

Etiopathogenic Aspects and Complex Conservative Treatment of Chronic Tonsillitis in Children

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Abstract - Background: Considering the role of palatal tonsils in the human body, medical professionals exercise cautiousness when considering tonsillectomy, especially in children, when the tonsil's physiological function is at its highest. Use of new diagnosis methods for measuring local and systemic immunity reactions, in correlation with a clinical evolution of the disease, will allow us in the future to gain in-depth knowledge about certain etiopathogenetic aspects of chronic tonsillitis.

Objective: 1. To explore some aspects of systemic immune reactions in chronic compensative tonsillitis. 2. To compare systemic immune reactions in chronic tonsillitis and adults. 3. To explore the efficacy of complex conservative treatment of children with compensative chronic tonsillitis.

Subjects and methods: 24 children and 13 adults with chronic compensative tonsillitis – immunological examinations, 180 children who were treated with conservative methods. Outcome measures: C-reactive protein, antistreptolysin O, absolute and relative amount of B lymphocytes, immunoglobulins – A, M, G, circulatory immune complexes, interleukins IL-4, IL-8, IL-1 β in blood serum.

Results: Interleukin-8 is 6.5 times higher in children than in adults ($p=0.047$), interleukin - 1 β is 17.4 times higher ($p=0.045$). Serum levels of IgA in adults is higher than in children ($p=0.038$), antistreptolysin – O titre is 1.4 times higher. We obtained positive results in 85% of cases treated with conservative methods.

Conclusion: The study of interleukin – 1 β and interleukin – 8 is useful in understanding the etiopathogenetic mechanisms of chronic compensative tonsillitis in children. Nonspecific immune factors play an important role in the immune response in chronic tonsillitis in children, while in adults the main role is held by a specific immune response. The dispensarisation of the children with chronic compensative tonsillitis and the complex conservative treatment, that include local and general immunostimulation, will decrease the number of complications and will improve the quality of life.

I. INTRODUCTION

The issues posed by chronic tonsillitis have surpassed the limits of ENT science. This disease is increasingly the object of study by representatives of theoretical medical science and various specialties of clinical medicine such as: pediatrics, rheumatology, nephrology, immunology, allergology, etc. Inflammatory processes located in tonsillar lymphatic tissue encourage development of human systemic complications and worsen their pathogenesis.

Human health is formed as a result of a complex interconnection between hereditary-constitutional peculiarities of the human body, the surrounding environment and society. The variation in the norm of human pathology by ethnic and geographic factors has already been ascertained. The prevalence of chronic tonsillitis in a population, according to various local and foreign sources, varies widely from 5 percent to 50 percent. Timely diagnosis and adequate treatment of chronic tonsillitis in children decreases the number of possible complications resulted from a source of chronic infection.

An epidemiological study of chronic tonsillitis in children from rural and urban regions of the Republic of Moldova conducted in year 2010 concluded that the average prevalence of this disease is quite high – 7.7 percent. Chronic tonsillitis is encountered more often after

the age of 12-13. A chronic or recurrent inflammatory-microbial pathology is a manifestation of general or local immunological abnormalities. Today, the poli-etiological aggression on the respiratory mucosa is continuously growing and expanding. Given the modification of microbial flora and its lack of sensitivity to antibacterial therapy, palatal tonsils are under increasing pressure to adjust and act as defense agents.

Considering the role of palatal tonsils in the human body, medical professionals exercise cautiousness when considering tonsillectomy, especially in children, when the tonsil's physiological function is at its highest^{2, 3, 4, 5}. Use of new diagnosis methods for measuring local and systemic immunity reactions, in correlation with a clinical evolution of the disease, will allow us in the future to gain in-depth knowledge about certain etiopathogenetic aspects of chronic tonsillitis. This will also enable medical professionals to develop new complex conservative treatment methods in order to stimulate healing and sanitation of local inflammatory processes. As a result, we will be able to witness a distinct difference between current treatment outcomes and future treatment outcomes as a result of local and general immune stimulation, which would probably ensure a faster and more complete evolution of reparative processes.

Stimulation of the anti-inflammatory and reparative processes in chronic tonsillitis is possible, but needs continuous research aimed at standardizing the new immunostimulatory and immunomodulatory drugs. It also

requires research of the mechanisms at work on cellular levels during this stimulation.

