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## EFEKTI RAZLIČITIH ANTIBIOTSКИH TERAPIJA AKUTNOG RINOSINUZITISA

### EFFECTS OF DIFFERENT ANTIBIOTICS IN THE TREATMENT OF ACUTE RHINOSINUSITIS

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#### Sažetak

**Uvod:** Sinusitisi su upale paranazalnih sinusa i mogu biti infektivne, alergijske ili autoimune prirode. Akutni rinosinuzitis najčešće je virusnog porekla i javlja se u okviru infekcije gornjih disajnih puteva. Ako je bakterijskog porekla, najčešći uzročnici su bakterije *Streptococcus*, *Pneumococcus* i *Haemophilus*. Neke upale mogu početi kao virusne, a da se kod 0,5% – 2% njih razvije tzv. bakterijska superinfekcija, tj. naknadna kolonizacija bakterijama. Sinusitisi uzrokovani virusima traju 7 – 10 dana, dok bakterijski mogu trajati duže.

**Cilj rada:** Cilj ove studije bio je da se uporede tri terapijska protokola u lečenju akutnog bakterijskog rinosinuzitisa.

**Materijal i metode:** Prospektivna klinička studija sprovedena na Klinici za bolesti uva, nosa i grla Kliničkog centra Niš od oktobra 2019. do januara 2020. godine, u koju su uključeni pacijenti sa akutnim bakterijskim rinosinuzitisom, kod kojih smo upoređivali efikasnost i bezbednost levofloxacina u trajanju 5 dana, levofloxacina u trajanju 10 dana sa efikasnošću tretmana amoxicilin-klavulonatom. Uključeno je 62 pacijenta sa kliničkim i radiološkim dokumentovanim simptomima.

**Rezultati:** Potvrda bakterijske etiologije ne radi se rutinski u kliničkoj praksi, pošto zahteva punkciju sinusa ili endoskopski pregled srednjeg nosnog hodnika. Kao posledica toga, izbor antibiotske terapije je empirijski. U našem istraživanju, koristili smo levofloxacina u trajanju od 5 dana (500 mg jednom dnevno), levofloxacina u trajanju od 10 dana (500 mg jednom dnevno) i amoxicilin-klavulonatom u trajanju od 10 dana (500 mg – 125 mg tri puta dnevno) i dobijeni rezultati pokazali su to da ne postoje statistički značajne razlike u pogledu izbora antibiotika i dužine primene terapije.

**Zaključak:** Nalazi ove studije sugerišu to da kratki kurs tretmana antibioticima ima sličnu efikasnost u odnosu na duži kurs lečenja bolesnika s akutnim, nekomplikovanim bakterijskim sinusitisom, onda kada je tretman indikovao.

**Cljučne reči:** akutni rinosinuzitis, antibiotik, terapija

#### Abstract

**Introduction:** Sinusitis is an inflammation of the paranasal sinuses and it can be infectious, allergic or autoimmune. Acute rhinosinusitis commonly has viral origin and occurs as part of the upper respiratory tract infections. The most common pathogens are *Streptococcus*, *Pneumococcus* and *Haemophilus influenzae*. Some inflammations may start as viral, but develop into bacterial superinfection, i.e., subsequent colonization of the bacteria in 0.5-2% of cases. Viral sinusitis lasts for 7–10 days, whereas bacterial may take longer.

**The aim:** The aim of this study was to compare three therapeutic protocols for the treatment of acute bacterial rhinosinusitis.

**Materials and Methods:** A prospective clinical study was conducted at the Ear, Nose and Throat Clinic, Clinical Center Nis from October 2019 to January 2020, and it involved patients with acute bacterial rhinosinusitis in whom we compared the efficiency and safety of levofloxacin administration for five and 10 days with the efficiency of amoxicillin clavulanate treatment. The study included 62 patients with documented clinical and radiological symptoms.

**Results:** Confirmation of bacterial etiology is not routinely performed in clinical practice since it requires antral puncture or endoscopic examination of the middle nasal meatus. Consequently, the choice of antibiotic therapy is empiric. In our study, we used levofloxacin for five (500 mg once a day) and 10 days (500 mg once a day) and amoxicillin-clavulanate for 10 days (500 mg–125 mg three times a day), and the results showed no statistically significant difference in regard to the choice of antibiotics and the duration of therapy.

**Conclusion:** The findings of this study suggest that a short course of antibiotic treatment has similar efficiency compared to a longer course of treatment of patients with uncomplicated acute bacterial sinusitis when treatment is indicated.

**Key words:** acute rhinosinusitis, antibiotics, therapy

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## Uvod

Sinusitisi su upale paranazalnih sinusa i mogu biti infektivne, alergijske ili autoimune prirode<sup>1-16</sup>. Najčešće se javljaju istovremeno sa upalama sluzokože nosne šupljine, te je adekvatniji naziv rinosinusitis<sup>1</sup>. Po trajanju mogu biti akutni (do 3 nedelje), subakutni (od 3 nedelje do 12 nedelja) i hronični (od 12 nedelja, pa sve do više meseci ili godina)<sup>2</sup>.

Prema tome koliko je paranazalnih šupljina i koju je paranazalnu šupljinu zapaljenje zahvatilo, upale delimo na monosinuzitise (sinusitis maxillaris, sinusitis ethmoidalis, sinusitis frontalis i sinusitis sphenoidalis), polisinzuzitise (kada su zahvaćeni sinusi sa jedne strane glave) i pansinuzitise (kada su zahvaćene sve paranazalne šupljine)<sup>3,4</sup>.

