ABSTRACTS

Friday, 21 September 2018
Poster Discussion Session I
13:45 – 14:45

P01 - Fraction Of Exhaled Nitric Oxide In Children Undergoing Allergen Immunotherapy For IgE-Mediated Food Allergy: Towards Precision Medicine

Stefania Arasi, Lucia Caminiti, Giuseppe Crisafulli, Laura Cannavò, Giulia Cafarella, Giovanni B Pajno
University of Messina, Messina, Italy

Background

The fraction of exhaled nitric oxide (eFeNO) is a non-invasive tool correlating to allergic airways inflammation and has been independently associated with increased food-specific IgE and the outcome of a food challenge. Oral immunotherapy (OIT) is the only active effective treatment for food allergy (FA). However, there are stil many gaps in OIT treatment. Furthermore, asthma is one of the major risk factors for OIT outcome. To our best knowledge this is the first study reporting the longitudinal evaluation of eFeNO in a pediatric cohort undergoing OIT.

Materials and methods

Prospective evaluation of eFeNO and sIgE with/without spirometry in collaborating children suffering from severe persistent IgE-mediated FA: before, during (half of the mantainance dose) and after a consolidate OIT protocol to cow's milk (CM) or hen's egg (HE). Informed written consent was obtained by parents before the treatment.

Results

We have so far enrolled 14 children (n male=10), aged 8 ± 4 (mean±SD) before the beginning of OIT with CM (n=9) and HE (n=5). Ten children have concomitant allergic asthma (A). eFeNO values have been successfully collected before, during and after OIT in each patient who completed the desensitization protocol (n=9). OIT is currently ongoing in the remaining 5 patients. Preliminary data show no significant differences in eFeNO values among the three time points. However, eFeNO values related with OIT outcomes. The highest FeNO values (>35 ppb) have been assessed in the 2 children who interrupted OIT during the build- up phase for concomitant severe A: one at the increasing dose of 17 ml and one at 150 ml of CM.

Conclusion

This preliminary data show the potential role of eFeNO in managing the up-dosing of OIT protocols in patients with bronchial hyperreactivity. This biomarker might be a

step forward in the perspective of a precision OIT, tailored on the single patients. However, this promising data need to be confirmed.

P02 - Macroarray Diagnostic And Sublingual Allergen Specific Immunotherapy Of Polysensitization Children

Olena Viktorivna Sharikadze
Shupyk National Medical academy of postgraduate education, Kiev, Ukraine

Background

The efficacy of allergen- immunotherapy in polysensitization children has not yet been fully resolved. The possibility of evaluating the full patient's sensitivity profile for making a decision about choosing a therapy regimen until recently was limited. The emergence of new diagnostic methods - gives the opportunity to review the old algorithms in the appointment of therapy. This is especially important in children.

Materials and methods

To evaluate the efficacy of the use of macro diagnostics for the appointment of an allergen immunotherapy in children.250 children aged 1-17 years with atopic dermatitis, allergic rhinitis and asthma were measured by MAD ALEX for the determination of the spectrum of sensitization to allergic components and extracts of the inhalation and food allergens to solve the issue of tactics of management and selection of the allergen of immunotherapy.

Results

In 250 examined patients, Ig E dependent reactions were found in 244 (97.6%). 25% of patients had a total IgE more than 1000 (kU/L). Sensitization to food allergens was found in 62% of which the most common were allergens - proteins of milk, eggs, fish, nuts. In 187 children, sensitization to inhalant allergens was detected. Polysensitization occurred in 165 children. Molecules of house dust mites p Der p23, Der p 7, r Der p 11 were found in 30% of patients. 15 % children has polysensitization which was associated with sensitization to minor timothy allergens Phl p7, Phl p 12.

Conclusion

The use of macro-diagnostics makes it possible to take into account the possibility of sensitization to molecules of allergens, which are crucial in the development of allergic symptoms, but are not decisive in extracts used for therapy. Knowledge of the profile of the child's sensitization allows for timely initiation of therapy taking into account the possible risks of developing side-effects and taking into account the reasons for the lack of effectiveness.

P03 - Adherence To Sublingual Immunotherapy In Real-Life

Polina Y. Shahid, Tihomir B. Mustakov
Departement of Clinical Allergy, UMHAT Alexandrovska, Sofia, Bulgaria

Background

Allergen immunotherapy (AIT) modifies the natural course and complications of allergic diseases. Adherence to therapy is important for its effectiveness, however such data is limited. Sublingual immunotherapy (SLIT), as any other long-term treatment, faces the problem of adherence and patient compliance is a major barrier to achieving optimal outcomes. The aim of our real-life study was to retrospectively evaluate adherence to sublingual immunotherapy across children of different ages.

Materials and methods

Our study population consisted of 81 children (50♂, 31♀) aged between 4 and 15 years (mean age 7.5y). AIT was indicated for respiratory allergic disorders. Sensitivity to aeroallergens such as pollens (38 children), mites (32) and molds (11) was confirmed by a positive skin prick test and specific IgE assay. Patients were divided into three groups based on their age: group A (4-6y), group B (7-12y) and group C (13-18y).

Results

Among 81 children who initiated SLIT, 47% completed 3 years of treatment and only 15% - 4 years. The total dropout rate was 53% (3rd year) and 85% (4th year). Group C showed a higher dropout rate (50%) than group A (44%) and group B (27%) did. Optimal adherence with SLIT was reached in children aged six and seven. The most common reasons for discontinuing SLIT were the inability to take the medication as scheduled, cost, concurrent illness, and adverse effects.

Conclusion

Allergen immunotherapy is relatively time-consuming and patients should receive adequate initial education about treatment duration and adherence benefits. Compliance measures such as electronic reminders and more frequent visits may be beneficial. Unsurprisingly, young children demonstrate better adherence probably due to parental involvement.

P04 - Oral Immunotherapy On Children With Cow's Milk Allergy

António Jorge Cabral, **Alexandra Rodrigues**, Carolina Freitas Fernandes, Graça Araújo, Ana Marques
Hospital Central do Funchal, Funchal, Portugal

Background

Cow's milk allergy (CMA) is the most common food allergy in young children and up to 20% maintain it until the second decade of life, representing a heavy burden for patients and their families. No cure is available and strict avoidance of the food allergen is the only therapeutic option to prevent anaphylactic reactions and to resolve chronic associated symptoms. However, the natural history is left unchanged with likely increased sensitization as well as lowering of the threshold of reactivity. Therefore an active treatment is required and oral immunotherapy (OIT) seems to be a promising treatment.

