

EVIDENCE BASED PRACTICE IN USING ANTIBIOTICS FOR ACUTE TONSILLITIS IN PRIMARY CARE PRACTICE

Valentina Risteska Nejashmikj¹, Snezana Stojkovska², Irena Kondova Topuzovska², Katarina Stavrikj¹

¹ Center for Family Medicine, Medical Faculty Skopje

² University Clinic for Infectious Diseases and Febrile Conditions, Medical Faculty Skopje, Republic of Macedonia

Corresponding author: Risteska Nejashmikj Valentina, Center for Family Medicine, Medical Faculty Skopje, st. 50 Divizija no.6 , 1000 Skopje, R Macedonia, tel: 070-216970, e-mail: valentina.nejasmic@gmail.com

ABSTRACT

The increased use of antibiotics for acute tonsillitis is a public health problem. 80% of the antibiotic prescriptions for acute tonsillitis are done in the Primary Care practice (PCP). The inappropriate use of the antibiotic causes bacterial resistance and treatment failure. Only patients with acute tonsillitis caused by Group A beta-hemolytic streptococcus (GAS) have benefit of the antibiotic treatment, which is a predict cause in 5-20%. In order to assess the antibiotic prescribing for acute tonsillitis by the doctors in the PCP in Macedonia we use the data from the national project about antibiotic prescribing for acute respiratory tract infections which was conducted in November 2014 during a period of 4 weeks as part of the E-quality program sponsored by the IPCRG. 86 general practitioners from Macedonia have participated. The group of 1768 patients, from 4 months to 88 years of age, with diagnosis of acute tonsillitis was analyzed. The antibiotic prescriptions according to the Centor score criteria were compared to the Cochran's guidelines which are translated and recommended as national guidelines. 88.8% of the patients with acute tonsillitis were treated with antibiotics, of which 52.9% with Centor score 0 to 2 were treated inappropriate. The diagnosis is mostly made based on the clinical picture and the symptoms. Only (23.6%) of the patients were treated with antibiotics (Penicillin V and cephalexin) according to the guidelines.

We concluded that there is a low adherence to the national guidelines. The clinical assessment is not accurate in determining the etiology. Also, there is a high nonadherence in prescribing the first choice of antibiotics. We emphasize the need to change the general practitioners' prescription behavior according to the guidelines.

Key words: Centor score, acute tonsillitis, irrational antibiotic prescribing, antibiotic prescribing.

INTRODUCTION

The majority of the respiratory tract infections (RTIs) are treated in the general practice. Most infections are caused by a virus, and antibiotics are therefore unlikely to have any clinical benefit. Antibiotic resistance is a major concern globally. Antibiotic consumption increases the likelihood for an individual to develop bacterial resistance. [1] In Macedonia there have been increasing levels of antibiotic use and antimicrobial

resistance. The national antimicrobial resistance surveillance data in 2015 showed high resistance, such as *Staphylococcus aureus* 43% resistant to meticillin, 20% *Streptococcus pneumoniae* resistant to penicillin as well as high resistance of Gram-negative bacteria: *Enterobacter spp* (50%) to vancomycin, *Klebsiella pneumoniae* (87%) and *Escherichia coli* (66%) to the third generation of cephalosporin. [2] Despite the widespread implementation and use of the guidelines, numerous studies showed inappropriately high level of use

of antibiotics. [3,4,5] The translated Cochrane guidelines have been provided by the Ministry of Health since 2007 in Macedonia, but the nonadherence to those guidelines continues. Concerning the antibiotic prescribing practices for tonsillitis in adults and children, the guidelines recommend antibiotic treatment only in patients who were likely to have Group A streptococcus infection based on the presence of at least 3 of 4 Centor criteria, or patients with two or more Centor criteria in the presence of a positive rapid antigen detection test (RADT). [6] More recently, the Centor score was modified by incorporating the patient's age, which allows the physician to place patients in low-, moderate-, or high-risk groups. The use of the McIsaac Modified Centor score has helped in decreasing the inappropriate antibiotic use by almost 88%. [7] For cases meeting the clinical and/or laboratory criteria of streptococcal tonsillitis the recommended agents include penicillin V or cephalexin, depending on the patient's antibiotic allergies. [8]

Factors influencing the antibiotic prescribing for respiratory tract infection are the doctors, the patients, and the pharmacy and health policies. [5] These factors may include the limited knowledge and experience of the medical practitioner, personal preference, and parental or patient pressure. [9,10] Antibiotic prescribing for acute tonsillitis varies in different European countries. Increased antibiotic prescribing is noted in South European countries. [11] Doctors have a key role in prescribing the antibiotics for acute tonsillitis. Centor Score Criteria and RADT can increase the diagnostic safety and greatly help in reducing of antibiotic prescribing in PCP. [12, 13, 14]

AIM

The purpose of this study was to assess the use of the national guidelines among the general practitioners in the antibiotic prescribing for acute tonsillitis in Macedonia.

