

THE EFFECT OF MAGNETO-LASER THERAPY ON THE PHENOTYPE OF BASOPHILS IN CHILDREN WITH ATOPIC ASTHMA

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Summary

In recent years there has been growing evidence to suggest a major role of basophils alongside eosinophils and mast cells in allergic inflammation.

The aim of this study was to analyze the dynamics of the basophil phenotypes after the use of magneto-laser therapy in children with atopic bronchial asthma. **Materials and methods.** A total of 66 children with mild persistent atopic bronchial asthma (aged 6 to 18 years old) were examined. Group A included 34 children who received magneto-laser therapy together with basic asthma treatment (low dose of inhaled corticosteroids). Group B included 32 children who received only basic asthma therapy. The level of CD203c⁺, CD203c⁺CD63⁺, CD203c⁺IgE⁺ basophils was determined in peripheral blood in the beginning of the study, after 2 weeks and after 3 months.

Results. A statistically significant decrease in the absolute levels of CD203c⁺CD63⁺ and CD203c⁺IgE⁺ basophils and in the relative level of CD203c⁺IgE⁺ among all CD203c⁺ basophils was determined in group A after magneto-laser therapy. The comparison of group A and group B indices revealed a significant difference between the relative level of CD203c⁺IgE⁺ basophils after 12-15 days from the beginning of the study. This indicator was significantly lower in group A than in group B ($p < 0.05$). The absolute level of CD203c⁺IgE⁺ basophils was significantly lower in group A in comparison with group B after 82-90 days ($p < 0.05$).

Conclusions. Magneto-laser therapy can change the phenotype of basophils in children with atopic bron-

chial asthma, causing suppression of proallergic parameters. Considering these results there is reason to believe, that it is possible to use this method as an additional immunocorrective treatment in patients with basophilic phenotype of atopic asthma.

Introduction

Chronic allergic inflammation is the morphological basis of hyperreactivity of the bronchial tree in patients with asthma [1]. Many cells play a role in this chronic inflammation, most prominently mast cells and eosinophils. In recent years, however, there has been growing evidence to suggest a major role for basophils in allergy despite being one of the rarest leucocytes [14]. Recent studies have shown that basophil responses, typically characterized by degranulation, correlate with the severity of allergic reactions. While basophils are an important early source for pro-allergic Th2-type cytokines, interleukins 4 and 13, studies show their ability to migrate into affected tissue and participate in the late phase allergic reactions. At this time we can conclude that basophils seem more likely to participate in allergic reactions than previously thought and their activation status serves as a useful diagnostic marker of clinical symptoms of allergy. Studies tend to support an essential role of basophils in perpetuating ongoing allergic disease, both at the level of directly increasing inflammation and maintaining immunomodulatory mechanisms responsible for the underlying allergic inflammation and Th2 immunity [14].

The dysfunction of the immune system, which develops due to the insufficiency of the immune response regulatory mechanisms, is the main part of the bronchial asthma pathogenesis [2]. It is known that physical factors are capable of directly altering the immunological reactivity by action on the lymphoid tissue, as well as indirectly through the nervous and endocrine systems. Laser radiation is one of

the physical factors capable of correcting immune disorders. It is suggested that the immunomodulating effect of this physical factor is related to the effect it has on the receptor apparatus of immunocompetent cells [3]. Based on available literature, laser radiation affects the surface membrane of the immunocompetent cell, including its receptors, cellular centrosomes and enzymes of the hexosomonophosphate shunt. The influence on these structures causes the immunomodulation effect of this radiation. The effect of low-intensity laser radiation on immunological parameters depends on their initial values and has evident modulating properties [4]. The combination of a magnetic field and laser radiation significantly increases the penetrating power of the lasers action, reduces its reflection at the interface of tissues and improves absorption. This interaction leads to an increase in the effectiveness of laser therapy [5].

Activation of basophils is realized through specific receptors on the membrane of these cells. Degranulation of basophils is accompanied by the appearance of activation molecules - CD203c and CD63. The most commonly recognized marker of blood basophils is CD203c (ectonucleotide pyrophosphatase (E-NPP3)).

The aim of this study was to analyze the dynamics of the basophil phenotypes in peripheral blood after the use of magneto-laser therapy in children with atopic bronchial asthma.

Materials and methods

The study included 66 children 6 to 18 years old. Children were divided into 2 groups: group A - patients receiving magneto-laser treatment and basic asthma therapy simultaneously and group B - children receiving only basic asthma therapy. Both groups of patients were compared by sex and age before inclusion in the study. There was no significant difference between the groups. (Table 1). All children had mild persistent atopic bronchial asthma. The diagnosis and the degree of severity of the disease were established and confirmed in the hospital according to international recommendations [6], based on the anamnesis and the clinical manifestation of bronchial asthma. The study was carried out according to the protocol of open controlled study. In the background both parallel groups of patients received

Table 1. Groups of children with bronchial asthma included in the study (Median [25-75%])

Note: n - is a number of patients in the group

Indicators	Group A (n=34)	Group B (n=32)
Age (years)	10,00 [7,00-13,00]	10,00 [7,00-14,00]
Sex, m / f	21/13	18/14

standard therapy for the main disease. The study was performed with the parents' informed consent of all children that were included in the research (Ethical Committee, protocol No. 3 dated May 11, 2017). Basic therapy was prescribed according to international consensus and treatment protocols. This therapy included inhaled glucocorticosteroids (i-GCS) in low doses and short-acting β 2-agonists as needed.

