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Original Research Article

Severe asthma in childhood and allergens

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Abstract

We evaluated the 29 children – 14 with Severe Asthma (SA) and 15 with moderate asthma – control group (CG). All children were tested for specific IgE. All SA children had concomitant allergic rhinitis in contrast to only 2 (13,3%) with CG. Higher eosinophil levels were found in SA group (p<0,05). 92,85% from SA group and 33.33% in CG had minimum 1 elevated antigen titer. The most common clinically significant allergens in SA were dermatophagoides, grass mix and cat, followed by alternaria and birch. Precise allergen detection could help for recommendation plan in patients who are unable to be tested.

Keywords: ACQ, Allergic rhinitis, nasal eosinophilia, severe asthma, specific IgE

INTRODUCTION

Atopy and allergy have long been associated with asthma and, to some degree, with severe asthma (SA). SA is a heterogeneous condition consisting of phenotypes such as eosinophilic asthma. Usually the presence of atopy or any allergic disease could interfere and obstacle the control of asthma. The association between severity of allergy and asthma is stronger in children.

In all patients, determining whether there is an association between specific IgE (as measured by skin prick testing or serum testing), on-going exposures and symptoms may help identify factors which contribute to asthma symptoms and exacerbations. Even specific recommendations on the use of sputum eosinophil count and exhaled nitric oxide to guide therapy, as well as treatment with anti-IgE antibody are provided.

MATERIAL AND METHOD

For a period of 6 months (Feb-Jul 2014) we evaluated medical history data of 29 children with asthma divided into two groups – 14 (6 girls, 8 boys) with severe asthma (SA) on high dose combined inhaled corticosteroids (ICS) and 15 (6 girls, 9 boys) with moderate asthma, matched by age to serve as a control group (CG).
For all children we performed:

- pulmonary function tests (PFT) (pre- and post-bronchodilator spirometry),
- nasal smears for eosinophil counts,
- drew blood for IgE against inhalation and food allergies antibodies detection
- ACQ* (Asthma Control Questionnaire, validated Bulgarian translation; interviewer-administered version for the age 6-10 years).

The specific IgE were assessed with in vitro semi-quantitive test with predesigned kit – Enzyme Allergo Sorbent Test (EAST), Euroimmune ® (Medizinische Labordiagnostica, Germany), Euroline Allergy Profile Pediatrics.

For the study an approval from our institutional board have been obtained. And before any intervention and test for all patients an informed consent was signed by both parents/legal guardians.

Statistics:

We used SPSS v. 19. Software. A p value of, 0.05 was considered statistically significant.

RESULTS AND DISCUSSION

The sex and age distributions between the two groups showed no significant difference (Table1). No significant

Table1. Summary statistics.

	SAG (n=14)	CG (n=15)	p*
Age (ys) (mean ± SD)	11,1±1,2	10,7±1,5	p>0,05
Gender (boys/girls)	8/6	9/6	p>0,05
FH – asthma (yes/no) (% yes)	7/7 – 50%	6/9 – 40%	p>0,05
FH - atopy (yes/no) (% yes)	7/7 – 50%	8/7- 53,33%	p>0,05
Allergic rhinitis (yes/no) (% yes)	14/0 – 100%	2/13 - 13,3%	p<0,05
SPT – positive (yes/no)	6/8 – 42,85%	3/12 – 20%	p<0,05
First symptoms (ys) (mean ± SD)	3,98±0,78	5,18±1,65	p=0,004
Age of asthma diagnosis (ys) (mean ± SD)	5,13±0,78	6,48±1,49	p=0,01
Time elapsed between first symptoms and diagnosis (ys) (mean ± SD)	1,14±0,52	1,3±0,49	p=0,44
PFT – FEV_1 (%pred.)(mean ± SD)	82,5%±4,79%	90,5%±3,52%	p=0,068
PTF – $MMEF_{25-75}$ (%pred) (mean ± SD)	51,21%±4,91%	66,06%±5,06%	p=0,051
PTF – BDR (□FEV_1%) (mean ± SD)	21,2%±4,68%	15,6±0,33%	p=0,051
Nasal eosinophilia (%)	8,45%±1,34%	4,32%±1,33%	p<0,05
Controller therapy (LtRA/ICS – low or medium dose/ ICS+LtRA/ ICS- high dose or CICS/ CICS+LtRA)	0/0/0/12/2	5/5/3/2/0	
Exacerbation last year (mean ± SD)	3±8,7	2,26±1,2	p=0,043
Hospitalizations last year (mean ± SD)	1,7±1,9	1,4±0,6	p= 0,047
ACQ (under 1,5/above 1,5)	3/11	10/5	p=0,09
(mean ± SD)	2,05±0,6	1,23±0,8	
Positive IgE in serum - yes/no – (%)	13/1 - 92,85%	5/9 - 33,33%	p<0,05
Significant IgE titer - yes/no – (%)	11/4 – 78,57%	2/13 – 13,3%	p<0,05

SAG – Severe asthma group, CG – Control group
FH – family history, LtRA-leucotrien receptor antagonist, ICS – inhaled corticosteroids, CICS- combined ICS, PFT- pulmonary function test; SPT- skin prick test; BDR – bronchodilator response; F-test, ANOVA.

difference was found in respect to family history of asthma (50% of SAG and 40% of CG) or atopy (50%, 53.3% respectively).

