1

¿Cómo de segura es la ITSL en tabletas?

Safety of Timothy Grass Sublingual Immunotherapy Tablet in Children: Pooled Analyses of Clinical Trials.

Halken S, Roberts G, Valovirta E, Nolte H, Hulstrøm V, Blaiss MS

J Allergy Clin Immunol Pract. 2020 Jan 15. pii: S2213-2198(20)30047-7. doi: 10.1016/j.jaip.2020.01.008. [Epub ahead of print]

ARTÍCULO DESTACADO

BACKGROUND

Timothy grass sublingual immunotherapy (SLIT)-tablets are indicated for children with allergic rhinitis with or without conjunctivitis (AR/C).

OBJECTIVES

To use pooled analyses to assess the short- and long-term tolerability and safety of timothy grass SLIT-tablet in children.

METHODS

Data from 9 double-blinded, randomized European or North American trials that included children with AR/C treated up to 3 years with once-daily timothy grass SLIT-tablet or placebo were pooled.

RESULTS

In all, 1818 (SLIT-tablet=923; placebo=895) subjects were included in the analysis. The frequency of treatment-emergent adverse events (AEs) was 86% in the SLIT-tablet and 83% in the placebo groups and of treatment-related AEs (TRAEs) was 59% and 23%, respectively. Most (98%) TRAEs were mild-to-moderate in severity. The two most common TRAEs with SLIT-tablet were oral pruritus (33%) and throat irritation (19%), which had a median onset of 1 day and recurrence of 14.5 and 5 days, respectively. In all, 8% of subjects in the SLIT-tablet and 2% in the placebo groups discontinued due to AEs. There were 7 serious AEs assessed as related to SLIT-tablet, 1 systemic allergic reaction (severe with a drop in blood pressure), 3 epinephrine administrations, no eosinophilic esophagitis events, and no serious airway obstructions. The safety profile was similar in subjects across geographic regions and with and without asthma.

CONCLUSIONS

Pooled data indicate that short- and long-term timothy grass SLIT-tablet is well tolerated in children, regardless of geographic region. AEs were generally local, mild, and transient allergic reactions.

2

El riesgo de la ITO con trigo.

Exercise-induced allergic reactions on desensitization to wheat after rush oral immunotherapy.

Furuta T, Tanaka K, Tagami K, Matsui T, Sugiura S, Kando N et al

Allergy. 2020 Jan 17. doi: 10.1111/all.14182. [Epub ahead of print]

BACKGROUND

The effect of oral immunotherapy (OIT) on wheat allergy is promising in terms of the potential to obtain desensitization; however, the frequency of exercise-induced allergic reactions on desensitization (EIARDs) and the associated risk factors remain to be determined.

METHODS

Twenty-five patients underwent rush OIT for wheat allergy, and 21 achieved the full-dose intake of wheat products (5 g of wheat protein). Exercise-provocation tests were repeatedly performed after the ingestion of a full-dose wheat product. The time-course of the levels of the specific IgEs (sIgE) to wheat extract, total gliadin, deamidated gliadin, recombinant gliadin components (α/β-,γ-,ω1,2- and ω-5-) and glutenin (high and low molecular weight) components were analyzed using ImmunoCAP® , ELISA or IgE immunoblotting.

RESULTS

Fourteen patients (66.7%) were diagnosed as EIARD+, which remained 5 years after rush OIT in 11 patients (52.4%). There were no differences in the clinical backgrounds of the EIARD+ and EIARD- patients. However, EIARD+ patients showed significantly higher sIgE levels to all gliadin and glutenin components than EIARD- patients before OIT. The sIgE levels to each component decreased equally after 1 and 2 years of OIT. On IgE immunoblotting, sera from all patients reacted to the multiple gluten bands, and some reacted to the water-soluble bands. The intensity of all IgE-reactive bands also became equally lighter after OIT.

CONCLUSIONS

EIARDs were frequently observed and remained for a long period after successful OIT for wheat allergy. None of the specific wheat components were found to contribute to EIARDs.

3

Alergia al cacahuete: todavía queda mucho por resolver.

Review Article: Unmet needs of children with peanut allergy: aligning the risks and the evidence.

Chan ES, Dinakar C, Gonzales-Reyes E, Green TD, Gupta R, Jones D et al

Ann Allergy Asthma Immunol. 2020 Jan 30. pii: S1081-1206(20)30037-5. doi: 10.1016/j.anai.2020.01.016. [Epub ahead of print]

BACKGROUND

Peanut allergy is a potentially severe and lifelong allergy, with few effective treatments or preventative measures.

OBJECTIVE

To convene an expert panel of allergists, pediatricians, and advocates to discuss and highlight unmet needs in the prevention and management of peanut allergies.

METHODS

Literature searches of PubMed were performed. The panel evaluated published data on the prevention of peanut allergy, treatment of existing peanut allergy, and management of reactions following unintentional peanut exposures.

RESULTS

Key unmet needs in the prevention and management of peanut allergy were identified, including: 1) enhancing and optimizing implementation of early peanut introduction as a means of preventing the development of peanut allergy; 2) developing knowledge translation strategies regarding the safety and efficacy data for current and emerging immunotherapies for peanut-allergic children to support their use in clinical practice; and 3) promoting understanding of true exposure risk in allergic individuals and ensuring access to epinephrine for accidental exposures that provoke severe reactions. Clinicians should help educate caregivers about the actual risks associated with peanut allergy, and its prevention and management so that treatment decisions can be evidence based rather than fear based. Support tools are needed to help address caregiver goals, expectations, and psychological barriers, as well as identify facilitators for prevention and treatment strategies.

CONCLUSIONS

There are significant unmet needs in our understanding of peanut allergy; addressing these needs will help to enhance understanding of how to most effectively prevent and treat peanut allergy, as well as educate the food-allergic and nonallergic community regarding current evidence-based practices.

4

Futuros retos de la ITE en asma alérgica.

Allergen immunotherapy for pediatric asthma: current evidence and knowledge gaps.

Passalacqua G, Landi M, Peroni DG

Curr Opin Allergy Clin Immunol. 2020 Jan 16. doi: 10.1097/ACI.0000000000000618. [Epub ahead of print]

PURPOSE OF REVIEW

The introduction of high-quality and standardized extracts for immunotherapy has renewed the interest in the treatment of pediatric allergic asthma that represents a high-prevalence disease.

RECENT FINDINGS

In addition to clinical trials, several systematic reviews and metaanalyses were published, confirming overall the clinical efficacy of allergen immunotherapy in pediatric asthma. In addition, new data on the preventive effect of the treatment on asthma onset were published. Despite this, many intriguing questions emerged, in parallel to the development of knowledge.

SUMMARY

Allergen immunotherapy is overall effective for the treatment of asthma in children, but a class-effect should not be claimed, rather the efficacy of each single product. According to the recent findings, the challenge for the future research will be to clarify: when to start immunotherapy in children, which are (if they exist) the predictive biomarkers for efficacy in the single individual, the magnitude of the preventive effect and the optimal duration of the treatment.

5

La ambigüedad del término “SLIT”

Clinical Aspects of Sublingual Immunotherapy Tablets and Drops.

Tankersley M, Han JK, Nolte H

Ann Allergy Asthma Immunol. 2020 Jan 7. pii: S1081-1206(19)31532-7. doi: 10.1016/j.anai.2019.12.025. [Epub ahead of print].

OBJECTIVE

Sublingual immunotherapy (SLIT) is administered via tablets (SLIT-T) or liquid drops (SLIT-D). In North America, currently four SLIT-T formulations are FDA approved for allergy immunotherapy and SLIT-D are an off-label use of subcutaneous immunotherapy (SCIT) extracts. The purpose of this review is to compare and contrast aspects of SLIT-T and SLIT-D including physical characteristics, mechanism of action, dosing, efficacy, safety, adherence, and cost.

DATA SOURCE

PubMed literature review (no limits), product prescribing information, and manufacturer websites.

STUDY SELECTION

Publications related to physical characteristics, mechanism of action, dosing, efficacy, safety, and adherence.

RESULTS

Published evidence indicates that tablet and drop formulations differ in regard to physical characteristics, dosing, and strength of evidence for efficacy. It is currently unknown if there are any differences in absorption and mechanism of action between the two formulations. Optimal dosing, efficacy, and safety have been established for SLIT-T. In contrast, in North America there is little support for efficacy of SLIT-D from randomized DBPC trials and dose ranges have not been appropriately evaluated. SLIT-T treat a single allergen whereas in the United States SLIT-D often contain multiple allergens to treat polysensitization. The safety profile of SLIT-T and SLIT-D appears similar, and both formulations are considered safer than SCIT.

CONCLUSIONS

Professional guidelines should make a clear distinction between SLIT-T and SLIT-D in their recommendations to minimize confusion with the umbrella term of SLIT.

6

Seguridad: la asignatura pendiente de la ITO con cacahuete.

Adverse events associated with peanut oral immunotherapy in children – a systematic review and meta-analysis.

Grzeskowiak LE, Tao B, Knight E, Cohen-Woods S, Chataway T

Sci Rep. 2020 Jan 20;10(1):659.

ABSTRACT

While peanut oral immunotherapy (POIT) represents a promising treatment for peanut allergies in children, safety concerns remain a common barrier to widespread adoption. We aimed to systematically assess available evidence to determine the risk and frequency of adverse events occurring during POIT, and examine study-level characteristics associated with their occurrence and severity. A systematic search of MEDLINE, EMBASE, and Web of Science was conducted through April 2019. Controlled and non-controlled studies evaluating POIT were eligible. Twenty-seven studies, involving 1488 subjects, were included. Adverse events to POIT were common and led to treatment discontinuation in 6.6% of children (95% CI 4.4-9.0; 27 studies, I2 = 48.7%). Adverse events requiring treatment with epinephrine occurred among 7.6% (4.5-11.4; 26 studies, I2 = 75.5%) of participants, at a rate of 2.0 per 10,000 doses (0.8-3.7; 15 studies, I2 = 64.4). Use of a rush treatment phase and targeting a higher maintenance dose were associated with a higher risk and frequency of epinephrine use, while using co-treatments in addition to POIT was associated with a lower risk of treatment discontinuation due to adverse events. While adverse events to POIT are common, this study provides promising explorative evidence that certain modifications to existing treatment protocols could significantly improve treatment outcomes.

7

¿Ha encontrado la alergia alimentaria un nuevo aliado?

New Developments in Non-allergen-specific Therapy for the Treatment of Food Allergy.

Long A, Borro M, Sampath V, Chinthrajah RS

Curr Allergy Asthma Rep. 2020 Jan 16;20(1):3.

PURPOSE OF REVIEW

The prevalence of food allergy is increasing. At the current time, there are no approved treatments for food allergy. Major limitations of immunotherapy are long treatment periods (months or years), frequent clinic visits, high costs, increased risk of adverse events during treatment, and lack of durability of desensitization. Additionally, it is allergen-specific, and in those allergic to multiple allergens, the length and cost of treatment are further increased. In this review, we summarize recent developments in novel non-allergen-specific treatments for food allergy.

RECENT FINDINGS

A number of monoclonal antibodies that block IgE or specific pro-allergenic cytokines or their receptors have shown promise in clinical trials for food allergy. The insight we have gained through the use of one drug for the treatment of an atopic disease is quickly being translated to other atopic diseases, including food allergy. The future for food allergy treatment with biologics looks bright.

8

ITE vs tratamiento convencional en rinitis alérgica perenne.

Effects of Perennial Allergen Immunotherapy in Allergic Rhinitis in Patients with/without Asthma: A-Randomized Controlled Real-Life Study.

Ünal D

Int Arch Allergy Immunol. 2020;181(2):141-148.

BACKGROUND

There have been very few studies in real-life settings comparing the treatment effects of allergen immunotherapy (AIT) and pharmacotherapy for perennial allergic rhinitis (AR).

OBJECTIVE

This study was performed to compare AIT and pharmacotherapy in terms of their effects on the symptom control and quality of life (QOL) of AR patients with/without asthma.

METHODS

A total of 250 patients diagnosed with AR with/without asthma were included and assigned to the immunotherapy (AIT plus pharmacological treatment) or control (pharmacological treatment only) group. Clinical and medication scores, QOL scores, and lung function (forced expiratory volume in one second as a percentage; FEV1%) were measured at baseline and 3 years after the start of treatment.

RESULTS

This study showed that there was clinical improvement in AR symptoms in the AIT group, whereas standard pharmacotherapy alone had no significant effect on nasal symptoms. The QOL and satisfaction scores, as evaluated with a visual analogue scale (VAS), were further improved compared to the pharmacotherapy group. There was a significant improvement in medication scores in both AIT groups. According to our results, while total asthma scores and asthma control test scores were significantly improved in the HDM AIT group, they did not change in the Parietaria pollen AIT group. In our study FEV1% was increased compared to the baseline value in the AIT group, but it was not statistically significant. On the other hand, FEV1% remained without any improvement in patients on standard pharmacotherapy.

CONCLUSIONS

Perennial AIT was found to be superior to pharmacotherapy in decreasing symptoms as well as in improving QOL scores in AR patients with/without asthma. HDM AIT was more effective for asthma symptoms than Parietaria pollen AIT.

9

Cómo minimizar las reacciones adversas de la ITE.

Allergy immunotherapy for inhalant allergens: Strategies to minimize adverse reactions.

Nelson HS

Allergy Asthma Proc. 2020 Jan 1;41(1):38-44.

BACKGROUND

Allergy immunotherapy (AIT), both subcutaneous immunotherapy (SCIT) and sublingual immunotherapy (SLIT), is an effective and safe treatment for allergic rhinitis and allergic asthma due to inhalant allergens. However, there are many variables in how it is administered.

OBJECTIVE

To review the evidence that suggests the optimal practice(s) to minimize adverse reactions to AIT.

METHODS

Articles that reported the results of various approaches to the practice of AIT and evidence-based guidelines were consulted for guidance about approaches that would minimize adverse reactions to AIT.

RESULTS

Evidence is presented that supports care in the preparation of allergy extracts for treatment; use of modified extracts; location for administration of SCIT and SLIT; risk factors for systemic reactions; AIT in patients on adrenergic blocking agents and angiotensin-converting enzyme inhibitors; use of premedication; the need for prescription of epinephrine autoinjectors; adjustments in dose for pollen seasons, interruptions in treatment, and for local and systemic reactions; and the safety in patients with autoimmune diseases and during pregnancy.

CONCLUSIONS

Although some of these variables have not been adequately studied, there are many studies that indicate practices that minimize the risk of adverse reactions for both SCIT and SLIT.

10

Una manzana al día para los alérgicos a abedul.

Allergen-specific immunotherapy with apples: Selected cultivars could be a promising tool for birch pollen allergy.

Nothegger B, Reider N, Covaciu CE, Cova V, Ahammer L, Eidelpes R et al

J Eur Acad Dermatol Venereol. 2020 Jan 17. doi: 10.1111/jdv.16201.

BACKGROUND

Most birch-pollen-allergic patients develop allergic cross-reactions to the major allergen found in apples Mal d1, known as pollen-related food allergy (prFA). This is due to a strong clinically relevant homology between the major allergen in birch Bet v 1 and Mal d 1. Daily apple consumption induces oral tolerance in prFA, but its effect on the inhalational allergy has not been investigated.

OBJECTIVES

As continuous apple consumption might also mitigate the inhalational allergy, this study aimed to uncover apple cultivars suitable for treatment of birch-pollen rhinoconjunctivitis and apple allergy in a controlled and established dosage.

METHODS

Patients (n=52) with birch-pollen allergy and prFA to apples were subjected to a Prick to Prick-Test (SPT) with 23 cultivars (red-fleshed-, old-traditional, and new-commercial). By SPT the apple parts flesh, peel-equatorial and peel-apical near the stalk were compared for their reactivity. One apple cultivar of each allergenicity class (low, middle, high) was subsequently tested in an oral provocation test (OPT).

RESULTS

According to the SPTs we provide a ranking of all 23 cultivars. Red-fleshed apples displayed the lowest reactivity, followed by old- and new cultivars. Four cultivars showed disagreement from their allergenicity class: Santana and Pink Lady®, new cultivars that provoked only low to moderate. In contrast, White Rosemary and Goldparmäne, two old cultivars, induced strong reactions. Skin reactivity increased from flesh to peel to stalk and SPT results could predict the severity of prFA of each allergenicity class.

CONCLUSIONS

Herein we propose a treatment protocol for allergen immunotherapy to birch-pollen and prFA with daily apple consumption. Red-fleshed-, old- and the new cultivars Santana and Pink Lady® provoke less allergic reactions and are suitable for initial induction. After a controlled and well tolerated increase of intake, also moderate and finally high allergenic apple cultivars should be integrated into treatment of birch-pollen allergenic patients.

1

Coste-efectividad de la ITE: cara a cara entre ITSC e ITSL.

Cost-effectiveness of grass pollen allergen immunotherapy in adults.

Di Bona D, Bilancia M, Albanesi M, Caiaffa MF, Macchia L

Allergy. 2020 Feb 24. doi: 10.1111/all.14246. [Epub ahead of print]

ARTÍCULO DESTACADO

BACKGROUND

Major scientific societies, such as the EAACI or the AAAAI, do not express any suggestion on which form of allergen immunotherapy (AIT) is to be preferred (subcutaneous immunotherapy, SCIT, vs. sublingual immunotherapy, SLIT). This choice could depend on their relative pharmacoeconomic value.

OBJECTIVES

To assess the cost-effectiveness of AIT for grass pollen, administered as SCIT or SLIT.

METHODS

We created a Markovian Model, to evaluate, in a hypothetical cohort of adult patients suffering from moderate-to-severe rhino-conjunctivitis with or without allergic asthma, the cost-effectiveness of SLIT (tablets, Grazax® and Oralair®) or SCIT (various currently available products, plus indirect non-medical costs, such as travel and productivity costs) in addition to pharmacological therapy, assuming a 9-year horizon to capture AIT long-term effects. The incremental cost-effectiveness ratio (ICER) was calculated assuming pharmacological therapy as the reference comparator.

RESULTS

In the base-case, SCIT was slightly more expensive, but more effective than SLIT, being the most cost-effective option (ICER for SCIT, €11,418; ICER for SLIT, €15,212). ICERs greater than €120,000 for both SCIT and SLIT was demonstrated in a scenario assuming that low treatment persistence rates, which are common in real-life, lead to absence of long-term AIT clinical benefit. Considering indirect non-medical costs SLIT resulted more cost-effective than SCIT (ICER for SCIT, €17,318; ICER for SLIT, €15,212).

CONCLUSIONS

In daily practice AIT for grass pollens may be a cost-effective option only in patients with low discontinuation rates. SCIT, which is less affected by this limitation than SLIT, seems the most cost-effective AIT form.

2

Efectividad de un alergoide de ácaros en práctica clínica habitual.

Real-world evidence of subcutaneous allergoid immunotherapy in house dust mite-induced allergic rhinitis and asthma.

Jutel M, Brüggenjürgen B, Vogelberg C, Richter H

Allergy. 2020 Feb 20. doi: 10.1111/all.14240. [Epub ahead of print]

BACKGROUND

The objective of this study was to analyze the effectiveness of allergen immunotherapy (AIT) with an allergoid in the treatment of house dust mites (HDM)-induced allergic rhinitis and/or asthma based on recent real-life data. The outcomes were measured using asthma incidence and consumption of corresponding medications as the indicator of persisting symptoms.

METHODS

In this retrospective cohort analysis of a German longitudinal prescription database, patients who received at least two relevant mite AIT prescriptions in two different successive seasonal cycles were compared with non-AIT patients who received at least three symptomatic allergic rhinitis (AR) prescriptions in successive mite seasons. Study endpoints included AR progression, asthma progression, asthma occurrence, and therapy adherence. We used multivariate regression analyses to estimate the effects of AIT, adjusting for relevant variables.

RESULTS

This study included 2,350 patients receiving a mite allergoid and 64,740 control patients. After up to 6 years of follow-up, patients treated with mite allergoid required significantly fewer AR and asthma prescriptions (59.7% versus 10.8%) than the control group, and the probability of asthma development was significantly lower. The adherence of patients receiving allergoid was 63.8% at the end of the second year and 38.6% at the end of the third year.

CONCLUSIONS

This real-world evidence confirms the good efficacy of subcutaneous AIT with HDM mite allergoid in the treatment of allergic rhinitis and/or asthma. Up to 6 years of follow-up revealed significant effects in allergic rhinitis by measuring the number of AR medications and demonstrating significant reductions in asthma medications.

3

Nuevas estrategias en alergia alimentaria: ¿Datos convincentes?

Molecular approaches to allergen-specific immunotherapy: are we so far from clinical implementation?

Pechsrichuang P, Jacquet A

Clin Exp Allergy. 2020 Feb 20. doi: 10.1111/cea.13588. [Epub ahead of print] Review.

ABSTRACT

Conventional allergen-specific immunotherapy (AIT), based on administrations of allergen extracts, represents up to now the unique protocol for the desensitization of allergic patients. Whereas the effectiveness of AIT was evidenced for the treatment of allergic rhinitis and allergic asthma, such strategy remains experimental for food allergies up to now. However, important issues are commonly associated with AIT as the quality of natural allergen extracts, the long duration and adverse side effects which negatively affect successful desensitization together with the patient compliance. The rapid progression of molecular allergology made possible the quest of safer, shorter and more effective immunotherapeutic approaches. The aim of this review is to provide an update on these different innovative recombinant derivatives including their efficacy but also their limitations. Despite of promising preclinical and early clinical studies, absence of convincing data in large Phase III trials precludes so far the translation of these immunotherapeutic candidates into the clinic.

4

Los médicos también necesitan entrenamiento.

Subcutaneous Immunotherapy Safety: Incidence per Surveys and Risk Factors.

Sánchez-Borges M, Bernstein DI, Calabria C

Immunol Allergy Clin North Am. 2020 Feb;40(1):25-39. doi: 10.1016/j.iac.2019.09.001.

ABSTRACT

Subcutaneous immunotherapy (SCIT) is effective for allergic rhinitis and conjunctivitis, asthma, and insect venom hypersensitivity. The risk of severe allergic reactions induced by SCIT remains low, and mild systemic reactions have recently shown a tendency to decline. However, near-fatal and fatal anaphylactic reactions may occur. Clinicians administering allergen-specific immunotherapy should receive specialized training and be aware of risk factors and preventive measures to avoid severe allergic reactions induced by SCIT.

5

Debemos apostar por el abordaje multidimensional de la alergia alimentaria.

CSACI guidelines for the ethical, evidence-based and patient-oriented clinical practice of oral immunotherapy in IgE-mediated food allergy.

Bégin P, Chan ES, Kim H, Wagner M, Cellier MS, Favron-Godbout C et al

Allergy Asthma Clin Immunol. 2020 Mar 18;16:20. doi: 10.1186/s13223-020-0413-7

BACKGROUND

Oral immunotherapy (OIT) is an emerging approach to the treatment of patients with IgE-mediated food allergy and is in the process of transitioning to clinical practice.

OBJECTIVE

To develop patient-oriented clinical practice guidelines on oral immunotherapy based on evidence and ethical imperatives for the provision of safe and efficient food allergy management.

MATERIALS AND METHODS

Recommendations were developed using a reflective patient-centered multicriteria approach including 22 criteria organized in five dimensions (clinical, populational, economic, organizational and sociopolitical). Data was obtained from: (1) a review of scientific and ethic literature; (2) consultations of allergists, other healthcare professionals (pediatricians, family physicians, nurses, registered dieticians, psychologists, peer supporters), patients and caregivers; and patient associations through structured consultative panels, interviews and on-line questionnaire; and (3) organizational and economic data from the milieu of care. All data was synthesized by criteria in a multicriteria deliberative guide that served as a platform for structured discussion and development of recommendations for each dimension, based on evidence, ethical imperatives and other considerations.

