**ORIGINAL ARTICLE**

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# Examining Antibiotic Use at an Education and Research Hospital in Turkey: Point Prevalence Results*

**Aims:** Antimicrobial drugs are among the most commonly prescribed drugs in hospitals. Inappropriate use of antibiotics leads to development of antimicrobial resistance. The aims of this study were to determine the rate of antibiotic usage in hospitalized patients, the reasons for antibiotic therapy, irrational uses, and the rates of irrational use in patients hospitalized in Ankara Education and Research Hospital.

**Materials and Methods:** A point prevalence surveillance study was performed on 27 April 2006 at Ankara Education and Research Hospital. Data of all hospitalized patients were collected.

**Results:** On the day of the study, 153 patients (36.2%) out of 422 in-patients were being given one or more antibiotics. In 64 of the patients (41.8%), antibiotic therapy was for treatment, and in 89 (58.2%) it was given as prophylaxis. Usage of antibiotics for either treatment or prophylaxis was appropriate in 69 patients (45.7%), whereas it was inappropriate in the remaining 84 patients (54.3%). Inappropriate use of antibiotics was more common in surgical clinics (62.7%) when compared with medical clinics (24.1%) (P<0.001).

**Conclusions:** Inappropriate usage of antibiotics was detected particularly in surgical clinics in our hospital. A strict surveillance of surgical patients and preparation of a local surgical prophylaxis guideline could help to improve the appropriate use of antibiotic treatment.

**Key Words:** Antibiotic use, appropriateness

## Türkiye'de Bir Eğitim Hastanesinde Antibiyotik Kullanımının İrdelenmesi: Nokta Prevalans Sonuçları

**Amaç:** Antibiyotikler hastanelerde en yaygın kullanılan ilaçlardır. Uygunsuz antibiyotik kullanımı ise dirence yol açan en önemli nedendir. Bu çalışmada Ankara Eğitim ve Araştırma Hastanesi'nde yatan hastalarda antibiyotik kullanımının oranını, nedenlerini, uygun olmayan kullanım ve oranını belirlemek amaçlandı.

**Materyal ve Metod:** Ankara Eğitim ve Araştırma Hastanesi'nde 27 Nisan 2006 tarihinde nokta prevalans çalışması yapıldı. Hastanede yatan tüm hastaların verileri daha önceden hazırlanmış bir forma kaydedildi.

**Bulgular:** Çalışmanın yapıldığı gün hastanede yatan 422 hastanın 153'üne (% 36.2) bir ya da daha fazla sayıda antibiyotik uygulandığı saptandı. Bu hastaların 64'üne (% 41.8) tedavi, 89'una (% 58.2) profilaksi amacı ile antibiyotik verilmekteydi. Tedavi ya da profilaksi amacıyla antibiyotik kullanan 69 olguda (% 45.7) antibiyotik kullanımı uygun olarak değerlendirildi. Kalan 84 olguda (% 54.3) uygunsuz antibiyotik kullanımı söz konusuydu. Uygunsuz kullanım oranının cerrahi branşlarda (% 62.7) dahili branşlara göre (% 24.1) daha fazla olduğu saptandı (P < 0.001).

**Tartışma:** Sonuç olarak hastanemizde özellikle cerrahi kliniklerde uygunsuz antibiyotik kullanımı olduğu saptandı. Cerrahi birimlerde yatan hastaların yakın izlemi ve hastane içinde kullanılmak üzere bir cerrahi profilaksi rehberinin hazırlanması bu birimlerde uygun antibiyotik kullanımına fayda sağlayabilir.

**Anahtar Sözcükler:** Antibiyotik kullanımı, kulanım oranı

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## Introduction

Antibiotics are among the most frequently prescribed drugs worldwide. According to results of studies carried out in European countries and the United States, 23-38% of in-patients are given some kind of systemic antibiotic treatment (1,2). Antibiotics take the lead among most commonly used drugs in Turkey and account for 20% of the drug market (3).

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Unfortunately, 20-50% of antibiotic treatment is used irrationally (4,5). The fact that one of the most important causes of acquiring resistance is the lack of rational antibiotic use has been reported in many studies and has taken its place in the literature as evidence (6-9). Inappropriate use of antibiotics leads to some undesired effects such as an increase in mortality and morbidity, drug toxicity, extended periods of hospitalization, and an increase in expenditures.

