



The Antibiotic Prescription Practice in Primary Health Care from the Pharmacist Perspective

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SUMMARY

Introduction: Antibiotic resistance is a growing problem. Adherence to national guidelines is one of the key factors necessary for the rational use of antibiotics.

Aim: The aim of the study was to examine characteristics of antibiotic prescribing practice in primary health care in Novi Sad.

Method: The analysis was designed as a descriptive, cross-sectional study based on the data obtained from the health institution Cvejić Pharmacy. The guidelines available to physicians at the time of prescribing were used to assess the compliance of the prescribed antibiotics with the guidelines. Additionally, the most frequently dispensed antibiotics for all diagnoses were recorded and results were expressed as a percentage of frequency of analyzed antibiotic prescriptions.

Results: The study has shown that antibiotic prescriptions make 5.48% of all prescriptions (719 out of 13115), 513 (71.35%) of which were established by national guidelines, and 206 (28.65%) for less frequent diagnoses which was not included in national guidelines. In the study sample, 297 (65.42%) terapeuthical regimes had adequate terapeuthical dosage. The most commonly prescribed antibiotic groups were: macrolides (35.18%), penicillins (28.68%) and cephalosporins (14.60%).

Conclusions: Irrational prescribing and dispensing of antibiotics is both national and global problem. It is necessary to pay close attention to antibiotics prescribing and dispensing. The focus should be on national guidelines and their extension.

Keywords: prescribing practice, guidelines, prescribing and dispensing antibiotics, bacterial resistance

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INTRODUCTION

Antibiotic resistance, caused by widespread and non-specific use of antibiotics, led to a global public health problem [1,2]. The World Health Organization has proclaimed important messages regarding the control and reduction of bacterial resistance. Adherence to local guidelines during prescribing and dispensing antibiotics is the most important one [3]. Almost half of the prescribed antibiotics have inadequate use. This leads to a decrease in their effectiveness [4,5]. Global antibiotic consumption has increased dramatically, 2.5 times over a 1.5-decade time span (2000-2015) [6]. This is a multilevel problem: this group of medicines is being prescribed for diagnoses for which no antibiotic use has been indicated at all, another problem is making the wrong choice of antibiotics for the treatment of bacterial infections, also there is the issue of adherence in making appropriate drug choices [7]. One important factor in reducing resistance is decreasing prescribing and dispensing of inappropriate antibiotic prescriptions [8]. Globally, 700000 people die from infections caused by resistant strains of bacteria. Unless rational action is taken on a global scale, it is predicted that millions of deaths a year caused by drug-resistance infections would happen by 2050 [9]. Nowadays, the European Medicines Agency is making efforts to find the best solution for the current problem. Furthermore, with the recent spread of bacterial resistance, there is no corresponding progress in the development of new antibiotic molecules. For those reasons, the attention will be carefully focused on boosting research, on development of new therapeutic entities on one hand, and providing guidelines for downsizing the use of existing antibiotics on the other hand. It is estimated that the European Union has been losing 1.5 billion euros annually at the expense of age-related bacterial resistance [10]. Considering that the vast majority of antibiotics are prescribed in primary care [11], we have decided to examine what prescribing practice is present in our country. National guidelines are contained in Pharmacotherapy Protocols in Primary Health Care – the most common diseases and conditions from 2014. Protocol selection is made according to therapy for the most common diagnosis (MCD) established by The National Health Insurance Fund (NHIF) [12].

AIM

The aim of the study was to examine characteristics of antibiotic prescribing practice in primary health care in Novi Sad.

