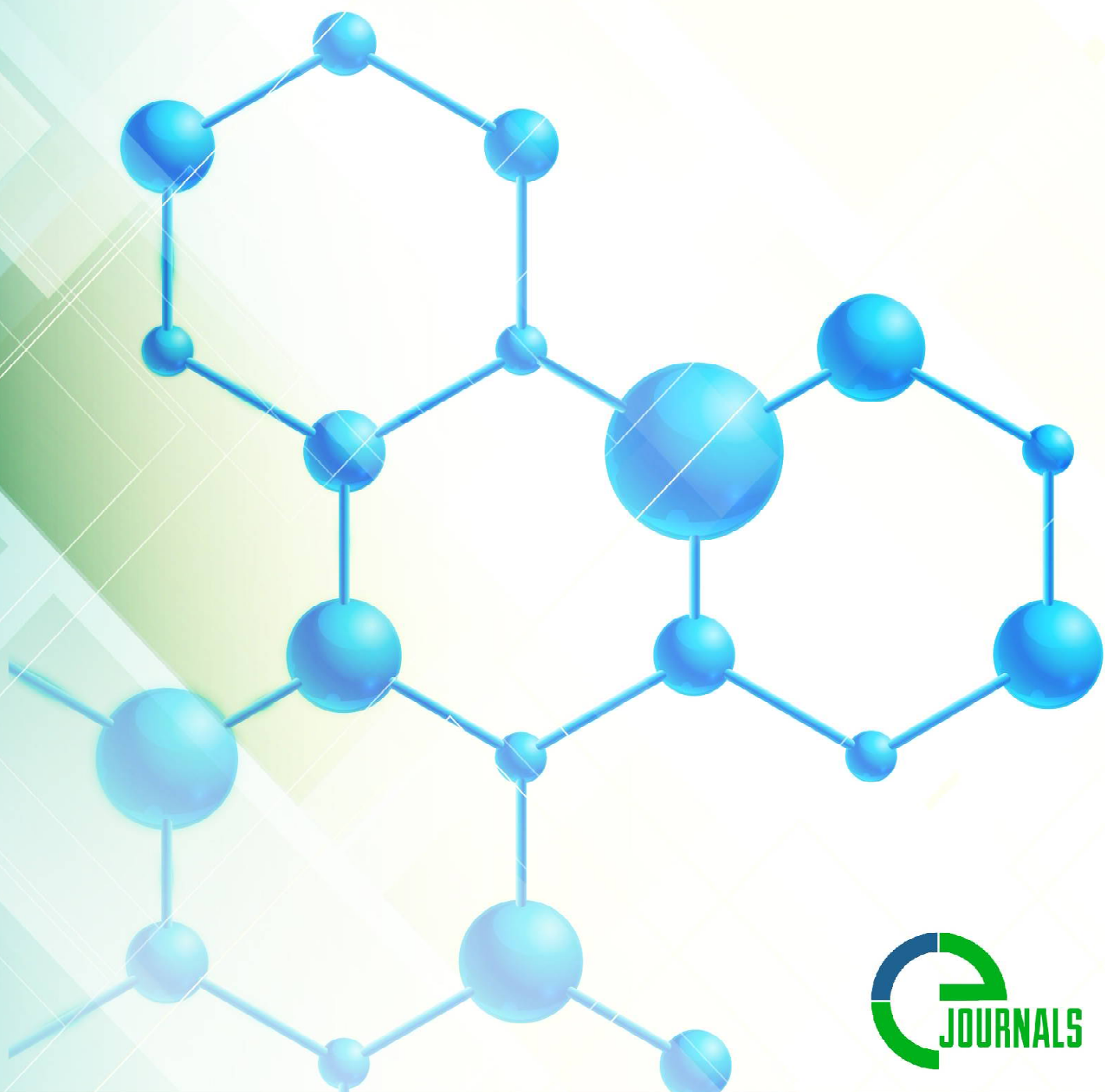


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IMMUNOLOGICAL ASPECTS OF DIAGNOSIS AND TREATMENT OF SICK CHILDREN WITH CHRONIC PURULENT MEDIUM OTITIS ON THE BACKGROUND OF CHRONIC HEPATITIS**Raxmatov A.A.
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Abstract: The immunograms of 93 sick children with chronic purulent otitis media on the background of chronic hepatitis (39 mesotympanitis and 54 epitympanitis) were studied. A comparative analysis of immunogram indices was carried out depending on the severity of inflammatory changes and the inclusion of imunofan in the therapy regimen. The results of the work showed that in sick children with chronic purulent otitis media against the background of chronic hepatitis, the immunogram reflects the peculiarities of the course of the inflammatory process. Chronic inflammatory process in the temporal bone and surgical trauma sharply suppress cellular and humoral immunity, which prompts the use of immunocorrectors in the scheme of postoperative treatment. The inclusion of imunofan in the therapy scheme allowed to completely normalize the immunogram indices in patients with epitympanitis and to improve the clinical course of the postoperative period.

