



Serum ECP and total IgE levels in children with acute laryngotracheobronchitis

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KEYWORDS

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Summary

Objective : Eosinophilic cationic protein (ECP) and immunoglobulin E (IgE) are important mediators of allergic inflammation and they are commonly used in the diagnosis and follow-up of allergic diseases. But serum levels of these molecules can also be elevated by some other diseases including viral infections. Acute laryngotracheobronchitis (ALTB) is an important viral infection of upper airway and serum levels of ECP and IgE may increase in patients with ALTb.

Methods : In the present study serum ECP and IgE levels were measured before treatment and on the third day and third week after treatment in 27 patients with ALTb aged 10 months to 5 years and were compared with a age matched healthy controls. All patients were treated with nebulized budesonide.

Results : We found that pre-treatment ECP levels were significantly higher than post-treatment third days and third weeks (28.3 ± 2.3 ng/ml versus 20.2 ± 3.2 ng/ml and 11.4 ± 1.1 ng/ml, respectively). Similarly, the mean pre-treatment serum IgE values were significantly higher than post-treatment values (131.6 ± 17.5 IU/ml versus 83.6 ± 12.4 IU/ml and 68.2 ± 6.7 IU/ml). A positive correlation was found between serum ECP and IgE values for pre-treatment and post-treatment third week values ($r = 0.62$, $p = 0.01$ and $r = 0.64$, $p = 0.01$, respectively). The pre-treatment serum ECP and IgE levels were significantly higher than those of controls (10.8 ± 1.5 ng/ml and 43.8 ± 6.6 IU/ml, respectively $p < 0.05$).

Conclusion : In this study it was shown that, serum ECP and IgE levels increase in the acute phase of infection and return to normal after treatment in patients with ALTb such as in allergic patients. This effect of ALTb on serum ECP and total IgE levels should be kept in mind and these parameters should not be used in the diagnosis and follow-up of allergic diseases in children who had had ALTb in recent weeks.

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1. Introduction

Acute laryngotracheobronchitis (ALTB) or viral croup is a disease of respiratory tract of children caused by parainfluenza virus (PIV) types 1 and 2, influenza virus, adenovirus, respiratory syncytial virus (RSV) and rhinoviruses [1]. It has been shown that viral agents lead to increase in the number of lymphocytes, eosinophils and related mediators in respiratory tract in both allergic and non-allergic patients [2]. The process in upper respiratory tract (URT) inflammation depends on either Th2 mediated allergic base or Th1 mediated infectious base [3]. Moreover, studies have shown that serum total immunoglobulin E (IgE) levels rise in respiratory tract infections caused by PIV, RSV and rhinoviruses [4]. Both IgE and eosinophilic cationic protein (ECP) are important markers of atopy and allergic inflammation so are commonly used in the diagnosis and following the allergic diseases. So all of other causes of increased IgE and ECP levels should be known before diagnosis of allergic diseases and activations. In this study, we investigated the effect of ALT on serum ECP and total IgE levels in children.

2. Patients and methods

Total 27 children (13 boys and 14 girls) with acute viral croup without history of previous attacks were randomly recruited from the state hospital pediatric outpatients department (Erbaa, Tokat, Turkey). Age-matched controls ($n:18$) were recruited among children with minor trauma without any history related to allergy or atopy. The diagnosis of viral croup was based on clinical (rhinorrhea, pharyngitis, mild cough and low-grade fever in the previous 1–3 days of admission and hoarse voice, normal or moderately inflamed pharynx on physical examination) and laboratory (“belfry” appearance on the neck radiograph, normal CRP and white blood cell counts, no pathogens throat cultures) findings [5]. The aim of the study was explained to the parents and verbal consents were taken. In addition to comprehensive pediatric and allergy history, all patients were thoroughly examined. Lung and lateral neck radiographies were obtained from all patients at the beginning of the study. All patients were given 2 mg nebulized budesonide and clinical response to this treatment was assessed with croup symptom scores [6] during 8 h follow-up period. Venous blood samples were taken just before and 3 days and 3 weeks after the budesonide treatment from all of the patients and once from the controls. Serum samples were stored at -30°C until studying. Serum ECP and total IgE levels were analyzed by chemilu-

minescence assay method (immulite one analyzer, DPC-Diagnostic Product Corporation, USA). Complete blood counting and leukocyte differentials were also made from all of the patients. The study protocol was approved by the ethics committee of the Hospital.