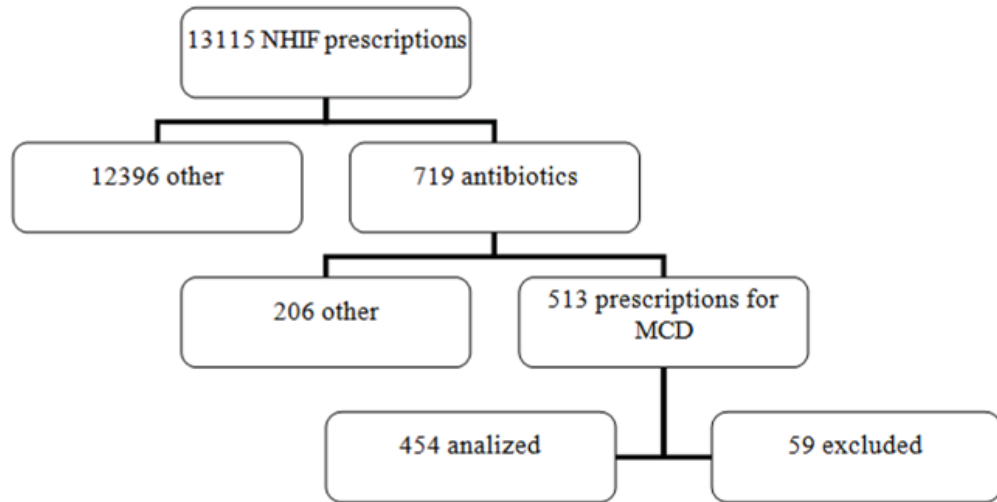
METHOD

The analysis was designed as a non-commercial, descriptive, cross-sectional study based on the data obtained from the health institution Cvejić pharmacy. Seven branches of the pharmacy in Novi Sad (the second-largest city by population in Serbia) were observed during January 2018. Data taken for analysis is related to dispensed antibiotics, which were prescribed according to prescription patterns funded by NHIF. Data was chosen randomly. Prescription patterns of dispensed antibiotics that are not recognized by NHIF for funding were not considered, due to the incompleteness of the data of the observed parameters.

Data regarding gender, age, diagnosis and prescribed/dispensed medicines were recorded. For each observed diagnosis, the frequency of each therapeutic choice was recorded. The same therapeutic choice was considered to be medicines with the same active pharmaceutical ingredient (API) in the same total therapeutic dose (TTD), from different producers. Prescriptions for antibiotics with dosage based on body weight were excluded from the study (excluded prescriptions) due to the lack of required data when classifying the prescribed medicine into one of four groups: appropriate medicine, appropriate but sub-dosed medicine, appropriate but supradosed medicines and inappropriate medicine.

This paper assess the compliance of the prescribed antibiotics with the available guidelines. Pharmacotherapy Protocols in Primary Health Care for the most common diseases and conditions from 2014, issued by NHIF, were used, written by national experts in the specific areas for which the guideline is intended [12]. The guidelines prescribe therapies for the most common diagnoses in primary health care (MCD). Only these diagnoses were observed to evaluate the compliance of the prescribed therapies with the guidelines in this study. The necessary minimum and maximum TTD for the individual diagnosis and each age category of patients were calculated based on the guidelines. The dispensed doses were compared with the calculated ones

Figure 1. Selection of prescriptions for analysis



to assess suitability. Additionally, the most frequently dispensed antibiotics for all diagnoses were recorded. The prescriptions selected for analysis are given in Figure 1.

Table 1. Features of prescriptions prescribed for MCD

* Prescriptions for most common diagnosis:
 J02 - Acute pharyngitis;
 J20 - Acute bronchitis;
 J00 - Acute nasopharyngitis;
 J03 - Acute tonsillitis;
 J01 - Acute sinusitis;
 J02.9 - Acute nonspecific pharyngitis;
 N30 - Cystitis;
 J04 - Acute laryngitis and tracheitis;
 H65 - Middle ear inflammation;
 L02 - Abscess, ulcer and group of ulcers;
 L08 - Other localized infections of the skin and subcutaneous infections.

** Other diagnosis:
 H60 - External ear inflammation;
 H66 - Purulent and nonspecific middle ear inflammation;
 I10 - Hypertension of unknown origin;
 J40 - Nonspecific acute or chronic bronchitis;
 J42 - Chronic nonspecific bronchitis;
 K21 - Gastro-esophageal reflux disease;
 N30 - Dyspepsia;
 N34 - Urethritis and vaginal inflammation;
 N40 - Prostatic hyperplasia;
 N76 - Vulvovaginitis;
 N72 - Cervicitis.

