The Pharma Innovation Journal 2016; 5(11): 01-04

www.ThePharmaJournal.com

The Pharma Innovation

ISSN: 2277- 7695
TPI 2016; 5(11): 01-04

www.thepharmajournal.com
Received: 01-09-2016
Accepted: 02-10-2016

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The pharmacologic correction of the immunological state in children with the bronchial asthma

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Abstract
These work devoted to investigation the bronchial asthma in children. The study involved 157 children with asthma in age from 6 to 18 years old. The control group consisted of 20 healthy children of similar age. The study was conducted in two phases. At the first stage we studied the features of the immune status and immunoreactivity. At the second one we explored the possibilities of correction of the detected changes with the different kinds of therapeutic approaches, namely, 49 children received standard therapy, 50 - standard therapy in combination with Beres Drops Plus and 58 children treated with standard therapy, Beres Drops Plus in combination with Likopid. During the treatment and monitoring we can observe the highest positive dynamics in almost all the indicators of phagocytic activity in patients with asthma treated with standard therapy in combination with Beres Drops Plus and Glyukozaminilmuramildipeptid (Likopid).

Keywords: Bronchial asthma, children, immunity

1. Introduction
Nowadays, a bronchial asthma (BA) is widespread in 300 times more than coronary heart disease, 33 times more than lung cancer and 20 times more than breast cancer, 15 times more than stroke, 5 times more than HIV [1].
Multivariate character of asthma, including genetic predisposition, environmental influences, immune and neural level of nonspecific hyperre activity and specific role of viral and microbial factors requires consideration of each additional component that can influence the course of asthma [1, 3, 5, 6]. Most researchers [3, 4, 6, 7] attribute asthma to allergic diseases, which are based on immunological mechanisms. Until now, their essence remains to be the subject of the research.
Initially operate nonspecific, and then specific mechanisms of reactivity. Nonspecific resistance of the organism factors directly involved at the beginning, during the development and in the final phase of the immune response. Phagocytosis, complement system, cytokines are singled out in the system of nonspecific resistance of the organism. These circumstances require a consideration of the severity of immune responses and their impact on the course of asthma in children [6-8].
Purpose of this work was to study the immunological status and immunore activity in children with asthma and the possible ways of correction of changes.

2. Materials and methods
The study involved 157 children aged 6 to 18 years, patients with asthma who were treated in the department of the Allergic Regional Pediatric Hospital in Ivano-Frankivsk. The diagnosis is verified by the Protocol of diagnosis and treatment of asthma in children (№ 767 from 27.12 in 2005). The control group consisted of 20 healthy children of similar age.
In the first stage, the state of nonspecific resistance of the organism was studied by the determination of phagocytosis (the method I. Petrov *et al*., 1984): phagocytic index (PI), phagocytic number (PN) in neutrophils.
Oxygen dependant metabolic activity of neutrophils was determined by nitroblue tetrazolium restoration (NBT-test) (method B. Park modifying by Viksman M.E., Mayanskoho M.N., 1982). We were spending the spontaneous and stimulated test calculation of NBT-positive neutrophils (N, %) and neutrophil activation index (AI, Relative Value Units.).
The second phase was carried out the exploring of the possibility of correcting the detected changes. With this aim, the children were divided into three groups: the first group received standard therapy (ST) for the control of asthma according to the Protocol; in the second group

ST was combined with the usage of Beres Drops Plus (BDP), produced by JSC "Beres Pharma" (Hungary) in the following way: 2 courses for 28 days with 2 months interval between. Dosage of BDP depended on the body weight: 20-40 kg - 20 drops 2 times a day, if the body weight is greater than 40 kg - 20 drops 3 times a day. Children of the third group except ST and BDP received the drug Likopid (ST+BDP + L). The drug Likopid belongs to a group of immunomodulators which is used in the following doses: 1 mg 1 g / day for 10 days in two courses with 1 month intervals between.

Statistic analysis of the results of research was carried out by using a standard computer program Microsoft Excel 97 and Statistic 5.0.

3. Results and discussion

The study of the dynamics of the immunological changes in children with asthma under the influence of selected technologies for drug research has shown their effectiveness in correcting the detected changes. However, the study found that the nature of the dynamics of immunological changes is largely determined by the choice of alternative therapy (Table 1).