Materials and methods

Thirty nine patients with documented CMA underwent OIT according to a standardized protocol that consists in increasing doses during the day in a hospital setting. A maintenance dosage is then continued at home for roughly two weeks and, at that time, new increase in dosage is made, under medical surveillance. The final desired dosage is 200mL per day that is ideally achieved after a 12 weeks period.

Results

Compliance to treatment was satisfactory, since only 3 patients didn't complete the protocol. One refused continuation after the initiation, 2 showed symptoms during the protocol, at 5mL and 7,5mL, severe enough to prevent dose increase. Two patients are completing procedure at the time of this abstract. The remaining cases completed the program and all are now able to tolerate cow's milk without any untoward effects or need for preventive drugs. Of these, one had suspended the protocol due to allergic symptoms, but was able to finish it one year later. Allergic reactions were common during the treatment, particularly when increasing the dose, with over half of the patients showing side-effects, usually requiring medication.

Conclusion

As shown in other studies, OIT helped these patients overcome their food allergy. The protocol used represents a safe and effective alternative approach in the management of milk allergic patients. Further attempts to standardize these procedures are necessary.

P05 - Sublingual immunotherapy with Pru P 3 –review of 7 cases

Maria João Vasconcelos, Alice Coimbra, Diana Silva
Serviço de Imunoalergologia, Centro Hospitalar de São João, EPE, Porto, Portugal

Background

In the Mediterranean area, lipid transfer protein (LTP) is a pan-allergen often associated with persistent severe systemic reactions. In this region, a large percentage of patients with food-dependent exercise induced anaphylaxis (FDEIA) are sensitized to LTP. The risk of severe reactions and the potential to react to a progressive number of LTP containing food makes this an important target for specific sublingual immunotherapy (SLIT) with the presumed primary culprit sensitizer - Pru p 3.

Aim

Evaluation of the management of patients with confirmed LTP food allergy treated with SLITPru p 3 and assessment of its efficacy and safety.

Materials and methods

A review of all patients treated with SLIT Pru p 3 between 2013 and 2016. The protocol was used according to the manufacturer's recommendations (Bioportugal®, ALK-Abelló). Efficacy was defined as negative peach challenge between 6 and 12 months of treatment and/or by negative oral challenges with previously allergic food. Adverse reactions were classified according to WAO grading system.

Results

Seven patients, 57% female, all with anaphylaxis to fresh fruits (peach, apple, orange) and/or walnuts and with positive LTP skin tests and/or specific IgE, (median of Pru p 3of 8.8 interquartile range [4.2-18.5] ISU) were included. The median age of onset of symptoms was 15 [12-19] years. During the 4-day build-up phase, 86% presented oral pruritis and/or angioedema and one presented a grade 2 systemic reaction. During the maintenance phase, no systemic reactions were reported. One patient completed the treatment successfully (36 months), 3 are currently under SLIT (12, 22 and 27 months of treatment) and 4 patients discontinued treatment (8, 12, 14 and 17 months). Two reported adherence difficulties, 1 emigrated and 1 stopped due to persistent symptoms. Tolerance to other LTP containing foods such as apple, strawberry, walnut, and hazelnut was achieved. Even in those who did not complete the treatment, tolerance to peach and other foods was maintained, even with exercise.

Conclusion

Immunotherapy with peach allergen extract was an effective and safe therapeutic option, even after twelve months of treatment, in this group of patients with Pru p 3 sensitization. Peach and other fresh fruits or walnuts that previously caused symptoms were tolerated. Oral tolerance induction was not confirmed, but desensitization was maintained even after stopping treatment

P06 - Steroid Sparing Effect Of Sublingual Immunotherapy: Real Life Study In Mono/Polisensitized Children With Asthma

Nilufer Galip(1), Arzu Babayigit(2), Nerin Nadir Bahceciler(2)
1. University of Kyrenia, Kyrenia, Cyprus
2. Near East University, Nicosia, Cyprus

Background

Retained modifying effect of AIT is tempting especially for pediatric allergists, as their major goal is to prevent asthma or cure asthma in the long-term. Based on the fact that, one of the major concerns of parents is corticophobia, avoidance or successful discontinuation of ICS for at least one year might be recommended as an objective parameter in evaluating the long-term success of AIT in childhood allergic respiratory diseases. Hereby, in this real life study we aimed to determine the impact of SLIT retrospectively in children with mild-moderate persistent asthma in terms of successful ICS discontinuation.

Materials and methods

All children up to 18 years of age with the diagnosis of allergic asthma with or without allergic rhinitis, followed by the Division of Paediatric Allergy and Immunology of Near East University Hospital and who were initiated allergen-specific (SLIT) between 2010-2014 were included in the study. Data on age, gender, duration of symptoms, diagnosis, number/type of allergens sensitized and mean daily dose of ICSs at initiation of IT were recorded from the Hospital database system, retrospectively. Children with maintained asthma control with no need of ICSs as controller medication for at least 6 months were defined as "ICS avoidance" patients.

Results

Ninety-children (mean±SD age 8,92±4,17yrs) were enrolled, 56,7%(n=60) being poly-sensitized. Mono, 2-simultaneous and multiple-pollen-mix allergen SLIT were prescribed in 84.4%, 17,8%, 7,8%, respectively. ICS was avoided in 70%, with no significant difference in mono/vs/poly-sensitized patients. ICS-avoidance rates in mono-allergen, pollen-mixture and 2-simultaneous-allergen SLIT were 93,6%, 83,3%, 73,7%, respectively. Longer-duration SLIT resulted in significantly more ICS-avoidance(p:0,0001).

Conclusion

SLIT with mono/multiple-mixed/simultaneous allergens in childhood asthma resulted in retained-avoidance of ICS. Steroid-sparing effect of SLIT in polysensitized children warrants further investigation.

Characteristics of the study population.

Table 1.