The present study used the point prevalence method and aimed to determine the rate of antibiotic use, irrational uses, and the rates of irrational use in patients who were hospitalized in Ankara Education and Research Hospital, Turkey.

## Materials and Methods

### Hospital Setting

The study was conducted at Ankara Education and Research Hospital, which is a tertiary facility with 600-bed capacity. There are four internal medicine and eight surgical units at the hospital; at the time of the study, intensive care units of neurology and neurosurgery, internal medicine, and surgery clinics had a capacity of 14, 12, and 8 beds, respectively, for active patient admission.

### Preauthorization Requirements Regarding Antibiotic Use

The hospital is under the purview of the Ministry of Health and at the time of the study, a limited use of antibiotics was applied in a legal regulation scope. According to this, antibiotic use was as follows:

1. Antibiotics that require the approval of a specialist in infectious diseases for their use: piperacillin-tazobactam, ticarcillin-clavulanate, cefoperazone-sulbactam, ceftazidime, cefepime, imipenem, meropenem, vancomycin, teicoplanin, caspofungin, liposomal amphotericin B, and voriconazole.

2. Antibiotics that require the signature of a specialist for use in the first 72 hours and the approval of an infectious diseases specialist if they are to be used longer than 72 hours: piperacillin, ticarcillin, carbenicillin, cefotaxime, ceftizoxime, ceftriaxone, cefoperazone, aztreonam, amikacin, isepamicin, netilmicin, tobramycin, ciprofloxacin, levofloxacin, ofloxacin, parenteral forms of pefloxacin and moxifloxacin, standard amphotericin B, and parenteral fluconazole.

3. Antibiotics that require the signature of a specialist for their use: ampicillin-sulbactam, parenteral forms of cefuroxime and clarithromycin, cefoxitin, loracarbef, nafcillin, rifabutin, rifampin, itraconazole, and anti-tuberculosis drugs.

### Data Collection

On 27 April 2006, between 8.00 AM and 5.00 PM, all the patients at the hospital were visited by a team of 12, consisting of specialists and residency trainees of our clinic. Patients hospitalized at the Infectious Diseases and Clinical Microbiology Department were not included in the study. All patients who were hospitalized in other clinics of the hospital were taken into the study. Data regarding the patients included were recorded by examining the nurse supervision forms and clinicians' orders.

Of all patients who used antibiotics, demographic features, departments in which they were hospitalized, diagnoses at hospitalization, performed surgeries if any, infection diagnoses, antibiotics used, indications of use, methods of application, doses and durations of application, and whether or not microbiological evaluation was performed were recorded on the standard evaluation forms prepared. Infections were classified as those acquired from the community and those acquired at the hospital, in accordance with the Centers for Disease Control (CDC) criteria.

### Assessment of Appropriateness of Antibiotic Use

Use of antibiotics was divided into two groups as appropriate and inappropriate. Inappropriate use was further divided into three subgroups as unnecessary, microbiologically inappropriate, and pharmacologically inappropriate.

*Unnecessary use:* defined as starting antibiotic treatment without a clinical or laboratory finding or any suspicious infectious sign and starting prophylactic antibiotic treatment in cases in which there is no prophylaxis indication.

*Microbiologically inappropriate use:* defined as antibiotic use despite the present indications and with a spectrum that does not include the causative agent, unnecessary wide spectrum antibiotic or reserve drug use when an alternative with a narrower spectrum is present, and as unnecessary combination treatment.

*Pharmacologically inappropriate use:* defined as use in inappropriate doses and durations and as use of a more

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toxic (having more side effects) agent when a less-toxic agent exists.

### Statistical Analysis

Data was analyzed using SPSS version 13.0 software. Chi-square tests were used for comparing the two groups. P<0.05 value was accepted as significant.

## Results

On the day of the study, 153 patients (36.2%) of the 422 in-patients were being given one or more antibiotics.

