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## **EFFECT OF ANTIBACTERIAL THERAPY ON THE CLINICAL COURSE OF STREPTOCOCCAL TONSILLOPHARYNGITIS IN CHILDREN**

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**Цитування:** Медичні перспективи. 2019. Т. 24, № 4. С. 69-74

**Cited:** Medicni perspektivi. 2019;24(4):69-74

**Key words:** group A  $\beta$ -hemolytic streptococcus, tonsillopharyngitis, children, antibacterial therapy

**Ключові слова:**  $\beta$ -гемолітичний стрептокок групи А, тонзилофарингіт, діти, антибактеріальна терапія

**Ключевые слова:**  $\beta$ -гемолитический стрептокок группы А, тонзиллофарингит, дети, антибактериальная терапия

**Abstract. Effect of antibacterial therapy on the clinical course of streptococcal tonsillopharyngitis in children.**

**Haiduk T., Cherhinets A., Shostakovych-Koretska L.** The aim of this study was to determine the effect of antibiotic therapy (AT) on the clinical course of streptococcal tonsillopharyngitis (STP) in children, depending on the timing of its administration, since the data on the need to start AT in the first days of the disease to achieve the effect are controversial. A retrospective analysis of inpatient medical records at "The Communal Dnipro City Clinical Hospital N 21 named after Professor Ye.G. Popkova" DRC" in the period from January 2012 to December 2018 was conducted. The inclusion criteria for the study were: 1) the diagnosis - tonsillopharyngitis; 2) the age of the patient: 3 to 18 yrs; 3) the exclusion of an alternative diagnosis (diphtheria, infectious mononucleosis, scarlet fever); 4) no complications; 5) positive results of the culture study on  $\beta$ -hemolytic streptococcus group A (GAS) (*Streptococcus pyogenes*) of the oropharyngeal swab. The study included 109 medical cards of children with STP. Depending on the timing of the onset of rational AT, all patients were divided into 5 groups. The first one consisted of 27 children who received AT from the 1st day of the disease, 2nd - 48 children (AT from the 2nd day), 3rd - 17 children (AT from the 3rd day) and the fourth - 7 children (AT from the 4th day), 5th - 10 children (AT from the 5th day). Clinical symptoms were evaluated by examining the patient with the main objective and subjective symptoms of STP. It was a retrospective open comparative study. All patients received the full recommended course of STP AT. The study showed no significant differences in the reduction of clinical symptoms of STP, regardless of the timing of antibiotic therapy (1-5 days from the onset of the disease) in almost half of patients with STP, which confirms the inadequacy of antibacterial therapy in children with tonsillopharyngitis. We believe that antibiotic therapy should only be used to prevent late complications in cases of children with tonsillopharyngitis only with a confirmed GAS etiology, and we propose the widespread use of the McIsaac Score, the Streptococcus Expression Test (RST) and the culture study of the oropharyngeal swab to confirm the etiology of GAS in children with tonsillopharyngitis to reduce the frequency of antibiotics overusing.

**Реферат. Вплив антибактеріальної терапії на клінічний перебіг стрептококового тонзилофарингіту в дітей.**

**Гайдук Т.А., Чергінєць А.В., Шостакович-Корецька Л.Р.** Метою цієї роботи було визначити вплив антибактеріальної терапії (АТ) на клінічний перебіг стрептококового тонзилофарингіту (СТФ) у дітей залежно від термінів її призначення, адже дані щодо необхідності початку антибактеріальної терапії в перші дні хвороби для досягнення ефекту є суперечливими. Проведено ретроспективний аналіз медичних карт стаціонарного хворого на клінічній базі КЗ «МКЛ №21 ім. професора Є.Г. Попкової» ДОР» м. Дніпро в період із січня 2016 по грудень 2018 року. Критеріями залучення до дослідження були: 1) діагноз - тонзилофарингіт; 2) вік пацієнта від 3 до 18 років; 3) виключення альтернативного діагнозу (дифтерія, інфекційний мононуклеоз, скарлатина); 4) відсутність ускладнень; 5) позитивні результати культурального дослідження мазка з ротоглотки на  $\beta$ -гемолітичний стрептокок групи А (GAS) (*Streptococcus pyogenes*). До дослідження було залучено 109 медичних карт дітей, хворих на СТФ. Залежно від термінів початку раціональної АТ усіх пацієнтів було розподілено на 5 груп. Першу склали 27 дітей, які отримували АТ з 1-ї доби захворювання, 2-у - 48 дітей (АТ з 2-ї доби), 3-ю - 17 дітей (АТ з 3-ї доби) та четверту - 7 дітей (АТ з 4-ї доби), 5-ту - 10 дітей (АТ з 5-ї доби). Оцінка клінічної симптоматики здійснювалась при огляді пацієнта за основними об'єктивними та суб'єктивними симптомами СТФ. Це було ретроспективне відкрите порівняльне дослідження. Усі пацієнти отримали повний рекомендований курс АТ СТФ. Проведене дослідження показало відсутність значущих