	TOTAL	Prescriptions for most common diagnosis*					
		J02	J20	J00	J03	J01	J02.9
GENDER							
Male	170 (33.14%)	77 (38%)	21 (30%)	17 (25%)	8 (19%)	8 (24%)	10 (31%)
Female	250 (48.73%)	100 (50%)	30 (43%)	26 (39%)	20 (48%)	25 (74%)	18 (56%)
Children	93 (18.13%)	24 (12%)	19 (27%)	24 (36%)	14 (33%)	1 (2%)	4 (13%)
AGE							
0-17	104 (20.27%)	30 (15%)	19 (27%)	24 (36%)	14 (33%)	5 (15%)	4 (13%)
18-35	81 (15.79%)	39 (19%)	5 (7%)	6 (9%)	16 (38%)	5 (15%)	5 (16%)
36-64	224 (43.67%)	93 (46%)	27 (39%)	28 (42%)	12 (29%)	21 (62%)	17 (53%)
>65	104 (20.27%)	39 (19%)	19 (27%)	9 (13%)	0 (0%)	3 (9%)	6 (19%)
TTD							
Analyzed	454 (88.50%)	190 (95%)	51 (73%)	52 (78%)	35 (83%)	34 (100%)	29 (90.5%)
Excluded	59 (11.50%)	11 (5%)	19 (27%)	15 (22%)	7 (17%)	0 (0%)	3 (9.5%)
	TOTAL	Prescriptions for most common diagnosis*					
		N30	J04	H65	L02	L08	Others**
GENDER							
Male	170 (33.14%)	9 (41%)	2 (25%)	4 (57%)	4 (80%)	1 (20%)	9 (45%)
Female	250 (48.73%)	13 (59%)	5 (62%)	0 (0%)	1 (20%)	3 (60%)	9 (45%)
Children	93 (18.13%)	0 (0%)	1 (13%)	3 (43%)	0 (0%)	1 (20%)	2 (10%)
AGE							
0-17	104 (20.27%)	0 (0%)	1 (13%)	4 (57%)	0 (0%)	1 (20%)	2 (10%)
18-35	81 (15.79%)	2 (9%)	0 (0%)	1 (14%)	0 (0%)	0 (0%)	2 (10%)
36-64	224 (43.67%)	7 (32%)	4 (50%)	0 (0%)	4 (80%)	3 (60%)	8 (40%)
>65	104 (20.27%)	13 (59%)	3 (37%)	2 (29%)	1 (20%)	1 (20%)	8 (40%)
TTD							
Analyzed	454 (88.50%)	22 (100%)	7 (87%)	6 (86%)	5 (100%)	5 (100%)	18 (90%)
Excluded	59 (11.50%)	0 (0%)	1 (13%)	1 (14%)	0 (0%)	0 (0%)	2 (10%)

RESULTS

The study has shown that antibiotic prescriptions make 5.48% of all prescriptions (719 out of 13115), 513 (71.35%) of which were established by national guidelines, and 206 (28.65%) for less frequent diagnoses which were not included into the national guidelines. The incidence of diagnoses in the examined sample was: J02 (39.18%), J20 (13.65%), J00 (13.06%), J03 (8.19%), J01 (6.63%), J02.9 (6.24%), N30 (4.29%), J04 (1.56%), H65 (1.36%), L02 (0.98%), L08 (0.97) and others (3.89 %). Most of the observed diagnoses were more frequent in female (49.5%) compared to male (32.5%), while the incidence in children (<18 years) was the

lowest (18%). The exceptions are diagnoses J00 (36%) and J03 (33%). The inappropriateness of antibiotic prescription was assessed via rate of sub- and supra- doses, as well as unsuitable indications. An example of an unsuitable indication was antibiotic prescription not recommended by national guidelines. The results of the most commonly prescribed diagnoses established by national guidelines are shown in Table 1 and Table 2. The results of the most commonly used antibiotic groups, as well as the most commonly used antibiotics, are shown in Chart 1 and Chart 2 respectively.

TTD	TOTAL	Prescriptions for most common diagnosis*					
		J02	J20	J00	J03	J01	J02.9
Appropriate	297 (65.42%)	140 (73.68%)	19 (37.25%)	43 (82.69%)	23 (65.71%)	19 (56%)	28 (96.55%)
Inappropriate	95 (20.93%)	27 (14.21%)	32 (62.75%)	8 (15.38%)	2 (5.71%)	11 (32%)	0 (0%)
Subdose	32 (7.05%)	16 (8.42%)	0 (0%)	1 (1.93%)	8 (22.86%)	3 (9%)	0 (0%)
Supradose	30 (6.60%)	7 (3.69%)	0 (0%)	0 (0%)	2 (5.72%)	1 (3%)	1 (3.45%)

TTD	TOTAL	Prescriptions for most common diagnosis*					Others**
		N30	J04	H65	L02	L08	
Appropriate	297 (65.42%)	0 (0%)	7 (100%)	4 (66.67%)	4 (80%)	0 (0%)	10 (55.55%)
Inappropriate	95 (20.93%)	3 (14%)	0 (0%)	0 (0%)	1 (20%)	4 (80%)	7 (38.88%)
Subdose	32 (7.05%)	0 (0%)	0 (0%)	2 (33.33%)	0 (0%)	1 (20%)	1 (5.57%)
Supradose	30 (6.60%)	19 (86%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Table 2. Frequency of analyzed antibiotic prescriptions for the most commonly prescribed diagnoses and their classification according to recommended TTD