Akutne upale paranazalnih šupljina najčešće prate akutne upale nosa. Akutne kataralne upale obično se ne dijagnostikuju i prođu nezapaženo i/ili su praćene kijavicom. U ovim slučajevima, pored jake kijavice, bolesnici se žale i na glavobolju<sup>5</sup>. Gnojne upale nadovezuju se na akutna kataralna stanja ili, pak, od početka postaju gnojna, ako za to postoje izvesni preduslovi kao, npr. masovna infekcija, loša ventilacija paranazalnih šupljina, oslabljene imunobiološke snage organizma, oslabljena lokalna reakcija sluzokože sinusa, itd.<sup>6</sup>.

Akutni rinosinusitis najčešće je virusnog porekla i javlja se u okviru infekcije gornjih disajnih puteva. Ako je bakterijskog porekla, najčešći uzročnici su bakterije Streptococcus, Pneumococcus i Haemophilus. Neke upale mogu početi kao virusne, a da se kod 0,5% – 2% njih desi tzv. bakterijska superinfekcija, tj. naknadna kolonizacija bakterijama. Sinusitisi uzrokovani virusima traju od 7 do 10 dana, dok bakterijski mogu trajati duže<sup>7,8</sup>.

Posebnu vrstu sinusitisa predstavljaju oni uzrokovani gljivicama. Po pravilu, javljaju se kod osoba sa bolestima i stanjima koja uzrokuju smanjeni imunitet, kao što su dijabetes i AIDS ili nakon transplantacija tkiva i organa i kod osoba na terapiji imunosupresivnim lekovima i mogu biti opasni po život zbog mogućeg brzog širenja infekcije i/ili mikotične seps<sup>4,5</sup>.

## Cilj rada

Cilj ove studije bio je da se uporede tri terapijska protokola u lečenju akutnog bakterijskog rinosinusitisa.

## Introduction

Sinusitis represents an inflammation of the paranasal sinuses and it can be infectious, allergic and autoimmune in nature<sup>1-16</sup>. They most often occur simultaneously with the inflammation of the mucous membrane of the nasal cavity, therefore, rhinosinusitis is a more appropriate name<sup>1</sup>. According to their duration, they can be acute - lasting up to three weeks, subacute - lasting three to 12 weeks and chronic - lasting more than 12 weeks up to several months or years<sup>2</sup>.

Depending on the number of paranasal cavities and which paranasal cavity was infected, inflammations are classified into monosinusitis (sinusitis maxillaris, sinusitis ethmoidalis, sinusitis frontalis and sinusitis sphenoidalis), polysinusitis (the sinuses on one side of the head are infected) and pansinusitis (all paranasal cavities are infected)<sup>3,4</sup>.

Acute inflammation of the paranasal cavities is most often accompanied by acute inflammation of the nose. Acute catarrhal inflammations are usually not diagnosed and go unnoticed commonly accompanied by sneezing. In such cases, patients also complain of headaches in addition to sneezing<sup>5</sup>. Purulent inflammations develop after acute catarrhal inflammations or they are purulent from the onset if certain preconditions are met, such as mass infection, poor ventilation of paranasal cavities, weakened immunobiological strength of the body, weakened local reaction of the sinus mucosa, etc.<sup>6</sup>.

Acute rhinosinusitis is most often of viral origin and it occurs as part of upper respiratory tract infection. If it is of bacterial origin, the most common causes are Streptococcus, Pneumococcus and Haemophilus influenzae. Some inflammations may start as viral with the so-called bacterial superinfection, i.e. subsequent bacterial colonization developing in 0.5–2% of cases. Sinusitis caused by viruses last for seven to 10 days whereas bacterial sinusitis can last longer<sup>7,8</sup>.

A special type is sinusitis caused by fungi. As a rule, these occur in people with diseases and conditions related to reduced immunity, such as diabetes, AIDS, tissue and organ transplantation, treatment with immunosuppressive drugs and they can be life-threatening due to the rapid spread of the infection and/or mycotic seps<sup>4,5</sup>.

## ***Materijali i metode***

Prospektivna klinička studija sprovedena je na Kinici za bolesti uva, grla i nosa Univerzitetskog kliničkog centra Niš od oktobra 2019. do januara 2020. godine, u koju su uključeni pacijenti sa akutnim bakterijskim rinosinuzitisom, kod kojih smo upoređivali efikasnost i bezbednost levofloxacina (500 mg jednom dnevno u trajanju od 5 dana ili 10 dana aplikovanja levofloxacina od 500 mg jednom dnevno) sa efikasnošću tretmana amoxicilin-klavulonata (500 mg – 125 mg tri puta dnevno tokom 10 dana). Uključeno je 62 pacijenta sa kliničkim i radiološkim dokumentovanim simptomima, od kojih su 20 bili lečeni levofloxacinom u trajanju 5 dana, 20 levofloxacinom u trajanju od 10 dana i 22 amoxicilinom i klavulonatom u trajanju od 10 dana.