RESULTS

The deliberative grid included 162 articles from the literature and media reviews and data from consultations involving 85 individuals. Thirty-eight (38) recommendations were made for the practice of oral immunotherapy for the treatment of IgE mediated food allergy, based on evidence and a diversity of ethical imperatives. All recommendations were aimed at fostering a context conducive to achieving objectives identified by patients and caregivers with food allergy. Notably, specific recommendations were developed to promote a culture of shared responsibility between patients and healthcare system, equity in access, patient empowerment, shared decision making and personalization of OIT protocols to reflect patients' needs. It also provides recommendations to optimize organization of care to generate capacity to meet demand according to patient choice, e.g. OIT or avoidance. These recommendations were made acknowledging the necessity of ensuring sustainability of the clinical offer in light of various economic considerations.

CONCLUSIONS

This innovative CPG methodology was guided by patients' perspectives, clinical evidence as well as ethical and other rationales. This allowed for the creation of a broad set of recommendations that chart optimal clinical practice and define the conditions required to bring about changes to food allergy care that will be sustainable, equitable and conducive to the well-being of all patients in need.

6

¡Inyecciones sin aguja para los niños!

Tolerance of needleless subcutaneous immunotherapy in children

Traina G, De Vuono A, Valluzzi R, Fierro V, Dahdah L, Artesani MC et al

Pediatr Allergy Immunol. 2020 Feb 14. doi: 10.1111/pai.13227. [Epub ahead of print]

ABSTRACT

Subcutaneous Allergen Immunotherapy (SCIT) is an effective treatment of respiratory allergy, but injections in children may cause pain, fear, and sometimes systemic adverse events. Needle-free injectors, who generate a "liquid needle" with a sufficient force to pass through the skin and enter the subcutaneous tissue, don't inject fluids directly into the vein. They have never been used for the delivery of SCIT. In this prospective, double-arm, randomized, patient-blinded, intra-individual multi-center clinical trial, we compared a needleless vs. a traditional administration of SCIT in children and adolescents with grass pollen or House Dust Mite (HDM) allergy.

7

¿Qué ocurre tras 3 inyecciones intralinfáticas de cedro de Japón?

Sustained effects of intralymphatic pollen-specific immunotherapy on Japanese cedar pollinosis.

Terada T, Omura S, Kikuoka Y, Suzuki M, Inaka Y, Inui T et al
Rhinology. 2020 Feb 24. doi: 10.4193/Rhin19.301. [Epub ahead of print]

BACKGROUND
Intralymphatic immunotherapy (ILIT) for allergic patients requires only a few intralymphatic injections of the allergen. However, the effectiveness and safety for Japanese cedar pollinosis are unclear. The objectives of this study were to clarify whether and how long ILIT is effective for pollinosis, and its safety.
METHODS
In an open pilot investigation followed by a double-blind, placebo-controlled study, patients with Japanese cedar pollinosis received 3 intralymphatic inguinal injections of the pollen extracts before the first pollen season. The symptom medication score (SMS), nasal provocation testing and scoring visual analogue scale (VAS) were assessed after the first-third seasons.
RESULTS
(1) Although mild adverse events were induced at the injected site, severe adverse events were not noted. (2) During the latter part of the first season, ILIT-treated patients (n=12) tended to show improved SMS compared to placebo-treated (n=6) without statistical significance. When assessed by nasal provocation testing and VAS scoring after the first season, the effectiveness of ILIT was significant. (3) The effects of ILIT continued until the second or third season. (4) Neither allergen-specific antibodies nor Treg/Breg cells changed in the peripheral blood.
CONCLUSIONS
ILIT was safe and effective for Japanese cedar pollinosis. The clinical effects remained for 1-2 years.

8

Nueva herramienta para la toma de decisiones conjunta.

Development and Acceptability of a Shared Decision-Making Tool for Commercial Peanut Allergy Therapies.

Greenhawt M, Shaker M, Winders T, Bukstein DA, Davis RS, Oppenheimer J et al
Ann Allergy Asthma Immunol. 2020 Feb 10. pii: S1081-1206(20)30076-4. doi: 10.1016/j.anai.2020.01.030. [Epub ahead of print]

BACKGROUND
Shared decision making (SDM) is the process through which patients and their medical provider mutually explore therapy goals, risks/benefits, and treatment options regarding medical care. Decision-aids are tools to help with the values clarification process and assess decisional needs and potential decisional conflicts.
OBJECTIVE
To develop and assess acceptability of a decision-aid for commercial peanut allergy therapies.
METHODS
The creation of this decision-aid occurred in three stages, including a qualitative study to assess decisional needs, development of a draft decision-aid through multiple iterations in accordance with international guidelines and decision-aid experts, and assessment of decisional acceptability, decisional conflict, and decisional self-efficacy related to using the decision-aid.
RESULTS
The decision-aid went through 9 iterations, resulting in a 4-page aid with 7 parts, explaining the therapies, the key risks and benefits of the therapy choices, the relative importance of key attributes of the therapies, and a self-check assessment regarding informational adequacy and how to take the next steps. Twenty-four subjects assessed the decision-aid, noting it had good acceptability, high decisional self-efficacy (mean score 91.9/100) and low decisional conflict (mean score 20.2/100). Respondents rated the information content as adequate and sufficient, and the information regarding the therapy choices as fair and balanced without a clear bias or presenting a “best choice”.
CONCLUSIONS
We have developed this decision-aid as a tool to help caregivers navigate the complexity of decision-making for peanut allergy treatment options. The decisión aid was noted to have good acceptability, with scores reflective of the instrument enhancing decisional self-efficacy and reducing decisional conflict.

9

En alergia alimentaria parece que lo mejor está todavía por llegar.

Food allergy immunotherapy: OIT and EPIT.

Kim EH, Burks AW
Allergy. 2020 Feb 7. doi: 10.1111/all.14220. [Epub ahead of print]

ABSTRACT
IgE-mediated food allergy remains a significant and growing problem across the globe. Of the various treatment modalities, oral immunotherapy (OIT) and epicutaneous immunotherapy (EPIT) have been the best studied. Across various studies of OIT for egg, milk, and peanut allergy, strong levels of desensitization have been shown. With egg and peanut OIT, a limited remission, or sustained unresponsiveness (SU), has further been demonstrated. These advances have been further validated by successful phase 2 and phase 3 studies of peanut OIT. EPIT, using daily administrations of a proprietary patch, demonstrated efficacy as well as safety and tolerability in parallel phase 2 studies; however, its phase 3 study did not meet its primary efficacy outcome. Despite its good track record of desensitization, the safety and tolerability of OIT has remained a question. EPIT, on the other hand, has proven safe and tolerable; however, the adequacy of its desensitization has remained to be determined. As OIT and EPIT continue their march toward regulatory review, optimizations for immunotherapy and novel therapies continue to be developed providing hope for food allergy patients everywhere.

10

Grandes lagunas de conocimiento en ITO: necesitamos más y mejores estudios.

Oral immunotherapy in pediatrics.

Arasi S, Castagnoli R, Pajno GB

Pediatr Allergy Immunol. 2020 Feb;31 Suppl 24:51-53.

ABSTRACT

IgE-mediated food allergy (FA) has been emerging as a public health priority, mainly in children. It represents a heavy burden for the entire society and not only for the patients and their families. There is evidence that in children with persistent FA, at least to cow's milk, hen's egg, and peanut, oral immunotherapy (OIT) may increase the reaction threshold to food allergen(s), while receiving active therapy (the so-called "desensitization"). Furthermore, OIT protects patients from the occurrence of severe reactions in the event of accidental ingestion of the culprit food during treatment. However, many gaps are still unsolved, including safety issues, identification of predictive biomarkers, and post-desensitization efficacy. This article briefly summarizes the current evidence and the main needs in OIT to stimulate the development of longitudinal, prospective, well-designed studies able to fill the current gaps soon.

1

En busca del biomarcador perfecto.

Basophil sensitivity reflects long-term clinical outcome of subcutaneous immunotherapy in grass pollen-allergic patients.

Schmid JM, Würtzen PA, Siddhuraj P, Jogdand P, Petersen CG, Dahl R et al

Allergy. 2020 Mar 7. doi: 10.1111/all.14264. [Epub ahead of print]

ARTÍCULO DESTACADO

BACKGROUND

Allergic rhinoconjunctivitis is a public health problem. Allergen Immunotherapy is an effective and safe treatment, that modifies the natural course of allergic disease and induces long-term tolerance.

OBJECTIVES

To correlate basophil and antibody biomarkers of subcutaneous immunotherapy to clinical outcomes and cellular changes in target tissue.

METHODS

To correlate basophil and antibody biomarkers of subcutaneous immunotherapy to clinical outcomes and cellular changes in target tissue.

RESULTS

Subcutaneous immunotherapy led to a 447-fold decrease in basophil sensitivity during the first treatment year. This remained 100-fold lower than baseline during the 3 year-treatment period and 10-fold lower during the follow-up year (n = 18, P = .03). Decrease in basophil sensitivity after three weeks of treatment predicted long-term improvement in seasonal combined symptom and medication scores ($\acute{\rho}$=-0.69, P = .0027) during three years of treatment. AUC of IgE-blocking factor correlated to nasal allergen challenge ($\acute{\rho}$ = 0.63, P = .0012) and SPT ($\acute{\rho}$ = 0.45, P = .03). Plasma cell numbers in the nasal mucosa increased during treatment (P = .02).

CONCLUSIONS

Decrease in basophil sensitivity after three weeks of subcutaneous allergen immunotherapy predicted the clinical outcome of this treatment.

2

El valor de la evidencia en vida real.

Allergen immunotherapy: what is the added value of real-world evidence from retrospective claims database studies?

Devillier P, Demoly P, Molimard M

Expert Rev Respir Med. 2020 Mar 4:1-8. doi: 10.1080/17476348.2020.1733417. [Epub ahead of print]

INTRODUCTION

Randomized controlled trials (RCTs) show that allergen immunotherapy (AIT) has proven long-term efficacy in patients with allergic rhinitis (AR). However, RCTs have limited generalizability and there is growing recognition that real-world evidence (RWE) is necessary to provide complementary data to those of RCTs, and corroborate their findings. Until recently, data from the real-world setting investigating the benefits of AIT for the treatment of patients with grass and birch pollen-associated AR were sparse, but new retrospective claims database studies from France and Germany have confirmed the sustained benefits of grass and birch pollen AIT in terms of significantly reduced progression of AR and asthma, and a significantly decreased risk of new-onset asthma.

AREAS COVERED

Here, we review the value of RWE used alongside data from traditional RCTs, and its potential strengths and limitations, and summarize the findings of the recent RWE studies investigating the benefits of AIT for the management of patients with grass and birch pollen-associated AR.

EXPERT OPINION

There is growing recognition of the necessity and value of RWE as a complement to data acquired in RCTs, to better understand the effects of AIT treatments in a broader, more representative patient population, and to help guide clinical decision-making.

3

¿Cómo se relaciona la ITO con leche y el crecimiento?

Regular intake of cow's milk with oral immunotherapy improves statures of children with milk allergies.

Emura S, Yanagida N, Sato S, Nagakura KI, Asaumi T, Okada Y et al

World Allergy Organ J. 2020 Mar 20;13(3):100108. doi: 10.1016/j.waojou.2020.100108

BACKGROUND

Children who avoid cow's milk (CM) because of food allergy may show disturbed growth. Calcium insufficiency, in particular, was reported among those who completely avoided dairy products. We retrospectively examined whether oral immunotherapy (OIT) affected the stature of patients who had completely avoided CM owing to their severe CM allergy.

METHODS

The CM-OIT group included subjects who had completely avoided milk their entire lives and were administered OIT between 2009 and 2013. The complete milk avoidance (CM-Avoid) group included subjects who were diagnosed with a CM allergy using oral food challenges between 2013 and 2014 who subsequently avoided CM completely. By examining clinical records and questionnaires, we investigated patient height changes over time. We calculated age- and sex-stratified height standard deviation scores (HtSDS) and analyzed changes in HtSDS retrospectively. The observation period was 1-2 years. To exclude pubertal growth spurts, we set the age criteria as less than 11 years in boys and less than 9 years in girls.

RESULTS

We recruited 29 patients (19 boys) for the CM-OIT group and 20 (9 boys) for the CM-Avoid group. The patients' median ages at the start of the observation period were 7.5 years (6.1-9.6) for boys and 6.8 years (5.8-7.8) for girls in the CM-OIT group, and 5.4 years (5.0-7.5) for boys and 5.7 years (5.0-7.1) for girls in the CM-Avoid group. The initial HtSDS in the CM-OIT group was -0.31 (median) and increased to -0.22 (median) after OIT (p = 0.016). In contrast, there was no significant change in HtSDS for the CM-Avoid group.

CONCLUSIONS

Physical growth of pediatric patients with severe CM allergies, who have avoided CM completely, could be improved by OIT for CM allergy.

5

Más allá de la ITE subcutánea y sublingual: la inmunoterapia transcutánea.

Solid-in-Oil Nanodispersions for Transcutaneous Immunotherapy of Japanese Cedar Pollinosis.

Kong Q, Kitaoka M, Wakabayashi R, Tahara Y, Kamiya N, Goto M

Pharmaceutics. 2020 Mar 7;12(3). pii: E240. doi: 10.3390/pharmaceutics12030240.

ABSTRACT

Japanese cedar pollinosis (JCP) is a common affliction caused by an allergic reaction to cedar pollen and is considered a disease of national importance in Japan. Antigen-specific immunotherapy (AIT) is the only available curative treatment for JCP. However, low compliance and persistence have been reported among patients subcutaneously or sublingually administered AIT comprising a conventional antigen derived from a pollen extract. To address these issues, many research studies have focused on developing a safer, simpler, and more effective AIT for JCP. Here, we review the novel antigens that have been developed for JCP AIT, discuss their different administration routes, and present the effects of anti-allergy treatment. Then, we describe a new form of AIT called transcutaneous immunotherapy (TCIT) and its solid-in-oil (S/O) nanodispersion formulation, which is a promising antigen delivery system. Finally, we discuss the applications of S/O nanodispersions for JCP TCIT. In this context, we predict that TCIT delivery by using a S/O nanodispersion loaded with novel antigens may offer an easier, safer, and more effective treatment option for JCP patients.

6

Nuevos algoritmos para medir el impacto de la ITE en la calidad de vida.

Application of a Mapping Function to Estimate Utilities for Ragweed Allergy Immunotherapy Trials.

Dick K, Briggs A, Brandi H

Pharmacoecon Open. 2020 Mar 9. doi: 10.1007/s41669-020-00205-y. [Epub ahead of print].

BACKGROUND

Ragweed pollen sensitivity is a common cause of allergic rhinitis (AR) worldwide. AR symptoms include itchy and runny eyes, sneezing, blocked nose, impaired sleep and social and emotional problems, which can have a significant impact on quality of life.

OBJECTIVE

The objective of this analysis was to estimate utilities for two pooled standardised quality (SQ) ragweed sublingual immunotherapy (SLIT) tablet trials by applying a previously developed mapping algorithm. This study validated the algorithm and extended its application to ragweed seasonal allergy trials. The mapping algorithm relates disease-specific quality-of-life scores to preference-based utilities that may be used to calculate quality-adjusted life-years (QALYs) in cost-effectiveness studies.

METHODS

A mapping algorithm based on a grass pollen allergy immunotherapy trial, GT-08 (EudraCT no. 2004-000083-27) was applied to pooled data from two ragweed pollen immunotherapy trials, P05233 (EudraCT 2008-003863-38) and P05234 (EudraCT 2008-003864-20) to generate EuroQoL 5-Dimensions, 3-Levels (EQ-5D-3L) utilities from Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) data.

RESULTS

The mean utility difference between the SQ ragweed SLIT tablet and placebo was 0.025 [95% confidence interval (CI) 0.011-0.038]. The SQ ragweed SLIT tablet showed an incremental quality-adjusted life-days (QALDs) benefit of 1.900 (95% CI 0.835-2.916) over 75 days.

CONCLUSIONS

Application of a previously developed mapping function allowed for the calculation of QALDs associated with the SQ ragweed SLIT tablet. The results showed a QALD benefit of the SQ ragweed SLIT tablet in P05233 and P05234 trials in the treatment of ragweed pollen-induced AR.

7

ITE y anafilaxia: ¿Cuál es el riesgo?

Safety of allergen immunotherapy in North America from 2008-2017: Lessons learned from the ACAAI/AAAAI National Surveillance Study of adverse reactions to allergen immunotherapy.

Bernstein DI, Epstein TEG

Allergy Asthma Proc. 2020 Mar 1;41(2):108-111. doi: 10.2500/aap.2020.41.200001.

ABSTRACT

In 2004, it was estimated that one fatal anaphylactic reaction (FR) occurred in every 2.4 million subcutaneous immunotherapy (SCIT) injection visits. Uncontrolled asthma was the most commonly cited factor that contributed to FRs. Results of the annual American College of Allergy, Asthma, and Immunology/American Academy of Allergy, Asthma and Immunology sponsored survey conducted among practicing allergists suggest that one nonfatal systemic reactions (SR) occurred in 0.15% of injection visits and in 0.7% of patients who were treated. Analysis of recent data indicated that FRs are 3.75-fold less frequent. Life-threatening grade 4 anaphylactic reactions are estimated to occur in 0.005% of patients who receive SCIT (or 1/160,000 injection visits). Analysis of data from annual surveys identified the following possible risk factors for SRs: a history of SRs to SCIT, the administration of injections in patients with uncontrolled asthma, use of accelerated buildup regimens, and never adjusting doses during the height of the allergy season. Delayed-onset SRs beginning >30 minutes after injections represented 15% of all SRs in clinics with 30-minute observation periods. The safety profile of sublingual immunotherapy is favorable, with no FRs yet identified for sublingual tablet or liquid formulations. Risk management should focus mainly on patients with uncontrolled asthma by withholding injections in such patients, with recent worsening in asthma symptoms and lung function (e.g., peak expiratory flow rate). Because nearly all FRs and SRs occur within 30 minutes of injections, a 30-minute observation period is recommended. Routinely prescribing epinephrine for all patients did not prevent severe SRs, likely due to poor adherence when SRs occurred. Also, no local or systemic infections were identified in 2.3 million patients attending 24.5 million injection visits, which allayed concerns over infections associated with compounding of allergen extracts by practicing allergists.

8

¿Vitamina D, ITE o vacunas bacterianas? Quizá todas ellas.

Immunologic Strategies for Prevention of Asthma

van Masson J, Portnoy JM

J Allergy Clin Immunol Pract. 2020 Mar;8(3):834-847. doi: 10.1016/j.jaip.2019.11.029.

ABSTRACT

A new understanding of factors leading to the development of asthma has pointed to potential primary, secondary, and tertiary prevention strategies. Some, such as genetic makeup, are not yet modifiable. Interventions targeting other factors such as maternal intake of vitamin D or environmental control can be used to decrease the risk of asthma development (primary prevention). The benefits of a diversified microbiome could be considered when recommending allergen avoidance and pet ownership. In addition to reducing symptoms, allergen immunotherapy is also worth considering for prevention of new sensitivities (secondary prevention) in addition to the development of asthma. Ongoing studies involving the use of bacterial vaccines and biologics may provide additional strategies for primary prevention of asthma and for reducing symptoms once it has developed (tertiary prevention). As the relative benefits of these strategies are defined, they should have an increasingly important place in the prevention and management of asthma.

9

¿Sabemos ya cómo detener la marcha atópica?

Halting the March: Primary Prevention of Atopic Dermatitis and Food Allergies

Fatima Bawany BA, Lisa A. Beck, MDb, Kirsi M. Järvinen, MD, PhD

J Allergy Clin Immunol Pract. 2020 Mar;8(3):860-875. doi: 10.1016/j.jaip.2019.12.005.

ABSTRACT

Atopic dermatitis (AD) is one of the most common inflammatory skin conditions, affecting 15% to 30% of children and 2% to 10% of adults. Population-based studies suggest that having AD is associated with subsequent development of other atopic diseases, in what is known as the "atopic march." We will provide an overview of studies that investigate primary prevention strategies for the first 2 diseases in the march, namely, AD and food allergies (FA). These strategies include emollients, breastfeeding, microbial exposures, probiotics, vitamin D and UV light, water hardness, and immunotherapy. Some studies, including randomized controlled trials on emollients and microbial supplementation, have found encouraging results; however, the evidence remains limited and contradictory. With regard to breastfeeding, microbial and lifestyle exposures, vitamin D and UV light, water hardness, and immunotherapy, the lack of randomized controlled trials makes it difficult to draw definitive conclusions. Current American Academy of Pediatrics guidelines support the idea that breastfeeding for 3 to 4 months can decrease AD incidence in children less than 2 years old. Recommendations regarding a direct relationship between breastfeeding on FA, however, cannot be made because of insufficient data. Regarding microbial supplementation, most guidelines do not recommend probiotics or prebiotics for the purpose of preventing allergic diseases because of limited evidence. Before definitive conclusions can be made regarding these interventions, more well-designed, longitudinal, and randomized controlled trials, particularly in at-risk populations, are required.

10

La dieta de eliminación debería ser cosa del siglo pasado.

Immunoglobulin E (IgE)-Mediated Food Allergy in Children: Epidemiology, Pathogenesis, Diagnosis, Prevention, and Management.

Barni S, Liccioli G, Sarti L, Giovannini M, Novembre E, Mori F

Medicina (Kaunas). 2020 Mar 4;56(3). pii: E111. doi: 10.3390/medicina56030111.

ABSTRACT

A food allergy is an immunoglobulin E (IgE)-mediated hypersensitive reaction to food, which consists in the appearance of allergic symptoms; it can vary from common urticaria to even fatal anaphylaxis. The prevalence of food allergies has been increasing in the past twenty years and it represents a major public health problem in industrialized countries. The mechanism that leads to food allergies is the lack of immunologic and clinical tolerance to food allergens. The diagnosis of IgE-mediated food allergies is based on the combined use of a detailed medical history, in-vivo, and in-vitro research of specific IgE, the elimination diet, and the double-blind placebo-controlled food challenge. The only currently available treatment for allergies is the strict elimination diet. This type of attitude, which we could define as "passive", does not overcome the risk of accidental reactions due to involuntary intake of the culprit food. For food allergy management, an "active" approach is urgently needed, such as specific allergen immunotherapy, which is currently under development and only used for research purposes. This article aims to give an updated review of IgE-mediated food allergies in pediatric populations in terms of epidemiology, pathogenesis, prevention, diagnosis, and management.

1

El diagnóstico molecular puede ser clave.

Molecular profiling of allergen-specific antibody responses may enhance success of specific immunotherapy.

Rodríguez-Domínguez A, Berings M, Rohrbach A, Huang HJ, Curin M, Gevaert P et al
J Allergy Clin Immunol. 2020 Apr 13. pii: S0091-6749(20)30479-6. doi: 10.1016/j.jaci.2020.03.029. [Epub ahead of print].

ARTÍCULO DESTACADO

BACKGROUND

House dust mites (HDM) are one of the most important allergen sources containing many different allergenic molecules. The analysis of patients from a double-blind, placebo-controlled allergen-specific immunotherapy (AIT) study indicated that patients may benefit to a different extent from AIT depending on their molecular sensitization profiles.

OBJECTIVES

To investigate in a real-life setting if stratification of HDM allergic patients according to molecular analysis may enhance AIT success.

