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Source / Izvornik: **Collegium Antropologicum, 2013, 37, 449 - 454**

Journal article, Published version
Rad u časopisu, Objavljena verzija rada (izdavačev PDF)

Permanent link / Trajna poveznica: https://urn.nsk.hr/urn:nbn:hr:105:851145

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Download date / Datum preuzimanja: **2025-03-20**

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Coll. Antropol. **37** (2013) 2: 449–454
Original scientific paper

Antibiotic Prescription Rate for Upper Respiratory Tract Infections and Risks for Unnecessary Prescription in Croatia

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A B S T R A C T

*Overprescribing of antibiotics in primary care has been recognized as public health problem. We investigated visits prescription rate of antibiotics to patients with upper respiratory tract infections (URTI) and unnecessary prescribtion for tonsillopharyngitis, in Croatia. In prospective observational **s**tudy in November 2007. 25 GPs in Croatia recorded all patients' visits with URTI episode according ICPC-2. Clinical status of patients with tonsillopharyngitis were categorized according to Centor Criteria. 689 visits were analysed, 82% of visits were initial. Antibiotics were prescribed in 44.7% visits with URTI. There were no significant differences in antibiotic prescription rates regarding non–clinical factors. Antibiotics were prescribed to patients with tonsillopharyngitis in 62.2% visits. Unnecessary antibiotics were prescribed (Centor 1,2) in 49.6% visits with tonsillopharyngitis. Logistic regression analysis showed significant differences in unnecessary antibiotic prescription rates only with respect to the workday – Wednesday, CI (1.117–2.671), p=0.0139. Leading antibiotic was amoxicillin + clavulonic acid, second was amoxicillin, the third were macrolides, the fourth was narrow spectrum penicillin and fifth were cephalosporins. This study shows over prescription for URTI. Unnecessary prescription for tonsillopharyngitis depend on non clinical factor – day of the week. This should be futher explored and help to improved prescribe antibiotics.*

***Key words**: antibiotics prescribing rate, unnecessary prescription, upper respiratory tract infections, general practitioners, Croatia*

Introduction

About 80% of all antibiotics for systemic use are prescribed in primary care. One half to two-thirds of these are prescribed for respiratory tract infections (RTI)[1–3]. Most patients with upper respiratory tract infections (URTI) have a mild viral or bacterial inflammation which are self-limiting, last 3–7 days, and do not require antibiotic treatment, only supportive care. Antibiotic treatment benefits mostly patients with A beta-hemolytic streptococcus infections (GABHS), which causes acute pharyngitis and tonsillitis in approximately 5–10% adults[4–6].

Over prescription of antibiotics for URTI has been recognized as a public health problem because it leads to increased risk of resistance to antibiotics[1–3]. In European countries there are high differences in prescription of antibiotics to outpatients[3,4]. Croatia was at 8th position among 32 countries in European Surveillance of Antibiotic Consumption (ESAC) (1997–2002) regarding defined daily doses per thousand inhabitants daily (DDD/TID)[1,2,7–10].

In Croatia 94% of antibiotics are prescribed to outpatients[7,8,10]. In Croatian study from 2000 antibotics was

Received for publication October 20, 2010

prescribed in 72.1% cases of pharyngitis[11]. In region (Niš, Serbia) the majority of antibiotics (70.5 %) in primary care were prescribed to patients with URTI (2005–2007)[12]. However, in Slovenia decrease in outpatient antibiotic consumption (18.6%) was noted in the period 1999–2002[13].

General practitioners (GP) report that they often prescribe unnecessary antibiotics because they think patients will be dissatisfied without a prescription and will reconsult if antibiotics are not prescribed[4,14,15]. Physicians also decide to prescribe antibiotics because of comorbidities, fear of further complications, in pressured socioeconomic contexts or patient's lifestyle, to working people[15,17,19]. Some studies found that antibiotics are mostly prescribed to certain age groups[16–18] and others show that antibiotics are mostly prescribed for pharyngitis, tonsillitis and sinusitis[18,19].

In Croatia in the year 2004 for a population of 4.38 million people primary health care was provided by 2.419 GP, one half had a specialist training in general practice/family medicine. The average size of a general practitioner's list in 2004 was 1784 patients, who each had on average 5.9 consultations per year[7]. GPs provide routine primary care on weekdays and emergency or urgent care provide it at night and at weekends. Antibiotics can be prescribed to outpatients only by primary care and emergency care doctors[7].

