51. Allergen immunotherapy and anti-immunoglobulin E

P262
Sublingual allergen extract immunotherapy in a rush pattern to reach the maintenance faster
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Introduction: Slit (sublingual immunotherapy) Rush immunotherapy was tried on some patients to evolve some faster and affordable immunotherapy modality to make the patient achieve the maintenance plateau within a very short time. Conventional method of immunotherapy is administered with long durations; rush immunotherapy is super fast methodology in attaining the maintenance/boosting module, which requires hospitalization and other precautionary methods, and multiple allergen vaccines to be administered within a short span of time. Also in this method, it was found that within 15-20 days the relief of the immunotherapy was reached.

Material & method: 186 patients out of which 48 with urticaria allergy and 138 with allergic Rhinitis & Bronchial Asthma were selected. The therapy consists of administration of four vials of allergen extracts, 1st vial: 1:25,00, 2nd vial 1:2,50, 3rd vial 1:25, and 4th vial 1:10 dil. The 1st & the 2nd concs were administered in daily 6 hourly schedules in a graphically rising manner. The patients had been given pre-medication. Blood examination and IgG & IgE level estimation were done before & after 8 weeks.

Results: Some of the patients showed local skin reactions which subsided without drugs and no systemic reaction was noted. There was substantial decrease in IgE & increased IgG level, significant & marked satisfactory relief was observed in the patients symptomatology, thus the procedure was graded as a very fast & affordable & SAFE immunotherapy.

P263
Adherence to sublingual immunotherapy in patients allergic to mites
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Background: Adherence is essential for effective treatment. Specific allergen immunotherapy (SIT) should be continued until the patient has had substantially reduced symptom free for 3 or 5 years. Sublingual immunotherapy (SLIT) is referred to improve adherence to SIT. The aim of this study was to identify factors that may influence adherence to SLIT.

Methods: We evaluated 610 patients (15-45 years), 54.4% male, monosensitised to house dust mites with moderate persistent rhinitis and mild persistent asthma, submitted to SLIT in the last 5 years. We analysed factors related to non adherence to SLIT.

Results: 81 patients (13%) suspended SLIT based on different motives: For 28 patients (35%), main reason for discontinuation of SLIT is inability to take medication according to schedule: 21 patients (26%) withdrew in the first 4 months because of local side effects. 14 patients (17%) due to symptoms resolution: they began to show a 30% improvement of their symptoms compared to the basal score, already 6 months after the start of the therapy. 10 patients (12%) “get bored” after 6 months of maintenance treatment. 5 patients (6%) stopped because they went to holidays or working habits, 3 patients (4%) due to respiratory recurrent infections. After quitting SLIT, 14 patients (17%) preferred subcutaneous specific immunotherapy.

Conclusions: The main cause of SLIT cessation was desertion, suggesting a need of a greater number of clinical appointments, at least during the first six months of treatment. Candidates to SLIT should be well selected to improve adherence to treatment. The ineffectiveness of SLIT could not be explained by non-adherence.
Pre-seasonal (PS) and maintenance (M) schedules of specific subcutaneous immunotherapy (SCIT) with allergens are used to treat patients suffering from seasonal allergic rhinitis. Which of them is more profitable? The aim of the study was to compare an efficacy of two schedules of SCIT, PS vs. M.

Fifty seven patients included into the study randomly divided into two groups: PS group (n=28) and M group (n=29). Allergolog® 906 – grass pollen (Allergopharma, Germany) was chosen to treat of them. SCIT lasted 3 years. Every year since 1st May-31st August diary cards were fulfilled. Intensity of symptoms (sneezing, nose itching, rhinorhoea, nasal obstruction, eye itching, lacrimation, eye reddening, cough and shortness of breath) and concomitant drug consumption were evaluated. Serum total and sIgE were evaluated before and after stopping SCIT. Intensity of a pollination was evaluated every year. Each individual from PS group was injected 30 times and obtained cumulative dose of 860629 IU/ml, whereas the one from M group - 414859 and 172892 IU/ml. In 2006 the highest concentration of grass pollen in the air was 197/m³, in 2007 much higher – 475/m³, and in 2008 – 247/m³. The highest intensity of the symptoms in both group were registered in the first season of SCIT (2006). No significant differences between PS and M were found. The intensity of the symptoms decreased in successive years of SCIT, and in M group was more evident. After SCIT the concentration of sIgE and slgE decreased significantly.

