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OPTIMIZATION OF ETIOLOGICAL DIAGNOSIS AND MANAGEMENT OF CHILDREN WITH ACUTE TONSILLOPHARYNGITIS

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Annotation. The article is devoted to an important clinical topic - the etiological diagnosis of acute tonsillopharyngitis in children, where the key aspect is the differential diagnosis between viral etiology and beta-hemolytic streptococcus group A, in order to prevent unjustified prescribing of antibiotics.

Key words: children, acute tonsillopharyngitis, etiological diagnosis, clinical manifestations, therapy

Introduction. Respiratory tract infections, in particular acute tonsillopharyngitis (ATF), are one of the main reasons for the unjustified prescription of antibacterial drugs in outpatient practice, with the frequency of their use reaching 75%. In the vast majority of cases, ATF has a viral etiology (associated with rhinoviruses, adenoviruses, enteroviruses, influenza viruses, parainfluenza, Epstein–Barr) and does not require systemic etiotropic therapy [1, 2]. Among bacterial pathogens, beta-hemolytic streptococcus group A (Streptococcus pyogenes, BHSA) is of the greatest clinical importance, accounting for 5% to 15% of cases in the adult population and 20-30% in the pediatric population [3]. The potential role of other bacterial agents such as group C and G streptococci, Streptococcus pneumoniae, Mycoplasma pneumoniae, and Chlamydophila pneumoniae is also discussed in the literature. The only definitive indication for systemic antimicrobial therapy of ATF in immunocompetent individuals is the proven streptococcal (BHSA) genesis of inflammation (with the exception of occasional rare cases of diphtheria or gonococcal lesions) [4]. The lack of convincing data on the involvement of other bacterial microorganisms in the formation of systemic complications of ATF, as well as the practical impossibility of differentiating the true etiological significance of such flora from transient bacterial carrier, require a critical attitude to the expediency of prescribing broad-spectrum antibacterial drugs without verifying the pathogen.

The clinical manifestations of ATF of streptococcal and non-streptococcal etiology are characterized by a high degree of similarity, however, there are a number of differential diagnostic signs. Acute manifestation of angina, manifestation in the age range from 5 to 15 years, febrile fever (38°C), cephalgia, abdominal syndrome, nausea and vomiting are pathognomonic for ATF associated with BHSA. An objective examination verifies pronounced hyperemia of the tonsils, palatine arches and posterior pharyngeal wall, the presence of loose layers in the lacunae, petechial enanthema on the hard palate, as well as painful anterior cervical lymphadenitis. Streptococcal infection is characterized by winter-spring seasonality and the presence of epidemiological contact with a patient with tonsillitis [5]. On the contrary, the viral etiology of ATF is supported by symptoms such as conjunctivitis, laryngitis, dysphonia (hoarseness of voice), cough, rhinorrhea, diarrheal syndrome, aphthous stomatitis and polymorphic exanthema. Despite the presence of these markers, the etiological verification of ATF, based solely on clinical and epidemiological data, is characterized by low specificity. The traditional bacteriological examination (cultural method) is still recognized as the "gold standard" of diagnosis, but it is characterized by high complexity and variability of results [6]. The main limitation of the method in routine clinical practice is the delay in obtaining results, which become available to the doctor only 48-72 hours after sampling the biomaterial. As a result, in outpatient settings, the decision to start antibacterial therapy is made empirically. Such tactics naturally lead to a high frequency of unjustified prescribing of systemic antimicrobials, which is associated with the risk of adverse drug reactions in the patient and the selection of resistant strains of pathogens in the population. Thus, the urgent task of pediatrics remains the search and implementation of new highly specific criteria that allow early differential diagnosis of bacterial and viral ATF, which is necessary to optimize initial therapy.

The purpose of the study: to study the features of the etiological diagnosis of acute tonsillopharyngitis in children and to determine the diagnostic value of general clinical and paraclinical indicators in verifying the non-streptococcal etiology of the disease in order to optimize treatment tactics.

