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Original Research Article

Diagnostic possibilities of ECP and eosinophilia in nasal mucosa in children with different types of rhinitis

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Abstract

Early diagnosis of rhinitis in children is important both for the therapy, as well as for prophylaxis of these diseases. The aim of this study is to evaluate the differential diagnostic possibilities of ECP in children with rhinosinusitis. In our study, 50 patients with clinical symptoms of rhinitis are divided in the following three groups: in Group 1 are included children with allergic rhinitis (n = 15, 30%), Group 2 – children with non-allergic rhinitis (n = 12, 24%) and Group 3 – non-allergic rhinitis with eosinophilia syndrome (n = 23, 46%). In each patient, ECP in serum and eosinophilia in nasal secretion were examined. The serum ECP levels were measured using immune methods (Pharmacia CAP). There is no statistically significant difference in the ECP levels between the three groups, although the mean ECP concentration is higher in asthmatics with allergic rhinitis. We found that the degree of allergic inflammation in allergic rhinitis with asthma can affect the serum ECP levels.

Keywords: Allergic rhinitis in children, bronchial hyperreactivity, bronchospasm, rhinosinusitis

INTORDUCTION

Rhinitis is characterized by one or more of the following symptoms: rhinorrhea with clear and watery, in some cases slightly mucoid characteristics, itchy nose, palate, oropharynx and ears; sneezing (especially paroxysmal); nasal congestion. Since the nose is an entrance to the respiratory system, rhinitis can be associated with sinusitis or Eustachian tube dysfunction.

Allergic rhinitis is a global health problem. According to statistical data 18.2% of Bulgarian children suffer from allergic rhinitis. It is close to the data for Europe 20-25%. Allergic rhinitis can be seasonal, perennial or professional (Almqvist et al., 2007; Beeh et al., 2000; Bousquet et al., 2004; Bousquet et al., 2008).

The most frequent cause for non-allergic rhinitis is acute viral infection. Other types of non-allergic rhinitis include vasomotor, hormonal, medication-induced and non-allergic rhinitis with eosinophilia syndrome. Very often the diagnosis of rhinosinusitis is made after X-ray examination, however the differential diagnosis between allergic and non-allergic rhinitis is of great importance for the therapeutic behavior, as well as for conduction of prophylaxis (Burgess et al., 2007; Casale and Dykewicz, 2004; Chanez et al., 1999).

In allergic rhinitis the following immunological cascade develops:

- The antigen is taken by antigen-presenting cells
- Antigens are processed and the epitope appears on the surface of MHC II cells.
- CD4 + cells interact with APC and release cytokines IL3, IL4, IL5 and GM-CSF.
- They stimulate IgE production by plasmatic cells, cell proliferation and infiltration in the nasal mucosa, as well as eosinophilia
- People with atopy produce IgE and develop Th2 lymphocyte reaction.

Eosinophilic cationic protein (ECP) is released by the activated eosinophils and is one of the most important mediators of allergic inflammation in the respiratory tract. Serum ECP levels>15 mg/L show allergic inflammation and require therapy (Crystal-Peters et al., 2002; Dixon et

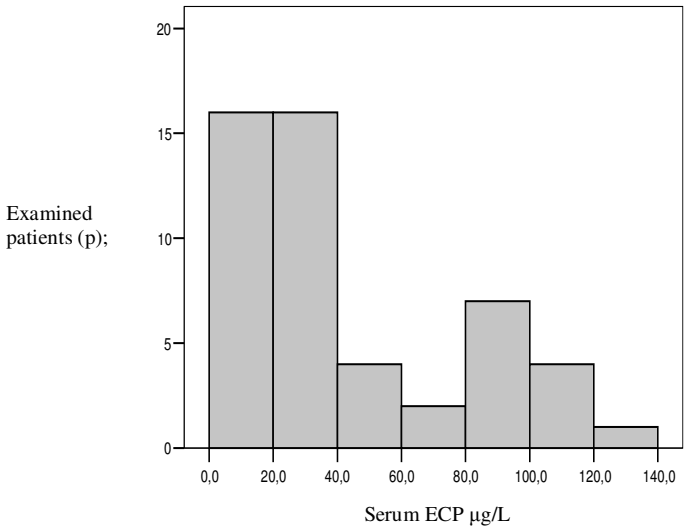

Figure 1. Serum ECP levels in the examined patients

al., 2006; Greisner et al., 1998).