Key words: chronic hepatitis, immunogram, cellular and humoral immunity, imunofan, chronic otitis media.

In the modern literature, there is a lot of data on the relationship between the development of surgical infection with pronounced changes in the immune system, which are classified as secondary immunodeficiency states [5, 6, 12]. The increase in the number of chronic inflammatory diseases of the middle ear against the background of chronic hepatitis and changes in their clinical course [1,9,13] dictate the need for an in-depth study of the mechanisms of development of this pathology and the development of ways of pathogenetic effects on the chronic inflammatory process. It is known that one of the reasons for the formation of chronic suppurative otitis media against the background of chronic hepatitis is a change in general and local immunity [3,7,14]. The main indicators of cellular and humoral immunity are united by the concept of "immunogram" [4, 5, 10, 11]. Imunofan is used to correct immunological disorders in the combination therapy of a number of diseases [2, 8,15]. However, information on the use of Imunofan in otorhinolaryngology, including in the treatment of epitympanitis, is not found in the literature.

Purpose: to study the parameters of the immunogram in patients with chronic suppurative otitis media and to evaluate the effectiveness of standard and combined therapy using imunofan.

Materials and methods. On the first day of hospitalization, immunograms of 93 patients with chronic purulent otitis media (51 men, 42 women) were examined. All examined patients, depending on the activity of the inflammatory process, were divided into three groups. The first consisted of 27 patients with mesotympanitis (code H66.1 according to the International Classification of Diseases) who received only conservative therapy. The second group consisted of 28 patients with epitympanitis (code H66.2), who simultaneously underwent sanitizing and functional operations on the middle ear. The third group included 38 patients with epitympanitis, who, due to the extensiveness of pathological changes (a significant amount of destructive destruction, large cholesteatoma, labyrinth fistula, sub- and epidural abscesses, paresis of the facial nerve), underwent only sanitizing surgery.

At discharge from the hospital, the immunogram was analyzed in 54 patients with epitympanitis, of which two groups were formed. The control group included 26 patients who underwent standard therapy (antibiotics, hyposensitizing drugs, symptomatic and local therapy) in the postoperative period, the main group consisted of 28 patients who, upon discharge from the hospital, the immunogram was analyzed in 54 patients with epitympanitis, of which two groups were formed. The control group consisted of 26 patients who received standard therapy (antibiotics, hyposensitizing drugs, symptomatic and local therapy) in the postoperative period, the main group consisted of 28 patients who received standard postoperative treatment with intramuscular administration of 1 ml of Imunofan every other day for 10 days. (5 injections). The material was processed using a set of descriptive statistics parameters implemented in the Microsoft Excel analysis package for Windows XP. Differences between relative and absolute values were determined using the critical values of the Student's test (t). Differences were considered significant at $t > T_{crit.}$, Corresponding to a significance level of $p < 0.05$.

The results of the study of immunograms of patients with chronic purulent otitis media indicated significant changes in the key links of both cellular and humoral immunity. In clinical groups, there is an increasing suppression of all links of immunity with an increase in the severity of the inflammatory process (Table 1). In the cellular link of immunity of patients of the first clinical group, although there is a decrease in the number and functional activity of phagocytes, significant differences in indicators were determined only by the number of active phagocytes - $1.7 \pm 0.17 \times 10^9 / L$ ($p < 0.05$ to the indicators of healthy donors). In patients of the second group, the suppression of cellular immunity increases; I percent of phagocytosis decreases to $49.4 \pm 2.9\%$ ($p < 0.05$), the phagocytic number to $4.610.31$ ($p < 0.05$), the number of active phagocytes is up to $1, 3 \pm 0.12 \times 10^9 / l$ ($p < 0.05$). In the third clinical group in none of the patients, the percentage of phagocytosis and the number of active phagocytes did not reach the lower limit of the reference interval, and the average figures were significantly lower than the average values of similar indicators in the first and second groups. The percentage of phagocytosis in the third group decreased to $38.9 \pm 3.6\%$ ($p < 0.05$), the phagocytic number - to 4.1 ± 0.45 ($p < 0.01$), the number of active phagocytes - to $1, 51 \pm 0.19 \times 10^9 / l$ ($p < 0.01$) (Table 1). The most profound depletion of the cellular link of immunity was found in patients with a long-term destructive cholesteatotic process in the temporal bone and recurrence of epitympanitis after a previously performed sanitizing operation.