Age (Mean ±SD)	8,92±4,17
Gender (M/F) (%)	65.3/34.4
DIagnosis (%)	25.6
Asthma	74.4
Asthma/Rhinitis	
Sensitization patterns (%)	28.9
HDM	50
HDM+other	12.2
One pollen	6.7
>1 pollen	2.2
Other	
Sensitization Status (%)	43,3
Monosensitized	56,7
Polisensitized	
Treatment	
ICS Use (%)	64,4
Dose of ICS (mcg) (Mean /range)	426,72 (200-500)
IT regimen (%)	
Multiple	27,8 (2-36)
Indoor+ Outdoor (Simultaneous)	17,8
Mixture pollen	7,8
Mono	74,4
Compliance to the SLIT (%)	
Completed	65
Interrupted by self decision	2.2
Compulsarily interrupted*	32.2

P07 - Sensitization Pattern To Aeroallergens And Food Allergens Among Pediatric Patients With Common Allergic Diseases

Pauline Florence Robles Santos Estrella(1), Marysia Stella Tiongco Recto(2), Madeleine W Sumpaico(2), Mary Ann Roldan Castor(2)
1. St. Luke's Medical Center, Quezon City, Philippines
2. UP-PGH, Quezon City, Philippines

Background

Aeroallergens and Food allergens associated with common allergic diseases may have change through the years.

Materials and methods

Cross sectional study of pediatric patients from January 2006 to December 2011 diagnosed with allergic rhinitis, bronchial asthma, atopic dermatitis and/or urticaria to determine the frequency of aeroallergens and/or food allergens.

Results

Two hundred eighty nine patients were included in the study. There were 180 male (62%) and 109 female (38%). The mean age was 9.07 years + 4.4 SD. Some patients were tested for aeroallergens or food allergens only. The frequency of common aeroallergens were as follows: Indoor – housedustmite 215/289 (74%), cockroach 147/289 (51%) and cat's hair 32/289 (11%). Outdoor allergens were grouped into grasses, weeds and tree pollens. Most common were as follows respectively: Johnson grass (Sorghum jalepense) 33/289 (11%), pigweed (Amaranthus spinosus) and mango tree pollen (Mangifera indica) 15/289 (5%). Food allergens were as follows: crabmeat and bagoong alamang 18/110 (16%), squid 13/110 (12%), shrimp 12/110 (11%), eggwhite 7/110 (6%), mussel 6/110 (5%), peanut and oyster 5/110 (4.5%), chocolate, cow's milk, chicken and rice grain 4/110 (4%).

Conclusion

Compared to previous studies, dustmite remains to be the most common indoor aeroallergen. There were no changes in the frequency of allergens associated with common allergic condition through the years.

Friday, 21 September 2018
Oral Abstract Presentation
17:45 – 19:15

O01 - Intensity Of Pain Associated With Subcutaneous Administration Immunotherapy In Pediatric Age

Cristiana Ferreira(1), Isabel Rezende(2), Arminda Guilherme(1), Ines Lopes(1)
1. CHVNG/E, Gaia, Portugal
2. CHPORTO, Porto, Portugal

Background

Allergen immunotherapy is the only treatment that can safely and effectively change the natural history of allergic diseases. In the literature, there are few studies evaluating the perception of pain associated with the administration of subcutaneous immunotherapy with allergens.

Materials and methods

To evaluate the intensity of pain associated with the subcutaneous injection of allergen immunotherapy in a paediatric population with respiratory allergy treated with allergen subcutaneous immunotherapy, followed in an Immunoallergology outpatient clinic. Possible correlations between the intensity of pain with demographic and clinical factors and/or manifested adverse reactions were also analysed.

During 4 consecutive weeks, nurses performed the evaluation of pain associated with subcutaneous injections of allergen immunotherapy in children (7 to 16 years-old), trought an anonymous questionnaire. This questionnaire used 2 different pain evaluation scales, according to the children's age: the selfreporting faces scale (score 0 to 10; 5 to 8 years of age) and the numeric scale (score 0 to 10; >8 year-old) and also identify any relation with demographic data, clinical data and with the occurrence of any adverse reactions.

Results

Of the fourty six patients included most were males, with rhinitis/rhinoconjuntivitis, receiving subcutaneous immunotherapy with mites. Doses varied between 0.25 and 0.5 mL. Seven local adverse reactions were recorded, all of them mild. 22% of patients did not mention any pain. Of the 36 patients that mentioned some pain, 33 indicated mild pain and only 3 rated pain as moderate. The median pain referred was 1 and the mean was 1.5. The maximum pain reported was of 6. No other significant differences in pain scores were noted between different groups of patients even considering patients with and without local reactions or in patient receiving divided injections in both arms.

Conclusion

In this study, subcutaneous allergen immunotherapy was shown to be only a mildly painful procedure, associated with only a few local reactions and therefore being a safe option for most of our allergic pediatrics patients.

O02 - Up-Dosing Phase Of A Cooked-Egg Oral Immunotherapy Protocol: Improving Security

Daniella Gereda, Adrianna Machinena, Jorge Mauledoux, Jaime Lozano, Davinia Vasquez, Mar Folque, Ana Maria Plaza, Montserrat Alvaro
Hospital Sant Joan de Deu, Barcelona, Spain

Background

Our group has previously published data regarding safety in a raw egg-OIT protocol, reporting adverse reactions in 7.6% of doses and many studies reported early discontinuation due to severe adverse events. More information about cooked egg (CE) Oral immunotherapy (OIT) safety is needed.

Aim

To evaluate the safety of the up-dosing phase of a CE-OIT protocol.

Materials and methods

Retrospective study. Children over 5 years with egg-allergy, clinical history, positive skin prick test (SPT ≥ 3 mm) and specific IgE (s-IgE > 0.35 KU/L) with a confirming oral food challenge (OFC) were included. All underwent a 28 step CE-OIT protocol, beginning with a 4-day initial schedule (18 steps) following up-dosing weekly intervals (10 steps) reaching a total dose of one well-done omelette (7.5g of egg protein). Patients did not receive pre medication. Data were collected for demographics, s-IgE, SPT, adverse events at OFC, and all dose-related reactions were registered during the up-dosing phase.