Conclusions: Both schedules, PS and M of SCIT with allergoid vaccine are effective in pollinosis patients, but M is more profitable.

P265
Pollen asthma treatment: Comparative efficacy study
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Background: Airborne pollen has always been one of the most common triggers of asthma, so there is vital need in efficient hypothesensibilisation.

Aims and objectives: The principal aim was to check efficacy of different combinations of inhaled corticosteroid/long-acting β2 agonist upheld by specific immunotherapy and/or montelukast.

Methods: In open-label, randomized, parallel group, one-year panel study were involved 468 patients with pollen asthma (moderate-to-severe airflow limitation, bronchitis symptoms, and a history of exacerbations). All participants had completed allergy examination (prick skin test), immunologic, and functional assessment concerning their asthma status. Participants were randomized in three equal groups, 156 patients each. First group got specific immunotherapy, second - montelukast (Singular), and third – both treatments. Entire population received budesonide/formoterol (Symbicort Turbuhaler) as well.

Results: After 52-week treatment first group exhibited strong remission in 68% of patients assigned, second group – in 61% patients, and third group – in 79% patients. These changes were statistically independent of patient’s age, sex, and smoking status (P<0.01).

Conclusions: Budesonide/formoterol in conjunction with allergen-specific immunotherapy and montelukast proved to be the most successful combination for curing pollen asthma.

P266
Omalizumab in asthmatics with IgE levels > 700 IU/ml
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Introduction: Omalizumab, a monoclonal antibody against IgE, has been effectively used to control symptoms and reduce steroid requirements in asthmatics with severe allergic asthma. Its use when IgE levels are < 30 IU/ml (786-10979) vs. 221 IU/ml (30-578) respectively (p<0.001). Age, gender, and weight were similar in both groups. Both, Group 1 and Group 2 had an improvement in asthma control based on the mean ACT pre and post treatment (15.6 vs. 18.9 [p=0.016] and 15.4 vs. 19 [p=0.006]) respectively. There was also a significant reduction in the frequency of systemic corticosteroid use during the 6 months pre and post treatment (2.58 vs. 0.96 and 2.62 vs. 1.23/steroid bursts respectively (p<0.001).

Conclusions: Omalizumab was effective in controlling asthma symptoms and reducing the need for systemic corticosteroids in patients with IgE levels > 700 IU/ml and produced clinical improvement similar to patients with IgE levels between 30-700 IU/ml.

P267
Effects of add-on omalizumab therapy on airway wall thickening in severe persistent asthma
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Background: Omalizumab has an important role in inhibiting the allergic inflammation, and it could possibly contribute to decreased airway remodeling in patients with asthma.

Aims and objectives: The aim of the study is to assess the effects of omalizumab on airway wall thickening using computed tomography (CT).

Methods: Twenty-eight patients with severe asthma were randomized to treat with conventional therapy with (n=13) or without omalizumab (n=15) for 16 weeks. Airway dimensions were assessed by CT, and wall area corrected for body surface area (WA/BSA), percentage wall area (WA%), wall thickness (T)/BSA at the right apical segmental bronchus were measured before and after treatment. The percentage of eosinophils in induced sputum, pulmonary function, and Asthma Quality of Life Questionnaire (AQLQ) were also measured.

Results: Treatment with omalizumab significantly decreased WA/BSA, WA% and T/BSA (p<0.01, each) whereas conventional therapy had no change. In the omalizumab group, there were significant decrease in the sputum eosinophils (p<0.01), and improved forced expiratory volume in 1s (FEV1), morning expiratory peak flow and the AQLQ score. The changes in FEV1% predicted and sputum eosinophils were significantly correlated with changes in WA% (r=0.88, p<0.001, and n=072, p<0.01, respectively).