Our hypothesis was that there is over prescription of antibiotics for URTI by GPs in Croatia. Because most URTI are resolved without antibiotics, prescription rates for this indication in primary care could be reduced.

Change in prescribing routine will be successful when based on a proper understanding of over-prescription of antibiotics for URTI in general practice. Therefore, the aim of the study was to find out the antibiotic prescribing rates per visit to patients with URTI episode and to establish which factors influence for unnecessary prescriptions.

Material and Methods

Setting and population

The present study was conducted in 2007 as a part of the planned activities of the Interdisciplinary Section for Antibiotic Resistance Control (ISKRA). ISKRA was founded by the Croatian Ministry of Health and Social Welfare within the framework of Matra Project (MAT 05/HR/9/2) with the aim of rationalizing antibiotic prescribing[21,22].

The study was conducted by GPs from all Medical Centres in Croatia, who were asked by Croatian Ministry of Health and Social Welfare to participate in the ISKRA study[21,22]. 51 GPs agreed to take part in the research and were given questionnaire and instructions via post or e-mail. When required, the board of researchers also conducted consultations via telephone on how to collect data. 25 GPs (18 women and 7 male, aged 37 to 64), which is 49.0%, completed the study. Their period of practice with the same population was 5 to 35 years and the total number of patients in their lists was 41 780. Study period was two weeks in November 2007, the time when common cold starts and before flu vaccination.

GPs recorded all visits with URTI episode during the study period. The following data were collected: day of the week, type of visit (initial or follow-up), patient age and sex, employment status. The URTI symptoms which were presented were recorded using ICPC-2 code: chills (A02), fever (A03), weakness (A04), feeling ill (A05), headache (R01), cough (R05), nose symptom (R08), throat symptom (R21), voice symptom (R23), abnormal sputum (R25), and earache (H01)[23]. GPs registered the duration of URTI symptoms in days prior to the consultation, and clinical status of the throat, nose, paranasal sinuses, lymph nodes, and ear (if examined). The prescription and type of antibiotic were recorded..

The URTI episodes where patients had comorbid lower respiratory tract infection, such as bronchitis, asthma, chronic obstructive pulmonary disease or pneumonia, were excluded from the analysis.

From patients with URTI we selected those with tonsillopharyngitis. Two independent investigators divided them on the basis of their recorded symptoms and clinical status in four groups according to Centor Criteria[24–27]. Centor Criteria for prediction of pharyngitis caused by GABHS include: temperature >38 °C or history of fever; absence of cough; swollen and tender anterior cervical nodes; and tonsillar swelling or exudate with redness of the pharynx and tonsils. The presence of three or four Centor Criteria (Centor 3,4) indicates a positive predictive value of 40–60% for GABHS, whereas the absence of three or four (Centor 1,2) has a negative predictive value of approximately 80% for GABHS. Some guidelines recommend prescription of antibiotics to patients with Centor 3,4 without the previous confirmation of GABHS pharyngitis by using GABHS rapid diagnostic test. In patients with Centor 1,2 only symptomatic therapy is recommended[13,22,24,25].

Statistics

Descriptive statistics was used to present the data. When there was more than one visit for the same URTI episode, each visit was analyzed separately. For analysis of different categories of visits/patients attributes and prescription/non-prescription of antibiotics the χ^2-test was applied. The most frequent categories of visits/patients attributes were selected as independent binary variables as predictors for unnecessary prescription of antibiotics in the logistic regression analysis. The level of statistical significance was set at $p<0.005$. All statistical analyses were performed with SAS (SAS Institute Inc. Cary. NC. USA).

Results

GPs recorded 756 visits for URTI episodes in the study period out of which 67 were excluded due to con-

comitant lower respiratory tract infection, so that 689 visits were analyzed. Patients were aged between 3 and 75 and the majority were female 398 (57.7%). Most visits were initial 569 (82%), and the rest were follow-up (Table 1). Among the follow-up visits (120), 78 (65.2%) initial visits were paid to the chosen GP, 15 (12.5%) to another GP, 14 (12.0%) to an emergency department, and 2 (6.3%) to a secondary health care institution. The most frequent URTI symptoms were presented as follows: throat symptoms (R21) (N=485), cough (R05) (N=380), fever (A03) (N=305), nose symptoms (R08) (N=290), general weakness (A04) (N=175), and headache (R01) (N=175). The symptoms were present for up to two days prior to the consultation in 38.2% of visits, up to five days in 39.5% of visits, and more than six days in 21.9% of visits.