Results

43 children, 70% boys. Median age at OFC: 9 years (7-12). 53.5% had other food allergies, 46.5% atopic dermatitis, 42% asthma, 21% allergic rhinitis. Median at baseline: total IgE 612 KU/L (243-1611), egg-white s-IgE 6.22 (1.87, 24.85), ovomucoid s-IgE 3.8 (1.8- 14.1), egg-white SPT 10.4 mm (7.4-12.6) and ovomucoid SPT 9.6 mm (7.3-11.7). 55.8% were anaphylactic before beginning our protocol. At OFC 51% of patients presented anaphylaxis (39.5% mild, 11.5% moderate), 41.9% urticaria, and 4.7% gastrointestinal symptoms. Only 2 patients did not perform OFC because of recent anaphylaxis. 76.7% of patients managed to finish the up-dosing phase, 23.3% withdrew. 6044 doses were administrated and adverse events occurred

in 3% of the doses. 7.3 % of adverse events/dose occurred within withdrawals while 1.4% occurred in patients who finished up-dosing phase. 28% had 1 anaphylaxis, 11.6% presented 2 or more anaphylaxis. Epinephrine was required in 14% of children. 100% of patients, who needed 2 or more epinephrines, dropped off our protocol. Only 1 patient required 4 epinephrines. From withdrawals 90% were anaphylactic at the initial OFC. 1 patient (4%) dropped off because he moved away. No significant difference was found in total IgE, s-IgE nor SPT between withdrawals and active patients.

Conclusion

We find our protocol a safer procedure than raw egg OIT, given the lower reaction/dose ratio. Discontinuation was associated with frequent mild- moderate reactions and anaphylaxis at OFC. All children who needed two or more epinephrines dropped off our CE-OIT protocol.

O03 - Deep Immunophenotyping Of Early And Late Cellular Events Shows Tolerance Induction By Successful High Dose CpG-Based Immunotherapy In A Murine Asthma Model

Guillem Montamat, Cathy Leonard, Olivia Domingues, Caroline Davril, Justine Heckendorn, Coralie Guerin, Markus Ollert
Luxemboug Institute of Health, Esch-Sur-Alzette, Luxembourg

Background

Allergen-specific immunotherapy (AIT) is the only curative treatment for perennial allergic rhinitis/asthma which can restore allergen immune tolerance with long term effects. CpG oligodeoxynucleotides (CpG-ODN) is a promising adjuvant for AIT shown to induce immune tolerance at high doses. Applying these properties to an AIT model, a successful high dose CpG-based AIT (hCpG-AIT) has been established in a murine allergic asthma model to the major cat allergen Fel d 1. This study aims to deeply phenotype cellular events at two crucial steps of this immunotherapy.

Materials and methods

Mice were sensitized by three i.p. injections containing a mixture of Fel d 1 and alum. Subsequently, the animals received three i.p injections of immunotherapy using a solution of Fel d 1 and CpG-ODN (1.05mg/kg). Finally, an allergen airway challenge was performed through nasal instillation. Twenty-four hours after the first AIT injection, spleen, mediastinal lymph nodes (MLN) and peritoneal cavity cells were isolated. Cells were also extracted from lungs, MLN and spleen after the complete course of hCpG-AIT and subsequent challenge. All the samples were immunophenotyped by mass cytometry. Three groups of animals were analyzed: allergic, hCpG-AIT treated and control.

Results

After the first CpG-AIT injection, the percentage of plasmacytoid dendritic cells (pDCs) was increased by 3-fold in the spleen and by 20-fold in the MLN in the hCpG-AIT group. Upon complete hCpG-AIT, a clear improvement of allergic parameters was found in the lungs, among which the relative numbers of eosinophils and mast cells were reduced by 20- and 10-fold respectively. High CpG-AIT also reduced the IL-13 expression from lung Th2 cells by 2-fold. In MLN, hCpG-AIT diminished the relative number of B cells by 20% and their CD69 expression by 50%. In addition, hCpG-AIT decreased the Gata3 expression in MLN Th2 cells by 50%. In the spleen, hCpG-AIT induced a 25% increase of the Treg ratio and a 15% increase of FoxP3 expression in these cells.

Conclusion

Using mass cytometry, a single cell high throughput immunophenotyping technology, we studied the early and late immune cell events in a high dose CpG-based AIT model. The analyses of the early events showed that hCpG-AIT caused pDCs upregulation in lymphoid organs. The characterization of the late events revealed a reduction of the allergic effector cells and Th2 response as well as the induction of systemic tolerance. These results will help to further understand how high dose CpG AIT modulates the immune system towards tolerance.

O04 - Eosinophilic Esophagitis In Paediatric Patients Undergoing Oral Immunotherapy For IgE-Mediated Milk Allergy

Mireia Arnan, Rosa Jiménez, Carmen Riggioni, Olga Dominguez, Monica Piquer, Yadira Gordon, Ana Maria Plaza, Montserrat Alvaro
Hospital Sant Joan de Déu, Barcelona, Spain

Background

Oral immunotherapy (OIT) has emerged as a promising allergen-specific therapy for patients with IgE-mediated food allergy, however it´s possible adverse events such as eosinophilic esophagitis (EoE) are still under investigation. Our aim was to describe clinical characteristics, evolution and treatment of children diagnosed with EoE during milk-OIT for IgE-mediated milk allergy.

Materials and methods

Retrospective study including IgE-mediated milk allergic patients, under 18 years of age, who underwent milk–OIT from 2007 to 2015. Follow-up was based on hospital protocol (approved by the ethics committee) and endoscopy was performed in all children who showed symptoms compatible with EoE. EoE diagnosis and treatment response was assessed histologically according to EAACI criteria 2011.

Results

178 children that underwent milk-OIT were recruited. EoE was confirmed in 3.37% of patients (n=6 /178), 50% were male. 50% of patients had multiple food allergies, 83% were sensitized to pneumoallergens and 33% had asthma. Median age at milk-OIT onset was 7.3yrs (range 4.4-13.8yrs). Median time between beginning milk-OIT and symptoms suggesting EoE was 6.63yrs (range 1-month to 9.29yrs). Median time between starting milk-OIT and EoE diagnosis was 7.9yrs (range 3.4 months to 9.8yrs). Most common symptoms were abdominal pain (4/6), dysphagia (3/6), impaction (2/6) and vomit (2/6). All patients who presented abdominal pain associated other symptoms.

With regards to treatment:

Three patients were PPI (proton pump inhibitor) responsive and none required withdraw of daily dose of milk to control EoE. Other two patients (also continuing milk doses), have responded to swallowed corticosteroids, and are currently undergoing treatment with PPI and waiting a re-evaluation. Dietary therapy was followed by the last patient (milk exclusion, 6-food and elemental diet) after trying PPI without response, and EoE resolution was only achived with swallowed corticosteroids.

Conclusion

In our population, milk-OIT children were diagnosed with EoE in 3.7% of patients. PPIs were a usefull first line treatment for patients with EoE+OIT. None of these patients required milk exclusion diet to control their esophagitis, being able to continue the treatment with milk in all cases. Our results confirm the need for long-term follow-up of patients undergoing milk-OIT. Whenever gastrointestinal symptoms are present, EoE should be ruled out. The exact role of milk-OIT as a trigger for EoE needs to be further investigated using prospective, longitudinal properly designed trials.

