

Antibiotic prescribing patterns for sore throat infections in a university-based primary care clinic

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BACKGROUND: Recent studies reveal that a high percentage (over 50%) of episodes for URTIs are treated with antibiotics, regardless of appropriateness or the necessity for prescription. We identified antibiotic prescriptions in a primary health care centre (PHC) and evaluated their suitability for sore throat infections. We also explored whether symptoms, signs, diagnosis and antibiotics prescribed differed by gender.

PATIENTS AND METHODS: We collected data on all patients visiting the centre over a period of 12 weeks with a main complaint of sore throat who were prescribed antibiotics after taking a blood count and throat culture. Patients older than 16 years of age were included in the study irrespective of sex, nationality, marital status, occupation or location of residence. The chi square (χ^2) statistical test was used in comparing categorical variables. A *P* value of <0.05 was considered significant.

RESULTS: During the period of study, 579 patients with upper respiratory tract infections (URTIs) presented to the health centre, from which 339 patients with a sore throat were enrolled. Of the study group, 48.7% (165) were male and 51.3% (174) female, with the majority of patients being under 30 years old (54.3%). Throat cultures were positive in 56 patients (16.5%). Most of patients were diagnosed as having pharyngitis (22.7%), and the most frequently prescribed medicine was an oral penicillin (39.1%). Two hundred eight-six patients (84.4%) had 2 or fewer Centor criteria.

CONCLUSIONS: Throat cultures were positive in only 16.5% of the patients prescribed antibiotics. This indicates that physicians in the health centre of the university are prescribing antibiotics inappropriately and inconsistently. This also highlights the need for more prescriber education, especially as the range of medications available to the general practitioner for prescribing increases.

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Upper respiratory tract infections (URTIs) are a very common health problem, not only among patients attending primary health care (PHC) clinics, but also among individuals in the community. During the winter season in particular there is an increase in patients.^{1,2} A sore throat is one of the most common presenting symptoms in PHC clinics.³ The cost of prescribing for this condition is one of the most important factors in the worldwide rise in healthcare costs, both in resources and time.^{4,5} Recent studies reveal that a high percentage (over 50%) of episodes for URTIs are treated with antibiotics, regardless of appropriateness or the necessity for prescription.^{6,7} For instance, two-thirds of all antimicrobial drugs prescribed by Dutch PHC physicians are for the treatment of URTIs.⁵ However, only a minority of patients presenting with a sore throat appear to harbor Group A β -hemolytic streptococci (GABHS), including carriers,⁸ and it is known that antibiotics have no benefit in the treatment of viral URTIs. In Turkey, the antibiotic market is equivalent to approximately \$2.7 billion US per year,⁹ indicating an irrational use of antibiotics. There is a widely held belief, held by both physicians and patients, that the cost of an antibiotic relates to its effectiveness. Turkish patients can buy antibiotics over the counter from pharmacies.¹⁰ Thus, a large number of patients may be unnecessarily exposing themselves to the risk of overuse of antibiotics, as well as the development of resistance, while putting a concomitant drain on health budgets.^{11,12} Furthermore, use

of the broad-spectrum antibiotics ampicillin and amoxicillin is most prevalent even though penicillin and erythromycin are the most appropriate antibiotics for URTIs of bacterial origin.^{9,13,14} Patient demand for antimicrobials, often contrary to the doctor's assessment that no such need exists, has increased unnecessary prescription.^{1,15} Such practices can in turn enhance a patient's belief in the need for antimicrobials even when there is no indication, further increasing pressure on those prescribing.¹⁶ Antibiotics may also be requested from pharmacies without a medical practitioner's prescription, a fact that has been reported as common practice in both developing countries and Western Europe.^{17,18}

This study was initiated to establish the pattern of presentation and management of sore throats in a PHC clinic, and to gather information on whether throat cultures have changed in relation to age, gender, clinical presentation and laboratory test results. We also compared the clinical diagnosis with the medicine prescribed, and compared the clinical features and demographic characteristics of male and female patients.

