



Inappropriate prescribing of antibiotics to the patients with acute bronchitis

Neadekvatno propisivanje antibiotika bolesnicima sa akutnim bronhitisom

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Abstract

Background/Aim. Inappropriate prescribing of antibiotics to the patients with acute bronchitis is frequent event in clinical practice with potentially serious consequences, although majority of treatment guidelines do not recommend it. The aim of this study was to reveal risk factors associated with inappropriate prescribing of antibiotics to the patients with acute bronchitis in primary healthcare. **Methods.** This case/control study included the adult patients with acute bronchitis during the initial encounter with a general practitioner. Prescription of an antibiotic was an event that defined the case, and patients without prescribed antibiotic served as controls. **Results.** Antibiotics (mostly macrolides and beta-lactams) were prescribed to the majority of patients with diagnosis of acute bronchitis (78.5%). A significant association was found between antibiotic prescription rates and patient age, whether an attending physician is a specialist or not and the average number of patients a physician sees per day [OR_{adjusted} was 1.029 (1.007–1.052), 0.347 (0.147–0.818) and 0.957 (0.923–0.992), respectively]. **Conclusion.** When there is primary care encounter with patients suffering from acute bronchitis, older patients are more likely to receive inappropriate antibiotic prescription, especially if their physician is without specialist training and has less patient encounters in his/her office daily.

Key words:

bronchitis; anti-bacterial agents; risk factors; comorbidity; medication errors; serbia.

Apstrakt

Uvod/Cilj. Neadekvatno propisivanje antibiotika bolesnicima sa akutnim bronhitisom česta je pojava u kliničkoj praksi, sa potencijalno ozbiljnim posledicama, iako većina vodiča za lečenje akutnog bronhitisa to ne preporučuje. Cilj naše studije bio je da se doprinese postojećim saznanjima o neodgovarajućem propisivanju antibiotika. **Metode.** Ova studija tipa slučaj/kontrola uključivala je odrasle bolesnike sa akutnim bronhitisom tokom prvog susreta sa lekarom opšte prakse. Propisivanje antibiotika je definisalo slučajeve, a bolesnici bez propisanog antibiotika služili su kao kontrola. **Rezultati.** Antibiotici (uglavnom makrolidi i beta-laktami) bili su propisani većini bolesnika sa dijagnozom akutnog bronhitisa (78,5%). Uočena je značajna povezanost između propisivanja antibiotika i starosti bolesnika, između propisivanja antibiotika i toga da li je lekar specijalista ili ne, kao i između propisivanja antibiotika i prosečnog broj bolesnika koje lekar pregleda tokom dana. Prilagođeni odnos šansi bio je [1,029 (1,007–1,052), 0,347 (0,147–0,818) i 0,957 (0,923–0,992), respektivno]. **Zaključak.** Prilikom prvog susreta bolesnika sa dijagnozom akutnog bronhitisa veću šansu da im antibiotik bude neadekvatno propisan imaju stariji bolesnici, posebno ako lekar nije specijalista i ako ima manji prosečan broj bolesnika u svojoj ordinaciji tokom dana.

Ključne reči:

bronhitis; antibiotici; faktori rizika; komorbiditet; lečenje, greške; srbija.

Introduction

Inappropriate antibiotic prescribing has been recognized as an important public health problem worldwide¹, because it contributes to development of antimicrobial resistance². According to the World Health Organization (WHO), inap-

propriate drug prescribing is denoted by unnecessary prescribing (overprescribing), omission, wrong selection of antibiotic, wrong dosage, incorrect duration of treatment, unnecessary expenses and unnecessary risk³. Any prescription event should be in accordance with the available evidence-based guidelines. A recent large cross-sectional survey con-

ducted in the United States found that 30% of outpatients oral antibiotic prescriptions, regardless of indications, could have been inappropriate, and for acute respiratory infections up to 50% of prescribed antibiotics could have been unnecessary⁴. Among the acute respiratory tract infections, the highest percentage of inappropriate antibiotic prescribing occurs in the adult patients with acute bronchitis⁴; one of the studies found that almost 80% of these patients had antibiotics prescribed, but inappropriateness rate was 100%⁵.