Materials and methods of research. A comprehensive examination of 105 children with a strictly verified diagnosis of AF was conducted in clinical conditions. According to the results of bacteriological examination of smears from the surface of the tonsils for the presence of hemolytic streptococcus group A (BHSA), all patients were divided into two observation groups. The first (I) group included 70 children with non-streptococcal ATF (NATF) and a negative culture result. The second (II) group consisted of 35 children with confirmed streptococcal ATF (SATF) and isolated BGSA culture. The average age of the examined patients was 8.63±0.49 years (95% CI 7.65–9.61). The proportion of boys in group I was 52.2%, in group II - 38.2% ($p>0.05$). According to the main anamnestic and demographic characteristics, the groups were comparable. At the time of hospitalization, all patients underwent a standard clinical examination with a point assessment of the severity of objective symptoms (points were awarded in proportion to the increase in the severity of ATF manifestations). The parameters of a detailed general blood test were evaluated as additional paraclinical markers potentially confirming the non-streptococcal nature of inflammation. The study was conducted in compliance with ethical standards, after the parents (legal representatives) of the children signed a form of voluntary informed consent. Statistical analysis of the obtained data was carried out using the StatSoft Statistica v. 6.0 software package. To assess the clinical information content of the studied indicators, the operational characteristics of the tests were calculated: sensitivity (HR), specificity (SP), the prognostic value of a positive result (PCPR) and the prognostic value of a negative result (PCR). In

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accordance with the principles of clinical epidemiology, the indicators of absolute (attributive) and relative risks, as well as the odds ratio (OR), were calculated with the calculation of the corresponding 95% CI. The critical significance level for testing statistical hypotheses was assumed to be 0.05.

The results of the study and their discussion. Upon hospitalization in the hospital in group I (NATF), an isolated diagnosis of ATF was established in 73.1±5.37% of patients, while the remaining 26.9±5.37% of children had a combined lesion in the form of tonsillitis with pharyngitis or rhinopharyngitis. In group II (SATF), isolated ATF and combined forms of lesion were recorded in 87.5±5.67% and 12.5±5.67% of cases, respectively (differences between the groups are statistically insignificant, p>0.05). An analysis of the nature of the inflammatory process showed that in group I, the catarrhal form of ATF was verified in 32.8±5.69% of children, and exudative tonsillopharyngitis in the remaining 67.2±5.69% of patients. In group II, these morphological forms of the disease occurred in 24.2±7.35% and 75.7±7.35% of cases, respectively; intergroup differences also did not reach statistical significance (p>0.05). Thus, an isolated assessment of the nosological form and nature of exudation on the tonsils did not allow us to reliably differentiate the streptococcal etiology of the process from non-streptococcal at the initial examination stage.

A comparative analysis of the clinical picture of tonsillitis at the onset of the disease did not reveal statistically significant differences in the nature of tonsillitis between the compared groups, although local inflammatory changes were visually more pronounced in patients with tonsillitis. Against the background of the therapy, the dynamics of symptom regression and their integral score in both groups practically coincided. Thus, in group I, the number of children with severe tonsillopharyngitis (the total score exceeded 45 points) at hospitalization was 30 people (42.6±6.00%), while in group II — 15 patients (44.1 ± 8.52%; p>0.05). Fever was the leading clinical symptom in both cohorts. In group I (NATF), subfebrile body temperature was recorded in 20.6% of patients, and in half of the cases (50.0%), the temperature reaction exceeded 38.5 °C. In patients of group II (SATF), subfebrility and febrile fever were verified in 35.3% and 58.8% of cases, respectively. An assessment of the operational characteristics showed that the presence of isolated subfebrility at the onset of the disease has high specificity (94.1%), but extremely low sensitivity (20.6%) in relation to verification of the non-streptococcal etiology of the process. Taking into account the fact that in 79.4% of cases false negative results were recorded when evaluating this parameter, the isolated use of the temperature reaction as a reliable etiological marker of ATF is impractical. Thus, the decision to abandon systemic antibacterial therapy should not be based solely on the nature of the febrile syndrome.

The presence of cough in children with inflammation of the palatine tonsils indicates a non-streptococcal etiology (NATF) with a specificity of 70.5% and a prognostic value of a positive result (PCPR) of 60.0%, however, this sign has a high frequency of false negative results (64.7%). The absence of intoxication syndrome is characteristic of NATF (specificity

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91.4%, PCR 75.2%), but it has an extremely low sensitivity (4.0%), and the absence of pronounced cephalgia (sensitivity 76.8%) also indicates a non-streptococcal etiology.

In clinical practice, it is generally accepted that the severity of layers on the palatine tonsils is directly proportional to the probability of streptococcal etiology of ATF. However, according to our data, this symptom has an extremely limited differential diagnostic value. At the onset of the disease, the intensity of the exudative component in the examined children in both groups did not differ significantly and amounted to 2.6±0.17 points in patients of group I, versus 2.9±0.23 points in patients of the comparison group ($p>0.05$). Evaluation of the revealed characteristics showed that the absence of pronounced exudate (less than 3 points) as a test confirming NATF is characterized by both low sensitivity (42.4%) and insufficient specificity (69.7%). The odds ratio (OSH) of NATF verification under this condition was 1.7 (95% CI: 1.0–3.0) with a post-test probability of outcome of only 8.3%.