Conclusions: These findings suggest that omalizumab reduced wall thickness and airway inflammation.
Severe uncontrolled asthma is a contraindication against allergen-specific immunotherapy due to increased risks of side effects and asthma exacerbations. Omalizumab (Xolair®) has been shown to be an effective treatment for patients suffering from severe allergic asthma and to increased safety of allergen Specific-immunotherapy SIT. We describe 3 patients (males, 28, 31 and 42 years) with severe asthma GINA III IV and total IgE ranging from 181 to 680 IU/ml undergoing a combination of Omalizumab and house dust mite-SIT. House dust mite (HDM) allergy was confirmed by clinical history, positive skin prick tests, elevated specific serum IgE and positive conjunctival challenge tests. In all 3 patients Omalizumab was initiated according to manufacturer’s recommendation. After 3 months in all patients asthma improved requiring less inhaled drugs and an improved quality of life. The felt effect of HDM exposure was also reduced but still present. Thus we added an allergen-specific immunotherapy with HDM as the asthma situation was stable. We opted for an ultra-rapid induction regimen with a total of 6 injections over 4 hours and a cumulative dose of 100'000 SQU. Patients were closely monitored. All patients tolerated the ultra-rapid induction very well. The maintenance regimen of the HDM extract was then injected on a monthly base. Also Omalizumab was continued on the initial dose. Omalizumab may enable induction of allergen-specific immunotherapy with HDM in severe asthma patients otherwise not accessible to this approach. The long term effect of this combined treatment will have to be further evaluated to judge clinical and pharmacoeconomical aspects.

Omalizumab is approved as add-on therapy for patients (age ≥ 6 years, European Union) with uncontrolled severe persistent allergic (IgE-mediated) asthma. Few studies have reported onomalizumab’s effectiveness on real-life outcomes in UK clinical settings. We report clinical outcomes in severe allergic asthma patients receiving omalizumab (150-600 mg q4wk or q2wk) at 3 UK centres (St Peter’s Hospital, Chertsey, Bradford Royal Infirmary, Colchester Hospital). Data were compared for 2-years pre-omalizumab and for the most recent assessment following omalizumab initiation. Patients (n=52; age 18–74 years) received omalizumab for an average of 982 days (range: 112–3839). 86.4% patients responded to treatment at 16 weeks. Following omalizumab, hospital admissions/bed days, A&E and GP visits decreased compared with pre-omalizumab (Table). Oral corticosteroid (OCS) use was also reduced post-omalizumab; mean maintenance dose of OCS pre- and post-omalizumab was 12.6 and 5.7 mg/day (n=45). Overall, mean [SD] improvement in AQLQ score was +1.39 [1.80]. Asthma control also improved post-omalizumab, as shown by an overall increase in mean [SD] ACT of +7.29 [4.64]. Patients not receiving OCS at baseline (n=14) achieved higher mean [SD] AQLQ scores compared with those on OCS at baseline (n=29; 2.29 [1.23] vs 1.36 [1.77]).

Severe persistent allergic asthma were or were not receiving continuous OCS. Percentages of patients reducing/stopping OCS use, changes in exacerbation rates, hospitalization and accident/emergency visit rates, overall responder rates and FEV1, all improved post-omalizumab (Table). Responses were similar when comparing those who were and those who were not on continuous OCS at baseline. In conclusion, the benefits of omalizumab in patients not receiving continuous OCS at baseline were at least as great as those in patients receiving continuous OCS at baseline.

The APEX study: A retrospective review of responses of severe allergic asthma patients to omalizumab on continuous or non-continuous oral corticosteroids in UK clinical practice

Results from this pooled analysis demonstrate the real-life effectiveness of omalizumab in a clinical setting, further supporting the efficacy of omalizumab shown in clinical trials.

ROMA (registry omalizumab in Malaga): Study of 84 patients

Purpose: Our objective is to describe the patients profile and the results observed in the patients treated with omalizumab in the three main hospitals of Malaga.

