Ruohao Fan, Weihong Jiang et al

OBJECTIVE

To evaluate the efficacy and safety of dust mite subcutaneous immunotherapy (SCIT) in monosensitized and polysensitized children with allergic rhinitis (AR).

METHODS

One hundred thirty children were enrolled and categorized into 2 groups: monosensitized to only dust mites and polysensitized to at least 1 additional allergen beyond dust mites. All patients received SCITtargeting dust mites for 3 years, followed by a 5-year monitoring period. The Total Nasal Symptom Score (TNSS), Symptom and Medication Score (SMS), Visual Analogue Scale (VAS), and Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) were assessed before SCIT (T0); at 1 (T1) and 2 (T2) years of SCIT; immediately after SCIT (T3); and 2 years post-SCIT (T5). Safety was assessed based on adverse events (AEs).

RESULTS

Fifty-one monosensitized and 50 polysensitized children completed the study. At T3, 47 monosensitized and 46 polysensitized children were effectively treated, with no significant between-group difference in efficacy ($P > .05$). The TNSS, SMS, VAS scores, and RQLQ score were significantly lower at T1, T2, T3, and T5 than at T0 in both groups ($P < .05$). The differences in the TNSS, SMS, VAS score, and RQLQ score between the 2 groups were nonsignificant at T0, T1, T2, and T3 ($P > .05$), but significant at T5 ($P < .05$). No serious AEs were reported.

CONCLUSION

Monosensitized and polysensitized children exhibited similar beneficial efficacy and safety after 3 years of dust mite SCIT. Monosensitized children derived more benefits 2 years after discontinuation.

9

Hablemos de regulación.

Allergen-specific immunotherapy and evidence: A European regulatory perspective.

Detlef Bartel, Andreas Bonertz, Diana Hartenstein, Stefan Kaul, Iris Lauer, Christina Reeb et al

Allergol Select . 2023 Dec 12:7:198-210.

ABSTRACT

Allergen immunotherapy (AIT) has been performed for 112 years. In this article we summarize regulatory standards and challenges based on scientific evidence on AIT. Most crucial and timely aspects concerning AIT are addressed from the regulatory perspective of the authors as employees of a national competent authority in Europe: (1) product specificity; (2) clinical efficacy; (3) treatment for adults and children (needs for extrapolation); (4) allergen exposure chambers; (5) biomarkers; (6) standardization; (7) real-world evidence (8) independent official batch release (benefit and challenges); (9) harmonization on the EU level. The Paul-Ehrlich-Institut (PEI), the Federal Institute for Vaccines and Biomedicines, in Langen near Frankfurt/Main in Germany, examines and evaluates the benefits and risks of AIT products within the course of clinical development, marketing authorization, and subsequently throughout their entire life cycle to ensure high-quality, safe, and effective AIT products.

10

¿Cuáles son los oficios de más “riesgo”?

Occupational anaphylaxis—Data from the anaphylaxis registry.

Margitta Worm, Veronika Höfer, Sabine Dölle-Bierke, Maria Beatrice Bilo, Karin Hartmann, Dominique Sabouraud-Leclerc et al

Allergy . 2023 Dec 13. doi: 10.1111/all.15974.

BACKGROUND

Epidemiologic data on occupational anaphylaxis is scarce, and there is a need of more knowledge about work-related anaphylactic episodes.

METHODS

Based on the data of the Anaphylaxis Registry, we identified cases related to occupational exposure and analyzed the elicitors, demographics, severity of clinical reaction and management.

RESULTS

Since 2017, 5851 cases with an information about the occupational relation of the anaphylactic episode were registered whereby 225 (3.8%) were assigned to be caused by an occupational allergen. The vast majority of these occupational anaphylaxis cases were caused by insects (n = 186, 82.7%) followed by food (n = 27, 12.0%) and drugs (n = 8, 3.6%). Latex elicited occupational anaphylaxis in only two cases. Beekeepers, gardeners, farmers, and individuals working in professions associated with food handling, for example, employees in restaurants, bakery, pastry, and cooks were most frequently affected. The comparison of the occupational insect venom-induced anaphylaxis to a group of non-occupational insect anaphylaxis in adults (n = 1842) revealed a significant younger age in occupational anaphylaxis (46 vs. 53 years), a predominance of bee-induced cases (38% vs. 17%), and a higher rate of venom immunotherapy in a primary care setting (3.3% vs. 1.3%, p = .044). In the occupational-versus non-occupational adults with food-induced anaphylaxis atopic dermatitis as concomitant atopic disease was observed more frequently (n = 486; 20% vs. 10%), although this was not significant.

CONCLUSION

Our data demonstrate the impact of venom allergy in work-related anaphylaxis. Foods and drugs are less frequently elicitors, and latex-induced occupational anaphylaxis was rare. More data are needed to determine risk factors associated with occupational anaphylaxis.