The intensity of pain in the throat was also almost identical in children of both groups. In patients of group I, this indicator averaged 2.96 points, and in patients of group II - 3.0 points. Thus, the results obtained convincingly demonstrate that an isolated assessment of the severity of local and general clinical symptoms of AF does not reliably differentiate the streptococcal etiology of the inflammatory process from non-streptococcal at the initial examination stage.

The presented clinical characteristics of ATF in children indicate that neither an isolated symptom of the disease nor their combined manifestation can serve as a reliable criterion for the differential diagnosis between HSA-induced infection and lesions of a different etiology. At the same time, it has been established that markers of systemic and local inflammatory response of the macroorganism are registered with a higher frequency in case of ATF than in case of non-streptococcal nature of the pathological process. In this regard, it is reasonable to assume that paraclinical indicators of inflammatory activity can act as additional criteria for etiological verification of the disease.

Analysis of the results of the hematological examination showed that in children with non-streptococcal and streptococcal ATF there are no significant differences in most parameters of the leukocyte formula, with the exception of the general frequency of leukocytosis. In particular, absolute leukocytosis in peripheral blood (more than 10.0 g/l) in group II (SATF) was significantly more often recorded than in group I (NATF) — in 44.1% versus 29.4% of cases, respectively ($p<0.05$). At the same time, an increased content of rod-shaped neutrophils (more than 15.0%) was detected in 47.1% of patients with NATF and in 38.2% of children with SATF ($p>0.05$). The proportion of patients with a segmented neutrophil level of more than 50.0% was 48.5% in group I and 41.1% in group II ($p>0.05$). The relative number of lymphocytes of more than 50.0% was determined in 13.2% of children with NATF and in 17.6% of patients in the comparison group, and these differences also did not have high statistical significance ($p>0.05$).

There were also no statistically significant differences in the characteristics of erythropoiesis between the compared groups. In group I patients, the number of erythrocytes

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in peripheral blood was 4.2±0.06 10^{12}/L (95% CI 4.10–4.32) with an average hemoglobin concentration of 129.6±1.78 g/l (95% CI 126.0–133.1) and a color index of 0.92±0.003 (95% CI 0.92–0.93). In the patients of the comparison group (group II), these indicators were 4.0±0.11 (95% CI 3.7–4.2) 10^{12}/l, 121.2±2.48 (95% CI 116.2-126.3) g/l and 0.94±0.03 (95% CI 0.88-1.0) ($p>0.05$), respectively.

The platelet count in patients with NATF averaged 234.3±5.78 (95% CI 220.1-248.4) 10^9/l. In the group of children with SATF, the average platelet count in peripheral blood was in the range of 337.0±6.28 (95% CI 330.0-352.0) 10^9/l ($p>0.05$). Considering that none of the isolated clinical or laboratory parameters simultaneously possessed a sufficient level of sensitivity and specificity to verify the etiology of acute inflammation of the palatine tonsils, the integrated use of clinical and paraclinical markers was justified. The integrative approach makes it possible to significantly improve the accuracy of differential diagnosis, verify NATF in a timely manner, and prevent the unjustified appointment of systemic antibacterial therapy in pediatric practice.

Conclusions:

1. At the onset of the disease and at the stage of hospitalization, the intensity of the main clinical manifestations of acute tonsillopharyngitis (ATF) in children in the compared groups had no statistically significant differences. At the same time, patients with non-streptococcal etiology of the process (NATF) were characterized by a significantly rarer and isolated manifestation of febrile fever (OR = 4.1), as well as a lower incidence of pronounced edema and layers on the palatine tonsils (OR=1.7), lymphadenopathy of the anterior cervical nodes and cough.

2. The parameters of the systemic inflammatory response of the macroorganism (according to a detailed hematological study) in children with NATF did not significantly differ from similar markers in patients with streptococcal etiology of the disease, with the exception of the general frequency of absolute leukocytosis.

3. A promising area of further research is the comprehensive study of additional highly specific paraclinical markers of ATF in children. The introduction of integrative scales and algorithms will allow timely verification of the non-streptococcal nature of inflammation, optimize initial empirical therapy, and significantly limit the irrational use of antibacterial agents in pediatric practice.

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