Methods: Retrospective study of clinical records. All the patients including are adult with not controlled severe allergic asthma condition. A data base has been created using software SPSS 15.0.

Results: 84 patients were included (70% women), with an average age of 51 years and FEV1: 64.7±18%. The 100% of the patients had some exacerbations and 20% needed hospitalization in the previous year. 9 patients were steroids-

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Poster Discussion
...design approach to measure epidemiology variables based on patient-level data. 770 patient charts were reviewed in designated towns in Germany/Italy, in collaboration with >200 primary care physicians (PCPs) and respiratory specialists (RS). This study sample represents >50% and >70% of local RS in these designated towns of Germany and Italy, respectively. Of patient charts evaluated, 4 patients were currently receiving omalizumab. Among 391 patients (12 PCP, 19 RS) were evaluated as omalizumab-eligible (i.e., fulfilled all product label criteria) but were not receiving the drug. Extrapolating to a national level, this yields >6500 eligible patients in Germany, >3200 in Italy. Furthermore, this study sample revealed a significant number of PCPs treating uncontrolled severe asthma patients without referral to RS; these patients are not consistently evaluated for FEV1, allergen sensitivity as well as a qualitative understanding of severe exacerbations, and day and night-time symptoms. This study suggests that significant numbers of omalizumab-naïve severe allergic asthma patients in Germany/Italy are eligible for omalizumab therapy; if treated, these patients may benefit from reduction in asthma exacerbations and improved asthma control and quality of life.

P278 Cytokine production profile of T-lymphocytes and frequency of regulator T-cells in patients with allergic asthma receiving anti-IgE therapy

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Omalizumab is a recombinant anti-IgE antibody with proven efficacy in severe allergic asthma. Little is known about immunological changes induced by decreasing free IgE during omalizumab therapy. In the present study T-lymphocyte cytokine profiles and frequency of regulatory T-cells before and during omalizumab therapy in patients with severe allergic asthma were examined. Twenty patients with severe allergic asthma (14 female) who met the criteria for CD4+ CD4+ T-lymphocytes were enrolled. Before and after 16 weeks of therapy peripheral blood mononuclear cells were isolated and activated with anti-CD3/anti-CD28 antibodies. Cells were processed for intracellular cytokine staining and frequency of CD4+ cytokine + inter leukin (IL) 4, 5, 10, 17, interferon (IFN-) positive cells was assessed. The frequency of CD4+ CD25+FOX-P3+CD127- regulatory T-cells was assessed.

Anti-IgE treatment did not lead to a significant change of intracellular IL 4, 5, 10 and IFN-y in CD4+ CD4+ T-lymphocytes (mean at baseline: IL-4 5.9±3.8%; IL-5 5.1±1.1%; IL-10 4.5±3.2%; IL-17 2.0±2.0%; IFN-γ 9.2±5.6%, intradividual difference in week +16: IL-4 1.3±3.8% p=0.164; IL-5 0.2±1.2% p=0.474; IL-10 3.3±5.0% p=0.774; IL-17-1.4±6.4% p=0.376; IFN-γ 2.0±4.5% p=0.056). Additionally, there was no significant change in frequency of regulatory T-cells (mean at baseline: Treg 11.4±5.7%; intradividual difference in week +16 Treg 0.4±5.9% p=0.730).

In this study there was no significant difference of the tested intracellular cytokines before and after anti-IgE therapy. Frequency of regulatory T-cells did not change significantly 16 weeks after initiation of anti-IgE therapy.

P277 Eligibility for treatment with omalizumab in Italy and Germany

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Omalizumab is an add-on therapy for patients with uncontrolled severe allergic asthma. In Europe, patients must fulfill a number of additional criteria to become eligible for omalizumab therapy, creating a challenge for epidemiology studies to quantify the potential patient pool. Thus, and in the absence of robust data, the number of omalizumab-eligible patients has remained unclear. To assess eligible patient numbers, the team employed an innovative chart-audit...