Table N 1

Average immunogram indices in patients with chronic purulent otitis media, depending on the severity of the inflammatory process

Indicator	Healthy donors	1 group n = 27
Leukocytes, x 10 ⁹ /л	5,4 ± 0,1	5,4 ± 0,23
Lymphocytes, x 10 ⁹ /л	1,7 ± 0,01	1,6 ± 0,12
T-lymphocytes are relative, %	53,9 ± 0,3	54,8 ± 5,6
T-lymphocytes absolute, x 10 ⁹ /л	0,95 ± 0,04	1,4 ± 0,22
B-lymphocytes are relative, %	14,7 ± 0,3	22,9 ± 0,9
B-lymphocytes are absolute, x 10 ⁹ /л	0,4 ± 0,01	0,53 ± 0,7f
Percentage of phagocytosis, %	82,8 ± 0,2	59,3 ± 2,5f
Phagocytic number	7,1 ± 0,1	6,9 ± 0,26
Number of active phagocytes, x 10 / л	2,7 ± 0,1	1,7 ± 0,17
Circulating immune complexes, ЕД	53,8 ± 0,2	31,2 ± 5,5
Immunoglobulin G, g/l	9,06 ± 0,1	11,2 ± 0,4
Immunoglobulin A, g/l	1,25 ± 0,1	1,48 ± 0,1
Immunoglobulin M, g/l	1,14 ± 0,1	0,6 ± 0,04.

The average leukocyte counts in all clinical groups were recorded within the permissible reference interval, increasing from the first group to the third, reaching in the latter significant differences with the indicators in healthy donors - $6.2 \pm 0.37 \times 10^9 / L$ ($p < 0.05$). In patients of the first and second groups, the intensity of humoral immunity was noted, expressed in an increase in the number of T- and B-lymphocytes, especially noticeable in young patients. In the third group, an adequate immunological response to the chronic process was not revealed. Despite the predominance of patients with severe inflammatory changes in the temporal bone, including recurrent and complicated ones, the absolute and relative numbers of T- and B-lymphocytes were within the permissible reference numbers (Table 1).

Increasing immunosuppression is also seen in other indicators of humoral immunity. In all clinical groups, both as a whole and throughout the sample, there is a decrease in the titer of circulating immune complexes. In the first group, their numbers were 3 ± 5.5 U in the second, they decreased to 30.7 ± 5.7 U in the third - to 21.2 ± 4.1 U. Similarly, the titers of immunoglobulin A decreased: from 1.48 ± 0.1 g / L in the first group, to 1.39 ± 0.1 g / L - in the second and 1.27 ± 0.1 g / L - in the third (Table 1).

The results of a comparison of indicators of cellular and humoral immunity in clinical ipynnax revealed an increasing, depending on the severity of inflammatory changes, immunodeficiency in patients with chronic purulent otitis media. This circumstance prompts the inclusion in the treatment regimen, especially of severe destructive cholesteatotic, recurrent and complicated epitympanitis, immunocorrective drugs.

Analysis of the results of the immunogram before discharge showed significant changes in the cellular and humoral immunity in patients with chronic purulent otitis media after the sanitizing surgical treatment. A similar condition after surgical treatment is described by many authors as "immunological paralysis" [5, 6]. So, in patients of the control group, a sharp decrease in phagocytic activity was noted. The percentage of phagocytosis in them was $29.4 \pm 3.1\%$ ($p < 0.05$ to the indices of healthy donors), the phagocytic number was 3.6 ± 0.41 , the number of active phagocytes was $1.2 \pm 0.1 \times 10^9 / L$ (reference interval $2.5 - 2.9 \times 10^9 / L$, $p < 0.05$) (Table 2). The data obtained confirm the fact of the immunosuppressive effect of surgical trauma and indicate the low immunocorrective efficacy of traditional therapy prescribed in the postoperative period.

It was noted that in the majority of patients who received only 29.4 standard therapy, the absolute and relative numbers of T- and B-lymphocytes were higher than in healthy donors, which affected the average values. Relative T-lymphocytes were $58.8 \pm 4.4\%$, absolute- $1.6 \pm 0.19 \times 10^9 / L$, B-lymphocytes - $21.5 \pm 0.19\%$ and $0.53 \pm 0.04 \times 10^9 / L$. At the same time, a sharp decrease in the functional activity of cells was stated. Low indices of circulating immune complexes - $22.4 + 4.9 U$ ($p < 0.05$ to the indices of healthy donors), immunoglobulin G- $8.9 + 0.58 g / l$, immunoglobulin A- $1.21 + 0.13 g / l$ and immunoglobulin M- $0.66 + 0.04 g / l$ (Table 2).

