

Scientific Journal of the Faculty of Medicine in Niš 2010;27(1):27-32

Original article ■

Outpatient Antibiotic Use In Primary Healthcare Of Niš Region

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SUMMARY

Monitoring of antibiotic prescribing promotes rational use of drugs, reduces costs and slows down the development of resistance. Upper respiratory tract infections (URIs) are common conditions managed in primary health care (PHC).

The aim of this study was to evaluate prescribing of antibiotics, especially in the treatment of URIs in PHC of Niš region and to identify the practice of drug overuse, underuse or inappropriate use. The data on outpatient use of antibacterials for systemic use was obtained by retrospective study and expressed as the number of defined daily doses (DDD) per 1000 inhabitants per day (DID), according to the WHO anatomic therapeutic chemical classification and DDD measurement methodology. The City Pharmacy Department provided automatic reports on antibiotics prescribed by physicians for certain diagnoses in the Niš region over the 2005-2007 period. In the same period, outpatient antibiotic use increased by 9.02% (22.83/ 25.96 DID). The most commonly prescribed drugs were semi-synthetics penicillins and macrolides. The greatest increase in antibiotics prescriptions was noted in azithromycin (by 164%). Out of the total number of antibiotics, 70.5% prescriptions were made for the treatment of URIs. Pharyngitis acuta was the most common indication for prescription of antimicrobial medicines (45.26%). Amoxicillin (33%) and cephalexin (35%) were most commonly prescribed antibiotics for this indication. This analysis shows the irrational use of antibiotics in primary health care in the Niš region, which requires an additional application of educational programs and monitoring of microbial sensitivity. The results will be the basis for further evaluation of rational use of antibiotics in primary health care.

Key words: antibiotic use, outpatients, defined daily dose, drug utilization

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INTRODUCTION

Analysis of antimicrobial drugs use offers insight in actual prescribing practice. The highest rates of antibiotic prescriptions for systemic use are in general practice. Upper respiratory tract infections (URIs) are one of the commonest diagnoses in primary health care (PHC), which are often treated with antibiotics (1,2). The use of antibiotics for upper respiratory tract infections is controversial. Any benefits have to be weighed against common adverse reactions (including rash, abdominal pain, diarrhoea and vomiting), cost and antibacterial resistance (3). Information about drug utilization among outpatients in Serbia is scanty and there are no available publications on the topic.

Monitoring of antibiotic prescribing promotes rational use of these drugs, reduces costs and slows down the progress of resistance (3-5). In total consumption, antibiotics took up 16.25% of drugs budget in Niš region in 2005. The analysis of consumption of antibiotics, based on the number of prescriptions, presents the basis for the estimate of rationality of URIs. To assess the antibiotic prescription, the analysis of the assumed etiology and antibiotic groups prescribed for URIs is needed, in order to provide some useful recommendations for the future. The aim of our study was to analyze the outpatient antibiotics utilization, especially in the treatment of URIs in PHC of Niš region, one of the biggest regions of south-east Serbia, during 2005-2007 period, and to identify practice of drug overuse, underuse or misuse.

METHODS

The data were obtained from the City Pharmacy Department which supplies approximately 350.000 inhabitants, through the network of 25 state - owned pharmacies.