відмінностей у зменшенні клінічних симптомів СТФ незалежно від термінів призначення антибактеріальної терапії (на 1-5 дні від початку захворювання) майже в половини пацієнтів зі СТФ. Таким чином, наші дані співпадають з більші ранніми дослідженнями, в яких повідомляється, що антибактеріальна терапія має незначний вплив на клінічний перебіг СТФ у дітей і має за мету, передусім, профілактику ускладнень. Ми вважаємо, що антибіотикотерапія має призначатися тільки для запобігання пізнім ускладненням у випадках тонзиллофарингіту в дітей лише з підтвердженою етіологією GAS, і пропонуємо широке застосування шкали McIsaac, експрес-тесту на стрептокок (RST) та бактеріологічне дослідження мазка з ротоглотки для підтвердження етіології GAS у дітей з тонзиллофарингітом з метою зниження частоти надмірного використання антибіотиків.

Group A  $\beta$ -hemolytic streptococcus (GAS) is one of the most common pathogens that infects children and adolescents with a wide variety of clinical manifestations, from relatively benign tonsillopharyngitis to invasive forms of GAS infection, life-threatening for infants [1, 5, 11]. Moreover, postponed GAS tonsillopharyngitis can cause severe complications in the form of acute rheumatic fever, post-streptococcal glomerulonephritis, and childhood autoimmune neuropsychiatric disorder (PANDAS) [1, 9, 10].

The relevance of the study of tonsillopharyngitis in children caused by GAS is due, to among other things, the high incidence of the disease in children aged 5-15 years – 9 to 12 cases of GAS tonsillopharyngitis per 100 patient-years [2]. Among all cases of pharyngitis in children, GAS etiology of tonsillopharyngitis is detected in 30-40% [10, 12].

Sore throat is one of the most common reasons for prescribing antibiotics in children and adults [13]. The aim of the antibacterial therapy of acute streptococcal tonsillopharyngitis is primarily the eradication of GAS, which leads not only to the reduction of symptoms and duration of the disease, but also to the prevention of the spread of infection, early and late complications associated with GAS [9, 11, 12, 13]. However, there are studies showing that antibiotics administration in the early days of the disease is not rational, since not always the etiology of tonsillopharyngitis is GAS, which causes purulent complications, acute rheumatic fever, poststreptococcal glomerulonephritis (PSGN), and others [7].

However, antibiotics are most effective when positive results are obtained from the oral oropharyngeal smear for GAS [4, 13].

There are studies that show a small effect of AT on pharyngitis with possible GAS etiology in the primary clinical evaluation of acute symptoms. At the same time, they showed that the onset of AT up to 10th day after the onset of symptoms effectively prevents the development of most complications (acute rheumatic fever, poststreptococcal glomerulonephritis, PANDAS), and the early administration of antibiotics before the confirmation of GAS etiology of tonsillopharyngitis, rarely is of urgent importance [6].

At the same time, some studies demonstrate a decrease in the duration of streptococcal tonsillopharyngitis (STP) symptoms on average by 16 hours in AT of STP [13].

The aim of this study was to determine AT effect on the STP clinical course in children depending on the timing of its administration.

#### MATERIALS AND METHODS OF RESEARCH

A retrospective analysis of inpatient medical records at “Communal Dnipro City Clinical Hospital N 21 named after Professor Ye.G. Popkova” of Dnipropetrovsk Regional Council” in the period from January 2012 to December 2018 was conducted. The inclusion criteria for the study were: 1) diagnosis - tonsillopharyngitis; 2) age of the patient from 3 to 18 years; 3) elimination of alternative diagnosis (diphtheria, infectious mononucleosis, scarlet fever); 4) lack of complications (paratonsillar abscess, acute otitis media, sinusitis, mastoiditis, purulent cervical lymphadenitis requiring surgical treatment, burn of the oropharynx); 5) positive results of GAS (*Streptococcus pyogenes*) culture study of a swab from the oropharynx.