MATERIAL AND METHODS

The data are used from the national project about antibiotic prescribing for acute respiratory tract infections, which was conducted in November 2014 as a part of the E-quality program supported by the International Primary Care Respiratory Group (IPCRG). The study was carried by 86 general practitioners from different areas of Macedonia. A written informed consent was obtained

from every doctor and a verbal informed consent from every patient and parent prior to fulfilling the questionnaires. The socio-demographic and medical data were obtained by means of personal or parental interviews. The survey was run from 3 November till 28 November 2014 (4 weeks). When the survey finished all the questioners were sent to the key researchers and the data base was established. The analyzed group contained 1768 patients, from 4 months to 88 years of age, with the diagnosis of acute tonsillitis J03 and J03.0 via the ICD-10CM diagnosis code. The antibiotic prescribing practice for acute tonsillitis has been compared with the Centor score criteria according to the actual national guidelines.

Statistical analysis. The data obtained were analyzing using STATISTICA for Windows version 7.

RESULTS

The total number of patients presented with acute tonsillitis was 1768. Only 295 patients (16.7%) had the diagnosis of streptococcal tonsillitis - J03.0, the rest of 1473 patients had the diagnosis of acute tonsillitis - J03. There is a difference in the distribution of the patients with acute tonsillitis by the age, with predomination of the group from 3-15 years old patients (45.2%). (Table 1)

The majority of the antibiotic prescriptions were not strictly in accordance with the guidelines. The results obtained with this study show that 1571 patients (88.8%) were treated with antibiotics. 832 patients (52.9%) had Centor score 0, 1 and 2, and they received antibiotics although they didn't need it. 650 (41.4%) patients had Centor score 3 and 4, with very low risk for streptococcal infections, and probably most of them didn't need antibiotics, but they were still given them. Only 89 patients (5.7%) with Centor score 5 received the appropriately antibiotics according to the guidelines. (Table 2)

The statistical analysis of the Chi (X^2) square test showed an increased antibiotic prescribing $p=0.005$ in the group of patients with Centor score 0, 1, 2 who are not for antibiotic treatment according to the guidelines. In the group of patients with Centor score 3, 4+5 it also showed an increased antibiotic prescribing, which is appropriate according the guidelines $p<0.005$.

1255 patients (71 %) of the total of patients (1768) didn't have any investigations. In 2.4% of the patients a microbiological smear was performed, in 3.6% a CRP test, and a peripheral blood sample in 373 (21.1%). In 33 patients (1.9%)

Table 1. Distribution of patients by age

Age groups	N (%)
< 3y	212 (12.0%)
3-15y	799 (45.2%)
15-44y	515 (29.1%)
>45y	242 (13.7%)

GAS tonsillitis should be treated with antibiotics, but in our survey 88.8% of the patients presented with acute tonsillitis were treated with antibiotics. In comparison to other countries, our level of harmonization with the guidelines is low similar to Pakistan were 98.5% of the patients were treated

Table 2. Distribution of patients according to the Centor sores and antibiotic treatment

Centor score	Number of patients	Treated with antibiotics	Without antibiotics
-1/0	192	165 (86%)	27(14%)
1	303	265 (87%)	38 (13%)
2	462	402 (87%)	60 (13%)
3	437	394 (90%)	43 (10%)
4	276	256 (93%)	20 (7%)
5	98	89 (91%)	9 (9%)
	1768	1571 (88.8%)	197(11.2%)

Table 3. Used antibiotics in patients with tonsillitis

Antibiotics	N (%)
Penicillin V	247 (15.7%)
Cephalosporin	272 (17.3%)
Amoxicillin	291 (18.5%)
Amoxicillin/clavulanic acid	622 (39.6%)
Macrolides	66 (4.2)
Intramuscular therapy	40 (2.5%)
Other antibiotics	33 (2.1%)

RADT was performed, of which 11 were negative. All 22 patients with positive RADT were treated with antibiotics.

