

Şanlıurfa'da Reçetesiz Antibiyotik Sıklığı ve Reçetelenen Antibiyotiklerin Uygunluğu*

[The Frequency of Antibiotics Sold Without a Prescription and the Appropriateness of Antibiotics Sold with a Prescription in Sanliurfa]

ÖZET

AMAÇ: Bu çalışmada, Şanlıurfa ilinde reçetesiz satılan antibiyotik sıklığının ve ilişkili risk faktörlerinin saptanması ve reçetelenen antibiyotiklerin tanıya göre uygunluğunun belirlenmesi amaçlandı.

YÖNTEM: Kesitsel tipteki bu çalışma, Eylül-Aralık 2010 tarihlerinde, eczanelere reçeteli veya reçetesiz antibiyotik almak için gelen hastalarda yapıldı. Araştırmanın evreni küme örnekleme metodu ile belirlendi ve 186 eczaneden 25 eczane basit rastgele yöntemle seçildi. Eczaneler araştırmacı tarafından ziyaret edildi. Anket formları katılımcılar tarafından dolduruldu.

BULGULAR: Eczanelerden 373 antibiyotik talebi değerlendirildi. Hastaların %98,6'sı (n=359) antibiyotikleri reçete ile almışlardı. Hastalara 39 farklı antibiyotik reçete edilmişti. Reçetelenen antibiyotiklerin %63,7'si uygun değildi. En sık reçetelenen antibiyotik ko-amoksilav idi.

Antibiyotiklerde uygunluğun solunum yolu enfeksiyonu tanısı konan reçetelerde en yüksek (%74,3) iken idrar yolu enfeksiyonu tanısında (%23,3) en düşük olarak tespit edildi (χ^2 : 68.8, $p<0.001$). Kamu hastanelerinde reçetelenen antibiyotik uygunluğunun (%53,7), sağlık ocaklarından (%72,1) ve özel sağlık kuruluşlarından (%64,7) daha düşük olarak saptandı ($p<0.05$). Reçetelerin %4,7'sinde antibiyotik yazılmasına karşın enfeksiyonla ilişkili bir tanı yoktu.

SONUÇ: Şanlıurfa'da reçetesiz antibiyotik kullanımının oldukça az, ancak uygun olmayan antibiyotik kullanımının yüksek olduğu saptandı. Reçetesiz antibiyotik kullanımı sağlık sistemindeki düzenlemeler ile önenebilir. Özellikle hekimlerin akılcı antibiyotik kullanımı konusundaki bilgilerinin pekiştirilmesi ve mezuniyet sonrasında eğitimlerin devam ettirilmesi gereklidir.

SUMMARY

AIM: The aim of this study was to determine the frequency with which antibiotics were sold without a prescription, to examine factors related to such practices and to determine the appropriateness of antibiotics sold with a prescription in Sanliurfa city center in Turkey.

METHOD: This cross-sectional study was carried out between September 6 and December 15, 2010, on patients who visited the pharmacies to ask for antibiotics with or without prescription. To determine the research sample the cluster sampling method was used and from 186 pharmacies, 25 pharmacies were selected at random. The pharmacies were visited and asked to complete a structured questionnaire.

RESULTS: 373 patients obtained antibiotics from pharmacies. The patients who received antibiotics by prescription comprised 98.6% (n=359) of all patients. A total 36 different antibiotics had been prescribed to the patients. Inappropriate prescription of antibiotics was documented in 63.7%. The most-prescribed antibiotic was co-amoxiclav (28.8%). The rate of inappropriate antibiotic prescriptions with the diagnosis of upper respiratory tract infection (77.8%) was highest, while the rate was lowest with the diagnosis of urinary tract infection (23.3%) (χ^2 : 68.8, $P<0.001$). The rate of inappropriate prescribed antibiotics in state hospitals (53.7%) was lower than the rate in primary health care centers (72.1%) and private hospitals and clinics (64.7%) (χ^2 : 10.4, $P=0.05$). There was no diagnosis of infection in 17 (4.7%) patients with prescriptions.

CONCLUSION: These results indicate that the use of antibiotics without prescription was low, while the rate of inappropriate antibiotic use was high in Sanliurfa. The use of antibiotics without prescription can potentially be prevented through interventions in the healthcare system. To prevent inappropriate antibiotic prescription, improvements to physicians' education must be implemented, even after graduation.