Phenotyping of the cells was carried out by a flow cytometer Cytomics FC 500 (Beckman Coulter Inc., USA) using monoclonal antibodies. The lysis solution OptiLyse C was used for the lysis of erythrocytes. The patients' immune status was evaluated before the study, 12-15 and 82-90 days after the start of therapy. At the beginning of the study, the level of CD203c⁺ basophils was measured. After that the relative levels of CD203c⁺CD63⁺ and CD203c⁺IgE⁺ were determined among these cells, and then the absolute level of these parameters was calculated.

The basophil phenotype indices CD203c⁺, activated basophils CD203c⁺CD63⁺ and CD203c⁺IgE⁺ were analyzed.

The apparatus that was used for the procedures of magneto-laser therapy had the following characteristics: a laser in the red spectral region with a wavelength of 0.67 ± 0.02 μ m, a near infrared laser with a wavelength of 0.78 ± 0.02 μ m, a constant magnetic headpiece with magnetic induction of 70 mT. The course of magneto-laser therapy in children with bronchial asthma is 7-10 procedures, which are conducted daily.

Statistical data analysis was carried out using the standard software package "Statistica 6.0". The Shapiro-Wilk criterion was used to identify the distribution type of the quantitative attribute. The median and interquartile range were used to describe the characteristic of distribution, which differs from the normal one. Non-parametric methods of statistical analysis were used: the Mann-Whitney test (to assess differences in two independent groups by the quantitative attribute). Differences were held statistically significant at $p < 0.05$.

Results

Statistically significant differences of the level of CD203c⁺ basophils between intervention and control groups were not established during the whole observation period (Table 2).

In group A, the relative level of CD203c⁺CD63⁺ basophils at the beginning of the study was 57.40% [41.90; 76.70%], whereas after 12-15 days the indicator decreased and was significantly lower than in group B ($p_{A2-B2} < 0,01$). After 82-90 days the level of this indicator in group A was still significantly lower than in group B ($p_{A3-B3} < 0,01$). The absolute level of CD203c⁺CD63⁺ basophils in group A decreased and after 82-90 days was significantly lower than the initial

Table 2. Comparative indicators of basophil phenotypes in children with bronchial asthma after treatment (Median [25-75%])

Note: * - significant differences within the group with $p_{1,2} < 0,05$; ** - significant differences within the group with $p_{1,3} < 0,05$

Indicator, units of measure	Group A (n=34)			Group B (n=32)			Reliability of differences between groups
	Before treatment (1)	12-15 day (2)	82-90 day (3)	Before treatment (1)	12-15 day (2)	82-90 day (3)	
CD203c ⁺ , basophils, cells / μ L	6,00 [2,00-20,00]	3,00 [2,00-12,00]	3,00 [2,00-5,00]	4,00 [3,00-5,00]	5,00 [3,00-6,00]	3,00 [2,00-3,00]	
CD203c ⁺ CD63 ⁺ % among CD203c ⁺ basophils	57,40 [41,90-76,70]	52,60 [33,30-71,90]	46,70 [26,70-63,80]	66,70 [52,80-74,60]	81,80 [58,30-89,50]	85,70 [77,80-88,60]	$p_{A2-B2} < 0,01$; $p_{A3-B3} < 0,01$
CD203c ⁺ CD63 ⁺ cells / μ L	3,52 [1,72-9,48]	1,63 [1,13-7,66]	1,64 [1,24-2,55]**	2,24 [1,67-2,70]	2,89 [1,68-4,82]	2,38 [1,30-2,64]	
CD203c ⁺ IgE ⁺ , % among CD203c ⁺ basophils	30,90 [27,40-38,90]	22,70 [17,30-29,40]*	31,70 [12,20-45,90]	39,50 [22,50-47,70]	31,60 [24,50-46,30]	40,00 [32,70-45,70]	$p_{A2-B2} < 0,05$
CD203c ⁺ IgE, cells / μ L	1,70 [0,69-4,60]	0,70 [0,50-1,70]*	1,05 [0,67-1,26]	1,58 [0,69-2,03]	1,58 [0,92-2,21]	1,20 [0,79-1,47]	$p_{A3-B3} < 0,05$

value (1,64 [1,24-2,55] cells / μ L vs 3,52 [1,72-9,48] cells / μ L; ($p_{1,3} < 0,05$).