METHODS

Serum and nasal secretion samples from HDM allergic patients (n=24) (baseline, 7, 15, 33 and 52 weeks) who had received one year treatment with a well-defined subcutaneous AIT form (Alutard SQ 510) were tested for IgE and IgG reactivity to 15 micro-arrayed HDM allergen molecules with ImmunoCAP ISAC technology. IgG subclass levels to allergens and peptides were determined by ELISA and IgG blocking was assessed by basophil activation. In vitro parameters were related to reduction of symptoms determined by combined symptom medication score (CSMS) and visual analogue (VAS).

RESULTS

Alutard SQ 510 induced protective IgG mainly against Der p 1 and Der p 2 and to a lower extent to Der p 23, but not to the other important allergens such as Der p 5, Der p 7 and Der p 21 showing better clinical efficacy in patients only sensitized to Der p 1 and/or Der p 2 as compared to patients with additional IgE specificities.

CONCLUSIONS

Stratification of HDM allergic patients according to molecular sensitization profiles and molecular monitoring of AIT-induced IgG responses may enhance success of AIT.

2

El efecto placebo: ¿la condena de los ensayos clínicos con ITE?

Placebo effects in allergen immunotherapy – an EAACI Task Force Position Paper.

Pfaar O, Agache I, Bergmann KC, Bindslev-Jensen C, Bousquet J, Creticos PS et al
Allergy. 2020 Apr 23. doi: 10.1111/all.14331. [Epub ahead of print].

ABSTRACT

The placebo (Latin "I will please") effect commonly occurs in clinical trials. The psychological and physiological factors associated with patients' expectations about a treatment's positive and negative effects have yet to be well characterized, although a functional prefrontal cortex and intense bidirectional communication between the central nervous system and the immune system appear to be prerequisites for a placebo effect. The use of placebo raises certain ethical issues, especially if patients in a placebo group are denied an effective treatment for a long period of time. The placebo effect appears to be relatively large (up to 77%, relative to pre-treatment scores) in controlled clinical trials of allergen immunotherapy (AIT), such as the pivotal, double-blind, placebo-controlled (DBPC) randomized clinical trials currently required by regulatory authorities worldwide. The European Academy of Allergy and Clinical Immunology (EAACI) therefore initiated a Task Force, in order to better understand the placebo effect in AIT and its specific role in comorbidities, blinding issues, adherence, measurement time points, variability, and the natural course of the disease. In this Position Paper, the EAACI Task Force highlights several important topics regarding the placebo effect in AIT such as i) regulatory aspects, ii) neuroimmunological and psychological mechanisms, iii) placebo effect sizes in AIT trials, iv) methodological limitations in AIT trial design and v) potential solutions in future AIT trial design. In conclusion, this Position Paper aims to examine the methodological problem of placebo in AIT from different aspects and also to highlight unmet needs and possible solutions for future trials.abs

3

¡La Blomia también existe!

Subcutaneous allergen immunotherapy for asthma: A randomized, double-blind, placebo-controlled study with a standardized Blomia tropicalis vaccine.

Castro-Almarales RL, Ronquillo-Díaz M, Álvarez-Castelló M, Rodríguez-Canosa J, González-León M, Enríquez-Domínguez I et al
World Allergy Organ J. 2020 Apr 10;13(4):100098.

BACKGROUND

Sensitization to Blomia tropicalis (Bt) is very frequent in the tropics, and particularly in Cuba, being a significant cause of allergic asthma. Allergen immunotherapy (AIT) with Bt can be a therapeutic option, however, placebo-controlled clinical trials have not been reported.

OBJECTIVE

To assess the therapeutic effect and safety of AIT for asthma using a standardized allergen vaccine of B. tropicalis by subcutaneous route, in allergic asthmatic patients exposed and sensitized to this mite species.

METHODS

A double-blind, placebo-controlled Phase II trial was conducted in 35 adults (18 with treatment and 17 with placebo), with mild to moderate asthma, predominantly sensitized to Bt. AIT was administered subcutaneously in increasing doses from 4 to 6000 Biological Units using a locally manufactured standardized extract (BIOCEN, Cuba). Patient assessment was performed using symptom-medication score (SMS), peak expiratory flow and skin reactivity relative to Histamine as measured by skin prick test (SPT).

RESULTS

The 12-month treatment achieved a significant ($p < 0.001$) decrease of SMS. Symptom score showed only 41% (CI: 26-61) of placebo values, whereas medication was 34.5% (22.4%-63.3%). Treatment was regarded clinically effective in 67% of patients (OR 32; 95%CI: 17 to 102). The effect size on symptoms and medication was higher than has been reported with equivalent allergen dosages of D. pteronyssinus and D. siboney in Cuban asthmatic patients. Skin reactivity to Bt was also significantly reduced ($p = 0.0001$), increasing 148-fold the allergen threshold to elicit a positive skin test. This desensitization effect was specific to Bt and did not modify the reactivity to Dermatophagoides. The change of specific skin reactivity was significantly ($p < 0.05$) correlated to clinical improvement. All adverse events were local with a frequency of 2.4% of injections.

CONCLUSIONS

The 12-month treatment achieved a significant ($p < 0.001$) decrease of SMS. Symptom score showed only 41% (CI: 26-61) of placebo values, whereas medication was 34.5% (22.4%-63.3%). Treatment was regarded clinically effective in 67% of patients (OR 32; 95%CI: 17 to 102). The effect size on symptoms and medication was higher than has been reported with equivalent allergen dosages of D. pteronyssinus and D. siboney in Cuban asthmatic patients. Skin reactivity to Bt was also significantly reduced ($p = 0.0001$), increasing 148-fold the allergen threshold to elicit a positive skin test. This desensitization effect was specific to Bt and did not modify the reactivity to Dermatophagoides. The change of specific skin reactivity was significantly ($p < 0.05$) correlated to clinical improvement. All adverse events were local with a frequency of 2.4% of injections.

4

La ITO con cacahuete NO es para todos.

Community Private Practice Clinical Experience with Peanut Oral Immunotherapy.

Afinogenova Y, Rubin TN, Patel SD, Powell RL, Gilo JM, Denno MN et al
J Allergy Clin Immunol Pract. 2020 Apr 2. pii: S2213-2198(20)30259-2. doi: 10.1016/j.jaip.2020.03.016. [Epub ahead of print].

BACKGROUND

Peanut oral immunotherapy is an effective treatment for desensitizing peanut-allergic patients, but the frequency of adverse reactions has limited its widespread use.

OBJECTIVE

To review the frequency of adverse reactions that patients on peanut oral immunotherapy experience during build-up and maintenance phases and explore factors that may contribute to adverse events.

METHODS

A retrospective chart review of children and adults with peanut allergy undergoing peanut oral immunotherapy at the New England Food Allergy Treatment Center in West Hartford, Conn was performed. Data on patient demographics, allergic profile, peanut allergy testing, and details of reactions in build-up and maintenance phases were collected. A systemic reaction was defined as one of the following: (1) severe reaction involving 1 system, such as generalized hives and/or angioedema; (2) 2 or more of the following symptoms: cutaneous or oral, respiratory, or gastrointestinal symptoms; (3) drop in blood pressure; or (4) need for epinephrine.

RESULTS

Data were available on 783 patients aged 3.5 to 48.3 years. During buildup, 78 patients (10%) experienced at least 1 systemic reaction, 660 (84%) at least 1 gastrointestinal adverse event, 369 (47%) at least 1 cutaneous adverse event, and 157 (20%) at least 1 respiratory adverse event. Thirty-four patients (4%) required epinephrine during buildup. Six hundred ninety-seven patients (89%) completed buildup and progressed to maintenance. During maintenance, 131 patients (19%) experienced at least 1 systemic reaction, 190 (27%) at least 1 gastrointestinal adverse event, 104 (15%) at least 1 cutaneous adverse event, and 50 (7%) at least 1 respiratory adverse event. Seventy-four patients (11%) required epinephrine during maintenance. None of the adverse events required hospitalizations, and there were no mortalities. Nine patients (1%) were diagnosed with eosinophilic esophagitis during buildup or maintenance. Increasing pretreatment peanut specific IgE levels were associated with increased odds of a systemic reaction during buildup. Increasing age, pretreatment peanut specific IgE level, and a systemic reaction in buildup were associated with increased odds of a systemic reaction during maintenance.

CONCLUSIONS

Peanut oral immunotherapy may be an effective and safe treatment for carefully selected peanut-allergic patients under the guidance of experienced providers. Specific patient characteristics and immunologic factors may help predict adverse events.

5

ITE y estación polínica.

Systemic and large local reactions during subcutaneous grass pollen immunotherapy in children.

Gur Cetinkaya P, Kahveci M, Esenboga S, Karaatmaca B, Soyer O et al

Pediatr Allergy Immunol. 2020 Apr 22. doi: 10.1111/pai.13261. [Epub ahead of print].

BACKGROUND

Subcutaneous immunotherapy (SCIT) is the allergen specific curative treatment of allergic rhintis. Adverse effects, most of which are local, can be observed during the immunotherapy. These adverse effects have been reported more frequently during the pollen season. The purpose of this study was to estimate the rate of local, large local and systemic reactions during the treatment, to determine the relationship between adverse reactions and the season in which these reactions occur, as well as the risk factors for adverse reactions during the grass pollen specific SCIT treatment in children.

METHODS

We retrospectively collected and analyzed the data of 261 children who administered grass pollen SCIT between 2008 and 2018.

RESULTS

A total of 261 children (177, 67.8% male), who received grass pollen SCIT, with a mean (±SD) age of 12.0±3.0 years at the initiation of SCIT were enrolled to the study. The number of the patients who experienced local and large local reactions were 109 and 30, respectively. In addition, the number of the patients with systemic reactions were 35. After the 12,284 injections, local reactions occurred in 357 (2.9%), and this was followed by systemic reaction as 55 (0.4%) and large local reactions as 40 (0.3%). Frequency of local ($p<0.001$) and systemic reactions ($p=0.003$) were higher during grass pollen season than out of the grass pollen season. In multivariate analysis, initiation of SCIT during the grass pollen season [OR:7.351, 95%CI:1.532-35.279, $p=0.013$] and experiencing local reactions [OR:4.214, 95%CI:2.159-8.224, $p<0.001$] were independent predictors for the development of large local and systemic reactions.

CONCLUSIONS

SCIT, in which only mild to moderate systemic reactions occurred, is safe for the treatment of allergic rhinitis in children. Our study revealed that previous local reactions and initiation of immunotherapy during the grass pollen season were the predictors for large local and systemic reactions during SCIT in children.

6

¿Cuánta similitud existe entre Parietarias?

Cross-reactivity between Parietaria judaica and Parietaria officinalis in immunotherapy extracts for the treatment of allergy to Parietaria.

Cancelliere N, Iglesias I, Ayuga Á, Enrique Miranda E

Biomed Rep. 2020 Jun;12(6):326-332. doi: 10.3892/br.2020.1297. Epub 2020 Apr 6.

ABSTRACT

Parietaria judaica and P. officinalis are the two most common subspecies of the Parietaria genus. P. judaica and P. officinalis have exhibited cross-reactivity in previous studies. P. judaica pollen is the main cause of allergy in the Mediterranean area. It has been shown that a high percentage of patients sensitized to P. judaica with allergic rhinitis (AR) have an increased risk of developing asthma. The present study aimed to confirm the cross-reactivity between P. judaica and P. officinalis and to evaluate the use of a single P. officinalis extract in patients allergic to both subspecies as a preferable option for the diagnosis and treatment of allergy in a highly pollinated area of the Spanish Mediterranean coast. The present study was a single centre, observational cross-sectional study of adult patients diagnosed with AR and/or bronchial asthma who were sensitized to Parietaria pollen. A total of 24 patients were enrolled in the study and included in the analysis. Allergovit® immunotherapy extracts were selected for the study based on the protein content (P. officinalis pollen extract). The results of an in vitro ELISA revealed that 79.1% (n=19) of the patient sera were reactive to immunotherapy extracts. ELISA inhibition assay of the IgE binding to P. officinalis demonstrated inhibition values >70% in the sera of highly reactive patients, confirming the cross-reactivity between the two Parietaria subspecies. In addition, all patients enrolled in the study exhibited double skin positivity against P. judaica and P. officinalis extracts, as assessed by the skin prick test, further supporting the in vivo reactivity between the two subspecies. The present study demonstrated that P. judaica and P. officinalis pollen extracts were highly cross-reactive, and that a unique P. officinalis pollen extract may be used for the diagnosis and immunotherapy of patients allergic to Parietaria.

7

ITE sublingual con un alergoide monomérico.

The role of allergoids in allergen immunotherapy: from injective to sublingual route.

Compalati E, Incorvaia C, Cavaliere C, Masieri S, Gargiulo A, Mistrello G et al

Eur Ann Allergy Clin Immunol. 2020 Apr 27. doi: 10.23822/EurAnnACI.1764-1489.142. [Epub ahead of print].

ABSTRACT

Allergen immunotherapy (AIT) is aimed at inducing tolerance to allergens, such as pollens, dust mites or moulds, by administering increasing amounts of the causative allergen through subcutaneous or sublingual route. The evidence of efficacy of AIT is high, but the issue of safety, especially for the subcutaneous route, must be taken into account. The search for safer AIT products aimed at reducing the allergenicity, and thus adverse reactions, while maintaining the immunogenicity, that is essential for effectiveness, gave rise to the introduction of allergoids, which were conceived to fulfill these requirements. In the first allergoids glutaraldehyde or formaldehyde were used as cross-linking agent to polymerize allergens, this resulting in high molecular weight molecules (200,000 to 20,000,000 daltons) which were significantly less allergenic due to a decreased capacity to bridge IgE on its specific receptor, while maintaining the immunogenicity and thus the therapeutic efficacy. In recent years further agents, acting as adjuvants, such as L-tyrosine, monophosphoryl lipid A, aluminium hydroxide, were added to polymerized extracts. Moreover, a carbamylated monomeric allergoid was developed and, once adsorbed on calcium phosphate matrix, used by subcutaneous route. At the same time, in virtue of its peculiarities, such allergoid revealed particularly suitable for sublingual administration. A lot of clinical evidences show that it is well tolerated, largely safer and effective. Importantly, the higher safety of allergoids allows faster treatment schedules that favor patient compliance and, according to pharmaco-economic studies, they might be more cost-effective than other AIT options.

8

Pasado, presente y futuro de la ITE.

Past, presence, and future of allergen immunotherapy vaccines.
Dorofeeva Y, Shilovskiy I, Tulaeva I, Focke-Tejkl M, Flicker S, Kudlay D et al
Allergy. 2020 Apr 6. doi: 10.1111/all.14300. [Epub ahead of print]

ABSTRACT

Allergen-specific immunotherapy (AIT) is an allergen-specific form of treatment for patients suffering from immunoglobulin E (IgE)-associated allergy; the most common and important immunologically mediated hypersensitivity disease. AIT is based on the administration of the disease-causing allergen with the goal to induce a protective immunity consisting of allergen-specific blocking IgG antibodies and alterations of the cellular immune response so that the patient can tolerate allergen contact. Major advantages of AIT over all other existing treatments for allergy are that AIT induces a long-lasting protection and prevents the progression of disease to severe manifestations. AIT is cost effective because it uses the patients own immune system for protection and potentially can be used as a preventive treatment. However, broad application of AIT is limited by mainly technical issues such as the quality of allergen preparations and the risk of inducing side effects which results in extremely cumbersome treatment schedules reducing patients compliance. In this article we review progress in AIT made from its beginning and provide an overview of the state of the art, the needs for further development, and possible technical solutions available through molecular allergology. Finally, we consider visions for AIT development towards prophylactic application.

9

El renovado interés en el asma pediátrica.

Allergen immunotherapy for pediatric asthma: current evidence and knowledge gaps.
Passalacqua G, Landi M, Peroni DG
Curr Opin Allergy Clin Immunol. 2020 Apr;20(2):162-167. doi: 10.1097/ACI.0000000000000618.

PURPOSE OF REVIEW

The introduction of high-quality and standardized extracts for immunotherapy has renewed the interest in the treatment of pediatric allergic asthma that represents a high-prevalence disease.

RECENT FINDINGS

In addition to clinical trials, several systematic reviews and metaanalyses were published, confirming overall the clinical efficacy of allergen immunotherapy in pediatric asthma. In addition, new data on the preventive effective of the treatment on asthma onset were published. Despite this, many intriguing questions emerged, in parellel to the development of knowledge.

SUMMARY

Allergen immunotherapy is overall effective fo the treatment of asthma in children, but a class-effect should not be claimed, rather the efficacy of each single product. According to the recent findings, the challenge for the future reseach will be to clarify: when to start immunotherapy in children, which are (if they exist) the predictive biomarkers for efficacy in the single individual, the magnitude of the preventive effect and the optimal duration of the treatment.

10

El novedoso enfoque del ensayo clínico “BOOM”

Protocol for a double-blind, randomized controlled trial on the dose-related efficacy of omalizumab in multi-food oral immunotherapy.
Langlois A, Lavergne MH, Leroux H, Killer K, Azzano P, Paradis L et al
Allergy Asthma Clin Immunol. 2020 Apr 17;16:25.

BACKGROUND

Previous proof-of-concept studies have shown that a short course of omalizumab can safely accelerate the oral immunotherapy schedule for multiple allergens simultaneously. Considering the high cost of medication, the dose-related efficacy of omalizumab at decreasing the duration of oral immunotherapy up-dosing phase must be objectively quantified before cost-benefit analyses can be performed. The primary objective of this trial will be to compare the efficacy of 2 omalizumab dosages to placebo at decreasing time-to-maintenance dose during a symptom-driven multi-food OIT protocol.

METHODS

A total of 90 participants aged 6 to 25 with multiple food allergies (3 or more) will be enrolled at four sites in Canada. Participants will be randomized to: (A) Omalizumab 8 mg/kg per month (n = 36); (B) Omalizumab 16 mg/kg per month (n = 36); or (C) Placebo (n = 18). Study drug will be administered at full dosage for 12 weeks, then progressively tapered at 50% dosage (8 mg/kg vs 4 mg/kg vs placebo) for 4 weeks and at 25% dosage (4 mg/kg vs 2 mg/kg vs placebo) for another 4 weeks. After a pre-treatment period of 8 weeks, participants will undergo an initial food escalation (IFE) to an OIT mix containing 3 allergens and start daily home dosing with biweekly increases until a target daily maintenance of 1500 mg protein is achieved. The amount escalated at each visit will vary based on treatment tolerance according to a standardized up-dosing algorithm. Participants will be followed for at least 12 months following the initial food escalation. The primary endpoint will be time from IFE to the target maintenance dose of 1500 mg protein. Time-to-event analytic methods, including the log-rank test, will be used to compare the 3 arms.

DISCUSSION

This trial uses a novel pragmatic approach to compare OIT with omalizumab to OIT without omalizumab in a blinded manner, which allows to single out the effect of this anti-IgE medication on treatment effectiveness speed without the recourse to predetermined schedules. The innovative patient-centered up-dosing algorithm allows to maximise treatment effectiveness speed without compromising patient safety, regardless of whether the patient is on omalizumab or not. This study will also provide novel prospective data to inform on the optimal and most cost-effective dosage for this indication.

1

Autoadministración de la ITA en tiempos de pandemia.

Health and Economic Outcomes of Home Maintenance Allergen Immunotherapy in Select Patients with High Health Literacy during the COVID-19 Pandemic: A Cost-Effectiveness Analysis During Exceptional Times.

Shaker MS, Mosnaim G, Oppenheimer J, Stukus D, Abrams EM, Greenhawt M

J Allergy Clin Immunol Pract. 2020;S2213-2198(20)30477-3.

ARTÍCULO DESTACADO

BACKGROUND

Allergen immunotherapy (AIT) is safe and effective but is typically administered under strict clinic observation to mitigate the risk of a systemic reaction to immunotherapy (SRIT). However, in the setting of the global coronavirus disease 2019 pandemic, alternative care models should be explored.

OBJECTIVE

To evaluate the cost-effectiveness of home immunotherapy self-administration (HITSA) in a highly idealized circumstance for provision of maintenance AIT in a shelter-in-place or other scenarios of unforeseen reduction in nonessential medical services.

METHODS

Markov modeling was used to compare in-office clinic AIT in selected patients using cohort analysis and microsimulation from the societal and health care perspectives.

RESULTS

Assuming similar SRIT rates, HITSA was found to be a cost-effective option with an incremental cost-effectiveness ratio of $44,554/quality-adjusted life-year when considering both incremental epinephrine autoinjector costs and coronavirus disease 2019 risks. Excluding epinephrine autoinjector costs, HISTA dominated other options. However, outside of pandemic considerations, HITSA was not cost-effective (incremental cost-effectiveness ratio, $198,877,286) at annual epinephrine autoinjector costs above $287. As the incremental HITSA SRIT rate increased above 15%, clinic AIT was the most cost-effective strategy. Excluding both pandemic risks and risk of motor vehicle accident fatality from round-trip clinic transit, clinic AIT dominated other strategies. Clinic AIT was the more cost-effective option at very high fatality relative risk for HITSA or at very low annual risk of contracting coronavirus disease 2019.

CONCLUSIONS

Under idealized assumptions HITSA can be a safe and cost-effective option during a global pandemic in appropriately selected patients provided home rates of SRIT remain stable.

2

La desescalada también aplica a las consultas de Alergología.

A Phased Approach to Resuming Suspended Allergy/Immunology Clinical Services.

Searing DA, Dutmer CM, Fleischer DM et al

J Allergy Clin Immunol Pract. 2020;S2213-2198(20)30486-4. [Epub ahead of print]

ABSTRACT

In early 2020, the first US and Canadian cases of the novel SARS-CoV-2 infection were detected. In the ensuing months, there has been rapid spread of the infection. In March 2020, in response to the virus, state/provincial and local governments instituted shelter-in-place orders, and non-essential ambulatory care was significantly curtailed, including allergy/immunology services. With rates of new infections and fatalities potentially reaching a plateau and/or declining, restrictions on provision of routine ambulatory care are lifting, and there is a need to help guide the allergy/immunology clinician on how to re-initiate services. Given COVID-19 will circulate within our communities for months or longer, we present a flexible, algorithmic best-practices planning approach on how to prioritize services, in 4 stratified phases of re-opening according to community risk level, as well highlight key considerations for how to safely do so. The decisions on what services to offer and how fast to proceed are left to the discretion of the individual clinician and practice, operating in accordance with state and local ordinances with respect to the level of non-essential ambulatory care that can be provided. Clear communication with staff and patients before and after all changes should be incorporated into this new paradigm on continual change, given the movement may be forward and even backward through the phases as this is an evolving situation.

3

La ITA en la práctica clínica habitual.

Clinical Practice of Allergen Immunotherapy for Allergic Rhinoconjunctivitis and Asthma: An Expert Panel Report.

Calderon MA, Waserman S, Bernstein DI et al

J Allergy Clin Immunol Pract. 2020;S2213-2198(20)30479-7. doi:10.1016/j.jaip.2020.04.071.

ABSTRACT

Allergen immunotherapy (AIT) reduces symptoms and medication use associated with allergic rhinitis with or without conjunctivitis and allergic asthma. Although several AIT guidelines exist, there remain unanswered questions about AIT that are relevant to everyday practice. Our objective was to prepare an evidence-based overview addressing the practical aspects of AIT in clinical practice based on published evidence and the experience of international experts in the field. Topics covered include interpretation and translation of clinical trial data into everyday clinical practice (e.g., allergen doses and treatment duration), assessment of risk and treatment of local and systemic allergic reactions, recommendations for improvement of AIT guidelines, and identification of appropriate data for seeking regulatory approval, to name a few. Many informational gaps in AIT practice need further evaluation as products and practices evolve.