The most prescribed antibiotics were amoxicillin/clavulonic acid in 622 patients (39.6%), amoxicillin (18.5%), and cephalosporin in 272 patients (17.3%). In 7.9% of the patients cephalexin was prescribed as the first line recommended antibiotic, while in 9.4% the second and third generation of cephalosporin. Penicillin V, the national guideline-recommended antibiotic, was prescribed in only 15.7% of cases. Although there is high resistance of Group A streptococcus to macrolides, only 40 (2.5%) of the patients were treated with it. Intramuscular therapy was administered in 33 patients (2.1%). (Table 3)

DISCUSSION

There is irrational and inappropriate prescribing of antibiotics and a broad spectrum of antimicrobial drugs in patients with acute tonsillitis in Macedonia. According to our guidelines around 20% of the patients who are highly suspected for

with antibiotics. [12] Antibiotic treatment of tonsillitis was performed in 24% of the patients in London, UK. [15] The Dutch study showed that 71% of the patients were treated according to the guidelines. [16]

Unnecessary antibiotic treatment received 832 patients (52.9%) of the patients with acute tonsillitis taking into account the Centor score and the national guidelines, but still there are doubts in the diagnostic safety. Using the Centor score has still not been included in the regular practice in Macedonia, but Macedonian doctors have the ability to recognize the patients for the antibiotic treatment ($p < 0.005$), but they don't have the ability to reduce the antibiotic prescribing in patients who don't need it ($p = 0.005$). Using Centor score can greatly help in reducing the antibiotic prescribing. [12, 17] Our study showed that it would be useful for general practitioners to use national guidelines and the McIsaac Modified Centor score as it is not costly, and is sensitive and specific enough to reduce the unnecessary antibiotic prescriptions. Based on our study, we recommend that the score-only approach would save antibiotics prescriptions for 52.9% of our patients with scores of 0, 1 or 2. Although without a RAST test option, more antibiotics would be prescribed to patients with a score of 3 or 4, and this percentage is better than the percentage of the patients that receive inappropriate antibiotics without a clinical score-based screening.

Centor score criteria include: 1. Body temperature $> 38^{\circ}\text{C}$ 2. Hyperemic, swollen tonsils with exudates 3. Increased and painful lymph node on the neck 4. Absence of cough 5. Age: 3-15

years score 1 point, 15-44 years 0 point, > 45 years -1 point. If each of these criteria is positive it is scored by 1 point. Patients with Centor score 4+5 points should receive empirical antibiotic treatment with benzathine phenoxymethyl penicillin for 10 days, and in patients with Centor score 2 or 3 points RADT needs to be performed, and antibiotic prescribing is necessary only in the positive test [9,10]. In our country RADT is expensive for the patients, and due to that we included the patients with Centor score 3 for empirical treatment.

Following the score approach would significantly reduce the unnecessary antibiotics prescriptions, but the clinical assessment is not accurate in determining the microbial etiology. The guideline recommends performing a throat swab in patients who are suspected for group A streptococci on the basis of the symptom score. Only 29% of the patients performed some laboratory tests, most of them blood count, which is not according to the guidelines. RADT is performed only in 1.9% and throat swab is taken only in 2.4%. Using RADT is limited for the primary care settings in Macedonia because it is not paid by the Insurance Fund.

RADT can further increase the diagnostics safety. [17, 18] Using the guidelines and the Centor score criteria can have an important impact on the treatment decisions by the doctors in the PHC, on the emergence of the antibiotic resistance; it can prevent the adverse effects of the antibiotics and reduce the unnecessary antibiotic prescriptions and antibiotic costs. [13, 19, 20]

Antibiotic prescriptions for acute tonsillitis corresponded poor with the recommended first-line choice in 23.6% of all prescriptions. The use of broad-spectrum antibiotics such as amoxicillin/clavulanic acid and cephalosporin second and third generation accounted for 39.6% and 9.4% of the GPs' prescriptions. This corresponds well with the national figures for the same time period from the Health Insurance Found where one third of all prescribed antibiotics are amoxicillin clavulanic acid. [21] The study in Ireland showed high prescription rate of antibiotics for acute tonsillitis in 78.05% of patients, of which 25.09% account for Co-amoxicillin while phenoxypenicillin in 42.7%. [5] In Pakistan penicillin was mostly prescribed (34.1%), especially amoxicillin/clavulanate; followed by macrolides (31.1%), especially the second-generation agents, and fluoroquinolones (14.8%). [12] In the Netherlands, about three-quarters of the prescribed antibiotics are the first-line choice. [16]