Acute bronchitis is a self-limiting inflammation of the large airways – bronchi, accompanied by a cough (productive or not) which can last up to 6 weeks, with absence of tachycardia, tachypnea, fever and abnormal findings on the chest examination⁶. In most cases, acute bronchitis is a viral infection. The most recent recommendations by the American College of Physicians state that antibiotic therapy should not be initiated in the patients with acute bronchitis, unless pneumonia is suspected⁶. Other available evidence-based guidelines also do not recommend prescription of antibiotics for acute bronchitis^{7,8}. A trend of increased adverse events rate in the acute bronchitis patients treated with antibiotics was found in a systematic review of 17 randomized clinical trials⁸.

Recent studies have shown that many factors may have an influence on inappropriate prescription of antibiotics⁹. These factors include a patient's history (comorbidities, age), clinical experience of physicians and a type of specialization¹⁰. Socio-economic factors, closely related to aspects such as the healthcare funding and reimbursement, number of generic drugs on the market and availability of diagnostic tests were also recognized as important². Some of the studies also showed relevance of patient's demand and satisfaction, doctor's unwillingness to accept uncertainty and risks and fear of complications^{9,11}. Findings from a cross-national study which included the data on prescription of antibiotics in primary care in 26 European countries demonstrated a significant correlation between antibiotic resistance and outpatient antibiotic use¹². Rational use of antibiotics is necessary in order to preserve their effectiveness in circumstances of growing antimicrobial resistance¹.

Despite the relevance of this problem, many issues in regard to the factors influencing inappropriate prescribing of antibiotics to the patients with acute bronchitis remain unresolved. The aim of this study was to reveal risk factors associated with inappropriate prescribing of antibiotics to the patients with acute bronchitis in primary healthcare.

Methods

The study included the adult patients with acute bronchitis (the code J20 according to the International Classification of Diseases, 10th version: ICD-10) during the initial encounter with a general practitioner at the Primary Health Care Centers at three cities in the Republic of Serbia (Kragujevac, Novi Pazar and Šabac) and one city in Republic of Montenegro (Bijelo Polje). The patients were treated at the Primary Health Care Centers during the year 2016.

This study was designed as an analytical, clinical observational, case/control study. There were two groups in the

study: the group of cases, who were prescribed an antibiotic at the initial encounter, and the group of controls, who were treated without an antibiotic. The data were collected from the patient files and the personal files of physicians employed at the Primary Health Care Centers. In each of the four cities the offices of Primary Health Centers already designated with number 1 or as “the first” were included in the study. The patients were enrolled consecutively, as their files were found in a patient registry of the health facilities where the study took place, starting from the index date of the study: January the 1st, 2016. Based on expected power of the study of at least 0.8, and on probability of type I error of maximum 0.05, the sample size was set on 200 patients. Further collection of data on the study sites was terminated after the target of 200 patients was reached. The last patient who entered the study was treated due to acute bronchitis on November the 17th, 2016. The study was approved by the local Ethics Committee (decision No 01-569/2, 26.01.2017.).

Inclusion criteria for the study patients were: both genders 18–70 years of age, diagnosis of acute bronchitis (ICD-10 code J20) established by a general practitioner and good general condition. The exclusion criteria were as the following: tachycardia (heart rate above 100 beats per minute), tachypnea (respiration rate above 24 per minute), fever above 38°C, abnormal respiratory sounds, age below 18 or above 70 years, chronic obstructive pulmonary disease – COPD, the patients undergoing chemotherapy or taking immunosuppressant, patients with asplenia, patients with hematological malignancy and pregnant or lactating women.

The following data were extracted from the patient or personal files: educational level of prescribers (general practitioner or specialist of general medicine); working experience in years; duration of employment at the study site; average number of patient encounters per physician per day; patients' gender; age; employment status of patients; the number of times the patients visited a physician in 2016; the Charlson Comorbidity Index; a patient being hypertensive or not; concomitant therapy: ACE inhibitors, diuretics, beta blockers, statins, other cardiovascular drugs, antidepressants, antipsychotics, sedatives, anticonvulsants or anticoagulants.