* Prescriptions for most common diagnosis:
 J02 - Acute pharyngitis;
 J20 - Acute bronchitis;
 J00 - Acute nasopharyngitis;
 J03 - Acute tonsillitis;
 J01 - Acute sinusitis;
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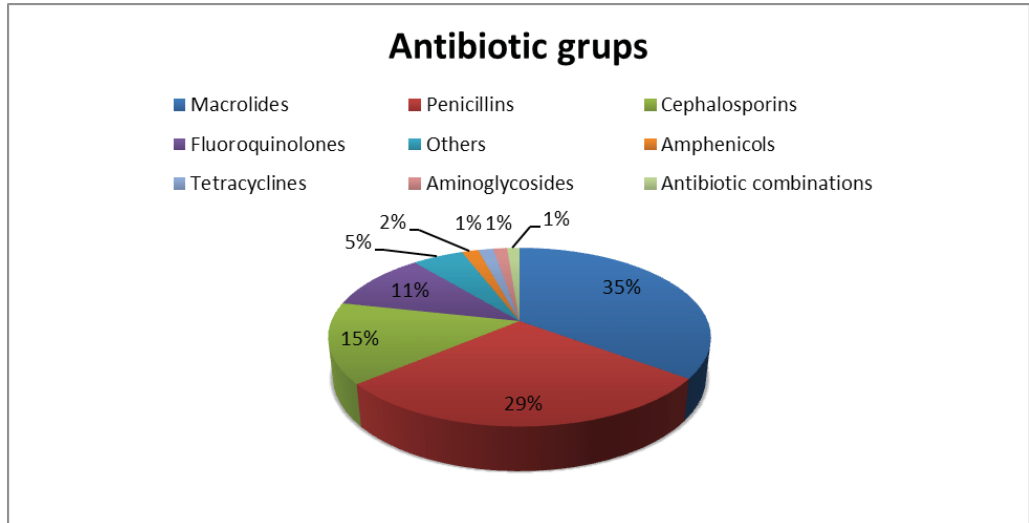
DISCUSSION

The vast majority of patients received the appropriate medication, but some did not receive the appropriate dose. In addition to the API, the guidelines prescribe the dose and duration of therapy for specific diagnoses. Based on this, we observed the minimum and maximum dose required for the overall treatment of infection given in the guidelines and the compliance of the dispensed medicines with the guidelines [12].

Due to the lack of data to evaluate the TTD (dosing is calculated in relation to body weight), 59 (11.5% of 513) patients were ex-

cluded from the study. The total number of analyzed TTD was 454. The highest percentage of TTD was in line with the observed guideline - 297 (65.42%). It was found that 62 (13.65 %) patients had a wrongly prescribed dose (adequate medicine, but underdosed 7.05 %, adequate medicine but overdosed 6.60 %) and 95 (20.93 %) received an antibiotic not given in the guidelines. Adherence to national primary health care guidelines was discussed in studies conducted in England, Germany, Cape Town, South Africa, as well as in the WHO pilot study [13 - 17]. Two studies conducted