Patients and Methods

The prospective study was conducted at the Medico-Social Centre of Osmangazi University, Eskisehir, Turkey, for 12 consecutive weeks starting 1 November 2002 to 31 January 2003. The Ethical Committee of Osmangazi University, School of Medicine approved this study. The patients provided informed consent to participate in the study. The health centre provides care for both the university staff, including hospital health care workers and students, and workers with no medical insurance. A patient population of approximately 50 000 is seen in a year. During the twelve weeks of the study, 579 patients with URTIs presented to the health centre. Of these, 339 adult patients (>16 years of age) visiting the centre with a main complaint of sore throat and also being prescribed antibiotics after examination were included in the study, regardless of sex, nationality, marital status, occupation, or location of residence. Physicians were free to prescribe any type of antibiotic. Patients not having a sore throat and also not being prescribed an antibiotic were excluded from the study, as were those who used antibiotics recently. No person taking part in the study was offered any financial incentive. The data were recorded in a previously designed form that included demographic characteristics, clinical diag-

nosis, and laboratory investigations of the patients. Patients were required to complete the first part of the questionnaire, concerning patient demographics and symptoms. Doctors completed the second part of the form after a clinical examination, which included an assessment of the present disease, diagnosis and a proposed antibiotic management plan. We then screened the patients prescribed antibiotics in terms of the presence of the four Centor criteria:¹⁹ history of fever, tonsillar exudates, absence of cough, and swollen tender anterior cervical lymph nodes. If antibiotics were prescribed, we requested that physicians order tests for white blood cells and assess neutrophilia, the erythrocyte sedimentation rate (ESR), anti-streptolysin O (ASO) levels, and C reactive protein as related to URTIs, rather than just take throat cultures prior to use of an antibiotic.

Technique, sample site, culture media, incubation condition and duration for the throat cultures. Physicians working in the PHC were taught to take throat cultures by the research team. Throat cultures were taken before the patient was given any antibiotic. The specimen was obtained by wiping the patient's throat with a cotton swab. Patients were asked to tilt the head back and open the mouth wide. With the tongue depressed, the care provider wiped the back of the throat and the tonsils with a sterile swab. The swab was applied to any area that appeared either very red or was discharging pus. The swab was removed gently without touching the teeth, gums, or tongue. It was then placed in a sterile tube for immediate delivery to the microbiology laboratory in our university. Obtaining the specimen took less than 30 seconds. When the throat swab reached the laboratory, it was wiped across a blood agar plate. The plate was allowed to incubate for 24-48 hours to allow the growth of bacteria. Laboratory results were usually available in 2 to 3 days.

The data was analyzed by the authors using SPSS for Windows (version 11.0). The results are given as means with standard errors (SE.) or 95% confidence intervals (95% CI). The χ^2 statistical test was employed in comparing categorical variables. A *P* value of <0.05 was considered significant, where appropriate.

Results

Three hundred and thirty-nine patients, including 165 (48.7%) males and 174 (51.3%) females, presented at our PHC clinic with sore throats and

were enrolled in this study. The majority of the patients (54.3%) were less than 30 years old, lived in the peripheral area of the city (50.7%), were civil servants or employees (52.5%), and were married (55.6%) (Table 1). Statistically, there was no difference between females and males with regard to age and residence (central or peripheral parts of the city), but occupation ($P<0.001$) and marital status ($P<0.05$) differed.

Pain and difficulty upon swallowing were the main symptoms, being reported by 61.1% and 83.0%, respectively, followed by headache (38.9%), nasal discharge (28.9%), dry cough (27.2%), and a feeling of weakness (26.3%). The least frequent presenting symptom was stomach ache (2.1%), followed by difficulty in hearing (4.7%), ear discharge (5.0%), and dry throat (5.9%). In general, symptoms were slightly more demonstrable in males than females, with few exceptions. There were statistically significant differences between males and females in productive cough, pain upon swallowing, and vomiting and sneezing ($P<0.05$ collectively), but the frequency of most symptoms was not different between the genders. The most frequent sign was pharyngeal erythema (40.1%), followed by temperature between 37.5 to 38.5°C (38.9%), sinus sensitivity by pressure (21.2%), tonsil enlargement (17.4%), and cervical lymph node enlargement (16.8%). In most cases (54.6%), temperature was lower than 37.5°C, with only 6.5% of the patients having a high fever. The clinical signs in males and females were similar, aside from tenderness of the cervical lymph node ($P=0.014$). Patients were most commonly diagnosed as having pharyngitis (22.7%), followed by acute bacterial rhinosinusitis (20.1%) and tonsillitis (19.5%) (Table 2). The least determined finding was laryngitis (1.8%). There were no statistically significant differences in diagnoses between males and females.