The study data were analyzed by the descriptive statistics and presented in tables. Mean was used as a measure of central tendency and standard deviation as a measure of dispersion for continuous variables. The values of categorical variables were presented as rates or percentages. After checking the normality of the data distribution for the continuous variables (Kolmogorov-Smirnov test), an appropriate parametric or nonparametric tests were applied (Student's *t*-test for independent samples or Mann-Whitney *U* test). Significance of differences in the rates of categorical variables' values were tested by the χ^2 test, or in case of low prevalence of particular categories by the Fisher's test. Null hypothesis was considered to be true if probability of difference was less than 0.05. An influence of potential risk factors on inappropriate prescribing of antibiotics was evaluated by the univariate and multivariate binary logistic regression analysis. The results were shown as crude and adjusted odds ratios (ORs) with corresponding 95% confidence intervals (CI). All

calculations were performed by the statistical program for social sciences (SPSS version 18).

Results

The study included 200 patients with acute bronchitis. There were 157 patients to whom antibiotics were prescribed (cases). The most common prescribed class of antibiotics were macrolides [66 (42.1%) patients], followed by beta lac-

tam antibiotics [52 (33.1%) patients] and beta lactam antibiotics with beta-lactamase inhibitor [15 (9.5%) patients]. Baseline characteristics of cases and controls are shown in Table 1. Significant differences between cases and controls were observed in the following features: the patients who got an antibiotic prescription were older ($p = 0.012$), had higher Charlson Comorbidity Index ($p = 0.044$) and were treated by an attending physician who did not have a specialization ($p = 0.032$).

Table 1

Baseline characteristics of cases and controls

Variable	Cases (n = 157)	Controls (n = 43)	Test value and significance of null hypothesis
Age of the patient (years), mean \pm SD	49.4 \pm 16.7	42.1 \pm 16.6	$U = 2528.5$ $p = 0.012^*$
Gender of the patient, n (%)			
female	90 (57.3)	27 (62.8)	$\chi^2 = 0.221$
male	67 (42.7)	16 (37.2)	$p = 0.638$
Employment status of the patient, n (%)			
unemployed	30 (20.3)	14 (32.6)	$\chi^2 = 5.385$
employed	61 (41.2)	20 (46.5)	$p = 0.068$
retired	57 (38.5)	9 (20.9)	
Number of the patient's visits to the doctor in the previous 12 months, mean \pm SD	8.3 \pm 5.7	7.3 \pm 6.1	$U = 2933.5$ $p = 0.187$
Hypertension, n (%)	74 (47.1)	14 (32.6)	$\chi^2 = 2.349$ $p = 0.125$
Charlson Comorbidity Index	1.2 \pm 1.5	0.9 \pm 1.8	$U = 2741.5$ $p = 0.044^*$
Chronic drug therapy [†] , n (%)	98 (62.4)	22 (51.2)	$\chi^2 = 1.344$ $p = 0.246$
The data about prescribers			
Age of the attending physician (years), mean \pm SD	49.8 \pm 6.9	49.6 \pm 6.4	$U = 3120.0$ $p = 0.445$
Gender of the attending physician, n (%)			
female	152 (96.8)	42 (97.7)	$\chi^2 = 0.085$
male	5 (3.2)	1 (2.3)	$p = 0.770$
Physician is a specialist, n (%)	71 (45.2)	28 (65.1)	$\chi^2 = 4.578$ $p = 0.032^*$
Working experience of the physician (years), mean \pm SD	21.4 \pm 8.8	21.9 \pm 8.0	$U = 3369.0$ $p = 0.985$
Number of the patients who chose the attending physician, mean \pm SD	1,623.0 \pm 302.5	1,601.8 \pm 245.0	$U = 3374.0$ $p = 0.996$
Average number of the patients the physician sees <i>per</i> day, mean \pm SD	32.9 \pm 10.3	35.7 \pm 11.5	$U = 2781.5$ $p = 0.074$
Distribution of cases and controls according to the study site, n (%)			
Kragujevac	111 (71)	29 (68)	
Novi Pazar	17 (11)	3 (7)	$\chi^2 = 0.367$
Šabac	13 (8)	7 (16)	$p = 0.947$
BijeloPolje	16 (10)	4 (9)	
Total	157 (100)	43 (100)	