O05 – Immunological Changes On Maintenance Phase Of Oral Immunotherapy With Cooked Hen´s Egg In Pediatric Patients

Jorge Alejandro Mauledoux, Adriana Machinena, Daniella Gereda, Jaime Lozano, Mar Folque, Marcia Dias, Ana Plaza, Montserrat Alvaro
Hospital Sant Joan de Deu, Barcelona, Spain

Background

Strict avoidance diet is the only accepted management for egg allergic children. Oral immunotherapy (OIT) might be an optional treatment, in order to achieve egg desensitization. Immunological positive markers of desensitization development might be measured as a predictor of success in OIT.

OBJETIVES: To describe immunological changes during, at least, a six month period of maintenance phase.

Materials and methods

Retrospective study and follow-up of egg allergic patients included in oral immunotherapy (OIT) with cooked hen´s egg. Allergic children over 5 years with a positive clinical history and skin prick test (SPT ≥ 3 mm) and/or specific IgE (sIgE > 0.35 KU/L) and a positive oral food challenge (OFC) were included. Clinical symptoms at OFC and in maintenance phase were registered. Measurement of s-IgE and SPT for hen´s egg and components: ovalbumin, ovomucoid, egg-white and yolk were obtained before the up-dosing phase (T0) and after 6 months period of maintenance phase (T1), taking 1 whole egg in a well-cooked omelet (7.5 gr of protein) 3 times a week by protocol. Non-parametric wilcoxon test was done for analysis.

Results

22 patients were included, 63.6% male. 54.5% had other food allergies, 50% atopic dermatitis, 31.8% asthma and 13.6% allergic rhinitis. Median age at the beginning of the protocol was 8y (SD 2.71). All patients underwent an OFC and 50% had anaphylaxis; epinephrine was administrated in 11.1% of them. The first control in maintenance phase (T1) was done at a mean time of 10.6 months (SD 2.76). In this period of OIT, 31.8% (n=7) had suffered anaphylaxis (6 mild, 1 moderate), no epinephrine was administrated, 30% had needed oral antihistaminic and 20% inhaled salbutamol. Statistical significance between s-IgE at T0 vs T1 was obtained: egg-white (80.2 vs 6.3 KU/L (p <0.001)); ovomucoid (20.3 vs 14.1 (p <0.001)); ovoalbumin (42.5 vs 2.1 (p <0.001)). Likewise for SPT: egg-white (9.9 vs 6.5 mm (p 0.009)); ovoalbumin (7.5 vs 4.3 mm (p 0.005)); ovomucoid (9.2 vs 6.4 (p 0.003)).

Conclusion

Immunological changes were obtained in both s-IgE and SPT for components of hen's egg with significant differences after, at least, 6 months of maintenance phase cooked egg OIT. By contrast on previous studies with raw egg OIT, no statistically significant results were obtained. It is necessary to continue a prolonged follow-up of these patients to determine the success of OIT.

O06 - 1,25-Dihydroxy Vitamin D3 Adjuvant Enhances Sublingual Immunotherapy Efficiency In Pediatric Asthma: A Controlled Clinical Trial

Lobna Abdelaziz Abdelazim Abdelaziz El-Korashi, Ola Elsayed Nafae, Lamiaa Gaber Zake, Nana Abdelrahman Mohamed
Zagazig University, Zagazig, Egypt

Background

Sublingual immunotherapy (SLIT) is an efficient and safe treatment for bronchial asthma which its immune mechanisms have been well investigated in the last few years. In this approach, gradually cumulated doses of the allergen are required to achieve clinical efficiency. 1,25-dihydroxy vitamin D3 is one of SLIT adjuvants that have been considered in improving the allergen availability to the immune system in order to enhance the SLIT efficiency and decrease the allergen dosing. Some murine models proved the role of 1,25-dihydroxy vitamin D3 in enhancing SLIT efficiency (1), although few clinical studies have been conducted in small cohorts of patients to test it in humans. Therefore, we evaluated the effect of combining 1,25-dihydroxy vitamin D3 with natural allergen extract of mixed grass pollens-specific SLIT in asthmatic children.

Materials and methods

Forty children, aged 5-18 years, with bronchial asthma were included in 6 months, randomized, placebo-controlled trial. The case group (n=20) received mixed grass pollen- specific SLIT adjuvanted with vitamin D while the placebo group (n=20) received natural allergen extract of mixed grass pollens-specific SLIT without any adjuvant. We assessed serum level of IL10 and IL17 before and after SLIT in both groups. Secondary outcomes including lung function, and serum level of Calcifediol were also measured.

Objectives: To compare the clinical efficiency and the serum level of IL10 and IL17 in children with bronchial asthma received mixed grass pollens -specific SLIT adjuvanted with 1,25-dihydroxy vitamin D3 with placebo group.

Results

When compared with the placebo group, SLIT adjuvanted with vitamin D group therapy showed more significant reduction of asthma symptoms and the medication score ($P < 0.001$ We also observed more significant reduction in serum level IL-17 (case group, $P = 0.032$; placebo group, $P = 0.021$) and more significant elevation in serum IL-10 level in the case group (case group, $P < 0.001$; placebo group, $P = 0.001$). We reported a significant improvement of forced expiratory volume in one second in the both groups (case group, $P = 0.012$; placebo group, $P =0 .017$) and there was a significant increase in serum level of Calcifediol in the case group ($P = 0.046$).

Conclusion

SLIT adjuvanted with vitamin D is an effective and safe modality of immunotherapy in treating pediatric asthma.

Saturday, 22 September 2018
Poster Discussion Session II
10:45 – 11:45

P08 - Evaluation Of IL-10/IL-17 Ratio As A Predictor Of Response To Allergen Immunotherapy In Children With Allergic Rhinitis

Catalina Cojanu(1), Liliana Rogozea(2), Ioana Agache(3)
1. Theramed Medical Center, Brasov, Romania
2. Transylvania University, Brasov, Romania
3. Faculty of Medicine, Brasov, Romania

Background

Allergic rhinitis (AR) is efficiently treated using allergen immunotherapy (AIT). No clinical or immunological biomarkers are validated as predictors of successful AIT. Increased serum IL-17 was suggested as a predictor of poor response to AIT in children with AR. IL-10 is described as a biomarker of induction of immune tolerance via AIT. Our hypothesis was that high IL-10/low IL-17 ratio is related to response to AIT.