Kriterijumi za uključenje u studiju bili su: starost od 18 godina, klinička dijagnoza akutnog bakterijskog rinosinuitisa (ABR) – prisustvo purulentne sekrecije iz nosa, facijalni bol i/ili pritisak prisutni više od 7 dana i manje od 28 dana. Svi pacijenti pregledani su prvog dana, od trećeg do petog dana, od osmog do petnaestog dana i na kraju studije, dvadeset osmog dana.

Merenje ishoda: 1. Efikasnost je merena prema kliničkom uspehu baziranom na pregledu pacijenta u momentu kontrole.

Izlečenje je definisano kao rezolucija znakova i simptoma ABR do nivoa koji je postojao pre pojave akutne bolesti i bez potrebe za novom terapijom antibioticima.

Neuspeh terapije definisan je kao prisustvo jednog simptoma ili znaka ili više simptoma ili znakova i/ili potrebom za dodatnom antimikrobnom terapijom ili promenom antimikrobne terapije.

2. Sigurnost je analizirana kod svih ispitanika koji su uzeli jednu dozu leka iz studije. Registrovani su svi prijavljeni neželjeni efekti.

## ***Rezultati***

Između oktobra 2019. i januara 2020. godine kod 62 pacijenta dijagnostikovano je akutni rinosinuzitis.

U ispitivanoj grupi bilo je 30 (48,39%) osoba muškog pola i 32 (51,61%) osobe ženskog pola ( $p > 0,05$ ) što znači da nije bilo statistički značajne razlike (Tabela 1).

Urađena analiza simptoma, koji su bili prisutni kod pacijenata tokom ispitivanja, pokazala je značajno češće pojavu kašalja (58 ispitanika; 93,55%), sekrecije iz nosa (53 ispitanika; 85,48%) i zapašenog nosa (50 ispitanika; 80,64%), a najmanje zastupljeni

## ***Aim of the study***

The aim of this study was to compare three therapeutic protocols in the treatment of acute bacterial rhinosinusitis.

## ***Material and Methods***

A prospective clinical study was conducted at the Ear, Nose and Throat Clinic of the Clinical Center Niš from October 2019 to January 2020. The study included patients with acute bacterial rhinosinusitis in whom we compared the efficiency and safety of levofloxacin (500 mg once a day for five days or 500 mg a day once a day for 10 days) with the efficiency of amoxicillin - clavulanate treatment (500 mg – 125 mg three times a day for 10 days). The study included 62 patients with clinically and radiologically documented symptoms who were treated with levofloxacin for five days (20 patients), levofloxacin for 10 days (20 patients), and amoxicillin and clavulanate for 10 days (22 patients).

The inclusion criteria were the following: age over 18 years, clinical diagnosis of ABR (acute bacterial rhinosinusitis), presence of purulent nasal secretions, facial pain and/or pressure for more than seven and less than 28 days. All patients were examined on day one, days three to five, days eight to 15 and at the end of the study on day 28.

Measurement of outcomes: 1. Efficiency was measured according to clinical success based on patient examination at the time of check-up.

Successful treatment was defined as the resolution of ABR signs and symptoms to the level before the acute disease onset and without the need for a new antibiotic therapy.

Failure of the treatment was defined as the presence of one or more symptoms or signs and/or the need for additional antimicrobial therapy or change in antimicrobial therapy.

2. Safety was analyzed in all subjects who took one dose of the medication listed in the study. All reported side effects have been documented.

## ***Results***

From October 2019 to January 2020, 62 patients were diagnosed with acute rhinosinusitis.

The examined group included 30 males (48.39%) and 32 (51.61%) females. No statistically significant difference was observed in this regard ( $p > 0.05$ ) (Table 1).

**Tabela 1.** Distribucija po polu  
**Table 1.** Distribution according to gender

	Distribucija po polu / Distribution according to gender	
Muški / Male	30	48.39%
Ženski / Female	32	51.61%
Ukupno / Total	62	100%

Vrednosti su prikazane kao broj (%)  
\*Hi-kvadrat test. +Nije statistički značajan  
Values in numbers (%)  
\*Chi-square test.+No statistical significance

**Tabela 2.** Ukupan broj pacijenata sa navedenim tegobama  
**Table 2.** Total number of patients with the listed complaints

	Ukupan broj pacijenata sa navedenim tegobama / Total number of patients with the listed symptoms	
Opšta slabost / Generalized weakness	7	11.29%
Jaka glavobolja / Severe headache	24	38.71%
Jak bol u sinusima / Severe sinus pain	20	32.26%
Zapušen nos / Nasal congestion	50	80.64% *
Bol u uhu / Ear pain	13	20.97%
Iskašljavanje / Expectoration	21	33.87%
Visoka temperatura / High fever	9	14.51%
Vrtoglavica / Dizziness	15	24.19%
Sekrecija iz nosa / Nasal discharge	53	85.48% *
Bol u grlu / Sore throat	18	29.03%
Kašalj / Coughing	58	93.55% *

Vrednosti su prikazane kao broj (%)  
\*Hi-kvadrat test+Statistički značajan  
Values in numbers (%)  
\*Chi-square test +Statistically significant

simptomi bili su opšta slabost (7 ispitanika; 11,29%) i visoka temperatura (9 ispitanika; 14,51%) ( $p < 0,05$ ) (Tabela 2).