4

Más allá de la ITA subcutánea y sublingual.

Intralymphatic immunotherapy for mountain cedar pollinosis: A randomized, double-blind, placebo-controlled trial.

Thompson C, Silvers S, Shapiro M

Ann Allergy Asthma Immunol. 2020;S1081-1206(20)30311-2. doi:10.1016/j.anai.2020.04.030.

BACKGROUND

Allergen immunotherapy can provide long-term benefits, including symptomatic relief and reduced disease progression, but requires a lengthy regimen that presents barriers to patient adherence. Thus, there is a need for improved approaches to immunotherapy. Recently, several clinical trials have reported successful results from intralymphatic immunotherapy.

OBJECTIVE

To evaluate the efficacy, safety and tolerability of intralymphatic immunotherapy for allergies caused by mountain cedar pollen in a proof-of-concept study.

METHODS

Twenty-one patients with allergic rhinoconjunctivitis due to mountain cedar pollen were randomized to receive three monthly intralymphatic injections of allergenic extract or placebo prior to the 2018-2019 mountain cedar pollen season. Safety was monitored during treatment thru the end of pollen season using structured and spontaneous reports. Clinical efficacy information was collected using a daily electronic diary of symptoms and allergy medication. Allergen-specific serum IgE was assessed before treatment and at the end of the study.

RESULTS

There were no serious adverse events or systemic reactions in either group. Four patients experienced mild injection-site reactions. Patients receiving intralymphatic immunotherapy experienced a significant improvement in allergy symptoms and medication use relative to patients receiving placebo ($p < 0.001$) and the active treatment group had lower average total combined scores on 20 of 27 days during peak pollen season ($p < 0.05$). There was not a significant difference between groups in changes to mean mountain cedar-specific serum IgE levels.

CONCLUSIONS

In this proof-of-concept trial, intralymphatic immunotherapy was well tolerated and reduced the symptoms and medication use associated with allergic rhinoconjunctivitis caused by mountain cedar pollen.

5

ITA subcutánea e ITA sublingual: cara a cara.

Subcutaneous and sublingual allergen-specific immunotherapy: a tale of two routes.

Incorvaia C, Ciprandi G, Nizi MC, Makri E, Ridolo E

Eur Ann Allergy Clin Immunol. 2020;10.23822/EurAnnACI.1764-1489.150. doi:10.23822/EurAnnACI.1764-1489.150.

ABSTRACT

Specific immunotherapy is the only treatment acting on the causes and not only on symptoms of respiratory allergy. It was first introduced as subcutaneous immunotherapy (SCIT) with the aim to induce immunological tolerance to the administered allergen(s). In the 1980s, sublingual immunotherapy (SLIT) was developed, mainly to improve the safety, which was a critical issue at that time. This article reviewed the available literature, including a large number of randomized controlled trials, meta-analyses, and real-life studies as well, on the outcomes of SCIT and SLIT concerning the treatment critical issues of the two routes, that are efficacy, safety, cost-effectiveness, and compliance to treatment. The efficacy of SCIT and SLIT is similar in respiratory allergy, providing, based on the induction of typical changes in the immunologic response, an early control of symptoms that steadily increases during the treatment and its efficacy lasts after the recommended duration of three years. Such results are the reason why SCIT and SLIT have economic advantage over symptomatic drugs.A

6

Complicaciones gastrointestinales de la ITO con cacahuete.

Gastrointestinal Eosinophil Responses in a Longitudinal, Randomized Trial of Peanut Oral Immunotherapy.

Wright BL, Fernandez-Becker NQ, Kambham N et al

Clin Gastroenterol Hepatol. 2020;S1542-3565(20)30676-5. doi:10.1016/j.cgh.2020.05.019.

BACKGROUND & AIMS

Gastrointestinal side effects are common during oral immunotherapy (OIT) and eosinophilic esophagitis (EoE) is a potential complication. We aimed to characterize eosinophilic gastrointestinal responses to peanut OIT, in which peanut protein is given orally, with incremental increases in dose over time.

METHODS

Twenty adults with IgE-mediated peanut allergy were randomly assigned to groups given peanut OIT (n=15) or placebo (n=5); 1 additional subject withdrew before randomization. Serial gastrointestinal biopsies were collected at baseline (n=21, 0 weeks), following dose escalation (n=10, 52 weeks), and during the maintenance phase (n=11, 104 weeks). Endoscopic findings were characterized using the EoE endoscopic reference score. Biopsies were assessed for eosinophils per high-power field (eos/hpf) and other pathology features using EoE histologic scoring system scores. We performed immunohistochemical analyses of eosinophil peroxidase deposition, quantified using automated image analysis.

RESULTS

At baseline, no subjects reported current gastrointestinal symptoms. However, 3 of the 21 subjects (14%) had esophageal peak eosinophil counts ≥15 eos/hpf and all subjects had dilated intercellular spaces (DIS). OIT induced or exacerbated esophageal eosinophilia (EE) at 52 weeks in most subjects (peak eosinophil counts >5 eos/hpf in 6 of 7 patients [86%]; peak eosinophil counts ≥15 eos/hpf in 4 of 7 patients [57%]). One subject met clinicopathologic criteria for EoE and withdrew; no significant changes in esophageal peak eosinophil counts were observed in the placebo group. EE in the OIT group corresponded with significant increases in EoE histologic scoring system scores and deposition of eosinophil peroxidase. In 4 of 6 participants (67%), OIT-induced EE and gastrointestinal eosinophilia resolved by the end of the maintenance phase. Gastrointestinal symptoms were not clearly associated with EE or gastrointestinal eosinophilia.

CONCLUSIONS

In this pilot study, we found that peanut OIT-induced EE and gastrointestinal eosinophilia are usually transient and are not always associated with gastrointestinal symptoms.

7

Aspectos clave de la ITA en niños.

EAACI Allergen Immunotherapy User's Guide.

Alvaro-Lozano M, Akdis CA, Akdis M et al
Pediatr Allergy Immunol. 2020;31 Suppl 25:1-101. doi:10.1111/pai.13189.

ABSTRACT

Allergen immunotherapy is a cornerstone in the treatment of allergic children. The clinical efficiency relies on a well-defined immunologic mechanism promoting regulatory T cells and downplaying the immune response induced by allergens. Clinical indications have been well documented for respiratory allergy in the presence of rhinitis and/or allergic asthma, to pollens and dust mites. Patients who have had an anaphylactic reaction to hymenoptera venom are also good candidates for allergen immunotherapy. Administration of allergen is currently mostly either by subcutaneous injections or by sublingual administration. Both methods have been extensively studied and have pros and cons. Specifically in children, the choice of the method of administration according to the patient's profile is important. Although allergen immunotherapy is widely used, there is a need for improvement. More particularly, biomarkers for prediction of the success of the treatments are needed. The strength and efficiency of the immune response may also be boosted by the use of better adjuvants. Finally, novel formulations might be more efficient and might improve the patient's adherence to the treatment. This user's guide reviews current knowledge and aims to provide clinical guidance to healthcare professionals taking care of children undergoing allergen immunotherapy.

8

¿Se puede tratar la alergia respiratoria local con inmunoterapia?

Allergen Immunotherapy for Local Respiratory Allergy.

Eguiluz-Gracia I, Ariza A, Testera-Montes A, Rondón C, Campo P
Curr Allergy Asthma Rep. 2020;20(7):23.

PURPOSE OF REVIEW

Local respiratory allergy (LRA) is an eosinophilic phenotype of chronic airway disease. Three entities have been described within the LRA spectrum: local allergic rhinitis (LAR) and local allergic asthma (LAA) in non-atopic patients, and dual allergic rhinitis (DAR) in atopic patients (coexistence of LAR and allergic rhinitis). In this article, we aim to review the current evidence on the therapeutic options for LRA.

RECENT FINDINGS

No controlled study has assessed the effect of standard therapy (oral antihistamines, intranasal or inhaled corticosteroids, bronchodilators) in LRA subjects. Three randomized clinical trials and one observational study demonstrated that allergen immunotherapy (AIT) is able to control nasal and ocular symptoms, decrease the need for rescue medication, and improve quality of life in LAR individuals. Nasal or inhaled steroids can be expected to improve eosinophilic inflammation in LRA patients but cannot change the natural course of the disease. Moreover, the long-term and disease-modifying effects of AIT in LRA subjects need to be investigated.

9

Alergia al gato: ITA con extracto polimerizado versus nativo.

Immunogenicity of a new allergoid from Felis domesticus.

González JPS, Hernández EB, Abellán AC, Peñalver-Mellado M
Allergol Immunopathol (Madr). 2020;S0301-0546(20)30074-4. doi:10.1016/j.aller.2020.02.008.

BACKGROUND

The chemical modification of allergens with glutaraldehyde improves safety while maintaining clinical efficacy, which permits the administration of higher doses of immunotherapy, reducing the risk of adverse reactions. The aim of this study is to evaluate the immunogenic capacity of a new cat dander polymer by immunizing mice and quantifying immunoglobulins in serum, in comparison with the non-modified allergen.

METHODS

The study consists of the immunization of three mice groups with the polymerized and the native extract, together with a negative control group. The immunoglobulin levels in serum have been measured by indirect ELISA. By means of the non-parametric Mann-Whitney U test, it was determined if there were significant differences in the values of specific antibodies between groups.

RESULTS

The group immunized with the allergoid showed significantly higher specific IgG and IgG1 values to dander allergens and specific IgG to the major allergen Fel d 1, while there were no significant changes in IgG2a and IgE values. These results could be due to a higher immunization dose. The vaccine formulation was based on the optimal defined dose for clinical efficacy of allergen immunotherapy.

CONCLUSIONS

This preclinical study carried out with the present assay has established that the allergoid of cat dander extract, as designed for its optimal use in allergen immunotherapy, produces a higher specific IgG than the native extract, in addition to showing significantly higher specific IgG1 levels, evidencing a greater effectiveness in immunization.

10

En la ITA, el dinero también importa (y mucho).

A non-stationary Markov model for economic evaluation of grass pollen allergoid immunotherapy.

Bilancia M, Pasculli G, Di Bona D

PLoS One. 2020;15(5):e0232753.

INTRODUCTION

Allergic rhino-conjunctivitis (ARC) is an IgE-mediated disease that occurs after exposure to indoor or outdoor allergens, or to non-specific triggers. Effective treatment options for seasonal ARC are available, but the economic aspects and burden of these therapies are not of secondary importance, also considered that the prevalence of ARC has been estimated at 23% in Europe. For these reasons, we propose a novel flexible cost-effectiveness analysis (CEA) model, intended to provide healthcare professionals and policymakers with useful information aimed at cost-effective interventions for grass-pollen induced allergic rhino-conjunctivitis (ARC).

METHODS

Treatments compared are: 1. no AIT, first-line symptomatic drug-therapy with no allergoid immunotherapy (AIT). 2. SCIT, subcutaneous immunotherapy. 3. SLIT, sublingual immunotherapy. The proposed model is a non-stationary Markovian model, that is flexible enough to reflect those treatment-related problems often encountered in real-life and clinical practice, but that cannot be adequately represented in randomized clinical trials (RCTs). At the same time, we described in detail all the structural elements of the model as well as its input parameters, in order to minimize any issue of transparency and facilitate the reproducibility and circulation of the results among researchers.

RESULTS

Using the no AIT strategy as a comparator, and the Incremental Cost Effectiveness Ratio (ICER) as a statistic to summarize the cost-effectiveness of a health care intervention, we could conclude that: SCIT systematically outperforms SLIT, except when a full societal perspective is considered. For example, for T = 9 and a pollen season of 60 days, we have ICER = €16,729 for SCIT vs. ICER = €15,116 for SLIT (in the full societal perspective).For longer pollen seasons or longer follow-up duration the ICER decreases, because each patient experiences a greater clinical benefit over a larger time span, and Quality-adjusted Life Year (QALYs) gained per cycle increase accordingly.Assuming that no clinical benefit is achieved after premature discontinuation, and that at least three years of immunotherapy are required to improve clinical manifestations and perceiving a better quality of life, ICERs become far greater than €30,000.If the immunotherapy is effective only at the peak of the pollen season, the relative ICERs rise sharply. For example, in the scenario where no clinical benefit is present after premature discontinuation of immunotherapy, we have ICER = €74,770 for SCIT vs. ICER = €152,110 for SLIT.The distance between SCIT and SLIT strongly depends on under which model the interventions are meta-analyzed.

CONCLUSIONS

Even though there is a considerable evidence that SCIT outperforms SLIT, we could not state that both SCIT and SLIT (or only one of these two) can be considered cost-effective for ARC, as a reliable threshold value for cost-effectiveness set by national regulatory agencies for pharmaceutical products is missing. Moreover, the impact of model input parameters uncertainty on the reliability of our conclusions needs to be investigated further.

1 La alergia en tiempos de COVID-19.

COVID-19 Pandemic: Practical Considerations on the Organization of an Allergy Clinic – An EAACI/ARIA Position Paper.

Pfaar O, Klimek L, Jutel M, Akdis CA, Bousquets J, Breiteneder H et al

Allergy 2020 Jun 12;10.1111/all.14453. doi: 10.1111/all.14453. Online ahead of print.

ARTÍCULO DESTACADO

BACKGROUND

The Coronavirus disease 2019 (COVID-19) has evolved as a pandemic infectious disease transmitted by the severe acute respiratory syndrome coronavirus (SARS-CoV-)2. Allergists and other health care providers (HCPs) in the field of allergies and associated airway diseases are in the front line, taking care of patients potentially infected with SARS-CoV-2. Hence, strategies and practices to minimize risks of infection for both HCPs and treated patients have to be developed and followed by allergy clinics.

METHODS

The scientific information on COVID-19 was analyzed by a literature search in Medline, Pubmed, national and international guidelines from the European Academy of Allergy and Clinical Immunology (EAACI), the Cochrane Library and the Internet.

RESULTS

Based on diagnostic and treatment standards developed by EAACI, on international information regarding COVID-19, on guidelines of the World Health Organization (WHO) and other international organizations as well as on previous experience, a panel of experts including clinicians, psychologists, IT experts and basic scientists along with EAACI and the "Allergic Rhinitis and its Impact on Asthma (ARIA)" inititiative have developed recommendations for the optimal management of allergy clinics during the current COVID-19 pandemic. These recommendations are grouped into nine sections on different relevant aspects for the care of patients with allergies.

CONCLUSIONS

This international Position Paper provides recommendations on operational plans and procedures to maintain high standards in the daily clinical care of allergic patients whilst ensuring necessary safety in the current COVID-19 pandemic.

2 Cumbre de expertos sobre ITO en alergia alimentaria.

Consensus Report from the Food Allergy Research and Education (FARE) 2019 Oral Immunotherapy for Food Allergy Summit.

Pepper AN, Assa'ad A, Blaiss M et al

J Allergy Clin Immunol. 2020;S0091-6749(20)30747-8. doi:10.1016/j.jaci.2020.05.027.

ABSTRACT

Food allergy is a major health problem affecting 5 to 10% of the population in developed nations, including an estimated 32 million Americans. Despite the large number of patients suffering from food allergies, up until the end of January 2020, no treatment for food allergies had been approved by the U.S. Food and Drug Administration (FDA). The only options were avoidance of food allergen triggers and acute management of allergic reactions. A considerable body of data exists supporting oral immunotherapy (OIT) as a promising, novel treatment option, including that for the now FDA-approved peanut OIT product, Palforzia. However, data for long-term quality of life improvement with OIT varies, depending on the measures used for analysis. Like many therapies, OIT is not without potential harms, and burdens, and the evaluation of patient-specific risk-benefit ratio of food OIT produces challenges for clinicians and patients alike, with many unanswered questions. Food Allergy Research & Education (FARE) organized the Oral Immunotherapy for Food Allergy Summit on November 6, 2019 modeled after the PRACTALL sessions between the European Academy of Allergy and Clinical Immunology (EAACI) and the American Academy of Allergy, Asthma and Immunology (AAAAI) to address these critical issues. Health care providers, patient representatives, researchers, regulators and food allergy advocates came together to discuss OIT and identify areas of common ground as well as gaps in existing research and areas of uncertainty and disagreement. The purpose of this paper is to summarize that discussion and facilitate collaboration among clinicians and patients to help them make better-informed decisions about offering and accepting OIT, respectively, as a therapeutic option.

3 ¿Algún biomarcador de respuesta a la ITSL de ácaros?

Association between biomarkers and house dust mite sublingual immunotherapy in allergic asthma.

Hoshino M, Akitsu K, Kubota K, Ohtawa J

Clin Exp Allergy. 2020;10.1111/cea.13686. doi:10.1111/cea.13686 [Epub ahead of print].

BACKGROUND

House dust mite (HDM) sublingual immunotherapy (SLIT) has demonstrated efficacy in clinical trials of patients with asthma. Airway inflammation is a characteristics of respiratory allergy, but its relationship to SLIT remain unclear.

OBJECTIVE

We evaluate the association between clinical outcomes with pulmonary function and biomarkers in before and after HDM SLIT (UMIN-Number 000022390).

METHODS

One hundred twelve patients with asthma sensitized to HDM were randomized to add-on 6 standardized quality (SQ)-HDM SLIT to pharmacotherapy or pharmacotherapy alone for 48 weeks. At baseline and end of study, biomarkers, blood eosinophils, serum IgE, serum periostin, fractional exhaled nitric oxide (FeNO), and spirometry and clinical symptoms were measured. Association between biomarkers and an increase in FEV1 of 120 ml or greater were analyzed.

RESULTS

SLIT demonstrated a significant reduction of serum periostin ($P < 0.001$), FeNO ($P < 0.01$), and increase in HDM specific IgE ($P < 0.05$), FEV1 ($P < 0.001$) and improvement of clinical symptom scores, when compared to pharmacotherapy. The change in FEV1 correlated with the changes in serum periostin ($r = 0.696$, $P < 0.001$) and the changes in FeNO ($r = 0.682$, $P < 0.001$). The independent predictor of improvement in airflow limitation were change in serum periostin ($r2 = 0.753$, $P = 0.013$) and FeNO ($P = 0.038$). Based on cutoff values derived by receiver operating characteristic analysis (periostin 30.9 ng/mL, FeNO 28.0 ppb), patients were distinguished responders from non-responders, but with no predictive value for blood eosinophils or total IgE. The proportion of patients with both high periostin and FeNO levels was significantly higher in responder than in non-responder ($P = 0.026$).

CONCLUSIONS AND CLINICAL RELEVANCE:

Adding HDM SLIT to pharmacotherapy resulted in reduced serum periostin and FeNO, and improved pulmonary function. Serum periostin and FeNO may be useful biomarkers for prediction of SLIT.

4

¿Huevo cocinado o huevo crudo?

Induction of sustained unresponsiveness after egg oral immunotherapy compared to baked egg therapy in egg-allergic children.

Kim EH, Perry TT, Wood RA et al

J Allergy Clin Immunol. 2020;S0091-6749(20)30810-1. doi:10.1016/j.jaci.2020.05.040.

BACKGROUND

While desensitization and sustained unresponsiveness (SU) have been shown with egg oral immunotherapy (OIT), the benefits of baked egg (BE) therapy for egg allergy have not been well studied.

OBJECTIVE

To evaluate the safety and efficacy of BE ingestion compared to egg OIT in participants allergic to unbaked egg but tolerant to BE tolerant but unbaked egg reactive children ages 3-16 years were randomized to 2 years of treatment with either BE or egg OIT.

METHODS

Double-blind, placebo-controlled food challenges (DBPCFC) were conducted after 1 and 2 years of treatment to assess for desensitization, and after 2 years of treatment followed by 8-10 weeks off of treatment to assess for SU. Mechanistic studies were conducted to assess for immune modulation. A cohort of BE reactive participants underwent egg OIT and identical DBPCFCs as a comparator group.

RESULTS

Fifty participants (median age 7.3 years) were randomized and initiated treatment. SU was achieved in 3 of 27 (11.1%) BE participants versus 10 of 23 (43.5%) egg-OIT participants (p=0.009). In the BE reactive comparator group, 7 of 39 (17.9%) participants achieved SU. More BE tolerant participants withdrew from BE versus egg OIT (29.6% versus 13%). Dosing symptom frequency in BE tolerant participants was similar with BE and egg OIT, but more frequent in BE reactive participants. Egg white-specific IgE, skin testing and basophil activation decreased similarly after BE and egg OIT.

CONCLUSIONS

Among children allergic to unbaked egg but tolerant to BE, those treated with egg OIT were significantly more likely to achieve SU compared to children ingesting BE.

5

Desarrollo de ITA para población pediátrica: la legislación no lo pone fácil.

Allergen Immunotherapy (AIT) in children: a vulnerable population with its own rights and legislation – summary of EMA-initiated multi-stakeholder meeting on Allergen Immunotherapy (AIT) for children, held at Paul-Ehrlich-Institut, Langen, Germany, 16.1.2019.

Mahler V, Mentzer D, Bonertz A et al

Clin Transl Allergy. 2020;10:28. Published 2020 Jun 29. doi:10.1186/s13601-020-00327-w.

ABSTRACT

Concerning development of medicinal products, children belong to a so-called “special population” for which additional legislation applies: Regulation (EC) No 1901/2006 on medicinal products for paediatric use sets up a system of requirements, rewards and incentives to ensure that medicinal products are researched, developed and authorized to meet the therapeutic needs of children. Allergen Immunotherapy (AIT) is believed to contain a strong potential for immunomodulatory effects inducing sustained clinical efficacy after cessation of treatment (disease modifying effect) and thereby may prevent the progression of the atopic march towards asthma manifestation. However, to this day only few data on long-term effects in general exist and even fewer in children. These are predominantly data from open studies, which are strongly influenced in their validity by the known placebo effect of AIT. Furthermore, there are no studies allowing for the conclusion that efficacy in adults are mirrored by a similar efficacy in children and thus, up to now, it is not possible to extrapolate data from adults to children. The Paediatric Committee (PDCO)-European Medicines Agency’s (EMA) scientific committee responsible for activities on medicines for children-initiated a Multi-Stakeholder Meeting on AIT for Children held at the Paul-Ehrlich-Institut in Langen, Germany, to provide a platform for discussion and exchange of thoughts to this topic between allergy experts from academia, regulators and AIT-manufacturers. The consented meeting minutes, conclusions and participants are presented.

6

El cacahuete y la ITA epicutánea.

An evaluation of factors influencing response to epicutaneous immunotherapy for peanut allergy in the PEPITES trial.

Fleischer DM, Chinthrajah S, Scurlock AM et al

Allergy Asthma Proc. 2020;10.2500/aap.2020.41.200047. doi:10.2500/aap.2020.41.200047.

BACKGROUND

Epicutaneous immunotherapy (EPIT) for peanut allergy is a potential novel immunotherapy that utilizes the unique cutaneous immunologic properties to induce desensitization. A randomized, double-blind, placebo-controlled Phase 3 trial (PEPITES) in peanut-allergic children 4-11 years demonstrated an epicutaneous patch (DBV712) with 250 micrograms peanut protein was statistically superior to placebo in inducing desensitization following 12 months of daily treatment.

OBJECTIVE

To investigate what baseline and in-study factors influenced response to DBV712 250 micrograms, with a focus on patch adhesion, by posthoc analysis of PEPITES data.

METHODS

A posthoc multivariate model built with log-transformed Month 12 eliciting dose (ED) as the dependent variable was used to assess the influence of baseline characteristics and patch adhesion. Baseline characteristics and treatment response were also evaluated by stratifying subjects into decile subgroups by patch detachment rates over the 12-month study.