Materials and methods

We evaluated 16 children with AR (mean age 8.13 ± 3.07 years old) ,13 (81%) boys, undergoing subcutaneous AIT (SCIT) for at least 2 years with house dust mites (14 cases, 87.5%) and grasses (2 cases, 12,5%). SCIT responders were defined as having no symptoms after natural allergen exposure, negative skin prick test and negative nasal provocation test for the SCIT allergen. Serum levels of IL-17 and IL-10 were measured using commercially available quantitative sandwich enzyme immunoassays. High IL-10/low IL-17 ratio at the end of SCIT was evaluated as a predictor of SCIT success in multiple regression analysis together with age at SCIT start, duration of SCIT, sensitization pattern (mono-/polysensitized), lack of asthma association, allergen type (seasonal/perennial), allergen avoidance, compliance to SCIT schedule, level of sensitization (low/high), low levels of serum IL-17.

Results

5 (31.3%) AR children fulfilled the criteria for SCIT responder. Serum IL-10 levels were increased in all patients receiving SCIT but with mean values higher in responders. 4 children had high serum IL-17, and all were non-responders. 12 children had a high IL-10/low IL-17 ratio, 5 of which were responders and 7 non-responders. All 4 cases with high IL-10/high IL-17 were encountered only in non-responders. However in the multiple regression analysis high IL-10/low IL-17 ratio did not reach statistical significance.

Conclusion

High IL-10/low IL-17 ratio did not predict response to SCIT in children with allergic rhinitis

P09 - Oral Immunotherapy for milk allergy using omalizumab: A case report

Yadira Y Gordón Trigueros, Carmen Riggioni Viquez, Olga Domínguez, Monica Piquer, Davinia Vásquez, Rosa Jiménez Feijoo, Ana M Plaza, Montserrat Alvaro Lozano
Hospital Sant Joan De Deu, Barcelona, Spain

Background

Omalizumab (OMZ) is a recombinant humanized monoclonal antibody that binds IgE. Currently it's approved for treating allergic asthma and chronic spontaneous urticaria. OMZ has also been used off-label for other allergic conditions including food allergy. Studies suggest that OMZ used during oral immunotherapy (OIT) for cow's milk allergy (CMA) can decrease the time required to reach maintenance dosing and adverse events, however the length of the OMZ treatment maintenance phase is still under debate.

Case report

A 13 years old female with the diagnosis of CMA at 8 months of age, after a moderate anaphylaxis with milk formula. She followed a strict cow's milk (CM) elimination diet but suffered adverse events with hidden CM allergen resulting in 2 moderate anaphylaxis. She was first seen by our pediatric allergy team at 5 years old, when she was diagnosed with CMA, severe allergic asthma and sensitization to cat dander and house dust mites. At 6 years old, she had persisting symptoms of asthma and exacerbations despite high-dose of long acting beta agonists in combination with corticosteroids, so it was prescribed OMZ showing clinical and spirometrical improvement. Six months after beginning treatment with OMZ, she started CM-OIT following a step-up protocol. The up-dosing phase lasted 5 months, no adverse events were reported and she was able to tolerate 200 ml of CM. During the first 4 years of maintenance phase, our patient had 200 ml CM daily as well as products containing CM protein. She only presented one mild adverse reaction associated with exercise as a cofactor in the first year of maintenance phase. OMZ was finally stopped at fifth year of treatment (11 years old), at that moment she had well controlled asthma without any maintenance treatment. During the first 6 months, she had no reactions with CM. After that, she started frequent mild reactions and 3 moderate anaphylaxis to CM (1 associated with cofactor) during the next 10 months. This required gradual adjustments of the CM-OIT. Finally, the patient was able to tolerate 100 ml CM without serious adverse events for the past 4 months.

Conclusion

OMZ is effective in protecting from adverse events during OIT. This effect disappears after the discontinuation even though having been used for 5 years. Thus, patients need to be carefully monitored after OMZ withdrawal. Large clinical trials are needed with the follow-up of patients who have received combined treatment with OMZ and CM-OIT to determine the effectiveness and length of treatment.

Table 1. Evolution of specific CM-IgE and fractions

Laboratory findings	**Initial (without OMZ)**	**Year 1 (OMZ + CM-OIT)**	**Year 4 (OMZ + CM-OIT)**	**Year 6 (1 year after stopping OMZ)**
Total IgE (KUI/L)	1477,00	1012,00	796,00	367,00
Specific CM-IgE (KU/L)	1022,00	474,00	86,90	>100
α-lactalbumin (KUI/L)	20,20	-	17,00	36,50
β-lactoglobulin (KUI/L)	41,50	-	11,80	25,90
Casein (KUI/L)	1856,00	676,00	>100	>100

P10 - Pediatric Anaphylaxis Cases Due To Allergen Immunotherapy In Tartu: A Single-Center Experience

Anneli Larionova, Mari Kivivare, Maire Vasar, Kaja Julge, Tiia Voor
Children' s Clinic of Tartu University Hospital, Tartu, Estonia

Background

Allergen immunotherapy is considered an effective treatment method that has been used on rhinitis, asthma and venom anaphylaxis, but its' use is limited due to potential

of producing systemic reactions (SRs). The estimated frequency of subcutaneous immunotherapy (SCIT) related SRs is 0.1-4 % of all injections. Our aim was to assess anaphylaxis cases due to allergen immunotherapy (AIT) in our center.

Materials and methods

A retrospective review of anaphylaxis cases (ICD-10 codes T78.0 – T78.2) consulted and admitted in Children' s Clinic of Tartu University Hospital between 2010 – 2014.

Results

During the study period, there were 3 patients diagnosed AIT-associated anaphylaxis. Interestingly all three cases occurred in December 2014, which was the third month of treatment (out of pollen season) and they all had reached the same phase of treatment. All patients were male, treated with standardized depot alum – adsorbed pollen (2 tree pollen, 1 grass pollen) extracts. Injections were applied subcutaneously by the same experienced nurse. We had a total of 63 anaphylaxis patients (68% male, M:F ratio 2:1). Main anaphylaxis triggers were food (65%), insect stings (17.5%) and idiopathic anaphylaxis (6.3%), followed by less frequent cause SCIT (4.8%). According to WAO subcutaneous immunotherapy systemic reaction grading system all reactions were classified as Grade 2, involving upper and lower respiratory symptoms and cutaneous symptoms in all and gastrointestinal symptoms in one patient. All patients stopped AIT because of systemic reactions. The total number of injections of SCIT during year 2014 was 527, according to this the frequency of SCIT related systemic reactions was 0.5%. No SRs have been reported on subcutaneous immunotherapy after this period.

