



## **Immunological Disorders in Headaches in Children**

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### **ABSTRACT**

This article presents the results of a comparative analysis of n-carriers of antigen-binding lymphocytes specifically sensitized to tissue antigens in children with various types of cephalgia in the intercostal period.

**Key words:** headache, migraine, tension headache, immunology, antigen-binding lymphocytes, tissue antigens, children.

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### **INTRODUCTION**

An important scientific achievement of recent years in the study of primary headaches was the creation of a new conceptual model, according to which its progressive course is recognized as one of the variants of the "natural history of the disease" [9]. The concept of close interrelation and mutual regulation of the nervous and immune systems serves as a theoretical basis for studying the role of immune mechanisms in the formation of PHB. The study demonstrated that patients with primary headaches are characterized by a high prevalence of concomitant somatic disorders, the structure of which is dominated by chronic, recurrent infectious-inflammatory and allergic diseases.

Currently, immunology is one of the most actively developing branches of knowledge, continuously expanding its borders due to its introduction into various areas of clinical medicine [7]. It is proved that the activity of the immune system is not limited to the detection and destruction of foreign antigens, and the idea of its ability to control non-immune functions of the body is becoming more and more firmly established [6]. In this regard, it is of considerable interest to study the immune status of patients with primary headaches [4,5,10,11,12].

Studying the role of the immune system in the progression of GBN and migraine is a relevant scientific direction. Our studies have shown a correlation between the progression of headaches and humoral factors of immunity, which leads to an aggravation of clinical and neurological symptoms in cephalgia, with a deterioration of somatic status [1,8]. Research prospects should include changing approaches to preventing the progression of cephalgia, which can improve the effectiveness of care for patients with primary headaches.

One of the main vocations of the body's immune system is to neutralize and eliminate large- and medium-molecular substances of endogenous origin that are foreign to the internal environment. Antigen-binding lymphocytes (ASL), specifically sensitized to tissue antigens (TA), show the depth of inflammatory processes in the organ tissue. The study of this indicator in the dynamics of the disease allows us to judge the intensity of the process, i.e. an increase in ASL in dynamics indicates an increase, and a decrease in ASL indicates a decrease in the intensity of these processes, which allows us to assess the degree of organ damage, as well as the effectiveness of therapy. [2,3].

### **MATERIAL AND METHODS**

97 children with primary headaches were examined on an outpatient basis at the clinic of the Tashkent Pediatric Medical Institute. The examined people were divided into 3 groups: group 1-children with a

diagnosis of simple migraine in 45 (46 %) patients and migraine with aura in 18 (19 %) patients, group 2-35 (35 %) children with a diagnosis of tension headache, group 3-a control group, which included 34 practically healthy people children of the same age.

The diagnosis was made using the ICGH III Classification of 2013 and was based on anamnestic and clinical neurological data. Additionally, the following paraclinical studies were performed for differential diagnosis of secondary headaches: MRI, EEG, and TCDG.

Depending on the treatment performed in the study, the subjects were divided into 2 groups: group 1 consisted of patients who received traditional therapy, which included non-steroidal anti-inflammatory drugs (ibuprofen, paracetamol, meloxicam), preparations of hydrocortisone acid (prednisolone, prednolone), preparations of the antioxidant group (mexidol, actovegin), vitamin B group preparations (Vitamin B complex, neuromultivit); group 2 patients combined traditional therapy with the use of an immunomodulator-Galavit.

For quantitative registration of antigen-binding lymphocytes (ASL) specifically sensitized to tissue antigens (TA) of various organs, the indirect rosette formation reaction (RNRO) was used according to the F. Yu. Garib method.

## RESULTS AND DISCUSSIONS

The results of a comparative analysis conducted in a group of children with GBN show that the initial value of antigen-binding lymphocytes specifically sensitized to tissue antigens of the brain, liver, thyroid gland and choroid between the corresponding indicators of the 2 groups practically do not differ (Table 1). However, a comparative analysis of indicators 1 and 2 does not show any significant differences in the 2 groups, with corresponding values of the control group, show that the most pronounced changes are noted in the brain tissue (5,38±0,33%; 5,22±0,21%; in the control group, 1,79±0,19%, respectively) and vasculature tissue (5,63±0,28%; 5,94±0,27% in the control, 1,88±0,11%, respectively, P<0.001) (Table 1).