When these 153 patients under antibiotic treatment were evaluated, it was determined that treatment or prophylaxis was appropriate in 69 patients (45.7%) while it was not appropriate in 84 patients (54.3%). In 75 of 84 patients, despite the presence of treatment indication, the given treatment or prophylaxis was not microbiologically or pharmacologically appropriate and in 9 patients treatment was started without an indication (Table 1).

Inappropriate use of antibiotics was significantly higher in surgery clinics when compared with internal diseases clinics (P < 0.001) (Table 2). In 64 patients in

Table 1. Distribution of determined reasons for inappropriate antibiotic use.

| Reason for inappropriateness | Number | % |
|---|---|---|
| Unnecessary use (no evidence of an infection or indication for prophylaxis) | 9 | 10.7 |
| Microbiologically inappropriate use | 3 | 3.6 |
| Microbiologically and pharmacologically inappropriate use | 15 | 17.9 |
| Pharmacologically inappropriate use | 57 | 67.9 |
| Dose and duration | 36 | 42.8 |
| Dose | 18 | 21.4 |
| Duration | 12 | 14.3 |
| Dose, duration, and toxicity | 3 | 3.6 |
| Dose and toxicity | 2 | 2.4 |
| Total | 84 | 100.0 |

whom antibiotics were used with the aim of treatment, it was detected that an infectious diseases consultation was requested in 28 (43.7%). Appropriateness of treatment was found significantly higher in those patients for whom an infectious diseases consultation was requested, when compared with patients for whom this consultation was

Table 2. Distribution of rates of antibiotic use and inappropriate antibiotic use by clinics.

| Department | Number of hospitalized patients | Rate of antibiotic use n (%) | Rate of inappropriate antibiotic use n (%) |
|---|---|---|---|
| Surgery Clinics | 257 | 110 (42.8) | 69 (62.7) |
| General surgery | 78 | 32 (41.0) | 20 (62.5) |
| Urology | 31 | 19 (61.3) | 14 (73.7) |
| Orthopedics | 28 | 18 (64.3) | 16 (88.9) |
| Plastic surgery | 29 | 17 (58.6) | 11 (64.7) |
| Gynecology | 30 | 11 (36.7) | 8 |
| Neurosurgery | 21 | 5 | 2 |
| Ophthalmology | 21 | 1 | 1 |
| Otorhinolaryngology | 19 | 7 | 5 |
| Internal Diseases Clinics | 143 | 29 (20.3) | 7 |
| Internal medicine | 79 | 19 (24.0) | - |
| Neurology | 25 | 3 | - |
| Physical therapy and rehabilitation | 30 | 4 (13.3) | 3 |
| Dermatology | 9 | 3 | 1 |
| Intensive care units | 22 | 14 (63.6) | 3 |
| Neurology-neurosurgery ICU | 6 | 4 | - |
| Internal medicine ICU | 9 | 4 | - |
| General surgery ICU | 7 | 6 | 3 |
| Total | 422 | 153 (36.2) | 84 (54.9) |

not requested (P<0.05). When the rate of inappropriate use according to the aims of treatment or prophylaxis was examined, it was found that in 9 (14.1%) of 64 patients who used antibiotics for treatment and in 75 (84.3%) of 89 patients who used antibiotics for prophylaxis, antibiotic use was determined as inappropriate (P < 0.001).

When the distribution of patients under antibiotic treatments was evaluated according to the causes of their hospitalization, it was found that 82 patients (53.6%) were hospitalized for elective surgery, 44 (28.8%) for medical treatment, and 27 (17.6%) for urgent surgical procedures.

Antibiotic use was aimed at treatment in 64 patients (41.8%) and for prophylaxis in 89 patients (58.2%). The clinics with the highest rates of antibiotic use were found as orthopedics (64.3%), urology (61.3%), and plastic surgery (58.6%), respectively. When antibiotic use in intensive care units was examined, it was demonstrated that general surgery (85.7%) had the highest rate, followed by the neurology-neurosurgery unit (66.6%) (Table 2).