During the three months, prescriptions for acute URTIs accounted for 61.7% of all antibiotics prescribed by the physicians. The study physicians wrote for a total of 16 different medical drugs with commercial trademarks. These drugs were classified into six different antibiotic classes. The most frequently prescribed antibiotics were penicillins (46.5%, including oral and intramuscular penicillins), cephalosporins (32.3%, including oral and intramuscular cephalosporins), and macrolides (26.8%) (Table 2). These three groups of antibiotics constituted 95.6% of all the antibiotics prescribed for acute URTIs. There were no differences between males and females in type

of antibiotic prescribed ($P>0.05$) (Table 2). Culture swabs were taken from all patients with URTIs who had been prescribed antibiotics, and only 56 (16.5%) were found to be positive. The isolated microorganisms from all the throat cultures were GABHS.

In a univariate analysis, pharyngeal petechiae, tonsillar enlargement, cervical lymph node enlargement, very high fever ($>38.5^{\circ}\text{C}$), acute bacterial rhinosinusitis, pharyngitis and increased CRP levels showed significant relationships with the results of cultures ($P<0.05$), but most factors, including age, were not statistically significant ($P>0.05$). Nearly all of positive culture results were obtained from patients between 16 to 45 years old (98.2%). Most of these patients were females (58.9%), most lived in the periphery of the city (47.0%) and most were civil servants by occupation (63.4%). The most common clinical signs were pharyngeal erythema (33.9%),

Table 1. Demographic characteristics of the study population.

Characteristics	Male n=165 (100%)	Female n=174 (100%)	Total n=339 (100%)
Age (years)			
16-30	85 (46.2)	99 (53.8)	184 (100)
31-45	69 (50.7)	67 (49.3)	136 (100)
46-60	8 (61.5)	5 (38.5)	13 (100)
61 and over	3 (50.0)	3 (50.0)	6 (100)
Settlement			
Central	41 (58.6)	29 (41.4)	70 (100)
Central-peripheral	47 (48.5)	50 (51.5)	97 (100)
Peripheral	77 (44.8)	95 (55.2)	172 (100)
Occupation*			
Academic personnel	40 (58.0)	29 (42.0)	69 (100)
University student	30 (53.6)	26 (46.4)	56 (100)
Civil servant/employee	90 (50.6)	88 (49.4)	178 (100)
Housewife	5 (13.9)	31 (86.1)	36 (100)
Marital status*			
Single	60 (54.1)	51 (45.9)	111 (100)
Married	79 (41.8)	110 (58.2)	189 (100)
Widow (er)	17 (63.0)	10 (37.0)	27 (100)
Divorced/separated	9 (75.0)	3 (25.0)	12 (100)

*Statistically significant males vs.females

Table 2. Clinical diagnosis and medicine prescribed by gender of the study population.

Diagnosis	Male n=165 (100%)	Female n=174 (100%)	Total n=339 (100%)
Diagnosis			
Acute sinusitis	15 (9.1)	20 (11.5)	35 (10.3)
Common cold infection	15 (9.1)	14 (8.1)	29 (8.6)
Acute otitis media	6 (3.6)	4 (2.3)	10 (2.9)
Laryngitis	5 (3.1)	1 (0.6)	6 (1.8)
Acute bacterial rhinosinusitis	40 (24.3)	28 (16.1)	68 (20.1)
Pharyngitis	34 (20.6)	43 (24.7)	76 (22.7)
Tonsillitis	30 (18.2)	36 (20.7)	66 (19.5)
Tonsillopharyngitis	15 (9.1)	21 (12.7)	36 (10.6)
more than one diagnosis	5 (3.1)	7 (4.0)	12 (3.5)
Antibiotic prescribed			
Oral Penicillin	57 (48.3)	61 (51.7)	118 (39.1)
Oral Cephalosporins	42 (48.3)	45 (51.7)	87 (28.8)
Oral Macrolides	42 (51.9)	39 (48.1)	81 (26.8)
Oral Fluoroquinolones	8 (66.7)	4 (33.3)	12 (4.0)
Oral Co-trimoxazol	1 (50.0)	1 (50.0)	2 (0.7)
Oral Doxycycline	1 (50.0)	1 (50.0)	2 (0.7)
IM Penicillins	11 (44.0)	14 (56.0)	25 (7.4)
IM Cephalosporins	3 (25.0)	9 (75.0)	12 (3.5)