SD – standard deviation; * – statistically significant; [†] – any of the following: statin, anticoagulant, ACE inhibitor, diuretic, beta blocker, or other cardiovascular drug, antidepressant, antipsychotic, sedative, antiepileptic drug.

Table 2

Crude and adjusted odds ratios (OR) of the risk factors for antibiotic prescribing

Risk factors	Crude OR (95% CI)	<i>P</i>	Adjusted [#] OR (95% CI)	<i>P</i>
Age of the patient	1.026 (1.005–1.047)	0.013*	1.029 (1.007–1.052)	0.010*
Attending physician is a specialist	0.442 (0.219–0.892)	0.023*	0.347 (0.147–0.818)	0.016*
Average number of the patients the doctor sees per day	0.976 (0.946–1.008)	0.139	0.957 (0.923–0.992)	0.015*

– adjusted for age of the physician, attending physician is a specialist, working experience of the physician, average number of the patients a physician sees per day, number of the patients who chose the attending physician, age of the patient; CI – confidence interval; * – statistically significant.

Table 3

The interactions between significant risk factors for antibiotic prescribing

Risk factors	Crude OR (95% CI)	<i>P</i>	Adjusted [#] OR (95% CI)	<i>P</i>
Age of the patient and attending physician is a specialist	0.991 (0.979–1.003)	0.157	0.963 (0.920–1.009)	0.117
Age of the patient and average number of the patients a physician sees per day	1.000 (1.000 – 1.001)	0.297	1.004 (1.001–1.006)	0.004*
Attending physician is a specialist and average number of the patients a physician sees per day	0.975 (0.958–0.993)	0.007*	1.035 (0.952–1.127)	0.419

– adjusted for age of the physician, attending physician is a specialist, working experience of the physician, average number of the patients a physician sees per day, number of the patients who chose the attending physician, age of the patient; OR – odds ratio; CI – confidence interval; * – statistically significant.

The results of both univariate and multivariate stepwise backward conditional binary logistic regression from the last step with satisfactory goodness of fit (Cox & Snell R square 0.097, Nagelkerke R^2 0.149, Hosmer-Lemeshow χ^2 14.356, $df = 8$, $p = 0.073$) with adjustment for potential confounders are shown in the Table 2. The variables entered the multivariate analysis were: age of the attending physician, gender of the physician, a physician is a specialist, working experience of the physician, an average number of patients the physician sees per day, a number of patients who chose the attending physician, age of the patient, gender of the patient, a number of patient's visits to the physician in the previous 12 months and the Charlson Comorbidity Index. A statistically significant association with the inappropriate antibiotic prescribing was found for the following variables: age of the patient, physician is a specialist and an average number of the patients the physician sees per day. The older patients were more likely to get an antibiotic prescription, whereas the patients who were treated by a physician who was a specialist and who was seeing a larger number of the patients per day were less likely to get an antibiotic prescription.

The interactions between significant risk factors for getting an antibiotic prescription were investigated (Table 3). A significant interaction was observed between the age of the patient and the average number of patients the physician was seeing per day after the adjustment for potential confounders. The odds ratio for interaction between being treated by a

physician with specialization and the average number of patients the physician was seeing per day after adjustment dropped down and its confidence interval included 1, was no longer statistically significant ($p > 0.05$).

Discussion

The results of our study showed that physicians prescribe antibiotics to majority of patients with diagnosis of acute bronchitis (78.5 %). Macrolides were prescribed the most frequently, while beta-lactams were in the second place. A significant association was found between the antibiotic prescription rates and patient age, whether attending physician is specialist or not and average number of the patients a physician sees per day. Antibiotics were prescribed to the older patients more frequently. On the other hand, antibiotics were less often prescribed by the physicians who are specialists and who had a larger number of the patients per day.