**Table 1: Indicators of antigen-binding lymphocytes in patients with tension headache of groups 1 and 2 before treatment (%)**

ASL to TAG	Norm (healthy) n -34	group 1	group 2
Brain	1,79±0,19	5,38±0,33*	5,22±0,21*
Liver	1,94±0,16	2,0000±0,0707	2,0606±0,05
Choroid	1,88±0,11	5,63±0,28*	5,94±0,27*
Thyroid	2,06±0,22	5,19±0,24*	4,78±0,15*

**Note:** \* - p < 0.05 – significance of differences with indicators of healthy individuals;

There was also a significant increase in ASL parameters specifically sensitized to thyroid TAG (5.19±0.24% in group 1; 4.44±0.18% in group 2 and 2.06±0.22% in the control group; P < 0.001). At the same time, it was found that the initial values of liver ASL to TAG indicators practically do not differ from those in the control group (2.00±0.07% in group 1; 2.06±0.15% in group 2 and 1.94±0.16% in the control; P > 0.05).

A comparative analysis of the initial values of ASL to TAG indicators within the group of examined subjects showed that the maximum increase in ASL to TAG of the brain and choroid was noted up to 8%, and ASL to TAG of the thyroid gland up to 7%.

In the dynamics of the disease, on the 20th day of treatment, the analysis of the results of the comparison groups relative to the control values showed that the intensity of the decrease in the values of ASL to the studied organs has significant differences in the 2 groups.

**Table 2: Dynamics of antigen-binding lymphocytes in patients with tension headache (%)**

ASL to TAG	Control (n=34)	group 1	group 2
Brain	1,79±0,19	5,38±0,33,33* 3,06±0,16*●	5,22±0,21,21* 2,56±0,12*● ■
the liver	1,94±0,16	2,0000±0,0707 1,94±0,07	2,06±0,15 1,94±0,11
Choroid	1,88±0,11	5,63±0,28* 3,56±0,24*●	5,94±0,27* 2,83±0,17* ■
the thyroid gland	2,06±0,22	5,19±0,24* 3,06±0,16*●	4,78±0,15* 2,11±0,08* ■

**Note:** \* - p < 0.05 – significance of differences with indicators of healthy individuals;

- - p <0.05 – significance of differences in the dynamics of diseases
- - P <0.05 – significance of differences relative to the indicators of group 1

There is a more intense decrease in all indicators in the group of patients where an immunomodulator was introduced into the treatment. So, if in group 1 the index of ASL to TAG of the brain in dynamics decreased by 1.8 times, in Group 2 by 2 times (Table 2), the same dynamics is observed with the indicators of ASL to TAG of the choroid (1.6 and 2.1 times, respectively) and to TAG of the thyroid gland (1.7 and 2.3 times, respectively).

At the same time, it should be noted that regardless of the methods of treatment, the values of ASL to TAG of the brain (3,06±0,16%; 2,56±0,12%; in the control group, 1,79±0,19%, respectively), the choroid (3,56±0,24%; 2,83±0,17% in the control, 1,88±0,11%, accordingly, P <0.001) in patients with GBN remain significantly different from the values in the control group.

We also performed a comparative analysis of ASL parameters specifically sensitized to TAG in the brain, liver, vascular membrane, and thyroid gland of children with migraines. According to the obtained results, significantly high initial values of antigen-binding lymphocytes relative to the control values are also noted, indicating deeper disorders in the brain in both groups 1 and 2 (7,00±0,18%; 7,33±0,28%; in the control group, 1,79±0,19%, respectively), vasculature tissue (7.35±0.19%; 7.67±0.29% and 1.88±0.11% P<0.05, respectively), thyroid gland (6.73±0,20%; 5,76±0,25%, respectively, and 2.06±0.22%, in the control; P<0.05) and relative to the values of patients with tension headache as in group 1 (5.38±0.33%; 4.94±0.20% and 5.19±0.24%, respectively), and 2 groups (5.22±0,21%; 6.39±0,29% and 4.44±0,18%, respectively), which are probably associated with a longer and more frequent impact on the tissues of negative factors that make up the mechanism of migraine development (Table 3)

**Table 3: Indicators of ASL to TAG organs in patients with tension headache and migraine in groups 1 and 2 before treatment (%)**