IM: intramuscular

pharyngitis (34.0%), tonsillar exudates (16.8%), tender cervical lymph nodes (12.5%), and a fever less than 37.5°C (48.2%). None had rales or rhonchi or acute exacerbation of bronchitis. Most had no sinus sensitivity by pressure (76.8%), leukocytosis less than 11 000/mm³ (87.5%), lymphocytosis less than 45% (91.0%), neutrophilia less than 70% (76.7%), ESR less than 10 (50.0%), and an ASO titer less than 160 (76.7%). More than two-thirds of positive culture results were obtained from patients with CRP higher than 5.

Two hundred and thirty-seven patients (69.9%) prescribed antibiotics showed one or two Centor criteria (Table 3). This score had a 60% (3/5) sensitivity and 16.7% (8/48) specificity. All Centor criteria, including absence of cough, tonsillar exudate, swollen tender anterior cervical lymph nodes and a history of fever showed significant relationships with the

results of cultures. Patients with tonsillar exudates, swollen tender anterior cervical lymph nodes, and a history of fever were culture positive more often than those not having these signs, and absence of cough was less frequent in those were culture positive.

Discussion

In this study, only a small number of cultures were found to be positive for GABHS (16.5%), a finding in line with the results of other studies conducted in Turkey as well as other countries, where the frequency ranged between 5% to 22%.²⁰⁻²³ The absence of any bacterial pathogen in 83.5% of cases in the study population indicates the probability of viral infection. Tests for other probable bacterial pathogens such as *Mycoplasma*, *Chlamydia*, *Corynebacterium diphtheria* and *Arcanobacterium* were not done since physicians working at the PHC did not inform the laboratory of symptoms related to those microorganisms even though they are of special importance in young adults. In our study, the majority of patients were younger than 30 years old. This may be attributed to the fact that the study was conducted at a university-based hospital, although this health centre generally serves civil servants and employees in addition to students.

Positive cultures were more frequent in patients with a high CRP (>5), suggesting the probability of a bacterial aetiology.³ In all of those having positive throat cultures, rales-rhonchi and acute exacerbation of bronchitis were absent. This reflects the fact that the numbers of those having to rales-rhonchi in combination with acute exacerbation of bronchitis were quite low (6 and 3, respectively). With these rather low numbers, it is difficult to conclude that throat cultures would be positive in the absence of rales-rhonchi or acute exacerbation of bronchitis. Studies on these relationships would be useful.

The place of antibiotic therapy in the management of the most common URTIs, such as sore throat or otitis media, tonsillitis and rhinosinusitis, has been the subject of great controversy.²⁴ The majority of patients presenting with URTIs (58.5%) were treated with antibiotics. These results indicate that PHC physicians in Turkey are prescribing antibiotics inconsistently, a practice in common with that in some other countries. Dutch and Saudi Arabian PHC physicians, for example, prescribe antibiotics during acute URTIs at a rate of 70% and 76.4%, respectively.^{3,6} Sixteen different antibiotics were given, with oral and intramuscular penicillins prescribed in 46.5% of cases. This finding

is high compared to previously reported work, where penicillins were used in 32.4% and 34.3% of cases.^{25,26} The high rate of penicillin prescribing could be related to the low cost, fewer side effects, proven effectiveness, safety, and the broad availability of the medication.^{27,28} Physicians may also be influenced by studies recommending penicillins.^{13,27,28} Yet, while penicillin was the drug of choice,^{13,27} most of the antibiotics (53.5%) in our study consisted of the most expensive ones such as the new macrolides and third-generation cephalosporins. This finding is in line with other studies showing that the rate of prescribed medicines, apart from penicillins, was more than 50%.^{25,26}

It is remarkable that PHC physicians use antibiotics both widely and inconsistently in treating URTIs. It could be argued that this high prescribing behaviour among Turkish physicians is influenced by education, the doctor-patient relationship, the fear of development of a secondary bacterial infection, the

price of drugs and the activity of marketing groups from the pharmaceutical industry- factors mentioned in a study conducted by Bradley.²⁹ Further factors could be related to conditions peculiar to Turkey, such as anxiety about being a specialist, and unlike in some developed countries, such as England, which has a register of patients per doctor, the Turkish physicians' workload is directed by the state health system, without regard to the number of patients a doctor must see daily.