Serious immunity changes are determined by primary (congenital) or secondary (acquired) immunodeficiency. Secondary immunodeficiency develops as a result of various exogenous factors (infections, avitaminosis, stress, environment pollution etc.). Immunoregulatory modifications⁶ are one of the leading causes of chronic tonsillitis pathogenesis.

The risk of a secondary immune deficiency is higher during the immunity formation period in children, when as a result of an antigenic action, the immune system may react inadequately. This reaction may be either insufficient or excessive, hyperactive. In triggering this reaction, both humoral and cellular factors are at play⁷.

The Ig A deficiency in local (secretory Ig A) and general (serum Ig A) immunity⁸ is one of the most frequent humoral insufficiency factor, which favors the development of chronic disorders of the upper respiratory tract. Secretory Ig A deficiency increases mucous permeability, amplifying penetration of allergens and bacteria in tissues^{9, 10, 11}.

Research conducted to date has confirmed the role of cytokines (IL -1 β , IL-4, IL-6, IL-8, interferon, etc.) in influencing the severity of inflammatory processes, as well as their effect on immune mechanisms^{6, 8, 12, 13}.

Consequently, we consider that a priority direction in the ENT pediatric field is the continuous study and development of prognostic criteria regarding the evolution of inflammatory processes in children with chronic tonsillitis. Another important direction is the justification of complex conservative treatment in order to maintain palatal tonsils as an important organ for local and systemic immunity..

II. AIM OF THE STUDY

1. To explore some aspects of systemic immunity reactions in chronic compensative tonsillitis.
2. To compare systemic immunity reactions in children and adults with chronic tonsillitis.
3. To explore the efficacy of complex conservative treatment of children with chronic compensative tonsillitis..

III. MATERIAL AND METHODS

24 children aged 2 to 14 y.o. (average age – 7.7 \pm 0.6 y.o.) and 13 patients aged 16 to 28 y.o (average age – 20.1 \pm 1.2 y.o) with chronic tonsillitis, have been examined, 180 children who were treated with conservative methods.

Immunologic examination included: total levels of leukocytes; absolute and relative levels of lymphocytes in patient blood; estimation of nonspecific protection factors in blood serum – C reactive protein (CRP), antistreptolysin O (ASO), rheumatoid factor; investigation of humoral immune factors – absolute and relative levels of B lymphocytes, serum immunoglobulins – A, M, G (IgA, IgM, IgG), circulatory immune complexes (CIC), determination of interleukin levels - IL-4, IL-8, IL-1 β in blood serum.

IV. CONCLUSION

A comparative analysis of the outcomes from 2 groups of patients, showed a series of differences among a number of indices. In children with chronic compensated tonsillitis increased levels of B-lymphocytes and total lymphocytes, increased levels of C reactive protein and rheumatoid factor, as well as elevated levels of interleukins – IL-4, IL-8, IL-1 β were observed. In adults, a quantitative increase of total leukocytes, antistreptolysin O titre and Ig A levels were noted. The data confirmed that children with chronic tonsillitis develop a higher immune reaction than adults, however not all the results were valid (Table 1).

In Table 1, we can see that, despite the absence of significant statistical correlation between the groups, activation of nonspecific immunity factors is greater in children with chronic tonsillitis than in adults. Changes in nonspecific immunity indices in chronic tonsillitis depend on the phase of the inflammatory process, on the onset and the length of the disease. These indices are higher during the acute period of the disease than during the reparative period. In a prolonged onset of the disease, it has been observed that these indices are decreasing, as a result of immune exhaustion.

Significant statistical correlations were observed in the children group where an increase in the absolute levels of lymphocytes ($p = 0.04$), interleukin – 8 ($p = 0.047$) and interleukin – 1 β level ($p = 0.045$) were noted. Average levels of interleukin-8 and interleukin - 1 β in children are 6.5 and, respectively, 17.4 times higher than in adults.

Interleukin - 8 and interleukin - 1 β represent antiinflammatory cytokines, which induce activation of nonspecific immunity factors, thus supporting the amplification of specific immune response^{2, 13}. Interleukin -1 β is one of the most important cytokines that control the inflammatory process. It acts first of all on the inflammatory portion of the tissue where antigenic stimulation takes place. It also increases the functional state of neutrophils and activates the complement components etc. The biological effect of interleukin-1 β on a systemic level is manifested through fever, leukocytosis and increase of lymphocyte functional activity, etc. Interleukin -8 also plays an important role in increasing the nonspecific immune response by supporting neutrophilic migration to antigen invading zone.