RESULTS

Multivariate analysis identified higher baseline ED and lower baseline peanut-specific IgE as the variables most predictive of higher Month 12 ED, followed by mean daily patch application duration, baseline SCORing Atopic Dermatitis(SCORAD) score, and age. By decile stratification, no association between patch detachment and treatment response was identified for 80% of DBV712-treated subjects. All DBV712-treated subjects, including those with the highest patch detachment rates, demonstrated treatment benefit measured by fold-changes in geometric mean ED.

CONCLUSION

We identified subject baseline characteristics of higher baseline ED and lower baseline peanut-specific IgE as most predictive of higher Month 12 ED. For the majority of treated subjects, patch detachment did not impact treatment response. A minority of subjects, highly sensitive to peanut at baseline, had lower prespecified responder rates and higher patch detachment rates, yet still benefited from treatment based upon fold-changes in ED.

7

El cacahuete y la ITA epicutánea: más allá.

Improvements in eliciting dose across baseline sensitivities following 12 months of epicutaneous immunotherapy (EPIT) in peanut-allergic children aged 4 to 11 years.

Greenhawt M, Kim EH, Campbell DE, Green TD, Lambert R, Fleischer DM

J Allergy Clin Immunol Pract. 2020;S2213-2198(20)30526-2. doi:10.1016/j.jaip.2020.05.030.

ABSTRACT

Post hoc analyses presented herein evaluate eliciting dose changes after epicutaneous immunotherapy treatment in clinical trials in a more insightful way than a binomial endpoint approach allows.

8

La ITA en asma podría tener un nuevo rival.

Asthma immunotherapy and treatment approaches with mesenchymal stem cells.

Akkoç T, Genç D

Immunotherapy. 2020;12(9):665-674. doi:10.2217/imt-2019-0194.

ABSTRACT

Asthma is a chronic inflammatory disease of the airways where exaggerated T helper 2 immune responses and inflammatory mediators play a role. Current asthma treatment options can effectively suppress symptoms and control the inflammatory process; however, cannot modulate the dysregulated immune response. Allergen-specific immunotherapy is one of the effective treatments capable of disease modification. Injecting allergens under the skin in allergen-specific immunotherapy can reduce asthma and improve the sensitivity of the lungs, however, has a risk of severe reactions. Mesenchymal stem cells have immunoregulatory activity with their soluble mediators and contact dependent manner. In this review, we focus on the current treatment strategies with mesenchymal stem cells in asthma as a new therapeutic tool and compare those with immunotherapy.

9

La importancia de las dosis.

Single-Center Noninferiority Randomized Trial on the Efficacy and Safety of Low- and High-Dose Rush Oral Milk Immunotherapy for Severe Milk Allergy.

Takaoka Y, Yajima Y, Ito YM et al

Int Arch Allergy Immunol. 2020;1-7. doi:10.1159/000508627.

INTRODUCTION

Oral immunotherapy (OIT) has been reported to be effective but associated with a risk of severe symptoms. Thus, an OIT method with decreased risk is required.

OBJECTIVES

We aimed to evaluate the efficacy and safety of low- and high-dose OIT regimens in children with severe milk allergy.

METHODS

Overall, 33 participants (median age, 9 years; median final dose of the milk oral food challenge [OFC], 2 mL) were included. The participants were randomly assigned to groups that received either a low (20 mL; n = 19) or high (100 mL; n = 14) maintenance target dose of OIT. The dose was gradually increased to the target dose in the rush escalation phase and was then maintained daily at home. The primary endpoint was the final OFC dose at 6 months of OIT. Adverse events during OIT were evaluated.

RESULTS

The final OFC dose after OIT was significantly higher than that before OIT in both groups (low-dose, p = 0.000; high-dose, p = 0.006), but there was no significant difference in the final OFC dose between the 2 groups (p = 0.767). In the maintenance phase, the high-dose group had significantly more severe symptoms than did the low-dose group (0.5%, 11/2,355 total intake events vs. 0.1%, 4/3,230 total intake events; p = 0.018).

CONCLUSIONS

An equally increased dose effect was observed for maintenance OIT doses of 20 and 100 mL in children with severe milk allergy. The risk of severe symptoms in the maintenance phase was lower in the low-dose group. A low-dose OIT regimen is recommended for severe milk allergy.

10

Ensayos clínicos en alergia alimentaria: más atención al paciente, por favor.

Outcomes for clinical trials of food allergy treatments.

Sim K, Mijakoski D, Stoleski S et al

Ann Allergy Asthma Immunol. 2020;S1081-1206(20)30418-X. doi:10.1016/j.anai.2020.06.023.

OBJECTIVE

Food allergy is a common condition which can have a significant impact on the quality of life of affected individuals and their caregivers. Recent years have witnessed an increased effort to identify new treatments for food allergy. Here we review the need to identify core outcomes for measurement in clinical trials of food allergy treatments.

DATA SOURCE

We reviewed literature regarding core outcome set development, the important role that these play in prioritising patient-relevant outcomes and the potential for core outcomes to accelerate the path to product marketing by allowing prompt and reliable evidence synthesis following trial publication.

STUDY SELECTION

We reviewed recent clinical trials of food allergy treatments in order to understand which outcomes have previously been measured; and reviewed available core outcome set initiatives for other allergic conditions in order to understand which other outcomes might be explored in future trials.

RESULTS

Clinical trials of food allergy treatments have largely focussed on outcomes which are relevant to investigators and to commercial investors, especially threshold of reactivity and immunological changes. Future trials should consider addressing patient important outcomes and should report the experiences of both adult and child participants and their caregivers.

CONCLUSION

There is a pressing need for core outcome set development for food allergy treatment trials.

1

El cacahuete y la ITA epicutánea: Volumen II.

Long-Term, Open-Label Extension Study of the Efficacy and Safety of Epicutaneous Immunotherapy for Peanut Allergy in Children: PEOPLE 3-Year Results.

Fleischer DM, Shreffler WG, Campbell DE et al

J Allergy Clin Immunol. 2020;S0091-6749(20)30957-X. doi:10.1016/j.jaci.2020.06.028. [Epub ahead of print]

ARTÍCULO DESTACADO

BACKGROUND

We previously reported the safety and efficacy of epicutaneous immunotherapy (EPIT™) for peanut allergy (250 μg, daily epicutaneous peanut protein; DBV712 250μg) in a 12-month randomized controlled study (PEPITES) of peanut-allergic children aged 4-11 years.

OBJECTIVE

To assess interim safety and efficacy of an additional 2 years of EPIT from the ongoing (5-year treatment) open-label extension PEOPLE study.

METHODS

Subjects who completed PEPITES were offered enrollment in PEOPLE. Following an additional 2 years of daily DBV712 250μg, subjects who had received DBV712 250μg in PEPITES underwent Month-36 double-blind, placebo-controlled, food challenge (DBPCFC) with an optional Month-38 sustained unresponsiveness (SU) assessment.

RESULTS

198 (93%) of 213 eligible subjects who had received DBV712 250μg in PEPITES entered PEOPLE, of whom 141 (71%) had assessable DBPCFC at Month 36. At Month 36, 51.8% (73/141) of subjects reached an eliciting dose (ED) of ≥1000 mg, compared with 40.4% (57/141) at Month 12. 75.9% (107/141) demonstrated increased ED compared to baseline. 13.5% (19/141) tolerated the full DBPCFC of 5444 mg. Median cumulative reactive dose increased from 144 to 944 mg. 18 subjects underwent an optional SU assessment; 14/18 (77.8%) maintained an ED of ≥1000 mg at Month 38. Local patch-site skin reactions were common but decreased over time. There was no treatment-related epinephrine use in years 2 or 3. Compliance was high (96.9%), and withdrawals due to treatment-related adverse events low (1%).

CONCLUSIONS

These results demonstrate that daily EPIT treatment for peanut allergy beyond 1 year leads to continued response from a well-tolerated, simple-to-use regimen.

2

El momento decisivo para los alérgicos al cacahuete.

Efficacy and safety of oral immunotherapy with AR101 in European children with a peanut allergy (ARTEMIS): a multicentre, double-blind, randomised, placebo-controlled phase 3 trial.

Hourihane JO, Beyer K, Abbas A et al

Lancet Child Adolesc Health. 2020;S2352-4642(20)30234-0. doi:10.1016/S2352-4642(20)30234-0.

BACKGROUND

Peanut allergy is the leading cause of food-related anaphylaxis. Current management options can negatively affect food allergy-related quality of life. We aimed to investigate the efficacy of an investigational oral biologic drug (AR101).

METHODS

The AR101 Trial in Europe Measuring Oral Immunotherapy Success in peanut-allergic children (ARTEMIS) trial was a multicentre, double-blind, randomised, placebo-controlled phase 3 trial done at 18 hospitals in Ireland, France, Germany, Italy, Spain, Sweden, and the UK. Children and adolescents with peanut allergy, aged 4-17 years, who developed dose-limiting symptoms to 300 mg or less peanut protein (equivalent to approximately one peanut kernel) during a double-blind placebo-controlled food challenge test at study entry were enrolled. Participants were randomly assigned (3:1) to receive daily doses of either AR101 oral immunotherapy (AR101 group) or a taste-masked placebo (placebo group). All participants, investigators, and care providers were masked to treatment allocation until the study was completed. Doses were increased every 2 weeks over 6 months until a dose of 300 mg was reached and maintained for 3 months. The primary endpoint was the proportion of participants in the intention-to-treat or safety population (defined as those participants who had been randomly assigned and had received at least one dose of the assigned drug) who could consume a single dose of 1000 mg (cumulative dose 2043 mg) peanut protein without developing dose-limiting allergic symptoms at an exit double-blind placebo-controlled food challenge after 9 months of treatment. Additional endpoints included safety (ie, the frequency and severity of adverse events) and changes in food allergy-related quality of life, assessed by use of age-appropriate Food Allergy Quality of Life Questionnaires (FAQLQs) and the Food Allergy Independent Measure (FAIM). The study is registered with ClinicalTrials.gov, NCT03201003 , and is completed.

FINDINGS

Between June 12, 2017, and Feb 15, 2018, 227 patients were screened, of whom 175 were randomly assigned to the AR101 group (n=132) and the placebo group (n=43). All primary and secondary endpoints were met. 77 (58%) of 132 participants in the AR101 group tolerated 1000 mg peanut protein at the exit food challenge versus one (2%) of 43 participants in the placebo group (AR101-placebo treatment difference 56·0% [95% CI 44·1-65·2], p<0·0001). Adverse events were reported by almost all participants. The maximum severity of adverse events reported was mild or moderate for most participants who received AR101 (mild, 66 [50%] of 132 participants; moderate, 63 [48%]; and severe, one [1%]) or placebo (mild, 24 [56%] of 43 participants; moderate, 18 [42%]; severe, none). Participants aged 8-12 years in the AR101 group reported improvements that exceeded the minimum clinically important difference between the two groups across all FAQLQ domains. Additionally, participants in the AR101 group and their caregivers reported improvements that exceeded the minimum clinically important difference in FAIM domains related to the perceived likelihood and outcomes of a severe allergic reaction.

INTERPRETATION

AR101 oral immunotherapy treatment led to rapid desensitisation to peanut protein, with a predictable safety profile that improved with treatment, and an associated improvement in self-reported and caregiver-reported food allergy-related quality of life. These patient-oriented outcomes provide invaluable data to help physicians, patients, and caregivers make informed, shared decisions on the management of peanut allergy.

3

La necesidad de nuevas formas de inmunoterapia con alérgenos.

Intralymphatic Immunotherapy improves grass pollen allergic rhinoconjunctivitis. A three-year randomized placebo-controlled trial.

Skaarup SH, Schmid JM, Skjold T, Graumann O, Hoffmann HJ

J Allergy Clin Immunol. 2020;S0091-6749(20)30964-7. doi:10.1016/j.jaci.2020.07.002.

BACKGROUND

Allergic rhinoconjunctivitis is a global health problem. Different Allergen ImmunoTherapy (AIT) regimes are marketed but have low adherence because they are expensive, complex and time consuming. New AIT forms are needed.

OBJECTIVE

In a three-year follow-up double-blinded randomized placebo-controlled trial we aimed to investigate effect of intralymphatic AIT (ILIT).

METHODS

Patients with grass pollen rhinoconjunctivitis were treated with either three ILIT injections and an ILIT booster one year later, three ILIT injection and a placebo booster or three placebo injections and a placebo booster. Primary outcome was improvement in a combined symptom and medication score, cSMS. A novel evaluation tool with a linear regression model of cSMS and grass pollen counts was developed. Secondary outcomes were changes in grass specific immunoglobulins and skin and nasal provocation tests to grass pollen.

RESULTS

36 patients were included. Log10 transformed cSMS was reduced by 0.30 (95%CI 0.11 - 0.49), p=0.002 equalling 48.5% (95%CI 24.5% - 62%), in the entirethree-year follow-up period, significant only in the first follow-up season but not in the second and third season. The regression model showed a 37%, p<0.001, reduction in cSMS. The booster injection had no additional. Secondary, repeated measures of IgE and IgG4 to grass, showed significant between-group difference and within-group change in the ILIT groups. No change in provocation test was found.

CONCLUSION

Intralymphatic immune therapy gives a substantial reduction in grass pollen allergy symptoms and use of rescue medication, significant in the first season after treatment. A booster injection had no additional effect.

4

ITO para alérgicos a proteínas de leche de vaca: cuanto antes, mejor.

As soon as possible in IgE-cow's milk allergy immunotherapy.

Boné Calvo J, Clavero Adell M, Guallar Abadía I et al

Eur J Pediatr. 2020;10.1007/s00431-020-03731-3.

ABSTRACT

Oral immunotherapy is a common treatment in cow's milk protein allergy. The Department of Pediatric Allergology at the Children's Hospital of Zaragoza performed a retrospective analysis of 335 infants under 1 year of age diagnosed with IgE-mediated cow's milk and early treated. Clinical evaluation, skin prick test, and serum-specific IgE level control were performed before starting and after finishing treatment. Upon completion of treatment, more than 98% of patients became tolerant to milk and no one presented serious adverse reactions. Nowadays, the remaining non-tolerant patients (1.8%) can take milk or derivatives daily-as prophylaxis-to a certain maximum dose and still remain asymptomatic. After immunotherapy, both positive skin prick tests and a progressive decrease in specific IgE levels were found, as desensitization to milk increased. Conclusion: Oral immunotherapy is a safe and effective treatment against allergy to cow's milk proteins in infants. Such treatment should be offered to the children's families from the first moment of diagnosis. What is known: • Cow's milk proteins are responsible for the earliest IgE-mediated allergic reactions in children. • Oral immunotherapy (OIT) is commonly used as cow's milk allergy treatment and it is proposed at different ages. What is new: • OIT it is an effective and safe method with no severe reactions at early ages. • The number of reaching successful treatments is awesome so we believe that immunity response can be molded at the first months of life, so the probability of success with infants is greater than in older children.

5

¿Serán las nanopartículas el futuro de la ITA?

New and old adjuvants in allergen-specific immunotherapy: With a focus on nanoparticles.

Feng Z, Yi X, Hajavi J

J Cell Physiol. 2020;10.1002/jcp.29941. doi:10.1002/jcp.29941.

ABSTRACT

Allergic diseases have remarkably increased in recent years. Nowadays, efforts for curing and management of these disorders are an important concern worldwide. Allergen-specific immunotherapy (ASIT) has recently gained more attention as a means for the management of allergic diseases. Adjuvants or helper agents are materials applied for better stimulating and shifting of protective responses, and these belong to an extremely diverse collection of complexes. The main function of adjuvants includes acting as depot foundations, transferring vehicles, and immunostimulators. Immunostimulatory adjuvants have gained increasing attention for ASIT. In this regard, the present study provides a review of old and new adjuvants used in allergen immunotherapy.

6

Inmunotoxinas como alternativa a la ITA tradicional.

Der p 1-based immunotoxin as potential tool for the treatment of dust mite respiratory allergy.

Lázaro-Gorines R, López-Rodríguez JC, Benedé S et al

Sci Rep. 2020;10(1):12255. Published 2020 Jul 23. doi:10.1038/s41598-020-69166-w.

ABSTRACT

Immunotoxins appear as promising therapeutic molecules, alternative to allergen-specific-immunotherapy. In this work, we achieved the development of a protein chimera able to promote specific cell death on effector cells involved in the allergic reaction. Der p 1 allergen was chosen as cell-targeting domain and the powerful ribotoxin α-sarcin as the toxic moiety. The resultant construction, named proDerp1αS, was produced and purified from the yeast Pichia pastoris. Der p 1-protease activity and α-sarcin ribonucleolytic action were effectively conserved in proDerp1αS. Immunotoxin impact was assayed by using effector cells sensitized with house dust mite-allergic sera. Cell degranulation and death, triggered by proDerp1αS, was exclusively observed on Der p 1 sera sensitized-humRBL-2H3 cells, but not when treated with non-allergic sera. Most notably, equivalent IgE-binding and degranulation were observed with both proDerp1αS construct and native Der p 1 when using purified basophils from sensitized patients. However, proDerp1αS did not cause any cytotoxic effect on these cells, apparently due to its lack of internalization after their surface IgE-binding, showing the complex in vivo panorama governing allergic reactions. In conclusion, herein we present proDerp1αS as a proof of concept for a potential and alternative new designs of therapeutic tools for allergies. Development of new, and more specific, second-generation of immunotoxins following proDerp1αS, is further discussed.

7

Para la alergia alimentaria, ¿inmunoterapia oral o sublingual?

Sublingual immunotherapy for food allergy and its future directions.

Schworer SA, Kim EH

Immunotherapy. 2020;12(12):921-931. doi:10.2217/imt-2020-0123.

ABSTRACT

Food allergy is an important medical problem with increasing prevalence throughout the world. Different approaches of food immunotherapy are being investigated including oral, epicutaneous and sublingual routes. Sublingual immunotherapy (SLIT) for food allergy involves placement of glycerinated allergen under the tongue daily to achieve allergen-specific desensitization. SLIT has been studied in the treatment of hazelnut, peach, apple, milk and peanut allergies with substantial focus on the treatment of peanut allergy. Phase II studies have shown SLIT for treatment of peanut allergy increases the tolerated dose of peanut by a substantial margin with fewer and less severe side effects than other modalities. This review discusses the mechanisms of SLIT, early studies of its use in food allergy and larger randomized controlled trials for treatment of peanut allergy. Future directions using the mechanisms involved in SLIT include oral mucosal immunotherapy for peanut allergy.

8

ITA en pacientes más mayores: ¿Qué pasa a largo plazo?

Long-term efficacy of injected allergen immunotherapy for treatment of grass pollen allergy in elderly patients with allergic rhinitis.

Bozek A, Cudak A, Walter Canonica G

Allergy Asthma Proc. 2020;41(4):271-277. doi:10.2500/aap.2020.41.200035.

BACKGROUND

The effect of prolonged allergen immunotherapy is still insufficiently known, especially in elderly patients.

OBJECTIVE

The effect after a 3-year course of injected allergen-specific immunotherapy (AIT) for grass pollen allergy in elderly patients with allergic rhinitis was observed.

METHODS

Thirty-eight elderly patients (mean ± standard deviation, 66.2 ± 2.7 years old) who received preseasonal injected AIT or placebo for grass pollen allergy were monitored for 3 years and compared with a placebo group. The combined symptom medication score (CSMS), serum level of immunoglobulin G4 (IgG4) to phleum pratense 5 (Phl p5) and quality of life were assessed immediately after AIT and 3 years later.

RESULTS

After AIT, the CSMS was significantly decreased from 2.15 (range, 1.27-3.00) to 1.13 (range, 0.79-1.36) ($p = 0.03$) and remained lower (1.41 ± 0.72 versus 2.41 ± 1.11) than that in the placebo group during the 3 years after AIT. Serum-specific IgG4 against increased during the course of AIT and remained at a high level during further observation. Quality of life, based on the Rhinoconjunctivitis Quality of Life Questionnaire, was significantly decreased in the patients who received AIT from 1.51 (95% confidence interval [CI], 1.21-1.84) to 1.01 (95% CI, 0.93-1.87) ($p < 0.05$) and was decreased to 0.97-1.26 (95% CI, 0.88-1.82) during the 3 years after discontinuation of AIT.

CONCLUSION

A prolonged positive effect after AIT for grass pollen allergy was observed in elderly patients with allergic rhinitis. Further trials are needed to confirm this effect.Clinical trial MC56871/12.

9

Los alérgicos al huevo necesitan estrategias terapéuticas más seguras.

Egg Allergy: Diagnosis and Immunotherapy.

Dona DW, Suphioglu C

Int J Mol Sci. 2020;21(14):E5010.

ABSTRACT

Hypersensitivity or an allergy to chicken egg proteins is a predominant symptomatic condition affecting 1 in 20 children in Australia; however, an effective form of therapy has not yet been found. This occurs as the immune system of the allergic individual overreacts when in contact with egg allergens (egg proteins), triggering a complex immune response. The subsequent instantaneous inflammatory immune response is characterized by the excessive production of immunoglobulin E (IgE) antibody against the allergen, T-cell mediators and inflammation. Current allergen-specific approaches to egg allergy diagnosis and treatment lack consistency and therefore pose safety concerns among anaphylactic patients. Immunotherapy has thus far been found to be the most efficient way to treat and relieve symptoms, this includes oral immunotherapy (OIT) and sublingual immunotherapy (SLIT). A major limitation in immunotherapy, however, is the difficulty in preparing effective and safe extracts from natural allergen sources. Advances in molecular techniques allow for the production of safe and standardized recombinant and hypoallergenic egg variants by targeting the IgE-binding epitopes responsible for clinical allergic symptoms. Site-directed mutagenesis can be performed to create such safe hypoallergens for their potential use in future methods of immunotherapy, providing a feasible standardized therapeutic approach to target egg allergies safely.

10

Alergia y nuevas tecnologías: un avance muy necesario.

Digital technologies for an improved management of respiratory allergic diseases: 10 years of clinical studies using an online platform for patients and physicians.

Salvatore Tripodi, Andrea Giannone, Ifigenia Sfika, Simone Pelosi, Stephanie Dramburg, Annamaria Bianchi, Antonio Pizzulli, Jakob Florack, Valeria Villella, Ekaterina Potapova, Paolo Maria Matricardi

Italian Journal of Pediatrics (2020) 46:105. https://doi.org/10.1186/s13052-020-00870-z.

BACKGROUND

Digital health technologies carry the great potential of assisting physicians in making well-informed diagnostic and therapeutic decisions. In allergy care, electronic clinical diaries have been recently used to prospectively collect patient data and improve diagnostic precision.

OBJECTIVE

This review summarizes the clinical and scientific experience we gathered over 10 years of using a digital platform for patients suffering from seasonal allergic rhinitis.

METHODS

The mobile application and back-office of AllergyMonitor (TPS software production, Rome, Italy) enable patients to record their daily allergy symptoms as well as drug and immunotherapy intake plus possible side effects in a customizable way. The results can be accessed by the patient and attending physician as concise reports via a smartphone or computer. This technology has been used in several clinical studies and routine practice since 2009.

RESULTS

Our studies showed that A) the etiological diagnosis of SAR may be supported by matching prospectively registered symptoms with pollen counts; B) it is possible to perform a short-term prediction of SAR-symptoms at individual level; C) the adherence to daily symptom monitoring can remain high (> 80%) throughout several weeks when prescribed and thoroughly explained by the treating doctor; D) the use of mobile technology can improve adherence to symptomatic drugs as well as allergen-specific immunotherapy and E) the choice of the correct symptom-severity-score is critical at patient level, but not at group level.

