Immunomodulatory effect of Broncho-Vaxom (B-V) in children with atopic bronchial asthma and dysfunction of T lymphocytes

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SUMMARY

Respiratory tract infections can stimulate bronchial hyperreactivity in atopic children. Many investigations demonstrate the dependences between infections and T cell dysfunction. The aim of this study was to assess immunomodulatory effect of Broncho-Vaxom in children with atopic bronchial asthma and concomitant recurrent respiratory tract infections.

Twenty five children (4-16 years old) were included in the study and a number of T cells by E-rosetting test according to WHO criteria, serum level of IgE (by fluorimetric method) were examined. Children were treated using a "prophylactic" schedule i.e. one capsule of B-V of 3.5 mg daily for 10 days during three consecutive months. After finishing of B-V therapy the significant increase, especially of total E-rosettes (56.1±11.0% before and 66.7±5.0% after therapy) and percentage of T cells (25.1±6.4 before and 31.1±8.4 after therapy) were observed. These changes have been correlated with clinical improvement manifested by a decrease of episodes number of infections. In our opinion in atopic bronchial asthma with concomitant recurrent respiratory tract infections the immunomodulation therapy should be performed.

Key words: atopic asthma; respiratory tract infection; T lymphocytes

Respiratory tract infections are the most common illnesses in childhood, comprising approximately 50% of all illness in children under 5 years and 30% of children 5–12 years old. The peak incidence of infections is between 2nd and 4th year and the number does not fall to the average adult pattern of four to six per year until 8–10 years. Over 90% of respiratory infections are due to viruses. It has been proved that atopy does not constitute a risk factor for an increase of the number of respiratory tract infections (10). Although infections (especially viral) in asthma patients very frequently exacerbate symptoms of bronchial reactivity via specific and non-specific reactions (2, 11, 12, 17).

Many investigations demonstrate the correlations between infections and abnormalities of immune response (4).

For many years bacterial extracts have been proposed to enhance the responsiveness of the immune system and to secure protection against bacterial infections (3, 6, 7, 13). One of them is lyophilised bacterial extract – Broncho-Vaxom (B-V) produced by OM Laboratories in Geneva.

The effectiveness of B-V in patients suffering from chronic bronchitis was demonstrated in many controlled double-blind clinical trials in both adults and children (8, 9, 15, 16).

The aim of this study was the evaluation of influence of B-V therapy on selected immunological parameters in children with atopic bronchial asthma with concomitant recurrent respiratory tract infections.

MATERIAL AND METHODS

A group of 25 children of both sexes, aged from 4 to 16 years (mean age 6.4±2.6) with atopic bronchial asthma and concomitant recurrent respiratory tract infections was examined. The diagnosis of atopic asthma was based on the WHO's criteria. Recurrent infections of the respiratory tract were diagnosed basing on the standing clinical criteria (more than 6 inflammatory episodes during 12 months prior to the examination). For the evaluation of T cells population E-rosetting test was selected with very simple quantitative method. The modification of E-rosetting test originally invented by Jondal and co-workers was used (5). The absolute number of T lymphocytes (ANTL) and the proportion of T lymphocytes in leucogram (LT%) were also measured.

Broncho-Vaxom was administered at a dose of 3.5 mg per day during the first 10 days of each 3 con-

secutive months (August, September and October). B-V therapy according to this schedule has been repeated twice (in the following year in January, February, March and August, September and October).

The clinical criteria for the evaluation of B-V efficacy were: the number of acute episodes of infections and the number of days of treatment with antibiotics. Additionally such symptoms as: dyspnoea, cough, expectoration were evaluated for each patient. The severity of symptoms was scored on the 5-point scale from 0 (absence) to 4 (very severe). Before and after each period of therapy the cumulative index of the symptom score was calculated. The clinical examination was carried out before and after finishing of each period of therapy and immunological examination – before and after finishing the whole therapy.

The results of the study have been shown as an arithmetical mean +/- standard deviation (SD). The differences between means of the results before and after Broncho-Vaxom therapy were measured with the rank test by Mann-Whitney accepting $p<0.05$ as a statistically significant difference.

In consideration of a wide differences of immunological results that have been observed before treatment, the examined group, for each analysing parameter, was divided into three subgroups: a – parameters above normal value, b – normal value, c – below the normal value. The control group consisted of 20 healthy children of both sexes, aged from 6 to 16 years, who were submitted to identical studies as a group of sick children.

RESULTS

The clinical effects of B-V therapy is presented in Figure 1. It shows a substantial decrease in the number of infection episodes by 78%, in the use of antibiotic therapy by 83%, expectorants by 48% and bronchodilators by 68%. Overall evaluation by the physicians indicated "very good" results in 60% of patients, "good" in 30% and "moderate" results in 10% of patients (Fig. 2).

In 25 atopic patients with concomitant recurrent respiratory tract infections the evaluation of the ability of T-lymphocytes to form rosettes with SRBC by E-rosetting tests was done. Before Broncho-Vaxom treatment there were noted rosettes value and percentage of T cells number in leucogram significantly lower than in the control group. After finishing of B-V treatment the significant increases in mean values of these parameters were noted (Tab. 1).

These changes were more pointed in subgroups a – above the normal value and c – below the normal value (Tab. 2). The most significant increases were found in parameters in c subgroup. At the same time parameter previously higher than the value of the norm level (a subgroup), significantly decreased. After three series of B-V the values of percentage of T cells in leucogram for all subgroups returned to the normal value.