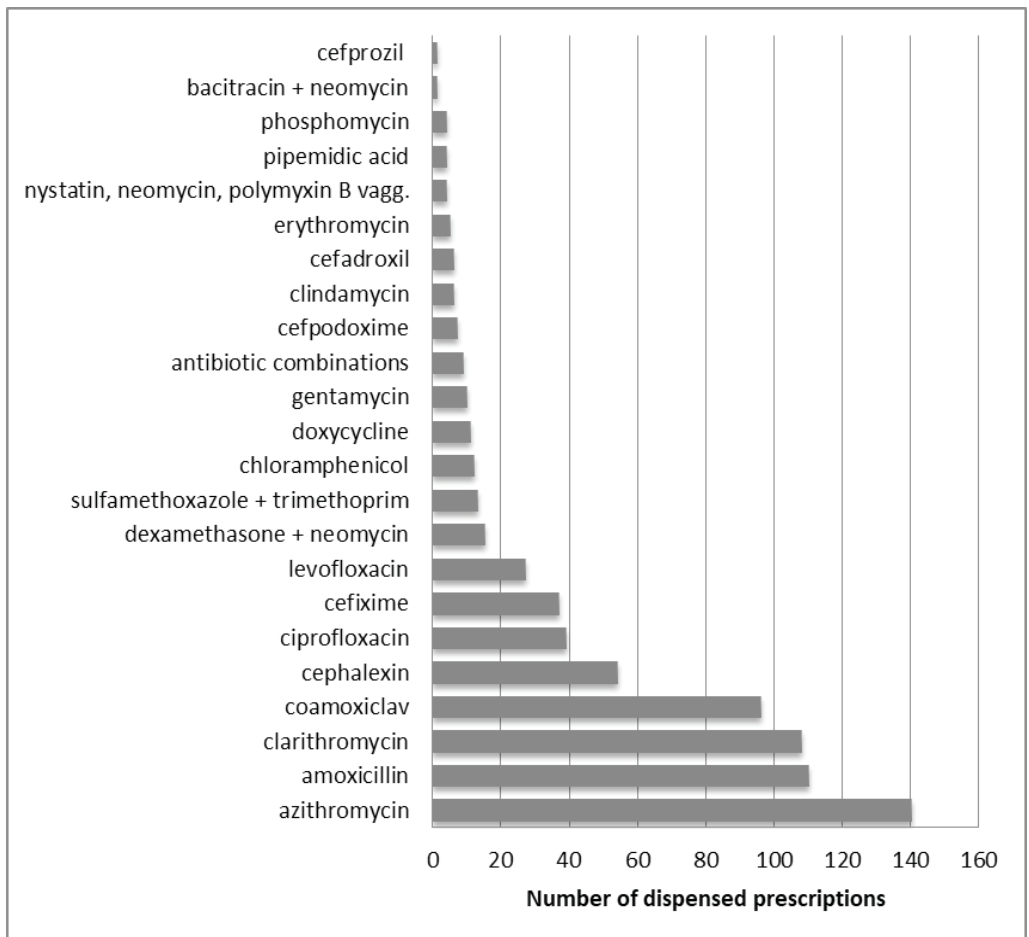
Chart 1. Most commonly used groups of antibiotics



in England have recorded low adherence rates to national guides [13,14]. A study conducted in Germany found that most antibiotic prescriptions (74.82%) were not in line with the guidelines, 95.66% of which were related to the diagnosis of acute bronchitis [15]. The smallest deviation from the guidelines, among the comparative trials of recent date, was found in

the survey conducted in Cape Town, South Africa, where a non-compliance with the guidelines was 54.6% of observed cases [16]. International guidelines promote raising awareness of the rational use of antibiotics, especially in case of therapy for acute respiratory infections, where routine antibiotic therapy is not recommended or it is rarely required [20, 21].

Chart 2. Most commonly used antibiotics



Out of 454 analyzed TTD, 404 (88.98%) were prescribed and issued for the treatment of acute respiratory. Acute pharyngitis was the most common diagnosis for which antibiotics were prescribed and 190 (41.85%) patients became ill with this infection. In 40-60% of cases, it is primarily of viral and 5-30% of bacterial origin [12]. In line with national guidelines were 140 (73.68%) of TTD. The second most frequent was bronchitis 51 (11.23%), which was of viral origin in 90% of cases [12,22,23]. Given the primary etiology of the disease, national guidelines suggest administration and prescribing of antibiotics only in the case of comorbidities or in people over 65 years of age. For the first two MCD, macrolide antibiotic was predominantly prescribed. Similar results were obtained in a study conducted in Italy where the MCD was acute pharyngitis (60.4%) and the second most frequent was acute bronchitis (18.2%) [11]. Globally, acute sinusitis in adults is usually of viral etiology. Antibiotics are prescribed if a patient's condition does not improve after 10 days, [12,18-20]. Levofloxacin, azithromycin and broad-spectrum penicillin were the most commonly prescribed antibiotics in our study. Current guidelines do not recommend macrolides or fluoroquinolones as the first-line antibiotics, therefore special attention should be given when diagnosing patients, as well as prescribing and dispensing appropriate therapy [12].

This study examined 719 (5.48%) antibiotic prescriptions issued by the pharmacy institution out of a total of 13115 NHIF prescriptions issued in January 2018. The most commonly prescribed antibiotic groups were macrolides (35.19%), penicillins (28.68%), cephalosporins (14.6%) and fluoroquinolones (9.18%). In 2008 an antibiotic consumption study was performed in the South Backa District (SBD) and the obtained results were compared with antibiotic consumption in Finland and Denmark during the same period. Penicillins were the most commonly prescribed antibiotics in all three countries [24]. The most commonly prescribed antibiotics in Romania in 2008 were broad-spectrum penicillins, second-generation cephalosporins and fluoroquinolones [25]. The results obtained from these studies show changes in the prescribing practices of primary care physicians. Macrolides were the most commonly prescribed antibiotics in our study with a proportion of 35.19%.

