

Association Between Systemic and Local Immune Response Parameters in Children with Bronchial Asthma

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Rationale: Immunoglobulin E (IgE) antibodies play an important effector role in bronchial asthma (BA) as well as the level of eosinophils in nasal and bronchial mucus, but there is evidence that T-cells and cytokines are also involved, although the association between these parameters is still unclear. The objective was to investigate the association between allergen-specific serum IgE levels, skin sensitivity, mucosal immune response (rhinocytological and bronchial sputum analyses) and cytokines production by blood mononuclear cells in children with BA.

Methods: 55 children aged 7-10 years with moderate BA were observed. Diagnosis was made using a clinical questionnaire, physical examination and skin prick tests (SPTs) to ten common allergens. All patients had investigation of lung functions and mucus eosinophil counts were measured.

Total and antigen specific IgE and IL-5, IL-10, γ -interferon levels were assessed by ELISA.

Results: Diagnosis of BA was confirmed by positive SPT to common allergens and increased levels of total and specific IgE. The results of FEV1 were complied with moderate BA. At the same time the count of mucus eosinophils significantly increased and correlated with skin sensitization, level of total and specific IgE and clinical manifestation of BA. These parameters also correlate with increasing production levels of IL-5 to 142 ± 5.4 p_{kg}/ml (N= 74.3 ± 3.3), IL-10 to 102 ± 7 p_{kg}/ml (N= 5.9 ± 0.25); and decreased production of γ -IFN to 301 ± 5 p_{kg}/ml (N= 331 ± 35); all were statistically significant (p<0.05).

Conclusions: The investigation confirmed that the level of total and allergen-specific IgE and mucus eosinophils directly correlates with Th2 cytokines production and clinical manifestation of BA in children.

ASSOCIATION BETWEEN SYSTEMIC AND LOCAL IMMUNE RESPONSE PARAMETERS IN CHILDREN WITH BRONCHIAL ASTHMA

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Introduction

Immunoglobulin E (IgE) antibodies play an important effector role in bronchial asthma (BA) as well as the level of eosinophils in nasal and bronchial mucus, but there is evidence that T-cells (Th2) and cytokines (IL-4, IL-5, IL-9, IL-10, IL-13 and granulocyte macrophage-colony stimulating factor- GM-CSF) are also involved, although the association between these parameters is still unclear.

The objective was to investigate the association between allergen-specific serum IgE levels, skin sensitivity, mucosal immune response (rhinocytological and bronchial sputum analyses) and cytokines production by blood mononuclear cells in children with BA.

Materials and Methods:

55 children (23 males and 32 females) aged 7-10 years with moderate BA were observed (Table 1). Asthma was diagnosed according to the criteria as described by the Global Initiative for Asthma and was established by symptoms of asthma and by improvement in the prebronchodilator forced expiratory volume in 1s

(FEV1) \geq 12% after administration of salbutamol (200 μ g).

And skin prick tests (SPTs) to common allergens: trees, grass, cat, dog, mites (*Dermatophagoides pteronyssinus* and *D. farinae*) and food (milk and egg) were performed. A negative control diluent and a positive control (10 mg/ml histamine) were included. A positive SPT was defined as giving a mean weal diameter of 3 mm or more at 15 min.

All patients had investigation of lung functions and mucus eosinophil counts were measured. FEV1 was measured by spirometer and the highest of three successive measurements was taken.

The number of eosinophils was measured in nasal secret and bronchial mucus and expressed as cells count ($\times 10^2$).

Total and antigen-specific IgE and IL-5, IL-10, γ -interferon levels were assessed by ELISA.

The normal limit of total IgE was 100 kU/l. Specific IgE was accepted positive if it was higher than 150 kU/l.

Results:

The characteristics of the patients who completed the study are given in Table 1.

There is also shown in Table 1 the results of FEV1 in our patients were 78,7 %, what complied with moderate BA.

All patients have a positive SPT to 4-5 allergens (Table 2). There was determined a total of 38 patients (50,9%) were sensitized to house dust mite; 21 patients (38,2%) to *D. pteronyssinus* and 16 patients (29,1%) to *D. farinae*; 26 patients (47,3%) to grasses and trees; 14 patients (25,5 %) to milk and 11 patients (20,0%) to egg. The level of serum total IgE (Table 1) and serum specific IgE, especially to *D. pteronyssinus* , *D. farinae*, milk and egg (Pic. 2) were significantly increased in all children with BA and it was statistically authentic ($p < 0.05$).