In case of antibiotic use with the aim of treatment, the most commonly diagnosed infectious disease was urinary infection (31.3%), followed by lower respiratory tract infection (26.7%) and soft tissue infection (22.0%). In 57.8% of these patients, culture sampling was performed prior to treatment and 82.8% of the antibiotherapy was started empirically. Of all the patients who were given antibiotics with the aim of treatment, 55 (85.9%) had community-acquired infections while 9 (14.1%) had hospital-acquired infections. In these patients, it was found that the most frequently used antibiotics were metronidazole (15.5%), third-generation cephalosporins (14.4%) and ampicillin-sulbactam (13.3%). It was detected that, of the 64 patients who were given antibiotics with the aim of treatment, 44 used a single antibiotic, while 20 were given two or more antibiotics.

The most frequently used antibiotics for prophylaxis were first-generation cephalosporins (56.9%), ampicillin-sulbactam (11.9%), and ceftriaxone (9.2%) (Table 3). In this prophylaxis subgroup, 78 patients were given a single antibiotic, while 11 used two or more antibiotics.

Of the total 153 patients, 31 (20.3%) were detected to use combined antibiotics.

When uses with the aim of treatment and as prophylactic were evaluated together, the most

Table 3. Distribution of antibiotics used for treatment and prophylaxis by classes of antibiotics.

| Antibiotic | For Treatment[a] n=90 | | For Prophylaxis[a] n=109 | | Combination n=68 | |
|---|---|---|---|---|---|---|
| | Appropriate | Inappropriate | Appropriate | Inappropriate | Appropriate | Inappropriate |
| Ampicillin-sulbactam | 9 | 3 | 2 | 11 | 2 | 2 |
| Amoxicillin-clavulanate | 3 | 2 | 2 | 1 | 1 | - |
| Piperacillin-tazobactam | 2 | - | - | | 1 | - |
| First-generation cephalosporins | 3 | 2 | 6 | 56 | 6 | 4 |
| Cefuroxime | 1 | 1 | 4 | 4 | 1 | - |
| Ceftriaxone | 12 | 1 | 5 | 5 | 7 | 1 |
| Cefoperazone-sulbactam | 3 | - | - | | 3 | - |
| Quinolones | 11 | - | - | 4 | 3 | - |
| Metronidazole | 12 | 2 | 3 | 3 | 15 | 2 |
| Carbapenems | 11 | - | - | | 6 | - |
| Glycopeptides | 4 | - | - | | 2 | - |
| Aminoglycosides | 3 | - | 1 | 2 | 4 | 2 |
| Other | 4 | 1 | | | 4 | 2 |
| Total | 78 | 12 | 23 | 86 | 55 | 13 |

[a] antibiotics used in combination are also included.

frequently used antibiotics within the combination were found as metronidazole, first- generation cephalosporin, and aminoglycosides, respectively.

## Discussion

One of the most effective approaches in preventing the spreading of multi-resistant microorganisms is to ensure appropriate antibiotic use. In the present study, 36% of hospitalized patients were under antibiotic treatment. Three years before this study, antibiotic use in the same hospital was examined with the same method and at that time this rate was found as 42.8% (10). Although minimal, the reason for this decrease may have been the legal regulation of limited antibiotic use, which started in 2003. However, biases resulting from the point prevalence method that may have led to this difference should not be discounted. According to the literature, nearly one-third of all hospitalized patients are given antibiotics in general (5,11-13). Nevertheless, different rates can also be seen with respect to the country and the hospital in which these studies are conducted. For instance, rate of antibiotic use was reported as 77.8% in a university hospital in China, while it was reported as 65% in a study conducted in Costa Rica (14,15). In a multi-center point prevalence study performed including 18 centers in Turkey, it was reported that antibiotics were ordered in 30.6% of patients on the day of the study (16). In other Turkish studies, similar rates were reported, and the rate of antibiotic use in hospitalized patients ranged between 16.6% and 39.4% (17-19).