Dužina trajanja simptoma pre javljanja lekaru pokazala je da se 29 (46,77%) pacijenata javilo lekaru u periodu kraćem od 7 dana od pojave simptoma, a 20 (32,26%) pacijenata u periodu 7 dana nakon pojave simptoma, dok preostalih 13 (20,97%) pacijenata kao odgovor nisu dali ni jedno ni drugo ( $p = 0,045$ ), što predstavlja statistički značajnu razliku (Tabela 3).

Od faktora rizika za nastanak oboljenja najčešće su prisutne pušačke navike, kod 41 (66,13%) pacijenta, devijacija septuma, kod 39 (62,90%) pacijenata, a najređe nosna polipoza, kod 6 (9,68%) pacijenata ( $p < 0,05$ ), što je statistički značajno (Tabela 4).

The analysis of symptoms present in patientson examination showed a significantly more frequent occurrence of coughing - 58 patients (93.55%), nasal discharge - 53 patients (85.48%) and nasal congestion - 50 patients (80.64%) and the least common symptoms were generalized weakness - 7 patients (11.29%) and high fever - 9 patients (14.51%), ( $p < 0.05$ ) (Table 2).

Duration of symptoms before reporting to the doctor showed that 29 patients (46.77%) reported to the doctor in less than seven days after the onset of symptoms, 20 patients (32.26%) reported after seven days from the onset and the remaining 13 patients (20.97%) did not provide an answer. A p value of 0.045 points to a statistically significant difference (Table 3).

Pošto su pacijenti pokazivali slične simptome, nasumičnim odabirom pacijente smo podelili u tri grupe. Ispitanici iz prve grupe koristili su levofloxacin 5 dana (500 mg jednom dnevno), druge grupe levofloxacin 10 dana (500 mg jednom dnevno), a treće amoxicilin-klavulonat 10 dana (500 mg – 125 mg tri puta dnevno) ( $p > 0,05$ ), što ne pokazuje statističku značajnost (Tabela 5).

Among the risk factors for the development of the disease, smoking habits are most often present in 41 patients (66.13%), deviated septum in 39 (62.90%) patients and least often present were nasal polyps in 6 (9.68%) patients. The findings have statistical significance ( $p < 0.05$ ) (Table 4).

**Tabela 3.** Dužina trajanja simptoma

**Table 3.** Duration of symptoms

	Dužina trajanja simptoma / Duration of symptoms				
			X	SD	CV
Kraće od 7 dana / Less than seven days	29	46.77%	5.27	0.69	0.13
Duže od 7 dana / More than seven days	20	32.26%	9.15	0.85	0.09
Drugo / For a long time	13	20.97%	14.46	1.45	0.10
Ukupno / Total	62	100%			

Vrednosti su prikazane kao broj (%)

\*Hi-kvadrat test+Statistički značajan

Values in numbers (%)

\*Chi-square test+Statistically significant

**Tabela 4.** Ukupan broj pacijenata sa pridruženim oboljenjima i faktorima rizika

**Table 4.** Total number of patients with associated diseases and risk factors

	Pridružena oboljenja i faktori rizika / Associated diseases and risk factors	
DM	12	19.35%
Nosna polipoza / Nasal polyps	6	9.68%
Devijacija septoma / Deviated septum	39	62.90% *
HOBP / COPD	32	51.61%
Pušačke navike / Smoking	41	66.13% *
Hronični alergijski rinitis / Chronic allergic rhinitis	15	24.19%
Alergija na penicilin / Penicillin allergy	14	22.58%

Vrednosti su prikazane kao broj (%)

\*Hi-kvadrat test+Statistički značajan

Values in numbers (%)

\*Chi-square test.+Statistically significant

**Tabela 5. Antibiotici**  
**Table 5. Antibiotics**

	Broj pacijanata / Number of patients	
Levofloxacin u trajanju od 5 dana / Levofloxacin 5 days	20	32.26%
Levofloxacin u trajanju od 10 dana / Levofloxacin 10 days	20	32.26%
Amoksisilin-klavulonat u trajanju 10 dana / Amoxicillin-clavulanate 10 days	22	35.48%
Ukupno / Total	62	100%

Vrednosti su prikazane kao broj (%)  
\*Hi-kvadrat test+Statistički nije značajan  
Values in numbers (%)  
\*Chi-square test+No statistical significance

**Tabela 6. Klinička uspešnost**  
**Table 6. Clinical success**

	Levofloxacin u trajanju od 5 dana / levofloxacin 5 days		Levofloxacin u trajanju od 10 dana / levofloxacin 10 days		Amoksisilin- klavulonat u trajanju od 10 dana / amoxicillin- clavulanate 10 days	
Na kraju lečenja / End of treatment	18/20	90%	19/20	95%	20/22	90.91%
Na kraju studije / End of study	15/20	75%	16/20	80%	17/22	77.27%

Vrednosti su prikazane kao broj/ukupan broj (%)  
\*Hi-kvadrat test+Nije statistički značajan  
Values in numbers (%)  
\*Chi-square test+No statistical significance

Na kraju lečenja levofloxacinom u trajanju od 5 dana 18/20 (90%) pacijenata pokazalo je kliničku uspešnost, lečenja levofloxacinom u trajanju od 10 dana kliničku uspešnost pokazalo je 19/20 (95%) pacijenata, lečenja amoksisilin-klavulonatom u trajanju od 10 dana kliničku uspešnost pokazalo je 20/22 (90,91%) pacijenta. Na kraju studije, prilikom lečenja levofloxacinom u trajanju od 5 dana kliničku uspešnost pokazalo je 15/20 (75%) pacijenata, lečenja levofloxacinom u trajanju od 10 dana kliničku uspešnost pokazalo je 16/20 (80%) pacijenata, lečenja amoksisilin-klavulonatom u trajanju od 10 dana kliničku uspešnost pokazalo je 17/22 (77,2%) pacijenta ( $p > 0,05$ ), što znači da nema statistički značajne razlike između grupa (Tabela 6).