According to the data obtained, we can clearly see the interconnection between antiinflammatory cytokine synthesis and increases in the nonspecific defense factors in children with chronic tonsillitis. This is a normal process in case of an inflammatory reaction. However, immune reactions resulting from the inflammatory process were not characteristic for adults with a similar diagnosis. There can be few explanations for this occurrence. First, considering the slow and lengthy nature of the disease, the visible decrease of antiinflammatory cytokines may be a result of immune exhaustion. Second, these patients could have displayed cytokine insufficiency from the start, which led to a chronic evolution of the inflammatory process.

Table 1. Systemic immunological parameters in children and adults with chronic compensative tonsillitis

Indices	Children (main group n=23)	Adults (control group n=13)	Validity level (p)
Total levels of leukocytes (*10 ⁹ /l)	7.42 ± 0.45	11.8 ± 4.44	0.3
Absolute levels of lymphocytes (*10 ⁹ /l)	2.92 ± 0.24	2.2 ± 0.11	0.04*
Absolute levels of B lymphocytes (*10 ⁹ /l)	3.09 ± 1.96	0.93 ± 0.09	0.4
C reactive protein –(CRP) (mg/ml)	1.43 ± 1.16	0	0.38
Rheumatoid factor (mg/ml)	1.87 ± 1.52	0	0.3
Antistreptolysin-O (ASO) (Iu/ml)	162.5 ± 45.53	216.67 ± 45.78	0.42
Serum immunoglobulin A (gr/l)	1.36 ± 0.16	1.92 ± 0.19	0.038*
Interleukin – 4 (pg/ul)	7.36 ± 2.13	4.66 ± 3.29	0.48
Interleukin – 8 (pg/ul)	229.09 ± 73.63	35.05 ± 14.64	0.047*
Interleukin – 1β (pg/ul)	191.19 ± 68.44	10.88 ± 4.28	0.045*

* Significantly different immunological parameters between the children and adult group with chronic tonsillitis (p < 0.05).

Despite the fact that the average level of serum IgA in adults and children with compensated chronic tonsillitis was within normal limits, the levels were statistically significantly higher in adults than in the children group (p=0.038). These results demonstrate that in case of chronic tonsillitis, a specific immune response prevails in adults. A higher antistreptolysin – O titre in adults (1.4 times higher) than in children also proves the presence of this specific immune response.

Taking into account immunological changes that develop in case of chronic compensative tonsillitis in children in our childrens clinic immunomodulator preparations like Ribomunil, IRS – 19, imudon are administered in addition to common local treatment of chronic compensative tonsillitis in children that allows to stimulate both specific and non-specific immunity. For a century a special attention has been paid to the development of new biomaterials to be used in regeneration of tissues. Cellular cultures are used to stimulate suppressed regenerative processes and they reduce local inflammations.

Taking into consideration the above mentioned a new method of local immunostimulation in case of chronic tonsillitis treatment was implemented in the childrens ENT Clinic. The method consists in the administration of autolymphocytes in the peritonsillar space. Being introduced autolymphocytes produce antiinflammatory cytokines and activate other immunocompetent cells in the respective region. The local immunity becomes better and the inflammatory process decreases that is correlated with a patients positive clinical state. No side-effects were noted after this method of treatment. We obtained positive results after the selection of conservative treatment modalities in 85% of cases.

V. CONCLUSION

The research has shown that nonspecific defense factors play an important role in children who suffer from chronic tonsillitis, while in adults the main role is played by a specific immune response. Comparative analysis of antiinflammatory cytokine synthesis by immunocompetent cells in chronic compensative tonsillitis demonstrated that this synthesis is much higher in children than in adults. In this regard, we recommend that studies of interleukin – 1 β and

interleukin – 8 levels should be conducted already at incipient stage of the disease in patients suffering from chronic tonsillitis. The dispensation of the children with chronic compensative tonsillitis and the complex conservative treatment, that include local and general immunostimulation, will decrease the number of complications and will improve the quality of life.

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