ASL to TAG	Control (n=34)	group 1	group 2
Brain	1,79±0,19	5,38±0,33,33* 7,00±0,18*●	5,22±0,21,21* 7,33±0,28*●
the liver	1,94±0,16	2,00±0,07 2,04±0,09	2,06±0,15 1,90±0,08
Choroid	1.88±0.11	5.63±0.28* 7,35±0,19*●	5,94±0,27* 7,67±0,29*●
the thyroid gland	2,06±0,22	5,19±0,24* 6,73±0,20*●	4,78±0,15* 5,76±0,25*●

**Note:** \* - p <0.05 – significance of differences with the control indicators;

● - p <0.05 – significance of differences in GBN parameters relative to patients with migraine

Numerator – ASL indicators of patients with GBN in the denominator - ASL indicators of patients with migraines

In the dynamics of the disease in patients with migraines, as well as in patients with tension headache, differences in the intensity of reduction of ASL to TAG indicators of organs were revealed, depending on the treatment tactics. A more intense decrease is observed in patients of the 2nd group of patients with the use of immunomodulators.

**Table 4: Dynamics of antigen-binding lymphocytes in patients with migraine in groups 1 and 2**

ASL to TAG	Control group (n=34)	group 1	group 2
Brain	1,79±0,19	<u>7,00.00±0,18,18*</u> 3,85±0,14*●	<u>7,33±0,28,28*</u> 3,00±0,11*●
the liver	1,94±0,16	<u>2,04±0,09</u> 2,00±0,08	<u>1,90±0,08</u> 1,95±0,06
Choroid	1.88±0.11	<u>7.35±0.19*</u> 4,23±0,15*●	<u>7,67±0,29*</u> 3,19±0,14*●
the thyroid gland	2,06±0,22	<u>6,73±0,20*</u> 3,19±0,11*●	<u>5,76±0,25*</u> 2,71±0,14*●

**Note:** \* - p <0.05 – significance of differences with indicators of healthy individuals; ● - p <0.05 – significance of differences in the dynamics of diseases

Thus, there is a decrease in the dynamics of the disease in the indicators of ASL to TAG of the brain in the 2nd group of patients with migraine by 2.4 times, while in the 1st group by 1.8 times, the vascular membrane by 2.4 and 1.7 times, and the thyroid gland by 2.2 and 2.1 times, respectively. It should be noted that on the 20th day of the examination, after treatment, both in group 1 and group 2, the values of ASL to TAG remain significantly higher compared to the control values of ASL to TAG of the brain, vascular membrane and thyroid gland, more significantly exceeding in patients 1 (2.2-2.3 times), than 2 groups (1.3-1.7 times) (Table 4.2).

A comparative analysis of the intensity of the decrease in the dynamics of the disease indicators in patients with GBN and patients with migraine showed that migraine has a more pronounced decrease in indicators than in GBN. It should be noted that the indicators for migraines remain significantly higher relative to the control values than the level of values for GBN. Thus, the average values of ASL to TAG indicators in patients with migraine in group 1 after treatment were to TAG of the brain  $3.85 \pm 0.14\%$ ; vasculature  $4.23 \pm 0.15\%$  and thyroid gland  $3.19 \pm 0.11$ , in group 2-  $3.00 \pm 0.11\%$ ;  $1.81 \pm 0.14\%$ ;  $3.19 \pm 0.14\%$  and  $2.71 \pm 0.14$ , respectively, while in GBN, the corresponding indicators in groups 1 and 2 of ASL to TAG of the brain had values of  $3.06 \pm 0.163$  and  $2.56 \pm 0.12\%$ ; vasculature  $3.00 \pm 0.17$  and  $2.83 \pm 0.17\%$ ; thyroid gland  $3.06 \pm 0.16$  and  $2.11 \pm 0.08\%$ , probably associated with deeper inflammatory processes in the tissues. These data are also confirmed by clinical and neurological indicators in patients with migraine and GBN, in the periods before and after treatment.

A comparative analysis of ASL indicators in the group of children with migraines with aura often shows higher values, which is evidence of deeper pathological processes in the organs (Table 5).