The results of this study have important implications: If injudicious use of antibiotics in URTIs continues in this way, the emergence and the prevalence of antimicrobial resistance as well as the costs of health care will ever increase.³⁰⁻³³ The emergence of resistance will threaten the efficacy of important pharmaceuticals such as penicillins and cephalosporins. For this reason, any strategy aimed towards the containment and reduction of antibiotic resistance

Table 3. Culture results according to Centor criteria.

Variables	Culture			χ^2	P*
	Positive (n=56; 16.5%)	Negative (n=283;83.5%)	Total (n=339)		
Number of Centor criteria				8.156 (df=4)	0.086
Absent	13 (26.5)	36 (73.5)	49 (14.5)	4.163	0.041
1	24 (18.9)	103 (81.1)	127 (37.5)	0.833	0.361
2	14 (9.1)	96 (91.9)	110 (32.4)	1.698	0.193
3	3 (6.9)	40 (83.1)	43 (12.7)	3.252	0.071
4	2 (20.0)	8 (80.0)	10 (2.9)	0.091	0.764
Centor criteria					
Absence of cough				24.341	0.0001
No	39 (28.7)	97 (71.3)	136 (40.1)		
Yes	17 (8.4)	186 (91.6)	203 (59.9)		
Tonsillar exudate				5.606	0.018
No	42 (14.5)	247 (85.5)	289 (85.2)		
Yes	14 (28.0)	36 (72.0)	50 (14.8)		
Swollen tender anterior cervical lymph nodes				4.551	0.033
No	31 (13.5)	198 (86.5)	229 (67.6)		
Yes	25 (22.7)	85 (77.3)	110 (32.4)		
History of fever (>37.5°C)				4.288	0.038
No	22 (12.5)	154 (87.5)	176 (51.9)		
Yes	34 (20.9)	129 (79.1)	163 (48.1)		

*For comparison of positive vs. negative cultures.

in the community must include surveillance of antibiotic consumption as well as an examination of all the factors that influence it.³⁴

According to data compiled by the Turkish drug and chemical industry, the total consumption of antibiotics from all drug use is over 20% in Turkey.³⁵ Antibiotics are used by approximately 25-35% of all patients presenting to hospitals in our country.³⁶ Considering that the costs of antimicrobials are rather high, something like \$2.7 billion US per year in this country,⁹ the position is worrying for the future. This results in financial costs being incurred by patients, wider manifestation of side effects, and weakening of the country's economy, with the routine prescription for sore throat enhancing patients' dependence to these drugs.

As noted by Wun, we must condemn indiscriminate prescribing and encourage quality prescribing.³⁷ Educational campaigns for the public on the uses and limitations of antibiotics are needed as part of any attempt to improve rational use of antimicrobials.³⁸ Such public campaigns are known to both increase public awareness of the existence and importance of bacterial resistance.³⁹ We found that the physicians working in the centre prescribed antibiotics

inappropriately. That is, most patients did not have three or four Centor criteria (286/339, 84.4%). This result showed that physicians prescribing antibiotics for URTIs did not consider the Centor criteria to be important. These criteria, which are evidence-based recommendations regarding evaluation and management of nonspecific URTIs, are approved by the Centers for Disease Control and Prevention (CDC), the American Academy of Family Physicians, and the American College of Physicians-American Society of Internal Medicine. Physicians in the PHC centers may not receive training on antibiotic prescribing rules, at either the student or post-graduate levels. In addition, we have found that no physician or health institution in Turkey prescribes antibiotics according to Centor Criteria.

In summary, this study suggests that injudicious antibiotic prescribing is rather high and should be reduced to modest levels. The Turkish Ministry of Health⁴⁰ has recently introduced new legal measures prohibiting the prescription of new macrolides and third-generation cephalosporins by primary health care physicians. We think that these types of restrictions would decrease inappropriate antibiotic use prescribed by physicians, and be cost-effective.

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