The clinical use of antibiotics was introduced in the early 1940s and a short time thereafter, their misuse and abuse potential were recognized (5). Studies to date have reported that 14-43% of the given antibiotic treatments were unnecessary (1,14,20). When inappropriate use is taken into consideration, irrational uses were reported in 28-65% (19,21-23). However, in studies carried out in Israel and Switzerland, appropriateness of antibiotic use has been reported at quite high rates (80 ± 9% and 71%, respectively) (24,25). In Turkey, despite antibiotics being used in 25-35% of patients admitted to the hospital, 40-50% of the cases were reported as misuses (17,26). In the multi-center study by Usluer et al. (16), it was reported that in antibiotics given with the aim of treatment, 25.8% of uses in clinically proven infections and 15.95% of uses in microbiologically documented

infections were inappropriate, while 33.07% of the prophylactic antibiotic uses were inappropriate. In Erbay et al.'s (18) study, rates for unnecessary use and inappropriate use were 27% and 35.8%, respectively. Irrational antibiotic use is the most important factor that contributes to resistance development. In the present study, more than half of the antibiotherapy (54.3%) was detected as inappropriate. In the same hospital, this rate was reported as 67% 3 years ago (10). This result suggests that the legislation about antibiotic restriction had a positive impact on the appropriateness of antibiotic use, but the effect was only limited and did not reach the desired levels. According to the Infectious Diseases Society of America (IDSA) guidelines published recently, preauthorization requirements can lead to a rapid and dramatic decrease in the use and expenditure of antibiotics (27).

Inappropriate antibiotic use was found significantly higher in surgery clinics when compared with internal diseases clinics. Use as prophylaxis (84.3%) was detected as inappropriate at an important level, when compared with the use aimed at treatment (14.1%). On the subject of rational antibiotic use, there are many problems regarding surgical prophylaxis in clinical practice (14, 28, 29). In a multi-centered study by Bailly et al. (28), it was declared that 58.3% of surgical prophylaxis was inappropriate.

In another multi-centered study conducted in Turkey by Hosoglu et al. (29), 88% of surgeons were reported as using more than one dose and 32% of them as giving prophylaxis with the wrong antibiotic. The other studies performed in Turkey stated that the majority of irrational antibiotic uses in surgery departments consisted of inappropriate prophylaxis (30,31). The most important reason for inappropriateness in surgical prophylaxis is the long duration of antibiotic use (32-34). In the present study, it was detected that duration of prophylaxis was long in 51 (57.3%) of 89 patients that were given prophylactic antibiotics.

In the present study, prophylaxis accounted for 60% of antibiotic use, while 40% was given with the aim of treatment. The rate of prophylaxis was higher than in the study of Usluer et al. (44%) and other studies performed in Turkey (28.8%-52.7%) (16,17,30,35). It was suggested that this situation may be relevant to the higher number of patients hospitalized in surgical clinics. Irrational usage of antibiotics could also be a reason for this situation

Evaluation of antibiotic use with the aim of treatment revealed that, although the Microbiology and Clinical Microbiology Clinic at the hospital in which the study was conducted worked 24/7, sampling for microbiological examination preceding treatment was not performed in approximately one-third of the patients. This rate is lower than the results of point prevalence study performed throughout the country and the data of the same hospital 3 years ago (10,16). This finding indicates that the awareness regarding the importance of performing culture sampling preceding empirical antibiotic therapy in clinical practice is increasing.

Among antibiotics given with the aim of treatment, cephalosporins and metronidazole ranked first. In a point prevalence study performed at 15 hospitals in Italy in 2000, penicillins and cephalosporins were reported as the most frequently used antibiotics (36). In the present study, when antibiotics used with the aim of treatment were taken into consideration together with prophylactic use, the most commonly used class of antibiotics was the same. Penicillins, and first- and second-generation cephalosporins are not limited antibiotics according to the

legal regulations in our country. We believe this could be a contributing factor to overuse of these antibiotics.

Combined antibiotic use was reported as 33% in the multi-center study performed by Usluer et al. (16). This rate was reported as 20.1% in the present study, with 24% reflecting inappropriate combined use.

In the present study, although the rate of antibiotic use in the hospital was acceptable when compared with other studies, more than half of it was inappropriate. Although the rate of starting empiric antibiotic therapy was high, the rate of culture sampling preceding treatment being low along with the higher inappropriate use in surgery clinics reveal that policies of antibiotic use in the hospital need to be reviewed in terms of rational antibiotic use. A close surveillance of the antibiotic use in surgery clinics and the structuring of new policies regarding surgical prophylaxis with the help of approaches such as the development of guidelines for local surgical prophylaxis and continuous education could contribute to improving the appropriate use of antibiotherapy.

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