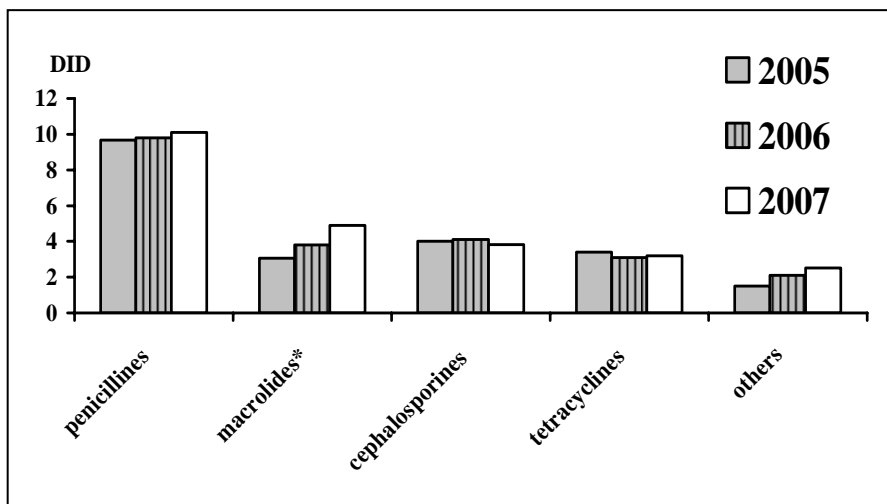
All data for 2005-2007 period were centrally collected, and analyzed. The City Pharmacy Department automatic report on antibiotics prescribed by physicians for certain diagnoses, especially URIs was used as data source. The data on outpatient use of antibacterials for systemic use were obtained by retrospective study and expressed as a number of DDD per 1000 inhabitants per day (DID; WHO version 2007) (6). All pharmaceuticals were classified by groups of anatomic therapeutic chemical (ATC) classification, data on outpatient use of antibacterials for systemic use (ATC J01 class; excluding parenteral antibiotics, antifungals and topical antibiotics). International classification of diseases (MKB-X revision) was to analyse the prescribed antibiotics (J02 - pharyngitis acuta, J04 - sinusitis acuta, J03 - tonsillitis acuta, J20 bronchitis acuta, N30 - cystitis, N39 - morbi tractus urinarii alii, J00 - nasopharyngitis acuta).

A study was taken to analyse the utilisation of antibiotics reimbursed by the Health Insurance Fund (HIF).

RESULTS

The total of 5.844.823 prescriptions was analyzed, with 1.112.270 (19.03%) being the prescriptions of antibiotics. In the three-year period of follow-up we registered an increase in the use of antibiotics by 9.02% (23.81/25.96 DID). The most utilized drugs were beta lactam antibiotics (13.79/13.16 DID).

The next most commonly used antibiotics were macrolides (3.05/5.17DID) and tetracyclines (3.65/2.89 DID) (Figure 1). The highest increase in prescribing was established for azithromycin (+164%; $p < 0.05$), owing to reimbursement by the Republic Fund for Health.



*($p < 0.05$); outpatient macrolides consumption was significantly increased from 2005 to 2007

Figure 1. Trends in antibiotic consumption in defined daily doses per 1000 inhabitants per day (DID) in Niš region from 2005 to 2007

Table 1. The top 10 prescribed antibiotics (ATC group J) in PHCs from 2005 to 2007 in DID and percentages

Antibiotics	DID (%)					
	2005		2006		2007	
Amoxicillin	6.95	(30.44)	7.15	(31.13)	6.70	(25.80)
Cephalexin	4.07	(17.82)	3.76	(15.69)	3.45	(13.28)
Doxycyclin	3.65	(15.98)	3.23	(13.48)	2.89	(11.13)
Erythromycin	3.05	(13.35)	3.10	(12.94)	3.41	(13.13)
Co-trimoxazole	3.03	(13.27)	2.87	(11.98)	2.23	(8.59)
Phenoxymethylpenicillin	2.65	(11.60)	2.28	(9.51)	2.51	(9.66)
Ciprofloxacin	0.29	(1.27)	0.38	(1.58)	0.23	(0.88)
Amoxicillin+clavul.acid	0.12	(0.52)	0.56	(2.33)	0.39	(1.50)
Azithromycin	-	-	0.56	(2.33)	1.48*	(5.70)
Roxitromycin	-	-	0.06	(0.25)	0.28	(1.07)
Total	23.81	100	23.95	100	25.96	100

*($p < 0.05$); Consumption of azythromycin significantly increased from 2005 to 2007; DID - defined daily doses per 1000 inhabitants per day

Table 1 shows utilization of the top 10 antibiotics in PHC in Niš region in DID and percentages.

In the period 2005-2007, the majority of antibiotics (70.5%) prescribed in PHC were for patients with URIs. The most commonly prescribed antibiotics are amoxicillin (28.5%), cephalexin (25.5%) and erythromycin (14.9%).