Conclusion

The incidence of severe systemic reactions due to SCIT is rare in our center. Although the risk factors for severe systemic reactions were absent, three anaphylactic reactions arose in a certain particular time period, which might have been caused by the properties of the allergen extract.

P11 - The Efficacy Of SLIT With Ambrosia And Artemisia In Children With Allergic Rhinoconjunctivitis

Hanna Kasianenko, Serhii Goncharuk, Yurii Bazhora
Odessa National Medical University, Odessa, Ukraine

Background

The aim of the study was to investigate the efficacy of the initial course of sublingual immunotherapy (SLIT) with ambrosia and artemisia in children with allergic rhinoconjunctivitis (ARC).

Materials and methods

We examined 330 children aged 5 to 18 years living in the southern regions of Ukraine, with ARC. Sensitization to major and minor components of weed allergens (ambrosia, artemisia) was determined using ImmunoCAP (Phadia) technology. Sensitization to the major component of ambrosia (w230 - nAmb a 1) was detected in 188 patients (58.93%), to the major component of artemisia (w231 - nArt v 1) in 48 (15.04%) patients. Combined sensitization was noted in 83 (26.01%) patients. Only 5 patients (1.52%) have sensitization to the major component of grass (g213-rPhlp1, rPhlp 5b), and 6 (1.82%) have sensitization to the minor component of grass (g214-rPhlp7, rPhlp 12). All patients with sensitization to the major components of ambrosia and artemisia (319 children) received the initial course of SLIT (Diater, Spain) after the flowering season. Criteria for exclusion from the group were: the presence of adenoid vegetations, complicated rhinosinusitis and conjunctivitis, wheezing.

Results

The efficacy of the treatment was assessed by the laboratory data after the completion of the SLIT course (sIgE, sIgG4, IgE total, ECP) in 186 patients. A decrease in sIgE was noted in 82.8%, a decrease in total IgE in 89.4%, ECP in 90.3% of patients. The increase was observed in sIgG4 in 74.7% of the subjects.
The dynamics of clinical symptoms was evaluated after one year of treatment according to the criteria: has not changed; episodic symptoms; decrease in the duration of seasonal symptoms; absence of symptoms. The initial treatment significantly reduced the symptoms of ARC and their duration in 254 children (79.6%); 12 (3.76%) episodes were occasional and 37 (11.6%) had no symptoms completely. Only in 16 (5.02%) clinical symptoms remained of the same intensity.
The amount of drug therapy (dosage of the drugs used during the flowering season) was evaluated according to the criteria: it did not change; decreased; drugs were not used. The amount of therapy did not change in 53 children (16.6%), decreased in 223 (69.9%). 41 children (12.6%) did not use medications.

Conclusion

The initial SLIT course is an effective method of treating children with seasonal ARC, which reduces the clinical symptoms, accompanied by the positive dynamics of laboratory indices, and contributes to a significant reduction in the amount of drug therapy in patients.

P12 - Factors That May Influence The Adherence On Specific Immunotherapy For The Treatment Of Allergic Respiratory Disease: A Pilot Study

Ingrid Johana Gil-Serrano, Cristina Blasco Valero, Blanca Vila-Indurain, Teresa Garriga Baraut
Pediatric allergy unit. Pediatric Pneumology section. Hospital Universitari Vall d'Hebron, Barcelona, Spain

Background

The allergic respiratory disease represents one of the most prevalent chronic disease in children; although allergen immunotherapy (AIT) has been demonstrated to be an effective treatment for the disease, there is not always a good adherence to this treatment. The aim of this study is to determine which factors may influence the adherence to AIT for allergic respiratory disease in our patients.

Materials and methods

Retrospective evaluation of 110 patients diagnosed of allergic rhinitis (AR) and/or allergic asthma (AA) on which subcutaneous AIT was first prescribed, with an inclusion period of one year. Demographical characteristics, allergological evaluation, and factors by which AIT was not initiated or not continued were evaluated.

Results

Mean age was 10 years (range=3-17), 60% (n=66) patients were males. Thirty-two percent (n=35) of the patients had AR, and 66.3% (n=73) had AA and AR. From the total patients, 9% (n=10) did not initiated AIT due to economic issues, and 6.3% (n=7) of patients did not initiated because of improvement of symptoms with conventional treatment (n=3) or parents didn't want to start this specific treatment (some of them had doubts on the efficacy of the treatment, n=4). On the other hand, 10% (n=11) of the patients who initiated the AIT did not continued the treatment, from which 1.8% (n=2) were due to economic issues, 1.8% (n=2) because of adverse events (both of them had bronchospasm), 4.5% (n=5) due to personal problems (most frequent was to have an unstable family for example divorced parents who were not able to go to each appointments), and 1.8% (n=2) for lack of response. One of the patients suspended AIT for improvement of symptoms after 8 months of treatment. As secondary findings: From all the patients, the most common composition of the AIT was House Dust Mite in 84.5% (n=93) children. Fifty-eight percent (n=64) of the patients had a complete response to AIT after a year (asymptomatic and/or needed promptly rescue medication), 13.6% (n=15) had partial response to AIT (still had some symptoms or need some rescue medication) and 5.4% (n=6) children had not responded (still had all symptoms and need all rescue medication).

Conclusion

The most influential factor for not starting AIT in our patients is due to economic problems. For patients who started AIT, the most influential factor for not continuing, was personal problems as not having a supportive family, economic issues and the presence of adverse reaction.

P13 - Utility Of Specific Allergen Immunotherapy On Physician's Prescription Of Medication Among Children With Allergic Rhinitis

Prapasri Kulalert
Division of Allergy and Immunology, Department of Pediatrics, Faculty of medicine, Thammasat University, Pathumthani, Thailand

Background

Allergic rhinitis is the common allergic disease in children. Intranasal corticosteroid, oral H1 antihistamine and antileukotirene are commonly prescribe in these children. Subcutaneous immunotherapy (SCIT) has been widely used for the treatment of allergic rhinitis in children. In daily practice, physicians usually step down medications in children who underwent immunotherapy if their clinical symptoms have well controlled. Physician's prescription patterns for allergic rhinitis medication is the appropriate parameter to show efficacy of immunotherapy. The aim of this study was to compare physician's prescription of medication before and after treatment with immunotherapy in children with allergic rhinitis.