In a study conducted in Italy in 2017, the most commonly prescribed were macrolides (32.5%), broad-spectrum penicillins (31.1%) and fluoroquinolones (14.2%) [11]. Italy is a country with a high consumption of antibiotics [26], especially for prophylactic purposes [27] and one of the countries with the fastest growth of antibiotic resistance [28]. Inappropriate use of antibiotics can lead to an increase in antibiotic resistance and, consequently, to an increase in morbidity and/or mortality rate, and costs of treatment, [29 - 31]. For almost every third diagnosis in this study (28.65%) there was no recommended therapy included in national guidelines. There are several reasons for the inappropriate use of antibiotics: failure to adhere to national guidelines, lack of knowledge and professional training, pressure from pharmaceutical companies, the financial benefit for physicians, and patient pressure on doctors to prescribe antibiotics even when they are not necessary [32-38]. One of the most important steps to slow down the development and spread of resistance is the rational use of antibiotics [39], per local guidelines, which are based on local antibiotic resistance maps [3]. Due to the implementation of new guidelines, adopted at the end of 2018, shortly after data collection for this study, it is extremely important to assess the adherence of rational use of antibiotics to the previous ones.

CONCLUSION

This study has shown a significant deviation of prescribing practice in primary care from national guidelines. The highest deviation was recorded in acute bronchitis and the most commonly prescribed antibiotic was azithromycin. For almost every third diagnosis in this study, the prescribed therapy was not included in national guidelines. Irrational prescribing and dispensing of antibiotics is a global problem. It is necessary to pay close attention to antibiotics prescribing and dispensing. The focus should be on adherence to national guidelines and their expansion.

This study has limitations in sense of short observation period, and a need for a larger sample pool from more pharmacies in order to acquire more representative data. Prescriptions for antibiotics with dosage based on body weight were excluded from the study. There was no information about special groups of patients who require particular doses calcu-

lations (including pregnant women, patients with kidney and liver disease etc). Prescriptions that were not funded by NHIF were not included in the study.

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CONFLICTS OF INTEREST

All authors declare no conflict of interest.

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Propisivačka praksa antibiotika u primarnoj zdravstvenoj zaštiti iz ugla farmaceuta

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KRATAK SADRŽAJ

Uvod: Antimikrobna rezistencija je globalni problem. Pridržavanje lokalnim smernicama prilikom propisivanja antibiotika je ključni faktor za njihovu racionalnu upotrebu. **Cilj:** Cilj studije je bio da se odrede karakteristike propisivačke prakse antibiotika u primarnoj zdravstvenoj zaštiti u Novom Sadu (Srbija).

Metoda: Ispitivanje je dizajnirano kao opservaciona, deskriptivna, retrospektivna studija zasnovana na podacima dobijenim iz zdravstvene ustanove apoteke Cvejić. Za procenu usklađenosti propisanih antibiotika sa smernicama, korišćene su smernice koje su bile dostupne lekarima u trenutku propisivanja kao najnovije. Posmatrana je potrošnja izražena kao procenat za svaki pojedinačni farmaceutski sastojak.

Rezultati: Studija je pokazala da su antibiotski recepti činili 5,48% svih recepata (719 od 13115), od toga 513 (71,35 %) recepata je propisano za najčešće dijagnoze, a 206 (28,65%) za manje učestale dijagnoze čije smernice nisu propisane nacionalnim vodičima. U ispitivanom uzorku 297 (65,42%) je imalo dobro propisanu dozu. Najčešće propisivane antibiotske grupe su bile: makrolidi (35,18%), penicilini (28,68%) i cefalosporini (14,60%).

Zaključak: Neracionalno propisivanje i izdavanje antibiotskih lekova je problem kako na nacionalnom nivou tako i na globalnom nivou. Potrebno je usmeriti dodatnu pažnju prilikom propisivanja i izdavanja lekova. Praćenje nacionalnih smernica je od ključne važnosti, kao i razmatranje o proširivanju isitih.

Ključne reči: propisivačka praksa, smernice, propisivanje i izdavanje antibiotika, bakterijska rezistencija

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