Thus, the average values of ASL to TAG indicators in patients with mirenia with aura in group 1 before treatment were brain TAG  $9.88 \pm 0.49\%$ ; liver  $3.63 \pm 0.31\%$ ; vascular membrane  $8.50 \pm 0.31\%$  and thyroid gland  $8.75 \pm 0.24$ , in group 2-  $9.40 \pm 0.34\%$ ;  $3.20 \pm 0.25\%$ ;  $8.60 \pm 0.31\%$  and  $8.30 \pm 0.31$ , respectively, while in GBN and migraine without aura, the corresponding indicators in the 1st group of ASL to TAG of the brain were  $5.38 \pm 0.33$  and  $7.00 \pm 0.18\%$ ; vascular membrane  $4.94 \pm 0.20$  and  $7.35 \pm 0.19\%$ ; thyroid gland  $5.19 \pm 0.24$  and  $6.730.20\%$  and in Group 2  $5.22 \pm 0.21$  and  $7.33 \pm 0.28\%$ ; liver  $2.39 \pm 0.19$ ; and  $1.81 \pm 0.14\%$ ; vasculature  $6.39 \pm 0.29$  and  $7.67 \pm 0.29\%$ ; thyroid  $4.44 \pm 0.18$  and  $5.76 \pm 0.25\%$  (Table 5).

In the dynamics of the disease in patients with migraine with aura after a course of traditional therapy, the positive dynamics of ASL indicators before treatment is the same in direction and severity, but, nevertheless, the values continue to differ significantly from the indicators in the control group (ASL to TAG).

**Table 5: Dynamics of antigen-binding lymphocytes in patients with migraine with aura in groups 1 and 2**

ASL to TAG	Control (n=34)	group 1	group 2
Brain	$1,79 \pm 0,19$	$9,88 \pm 0,49,49^*$ $5,63 \pm 0,43^* \bullet$	$9,40 \pm 0,34,34^*$ $3,30 \pm 0,26^* \bullet$
the liver	$1,94 \pm 0,16$	$2,13 \pm 0,12$ $1,88 \pm 0,12$	$2,10 \pm 0,18$ $1,80 \pm 0,15$
Choroid	$1.88 \pm 0.11$	$8.50 \pm 0.31^*$ $4,50 \pm 0,18^* \bullet$	$8,50 \pm 0,31^*$ $3,50 \pm 0,22^* \bullet$
the thyroid gland	$2,06 \pm 0,22$	$8,75 \pm 0,24^*$ $5,00 \pm 0,25^* \bullet$	$8,30 \pm 0,70^*$ $2,90 \pm 0,23^* \bullet$

**Note:** \* -  $p < 0.05$ -significance of differences with indicators of healthy individuals;  $\bullet$  -  $p < 0.05$  - significance of differences in the dynamics of brain diseases were  $-3.50 \pm 0.20$ ;  $8.94 \pm 0.40$  and in the control  $1.79 \pm 0.19\%$ , respectively; vasculature  $3.44 \pm 0.17$ ;  $8.06 \pm 0.25\%$  and in the control  $1.88$  thyroid gland  $2.94 \pm 0.17$ ;  $8.39 \pm 0.41$  and  $2.06 \pm 0.22\%$ , respectively) (Table 5).

A comparative analysis of the average values as a result of the course of therapy in the group of patients with HDN, migraine and migraine with aura shows an equally significant decrease in all studied indicators, with the exception of ASL to TAG of the liver in HDN and in patients with migraine, while in migraine with aura, a slight increase in ASL to TAG of the liver was noted, deeper disorders in this form of the disease that require certain additional adjustments in therapy.

**CONCLUSIONS**

According to the comparative analysis of the intensity and multiplicity of reduction in the level of ASL to TAG, a certain effectiveness of traditional methods of therapy was revealed, but the inclusion of an immunomodulator in the treatment regimen, according to the results of ASL indicators, specifically sensitized to TAG of the brain, vascular membrane and thyroid gland, showed a more significant decrease in the initial values of patients with cephalgia. This is also true in the dynamics of the disease, but taking into account the continued reliably high average values of ASL to TAG of the brain, vascular membrane, and thyroid gland in children with tension headache, migraine, and migraine with aura relative to the indicators in the control group, we can probably say that the inflammatory process of various severity continues in the body of some patients, which in turn, it requires continuing treatment or making certain adjustments to the traditional treatment regimens.

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