As it is shown on Pic. 1A and Pic. 1B the count of mucus eosinophils (as well in nasal secret as in bronchial mucus) was significantly increased. And bronchial

epithelium was destroyed and the augmentation of the columnar cells count was revealed there

These results were the most important evidence of our investigation purpose because they correlated with skin sensitization (positive SPT), increasing level of total and allergen-specific serum IgE and clinical manifestation of bronchial asthma in children

More of that we found also the direct correlation between these parameters and increasing the production of cytokines level. As it is shown on Pic. 3 in all our patients the level of IL-5 increased to 142 ± 5.4 pkg/ml compared with normal date ($N=74.3 \pm 3.3$), the production of IL-10 increased to 102 ± 7 pkg/ml ($N=5.9 \pm 0.25$); and the level of γ -IFN production decreased to 301 ± 5 pkg/ml ($N=331 \pm 35$). All these results were statistically significant ($p < 0.05$).

Discussion:

The increasing of the of cytokines production level (IL-4 and IL-5) by peripheral mononuclear cells induce the expression of cell adhesion molecules on inflamed endothelium and epithelial production of chemokines, leading to the recruitment of inflammatory cells, stimulating the production of IgE by B cells and causing bronchial hyper-reactivity.

IL-5 is known as an important cytokine for the growth, differentiation and activation of tissue eosinophils.

Although IL-10 is often described to have an immunosuppressive effect on both Th1/Th2 cells, it can also favour the polarization to Th2 cells. The presence of IL-10 at the site of T cell differentiation diminishes the secretion of IL-12, thereby indirectly attenuating the differentiation of Th1 cells.

All this immunological mechanism found the reflection in the results of our clinical investigation and proved the interaction between systemic and local immune response in bronchial asthma children, what was confirmed by

cytokines production, total and allergen-specific IgE levels and the count of mucus eosinophils.

Conclusions:

The investigation confirmed that the level of total and allergen-specific IgE and mucus eosinophils count directly correlate with Th2 cytokines production and clinical manifestation of bronchial asthma in children.