Pharyngitis acuta (J02) was the most common indication for prescription of antibiotics (45.26%) in URIs (Table 2). At the therapy of J02, amoxicillin and cephalexin were most commonly indicated antibiotics (33% and 35%), respectively (Figure 2).

It was shown that macrolides were used the most for the treatment of acute bronchitis (51.45 %). The total number of prescriptions for consumption of antibiotics was increased by 14%, while the cost was increased by 28% compared to 2005.

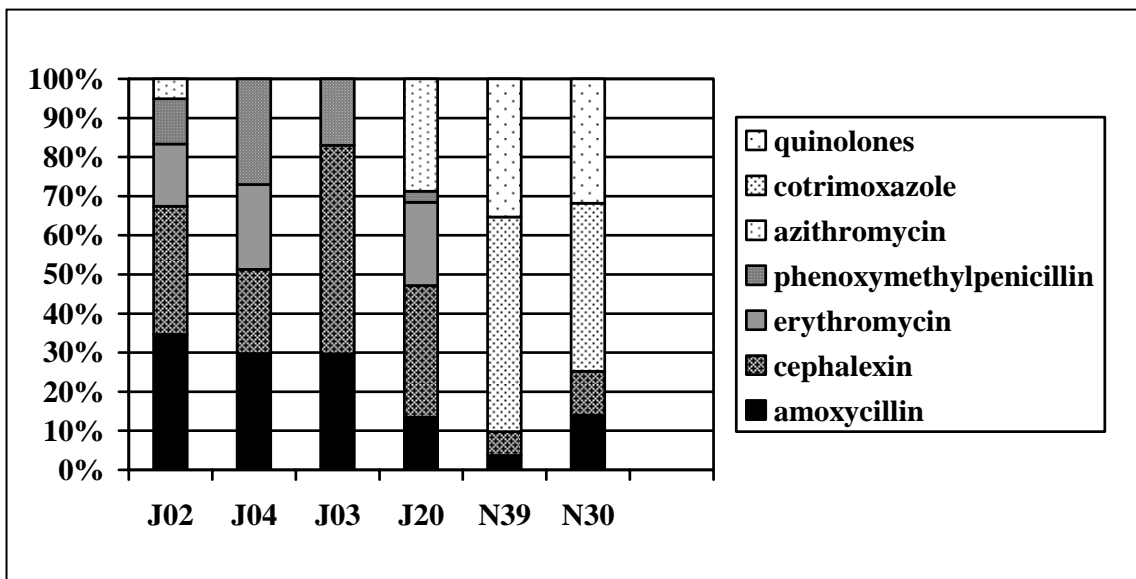
Out of the total number of antimicrobial medicines, 10.75% prescriptions were made for the treatment of urinary tract infections. The most commonly prescribed antimicrobial medicines are cotrimoxazole (45%) and pipemidic acid (29%). The total consumption of cotrimaxazole was in decline compared to year 2005 (26.18%).

Table 2. The most common infections in PHCs and antibiotic use

ICD (X revision)	Diagnosis	DID	Number of prescriptions	%	PID
J02	Pharyngitis acuta	11.53	503.470	45.26	3.94
J03	Sinusitis acuta	3.92	182.840	16.44	1.43
J20	Bronchitis acuta	2.36	115.920	10.42	0.91
N30	Cystitis	2.21	116.770	10.52	0.91
N39	Morbi tractus urinarii alii	1.28	54.270	4.88	0.42
J03	Tonsillitis acuta	0.71	33.000	2.93	0.25
	Other	2.56	106.000	9.44	0.83
	Total	24.57	1.112.270	100	8.69

ICD - international classification of diseases, DID - defined daily doses per 1000 inhabitants/day

PID - number of packages per 1000 inhabitants/day



J02-pharyngitis ac, J04-sinusitis ac, J03-tonsillitis ac, J20-bronchitis ac, N39-morbi tractus urinarii allii, N30-cystitis

Figure 2. The most commonly prescribed antibiotics for treatment of infections

DISCUSSION

In modern clinical practice, analyzing drug utilization is important tool for achieving rational drug therapy. It is necessary for identification of a problem, and then for following effectiveness of corrective interventions, undertaken by the management of a health facility.