CONCLUSION

The studies and clinical practice based on the use of AllergyMonitor have proven the reliability and positive impact of a digital platform including an electronic diary (eDiary) on the diagnostic precision of SAR in poly-sensitized patients as well as patient adherence to both, drug therapy and allergen immunotherapy.

1

Las “ómicas” en la inmunoterapia con alérgenos.

Exploring novel systemic biomarker approaches in grass-pollen sublingual immunotherapy using omics.

Barker-Tejeda TC, Bazire R, Obeso D et al

Allergy. 2020;10.1111/all.14565. doi:10.1111/all.14565. [Epub ahead of print]

ARTÍCULO DESTACADO

BACKGROUND

Sublingual allergen-specific immunotherapy (SLIT) intervention improves the control of grass pollen allergy by maintaining allergen tolerance after cessation. Despite its widespread use, little is known about systemic effects and kinetics associated to SLIT, as well as the influence of the patient sensitization phenotype (Mono- or Poli-sensitized). In this quest, omics sciences could help to gain new insights to understand SLIT effects.

METHODS

47 grass-pollen-allergic patients were enrolled in a double-blind, placebo-controlled, multicenter trial using GRAZAX® during 2 years. Immunological assays (sIgE, sIgG4 and ISAC) were carried out to 31 patients who finished the trial. Additionally, serum and PBMCs samples were analyzed by metabolomics and transcriptomics, respectively. Based on their sensitization level, 22 patients were allocated in Mono or Poli-sensitized groups, excluding patients allergic to epithelia. Individuals were compared based on their treatment (Active/Placebo) and sensitization level (Mono/Poli).

RESULTS

Kinetics of serological changes agreed with those previously described. At two years of SLIT, there are scarce systemic changes that could be associated to improvement in systemic inflammation. Poli-sensitized patients presented a higher inflammation at inclusion, while Mono-sensitized patients presented a reduced activity of mast cells and phagocytes as an effect of the treatment.

CONCLUSIONS

The most relevant systemic change detected after two years of SLIT was the desensitization of effector cells, which was only detected in Mono-sensitized patients. This change may be related to the clinical improvement, as previously reported, and, together with the other results, may explain why clinical effect is lost if SLIT is discontinued at this point.

2

¿Cómo son los pacientes españoles alérgicos al veneno de abeja?

Api m 6 and Api m 10 as Major Allergens in Patients with Honeybee Venom Allergy.

Vega-Castro A, Rodríguez-Gil D, Martínez-Gomariz M, Gallego R, Peña MI, Palacios R

J Investig Allergol Clin Immunol. 2020;0. doi:10.18176/jiaci.0639 [Epub ahead of print].

BACKGROUND

Component resolved diagnosis can be very valuable for the diagnosis and treatment of honeybee venom allergy (HVA) patients. Our aim is to study whether any of the allergens not included in the usual diagnostic platforms are relevant in our population.

METHODS

The allergenic sensitization profile of Spanish patients who suffered a systemic reaction after a honeybee sting and were diagnosed with HVA was studied by immunoblotting using raw autochthonous Apis mellifera venom obtained and characterized by SDS-PAGE and mass spectrometry and with a commercial assay (ImmunoCAP).

RESULTS

Allergens described in the International Union of Immunological Societies (IUIS) database were detected in the A. mellifera raw venom extract used, except Api m 12. Sera from 51 patients with a median age of 46.2 years (interquartile range 35.6-54.6) were analyzed. Api m 1 and Api m 10 were detected as major allergens (88.2% and 74.5% respectively) using ImmunoCAP. Moreover, Api m 6 (85.4%) was found by immunoblotting.

CONCLUSION

Api m 1, Api m 6 and Api m 10 are major A. mellifera venom allergens recognized in our population.

3

Se vislumbran nuevas formulaciones en el horizonte

Formulations for Allergen Immunotherapy in Human and Veterinary Patients: New Candidates on the Horizon.

Pali-Schöll I, DeBoer DJ, Alessandri C, Seida AA, Mueller RS, Jensen-Jarolim E

Front Immunol. 2020;11:1697. Published 2020 Aug 4. doi:10.3389/fimmu.2020.01697.

ABSTRACT

Allergen immunotherapy is currently the only causal treatment for allergic diseases in human beings and animals. It aims to re-direct the immune system into a tolerogenic or desensitized state. Requirements include clinical efficacy, safety, and schedules optimizing patient or owner compliance. To achieve these goals, specific allergens can be formulated with adjuvants that prolong tissue deposition and support uptake by antigen presenting cells, and/or provide a beneficial immunomodulatory action. Here, we depict adjuvant formulations being investigated for human and veterinary allergen immunotherapy.

4

El eterno debate en ITA con venenos: ¿qué pauta elegir?

Comparison of the Safety Profiles of 3 Different Hymenoptera Venom Immunotherapy Protocols: A Retrospective 2-Center Study of 143 Patients.

Pospischil IM, Kagerer M, Cozzio A et al
Int Arch Allergy Immunol. 2020;1-7. doi:10.1159/000509187 [Epub ahead of print].

INTRODUCTION
Venom immunotherapy (VIT) is highly effective and the treatment of choice for patients with a history of systemic anaphylactic reactions to a Hymenoptera sting. It has been assumed that VIT protocols with a rapid dose increase during the induction phase are associated with a higher frequency of systemic reactions (SR); however, study data addressing this issue are conflicting.
OBJECTIVE
The aim of this study was to compare the safety of 3 different Hymenoptera VIT protocols (half-day ultra-rush, 3-day rush, 3-week cluster).
METHODS
This retrospective 2-center study included 143 Hymenoptera venom-allergic patients, who underwent 147 VIT procedures during the years 2015-2018. Twenty cluster, 75 rush, and 52 ultra-rush VIT protocols were performed with honeybee (54 protocols) and wasp (93 protocols) venom. All documented side effects were classified into large local and SR (Ring and Messmer classification).
RESULTS
SR were observed during 11 (7.5%) VIT procedures and did not exceed severity grade II. SR occurred more frequently in cluster compared to accelerated protocols. This result was observed for both honeybee (cluster: 25%, rush: 8.7%, and ultra-rush: 15.8%) and wasp VIT (cluster: 12.5%, rush: 0%, and ultra-rush: 6.1%), though the differences were statistically significant only in the wasp VIT subgroup. Honeybee venom elicited more SR than wasp venom (14.8 and 3.2%, respectively, p = 0.01). The risk for SR did not depend on age, sex, concomitant antihypertensive medication, hypertryptasemia, or severity of the index sting reaction.
CONCLUSION
Accelerated VIT protocols, namely, rush and ultra-rush protocols are safe therapeutic options for Hymenoptera venom-allergic patients and displayed fewer SR than cluster VIT protocols in our study.

5

La perspectiva del paciente alérgico al cacahuete.

Improvements in Quality of Life in Children Following Epicutaneous Immunotherapy. (EPIT) for Peanut Allergy in the PEPITES and PEOPLE Studies.

DunnGalvin A, Fleischer DM, Campbell DE et al
J Allergy Clin Immunol Pract. 2020;S2213-2198(20)30831-X. doi:10.1016/j.jaip.2020.08.015 [Epub ahead of print]

BACKGROUND
Food allergy quality of life (FAQL) is impaired in children with peanut allergy. Food Allergy Quality of Life Questionnaires (FAQLQs) provide disease-specific insight into the burden of peanut allergy and potential FAQL changes following peanut immunotherapy.
OBJECTIVE
To examine FAQL changes in children following treatment with epicutaneous immunotherapy (EPIT) for peanut allergy (250μg, daily epicutaneous peanut protein; DBV712 250μg).
METHODS
FAQL was prospectively measured using the FAQLQ parent proxy form (FAQLQ-PF, for children aged ≤12 years) and child form (FAQLQ-CF, child rated if aged ≥8 years) during the 12-month double-blind, randomized, controlled PEPITES trial and the initial 12 months of the open-label PEOPLE follow-up study. Data were analyzed for between-group differences after treatment unblinding.
RESULTS
FAQLQ from placebo participants (-PF: 96; -CF: 47) and treatment group participants (-PF: 209; -CF: 105) were analyzed. Twenty-four-month global FAQL scores (FAQLQ-PF/CF) were significantly improved in the treatment versus placebo group (least squares [LS] mean 0.34, P=0.008 and 0.46, P=0.023, respectively). At 24 months, there was significant FAQLQ-PF score improvement in participants initially randomized to treatment who met the efficacy primary endpoint (n=74, LS mean 0.55, P<0.001) and in participants with any eliciting dose increase (n=127, LS mean 0.66, P<0.001). FAQLQ-PF improvements were observed in social dietary limitations (P=0.002), food-related anxiety (P=0.029), and emotional impact (P=0.048) domains. FAQLQ-CF improvements were observed in risk of accidental exposure (P=0.002) and allergen avoidance (P=0.04) domains. Nearly all outcomes met a non-treatment context MCID previously cited for FAQLQ.
CONCLUSION
EPIT treatment was observed to be associated with significant global and domain-specific FAQL improvement (FAQLQ-PF/-CF), largely driven by increases in eliciting dose, in children with peanut allergy.

6

Probióticos y alergia.

Probiotics function and modulation of the immune system in allergic diseases.

Eslami M, Bahar A, Keikha M, Karbalaei M, Kobyliak NM, Yousefi B
Allergol Immunopathol (Madr). 2020;S0301-0546(20)30113-0. doi:10.1016/j.aller.2020.04.005

ABSTRACT
Allergic diseases have been a global problem over the past few decades. The effect of allergic diseases on healthcare systems and society is generally remarkable and is considered as one of the most common causes of chronic and hospitalized disease. The functional ability of probiotics to modulate the innate/acquired immune system leads to the initiation of mucosal/systemic immune responses. Gut microbiota plays a beneficial role in food digestion, development of the immune system, control/growth of the intestinal epithelial cells and their differentiation. Prescribing probiotics causes a significant change in the intestinal microflora and modulates cytokine secretion, including networks of genes, TLRs, signaling molecules and increased intestinal IgA responses. The modulation of the Th1/Th2 balance is done by probiotics, which suppress Th2 responses with shifts to Th1 and thereby prevent allergies. In general, probiotics are associated with a decrease in inflammation by increasing butyrate production and induction of tolerance with an increase in the ratio of cytokines such as IL-4, IL-10/IFN-γ, Treg/TGF-β, reducing serum eosinophil levels and the expression of metalloproteinase-9 which contribute to the improvement of the allergic disease's symptoms. Finally, it can be said that the therapeutic approach to immunotherapy and the reduction of the risk of side effects in the treatment of allergic diseases is the first priority of treatment and the final approach that completes the first priority in maintaining the condition and sustainability of the tolerance along with the recovery of the individual.

7

ITO con leche: ¿la más peligrosa?

Patient Characteristics and Risk Factors for Home Epinephrine-Treated Reactions During Oral Immunotherapy for Food Allergy.

Nachshon L, Schwartz N, Tsviban L et al

J Allergy Clin Immunol Pract. 2020;S2213-2198(20)30744-3. doi:10.1016/j.jaip.2020.07.034 [Epub ahead of print]

BACKGROUND

Oral immunotherapy (OIT) is effective in desensitizing food-allergic patients but adverse events limit its applicability.

OBJECTIVE

To identify risk factors for home epinephrine-treated reactions during the build-up phase of OIT.

METHODS

A retrospective cohort study of patients older than 3.7 years undergoing OIT for food allergy at Shamir Medical Center between April 2010 and March 2019. All patients with a final disposition of full desensitization, partial desensitization, or failure were analyzed. Risk factors and outcome of home epinephrine-treated reactions were examined.

RESULTS

A total of 1037 patients (mean age, 8.4 years) who underwent 1100 OIT treatments (milk, n = 710; peanut, n = 213; egg, n = 50; sesame, n = 57; and tree nuts, n = 70) reached a final disposition and were analyzed. Full desensitization was achieved in 763 (69.4%) treatments, partial desensitization in 219 (19.9%), and 118 (10.7%) failed. Epinephrine was administered to 121 patients (11.7%) during 10.8% of treatments. Milk OIT was a significant risk factor both for epinephrine-treated reactions (odds ratio, 2.15; 95% CI, 1.25-3.68) and for low rate of full desensitization following such reactions compared with nonmilk OIT (18.2% vs 73.9%, respectively; P < .0001). Risk factors during milk OIT included asthma, pre-OIT reaction severity, lower tolerated dose, and epinephrine-treated reactions during clinic updosing, whereas risk factors during nonmilk OIT were male sex and lower tolerated dose.

CONCLUSIONS

Milk OIT poses a significant risk for home epinephrine-treated reactions during OIT and for poor outcome following such reactions. Together with the additional risk factors described for both milk and nonmilk OIT, this information may assist in patient selection for treatment.

8

¿Qué ocurre durante la ITO con cacahuete?

Transcriptional changes in peanut-specific CD4+ T cells over the course of oral immunotherapy.

Wang W, Lyu SC, Ji X et al

Clin Immunol. 2020;219:108568. doi:10.1016/j.clim.2020.108568 [Epub ahead of print]

ABSTRACT

Oral immunotherapy (OIT) can successfully desensitize allergic individuals to offending foods such as peanut. Our recent clinical trial (NCT02103270) of peanut OIT allowed us to monitor peanut-specific CD4+ T cells, using MHC-peptide Dextramers, over the course of OIT. We used a single-cell targeted RNAseq assay to analyze these cells at 0, 12, 24, 52, and 104 weeks of OIT. We found a transient increase in TGFβ-producing cells at 52 weeks in those with successful desensitization, which lasted until 117 weeks. We also performed clustering and identified 5 major clusters of Dextramer+ cells, which we tracked over time. One of these clusters appeared to be anergic, while another was consistent with recently described TFH13 cells. The other 3 clusters appeared to be Th2 cells by their coordinated production of IL-4 and IL-13, but they varied in their expression of STAT signaling proteins and other markers. A cluster with high expression of STAT family members also showed a possible transient increase at week 24 in those with successful desensitization. Single cell TCRαβ repertoire sequences were too diverse to track clones over time. Together with increased TGFβ production, these changes may be mechanistic predictors of successful OIT that should be further investigated.

9

China y sus pólenes.

Artemisia annua- sublingual immunotherapy: first step to cross the chasm.

Xian M, Zhang L

Allergy. 2020;10.1111/all.14539. doi:10.1111/all.14539 [Epub ahead of print]

BACKGROUND

Artemisia annua is an important autumnal pollen allergen for seasonal allergic rhinitis (SAR) in northern China. To date, no study has investigated allergen immunotherapy with A annua. We aimed to investigate the efficacy and mechanisms underlying A annua-sublingual immunotherapy (SLIT).

METHODS

This was a randomized, double-blind, placebo-controlled phase III clinical trial involving 71 SAR patients, randomized to SLIT with A annua extract (n = 47) or placebo (n = 24) for 32 weeks. Total nasal symptom score (TNSS; primary clinical end point) was evaluated at baseline (peak pollen phase (PPP) in the previous year), initiation of A annua-SLIT, 1st PPP during SLIT, end of SLIT and 2nd PPP during follow-up. Blood samples and nasal secretions were collected at beginning and after SLIT for assessment of T cells and inflammatory mediators. Safety was assessed according to adverse events (AEs) reported.

RESULTS

Artemisia annua-SLIT significantly reduced TNSS to a greater level from baseline (from 9.45 ± 1.68 to 6.16 ± 2.27) than placebo (from 9.29 ± 2.09 to 9.05 ± 2.40) at the 1st PPP (P < .001) and sustained the improvement in symptoms throughout to the 2nd PPP. Preseasonal A annua-SLIT for 16 weeks significantly decreased Th2 cells, increased nTreg and Tr1 cells in blood; and increased cystatin 1 (CST1) in nasal secretion after 16 and 32 weeks compared with pretreatment. Overall, 17/47 patients experienced mild local AEs and 2 patients mild systemic AEs, after A annua-SLIT.

CONCLUSION

Artemisia annua-SLIT is an efficacious and safe treatment in patients with A annua SAR.

10

¿Quién es el rival más fuerte? ¿Y el más débil?

Therapeutic perspectivs in food allergy.

Francesco Marcucci, Chiara Isidori, Alberto Argentiero, Cosimo Neglia, Susanna Espósito

Transl Med. 2020 Aug 5;18(1):302. doi: 10.1186/s12967-0200-02466-x.

BACKGROUND

In the last twenty years, several studies have been conducted in the search for new therapeutic strategies in patients with food allergy; in particular, after the failure of injection immunotherapy, three different routes of administration, oral immunotherapy (OIT), sublingual immunotherapy (SLIT), and epicutaneous immunotherapy (EPIT), have been teste. The aim of this manuscript is to review OIT, SLIT and EPIT clinical trials on food allergies and to suggest advantages an limits of the different routes of immunotherapy administration.

MAIN BODY

Of the three different routes of immunotherapy used in the treatment of food allergy, OIT is, at present, the only one actually able to induce an increase in tolerance in the majority of patients. However, its use is affected by serious secondary effects, such as major abdominal symptoms and anaphylaxis. The combination with omalizumab reduces the percentage of serious side effects. There are not many studies with SLIT for food allergy, but they have nevertheless shown that it is possible to obtain an increase in tolerance; however, this increase is modest in comparison with that obtained by OIT. EPIT, performed through the diffusion of allergens on intact skin, is the most recent form of immunotherapy. Although there are many works on EPIT carried out in laboratory animals, only few clinical studies have been published in humans. EPIT, unlike OIT and SLIT, is not responsible for systemic secondary effects such as anaphylaxis and eosinophilic oesophagitis but only for local an mild effects in areas where the devices are applied. Moreover, EPIT is characterized by high patient adherence.

CONCLUSION

OIT seems to have a prevalent application in patients who do not report previous symptoms of systemic or gastroenteric anaphylaxis, while SLIT and EPIT, in particular, could be more preferentially used in patients with a risk of anaphylaxis.

1

Estudios de ITSL y asma: seriedad, por favor.

Sublingual immunotherapy for asthma.

Fortescue R, Kew KM, Leung MST

Cochrane Database Syst Rev 2020 Sep 14;9:CD011293.

ARTÍCULO DESTACADO

BACKGROUND

Asthma is a common long-term respiratory disease affecting approximately 300 million people worldwide. Approximately half of people with asthma have an important allergic component to their disease, which may provide an opportunity for targeted treatment. Sublingual immunotherapy (SLIT) aims to reduce asthma symptoms by delivering increasing doses of an allergen (e.g. house dust mite, pollen extract) under the tongue to induce immune tolerance. Fifty-two studies were identified and synthesised in the original Cochrane Review in 2015, but questions remained about the safety and efficacy of sublingual immunotherapy for people with asthma.

OBJECTIVES

To assess the efficacy and safety of sublingual immunotherapy compared with placebo or standard care for adults and children with asthma.

AUTHORS' CONCLUSIONS

Despite continued study in the field, the evidence for important outcomes such as exacerbations and quality of life remains too limited to draw clinically useful conclusions about the efficacy of SLIT for people with asthma. Trials mostly recruited mixed populations with mild and intermittent asthma and/or rhinitis and focused on non-validated symptom and medication scores. The review findings suggest that SLIT may be a safe option for people with well-controlled mild-to-moderate asthma and rhinitis who are likely to be at low risk of serious harm, but the role of SLIT for people with uncontrolled asthma requires further evaluation.

2

Las tabletas de ácaros dan un paso adelante.

A 300°IR sublingual tablet is an effective, safe treatment for house-dust-mite-induced allergic rhinitis: an international, double-blind, placebo-controlled, randomized Phase III clinical trial.

Demoly P, Corren J, Creticos P, De Blay F, Gevaert P, Hellings P, Kowal K, Le Gall M, Nenasheva N, Passalacqua G, Pfaar O, Tortajada-Girbés M, Vidal C, Worm M, Casale TB

J Allergy Clin Immunol. 2020 Sep 2;S0091-6749(20)31221-5. doi: 10.1016/j.jaci.2020.07.036. [Online ahead of print]

BACKGROUND

Allergic rhinitis (AR) induced by house dust mites (HDMs) is a highly prevalent but often underdiagnosed and undertreated/untreated chronic disease. It often has a negative impact on sleep, work, leisure activities, and health-related quality of life. Allergen immunotherapy is a proven, safe treatment for respiratory allergies.

OBJECTIVE

To assess the efficacy and safety of a 300 index of reactivity (IR) sublingual tablet formulation of Dermatophagoides pteronyssinus: Dermatophagoides farinae 1:1 extract in adolescents (aged ≥12) and adults with moderate-to-severe HDM-induced AR.

METHODS

In a Phase III, international, double-blind, placebo-controlled, randomized clinical trial, participants received approximately 12 months of treatment with placebo or the 300°IR tablet. The primary endpoint was the average total combined score (aTCS) during 4 weeks at the end of the treatment period.

RESULTS

1,607 participants were randomized, and 1,476 (including 555 (37.6%) with concomitant mild controlled asthma at inclusion) comprised the full analysis set. Over the primary evaluation period, the least squares mean aTCS in the 300°IR group (3.62) was significantly lower ($p<0.0001$) than in the placebo group (4.35), with a relative least squares mean difference of -16.9% [95% confidence interval: -24.0%; -9.2%]. All pre-specified secondary endpoints were consistently improved in the 300°IR group, relative to placebo. The 300°IR tablet was generally well tolerated. Treatment-related adverse events (mainly mild or moderate local reactions) were reported for 51.0% of the patients in the 300°IR group and 14.9% in the placebo group.

CONCLUSION

The 300°IR sublingual HDM tablet is an effective, safe treatment for HDM-induced AR. (NCT02443805, EudraCT 2014-004223-46) CLINICAL IMPLICATIONS: A 300 index of reactivity sublingual tablet formulation of Dermatophagoides pteronyssinus: Dermatophagoides farinae extract is a safe, effective treatment for moderate-to-severe house-dust-mite-induced allergic rhinitis.

3

Vía intradérmica: ¿ha venido para quedarse?

Intradermal Phleum pratense allergoid immunotherapy. Double-blind, randomised, placebo-controlled trial.

Sola Martínez FJ, Barranco Jiménez RM, Martín García C et al

Clin Exp Allergy 2020 Sep 18. doi: 10.1111/cea.13740. [Online ahead of print].

BACKGROUND

In allergology, the intradermal approach is generally used to establish an etiological diagnosis, with limited experience in specific allergen immunotherapy.

OBJECTIVE

To evaluate the efficacy and safety of immunotherapy with an allergen extract of glutaraldehyde-polymerised Phleum pratense, administered intradermally, in patients with rhinoconjunctivitis sensitized to grass pollen.

METHODS

Multicentre, randomised, double-blind, placebo-controlled clinical trial in patients from 12 to 65 years of age with rhinitis or rhinoconjunctivitis, with or without asthma, due to grass pollen allergy. Patients were divided into three groups and received a total of 6 doses in a weekly interval, of either placebo; 0.03 μg or 0.06 μg of protein per dose of Phleum pratense allergoid. The primary objective was to evaluate the combined symptoms and medication consumption score (CSMS). The secondary objectives were symptoms and medication, tolerance to the conjunctival provocation test, specific IgE and IgG4 antibodies and the safety profile according to the WAO scale.

RESULTS

The dose of 0.06 μg of protein proved to be effective versus the placebo by significantly reducing CSMS and increasing tolerance to the allergenic extract in the conjunctival provocation test, after the first pollen season. This group showed a significant reduction in specific IgE after the second pollen season relative to the baseline. There were no variations in IgG4 levels. Only one grade 2 systemic reaction was recorded.