Pojava neželjenih efekata kod pacijenata lečenih levofloxacinom tokom 5 dana bila je prisutna kod 6/20 (30%) pacijenta, kod pacijenata lečenih levofloxacinom tokom 10 dana bila je prisutna kod 8/20 (40%) pacijenata, a kod pacijenata lečenih amoksisilin-klavulonatom kod 11/22 (50%)

Since the patients had similar symptoms, we randomly divided the patients into three groups. The first group used levofloxacin for five days (500 mg once a day), the second group used levofloxacin for 10 days (500 mg once daily) and the third group was administered amoxicillin-clavulanate for 10 days (500 mg – 125 mg three times a day). ( $p > 0.05$ ) which shows no statistical significance (Table 5).

At the end of a 5-day levofloxacin treatment, clinical success was recorded in 18/20 (90%) patients. Clinical success was achieved in 19/20 (95%) patients treated with levofloxacin for 10 days and in 20/22 (90.915) patients treated with amoxicillin-clavulanate for 10 days. At the end of the study, clinical success was achieved in 15/20 (75%) patients treated with levofloxacin for five days, 16/20 (80%) patients treated with levofloxacin for 10 days, and 17/22 (77.2%) patients treated with amoxicillin-clavulanate for 10 days. The p-value was  $p > 0.05$  which means that there was no statistically significant difference between the groups (Table 6).

pacijenta ( $p < 0,05$ ), što je statistički značajno. Prekid tretmana lečenih levofloxacinom u trajanju od 5 dana bio je sproveden kod jednog pacijenta od 20 (5%) pacijenta, levofloxacinom u trajanju od 10 dana kod jednog pacijenta od 20 (5%) pacijenata, a amoxicilin-klavulonatom kod 2/22 (9,09%) pacijenta ( $p < 0,05$ ), što je statistički značajna razlika. Najčešće prisutni simptomi bili su dijareja, kod 3 pacijenta od 20 (15%) pacijenata i nauzeja, kod jednog pacijenta od 20 (5%) pacijenata lečenih levofloxacinom tokom 5 dana, dijareja kod 4 pacijenta od 20 (20%) pacijenata i nauzeja kod dva pacijenta od 20 (10%) pacijenta lečenih levofloxacinom tokom 10 dana, dijareja kod 7 pacijenata od 22 (31,82%) pacijenta i nauzeja kod 3/22 (13,63%) pacijenta lečenih amoxicilin-klavulonatom ( $p < 0,05$ ), što je statistički značajno (Tabela 7).

Side effects in the group treated with levofloxacin for 5 days were recorded in 6/20 (30%) patients. The group treated with levofloxacin for 10 days had 8/20 (40%) patients with side effects and the group treated with amoxicillin-clavulanate had 11/22 (50%) patients with side effects, the p-value was  $p < 0.05$  which is statistically significant. With regard to discontinuation of treatment, the group treated with levofloxacin for five days had 1/20 (5%) patient; the group treated with levofloxacin for 10 days had 1/20 (5%) patient and the amoxicillin-clavulanate had 2/22 (9.09%) patients. For this criterion,  $p < 0.05$  which points to a statistically significant difference. The most common adverse effects were diarrhea in 3/20 (15%) patients and nausea in 1/20 (5%) patient treated with levofloxacin for five days; diarrhea in 4/20 (20%) patients and nausea in 2/20 (10%) patients treated with levofloxacin for 10 days; and diarrhea in 7/22 (31.82%) and nausea in 3/22 (13.63%) patients treated with amoxicillin-clavulanate. Here,  $p < 0.05$ , which is statistically significant (Table 7).

**Tabela 7. Analiza sigurnosti leka**  
**Table 7. Drug safety analysis**

Tretman / Treatment	Najmanje 1 neželjeni efekat vezan za tretman / Minimum one side effect related to treatment	Prekid tretmana / Discontinuation of treatment	Neželjeni efekti /Side effects	
			Dijareja / Diarrhea	Nauzeja / Nausea
Levofloxacin u trajanju od 5 dana / Levofloxacin 5 days	6/20 (30%)	1/20 (5%)	3/20 (15%)	1/20 (5%)
Levofloxacin u trajanju od 10 dana / Levofloxacin 10 days	8/20 (40%)	1/20 (5%)	4/20 (20%)	2/20 (10%)
Amoxicillin-clavulanate	11/22 (50%)	2/22 (9.09%)	7/22 (31.82%)	3/22 (13.63%)

Vrednosti su prikazane kao broj/ukupan broj (%)

\*Hi-kvadrat test+Statistički značajan

Values in numbers/total numbers (%)

\*Chi-square test+Statistically significant

## Diskusija

Rinosinusitis (RS) spada među najčešća stanja u medicini, od kojeg oboli oko 15% odraslih godišnje. Prethodne studije pokazuju da je visoka stopa propisivanja antibiotika radi lečenja RS u preko 80% slučajeva akutnog RS i preko 50% slučajeva hroničnog RS<sup>2,3</sup>. Dobijeni rezultati pokazali su to da nema statistički značajne razlike od oboljevanja od RS u pogledu pola u ispitivanoj grupi (Tabela 1). U Americi, pokazana je veća učestalost kod žena, što se može tumačiti i efektima klime i podneblja.