Our study indicated high prescribing rates of antibiotics in Niš region, when compared with some developed countries in Europe (Netherlands, Norway) and the USA (7-9). The European Surveillance of Antimicrobial Consumption (ESAC programme) collected data from 35 countries, showing that antibiotic use was the highest in southern European countries (7,8). Total outpatients antibiotic use in 2003 varied by factor by 3.2 between the country with the highest (31.4DID in Greece) and the country with the lowest (9.8 DID in the Netherlands) use (5,7,8). Prescription of antibiotics in Europe remained at a median level of 20 DID in the period 1997-2002. A study comparing outpatient antibiotic consumption in the USA showed it to be similar to that in the southern European countries, but macrolides, particularly azithromycin, are among the first-line agents prescribed in the USA for respiratory infections (9). In Europe, patients are more likely to receive a betalactam; and when a macrolide is indicated, clarithromycin is more likely to be prescribed than azithromycin (9-11). Penicillins represented the most frequently prescribed antibiotics in European countries, ranging from 31% (Finland) to 63% (Denmark) of the total outpatient antibiotic use, which is similar to our results (42%) (2).

Many reasons have been proposed to explain these large differences in consumption of antibiotics in

different countries including the incidence of community-acquired infections and factors which could result in differences in this incidence, culture determinants, social determinants, health care structures, resources and utilization, knowledge about antibiotics, pharmaceutical market and regulatory practices (12).

Antibiotic use in the treatment of respiratory tract infections is common in primary care, although the benefit of antibiotic therapy is questionable, their prescription is very frequent (13). This survey showed tendency of PHC physicians to more frequently prescribe wide-spectrum antibiotics.

Pharmacoepidemiologic analysis of outpatients' use of antimicrobial drugs in the treatment of URIs in Montenegro showed similar results (5). In the Netherlands, high prescribing was present for patients with sinusitis-like complaints (67%) (10,11). Amoxicillin was the most frequently used antibiotic for the treatment of URIs, similar to our results (2,5). Over prescribing was highest in tonsillitis and bronchitis (71% vs. 63%, respectively) in Netherlands (10).

Cross sectional observational study with clinicians from 14 primary care research networks in 13 European countries showed that acute cough is a major reason for antibiotic prescribing in primary care, with many prescriptions resulting in no clinical benefit (14). In total, Amoxicillin was the most common antibiotic prescribed, but this ranged from 3% of antibiotics prescribed in the Norwegian network to 83% in the English network (15, 16). Considerable variation in antibiotic prescribing for acute cough remains throughout Europe even after adjustment for illness severity, comorbidity, temperature, age, duration of illness before to consultation, and smoking status. Recovery is not meaningfully influenced by variation in antibiotic prescribing (14).

Our data also confirmed the insufficient use of macrolides (12.8% in 2005, 18.8% in 2007). As safe and well-tolerated antibiotics, macrolides play a key role in the treatment of community-acquired URI infection (17). Their broad spectrum of activity against gram-positive cocci, atypical pathogens, *H. Influenzae* (azithromycin and clarithromycin), and *Moraxella catarrhalis* and were alternatives for patients allergic to beta-lactams. International study exploring antibiotic prescribing showed that macrolides were prescribed to 26% of patients, ranging from 4% in Utrecht to 50%, 45%, and 38% in the Bratislava, Milan, and Lodz networks, respectively (14).

An antibiotic prescribing was in correlation with current protocol for treatment of URIs, mostly, issued by the Serbian Ministry of Health in 2005.

This analysis shows high use of antibiotics in acute pharyngitis in outpatients in Niš region, although an overwhelming majority of URIs are of viral origin, indicating the need for additional application of educational programs. Examination of the relationship between ambulatory antibiotic prescribing for respiratory tract infections was inversely associated with hospital admissions for respiratory tract infections (4).

There has been an interest in ways to reduce antibiotic prescribing. One way is to delay the use of prescribed antibiotics by more than 48 hours for acute

upper respiratory tract infections. Such methods have been shown to reduce prescribing (18-20). Reduction of prescriptions is possible by using timely laboratory examinations to determine etiological agents of infections (20).