2.1. Statistical analysis

The study data were analyzed with SPSS software program. Student’s *t*-test was used for comparison of groups consisted of independent, normally distributed data. For defining of relation between serum ECP and total IgE values Pearson correlation analysis was used. $p < 0.05$ values was accepted as statistically significant.

3. Results

The patients aged 10 months to 5 years (mean 2.1 ± 1.9 years) and the controls 9 months to 5 years (mean 2.0 ± 1.8 years). None of patients had premature birth, birth trauma, short or long durational intratracheal intubation, hoarseness and silent cry beginning from birth, weaning problems, difficulty in swallowing, frequent vomiting which may indicate gastroesophageal reflux, long durational stridor or cough that change with position or family history for allergic diseases. Moreover, none of the patients had previous allergic disease including asthma, serious febrile illness or history of surgery for cardiovascular system disease.

Physical examination revealed no pathological symptoms except ALT symptoms in all patients and subfebrile fever 12 children. Chest films were normal in all patients and lateral cervical films revealed hypopharyngeal distention and “pen tip” or “belfry” appearance. Blood counting and differentials were normal in all patients.

All patients were analyzed 2, 4, 6 and 8 h after budesonide treatment for ALT symptom scores. The mean symptom scores were ≤ 2 at fourth hour and ≤ 1 at eighth hour. None of the patients needed additional budesonide or any other medical treatment.

A significant difference was found between mean serum ECP levels before treatment (28.3 ± 2.3 ng/ml) and ECP levels 3 days (20.2 ± 3.2 ng/ml, $p < 0.05$) and 3 weeks (11.4 ± 1.1 ng/ml, $p < 0.001$) after treatment (Table 1). Difference between mean serum IgE levels before treatment (131.6 ± 17.5 IU/ml) and IgE levels 3 days (83.6 ± 12.4 IU/ml, $p < 0.05$) and 3 weeks (68.2 ± 6.7 IU/ml, $p < 0.01$) after treatment also was significant (Table 1). An evident correlation was found between serum ECP

Table 1 The mean serum ECP and total IgE values in patients and controls

	Pre-treatment	Post-treatment day 3	<i>p</i>	Post-treatment week 3	<i>p</i> ^a	Controls	<i>p</i> ^b
ECP (ng/ml)	28.3 ± 2.3	20.3 ± 3.2	<0.05	11.4 ± 1.1	<0.001	10.8 ± 1.5	<0.001
IgE (IU/ml)	131.6 ± 17.5	83.6 ± 12.4	<0.05	68.2 ± 6.7	<0.01	43.8 ± 6.6	<0.001

^a Comparison of values of pre-treatment and post-treatment (3 weeks).

^b Comparison of values of pre-treatment and control group.

levels before treatment and ECP levels 3 weeks after treatment ($r = 0.62$, $p = 0.01$ and $r = 0.64$, $p < 0.01$, respectively). A significant difference was found between mean serum ECP levels before treatment and control ECP levels (10.8 ± 1.5 ng/ml) and mean IgE values before treatment and control IgE values (43.8 ± 6.6 IU/ml, for each $p < 0.001$) (Table 1).

During long-term follow-up eight patients had more ALTB attacks (one patient had three attacks, three patients had two and four patients had one attack) and pre-treatment ECP levels of these were significantly higher than those who had no recurrences (37.5 ± 2.9 ng/ml versus 24.4 ± 2.9 ng/ml, $p < 0.01$). But, pre-treatment serum IgE levels were similar between two groups (133.7 ± 18.7 IU/ml and 130.7 ± 24 IU/ml, $p < 0.05$, respectively) (Table 2). Serum ECP levels and IgE values 3 weeks after treatment of eight patients with recurring attacks (13.5 ± 1.6 ng/ml and 78 ± 10.4 IU/ml, respectively) were also similar to those not having another attacks (10.5 ± 1.4 ng/ml and 64.1 ± 8.4 IU/ml, respectively, $p < 0.05$) (Table 2).