Simptomi sinusitisa su bol iznad zahvaćenog sinusa u vidu probadanja, koji se pojačava pri saginjanju i kašlju, osećaj pritiska ili punoće u predelu sinusa, glavobolja, zapušenost nosa, bol u uhu, pojačana sekrecija iz nosa kako spređa, tako i slivanjem u grlo, koja može da varira od vodenaste pa do gnojne, slabost, malaksalost, povišena telesna temperatura, napetost i edem lokalno. Nekađ se mogu javiti i krvarenje iz nosa i bol lociran u nekim specifičnim delovima glave, u zavisnosti od zahvaćenog sinusa – bol u zubima i prednjoj strani obraza, kod maksilarnog sinusa, u očima, slepoočnici i temenu, kod etmoidalnog i sfenoidalnog sinusa<sup>9</sup>. Dobijeni rezultati pokazali su to da su u ispitivanoj grupi najčešći simptomi bili kašalj, sekrecija iz nosa i zapušen nos (Tabela 2), što se slaže sa podacima iz literature<sup>8,9,10,11</sup>. U pogledu perioda javljanja lekaru, većina obolelih zatražila je lekarsku pomoć u periodu kraćem od 7 dana od pojave simptoma (Tabela 3).

Uzročnici u sinus, u daleko najvećem broju slučajeva, dospevaju preko nosa, a samo retko nekim drugim putem, kao što je preko krvi ili direktnim unošenjem, npr. preko povrede<sup>7,9,12,13</sup>. Takođe, upala maksilarnog sinusa može poticati od zapaljenskog procesa na korenu zuba, ako koren štrči u sinusnu šupljinu ili je proces na korenu uznapredovao ili je zapušten. Neka stanja, kao što su anatomski deformiteti, alergija, zamor i prethodna infekcija sinusa mogu uticati na češću pojavu bakterijske superinfekcije, zbog narušavanja normalne fiziologije sinusa<sup>12</sup>. Sinusitis mogu uzrokovati i hemijski iritansi, kao što su duvanski dim, isparenja hlora i drugih hemijski agresivnih susptanci, koje srećemo u industriji ili domaćinstvu. Dobijeni rezultati pokazali su to da su u ispitivanoj grupi najčešća pridružena oboljenja i simptomi devijacija septuma, pušačke navike i HOBP, što je u saglasnosti sa podacima iz literature<sup>4,6,10</sup> (Tabela 4).