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INTRODUCTION

The discovery of anti-infective agents that can be used to prevent and treat many serious infections is one of the most important developments in modern medicine. Antibiotics comprise 3-25% of

prescriptions and 15-30% of drug expenditures, the largest proportion of any therapeutic group of drugs (1-3). In the United States, antibiotics constitute approximately one third of hospital drug budgets, and more than half of this budget is spent on combating resistant bacterial infections (4). The introduction of

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Anahtar Kelimeler:

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new antibiotics has, unfortunately, contributed to the problem of inappropriate antimicrobial usage. Misuse and abuse of antibiotics exacerbates important problems such as the development of antimicrobial resistance, treatment failures, drug toxicities, the rising incidence of serious nosocomial infections and increases in cost containment (5).

Inappropriate antibiotic use is a global problem. Studies have reported that 14-43% of antibiotic treatments are unnecessary (6,7). Moreover, it is estimated that >50% of antibiotics used worldwide are purchased privately and without a prescription from pharmacies or markets (8). In developing countries, the use of antibiotics without medical guidance is facilitated by inadequate regulation of the distribution and sale of prescription drugs (9,10).

In Turkey, antibiotics are the most commonly used drugs and account for 20% of the drug market (11). Additionally, many drugs, including antibiotics, are sold without a prescription in Turkey (12). Previous studies have suggested that the purchase of drugs without a prescription is also common in Sanliurfa, which is where the present study was conducted. In pharmacies in the city center of Sanliurfa, approximately 75% of pharmacy staff suggested medical treatment to the patients rather than referring them to doctors, and the majority of the antibiotics suggested were inappropriate (13).

The aim of this study was to determine the frequency with which antibiotics were sold without a prescription, to examine factors related to such practices and to determine the appropriateness of antibiotics sold with a prescription in Sanliurfa city center in Turkey.

MATERIAL and METHOD

Study Area

Sanliurfa city, where this study was conducted, is located in the Southeastern Anatolian region of Turkey, which is one of the least developed regions in the country. In this region, 43% of the economy is based on agriculture (14). The education level in the population is extremely low (63.2% of women and 39.3% of men are illiterate), and both access to health care and service utilization are limited; the home delivery rate is 45.9%, and the infant mortality rate is 38 per 1000 live births (15).

Study design

This cross-sectional study was carried out between September 6 and December 15, 2010 on patients who visited the pharmacies in Sanliurfa to ask for antibiotics with or without prescription.

Written informed consent was obtained from all participants, and the study protocol was approved by the Ethical Committee of Harran University Medical Faculty.

Selected participants

Participants were selected from patients who had prescriptions for antibiotics and those who demanded antibiotics without a prescription.

Data collection

Pharmacists, the pharmacy technician (second responsible staff) in the pharmacies and the patients in the pharmacies were asked to complete a structured questionnaire. The first part of the questionnaire requested demographic information (age, gender, institution of practice, duration of occupational practice and social insurance) from the participants.

The second section consisted of questions to be answered by the interviewer herself through observations in the pharmacies; these questions included whether the patient had a prescription for antibiotics, how the pharmacist or staff responded to the patient's request and whether the prescribed antibiotic was appropriate to the diagnosis.

Before the visits to the pharmacies, a pilot study was performed to refine the questionnaire. Three visits to randomly selected pharmacies were conducted to test whether the questionnaires were sufficient to provide the required data. Pharmacy visits began after the questionnaires were corrected.

Number of pharmacies to be visited

At the time of this study, there were 186 pharmacies in Sanliurfa city center. To determine the research sample the cluster sampling method was used. The people who wanted antibiotics (with or without a prescription) at each pharmacy in a day determined the sampling unit of the study (16). A pilot study was conducted with random selection and sampling of 10 pharmacies. One pharmacy was visited each day, and each visit lasted between 9 am and 4 pm. During these visits, the interviewer

observed how many patients wanted antibiotics and how many of these patients had prescriptions.

From 186 pharmacies, 25 pharmacies were selected at random, using a random number table. These pharmacies were then visited by the interviewer. One pharmacy was visited each day. The study subjects included patients with or without prescriptions who demanded antibiotics between 9 am and 4 pm.

The antibiotics and the diagnosis were examined from the prescriptions of the patients by an Infectious Diseases and Clinical Microbiology specialist. The appropriateness of the antibiotics prescribed to the patients was evaluated according to general antibiotic usage criteria with the help of guidelines (5, 17).