CONCLUSIONS & CLINICAL RELEVANCE

Intradermal immunotherapy with P. pratense allergoid has been shown to be effective and safe, reducing CSMS, increasing tolerance to the conjunctival provocation test and reducing IgE levels.

4

En la alergia al cacahuete, (de momento) toda idea es buena.

Study protocol of a multicentre, randomised, controlled trial evaluating the effectiveness of probiotic and peanut oral immunotherapy (PPOIT) in inducing desensitisation or tolerance in children with peanut allergy compared with oral immunotherapy (OIT) alone and with placebo (the PPOIT-003 study).

Lozinsky AC, Loke P, Orsini F et al

BMJ Open 2020 Sep 9;10(9):e035871. doi: 10.1136/bmjopen-2019-035871.

INTRODUCTION

Peanut allergy is the the most common cause of life-threatening food-induced anaphylaxis. There is currently no effective long-term treatment. There is a pressing need for definitive treatments that improve the quality of life and prevent fatalities. Allergen oral immunotherapy (OIT) is a promising approach, which is effective at inducing desensitisation; however, OIT has a limited ability to induce sustained unresponsiveness (SU). We have previously shown that a novel treatment comprising a combination of the probiotic Lactobacillus rhamnosus CGMCC 1.3724 with peanut OIT (Probiotic Peanut Oral ImmunoTherapy (PPOIT)) is highly effective at inducing SU, with benefit persisting to 4 years after treatment cessation in the majority of initial treatment responders. Here we describe the protocol for a Phase IIb multicentre, double-blind, randomised, controlled trial (PPOIT-003) with dual primary objectives to evaluate the effectiveness of PPOIT at inducing SU (assessed at 8 weeks after treatment cessation) compared with placebo treatment and peanut OIT alone, in children with peanut allergy.

METHODS AND ANALYSIS

200 children 1 to 10 years of age with current peanut allergy confirmed by failed double-blind placebo-controlled food challenge (DBPCFC) at study screening will be recruited from three tertiary paediatric hospitals in Australia. There are three intervention arms-PPOIT, peanut OIT alone or placebo. Interventions are administered once daily for 18 months. The dual primary outcomes are: (1) the proportion of children who attain 8-week SU in the PPOIT group versus placebo group and (2) the proportion of children who attain 8-week SU in the PPOIT group versus OIT group.

ETHICS AND DISSEMINATION

This study has been approved by the Human Research Ethics Committees at the Royal Children's Hospital (HREC 35246) and the Child and Adolescent Health Service (RGS 2543). Results will be published in peer-reviewed journals and disseminated via presentations at international conferences.

5

¿Son los metaanálisis la panacea?

Sublingual Immunotherapy versus Placebo in the Management of Grass Pollen-Induced Allergic Rhinitis in Adults: A Systematic Review and Meta-analysis.

Boldovjáková D, Cordoni S, Fraser CJ, Love AB, Patrick L, Ramsay GJ, Ferguson ASJ, Gomati A, Ram B

Clin Otolaryngol 2020 Sep 26. doi: 10.1111/coa.13651. [Online ahead of print].

INTRODUCTION

Allergic rhinitis (AR) is a common inflammatory condition of the nasal mucosa affecting approximately 20% of the population worldwide. Current therapies include intranasal antihistamines, corticosteroids, subcutaneous and sublingual immunotherapy (SLIT). This review and meta-analysis assesses the efficacy of SLIT in the management of grass pollen-induced AR in adults.

METHODS

Ovid EMBASE, Ovid EBM Reviews, Cochrane Central Register of Controlled Trials, Ovid MedLine and PubMed were searched using the following terms: 'sublingual immunotherapy', 'SLIT', 'rhinitis', 'allergic rhinitis', 'rhinosinusitis' and 'rhino-conjunctivitis'. All included studies were double-blind, placebo-controlled and randomised trials. Primary outcome was symptom score and secondary outcome included quality of life and safety profile. Meta-analysis of symptom improvement was carried out.

RESULTS

Six studies were identified with 979 subjects randomly allocated to SLIT and 992 to a placebo control. All studies reported an improvement in symptoms with SLIT, with five reaching statistical significance ($p < 0.05$). Four studies reported statistically significant improvement in quality of life ($p < 0.05$). Oral pruritus was the most common adverse event reported. The overall risk of bias was high in 50% of the studies.

CONCLUSIONS

SLIT was a safe and effective treatment for grass pollen-induced AR in adults and therefore consideration should be given to its use for moderate-to-severe disease in the UK wide population.

6

Cómo predecir la seguridad de la SLIT.

Risk Factors for Safety of Allergen-Specific Sublingual Immunotherapy in Children with Allergic Rhinitis.

Liu W, Zeng Q, Yan S, Sun C, Tang Y, Luo R

Int Arch Allergy Immunol 2020 Sep 16;1-7. doi: 10.1159/000508523. [Online ahead of print]

ABSTRACT

A good compliance often attributes to good efficacy and safety of sublingual immunotherapy (SLIT). However, few studies have been conducted on the safety of SLIT treatment in children. We aimed to confirm the pretreatment parameters to predict the safety in children who underwent SLIT. 601 children with allergic rhinitis (AR) treated with SLIT were enrolled in this study. Baseline clinical information and laboratory parameters were collected. The clinical response and adverse events (AEs) were recorded and evaluated. A multivariate logistic regression model was established to confirm the predictors for AEs. The AEs were reported in 75 children (13.8%). The serum-specific IgE (s-IgE) level was significantly correlated with the occurrence of AEs by multivariate logistic regression analysis. Our receiver operating characteristic (ROC) analysis of the serum s-IgE levels >21.6 IU/mL had the best sensitivity (83.7%) and specificity (76.7%) to predict safety. The serum s-IgE level was significantly correlated with safety of SLIT in children, which may be helpful for patient selection before SLIT.

7

A cada paciente, lo suyo.

Personalized Medicine for allergy treatment: allergen immunotherapy still a unique and unmatched model.

Incorvaia C, Al-Ahmand M, Ansótegui I et al

Allergy. 2020 Sep 1. doi: 10.1111/all.14575. [Online ahead of print].

ABSTRACT

The introduction of personalized medicine (PM) has been a milestone in the history of medical therapy, because it has revolutionized the previous approach of treating the disease with that of treating the patient. It is known today that diseases can occur in different genetic variants, making specific treatments of proven efficacy necessary for a given endotype. Allergic diseases are particularly suitable for PM, because they meet the therapeutic success requirements, including a known molecular mechanism of the disease, a diagnostic tool for such disease, and a treatment blocking the mechanism. The stakes of PM in allergic patients are molecular diagnostics, to detect specific IgE to single allergen molecules and to distinguish the causative molecules from those merely cross-reactive, pursuit of patient's treatable traits addressing genetic, phenotypic and psychosocial features, and omics, such as proteomics, epi-genomics, metabolomics and breathomics, to forecast patient's responsiveness to therapies, to detect biomarker and mediators, and verify the disease control. This new approach has already improved the precision of allergy diagnosis and is likely to significantly increase, through the higher performance achieved with the personalized treatment, the effectiveness of allergen immunotherapy by enhancing its already known and unique characteristics of treatment that acts on the causes.

8

Cambio de panorama diagnóstico y terapéutico.

Biomarkers for diagnosis and prediction of therapy responses in allergic diseases and asthma.

Breitender H, Peng, YQ, Agache I et al

Allergy. 2020 Sep 7. doi: 10.1111/all.14582. [Online ahead of print].

ABSTRACT

Modern health care requires a proactive and individualized response to diseases, combining precision diagnosis and personalized treatment. Accordingly, the approach to patients with allergic diseases encompasses novel developments in the area of personalized medicine, disease phenotyping and endotyping, and the development and application of reliable biomarkers. A detailed clinical history and physical examination followed by the detection of IgE immunoreactivity against specific allergens still represents the state of the art. However, nowadays, further emphasis focuses on the optimization of diagnostic and therapeutic standards and a large number of studies have been investigating the biomarkers of allergic diseases, including asthma, atopic dermatitis, allergic rhinitis, food allergy, urticaria and anaphylaxis. Various biomarkers have been developed by omics technologies, some of which lead to a better classification of distinct phenotypes or endotypes. The introduction of biologicals to clinical practice increases the need for biomarkers for patient selection, prediction of outcomes and monitoring, to allow for an adequate choice of the duration of these costly and long-lasting therapies. Escalating healthcare costs together with questions about the efficacy of the current management of allergic diseases require further development of a biomarker-driven approach. Here, we review biomarkers in diagnosis and treatment of asthma, atopic dermatitis, allergic rhinitis, viral infections, chronic rhinosinusitis, food allergy, drug hypersensitivity and allergen immunotherapy with a special emphasis on specific IgE, the microbiome and the epithelial barrier. In addition, EAACI guidelines on biologicals are discussed within the perspective of biomarkers.

9

El futuro ya está aquí.

iTRAQ-based proteomic analysis reveals potential regulatory networks in dust mite-related asthma treated with subcutaneous allergen immunotherapy.

Bai J, Zhong JY, Liao W et al

Mol Med Rep 2020 Nov;22(5):3607-3620. doi: 10.3892/mmr.2020.11472. Epub 2020 Sep 1.

ABSTRACT

Asthma is one of the most common childhood chronic diseases worldwide. Subcutaneous immunotherapy (SCIT) is commonly used in the treatment of house dust mite (HDM)-related asthma in children. However, the therapeutic mechanism of SCIT in asthma remains unclear. The present study aimed to investigate the molecular biomarkers associated with HDM-related asthma in asthmatic children prior and subsequent to SCIT treatment compared with those in healthy children via proteomic analysis. The study included a control group (30 healthy children), -Treatment group (30 children with HDM-related allergic asthma) and +Treatment group (30 children with HDM-related allergic asthma treated with SCIT). An isobaric labeling with relative and absolute quantification-based method was used to analyze serum proteome changes to detect differentially expressed proteins, while functional enrichment and protein-protein interaction network analysis were used to select candidate biomarkers. A total of 72 differentially expressed proteins were detected in the -Treatment, +Treatment and control groups. A total of 33 and 57 differentially expressed proteins were observed in the -Treatment vs. control and +Treatment vs. control groups, respectively. Through bioinformatics analysis, 5 candidate proteins [keratin 1 (KRT1), apolipoprotein B (APOB), fibronectin 1, antithrombin III (SERPINC1) and α-1-antitrypsin (SERPINA1)] were selected for validation by western blotting; among them, 4 proteins (KRT1, APOB, SERPINC1 and SERPINA1) showed robust reproducibility in asthma and control samples. This study illustrated the changes in proteome regulation following SCIT treatment for asthma. The 4 identified proteins may serve as potential biomarkers prior and subsequent to SCIT treatment, and help elucidate the molecular regulation mechanisms of SCIT to treat HDM-related asthma.

10

Los últimos avances en el campo de la alergia y la ITA.

Mechanisms of allergen-specific immunotherapy and allergen tolerance.

Kucuksezer UC, Ozdemir C, Cevhertas L, Ogulur I, Akdis M, Akdis CA
Allergol Int. 2020 Sep 5;S1323-8930(20)30103-9. doi: 10.1016/j.alit.2020.08.002. [Online ahead of print]

ABSTRACT

Allergen-specific immunotherapy (AIT) is the mainstay treatment for the cure of allergic disorders, with depicted efficacy and safety by several trials and meta-analysis. AIT impressively contributes to the management of allergic rhinitis, asthma and venom allergies. Food allergy is a new arena for AIT with promising results, especially via novel administration routes. Cell subsets with regulatory capacities are induced during AIT. IL-10 and transforming growth factor (TGF)-β are the main suppressor cytokines, in addition to surface molecules such as cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4) and programmed cell death protein-1 (PD-1) within the micro milieu. Modified T- and B-cell responses and antibody isotypes, increased activity thresholds for eosinophils, basophils and mast cells and consequent limitation of inflammatory cascades altogether induce and maintain a state of sustained allergen-specific unresponsiveness. Established tolerance is reflected into the clinical perspectives as improvement of allergy symptoms together with reduced medication requirements and evolved disease severity. Long treatment durations, costs, reduced patient compliance and risk of severe, even life-threatening adverse reactions during treatment stand as major limiting factors for AIT. By development of purified non-allergenic, highly-immunogenic modified allergen extracts, and combinational usage of them with novel adjuvant molecules via new routes may shorten treatment durations and possibly reduce these drawbacks. AIT is the best model for custom-tailored therapy of allergic disorders. Better characterization of disease endotypes, definition of specific biomarkers for diagnosis and therapy follow-up, as well as precision medicine approaches may further contribute to success of AIT in management of allergic disorders.

1

Avanzando en la Medicina de Precisión de la alergia a himenópteros.

Precision Medicine in Hymenoptera Venom Allergy: Diagnostics, Biomarkers, and Therapy of Different Endotypes and Phenotypes.

Simon Blank, Johannes Grosch , Markus Ollert, Maria Beatrice Bilò

Front Immunol. 2020 Oct 22;11:579409. doi: 10.3389/fimmu.2020.579409

ABSTRACT

Allergic reactions to stings of Hymenoptera species may be severe and are potentially fatal deviations of the immunological response observed in healthy individuals. However, venom-specific immunotherapy (VIT) is an immunomodulatory approach able to cure venom allergy in the majority of affected patients. An appropriate therapeutic intervention and the efficacy of VIT not only depend on a conclusive diagnosis, but might also be influenced by the patient-specific manifestation of the disease. As with other diseases, it should be borne in mind that there are different endotypes and phenotypes of venom allergy, each of which require a patient-tailored disease management and treatment scheme. Reviewed here are different endotypes of sting reactions such as IgE-mediated allergy, asymptomatic sensitization or a simultaneous presence of venom allergy and mast cell disorders including particular considerations for diagnosis and therapy. Additionally, phenotypical manifestations of venom allergy, as e.g. differences in age of onset and disease severity, multiple sensitization or patients unsusceptible to therapy, are described. Moreover, biomarkers and diagnostic strategies that might reflect the immunological status of the patient and their value for therapeutic guidance are discussed. Taken together, the increasing knowledge of different disease manifestations in venom hypersensitivity and the growing availability of diagnostic tools open new options for the classification of venom allergy and, hence, for personalized medical approaches and precision medicine in Hymenoptera venom allergy.

2

¿Empezamos a hablar de células T foliculares cooperadoras y reguladoras?

Roles of follicular helper and regulatory T cells in allergic diseases and allergen immunotherapy.

Yao Y, Chen CL, Yu D, Liu Z

Allergy. 2020 Oct 24. doi: 10.1111/all.14639. [Epub ahead of print].

ABSTRACT

Allergic diseases are characterized by overactive type 2 immune responses to allergens and immunoglobulin E (IgE)-mediated hypersensitivity. Emerging evidence suggests that follicular helper T (TFH) cells, rather than type 2 T-helper (TH 2) cells, play a crucial role in controlling IgE production. However, follicular regulatory T (TFR) cells, a specialized subset of regulatory T (TREG) cells resident in B-cell follicles, restricts TFH cell-mediated help in extrafollicular antibody production, germinal center (GC) formation, immunoglobulin affinity maturation, and long-lived, high-affinity plasma and memory B-cell differentiation. In mouse models of allergic asthma and food allergy, CXCR5+ TFH cells, not CXCR5– conventional TH 2 cells, are needed to support IgE production, otherwise exacerbated by CXCR5+ TFR cell deletion. Upregulation of TFH cell activities, including a skewing toward type 2 TFH (TFH 2) and IL-13 producing TFH (TFH 13) phenotypes, and defects in TFR cells have been identified in patients with allergic diseases. Allergen immunotherapy (AIT) reinstates the balance between TFH and TFR cells in patients with allergic diseases, resulting in clinical benefits. Collectively, further understanding of TFH and TFR cells and their role in the immunopathogenesis of allergic diseases creates opportunities to develop novel therapeutic approaches.

3

La conjuntivitis alérgica también existe.

Allergic conjunctivitis in children: current understanding and future perspectives.

Vazirani J, Shukla S, Chhawchharia R, Sahu S, Gokhale N, Basu S

Curr Opin Allergy Clin Immunol. 2020 Oct;20(5):507-15.

PURPOSE OF REVIEW

The rising global burden of allergic diseases, particularly in the pediatric population, is of serious concern. Ocular allergy is one of the most common ocular pathologies met in clinical practice. A large proportion of children and adolescents suffer from allergic eye diseases (AEDs), which affect their quality of life. The available treatments and surgical modalities have their limitations and side effects. Therefore, the development of novel and alternate strategies is the need of the hour and requires a timely review of currently available knowledge.

RECENT FINDINGS

The current review covers the incidence and prevalence of AEDs, factors influencing occurrence and severity of AED (age, sex, socioeconomic status etc.), underlying mechanisms, role of allergy testing and immunotherapy in children, development of diagnostic markers and novel therapies including cells and molecules.

SUMMARY

Understanding the demographics, clinical patterns and risk factors of AED can help formulate appropriate preventive and therapeutic strategies for the effective management of this common cause of ocular morbidity. The future therapeutics for AED seems to rely primarily on cells (mesenchymal stem cells, Tregs, mast cells), cell products, molecules with immunosuppressive potential and immunotherapy.

4

ITA en niños asmáticos: las guías siguen sin ponerse de acuerdo.

Safety, Efficacy, and Preventive Role of Subcutaneous and Sublingual Allergen Immunotherapy for the Treatment of Pediatric Asthma.

Giannetti A, Ricci G, Procaccianti M, Santoro A, Caffarelli C

J Asthma Allergy. 2020;13:575-587. Published 2020 Nov 10. doi:10.2147/JAA.S234280.

ABSTRACT

Allergen-specific immunotherapy is currently the only treatment with the potential to modify and prevent progression of allergic asthma in children. In clinical practice, it is available in two forms: subcutaneous immunotherapy and sublingual immunotherapy. Trials and meta-analyses showed both the safety and the short- and long-term benefits of allergen-specific immunotherapy in asthmatic children. However, its use and role in asthma remains controversial, since studies are largely heterogeneous. This is mainly due to the lack of consensus on the optimal primary outcome to be considered for clinical trials evaluating the efficacy of allergen-specific immunotherapy in asthma. Therefore, well-conducted researchis needed using standardized and validated tools to evaluate key outcomes in asthmatic children.

5

El marco regulatorio de la ITO: Palforzia como (buen) ejemplo.

Oral Immunotherapy for Food Allergy-a US Regulatory Perspective.

Hise K, Rabin RL

Curr Allergy Asthma Rep. 2020 Oct 15;20(12):77.

ABSTRACT

The recent approval of Palforzia for treatment of peanut allergy by the US Food and Drug Administration (USFDA) predicts that additional products for oral immunotherapy (OIT) are on the horizon. In this article, the authors review the legal framework by which the USFDA regulates products for OIT of food allergy and the clinical data that demonstrated that the safety and effectiveness profile of Palforzia supported approval and conclude with a discussion of oral food challenge (OFC) as a clinical endpoint to demonstrate safety and effectiveness of OIT products.

6

Nuevos (posibles) beneficios del yogur fermentado.

Effect of Low-Immunogenic Yogurt Drinks and Probiotic Bacteria on Immunoreactivity of Cow's Milk Proteins and Tolerance Induction-In Vitro and In Vivo Studies.

Wróblewska B, Kaliszewska-Suchodoła A, Fuc E et al

Nutrients. 2020;12(11):3390. Published 2020 Nov 4. doi:10.3390/nu12113390

ABSTRACT

There is no effective therapy for milk allergy. The role of lactic acid bacteria (LAB) and probiotics in protection against allergy-related outcomes is still under investigation. The aim of the study was to evaluate the immunomodulative and therapeutic potential of yogurt drinks in cow's milk allergy (CMA) management. We compared immunoreactivity of α-casein (α-CN), β-casein (β-CN), κ-casein (κ-CN), α-lactalbumin (α-LA), and β-lactoglobulin (β-LG) in 27 yogurt drinks fermented with different basic yogurt cultures, or yogurt cultures enriched with Lactobacillus plantarum and/or Bifidobacterium lactis strains, by competitive ELISA assay. Drinks with the lowest antigenic potential were used as allergoids for CMA therapy. BALB/c mice were sensitized via intraperitoneal injection of α-CN + β-LG mixture with aluminum adjuvant, and gavaged with increasing doses of selected low-immunogenic drinks (YM—basic, or YM-LB—enriched with L. plantarum and B. lactis) to induce tolerance. Milk- or phosphate-buffered saline (PBS)-dosed mice served as controls. Compared to milk, the immunoreactivity of proteins in drinks increased or decreased, depending on the bacterial sets applied for fermentation. Only a few sets acted synergistically in reducing immunoreactivity. The selected low-immunogenic drinks stimulated allergic mice for profiling Th2 to Th1 response and acquire tolerance, and the effect was greater with YM-LB drink, which during long-lasting interventional feeding strongly increased the secretion of regulatory cytokines, i.e., IL-10 and TGF-β, and IgA and decreased IL-4, IgE, and anti-(α-CN + β-LG) IgG1. The studies revealed variations in the potency of yogurt bacteria to change allergenicity of milk proteins and the need for their strict selection to obtain a safe product for allergy sufferers. The YM-LB drink with reduced antigenic potential may be a source of allergoids used in the immunotherapy of IgE mediated CMA, but further clinical or volunteer studies are required.

7

¿Qué biomarcadores tenemos en la ITA para la alergia a alimentos?

Immunological Outcomes of Allergen-Specific Immunotherapy in Food Allergy.

Schoos AM, Bullens D, Chawes BL et al

Front Immunol. 2020;11:568598. Published 2020 Nov 3. doi:10.3389/fimmu.2020.568598.

ABSTRACT

IgE-mediated food allergies are caused by adverse immunologic responses to food proteins. Allergic reactions may present locally in different tissues such as skin, gastrointestinal and respiratory tract and may result is systemic life-threatening reactions. During the last decades, the prevalence of food allergies has significantly increased throughout the world, and considerable efforts have been made to develop curative therapies. Food allergen immunotherapy is a promising therapeutic approach for food allergies that is based on the administration of increasing doses of culprit food extracts, or purified, and sometime modified food allergens. Different routes of administration for food allergen immunotherapy including oral, sublingual, epicutaneous and subcutaneous regimens are being evaluated. Although a wealth of data from clinical food allergen immunotherapy trials has been obtained, a lack of consistency in assessed clinical and immunological outcome measures presents a major hurdle for evaluating these new treatments. Coordinated efforts are needed to establish standardized outcome measures to be applied in food allergy immunotherapy studies, allowing for better harmonization of data and setting the standards for the future research. Several immunological parameters have been measured in food allergen immunotherapy, including allergen-specific immunoglobulin levels, basophil activation, cytokines, and other soluble biomarkers, T cell and B cell responses and skin prick tests. In this review we discuss different immunological parameters and assess their applicability as potential outcome measures for food allergen immunotherapy that may be included in such a standardized set of outcome measures.

8

La Vitamina D podría convertirse en un nuevo adyuvante.

High dose vitamin D 3 empowers effects of subcutaneous immunotherapy in a grass pollen-driven mouse model of asthma.

Laura Hesse, N van Ieperen, Arjen H Petersen , J N G Oude Elberink, Antoon J M van Oosterhout, Martijn C Nawijn

Sci Rep. 2020 Nov 30;10(1):20876. doi: 10.1038/s41598-020-77947-6.