Table 1: Dynamics of the indicators of phagocytosis in children with bronchial asthma during the treatment with different variants of therapy

Indicators	Before the treatment[1]	During the discharging[2]	Long-term observation		Healthy[5] (n=20)
			in 3 months[3]	in 6 month[4]	
Standard treatment n=49, (%)					
PI, %	28,1±1,1	39,0±0,9	42,2±1,1	54,3±1,2	64,8±1,8 P_{1-5}<0,05 P_{2-5}<0,05 P_{3-5}<0,05
PN, RVU	3,5±0,09	3,9±0,08	4,5±0,08	5,6±0,09	7,5±0,06 P_{1-5}<0,05 P_{2-5}<0,05 P_{3-5}<0,05 P_{4-5}<0,05
NBT-test spontaneous : -AI (RVU).	0,09±0,01	0,10±0,01	0,10±0,01	0,11±0,01	0,15±0,02 P_{1-5}<0,05 P_{2-5}<0,05 P_{3-5}<0,05
-N, %	8,0±0,01	8,7±0,01	9,0±0,01	11,0±0,01	12,0±0,07 P_{1-5}<0,05 P_{2-5}<0,05
NBT stimulated: -AI (RVU).	0,7±0,01	1,0±0,01	1,2±0,01	1,2±0,03	1,2±0,02 P_{1-5}<0,05
-N,%	41,3±0,01	49,6±0,06	52,4±0,05	61,1±0,06	76,3±0,05 P_{1-5}<0,05 P_{2-5}<0,05 P_{3-5}<0,05 P_{4-5}<0,05
Standard treatment + Drops Beres Plus (n=50), %					
PI, %	28,0±1,2	46,0±0,9	50,4±1,2	62,3±1,2	64,5±1,9 P_{1-5}<0,05 P_{2-5}<0,05 P_{3-5}<0,05
PN, RVU	3,5±0,09	4,2±0,08	4,9±0,07	6,2±0,09	7,7±0,05 P_{1-5}<0,05 P_{2-5}<0,05 P_{3-5}<0,05
NBT-test spontaneous : -AI (RVU).	0,09±0,02	0,10±0,01	0,11±0,02	0,12±0,01	0,14±0,02 P_{1-5}<0,05
-N, %	8,1±0,01	9,0±0,01	9,1±0,01	11,0±0,01	12,1±0,06 P_{1-5}<0,05
NBT stimulated: -AI (RVU).	0,7±0,01	1,2±0,01	1,6±0,01	1,3±0,03	1,3±0,01 P_{1-5}<0,05
-N, %	41,8±0,05	52,2±0,06	59,8±0,04	67,2±0,06	76,5±0,04 P_{1-5}<0,05 P_{2-5}<0,05 P_{3-5}<0,05
Standard treatment + Drops Beres Plus + Likopid (n=58), %					
PI, %	29,0±1,1	47,1±0,9°	50,4±1,2	68,3±1,2°	65,0±1,7 P_{1-5}<0,05 P_{2-5}<0,05 P_{3-5}<0,05
PN, RVU.	3,7±0,09	4,2±0,08	4,7±0,09	6,8±0,09°	7,6±0,05 P_{1-5}<0,05 P_{2-5}<0,05 P_{3-5}<0,05
NBT-test spontaneous : -AI (RVU	0,09±0,03	0,10±0,01	0,11±0,03	0,12±0,01	0,15±0,02 P_{1-5}<0,05

-N, %	8,0±0,03	9,0±0,01	9,0±0,02	11,1±0,01	12,1±0,06 P_{1-5}<0,05
NBT stimulated: -AI (RVU).	0,8±0,02	1,2±0,01	1,7±0,02	2,0±0,03°ʌ	1,3±0,01 P_{1-5}<0,05
-N, %	41,0±0,01	52,4±0,06	61,0±0,04°	77,2±0,06°ʌ	76,4±0,05 P_{1-5}<0,05 P_{2-5}<0,05 P_{3-5}<0,05
Notes:	1. P - probability of difference to performance (1), (2) treatment and prolonged observation in 3 (3) and 6 (4) months and healthy (5) 2. * - Probability performance difference relative to values in patients using standard therapy and standard therapy in combination with drops Beres Plus, ° - standard therapy and standard therapy in combination with Beres Plus drops and Likopid; ʌ - standard therapy in combination with drops Beres Plus and standard therapy in combination with Beres Plus drops and Likopid (P<0.05)				