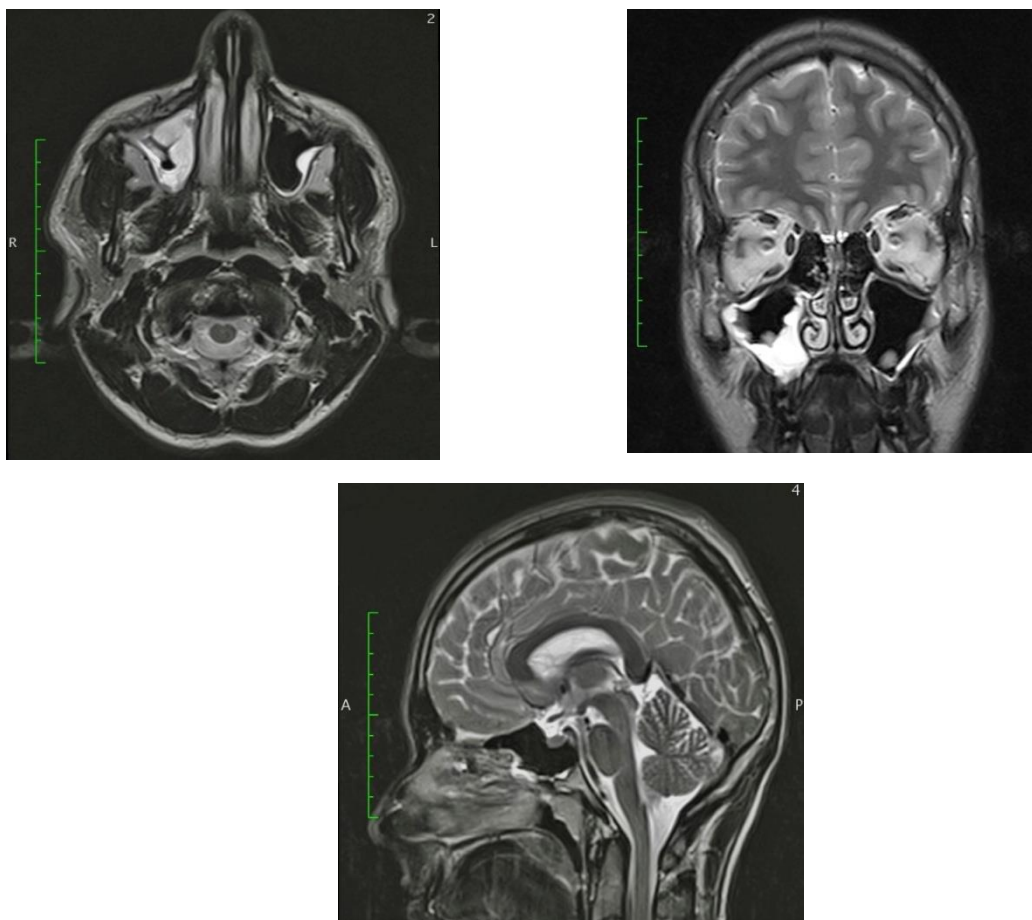
## Discussion

Rhinosinusitis (RS) is one of the most common medical conditions affecting 15% of adults each year. Previous studies have shown a high rate of prescribing antibiotics to treat RS, namely, over 80% in cases of acute RS and over 50% in chronic RS cases<sup>2,3</sup>. The obtained results showed that there was no statistically significant difference in the incidence of RS with regard to gender in the study groups (Table 1). In USA, a higher incidence has been recorded among women, which can be explained by the effects of climate and region.

Sinusitis symptoms include a stabbing pain above the affected sinus, which increases upon bending and coughing, a feeling of pressure or fullness in the sinus area, headache, nasal congestion, ear pain, increased secretion from the nose both to the frontal area and in the throat with the secretion varying from watery to purulent. The symptoms also include weakness, fatigue, fever, tension and local edema. Depending on the affected sinus, bleeding from the nose and pain located in some specific parts of the head can sometimes occur - pain in the teeth and front of the cheeks with maxillary sinus; pain in the eyes, temples and the top of the head with ethmoidal and sphenoid sinuses<sup>9</sup>. The obtained results showed that the most common symptoms were coughing, nasal secretion and nasal congestion (Table 2), which is in line with literature data<sup>8,9,10,11</sup>. With regard to the period of reporting to the doctor, the majority of patients sought medical help within the period of time less than seven days from the onset of symptoms (Table 3).

In most cases, causative agents reach the sinus through the nose, rarely in some other way, such as through blood or by direct intake, e.g., through injury<sup>7,9,12,13</sup>. Also, inflammation of the maxillary sinus can occur from the inflammatory process at the root of the tooth if the root protrudes into the sinus cavity or if the process at the root is advanced or neglected. Some conditions, such as anatomical deformities, allergies, fatigue, previous sinus infection may lead to more frequent bacterial superinfections due to disruption of normal sinus physiology<sup>12</sup>. Sinusitis can also be caused by chemical irritants, such as tobacco smoke, chlorine fumes and fumes from other chemically aggressive industrial or household substances. The obtained results showed that the most common associated diseases and symptoms in the tested groups were septal deviation, smoking and COPD, which is in accordance with the literature data<sup>4,6,10</sup> (Table 4).





**Slika 1,2,3.** Triplanarni prikaz akutnog zapaljenja maksilarnog i sfenoidnog sinusa  
**Figure 1,2,3.** Triplanar presentation of acute inflammation of the maxillary and sphenoid sinuses

Važno je zapamtiti da „abnormalni” radiološki nalazi, koji uključuju sinuse, ne potvrđuju nužno dijagnozu akutnog rinosinusitisa, jer 42% normalnih osoba može pokazati neki oblik abnormalnog zadebljanja sluzokože sinusa na CT-u<sup>11</sup>. Podjednako važno, snimanje ne može razlikovati virusni i bakterijski rinosinusitis, tako da se u smernicama za lečenje akutnog bakterijskog rinosinusitisa ističe to da nije potrebno pre davanja terapije raditi radiološku dijagnostiku, nego tek u slučaju neuspeha terapije i preteće komplikacije. Preporuka je da se radi kompjuterizovana tomografija paranazalnih sinusa.

Terapijske smernice uglavnom podržavaju 10 – 14 dana antibiotskog režima kod pacijenata sa akutnim bakterijskim sinusitom<sup>5,6,7,15,16</sup>. Međutim, nivo dokaza za takvu preporuku prilično je slab. Takođe, duže lečenje antibioticima može imati nedostake u poređenju sa kraćim vremenom korišćenja antibiotika, koje može biti jednako uspešno, kao što su povećanje bakterijske rezistencije, veća toksičnost i veća cena lečenja.

It is important to remember that “abnormal” radiological findings which include the sinuses do not necessarily confirm the diagnosis of acute rhinitis because 42% of otherwise healthy people can show some form of abnormal thickening of the sinus mucosa on CT scan<sup>11</sup>. Of equal importance is the fact that imaging cannot distinguish between the viral and bacterial rhinosinusitis so the guidelines for the treatment of acute bacterial sinusitis emphasize that it is not necessary to do radiological diagnostics before administering treatment but only in case of treatment failure and threatening complications. The recommendation is to perform computed tomography of the paranasal sinuses.

Therapeutic guidelines generally support 10 – 14 days of antibiotic treatment in patients with acute bacterial sinusitis<sup>5,6,7,15,16</sup>. However, the amount of evidence for such a recommendation is rather small. In addition, longer antibiotic treatment may have disadvantages compared to shorter antibiotic administration, which can be just as successful.