Majority of guidelines for appropriate use of antibiotics suggest that antibiotics should not be prescribed to the patients with acute bronchitis at first encounter^{6,8}. Despite these recommendations, physicians continue to prescribe antibiotics to many patients with acute bronchitis¹³. The prescribing rate in our study is not discordant with other reports, where over 65% of patients with acute bronchitis received antibiotics^{10,14,15}. Macrolides are the most commonly pre-

scribed antibiotics to the patients with acute bronchitis, being either on the first¹⁶ or second place^{10,17,18} according to absolute volume of prescriptions, competing only with beta-lactams. This is not surprising, considering that these antibiotic groups are active against the majority of bacteria causing outpatient respiratory infections⁶. The probable reason for such behavior of prescribers could be fear of missing bacterial infection if abstaining from antibiotics and of consequent deterioration of patient condition which may be ascribed to the prescriber as neglect or professional mistake. The prescribers than could snatch at antibiotics to ensure treatment efficacy, counting on relatively low rate of adverse effects in this group of drugs.

The association between antibiotic prescribing and the age of patients with acute bronchitis (older patients are more likely to get an antibiotic prescription) found in our study was also reported by others^{16,19-21}. Kroening-Roche et al.²¹ showed that the patients being 50 and older had 1.7 times higher chance to receive antibiotic for acute bronchitis than younger patients. A reason for more frequent prescribing of antibiotics to elderly patients with acute bronchitis is a fear of misdiagnosis or complications like pneumonia, which has a high mortality rate in the elderly¹³. The elderly patients are also more expectant than the younger ones, which builds up the pressure on prescribers who may be tempted to satisfy their patients by “giving” them antibiotics. On the other hand, some of the studies showed that the employed patients are more likely to get an antibiotic prescription for acute bronchitis, because they make a pressure on a physicians believing wrongly that antibiotics would bring them back to their job sooner^{19,22,23}. This effect was not reproduced in our study, probably reflecting different attitude to job of workers in transitional countries, like Serbia.

Several studies showed that years of medical training are inversely related to the frequency of prescribing antibiotics to the patients with acute bronchitis. The residents less frequently prescribe antibiotic for acute upper respiratory tract infections than the physicians without specialization²⁴. Knowledge of primary care physicians in regard to treatment

of acute bronchitis could be better, as reported by Ackerman et al.²⁵ who found that 31% of physicians believed that prescribing antibiotics for acute bronchitis was a standard of care. Probably prolonged medical training brings deeper insight to the nature and appropriate treatment of the diseases which are frequently encountered in the general practice. Besides, it is more probable that the prescribers with a higher level of professional training are acquainted with current treatment guidelines, and therefore less likely to prescribe drugs inappropriately.

Inappropriate prescribing of antibiotics to the patients with acute bronchitis was reported to be more frequent if physicians had more patient encounters per day. It was explained by lack of time during the working hours, so it was easier a physician to prescribe an antibiotic than to explain to the patient why it was not necessary^{26,27}. In our study the opposite was found, probably because an average number of patients per day was lower than in previous studies, letting other factors get involved, i.e., knowledge and experience of the attending physicians. The rate of patient encounters per prescriber is actually a composite indicator, which could be interpreted only if all details of local settings are known. It could be an indicator of prescribers' work overload due to insufficient staffing, but also of quality of care an individual prescriber offers to the patients, as he or she will have more patients who want to be cared for than other physicians. The first interpretation is more likely in Serbian settings, as understaffing is a serious problem at all levels of healthcare during the last decade.

Conclusion

Inappropriate prescribing of antibiotics to the patients with acute bronchitis is frequent phenomenon, although it is contrary to the recommendations of current therapy guidelines. Older patients are more likely to receive inappropriate antibiotic prescription, especially if their physician is without specialist training and has less patient encounters in his/her office daily.

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