Antibiotics for URTI were prescribed in 308 (44.7%) out of 689 visits (Table 1). There were no significant differences in antibiotic prescription rates with respect to patient age (p=0.533), sex (p=0.586), to initial and follow-up visits (p=0.323), with respect to visits by the day of the week (p=0.091), with respect to the employment status (p=0.078).

Tonsillopharyngitis was diagnosed in 442 out of 689 visits with URTI on the basis of patient's clinical status according to the Centor Criteria. Centor 4 was present in 11.3% visits and Centor 3 was present in 27.6% visits. Centor 1,2 were present in 61.0% visits. Antibiotics were prescribed in 275 (62.2%) out of 442 visits for tonsillopharyngitis. Antibiotics were prescribed in 81.9% visits for Centor 3,4 and in 49.6% visits for Centor 1,2 (Table 2). We found significant differences in antibiotic prescription rates with respect to Centor 3,4 in contrast to Centor 1,2 (p<0.001) (Table 2).

Antibiotics were unnecessarily prescribed for Centor 1,2 in 134 (49.6%) out of 270 visits (Table 2). For Centor 1,2 antibiotics were unnecessarily prescribed more often when symptoms persisted 3–5 days prior to the consultation 51 (38.1%) and also for employed patients 39 (78.0%), for age group 21 to 45 in 50 (37.3%). GPs decided to prescribe antibiotics more often during the mid-

TABLE 1
ANTIBIOTIC VISITS PRESCRIPTION RATE FOR UPPER RESPIRATORY TRACT INFECTION (URTI) IN GENERAL PRACTICE IN CROATIA

	No. of visits for URTI	No. (%) of visits antibiotic prescriptions for URTI	p*
No. of visits	689	308 (44.7)	
Patient age (years):			
<6	61	23 (37.7)	
6–20	206	86 (41.7)	
21–45	224	105 (46.9)	0.533
46–70	147	72 (48.9)	
>70	51	22 (43.1)	
Patient sex:			
men	291	127 (43.6)	0.586
women	398	181 (45.4)	
Type of URTI visit:			
initial	569	244 (42.8)	0.323
follow-up	120	64 (53.3)	
Visit by the day of the week:			
Monday	149	63 (42.2)	
Tuesday	138	60 (43.5)	
Wednesday	141	68 (48.2)	0.091
Thursday	145	56 (38.6)	
Friday	116	61 (52.5)	
Employment:			
Children and school age	168	88 (52.3)	
Employed	246	126 (51.2)	0.078
Unemployed	273	100 (36.6)	

*χ^2-test, Statistically significant p<0.005; There were no significant differences in antibiotic prescription rates for URTI with respect to non-clinical factors

TABLE 2
ANTIBIOTIC VISITS PRESCRIPTION RATE FOR TONSILLOPHARYNGITIS, ACCORDING CENTOR CRITERIA

	No. (%) of visits for tonsillopharyngitis, according Centor Criteria	No. (%) of visits antibiotic prescriptions for tonsillopharyngitis, according Centor Criteria	p*
No. of visits for tonsillopharyngitis	442	275 (62.2)	
Centor Criteria			
1	136 (30.7)	56 (41.1)	
2	134 (30.3)	78 (58.2)	<0.001
3	122 (27.6)	100 (87.9)	
4	50 (11.3)	41 (82.0)	
Centor 1,2	270 (61.0)	134 (49.6)	
Centor 3,4	172 (38.9)	141 (81.9)	<0.001

*χ^2-test, Statistically significant p<0.005; Significant differences in antibiotic prescription rates were found with respect to clinical entity tonsillopharyngitis Centor 3, 4 in contrast to Centor 1,2

TABLE 3
LOGISTIC REGRESSION ANALYSIS OF THE MOST FREQUENT CATEGORIES OF VISITS/PATIENTS ATTRIBUTES FOR UNNECESSARY PRESCRIPTION OF ANTIBIOTICS FOR TONSILOPHARYNGITIS

Visits / patients attributes	OR	95 % CI	p
Age	1.137	0.708–1.824	0.5955
Employment	1.199	0.754–1.907	0.4429
First visits	0.977	0.643–1.484	0.9118
Week day	1.727	1.117–2.671	0.0139
Duration symptoms	0.923	0.624–1.365	0.6891

Logistic regression analysis showed significant differences in unnecessary antibiotic prescription rates for tonsillopharyngitis only with respect to the day of the week (Wednesday) CI (1.117–2.671), p=0.0139.

dle of the week-Wednesday 38 (28.4%). Perceived frequency inside groups was analysed by logistic regression analysis and significant difference in unnecessary antibiotic prescription rates for tonsillopharyngitis was found only with respect to the day of the week-Wednesday (p=0.0139) (Table 3).