The aim of the present study is to prove the differential diagnostic possibilities of ECP and eosinophils in nasal mucosa in children with different types of rhinitis.

MATERIALS AND METHODS

Participants in the study

50 children with respiratory allergy admitted in SBALBB "Sv. Sofia" city of Sofia during the period August 2012 – April 2013 were examined.

Both sexes are equally represented (boys – 48% (n=24), girls – 52% (n=26)). The children were divided in 2 groups – Allergic rhinitis (AR) and Non-allergic rhinitis (NAR).

Inclusion criteria

- history for frequent rhinitis – time period, frequency and severity
- information for preceding viral or bacterial infection
- family history for bronchial asthma and hay fever on maternal, paternal side and in first degree relatives
- repeated antibiotic therapy without effect over the symptoms

Screening for rhinitis

- CBC with differential count
- Eosinophil count in nasal secretion
- ECP in serum
- X-ray data for rhinosinusitis
- Microbiological examination of nasal secretion
- Pulmonary function test

Laboratory analysis

ECP examination

ECP is examined using fluoro-immunoanalysis UniCAP System ECP FEIA (Pharmacia Diagnostics AB, Uppsala, Sweden) of UniCAP 100. The test is a sandwich immune method. The sensitivity of the method is > 2 µg/L.

Examination of eosinophils in nasal secretion

Nasal secretion is taken and two cytological specimens stained with hematoxylin-eosin and Romanowski-Giemsa are prepared. 500 cells are counted and the ratio of neutrophils and eosinophils among them is determined as a percentage.

Statistical analysis

Statistical processing of data is carried out with statistical package SPSS Version 13. The significance level at which null hypothesis is rejected is $p < 0,05$. The following methods for analysis were used: Descriptive analysis, when searching for statistical relationships between quantitative variables, parametric (t-test) and non-parametric methods (Mann-Whitney U-test) are used.

RESULTS

The results from observation and examination of 50 children with history and clinical data for rhinitiss are