#### Definitions of antibacterial therapy of STP

In the study we used the concept of rational (according to clinical guidelines) and irrational use of antibiotics for STP treatment [3, 4, 13]. By rational AT we mean that the patient received any antibacterial agents systemically from the group of  $\beta$ -lactams, macrolides, linkosamides. By irrational AT we mean that the patient was treated systemically with antibiotics of the aminoglycoside group, trimethoprim / sulfamethoxazole, or exclusively with topical antibiotics and antiseptics, or with traditional medicine methods and homeopathic preparations monotherapy.

#### Characteristics of the contingent of the study

According to the above criteria, the study included 109 medical cards of children with STP. Depending on the timing of a rational AT starting, all patients were divided into 5 groups. The first one consisted of 27 children who received AT from the 1st day of the disease, 2nd - 48 children (AT from the 2nd day), 3rd – 17 children (AT from the 3rd day) and the fourth – 7 children (AT from the 4th

day), 5th – 10 children (AT from the 5th day). Characteristics of groups are given in Table 1.

As an add-on therapy, all patients received antipyretics as needed (paracetamol, ibuprofen, metamizole).

#### *Evaluation of STP clinical symptomatology*

The clinical symptomatology was evaluated at the patients' examination by the main objective (fever, hyperemia and edema of the tonsils, layers on the tonsils, tonsillar lymph nodes enlargement) and subjective (sore throat, pain in tonsillar lymph nodes) symptoms of STP. Each symptom was evaluated as either positive (positive) or absent (negative).

#### *Research design*

This is a retrospective open comparative study. Comparison of evaluation data of STP clinical symptomatology between groups was carried out on the 2nd day from the onset of the disease between the 1st and 2nd groups, on the 3rd day - between the 1st, 2nd and 3rd groups, on the 4th day - between the 1st, 2nd, 3rd and 4th groups, as well as on the 5th and 10th days among all the experimental groups.

#### *Statistical analysis*

Comparison of the indicators between the groups was performed using the corrected Yeats method ( $\chi^2$ ). The results were considered reliable at  $p \leq 0.05$ .

Table 1

Characteristics of study groups

Indicator	Groups				
	1-st	2-nd	3-rd	4-th	5-th
Number, n	27	48	17	7	10
Age, years					
Interval	5-18	4-17	4-18	4-13	4-12
M±m	12,4±3,8	11,3±4,0	11,7±3,6	6,6±2,1	6,4±2,1
95% CI	10,8-14,2	10,2-12,5	9,8-13,7	4,1-9,9	4,0-9,5
Sex: m, n (%) / f, n	13(48,1)/14	29(60,4)/19	10(58,8)/7	4(57,1)/3	6(60)/4
Rational AT, n (%)					
Penicillins	3 (11,1)	7 (14,6)	2 (11,8)	0	0
Aminopenicillins	3 (11,1)	4 (8,3)	3 (17,7)	3 (42,9)	5 (50)
Cephalosporins	17 (63,0)	30 (62,5)	9 (52,9)	3 (42,9)	1 (10)
Macrolides	4 (14,8)	7 (14,6)	2 (11,8)	1 (14,2)	4 (40)
Lincosamides	0	0	1 (5,8)	0	0

## RESULTS AND DISCUSSION

All 109 patients completed the study and received the full recommended AT (from 5 to 10 days depending on the pharmacology group of a drug) of STP course.

The results of a comparative analysis of STP clinical symptoms evaluation between the 1st, 2nd, and 3rd groups on the 2nd and 3rd days from the start of rational AT showed that 100% of cases (92 patients) had all 6 symptoms that were evaluated.

In addition, there were no probable differences in the frequency of STP clinical manifestations bet-

ween the groups, depending on the timing of the beginning of rational AT of STP both on the 4th and 5th day of the disease (Table 2, 3).