Leading antibiotic to patients with URTI was amoxicillin + clavulonic acid in 78 (2.3%), out of 308, second was amoxicillin in 75 (24.3%), out of 308, followed by macrolides 68 (22.0%), narrow spectrum penicillin 36 (11.6%) and I,II,III generations of cephalosporins 31 (10.1%). The rest (6.4%) were sulfonamides and tetracyclines.

Discussion

Main finding of the study

In our study 82% of visits to chosen GP for URTI were initial and only one. Among follow up visits 120 (12.0%) initial visits were paid to the emergency units. Antibiotics were prescribed in 44.7% visits to patients with URTI and in 62.2% visits to patients with tonsillopharyngitis.Unnecessarily prescribed antibiotics to patients with tonsillopharyngitis (Centor 1,2) were found in 134 (49.6%) out of 270 visits.

Logistic regression analysis showed significant differences in unnecessary antibiotic prescription rates for tonsillopharyngitis only with respect to the day in the working week (Wednesday) CI (1.117–2.671, p=0.0139).

Leading antibiotics to patients with URTI was amoxicillin + clavulonic acid, second was amoxicillin, on the third place were macrolides, on the fourth was narrow spectrum penicillin and fifth were cephalosporins.

In literature antibiotic prescribing rates per visit to patients with URTI episode varied from 16% and 21% (Dutch, 2000, 2001)[17,19], 45% for RTI (Sweden 1999–2005)[28–30], 46% for RTI (USA 1999)[31], 72.1% for tonsillopharyngitis (Croatia 2000)[11], 70.5% for URTI (Serbia 2005–2007)[12], 65.6% for tonsillopharyngitis (Bosnia – Mostar 2005–2006)[20].

According to our study, patients who visited their chosen GP had one initial visit for URTI episodes in 82% visits compared to 90% to 95% in literature [5,20]. In our study most follow up visits may be due to administrative reasons (school children and working people who need sick leave note) or GPs' insistence on another check up.

Interestingly, among the follow-up visits (120), 14 (12.0%) initial visits were paid to emergency department. However, we do not know how many patients asked for help only in emergency units and how many antibiotics they were prescribed without ever visiting their GP[7]. It is well known that patients visit emergency units for infectious diseases more often during the weekend[28,30].

Most visits were paid in the phase of URTI episode, i.e., within the first two to five days. This may be due to the fact that in most cases URTI symptoms last 3–7 days or because patients might fear complications[3–5]. Also, patients with URTI and chronic conditions seek medical help earlier than other patients[17,19].

We did not find significant difference in antibiotic prescription rate for URTI in respect to non-clinical factors by bivarite analysis. Previous research has shown considerable variation in prescribing antibiotics attributable to non-clinical factors[14–20].

In our study distribution of Centor Criteria to patients with tonsillopharyngitis are in accordance with previous findings reporting that 10–18% patients with tonsillopharyngitis have Centor 4[5,24–27].

Patients with tonsillopharyngitis meeting Centor 3,4 were prescribed antibiotics significantly more often than patients with only Centor 1,2. However, according to this methodology GPs decided to prescribe unnecessary antibiotics in the presence Centor 1,2 in 48.7% visits. Our results show significant unnecessary antibiotic prescription in mid week, to be more precise, on Wednesdays. These results cannot be explained by morbidity itself.

Why does a GP prescribe unnecessary antibiotics for tonsillopharyngitis depending on the day of the week – Wednesdays?

In literature we found increased antibiotic prescription on Fridays in primary care and at the weekend in emergency units[32,33]. The prescription of antibiotics on Fridays was higher than on the other workdays because of smaller availability of GPs during the forthcoming weekend[14,25,32,33]. There was also seasonal fluctuation of antibiotic prescribing – peaks before Christmas and during influenza activity because influenza often leads to bacterial complications that require treatment[29].