4. Discussion

The mechanism underlying the inflammation in URT may be allergic or infectious [3]. It has been postulated that viral infections seen in childhood led to eosinophil activation and eosinophilic mediator increase in respiratory tract in allergic and non-allergic conditions [2]. Increased ECP levels in nasal secretions in most of children with URT infections like children with continuous wheezing indicate presence of eosinophilic allergic inflammation [7] IgE plays an important role in bronchial inflammation with limited action of IL-5 that lead to respira-

tory tract eosinophil migration and ECP secretion [8]. It has been reported that serum total IgE levels increased in 97% of children with otitis media with effusion and ECP levels in effusion fluid increased in 87.5% of the same patients [9]. It is speculated that there is similar inflammatory cell response against viral antigens in URT mucosa [9,10]. Increased serum ECP levels are accepted as a reflection of eosinophilic activation and allergic inflammation in bronchial asthma and other allergic diseases [11]. Moreover, total serum IgE levels had been shown to be increased in PIV, RSV and rhinovirus infections [3]. As it has not been shown in previous studies, we planned to assess whether serum ECP and total IgE values rise in ALTB, characterized by laryngeal and subglottic tissue inflammation as in allergic diseases.

In addition to some important allergic diseases, such as asthma and allergic rhinitis, serum ECP levels may also increase in some viral infections including RSV infections [12,13]. Higher serum ECP concentration during the acute phase of bronchiolitis may be a specific predictor of wheezing after bronchiolitis [13]. In our study, we tested continuation of eosinophilic activation by measuring serum ECP levels 3 days and 3 weeks after the treatment. However, Fraenkel et al. [2] reported that T cell activation mediated by increased IgE and eosinophilic inflammation have short duration in non-atopic conditions with wheezing. In our study decreased values found 3 days and 3 weeks after treatment in children with ALTB in comparison to pre-treatment values may be explained with the anti-inflammatory effects of corticosteroids or by short duration of eosinophilic inflammation.

Fujisawa et al. [14] suggested that serum ECP might be a useful marker for monitoring and predicting the clinical course in childhood asthma. They

Table 2 Serum ECP and total IgE levels in patients having recurrent croup attacks and no recurrences

	Pre-treatment		<i>p</i>	Post-treatment (3 weeks)		<i>p</i>
	Recurrent attacks (+) <i>n</i> = 8	Recurrent attacks (-) <i>n</i> = 19		Recurrent attacks (+) <i>n</i> = 8	Recurrent attacks (-) <i>n</i> = 19	
ECP (ng/ml)	37.5 ± 2.9	24.4 ± 2.7	<0.01	13.5 ± 1.6	10.5 ± 1.4	>0.05
IgE (IU/ml)	133.7 ± 18.7	130.7 ± 24	>0.05	78 ± 10.4	64.1 ± 8.4	>0.05

showed higher serum levels of ECP in initially asymptomatic patients who later had asthma attacks than those who remained asymptomatic. Similarly, in our study during long-term follow-up period serum ECP levels were higher in eight patients who had recurring ALTB attacks when compared to those who hadn't experienced more attacks. But, IgE values did not differ between two groups. On the other hand, there was no difference in serum ECP and IgE levels 3 weeks after treatment between two groups with and without recurrences. This may be as a result of transient inflammation of the airway.

It is reported that in children with BA inhaled budesonide improves asthma symptoms and lung functions and decreases serum ECP levels [15]. Similarly in children with ALTB nebulized budesonide treatment have been found to cause significant improvement in symptom scores after 4 h, decrease hospitalization rates and durations and have no difference in regard to effectiveness with dexamethasone [16]. In our study, all children with ALTB received nebulized budesonide and significant decrease in serum ECP and total IgE levels were seen in addition to clinical improvement.

Previous studies have shown that serum IgE values in acute phase of respiratory tract infections caused by viruses (e.g. parainfluenza virus) increase in comparison to improvement phase of the patients or healthy controls [4,7]. Our study also showed significant differences between pre and post-treatment IgE levels.

We concluded that serum ECP and IgE levels significantly rise in acute phase of ALTB like in allergic diseases and decrease after treatment with corticosteroid and higher initial levels of ECP are seen in patients who later may have recurrent ALTB attacks. So serum ECP and total IgE levels should not be used in the diagnosis and follow-up of allergic diseases in children who had had ALTB in recent 3 weeks.

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