The pharmacy system in Turkey: In Turkey, the pharmacy system is privatized. Each pharmacist can open and operate his or her own pharmacy. Under the law, no one but the pharmacist can apply the pharmacy in profession. Other staff, who may not have educations commensurate with pharmacy practice, work under the pharmacist's supervision (18).

Health insurance system: Health insurance in Turkey is provided by social security institutions and private insurance companies. With the help of government-supplied health insurance, patients get pay only 20% of their medical costs; the rest is paid by the government. There are 2 different health insurance systems in Turkey: Social Security insurance and the Free Health Services Card (also called "green card"; a form of health insurance supplied to poor people by the Turkish government and utilized by many families.) (15).

Statistical analysis

The software package SPSS 11.5 was used to generate descriptive statistics like number, percentage, mean and standard deviation. Chi-square

tests were performed to compare the differences between groups.

For the statistical analysis we assigned state hospitals and university hospital as public hospitals in the health institution variable.

RESULTS

In this study, 373 patients obtained antibiotics from 25 pharmacies. In 21 (84%) of the pharmacies, the pharmacist was present at the pharmacy at some point when the interviewer was there; in 4 (16%) pharmacies, the pharmacist was never present.

Of the patients visiting the pharmacies, 88.6% (n=323) lived in the city center, and 13.4% (n=50) lived in a rural area.

A primary health care center was within walking distance of 83.9% (n=313), and the hospital was within walking distance of 43.2% (n=161) of the patient's houses.

Insurance was distributed as follows: 234 patients (62.7%) had social security insurance; 133 patients (35.7%) had the free health services card, and 6 patients (1.6%) did not have any health insurance. The health insurance coverage of the patients who obtained antibiotics with and without prescriptions is shown in Table 1.

The patients who received antibiotics by prescription comprised 98.6% (n=359) of all patients.

The health institution where the patient was examined and the appropriateness of the recommended antibiotics are shown in Table 2.

The following were the most frequent diagnoses stated on prescriptions: upper respiratory tract infections (uRTIs; common cold, acute pharyngitis, acute sinusitis and acute otitis media) (44.5%), lower respiratory tract infections (LRTIs) (19.0%), mouth/dental infections (8.8%), urinary tract infections (UTIs) (8.2%) and acute gastroenteritis (4.4%).

Table 1: The health insurance coverage of the patients who obtained antibiotics with and without prescriptions.

Health insurance coverage	With prescription		Without prescription		Total		P**
	N	%*	N	%*	N	%*	
Social Security Insurance or Free Health Services Card	359	98.6	8	88.9	367	98.4	0.13
Do not have any health insurance coverage	5	1.4	1	11.1	6	1.6	
Total	364	100.0	9	100.0	373	100.0	

*Column percentage, ** fisher's exact test

Table 2: The health institution where the patient was examined and the appropriateness of the recommended antibiotics.

Health institution	Appropriate		Inappropriate		Total		P
	N	%*	N	%*	N	%**	
Primary health care centers	43	27.9	111	72.1	154	42.3	0.05
Public hospitals [§]	62	46.3	72	53.7	134	36.8	
Private hospitals and clinics	27	35.5	49	64.5	76	20.9	
Total	132	36.3	232	63.7	364	100.0	

[§]State hospitals and university hospital, *Row percentage, ** Column percentage

The diagnosis written in each prescription and the appropriateness of the prescribed antibiotic/antibiotics for each diagnosis are shown in Table 3. There was no diagnosis of infection in 17 (4.7%) patients with prescriptions.

A total of 36 different antibiotics had been prescribed to the patients by physicians. The 7 most-prescribed antibiotics were amoxicillin/clavulanic acid (co-amoxiclav) (28.8%), cefuroxime axetil (14.2%), cefazolin (5.2%), sulbactam/ampicillin (4.9%), cefixime (4.1%), ciprofloxacin (3.9%) and clarithromycin (3.4%).

Cefuroxime axetil (20.6%) and co-amoxiclav (15.8%) were the most-prescribed inappropriate antibiotics with the diagnosis of uRTIs. Sulbactam/ampicillin (28.0%) and cefixime (17.2%) were the most-prescribed inappropriate antibiotics with the diagnosis of IUTIs. Cefazolin (25.7) was the most-prescribed inappropriate antibiotic with the diagnosis of mouth/dental infections.