Materials and methods

This study was a one-group, before-after design (self-controlled design) in children under 15 years old who was diagnosed allergic rhinitis and underwent allergen specific immunotherapy at the Pediatric Allergy Clinic of Thammasat Hospital, Pathumthani, Thailand. Total amount of allergic rhinitis medication 1 year before and 1 year after underwent immunotherapy were collected. The primary outcome was to compare amount of medication before and after immunotherapy. Outcome measures were analyzed using paired t-tests for normally distributed data and Wilcoxon signed-rank test for skewed data.

Results

A total chart of 10 children were reviewed, of which 7 (70%) were male. The mean age was 12.7 ± 1.6 years. 6 (60%) children were treated with mite immunotherapy, 3 (30%) children were treated with mite and cockroach immunotherapy, and 1 (10%) were treated with cockroach immunotherapy, respectively. Intranasal steroid was prescribed 8.4 ± 3.9 bottles before initiation immunotherapy and 4 ± 3.7 bottles after initiation immunotherapy, p-value < 0.01. Oral H1-antihistamine was prescribed

265.5 ± 92.9 tablets before initiation immunotherapy and 171.5 ± 94.2 tablets after initiation immunotherapy, respectively, p-value = 0.02. Oral antileukotrienes was prescribed 257.5 ± 105.8 tablets before initiation immunotherapy and 99.4 ± 90.3 tablets after initiation immunotherapy, respectively, p-value =0.01.

Conclusion

Immunotherapy is effectiveness in children with allergic rhinitis. Our studies showed pattern of physician's prescription of medication was significant decrease after treatment with immunotherapy.

P14 - Acceptance Of Sublinguial Immunotherapy By Parents For Their House Dust Mite Sensitive Children With Recurrent Wheeze And Or Nocturnal Cough

Purushotam Dan
Mandore sattelite hospital, Jodhpur, India

Background

Allergen immunotherapy is known for more than 100 years and it is only treatment strategy having disease modifying capability .But traditional subcutaneous immunotherapy is less popular in paediatric patients because of potential side effects and painful injections.We did a survey at our out patient clinic to know acceptibility of sublingual immunotherapy in parents for their symptomatic mite sensitive children.

Materials and methods

Between january 2017 to december 2017 children between age of 6 to 10 years attending our clinic with history of recurrent wheeze and nocturnal cough were tested for selected indoor allergens.Parents of house dust mite sensitive children were counselled about specific avoidance measures.They were told about potential disease modifying capability of sublingual immunotherapy,its potential benifits and short comings and then they were given option to enroll for sublingual immunotherapy for their symptomatic children.In sublingual immunotherapy we used here glycerinated extract of house dust mite.Parents were demonstrated how drop should be held under the tongue for a specific period of time,and then residual swallowed.

Results

Total 30 children tested positive for house dust mite.Out of 30 symptomatic children who were tested positive for house dust mite, 12 had parentral history of asthma or allergic rhinitis,among these parents when asked to enroll for sublingual immunotherapty, 10 out of 12 parents[>80%] enrolled for subligual immunotherapy for their children.Rest 18 parents of mite sensitive symptomatic children without parentral history of allergic disease when asked to enroll for sublingual immunothwerapy,7[>35%]chose for sublingual immunothjerapy. Overall more than

50%,17 out of 30 parents were ready to be enrolled for sublingual immunopthjerapy for their children.

Conclusion

Sublingual immunotherapy is well accepted by parents for their house dust mite sensitive symptomatic children specially more with positive parentral history.

Symptomatic house dust mite children with negative parentral history of allergic disease.	Symptomatic house dust mite children with negative parentral history of allergic disease.

P15 - Evaluation Of PD-1 Expression On Different Subpopulations Of T-Lymphocytes In Donors And Patients With Allergic Rhinitis

Nadezhda Knauer, Ekaterina Pashkina, Yulia Konyakhina, Daria Demina, Vera Nepomnyaschikh, Marina Leonova, Vladimir Kozlov
Research institute of fundamental and clinical immunology, Novosibirsk, Russia

Background

The pathogenesis of allergy includes different mechanisms, such as increasing of number of activated effector cells or decreasing of number of cells with suppressive activity. Thus, the evaluation of markers of activation and suppression such as PD-1 and CD25 on T-lymphocytes in healthy donors and patients with allergy before and after the allergen-specific immunotherapy (ASIT) can be interesting.

Materials and methods

There were 5 groups 6 persons each included in the study: healthy volunteers (group I, age 21,5 (20;28)); naïve patients with allergic rhinitis (AR) before and after the first course of ASIT (groups II and III respectively, age 32 (19;46)); patients who had previous courses of ASIT before and after the new course (groups IV and V respectively; age 36 (20;52)). All patients had sensitization to birch pollen allergens of dust mite allergens confirmed by skin prick tests. Peripheral blood mononuclear cells were extracted from heparinized blood, then they were stained for flow cytometry. Statistical analysis was made by using Mann-Whitney and Wilcoxon criteria, the result was considered as significant in the case $p<0,05$.

Results

We found the significant decrease of CD4+CD25+cells after the therapy in patients with several courses of ASIT in the past. Donors had higher amount of CD4+CD25hiPD-1+cells than patients before the first course of ASIT and patients with ASIT in the past before and after the new course. There was the significant increasing of CD4+PD-1+ cells after therapy in both groups (groups III and V). Donors had the lower amount of CD8+CD25+cells than patients. The level of CD8+CD25+PD-1+cells is less in the donors group than in patients after therapy, the amount of these cells increases significantly after therapy.

Conclusion

We found the decreasing of CD4+lymphocytes expressing CD25, which can be considered as the marker of activation, after the therapy, however the number of CD8+CD25+ cells increases in patient groups. In the same time, the number of CD4+CD25hi cells associated with the population of T-regulatory cells had higher level of PD-1-expression in donor group than in patient groups. The number of cells expressing PD-1, which can regulate negatively the immune response, increases after therapy. These results can confirm the hypothesis that allergic diseases can be associated not only with increasing the number of activated effector cells, but with reduction of subpopulations with suppressive activity. The data also demonstrate the changing of balance between activating and suppressing of immune response after the immunotherapy.