Analysis of the factors of nonspecific protection of children with asthma in the background of ST at the discharge from the hospital on indicators of spontaneous NBT-test showed insufficient degree of stimulation of phagocytic cells and their low capacity for killing, and was evidenced by a significant increase in PI (%) of (28, 1 ± 1, 1) to (39, 0 ± 0, 9) (P<0,05) and a tendency to increase PN. Dynamics of stimulated NBT test during the child's stay in hospital showed that ST performed virtually no impact on the performance of the stimulated NBT test. Thus obtained at the first control level AI (RVU) and N (%) though were higher than comparable to treatment, but significantly lower than in healthy controls (p<0,05). Moreover, for the whole period of observation none of the index of the stimulated NBT test was not normalized compared with the corresponding referent data.

Under the influence of combined therapy of ST + DBP in children with asthma the vector of orientation disorders of phagocytosis was significantly less and biased toward the deficit compared with a group of pediatric patients treated with ST only. Thus, the percentage of phagocytic cells was significantly reduced in the early treatment group compared to the healthy (p<0,05), however, since the discharge from the hospital and during the long-term observation we can admitt a significant increase in this indicator, which was close to the level of healthy (p<0,05). A similar positive result was received in PN during treatment with ST + DBP compared to the healthy group.

Regarding the indicators of spontaneous NBT-test, we observed the tends to increase the degree of stimulation of phagocytic cells and their higher capacity for killing in patients with asthma (p<0, 05) treated with ST + DBP compared with the group of patients treated with ST only. Similar dynamics were observed for an extended supervision: three and six months.

Stimulated NBT test showed significantly higher potential activity of phagocytic cells and completeness of phagocytosis in children with asthma who received ST + DBP on those in ST group compared with healthy (p<0,05). Thus, the performance of AI (RVU) and N (%) before treatment were (0,7 ± 0,01) and (41,8 ± 0,05), respectively, and were significantly higher than similar at discharge from hospital, namely, (1,2 ± 0,01) and (52,2 ± 0,06) (p<0,05), but remained significantly lower than in healthy controls (p<0,05). During the long-term observation we fixed the similar pattern.

The improved therapy of asthma with the inclusion of complex treatment of Beres Drops Plus and Likopid is characterized by the effective correction of violations of phagocytic status. In particular, under the influence of the therapeutic complex we noticed likely a significant growth rate as phagocytic cells and PN at the beginning of the treatment of children with asthma compared with the other therapeutic approaches (P<0,05). Most clearly changes obtained over a long observation. In addition, stimulated NBT test showed a higher potential activity of phagocytic cells and completeness of phagocytosis in children who received ST + DBP + L than such groups with a different therapeutic approach (p<0,05). Thus, under the influence of combined therapy over a period of the long-term observation AI (RVU) and N (%) increased significantly and substantially increased the chance of effective correction in children with asthma, who approached the data with the results of previous therapy during the entire period of observation.

We established that the oxygen dependant microbocideness of the neutrophils maximum increased in the course of treating patients with asthma using the combined therapy with the inclusion of complex treatment except Beres Drops Plus Likopid (p<0, 05), which gives the reason to think about the relationship between activation of blood neutrophils, severity of chronic inflammation in the airways common in asthma and exposure inherent immunomodulatory drugs.

In addition, it should be noted that the degree of the dynamics of the immunological status is clearly determined not only by the variant, but by the term of the drug therapy.

4. Conclusions

During the treatment and long-term observation with usage of the various medicinal approaches shows the most positive trend in almost all the indicators of phagocytic activity in patients with asthma who received ST + DBP+ L.

In our opinion, the given results indicate the possibility of entry of such drugs in complex therapy of asthma, which would achieve better control of the disease compared with the traditional basic therapy with the additional adjustment of dose and duration of treatment with the drug in such children.

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