Among 9 patients who obtained antibiotics without prescription, 7 (77.8%) of them requested antibiotics, while 2 patients (22.2%) had particular antibiotics proposed to them by the pharmacy staff. None of these 9 patients was directed to a physician by the pharmacist or the other pharmacy staff.

No statistically significant difference was found between patients whose houses were within walking distance of the hospital or primary health care center and those whose houses were not within walking distance in terms of use of antibiotics without a prescription (χ^2 : 2.03, $P=0.19$).

No statistically significant difference was found in terms of the patient's educational level and use of antibiotics without a prescription (χ^2 : 5.76, $P=0.56$).

A statistically significant difference in the rates of antibiotic use without prescription was also found between patients with and without health insurance (χ^2 : 5.26, $P=0.02$) (Table 1).

According to general antibiotic usage criteria, inappropriate prescription of antibiotics was

documented in 63.7% of these prescriptions. The rate of inappropriate antibiotic prescriptions with the diagnosis of uRTI (77.8%) was highest, while the rate was lowest with the diagnosis of UTI (23.3%). The difference was statistically significant (χ^2 : 68.8, $P<0.001$).

The rate of inappropriate antibiotics prescriptions in state hospitals (53.7%) was lower than the rate in primary health care centers (72.1%) and private hospitals and clinics (64.7%). The difference was statistically significant (χ^2 : 10.4, $P=0.05$) (Table 2).

DISCUSSION

Worldwide, more than 50% of all medicines are prescribed, dispensed, or sold inappropriately. Moreover, approximately one-third of the world's population lacks access to essential medicines. The most common aspects of inappropriate use of medicines are as follows: the use of too many medicines per patient, use of antimicrobials for non-bacterial infections, failure to prescribe in accordance with clinical guidelines and inappropriate self-medication (19). Excessive use of antibiotics is partly attributable to inappropriate prescriptions by physicians. Inappropriate and excessive use of the antibiotics in both the hospital environment and outpatient clinics contributes to increased antimicrobial resistance, which is becoming a global public health problem (20). Studies have shown that 20-70% of the antibiotic use in hospitals in Turkey is inappropriate (12, 21, 22). Overuse of antibiotics was found to be widespread in another study from Samsun in 1999 (23). In the same study, inadequate antibiotic prescription was documented in 29.7% of antibiotic prescriptions. The results from the present study showed a higher (63.7%) rate of inappropriate antibiotic use in outpatient clinics. These findings indicate that even physicians are insufficiently aware of the repercussions of antimicrobial misuse.

Table 3: The diagnosis written in each prescription and the appropriateness of the prescribed antibiotic/antibiotics for each diagnosis.

Diagnosis	Appropriate		Inappropriate		Total	
	N	%*	N	%*	N	%**
Upper respiratory tract infection	36	22.2	126	77.8	162	44.5
Lower respiratory tract infection	34	49.3	35	50.7	69	19.0
Mouth-dental infection	18	56.3	14	43.8	32	8.8
Urinary infection	23	76.7	7	23.3	30	8.3
Non-infectious diagnosis	0	0.0	17	100.0	17	4.7
Acute gastroenteritis	6	37.5	10	62.5	16	4.4
Acute gastroenteritis + upper respiratory tract infection	1	9.1	10	90.9	11	3.0
Soft tissue infection	8	80.0	2	20.0	10	2.7
Upper respiratory tract infection + lower respiratory tract infection	2	28.6	5	71.4	7	1.9
Pelvic inflammatory infection	4	57.1	3	42.9	7	1.9
Tonsillitis + urinary tract infection	0	0	3	100.0	3	0.8
Total	132	36.3	232	63.7	364	100.0

*Row percentage , **Column percentage

Educational intervention should be implemented to improve antibiotic-prescribing habits. In the present study, it was found that the rate of inappropriate antibiotic prescription in state hospitals, where specialist physicians examine the patients, was lower compared with both primary health care centers and private hospitals and clinics, where the patients are examined mostly by general practitioners. Similar results were found by Quijano et al. in their study showing that doctors-in-training prescribed antibiotics more rationally than practicing physicians (24). We conclude that medical education on the subject of antibiotics and other therapeutic services that should continue throughout the physician's practicing lifetime and should be better-covered in postgraduate training.