This is of importance taking into account the increased bacterial resistance in Macedonia. In *Escherichia coli*, resistance rates for cephalosporin are 73% and the resistance to penicillin among clinical isolates of *Streptococcus pneumoniae* is 18.75% in 2015. [2] To date, *S. pyogenes* has remained universally susceptible to penicillin. Therefore, penicillin remains the first-line drug of choice for pharyngeal infections, as well as for complicated or invasive infections. [22]

This study clearly indicates that the guidelines need to be disseminated at a local level with a focus on reducing the antibiotics prescribing for minor respiratory conditions and on reducing the broad-spectrum antibiotics prescribing whenever necessary. Although the guidelines have been established since 2007 the nonadherence to these guidelines continues. The Ministry of Health started an intensive education of GP in Macedonia in the period of 2015-2017. Also, it is particularly important to increase the public awareness regarding the appropriate antibiotics use to decrease the patient pressure on GPs for the prescription.

CONCLUSION

We concluded that there is an increased and inappropriate prescribing of antibiotics and a broad spectrum of antimicrobial drugs in patients with acute tonsillitis in Macedonia. 88.8% of the patients presented with acute tonsillitis were treated with antibiotics. The most prescribed drug was amoxicillin-clavulanate. There is a low adherence to the national guidelines and the clinical assessment is not accurate in determining the etiology. Also, there is highly prevalent nonadherence in prescribing the first choice of antibiotics. The use of the guidelines and the Centor score criteria can help in rational prescribing, but it should be supported with laboratory tests (RADT or Microbiological smear) to verify the streptococcal infection especially with Centor score 3. We emphasize the need to change the general practitioners' prescription behavior according to the guidelines. Education of the doctors by improving the communication skills, using the Centor score, RADT or microbiological smear, assisted by changes in the Insurance Fond, the Ministry of Health, patients education and broad education of the population with increasing the awareness of the inappropriate use of antibiotics for acute tonsillitis are needed.

Conflict of interest. We do not have a conflict of interest to declare.

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МЕДИЦИНА БАЗИРАНА НА ДОКАЗИ ВО КОРИСТЕЊЕ НА АНТИБИОТИЦИ ЗА АКУТЕН ТОНЗИЛИТИС ВО ПРИМАРНА ЗДРАВСТВЕНА ПРАКСА

Валентина Ристеска Нејашмиќ¹, Снежана Стојковска², Ирена Кондова Топузовска², Катарина Ставриќ¹

¹ Центар за семејна медицина, Медицински факултет Скопје,

² Универзитетска клиника за инфективни болести и фебрилни состојби, Медицински факултет Скопје, Република Македонија

Резиме

Зголемената употреба на антибиотици за акутен тонзилитис претставува јавно здравствен проблем. 80% од сите пропишани антибиотици за акутен тонзилитис се пропишани во Примарна здравствена заштита (ПЗЗ). Несоодветното пропишување на антибиотици предизвикува бактериска резистенција и неуспех во третманот. Само пациентите со акутен тонзилитис предизвикан од бета хемолитичен стрептококус од Гр А (ГАС) имаат корист од антибиотски третман, за кој се предвидува дека е застапен во 5-20% од случаите со акутен тонзилитис. Со цел да се процени пропишувањето на антибиотици на докторите од ПЗЗ во Македонија, за акутен тонзилитис, ние ги искористивме податоците добиени од Националниот проект за употреба на антибиотици за акутни респираторни инфекции кој беше спроведен во Ноември 2014 година како дел од Е-Програмата за квалитет. 86 матични доктори од Македонија зеао учество. Беше анализирана група од 1768 пациенти на возраст од 4 месеци до 88 години со дијагноза на акутен тонзилитис. Пропишувањето на антибиотици беше споредувано според Центор скор критериумите од Кохрановите упатства кои се користат како национални упатства. 88.85% од пациентите со акутен тонзилитис добиле антибиотски третман од кои 52.9% со Центор скор 0 до 2 кои се лекувани непотребно со антибиотик. Дијагнозата во најголем број на случаи е базирана на клиничката слика и симптоми. Само 19.9% од пациентите биле третирани со антибиотици (Пеницилин В и цефалоспорини) согласно националните упатства.

Нашиот заклучок е дека постои слабо придржување до националните упатства. Клиничката проценка не е соодветна во потврдување на етиологијата. Исто така постои зголемено непридржување кон препишување на антибиотици од прва линија на избор. Се наметнува потреба од промена на однесувањето на општите лекари во поглед на препишување согласно упатствата.

Клучни зборови: Центор скор, акутен тонзилитис, ирационално препишување на антибиотици, пропишување на антибиотици.