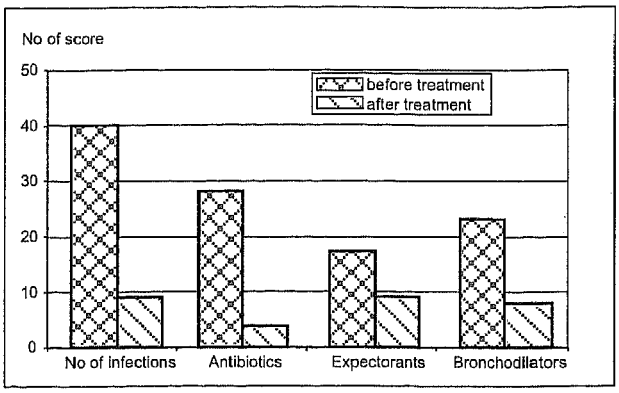

Fig. 1. Influence of B-V therapy on the clinical parameters in 25 children with atopic bronchial asthma and recurrent respiratory tract infections.

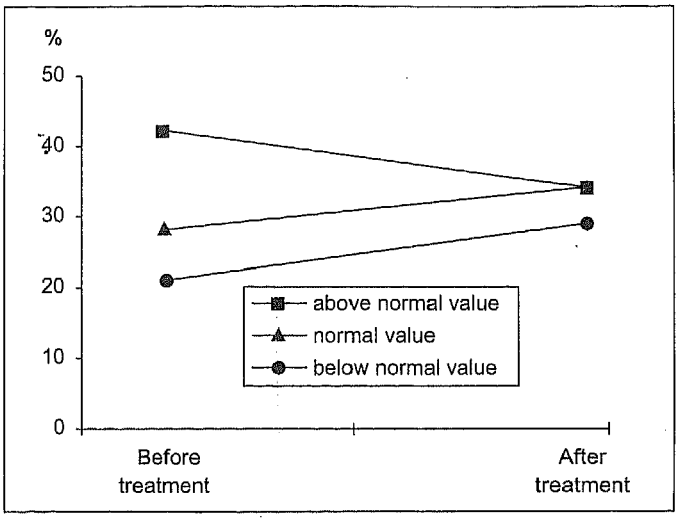

Fig. 2. Influence of B-V therapy on percentage of T lymphocytes in leucogram in children with atopic bronchial asthma and recurrent respiratory tract infections.

Table 1. Immunological parameters in children with atopic bronchial asthma and recurrent respiratory tract infections

Parameter	Before treatment	After treatment	Control group
Age (years)	6.4±2.6	7.3±2.6	6.7±2.1
Leukocytes (G/l)	8.4±2.2	7.5±2.1	7.9±2.2
Lymphocytes (%)	45.6±11.2	46.7±10.2	40.5±12.3
Total ros. (%)	56.1±11.0*	66.7±5.0	74.3±4.9
ANTC (G/l)	2.1±0.9	2.3±0.8	2.5±0.2
% IT in leukogram	25.1±6.4*	31.3±8.4	32.0±3.0

*p<0.05

Table 2. Effect of B-V therapy in children with atopic bronchial asthma and recurrent respiratory tract infection in subgroups: a – above normal value, b – normal value, c – below normal value

Evaluated parameters	Before treatment	After treatment
Lymphocytes (%)		
a	54.5±7.2	52.1±9.8
b	39.1±4.1	45.8±10.6
c	19.0±7.0*	50.0±19.7
Total ros. (%)		
b	68.7±4.4	64.3±5.3
c	54.1±7.4*	64.9±5.2
ANTC (G/l)		
a	3.7±0.5*	2.9±0.5
b	2.2±0.3	2.2±0.4
c	1.2±0.1*	2.0±1.0
% IT in leukogram		
a	40.8±5.2	33.6±4.5
b	29.2±4.0	33.8±10.1
c	20.3±2.6*	30.0±7.1

* $p<0.05$

DISCUSSION

The aim of this study was the quantitative evaluation of cellular immunity parameters in children with atopic bronchial asthma and recurrent respiratory tract infections. Each of the children before B-V therapy was ineffectively treated with antibiotics. In the investigations performed before starting the B-V therapy, both the total E-rosettes and absolute number of T lymphocytes in leucogram were significantly lower in comparison with the results obtained in the control groups. An open question remains, whether the observed disorders are a cause, or rather a result of the observed clinical changes.

Recognition of asthma as an inflammatory process continuing even during the remission has specific therapeutic consequences (1, 2, 14, 18). In the treatment of atopic asthma, in addition to the bronchodilators, to the anti-inflammatory agents (e.g. Nedocromil sodium, Disodium cromoglycate) in a mild process, and as potent as steroids (inhalatory and systemic) in a severe course of the disease, are recommended. The necessity of frequent administration of corticosteroids and antibiotics in the treatment of asthmatic patients may also depress the immunological response (6, 7, 13).

The results of immunological assessment presented in this paper concerned with the children with bronchial asthma and recurrent respiratory tract infections. A deficiency within the quantitative parameters characterising T lymphocytes population was found in the analysed group with the clinical course of disease, often requiring a use of immunosuppressive drugs. In the presented cases we proved that prophylactic use of the immunocorrectional drugs such as B-V induced both, clinical and immunological improvement.

CONCLUSIONS

In our opinion:

1. Treatment with B-V should be applied during long time (more than 1 series).
2. The estimation and progress of therapy have to be immunologically monitored.
3. The results of this evaluation may be used as the recommendations for a continuing or finishing therapy.

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