ABSTRACT

Allergen-specific immunotherapy (AIT) has the potential to provide long-term protection against allergic diseases. However, efficacy of AIT is suboptimal, while application of high doses allergen has safety concerns. The use of adjuvants, like 1,25(OH)2VitD3 (VitD3), can improve efficacy of AIT. We have previously shown that low dose VitD3 can enhance suppression of airway inflammation, but not airway hyperresponsiveness in a grass pollen (GP)-subcutaneous immunotherapy (SCIT) mouse model of allergic asthma. We here aim to determine the optimal dose and formulation of VitD3 for the GP SCIT. GP-sensitized BALBc/ByJ mice received three SCIT injections of VitD3-GP (30, 100, and 300 ng or placebo). Separately, synthetic lipids, SAINT, was added to the VitD3-GP-SCIT formulation (300 nmol) and control groups. Subsequently, mice were challenged with intranasal GP, and airway hyperresponsiveness, GP-specific IgE, -IgG1, and -IgG2a, ear-swelling responses (ESR), eosinophils in broncho-alveolar lavage fluid and lung were measured. VitD3 supplementation of GP-SCIT dose-dependently induced significantly enhanced suppression of spIgE, inflammation and hyperresponsiveness, while neutralizing capacity was improved and ESR were reduced. Addition of VitD3 further decreased Th2 cytokine responses and innate cytokines to allergens in lung tissue by GP-SCIT. However, addition of synthetic lipids to the allergen/VitD3 mixes had no additional effect on VitD3-GP-SCIT. We find a clear, dose dependent effect of VitD3 on GP-SCIT-mediated suppression of allergic inflammation and airway hyperresponsiveness. In contrast, addition of synthetic lipids to the allergen/VitD3 mix had no therapeutic effect. These studies underscore the relevance of VitD3 as an adjuvant to improve clinical efficacy of SCIT treatment regimens.

9

¿Qué ocurre con la ITA subcutánea en Canadá?

A single centre retrospective study of systemic reactions to subcutaneous immunotherapy.

Robertson K, Montazeri N, Shelke U, Jeimy S, Kim H

Allergy Asthma Clin Immunol. 2020;16:93. Published 2020 Nov 2. doi:10.1186/s13223-020-00491-5.

BACKGROUND

Subcutaneous immunotherapy (SCIT) is the standard approach for treating patients with sensitizations to aeroallergens. However, immunotherapy can trigger severe systemic reactions if delivered inappropriately or to high risk patients. We sought to characterize and quantify SCIT systemic reactions requiring epinephrine administration during a 6-year period in a Canadian setting following the recommendations for components and dosages published in the 2010 Canadian Society of Allergy and Clinical Immunology (CSACI) Immunotherapy Manual.

METHODS

A single centre retrospective chart review was performed for all patients with systemic reactions to subcutaneous immunotherapy requiring intramuscular epinephrine injection between January 2011 and October 2017. Each systemic reaction requiring epinephrine was reviewed for baseline patient characteristics, details of the reaction, and reaction severity. Research ethics approval was obtained through McMaster University.

RESULTS

28 of 380 patients experienced a systemic reaction requiring epinephrine administration, with an incidence rate of 1 per 1,047 injection visits (0.095%). 26 of the 28 reactions occurred within the mandatory 30-minute observation period post allergen immunotherapy. Of the 28 patients that experienced a systemic reaction to SCIT, 11 patients had asthma and 5 patients had a history of possible food allergy. All of the systemic reactions occurred during injections from vial number 4, and five patients reacted to their first shot of a re-ordered extract. 10 of the 28 patients required more than one intramuscular injection of epinephrine, and 20 of 28 patients were transferred to the hospital by ambulance.

CONCLUSIONS

This is the first Canadian study to review patients with systemic reactions to subcutaneous immunotherapy. Several best practice methods were employed throughout the study to optimize subcutaneous delivery of immunotherapy extract, and our recorded per injection incidence rate for systemic reactions was comparable or below the rate published in similar studies. The recommendations in the CSACI Immunotherapy Manual provide an approach to standardizing prescriptions for SCIT to maximize immunotherapy efficacy and reduce the risk of systemic reactions, though similar studies in larger multicenter settings are needed to confirm these observations. These observations provide important objective information to clinicians about the potential risks for systemic reactions in patients considering SCIT.

10

Manejo personalizado de los alérgicos (o no) a ácaros.

Precision Medicine in House Dust Mite-Driven Allergic Asthma.

Ibon Eguiluz-Gracia, Francisca Palomares, Maria Salas, Almudena Testera-Montes, Adriana Ariza, Ignacio Davila, Joan Bartra, Cristobalina Mayorga, Maria Jose Torres, Carmen Rondon

J Clin Med. 2020 Nov 26;9(12):E3827. doi: 10.3390/jcm9123827.

ABSTRACT

House dust mites (HDMs) are the allergenic sources most frequently involved in airway allergy. Nevertheless, not every sensitized patient develops respiratory symptoms upon exposure to HDM, and there is a clinical need to differentiate allergic asthmatics (AAs) from atopic non-allergic asthmatics with HDM sensitization. This differentiation sometimes requires in vivo provocations like the bronchial allergen challenge (BAC). Interestingly, recent data demonstrate that non-atopic patients with asthma can also develop positive BAC results. This novel phenotype has been termed local allergic asthma (LAA). The interest in identifying the allergic triggers of asthma resides in the possibility of administering allergen immunotherapy (AIT). AIT is a disease-modifying intervention, the clinical benefit of which persists after therapy discontinuation. Recently, new modalities of sublingual tablets of HDM immunotherapy registered as pharmaceutical products (HDM-SLIT tablets) have become commercially available. HDM-SLIT tablets have demonstrated a robust effect over critical asthma parameters (dose of inhaled corticosteroids, exacerbations, and safety), thus being recommended by international guidelines for patients with HDM-driven AA. In this review, we will summarize the current knowledge on the phenotype and endotype of HDM-driven AA, and LAA, address the difficulties for BAC implementation in the clinic, and discuss the effects of AIT in AA and LAA.

1

Avanza la inmunoterapia epicutánea de cacahuete.

Consortium for Food Allergy Research (CoFAR). Epicutaneous Immunotherapy for Treatment of Peanut Allergy: Follow-up from the Consortium for Food Allergy Research.

Scurlock AM, Burks AW, Sicherer SH, Leung DYM, Kim EH, Henning AK et al

J Allergy Clin Immunol. 2020 Dec 5:S0091-6749(20)31701-2.

ARTÍCULO DESTACADO

BACKGROUND

CoFAR investigators previously reported 52-week outcomes from a randomized, controlled trial of peanut EPIT, observing modest and statistically significant induction of desensitization, highest in children ages 4-11 years.

OBJECTIVES

To evaluate changes in efficacy, safety, and mechanistic parameters following extended open-label peanut EPIT.

METHODS

Peanut-allergic participants (4-25 years) received 52 weeks of placebo (PLB), Viaskin Peanut 100 mcg (VP100) or 250 mcg (VP250), then crossover to VP250 for placebo (PLB-VP250) and VP100 (VP100-VP250) participants and continuation of treatment for VP250 participants (total=130 weeks of active EPIT). Efficacy was assessed by DBPCFC (5044 mg peanut protein) and adherence, safety and mechanistic parameters were evaluated.

RESULTS

At week 130, desensitization success was achieved in 1/20 (5%) PLB-VP250, 5/24 (20.8%) VP100-VP250, and 9/25 (36%) VP250 participants with median successfully consumed dose (SCD) change from baseline of 11.5 mg, 141.5 mg, and 400 mg, respectively. Median age (years) for week 130 desensitization success was 6.2 years (IQR:5.2,9.1) versus 9.4 years (IQR:7.6,12.8) for failures ($p<0.001$). Adherence was 96%. Adverse reactions were predominantly local patch-site reactions. Significant increases in peanut- and Ara h2-specific IgG4 observed at week 52 persisted to week 130. By a post-hoc analysis, there were no statistically significant increases from week 52 to week 130 in either desensitization success or SCD.

CONCLUSION

Extended treatment with VP250 was well-tolerated and desensitization observed at week 52 persisted between weeks 52 and 130. Treatment success was observed predominantly in younger participants with younger age at initiation of active therapy an important predictor of success.

2

ITO con cacahuete: ¿Durante cuánto tiempo?

Continuous and daily oral immunotherapy for peanut allergy: results from a 2-year open-label follow-on study.

Vickery BP, Vereda A, Nilsson C, du Toit G, Shreffler WG, Burks AW et al

J Allergy Clin Immunol Pract. 2020 Dec 24:S2213-2198(20)31361-1.

BACKGROUND

The randomized, controlled PALISADE trial demonstrated the benefit of daily oral immunotherapy with PeanuT (Arachis Hypogaea) allergen powder-dnfp (PTAH, formerly AR101) in peanut-allergic children and adolescents.

OBJECTIVE

ARC004, the open-label follow-on study to PALISADE, used five dosing cohorts to explore PTAH treatment beyond 1 year and alternative dosing regimens in peanut-allergic individuals.

METHODS

Active arm (PTAH-continuing) PALISADE participants who tolerated 300-mg peanut protein at the exit double-blind placebo-controlled food challenge (DBPCFC) and placebo arm (PTAH-naïve) participants could enter ARC004. PTAH-continuing participants were assigned to receive daily (Cohorts 1 and 3A) or non-daily (Cohorts 2, 3B, and 3C) dosing regimens; PTAH-naïve participants were built up to 300-mg/day PTAH, followed by maintenance dosing. At study completion, participants underwent an exit DBPCFC with doses up to 2000-mg peanut protein. Data were assessed using descriptive statistics.

RESULTS

Overall, 358 (87.5%) eligible participants (4-17 years) entered ARC004 (PTAH-continuing, n=256; PTAH-naïve, n=102). Among PTAH-continuing participants, exposure-adjusted adverse event (AE) rates were 12.94-17.54/participant-year (PY) and 25.95-42.49/PY in daily and non-daily dosing cohorts, respectively; most participants (83%) experienced mild or moderate AEs. Daily dosing cohorts appeared to have higher desensitization rates than non-daily dosing cohorts. Of all PTAH-continuing cohorts, Cohort 3A had the longest daily dosing duration and the highest desensitization rates. Changes in immune markers with PTAH continuation demonstrated ongoing immunomodulation. Outcomes in PTAH-naïve participants mirrored those of the PALISADE active arm.

CONCLUSION

Continued daily PTAH treatment beyond 1 year showed sustained safety and efficacy. Ongoing immunomodulation was observed during the second year of treatment.

3

Cuanto más rápido, ¿mejor?

Safety and tolerability of venom immunotherapy: Evaluation of 581 rush- and ultra-rush induction protocols (safety of rush and ultra-rush venom immunotherapy).

Stock R, Fischer T, Aßmus K, Zoeller N, Ackermann H, Kaufmann R et al

World Allergy Organ J. 2020 Dec 15;14(1):100496.

BACKGROUND

Current literature is inconsistent regarding the risk of severe side effects using accelerated induction protocols in Hymenoptera venom immunotherapy (VIT). In addition, several data indicate the influence of purity grade of venom preparation on tolerability. We evaluated the safety and tolerability of ultra-rush and rush build-up protocols using purified and non-purified venom preparations.

METHODS

Retrospective single-center study of 581 VIT inductions (325 ultra-rush and 256 rush protocols) from 2005 to 2018 in 559 patients with bee and vespid venom allergy using aqueous purified (ALK SQ®) for ultra-rush protocol and aqueous non-purified (ALK Reless®) venom preparations for rush protocol.

RESULTS

Urticaria (8% vs. 3.1%, p = 0,013) and dose reductions (4.3% vs. 1.2%, p = 0,026) were significantly more frequent in the ultra-rush group. Overall rate of moderate-to-severe side effects (anaphylaxis ≥≥ grade 2 according to Ring and Meβmer) was low and did not differ significantly between protocols (p = 0.105). Severe events (grade 4 anaphylaxis) were not reported. Discontinuation rate was very low in both cohorts (0.6% vs 1.2%). The higher purity grade of venom preparations in the ultra-rush cohort did not improve tolerability. The bee venom group showed a non-significant trend towards higher incidence of mild reactions (urticaria), resulting in more frequent dose reductions and antiallergic therapy.

CONCLUSION

Rush and ultra-rush protocols show an excellent safety profile with only infrequent and mild anaphylactic reactions in bee and vespid venom allergy. Ultra-rush immunotherapy reduces the duration of the inpatient build-up phase setting and thus is viewed by the authors as preferred treatment in Hymenoptera venom allergic patients.

4

Lo que sabemos y lo que (todavía) no sabemos acerca de la ITA.

Mechanisms of Allergen Immunotherapy in Allergic Rhinitis.

Drazdauskaitė G, Layhadi JA, Shamji MH

Curr Allergy Asthma Rep. 2020 Dec 12;21(1):2.

PURPOSE OF REVIEW

Allergic rhinitis (AR) is a chronic inflammatory immunoglobulin (Ig) E-mediated disease of the nasal mucosa that can be triggered by the inhalation of seasonal or perennial allergens. Typical symptoms include sneezing, rhinorrhea, nasal itching, nasal congestion and symptoms of allergic conjunctivitis. AR affects a quarter of the population in the United States of America and Europe.

RECENT FINDINGS

AR has been shown to reduce work productivity in 36-59% of the patients with 20% reporting deteriorated job attendance. Moreover, 42% of children with AR report reduced at-school productivity and lower grades. Most importantly, AR impacts the patient's quality of life, due to sleep deprivation. However, a proportion of patients fails to respond to conventional medication and opts for the allergen immunotherapy (AIT), which currently is the only disease-modifying therapeutic option. AIT can be administered by either subcutaneous (SCIT) or sublingual (SLIT) route. Both routes of administration are safe, effective, and can lead to tolerance lasting years after treatment cessation. Both innate and adaptive immune responses that contribute to allergic inflammation are suppressed by AIT. Innate responses are ameliorated by reducing local mast cell, basophil, eosinophil, and circulating group 2 innate lymphoid cell frequencies which is accompanied by decreased basophil sensitivity. Induction of allergen-specific blocking antibodies, immunosuppressive cytokines, and regulatory T and B cell phenotypes are key pro-tolerogenic adaptive immune responses.

CONCLUSION

A comprehensive understanding of these mechanisms is necessary for optimal selection of AIT-responsive patients and monitoring treatment efficacy. Moreover, it could inspire novel and more efficient AIT approaches.

5

Biopartículas: el futuro puede estar en sus manos.

Design, production and immunomodulatory potency of a novel allergen bioparticle.

V. Gomord, V Stordeur, AC Fitchette, ED. Fixman3, G Tropper, L Garnier et al

PLoS One 2020 Dec 1;15(12):e0242867. doi: 10.1371/journal.pone.0242867. eCollection 2020.

ABSTRACT

Allergen immunotherapy (AIT) is the only disease-modifying treatment with evidence for sustained efficacy. However, it is poorly developed compared to symptomatic drugs. The main reasons come from treatment duration implying monthly injections during 3 to 5 years or daily sublingual use, and the risk of allergic side-effects. To become a more attractive alternative to lifelong symptomatic drug use, improvements to AIT are needed. Among the most promising new immunotherapy strategies is the use of bioparticles for the presentation of target antigen to the immune system as they can elicit strong T cell and B cell immune responses. Virus-like particles (VLPs) are a specific class of bioparticles in which the structural and immunogenic constituents are from viral origin. However, VLPs are ill-suited for use in AIT as their antigenicity is linked to structure. Recently, synthetic biology has been used to produce artificial modular bioparticles, in which supramolecular assemblies are made of elements from heterogeneous biological sources promoting the design and use of in vivo-assembling enveloped bioparticles for viral and non-viral antigens presentation. We have used a coiled-coil hybrid assembly for the design of an enveloped bioparticle (eBP) that present trimers of the Der p 2 allergen at its surface, This bioparticle was produced as recombinant and in vivo assembled eBPs in plant. This allergen biotherapeutic was used to demonstrate i) the capacity of plants to produce synthetic supramolecular allergen bioparticles, and ii) the immunomodulatory potential of naturally-assembled allergen bioparticles. Our results show that allergens exposed on eBPs induced a very strong IgG response consisting predominantly of IgG2a in favor of the TH1 response. Finally, our results demonstrate that rDer p 2 present on the surface of BPs show a very limited potential to stimulate the basophil degranulation of patient allergic to this allergen which is predictive of a high safety potential.

6

ITO y esofagitis eosinofílica.

Eosinophilic esophagitis as a complication of food oral immunotherapy.

Jin H, Trogen B, Nowak-Wegrzyn A

Curr Opin Allergy Clin Immunol. 2020 Dec;20(6):616-23.

PURPOSE OF REVIEW

Food oral immunotherapy (OIT) has emerged as way to mitigate serious allergic reactions including life-threatening anaphylaxis related to accidental ingestion. However, gastrointestinal-related adverse effects of OIT have been reported and are often cited as reasons for discontinuation of therapy. We summarize recent research on the prevalence of eosinophilic esophagitis (EoE) in patients undergoing OIT.

RECENT FINDINGS

We examined 12 recent studies on OIT for peanut, milk, walnut, egg, and wheat, which enrolled a total of 620 patients. Gastrointestinal symptoms were common during OIT, and while generally mild, 24 (3.9%) patients from the reviewed studies reported gastrointestinal symptoms that were significant enough to prompt discontinuation of OIT. Of these, two (0.3% of the total 620 patients or 8.3% of those with gastrointestinal symptoms) patients had biopsy-confirmed EoE. One of these patients was subsequently found to also have ulcerative colitis that had been previously undiagnosed.

SUMMARY

EoE is a rare but concerning side effect of OIT. More research is needed to better elucidate both the OIT-related and patient-related factors that may predispose individuals to develop EoE. The presence of comorbid conditions and/or preexisting subclinical esophageal eosinophilia may account for some of cases of EoE identified during OIT.

7

¿Qué pasa antes, durante y después de la ITO? El TAB nos da algunas pistas.

Oral Immunotherapy and Basophil and Mast Cell Reactivity in Food Allergy.

Paranjape A, Tsai M, Mukai K, Hoh RA, Joshi SA, Chinthrajah RS et al

Front Immunol. 2020 Dec 14;11:602660.

ABSTRACT

Basophil activation tests (BATs) can closely monitor, in vitro, a patient's propensity to develop type I hypersensitivity reactions. Because of their high specificity and sensitivity, BATs have become promising diagnostic tools, especially in cases with equivocal clinical histories, skin prick test results, and/or levels of specific IgE to allergen extracts. BATs also are useful as tools for monitoring the effects of treatment, since oral immunotherapy (OIT) studies report a diminution in patients' basophil responsiveness over the course of OIT. This review will discuss the BAT findings obtained before, during, and after OIT for food allergy. We will mainly focus on the association of basophil responsiveness, and alterations in basophil surface markers, with clinical outcomes and other clinical features, such as blood levels of specific IgG and IgE antibodies. The detailed analysis of these correlations will ultimately facilitate the use of BATs, along with other blood biomarkers, to differentiate short-term desensitization versus sustained unresponsiveness and to improve treatment protocols. Given the critical anatomic location of mast cells adjacent to the many IgE+ plasma cells found in the gastrointestinal tissues of allergic individuals, we will also discuss the role of gastrointestinal mast cells in manifestations of food allergies.

8

Adherencia en la vida real.

Real-world mapping of allergy immunotherapy in the United States: The argument for improving adherence.

Stone B, Rance K, Waddell D, Aagren M, Hammerby E, Tkacz JP

Allergy Asthma Proc. 2020 Dec 23.

BACKGROUND

There is a dearth of real-world evidence studies focused on allergy immunotherapy (AIT) use among patientswith allergic rhinitis (AR).

OBJECTIVE

This study examined claims data of AR patients residing in the United States to assess patient characteristicsand health outcomes.

METHODS

AR patients were identified in the IBM MarketScan database between January 1, 2014, and March 31, 2017. Patients receiving AIT were identified with relevant billing codes (earliest AIT claim for vaccine as the index date); patientswithout AIT were identified with claims that contained a diagnosis code for AR (earliest AR claim as the index date). All the patients were required to have continuous enrollment 12 months prior to and following their index date. AIT patients reaching 25+ injection claims were analyzed as a separate maintenance cohort. Patients were assessed for demographic characteristics, comorbid conditions, and health care utilization.

RESULTS

A total of 2,334,530 AR patients were included; 103,207 had at least one AIT claim, with 45,279 (43.9%) of thesepatients reaching maintenance. Patients who reached AIT maintenance presented higher rates of baseline comorbidities than both the full AIT cohort and the patients with no AIT claims, including asthma (34.6% versus 30.1% versus 7.5%) and upper respiratory tract infections (63.1% versus 60.3% versus 34.2%). From baseline to follow-up, maintenance AIT patients demonstrated reductions in all AR-related comorbidities assessed, along with reductions in all-cause and AR-related service utilization.

CONCLUSION

Patients initiating AIT presented the greatest need for therapeutic intervention, as evidenced by higher allergy-related comorbidities; those who reached maintenance demonstrated improved outcomes following the initiation oftherapy. Continued efforts to increase patient awareness and adherence to AIT are needed.

9

La carrera de los biomarcadores: ¿quién va ganando?

Serum Periostin as a Biomarker for Predicting Clinical Response to House Dust Mite Sublingual Immunotherapy in Allergic Rhinitis.

Hoshino M, Akitsu K, Kubota K, Ohtawa J

J Allergy Clin Immunol Pract. 2020 Dec 5:S2213-2198(20)31269-1.

BACKGROUND

House dust mite (HDM) sublingual immunotherapy (SLIT) has proven to be effective for allergic rhinitis (AR), but its efficacy varies among patients. No candidate biomarkers for prediction of response to SLIT are available. Periostin, a matricellular protein, is involved in pathophysiology of AR, and its serum levels reflect airway allergic inflammation.

OBJECTIVE

To evaluate the relationship between serum periostin levels and current rhinitis control before and after standardized quality (SQ)-HDM SLIT, and to investigate the role of periostin in predicting clinical response.

METHODS

One hundred eleven subjects with HDM-induced AR were randomized to receive either SLIT plus pharmacotherapy or pharmacotherapy alone, for 48 weeks. At enrollment and the end of study, clinical characteristics and biomarkers that included serum periostin, serum HDM-specific IgE (s-IgE), total IgE, blood eosinophil counts, and Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) were measured. The association between clinical indices or biomarkers and clinical response to SLIT was analyzed.

RESULTS

A response to SLIT was recorded in 64% (32 of 50) patients. High serum periostin levels (>30.2 ng/mL) were associated with an effective response to SLIT, and the magnitude of RQLQ improvement was correlated with the level of serum periostin. The sensitivity and specificity based on receiver operating characteristic analysis for periostin were higher than those of s-IgE. Multivariate regression analysis showed that serum periostin was an independent factor for SLIT responders.

CONCLUSIONS

Serum periostin appears to be a useful biomarker for predicting the response to SQ-HDM SLIT in patients with AR.

10

La (no tan) conocida alergia al caballo.

Equine Hypersensitivity: the Dark Horse of Allergy.

Davenport J, Smith D

Clin Rev Allergy Immunol. 2020 Dec;59(3):352-58.

ABSTRACT

A significant amount of medical literature has been published on the prevalence and treatment modalities of allergies to common household pets like dogs and cats. Although sensitization rates to horses are high in many urban areas, allergies to horses are rarely discussed. In order for allergists to treat effectively horse-allergic patients, they must be aware of various clinical presentations and treatment modalities that exist. A literature search was conducted in PubMED using the terms horse, immunotherapy, inhalant allergies, and food allergy limited to human studies from any period. What follows is a review of the prevalence, clinical presentations, and treatment modalities of horse aeroallergens and food allergies.