CONCLUSIONS

The analysis of antibiotic drugs' use offers insight in actual prescribing practice. In general, antibiotic prescribing was mostly in correlation with current protocol for treatment, however, the most commonly prescribed antibiotics are inappropriately used in therapy of acute pharyngitis, although an overwhelming majority of URIs are of viral origin.

Further studies about patterns of bacterial resistance to antibiotics and pharmacoeconomic aspect of pharmacotherapy are needed to estimate fully whether the prescription of antibiotics is rational or not. Additional continuing education of physicians and pharmacist from independent sources should be organized and proper education should be provided to patients.

The obtained results will be the basis for further evaluation of the rationality of antibiotic use in primary healthcare.

References

1. Van Roosmalen MS, Braspenning JCC, De Smet PA, Groel RP. Antibiotic prescribing in primary care: first choice and restrictive prescribing are two different traits. *Qual Saf Health Care* 2007;16(2):105-9.
2. Parmar DM, Jadav SP, Shah BK. Can azithromycin be substituted for amoxy cillin in upper respiratory tract infections. *Indian J Pharm* 2007; 39(1):55-6.
3. Spurling GK, Del Mar CB, Dooley L, Foxlee R. Delayed antibiotics for symptoms and complications of respiratory infections. *Cochrane Database Syst Rev* 2007;(3):CD004417.
4. Mainous AG 3rd, Saxena S, Hueston WJ, Everett CJ, Majeed A. Ambulatory antibiotic prescribing for acute bronchitis and cough and hospital admissions for respiratory infections: time trends analysis. *J R Soc Med* 2006; 99(7):358-62.
5. Duborija-Kovačević N. Antibiotic prescribing of the Republic Health Insurance Fund of Montenegro in the period 2000-2004: Effects of drug utilization reform strategy. *Med Pregl* 2006; 59(5-6):235-40.
6. WHO. ATC index with DDDs. World Health Organization: World Health Organisation Collaborating Centre for Drug Statistics Methodology, 2003-2005. [accessed 2008 June 28]
Available from: <http://www.whocc.no/atcddd>
7. Stimac D, Vukušić I, Culig J. Outpatient use of systemic antibiotics in Croatia. *Pharm World Sci* 2005; 27(3):230-5.
8. Goossens H, Ferech M, Vander Stichele R, Elseviers M. ESAC Project Group. Outpatients antibiotic use in Europe and association with resistance: a cross-national database study. *Lancet* 2005; 36:579-87.
9. Rutschmann OT, Domino ME. Antibiotics for Upper Respiratory Tract Infections in Ambulatory practice in United States, 1997-1999: Does Physician Specialty Matter. *J Fam Pract* 2004;17:196-200.
10. Akkerman AE, Kuyvenhoven MM, van der Wouden JC, Verheij TJ. Determinants of antibiotic overprescribing in respiratory tract infections in general practice. *J Antimicrob Chemother* 2005; 56(5):930-6.
11. Akkerman AE, van der Wouden JC, Kuyvenhoven MM, Dieleman JP, Verheij TJ. Antibiotic prescribing for respiratory tract infections in Dutch primary care *J Antimicrob Chemother* 2004; 54(6):1116-21.
12. Goossens H. Antibiotic consumption and link to resistance. *Clin Microbiol Infect* 2009;15(3):12-15.
13. Gonzales R, Steiner JF, Sande MA. Antibiotic prescribing for adults with colds, upper respiratory tract infections, and bronchitis by ambulatory care physicians *JAMA* 1997; 278(11):1-8.