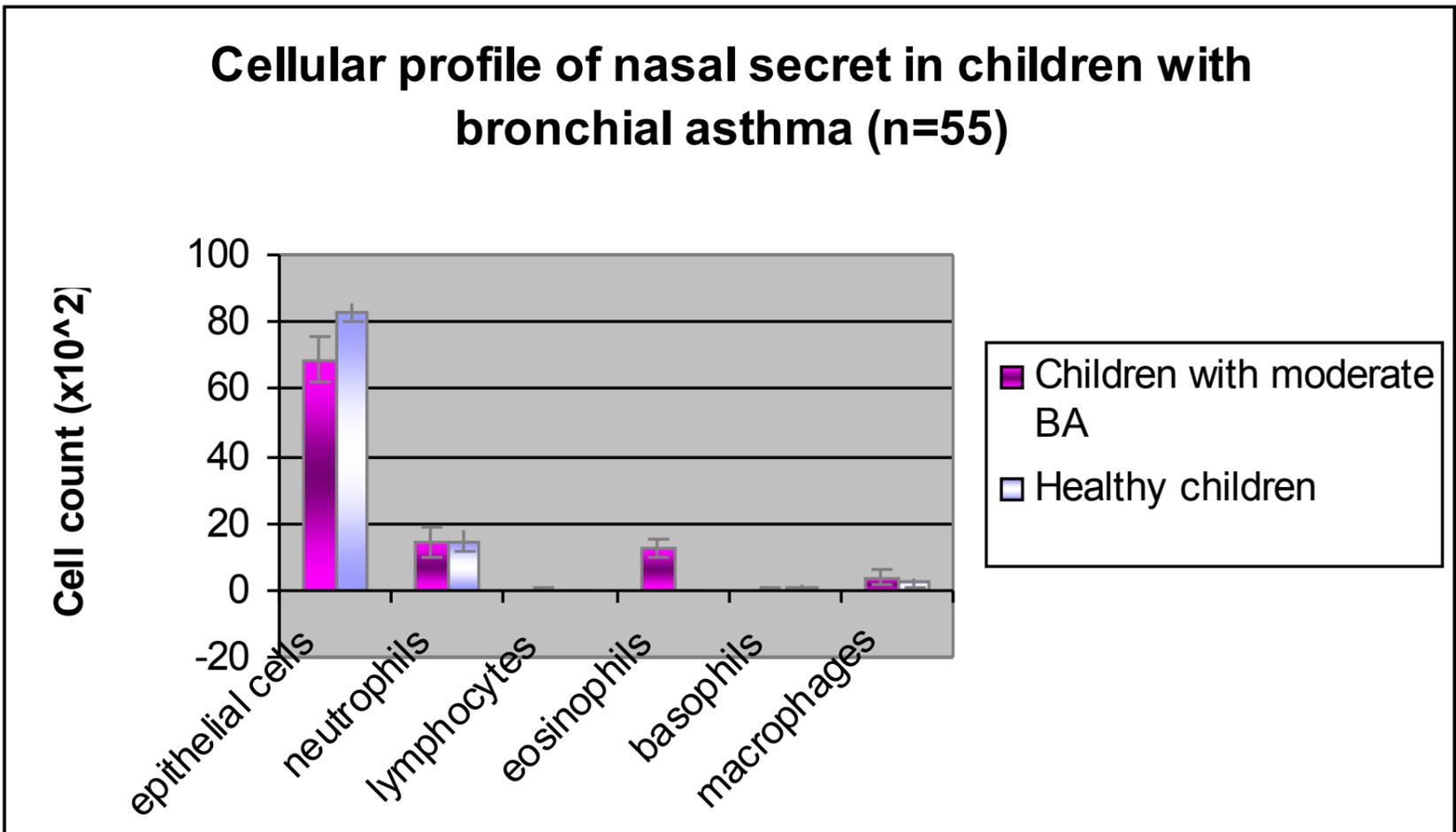
Table 1: Characteristics of patients

Children	55
Gender	Male 23 ; female 32
Age	7-10 years
Asthma symptoms (score)	7,0
History of Bronchial Asthma	3.5±1.2 years
Total IgE	410,5 ±72,0 kU/l
FEV1	78.7

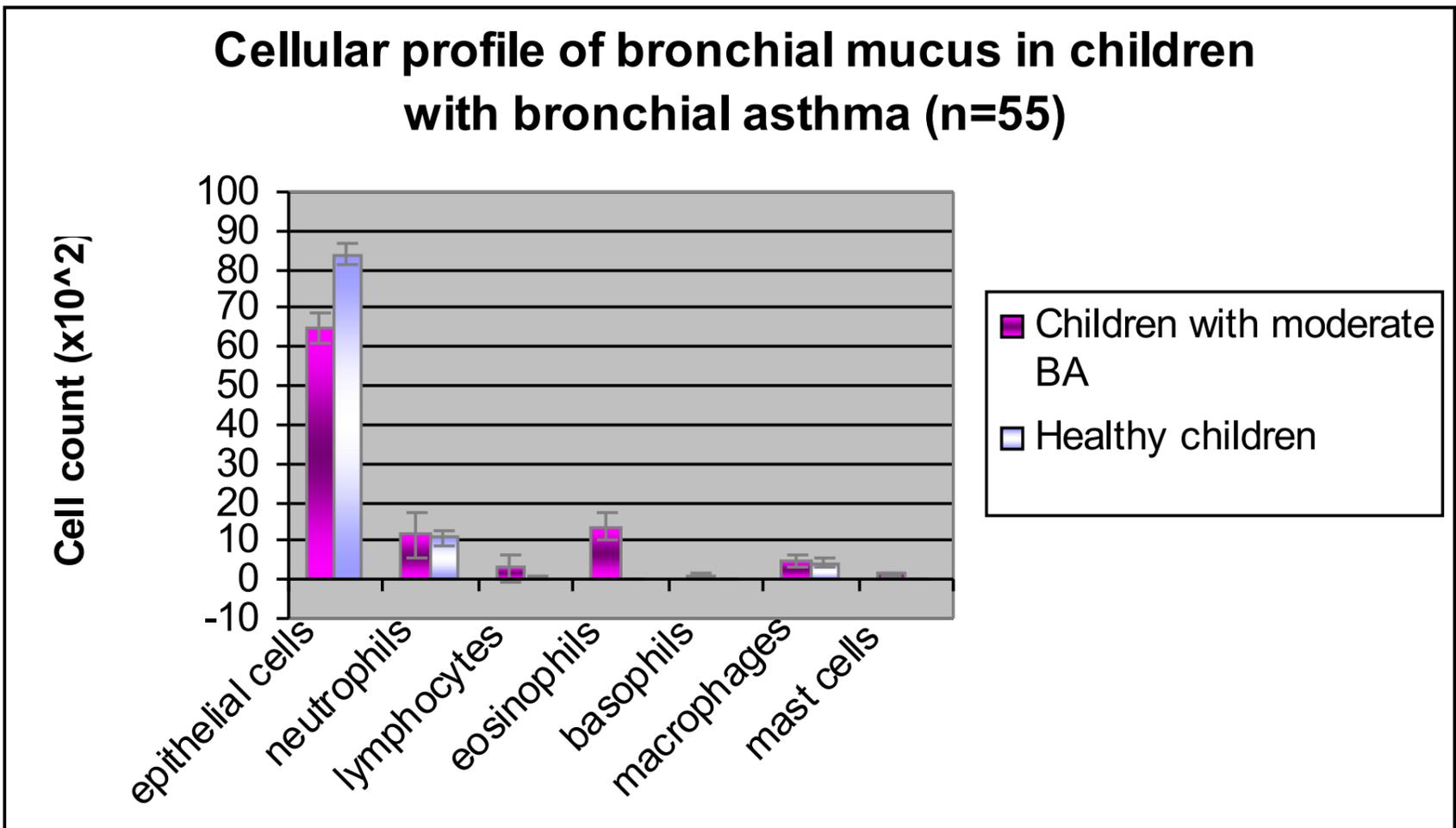
Table 2: Sensitisation to allergen extracts in children with BA (n=55)