The children with SA showed tendency for lower scores in ACQ and PFT without statistical significance (p>0,05).

Despite the normal pre-bronchodilator FEV1 ≥ 80%, the majority of children in both groups showed relatively low MMEF25-75%pred, but lower in SAG. Statistical difference wasn't established between the two groups (p = 0.068 for FEV 1 and p = 0.051 for MSED25-75%). The relatively low MMEF25-75%pred is another confirmation of the small airways impairment where inflammation persists despite the good asthma control.

All patients showed a positive bronchodilator response (ΔFEV1≥12% and 200ml). The average improvement for FEV1 value in the SA group was 5% higher compared with the CG without statistical significance (p = 0.051), but can be considered as a trend.

All children with SA had concomitant allergic rhinitis (AR) in contrast with the control group, where only 2 (13,3%) had also AR. The nasal smears had higher eosinophil levels in SA group (p<0,05). 92, 85% (13 children) from SA group and 33.33% from the CG (5 children) had at least one elevated IgE titer (≥0.7 kU/l).

High and very high antibody titer (with clinical significance) was noted in 11 children with SA and 2 in CG. The most common clinically significant allergens in SA group are Dermatophagoides pt. and fa.(d1, d2- 7 patients), grass mix (gx- 5 patients) and cat (e1- 4 patients). Alternaria alt.– m6 and birch- t3 were also found in 3 and 2 patients respectively. In the CG 1 patient had high titer against cat and the other against grass mix. (Figure 1 and 2)

The presence of poor control (ACQ), respectively impaired pulmonary function (baseline and BDR) corresponding to the related frequent exacerbations and need for hospitalization is expected and described by other authors in patients with SA. ((Chung et al., 2014; Frith et al., 2011; Juniper et al., 1999; Redder et al., 2009).

Allergic rhinitis is widely described and defined as a risk factor for asthma. Many patients with AR have an increased nonspecific bronchial hyper-reactivity and three times higher risk for asthma (Fitzpatrick and Teague, 2006; Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2014; Pinard et al., 2014).

All patients in our study with SA have concomitant AR, which would justify the need for local (nasal corticostero-