Potvrda bakterijske etiologije ne radi se rutinski u kliničkoj praksi, pošto zahteva punkciju sinusa ili endoskopski pregled srednjeg nosnog hodnika. Kao posledica toga, izbor antibiotske terapije je empirijski, u većini slučajeva, među antibioticima potencijalno efektivnim prema najčešćim izazivačima infekcije gornjeg respiratornog trakta, a prema smernicama za lečenje akutnog bakterijskog rinosinuzitisa<sup>5,6,7</sup>.

Smernice preporučuju da se odraslima sa blagom formom bolesti, koji nisu lečeni prethodno antibioticima, kao preporuka inicijalnog tretmana, ordinira: amoxicillin/clavulanate, amoxicillin (1,5 g/dnevno – 3,5 g/dnevno), cefpodoxime proxetil ili cefuroxime. Odraslima sa blagom formom bolesti, koji su u prethodnom periodu od 4 nedelje do 6 nedelja lečeni antibioticima i kod odraslih sa srednje teškom formom bolesti preporuka je da se ordinira: amoxicillin/clavulanate, amoxicillin (3 g – 3,5 g), cefpodoxime proxetil ili cefixime. Kod odraslih sa srednje teškom formom bolesti, koji su lečeni antibioticima u prethodnom periodu od 4 nedelje do 6 nedelja preporučeni antibiotici za lečenje su: amoxicillin/clavulanate, levofloxacin, moxifloxacin, ili doxycyclin<sup>1-16</sup>. U našem istraživanju koristili smo levofloxacin u trajanju od 5 dana (500 mg jednom dnevno), levofloxacin u trajanju od 10 dana (500 mg jednom dnevno) i amoksicilin-klavulonat u trajanju od 10 dana (500 mg – 125 mg tri puta dnevno), a dobijeni rezultati pokazali su to da ne postoje statistički značajne razlike u pogledu izbora antibiotika i dužine primene terapije. Dobijeni rezultati su u skladu sa podacima iz literature<sup>1,3,4,15</sup> (Tabela 6). Muhamad i sar. saopštavaju slične rezultate u studiji, koja upoređuje ove dve grupe antibiotika<sup>15</sup>. Burić i sar. ispituju i promenu bakterijske flore kod postojanja oroantralne fistule i bakterijskog sinuzitisa, što ukazuje na širi značaj ispitivanja upotrebe antibiotske terapije kod bolesnika sa sinuzitisom<sup>12</sup>. Tokom istraživanja zapaženo je to da je pojava neželjenih efekata nešto češća kod pacijenata koji su koristili amoksicilin-klavulonat i da je kod njih primećena veća neuspešnost terapije u odnosu na pacijente koji su koristili levofloxacin (Tabela 7).

The disadvantages include increased bacterial resistance, higher toxicity, higher treatment cost. The confirmation of bacterial etiology is not routinely done in clinical practice as it requires antral puncture or endoscopic examination of the middle nasal meatus. Consequently, the choice of antibiotic treatment is in most cases empirical and includes antibiotics potentially effective against the most common causes of upper respiratory tract infections and according to the guidelines for the treatment of acute bacterial rhinosinusitis<sup>5,6,7</sup>.

The guidelines recommend: Adults with mild disease who have not received antibiotics: Amoxicillin/clavulanate, amoxicillin (1.5–3.5 g/day), cefpodoxime proxetil, or cefuroxime is recommended as initial therapy. Adults with mild disease who have had antibiotics in the previous 4–6 weeks and adults with moderate disease: Amoxicillin/clavulanate, amoxicillin (3–3.5 g), cefpodoxime proxetil, or cefixime is recommended. Adults with moderate disease who have received antibiotics in the previous 4–6 weeks: Amoxicillin/clavulanate, levofloxacin, moxifloxacin, or doxycycline is recommended. In our study, we used levofloxacin for five days (500 mg once a day), levofloxacin for 10 days (500 mg once a day) and amoxicillin-clavulanate for 10 days (500 mg–125 mg three times a day). The obtained results showed that there are no statistically significant differences regarding the choice of antibiotic and the length of treatment. Our results are in accordance with the literature data<sup>1,3,4,15</sup> (Table 6). Muhamad et al. reported similar results in a study comparing these two groups of antibiotics<sup>15</sup>. Buric et al. also examined the change in bacterial flora in the presence of oroantral fistula and bacterial sinusitis, which points to a wider importance of testing the use of antibiotic treatment in patients with sinusitis<sup>12</sup>. During the study, it was noticed that the occurrence of side effects is somewhat more common in patients who used amoxicillin-clavulanate and that failure of treatment was also more common in this group compared to patients who used levofloxacin (Table 7).

## Zaključak

Nalazi ove studije sugerišu na to da kratki kurs tretmana antibioticima ima sličnu efikasnost u odnosu na duži kurs lečenja bolesnika sa akutnim, nekomplikovanim bakterijskim sinusitisom, onda kada je tretman indikovano. Ipak, treba podvući značaj lekarske procene, tako da antimikrobna terapija ne treba neprimereno da se ograniči kod pacijenta koji nije adekvatno reagovao na propisanu terapiju.

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## Conclusion

The findings of this study suggest that a short antibiotic treatment has similar efficiency compared to a longer course in patients with acute uncomplicated bacterial sinusitis when this treatment is indicated. However, the importance of medical assessment should be underlined so that antimicrobial therapy should not be inadequately limited in patients who have not had a proper response to prescribed therapy.

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