Moreover, on the 4th day from the onset of the disease, the fever, patch on the tonsils, sore throat and tenderness of the tonsillar lymph nodes remained almost in ½ patients in all comparison groups regardless of AT timing. Hyperemia and edema of the tonsils, increased tonsillar lymph nodes were present in all patients with STP.

Table 2

**Comparison of STP clinical manifestations under the influence of rational AT,  
depending on the date of its beginning, on the 4th day of the disease**

Symptom	Group				Probability of difference
	1-st	2-nd	3-rd	4-th	
Fever, n (%)	12 (44,4)	28 (58,3)	7 (41,2)	4 (57,1)	$\chi^2=2,88$ ; K=3; p<0,3
Hyperemia and swelling of the tonsils, n (%)	27 (100)	48 (100)	17 (100)	7 (100)	N
Patch on the tonsils, n (%)	18 (66,6)	27 (56,3)	10 (58,8)	4 (57,1)	$\chi^2=0,58$ ; K=3; p<0,5
Enlargement of tonsillar lymph nodes, n (%)	27 (100)	48 (100)	17 (100)	7 (100)	N
Sore throat, n (%)	12 (44,4)	21 (43,8)	9 (52,9)	4 (57,1)	$\chi^2=1,0$ ; K=3; p<0,4
Morbid tonsillar lymph nodes, n (%)	8 (29,6)	25 (52,1)	7 (41,2)	2 (28,6)	$\chi^2=4,2$ ; K=3; p<0,2

Note. N - not subject to statistical processing due to the lack of difference (100% have a sign).

However, significant reduction or absence of these symptoms (fever, patches on the tonsils, sore throat and soreness of tonsillar lymph nodes) was noted in all patients in comparative groups on the 5th day from the onset of the disease.

We did not find any cases of complications of STP in the form of paratonsillar abscess, acute otitis media, sinusitis, mastoiditis, purulent cervical lymphadenitis which would require surgical treatment throughout the observation period.

Table 3

**Comparison of STP clinical manifestations under the influence of rational AT,  
depending on the date of its beginning, on the 5th day of the disease**

Symptom	Group					Probability of difference
	1-st	2-nd	3-rd	4-th	5-th	
Fever, n (%)	2 (7,4)	6 (12,5)	1 (5,9)	1 (14,3)	1 (10)	$\chi^2=2,6$ ; K=4; p<0,4
Hyperemia and swelling of the tonsils, n (%)	27 (100)	48 (100)	17 (100)	7 (100)	10 (100)	N
Patch on the tonsils, n (%)	1 (3,7)	3 (6,3)	1 (5,9)	1 (14,2)	1 (10)	$\chi^2=1,37$ ; K=4; p<0,4
Enlargement of tonsillar lymph nodes, n (%)	27(100)	48 (100)	17 (100)	7 (100)	10 (100)	N
Sore throat, n (%)	0	1 (2)	1 (5,8)	0	0	$\chi^2=0,002$ ; K=4; p<0,5
Morbid tonsillar lymph nodes, n (%)	0	1 (2)	0	0	0	$\chi^2=0,001$ ; K=4; p<0,5

Note. N - not subject to statistical processing due to the lack of difference (100% have a sign).

The study showed no significant differences in the reduction of clinical symptoms of STP, regardless of the timing of the antibiotic therapy administration (1-5 days from the onset of the disease) in almost half of patients with STP. The obtained data are consistent with the results of the Cochrane systematic review of the antibiotics administration in tonsillopharyngitis (27 studies, of which only 3 were conducted exclusively in children). It has been shown that sore throat and

fever have reduced in the course of antibiotic treatment in only half of patients with STP. Moreover, in one week in about 90% of patients treated and those who did not receive the etiotropic drug, the symptoms were no longer present [3, 7].

#### CONCLUSION

Thus, our research data support previous studies that the antibacterial therapy has a little if any effect on the clinical course of streptococcal tonsillopharyngitis in children. We consider antibiotics

therapy to be prescribed just for prevention of the late complications in cases of tonsillopharyngitis in pediatric patients with confirmed GAS etiology only. We offer extensive applying of the McIsaac score [8], RST, and a culture smear to confirm the

etiology of GAS in children with tonsillopharyngitis in order to reduce the incidence of antibiotics overusing.

Conflict of interest. Authors declare no conflicts of interest.

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The article was received  
2019.06.28