Self-medication with antibiotics is another problem in various European countries, especially in the southern and eastern regions (25, 26). In Greece, it was shown that a high proportion of the rural adult population uses antibiotics without medical prescription, especially for high fevers and common colds (27). In Spain, 31% of antibiotics consumed were found to be dispensed by community pharmacies without prescription (28). In Malta, according to Borg and colleagues, 19% of study participants admitted to self-medication with

antibiotics, which were provided without prescription by local pharmacies in 85% of cases (29).

In Turkey, the law still allows patients to obtain antibiotics from pharmacists without any medical prescription. The rate of antibiotic use without medical prescription was found to be high in some studies from Turkey (13, 30), where to obtain a prescription, a patient must be examined in a health institution. The cost of the medicines is sometimes less than the consultation fee, which may be one reason that self-medication with antibiotics is preferred. In the present study, it was found that patients without any health insurance had higher rates of antibiotic use without prescription; however, the results of the present study showed a low overall percentage (1.4%) of antibiotic use without prescription. Health insurance coverage in Turkey makes prescribed drugs much cheaper or free of charge; therefore, most patients prefer to buy the drugs with prescriptions, as in our study.

The role of the pharmacist is to inform and guide the patients and to give them the drugs prescribed by their physicians (31). According to Togoobaatar et al., the prevalence of non-prescribed antibiotic use for young children was high in Ulaanbaatar; amoxicillin was the most commonly used antibiotic (58%) and pharmacies were the main source (86%) of non-prescribed antibiotics (32). In our study, none of the

patients who wanted antibiotics but did not have a prescription were directed to a physician by the pharmacist or the other pharmacy staff. We conclude that there is a need for better communication between physicians and pharmacists.

The European Surveillance of Antimicrobial Consumption (ESAC) project collected data on antibiotic use in Europe. In this survey, it was found that in 25 European countries, between 1997 and 2003, penicillins were the most-prescribed outpatient antibiotics among the major antibiotic classes (penicillins, cephalosporins, macrolides, lincosamides, streptogramins and quinolones) (33). Among the antibiotics prescribed by physicians in our study, co-amoxiclav (28.8%) was most frequently prescribed. Similarly, in a study conducted by Avci et al. in Turkey, co-amoxiclav was found to be the most frequently prescribed antibiotic (26.4%) (34). Physicians prefer broad-spectrum antibiotics to narrow-spectrum antibiotics. The decrease in the consumption of narrow-spectrum penicillins and the increasing use of co-amoxiclav and quinolones is in accordance with the international trend towards prescribing more broad-spectrum and newer antimicrobial agents (36). This tendency is a serious issue, contributing to the development of bacterial resistance, increased drug toxicities and increases in cost containment (5). Plachouras et al. found that in Greece, co-amoxiclav was dispensed in all examined cases without prescription.

With regard to the diagnosis stated on prescriptions, uRTIs were diagnosed with the highest frequency (45.4%) and also had the highest frequency of inappropriate antibiotic usage. UTI, which was the fourth-most-frequent diagnosis in the present study, was one of the most common infections found in previous studies as well (37, 38). This study was conducted in autumn (flu season in the Northern hemisphere), which may be the reason that the rate of RTIs is high.

We found that the use of unprescribed antibiotics is less frequent than has been suggested by recent literature, despite the low education level of study participants and the conditions of this region. It is postulated that most of the participants had a form of health insurance (including the government-issued "green card" for people in poverty) and that they do not want to spend money on antibiotics. Despite the accessibility of health services and very minor obstacles to accessing health insurance, the use of unprescribed antibiotics persists for reasons that cannot be explained in this study, and the use of unprescribed antibiotics is not being prevented by the pharmacists. These results indicate that the use of

antibiotics without prescription can potentially be prevented through interventions in the healthcare system.

Inappropriate antibiotic use with prescription and antibiotic use without prescription present an important and serious problem, one that is best addressed by a multisectoral approach, as follows:

1. The populations' economy needs to be improved.
2. There should be intensive efforts to educate the patients about drugs and their use.
3. Drugs, especially antibiotics, should be available only by prescription
4. Non-pharmacist pharmacy staff in Turkey must be educated about appropriate drug use.
5. In order to prevent inappropriate antibiotic prescription, improvements to physicians' education must be implemented, and the physicians should continue to develop their knowledge, even after graduation.

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