House dust mite	D. pteronys.	D. farinae	Grasses and trees	Milk	Egg
28	21	16	26	14	11
50,9%	38,2%	29,1%	47,3%	25,5%	20,0%

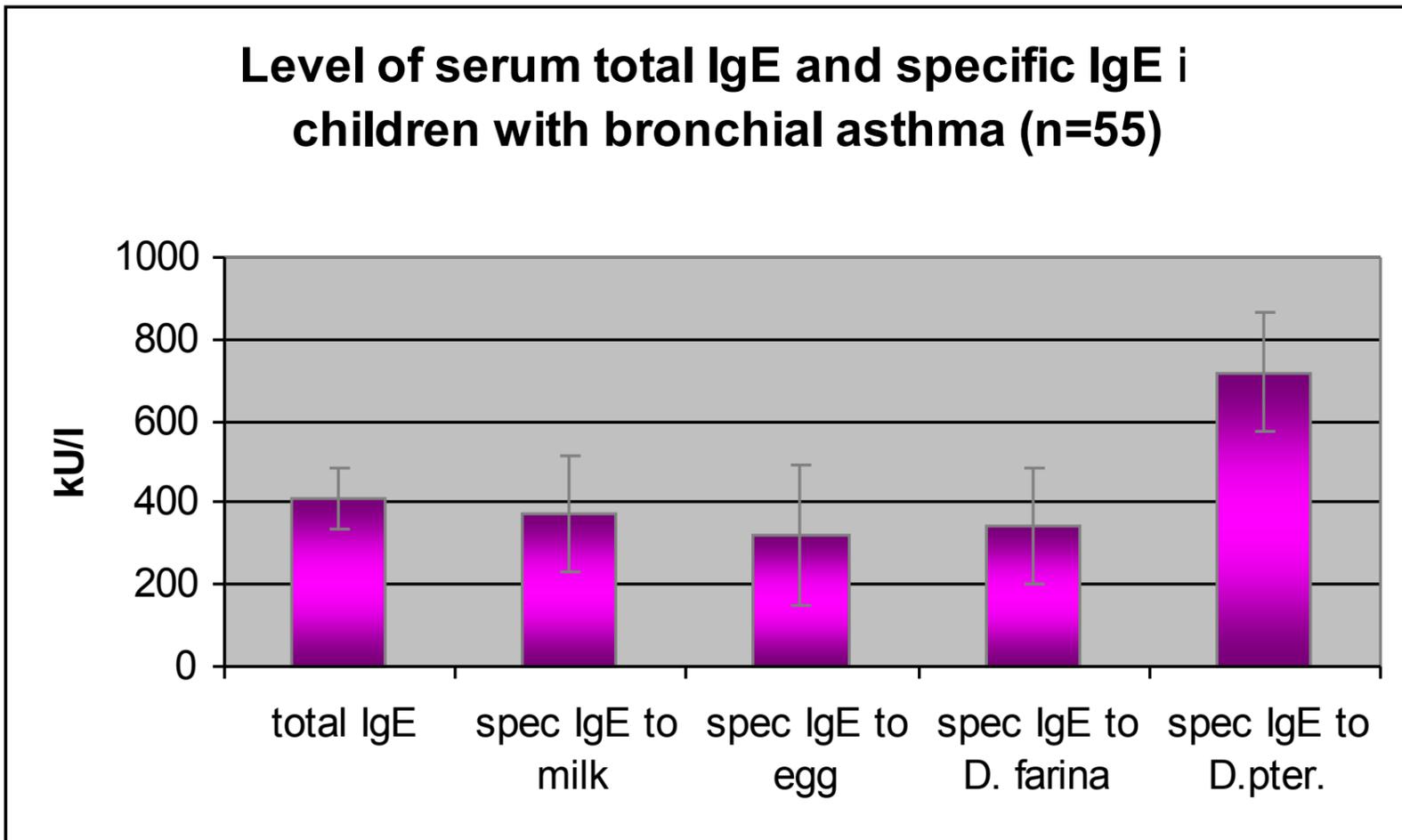
Picture 1A



Picture 1B



Picture 2



Picture 3