14. Butler CC, Hood K, Verheij T, Little P, Melbye H, Nuttall J, Kelly MJ, Mölsted S, Godycki-Cwirko M, Almirall J, Torres A, Gillespie D, Rautakorpi U, Coenen S, Goossens H. Variation in antibiotic prescribing and its impact on recovery in patients with acute cough in primary care: prospective study in 13 countries. *BMJ* 2009; 338:b2242.
15. Ferech M, Coenen S, Malhotra-Kumar S, Dvorakova K, Hendrickx E, Suetens C, Goossens H; ESAC Project Group. European Surveillance of Antimicrobial Consumption (ESAC): outpatient antibiotic use in Europe. *J Antimicrob Chemother* 2006; 58(2):401-7.
16. Coenen S, Muller A, Adriaenssens N, Vankerckhoven V, Hendrickx E, Goossens H, ESAC Project Group. European Surveillance of Antimicrobial Consumption (ESAC): outpatient parenteral antibiotic treatment in Europe. *J Antimicrob Chemother* 2009; 64(1):200-5.
17. Wierzbowski AK, Hoban DJ, Hisanaga T, DeCorby M, Zhanel GG. The use of macrolides in treatment of upper respiratory tract infections. *Curr Allergy Asthma Rep* 2006; 6(2):171-81.
18. Ranji SR, Steinman MA, Shojania KG, Gonzales R. Interventions to reduce unnecessary antibiotic prescribing: a systematic review and quantitative analysis. *Med Care* 2008; 46(8):847-62.
19. Smeets HM, Kuyvenhoven MM, Akkerman AE, Weschen I, Schouten GP, van Essen GA, Verheij TJ. Intervention with educational outreach at large scale to reduce antibiotics for respiratory tract infections: a controlled before and after study. *Fam Pract* 2009; 26(3):183-7.
20. Metz-Gercek S, Maieron A, Strauss R, Weininger P, Apfalter P, Mittermayer H. Ten years of antibiotic consumption in ambulatory care: trends in prescribing practice and antibiotic resistance in Austria. *BMC Infect Dis* 2009; 13(9):61-5.

UPOTREBA ANTIBIOTIKA U PRIMARNOJ ZDRAVSTVENOJ ZAŠTITI U NIŠKOM REGIONU

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Sažetak

Analiza potrošnje antimikrobnih lekova, na osnovu broja propisanih recepata, predstavlja osnovu za procenu racionalnosti terapije. Infekcije gornjeg respiratornog trakta (GRTi) su najčešća indikacija za propisivanje antibiotika u primarnoj zdravstvenoj zaštiti. Cilj našeg rada bio je analiza potrošnje antibiotika u primarnoj zdravstvenoj zaštiti niškog regiona, posebno u lečenju GRTi. Na osnovu broja propisanih recepata u ambulantnim uslovima, korišćenjem *Anatomical Therapeutic Chemical/Defined Daily Dose* metodologije, analizirali smo propisivanje antibiotika u niškom regionu tokom perioda 2005-2007. godine i dobijene rezultate izrazili kao broj definisanih dnevnih doza (DDD)/1000 stanovnika/dan. Studija je retrospektivna, zasnovana na podacima dobijenim iz Centralne apoteke grada Niša. Utvrđen je porast propisivanja antibiotika za 9.02% (22.83/ 25.96 DDD) u ispitivanom periodu. Najčešće propisivani antibiotici su: polusintetski penicilini i makrolidi. Najveći porast u propisivanju antibiotika zabeležen je kod azitromicina (0.26:0.70 DDD, 164%). Od ukupnog broja antimikrobnih lekova, za lečenje GRTi propisano je 70.5% recepata. Pharyngitis acuta je bila najčešća indikacija za propisivanje antimikrobnih lekova (45.26%). Amoksisicilin (33%) i cefaleksin (35%) su najčešće propisivani antibiotici za navedenu indikaciju. Ukupan broj propisanih antibiotika je povećan za 14%, dok su finansijski izdaci za antibiotike porasli za 28% u poređenju sa 2005. godinom. Ova analiza pokazuje neracionalnu upotrebu antibiotika u primarnoj zdravstvenoj zaštiti u niškom regionu, što zahteva dodatnu primenu edukativnih programa i praćenje mikrobiološke osetljivosti. Dobijeni rezultati biće osnova za dalju procenu racionalnosti upotrebe antibiotika u primarnoj zdravstvenoj zaštiti.

Ključne reči: antibiotici, ambulantni bolesnici, definisana dnevna doza, upotreba lekova