A explanation or reasons for our results is that GP think that patients will be dissatisfied without a prescription and will reconsult in two days, which means on Friday. Other reason is that GP often prescribe unnecessary antibiotics due to their own work overload and insufficient time to spend with patients, this might depend on the day of the week and in this case it is Wednesdays[35,38]. The reasons should be further explored, which

may help to reduce unnecessary antibiotics prescriptions.

The choice of antibiotics is one of quality indicators for treatment URTI/ tonsillopharyngitis classified according ICPC-2: narrow-spectrum-penicillin, broad-spectrum penicillin+clavulonic acid, macrolides, cephalosporins[23,31,38–40]. In our study we found lower consumption of narrow spectrum penicillins which is a reflection of the shortage of these products on the Croatian market[38]. Therefore, the risk of resistance of microorganisms to broad-spectrum penicillin+clavulonic acid and, macrolides could be expected[38]. In Sweden of all prescribed antibiotics for RTI 60% were narrow spectrum penicillins[28,30] and in Norway 37%[41]. However, in our region broad-spectrum penicillin was antibiotic of first choice[9,12].

Intervention

ISKRA has been providing GP training in all regions since 2007, which includes lectures and distribution of published guidelines[21,22,38]. Results of this study will be sent to all GPs who participated in the research, and also will be present in next training[42–44]. Following the intervention research should be conducted on a larger scale and in the course of several seasons.

Conclusion

This study shows over prescription for URTI. Unnecessary prescription for tonsillopharyngitis depend on non clinical factor – day of the week. This should be futher explored and help to improved prescribe antibiotics.

Limitations of the Study

This study was relatively simple to conduct during two weeks before expected peak of common cold and flu vacctination and it entailed small extra workload for the participants[28,29].

In our research we did not use GP electronic records as a source of data. Our results were based on the data on URTI episodes prospectively collected and recorded by 25 GPs according to the ICPC-2 during the visits. Due to GPs work overload and insufficient time to spend with patients, all URTI visits may not have been recorded. However, these limitations are also present in other similar studies[17].

Acknowledgements

We thank the GPs who voluntarily participated in this study and recorded all consultations of patients with URTI in the study period.

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STOPA PROPISIVANJA ANTIBIOTIKA ZA INFEKCIJE GORNJEG DIŠNOG TRAKTA I RIZICI ZA NEPOTREBNO PROPISIVANJE ANTIBIOTIKA U HRVATSKOJ

S A Ž E T A K

Povećano propisivanje antibiotika u primarnoj zaštiti je prepoznato kao javno zdravstveni problem jer dovodi do povećanja rezistencije na antibiotike. Istražili smo propisivanje antibiotika po posjetu liječniku opće medicine u tijeku episode bolesti infekcija gornjeg respiratornog trakta (IGRT). Potom smo istražili nepotrebno propisivanje antibiotika pacijentima s tanzilofaringitisom u općoj medicini u Hrvatskoj. Studija je bila prospektivna, a provedena je u studenom 2007. godine. 25 liječnika opće medicine bilježili su sve posjete pacijenata s epizodom bolesti – IGRT prema ICPC-2. Klinički status pacijenata s epizodom tonzilofaringitisa određen je prema Centor Criteria klasifikaciji. Analizirano je 689 posjeta, od čega su 82% bili prvi posjeti. Antibiotici su propisani u 44,7% posjeta pacijentima sa IGRT. Nismo našli statistički značajnu razliku u propisivanju antibiotika prema nekliničkim čimbenicima za pacijente s IGRT. Antibiotici su propisani u 62,2% posjeta pacijentima sa tonzilofaringitisom. Za klinički status tonzilofaringitisa Centor 1 i 2, u 49,6% posjeta nepotrebno su propisani antibiotici. Logistička regresijska analiza pokazuje značajnost razlike za nepotrebno propisivanje za dane u tjednu – srijeda, CI (1,117–2,671), p=0,0139. Od propisanih antibiotika na prvom je mjestu amoksicilin + klavulonska kiselina, na drugom amoksicilin, na trećem mjestu su makrolidi, na četvrtom usko spektralni penicilini, a na petomu cefalosporini. Studija pokazuje povećano propisivanje antibiotika za IGRT u Hrvatskoj. Nepotrebno propisivanje za pacijente s tonzilofaringitisom ovisi o nekliničkim čimbenicima, dan u tjednu – srijeda. Nalaz će se istražiti u sljedećim studijama s ciljem smanjenja propisivanja antibiotika u općoj medicini.