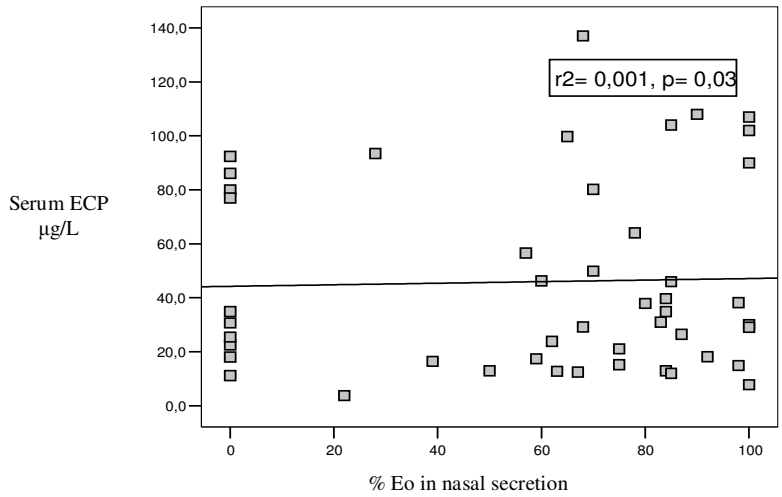

Figure 2. Relationship between serum ECP and Eo in nasal secretion

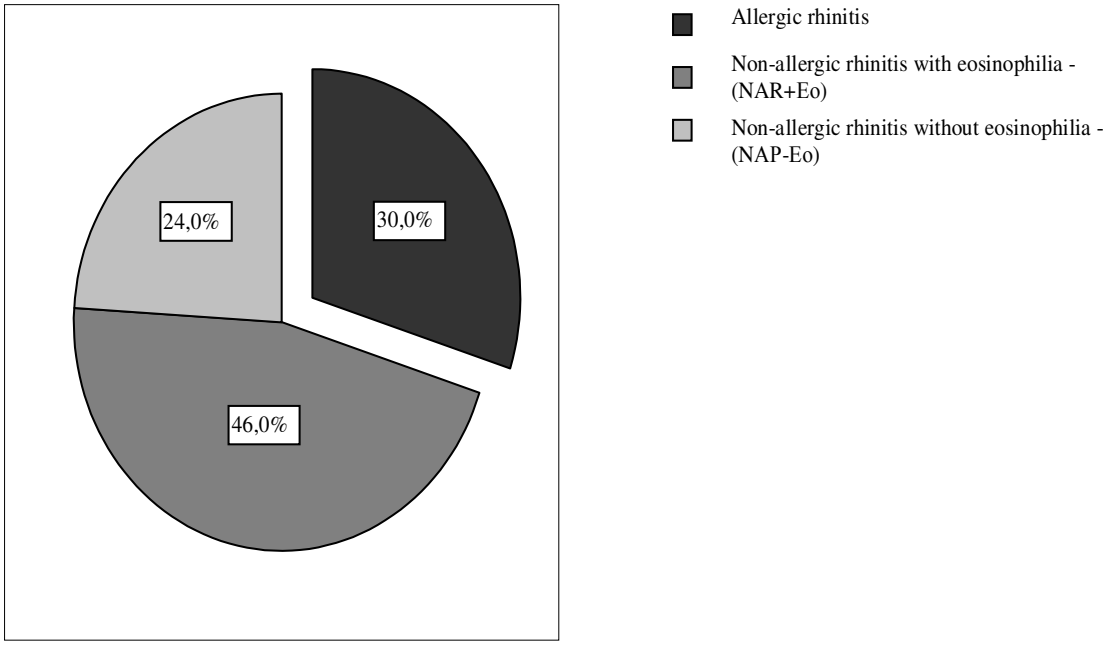

Figure 3. Group distribution

analyzed. Both sexes are equally represented (boys – 48% (n=24), girls – 52% (n=26)). 60% of the examined children are with family history for allergic diseases.

The examination for chronic bacterial carrier state showed mixed flora - *Staph. aureus* and *H.influenzae* in nasal and/or throat secretion in 6 of the children.

The serum ECP values vary from 3,8 to 1372 µg/L (mean 44,52 µg/L), Figure 1

80% (n=40) of the examined children have high values of serum ECP >11.22 µg/L.

Correlational relationship between serum ECP and nasal eosinophilia was found (Spearman test, p=0.03), Figure 2

Based on presence of eosinophilia in nasal secretion > 10%, the children with NAR were divided in two groups: Non-allergic rhinitis with eosinophilia (NAR+Eo)- 23 (66%) and Non-allergic rhinitis without eosinophilia (NAP-Eo)- 12 (34%), Figure 3

In 11 (73%) of the children with AR there is family history for allergic diseases, however it does not reach statistical significance due to the small group (Fisher test, p=0.08).

Children with history for recurrent broncho obstructive manifestations and positive broncho provocation test with physical exertion forming the Asthmatics group are 26 (52%). Their distribution in the three groups is as follows:

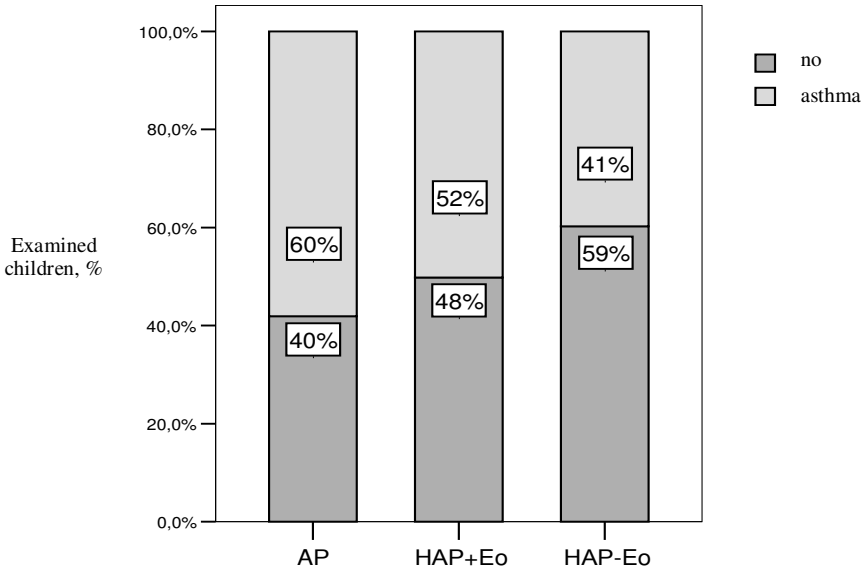

Figure 4. Ratio of asthmatics in the three groups

60% of the children with AR have asthma, compared to 52% for NAR+Eo and 41% for NAR-Eo, the difference does not reach statistical significance (Fisher test,p=0.6), Figure 4

Statistically significant difference in the serum ECP concentration among the three groups was not found (ANOV test, p= 0.8).

DISCUSSION

In 1998, three large expert committees came up with recommendations for differentiation between allergic and non-allergic rhinitis. Non-allergic rhinitis with eosinophilia syndrome is a clinical syndrome that includes symptoms of allergic rhinitis, at which atopy is excluded and in nasal secretion there is more than 20% eosinophils. The pathophysiology is not well understood, but the key component includes chronic eosinophilic nasal inflammation frequently accompanied by development of polyposis (Guerra et al., 2002; Leynaert et al., 2000; Linneberg et al., 2002).

Among the children examined by us, 30% are with Allergic rhinitis compared to 24% with non-allergic rhinitis and eosinophilia.

The mean age of onset in our group of children is 3, 2 years for AR and 4 years for NAR+Eo. This is in accordance with results reported by several other authors (Lundbäck, 1998; Settipane et al., 1994).

Family history for allergic diseases is a strong risk factor for allergic rhinitis- it was present in 73% of children with AR in our group. According to Wang et al. in presence of family history for both parents, the risk for AR is 70% and in presence of family history for only one parent, the risk falls to 50%.

AR is associated with asthma in 40% of the patients, as 80% to 95% of the patients with allergic asthma have allergic rhinitis. In 1999 for the first time under WHO guidance, an international expert group developed ARIA (The Allergic Rhinitis and its Impact on Asthma), later updated in 2008 and 2010, where the importance of these relationships is underlined.

There is no difference between the symptoms of allergic and non-allergic rhinitis. Eosinophils are main effector cells participating in the pathogenesis of allergic inflammation. The activated eosinophils release toxic protein granules. In this study, we evaluate the degree of nasal eosinophilia in children with allergic and non-allergic rhinitis and the eosinophil activation by measuring the serum ECP level. Correlation between nasal eosinophilia and serum ECP was found.

In the present study the lowest degree of eosinophilia was found in children with AR (78%). The ECP level reflects eosinophil activation and degranulation in target organs. Therefore, at follow-up of eosinophil activity, ECP measurement can be more effective and reliable indicator.

Increased serum ECP is considered a marker for allergic inflammation, however we are not able to evaluate its diagnostic value due to absence of control group of children. We also didn't find statistically significant difference between the ECP levels in the three groups of patients, although in all children with Asthma and AR, the ECP concentration was above the norm.

The first report about ECP published in 1977 reports for correlation between serum ECP level and eosinophil count in peripheral blood. Nowadays ECP is used as a diagnostic and prognostic marker for the risk of asthma in children with recurrent broncho obstructive manifestations.

Regardless of the small number examined children,

we believe that measurement of ECP and eosinophils in nasal mucosa give us reason to continue the study with the desire to create a differential diagnostic algorithm for differentiation between allergic and non-allergic rhinitis.

CONCLUSION

1. Family history for allergic diseases is a strong risk factor for allergic rhinitis - it was present in 73% of children with AR in our study
2. We evaluate the degree of nasal eosinophilia in children with allergic and non-allergic rhinitis and the eosinophil activation by measuring the serum ECP level. Correlation between nasal eosinophilia and serum ECP was found.
3. We didn't find statistically significant difference between the ECP levels in the three groups of patients, although in all children with Asthma and AR, the ECP concentration was above the norm
4. Increased serum ECP is considered a marker for allergic inflammation, however we are not able to evaluate its diagnostic value due to absence of control group of children

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