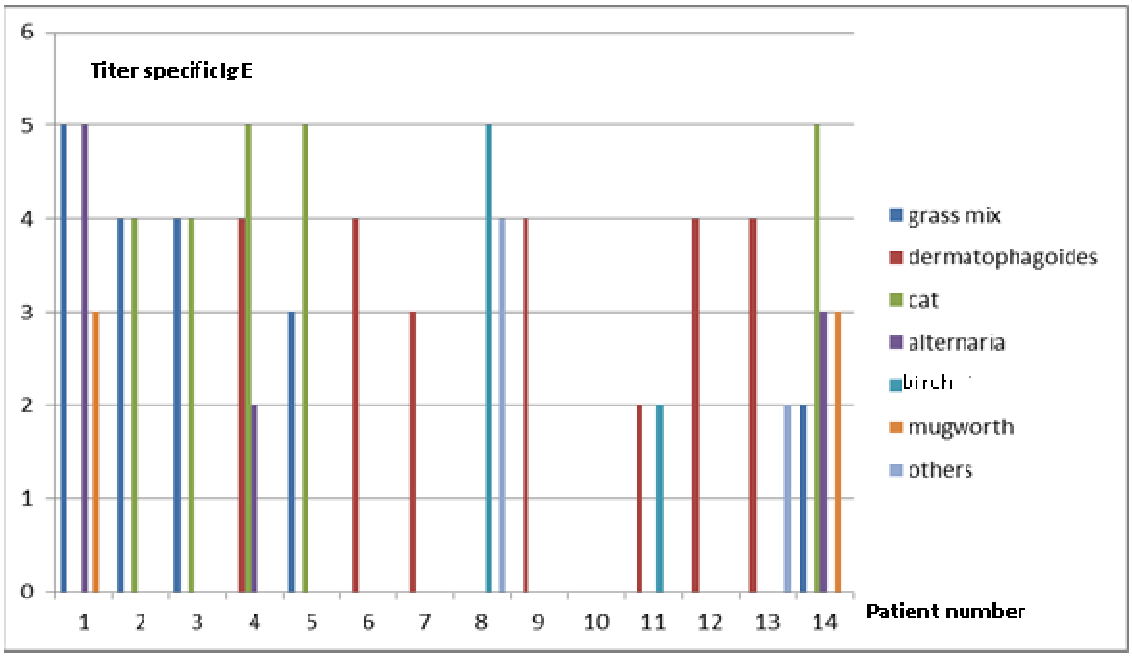

Figure 1. Clinically significant elevated specific IgE titers in the SAG patients
(Others – Dog, Horse, Cladosporium her., Aspergillus fum., Egg white, Wgg yolk, Cow's milk, Codfish, α – Lacatoalbumin, β – Lactoglobulin, Casein, Bovine serum albumin, Wheat flowr, Rice, Soybean, Peanut, Hazelnut, Carrot, Potato, Apple, CCD marker).

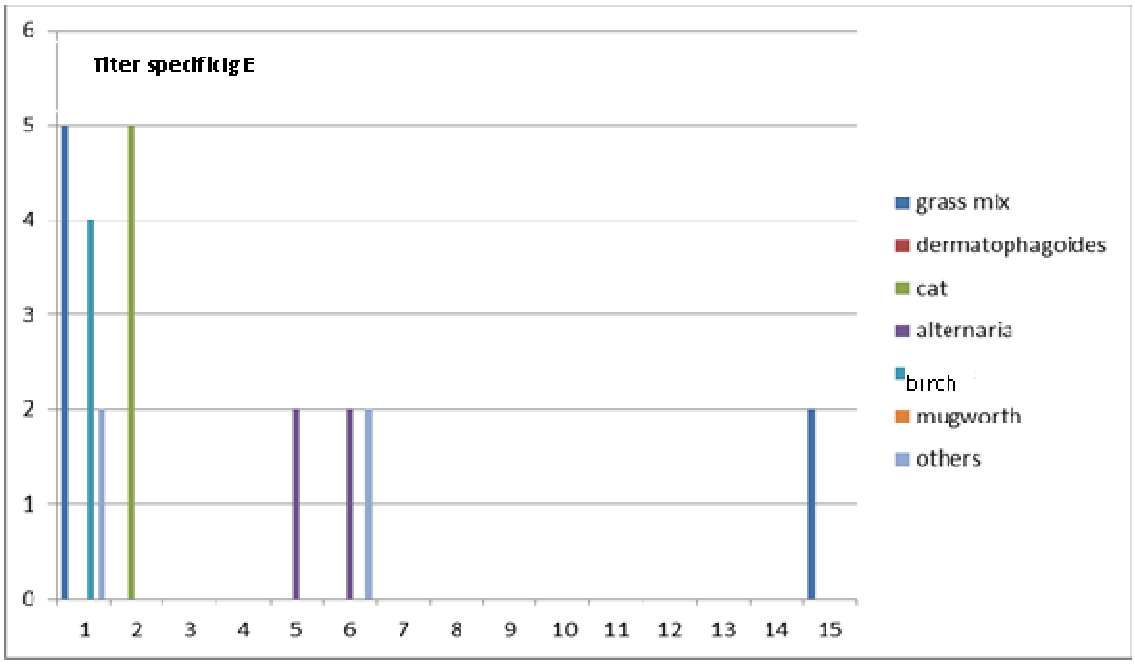

Figure 2. Clinically significant elevated specific IgE titers in the CG patients
(Others – Dog, Horse, Cladosporium her., Aspergillus fum., Egg white, Wgg yolk, Cow's milk, Codfish, α – Lacatoalbumin, β – Lactoglobulin, Casein, Bovine serum albumin, Wheat flowr, Rice, Soybean, Peanut, Hazelnut, Carrot, Potato, Apple, CCD marker).

ids) and systemic anti-allergic treatment (oral antihistamines), not as asthma controllers, but as AR medications which in turn would help to achieve better control to the underlying disease.

Sensitization to allergens from different sources is frequently observed in children with persistent asthma. The presence of allergy affects the disease course, as well as the symptoms manifestation. It is believed that persisting exposure to aeroallergens increased the bronchial inflammation and the exacerbation risk in SA patients (Sherrill et al., 1995). In order to define the strategy to avoid allergen exposure, international protocols include specific IgE testing for comorbidity identifying.

Our results demonstrate that children with SA were most sensitized to dust mites, grass mix, Alternaria alt., birch and cat. This suggests the idea that the recommendations for avoiding allergens for patients with SA have to include these 5 components and do not have to avoid foods (except in case of history of food allergen allergic reaction) and other pets. The last one can lead to stress and further deterioration of the disease control.

CONCLUSION

Precise detection of the allergen could help not only in maintaining better control in SA patients with avoidance technique, but also in designing a recommendation plan in patients who are unable to be tested.

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