Table 2

Average indices of the immunogram in patients with epitympanitis before discharge from the hospital, depending on the use of Imunofan

Indicator	Healthy donors	Standard therapy p = 26	+ Imu nof
Leukocytes, x 10 ⁹ /л	5,4 ± 0,1	5,7 ± 0,17	5,5 ±
Lymphocytes, x 10 ⁹ /л	1,7 ± 0,01	1,69 ± 0,08	1,7 1
T-lymphocytes are relative, %	53,9 ± 0,3	58,8 ± 4,4	69, 1
T-lymphocytes absolute, x 10 ⁹ /л	0,95 ± 0,04	1,6 ± 0,19 j	1,4 ± 0,
B-lymphocytes are relative, %	14,7 ± 0,3	21,5 ± 0,19f	16, 2 ±
B-lymphocytes are absolute, x 10 ⁹ /л	0,4 ± 0,01	0,53 ± 0,04f	0,4 7 ±
Percentage of phagocytosis, %	82,8 ± 0,2	29,4 ± 3,11	71, 3
Phagocytic number	7,1 ± 0,1	3,6 ± 0,4II	8,7 ±
Number of active phagocytes, x 10 /л	2,7 ± 0,1	1,2 ± 0,1 J,	2,6 ± 0,
Circulating immune complexes, ЕД	53,8 ± 0,2	22,4 ± 4,9	51, 9 ±
Immunoglobulin G, g/l	9,06 ± 0,1	8,9 ± 0,58	13, 1
Immunoglobulin A, g/l	1,25 ± 0,1	1,31 ± 0,13	1,4 5
Immunoglobulin M, g/l	1,14 ± 0,1	0,66 ± 0,04	1,0 3 ± 0

Note. Significant differences with indicators in healthy subjects (p 0.05) are highlighted in bold, arrows are indicators that go beyond the reference interval.

The inclusion of Imunofan in the scheme of postoperative treatment of patients with chronic purulent otitis media allowed to normalize most of the parameters of cellular and humoral immunity by the time of discharge from the hospital. The percentage of phagocytosis in this group of patients was $71.3 \pm 4.4\%$ ($p < 0.05$ to the control), the phagocytic number was 8.7 ± 0.62 ($p < 0.05$ to the control), the number of active phagocytes was $2,6 \pm 0.19 \times 10^9 / L$ ($p < 0.05$ to control). Although the absolute and relative numbers of T- and B-lymphocytes were determined at the level of the maximum figures of the reference interval, they did not differ significantly from those in patients who received standard therapy (Table 2).

The use of Imunofan activated the functional activity of immunocytes. On average, all the studied parameters of humoral immunity were determined at the level of the upper limit of the reference interval and significantly differed from those in patients treated according to the traditional scheme ($p < 0.05$). Thus, the average levels of circulating immune complexes increased to $51.9 \pm 5.21 U$, immunoglobulin G - up to $13.1 \pm 0.63 g / l$, immunoglobulin A - up to $1.55 \pm 0.09 g / l$, immunoglobulin M - up to $1.03 \pm 0.06 g / l$ (Table 2).

Imunofan combined therapy in the postoperative period of patients with epitympanitis significantly reduced the percentage of patients with a high degree of immunological deficiency. By the time of discharge from the hospital, in 82.6% of patients who received only standard therapy, at least 5 parameters of the immunogram went beyond the reference interval. Imunofan administration reduced the proportion of patients with such immunological disorders to 14.8% ($p < 0.05$).

The beneficial effect of using imunofan in the postoperative period in patients with epitympanitis is noticeable not only in the restoration of the immunological, but also in the positive changes in the clinical status of patients. In most patients, by the time of discharge from the hospital (8-12 days), exudation from the postoperative cavity was scarce, and areas of epidermis began to appear.

Thus, in patients with chronic purulent otitis media, the immunogram reflects the characteristics of the course of the inflammatory process, which must be taken into account in the diagnosis and in the treatment regimen. A chronic inflammatory process in the temporal bone and surgical trauma sharply suppresses cellular and humoral immunity, which prompts the use of immunocorrectors in the scheme after surgical treatment. The inclusion of Imunofan in the therapy scheme allowed to completely normalize the immunogram indices in sick children with epitympanitis and to improve the clinical course of the postoperative period.

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