In group A, the relative level of CD203c⁺IgE⁺ basophils at the beginning of the study was 30.90% [27.40-38.90%]. After 12-15 days the indicator decreased to 22.70% [17.30-29.40%], which is significantly lower in comparison with the initial values ($p_{1,2} < 0,05$). The absolute levels of CD203c⁺IgE⁺ basophils in group A after 12-15 days were also significantly lower (0,7 [0,5-1,07] compared to the levels before treatment (1,07 [0,69-4,60]) ($p_{1,2} < 0,05$). Although during the observation period in group B this indicator increased, however no statistically significant differences were found within the group.

When comparing the levels of CD203c⁺IgE⁺ between groups, significantly lower relative level of CD203c⁺IgE⁺ basophils after 12-15 days were observed in group A 22,70 [17,30-29,40] than in group B (31,60 [24,50-46,30]) ($p_{A2-B2} < 0,05$). Despite the increase in absolute levels of CD203c⁺IgE⁺ basophils in group A in 82-90 days (1,05 [0,67-1,26]), this index was significantly lower in comparison with group B (1,20 [0,79-1,47]) ($p_{A3-B3} < 0,05$).

Discussion

Taking into consideration that the dysfunction of the immune system forms the basis of the bronchial asthma development, the treatment that changes immunological indicators is pathogenetic and the most effective [2]. It is known that mast cells and basophils play a major role in the induction of allergic diseases [7]. An increased level of activated basophils is observed in patients with bronchial asthma [8]. It should be noted that the number of these cells is increased not only in blood, but also in the sputum of patients with atopic asthma. A correlation between the level of

basophils in sputum and eosinophils in both blood and the respiratory tract was found [9]. Degranulation of basophils is accompanied by the appearance of activation molecules - CD203c and CD63 [10, 11, 12].

The study revealed that there was a statistically significant decrease in the absolute level of CD203c⁺CD63⁺ basophils and relative and absolute levels of CD203⁺IgE⁺ basophils after the magneto-laser therapy in children with atopic bronchial asthma. The results obtained during the course of our study, along with other published data show that basophils can serve as a marker of the basophilic phenotype of atopic asthma.

The determination of the number of activated basophils is a new, prospective test, both valid for the diagnosis of allergy and for evaluation of treatment effectiveness [12, 13]. Thus, the data obtained in the study makes it possible to conclude that the involvement of magneto-laser therapy in the treatment of children with bronchial asthma is accompanied by positive dynamics of the immune status indicators. Expanding the knowledge about the mechanism of action of this physical factor will allow justified use of magneto-laser therapy in children with this allergic pathology. The use of magneto-laser therapy in patients can be an additional method of treatment, as well as a correction method of immunological disorders observed in bronchial asthma.

Conclusions

1. After the application of magneto-laser therapy in combination with basic treatment the phenotype of basophils changes, the absolute level of CD203⁺CD63⁺ and the relative and absolute levels of CD203c⁺IgE⁺ basophils decrease.

2. In the group of children receiving only basic asthma therapy the relative levels of CD203⁺CD63⁺ and

CD203c⁺IgE⁺ basophils were significantly higher after 12 - 15 days from the beginning of the study compared to the indices of patients whose treatment included magneto-laser therapy.

3. Magneto-laser therapy can be used as an additional method of treatment in atopic bronchial asthma.

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LAZERINĖS MAGNETINĖS TERAPIJOS ĮTAKA BAZOFILŲ FENOTIPAMS ATOPINE ASTMA SERGANTIEMS VAIKAMS E.Asiryne, P.Novikov, V.Matsiushchanka, N.Titova, L.Vaidelys, G.Griciūnaitė

Raktažodžiai: bronchų astma, magnetinė lazerio terapija, bazofilai, bazofilų fenotipai.

Santrauka

Paskutiniaisiais metais pateikiama vis daugiau duomenų apie bazofilų reikšmę alerginiame uždegime.

Tyrimo tikslas. Išanalizuoti bazofilų fenotipų pokyčius astma sergantiems vaikams taikant lazerinę magnetinę terapiją.

Tyrimo metodai. Tyrime dalyvavo 66 lengva persistuojančia astma sergantys 6-18 m. amžiaus vaikai. Grupei A priskirtiems 34 vaikams šalia įprasto astmos gydymo (mažos dozės įkvepiamojo kortikosteroido) buvo taikoma lazerinė magnetinė terapija. Grupėje B 32 vaikai gavo įprastą bazinį astmos gydymą. Bazofilų CD203c⁺, CD203c⁺CD63⁺, bei CD203c⁺IgE⁺ kiekis periferiniame kraujyje vertintas tyrimo pradžioje, po 2 sav. ir po 3 mėn.

Išvados. Tyrimas parodė, kad lazerinė magnetinė terapija, slopindama proalerginius veiksnius, gali keisti bazofilų fenotipus astma sergančių vaikų periferiniame kraujyje. Rezultatai leidžia manyti, kad lazerinė magnetinė terapija, kaip papildomas imunokorekcinis gydymas, gali būti taikomas astma sergantiems pacientams, kurių alerginiame uždegime dalyvauja bazofilai.

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