

Critical evaluation of antimicrobial use - A Turkish university hospital example

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Abstract

Introduction: Antimicrobials are being used unnecessarily for different reasons. The aims of this study were: assessment of the quality of antimicrobial use and determination of the factors related to correct use.

Method: Antimicrobial practice at Dicle University Hospital (DUH) was evaluated with a point prevalence approach. Using a standardized data collection form, the patients' data (clinic, epidemiology, laboratory and antimicrobial use) was collected. Possible influential factors on antimicrobial use were examined.

Results: In the surveillance study 1,350 inpatients were evaluated; 461 (34.1%) of them were using antimicrobials for treatment and 187 (13.9%) for prophylaxis. Antimicrobial indication was found in 355 of 461 patients (77.0%), and the number of antimicrobials was 1.8 per patient in the treatment group. The most common reason for antimicrobial use was community-acquired infection (57.9%). Pneumonia (20.4%), skin and soft tissue infections (9.11%) and urinary tract infections (7.9%) were the most common infectious diseases. Positive culture results were available for 39 patients (8.5.0%) when antimicrobial treatment started. All steps of antimicrobial use were found appropriate in 243 patients (52.7%).

In multivariate analyses, clinical manifestation of infection at the beginning ($p < 0.001$), presence of leukocyte counting ($p < 0.001$) and prescription by an infectious disease specialist were found significantly positive factors for wholly appropriate antimicrobial use. Hospitalization with a diagnosis other than infection was found a significantly negative factor for appropriate antimicrobial use ($p = 0.001$).

Conclusion: The quality of antimicrobial use could be improved with better clinical and laboratory diagnosis and consultation with infectious diseases specialists

Key words: antimicrobial use; quality evaluation; related factors

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Introduction

Antimicrobials are being used unnecessarily and with inappropriate characteristics, for different reasons. Thus, antimicrobial resistance has become one of the most important issues over the last 20 years. Many studies have focused on the influential factors of antimicrobial use, as well as aiming to determine the criteria for optimal quality of antimicrobial therapy [1-3]. It is generally accepted that the ideal antimicrobial use should be combined with maximal efficacy, minimal toxicity and the lowest cost. The quality of antimicrobial prescriptions depends on multiple factors. One of the most important factors is the knowledge of its prescribers. In the prescription of antimicrobials, the host factors, the virulence of microorganisms, the pharmacokinetics and the

pharmacodynamics of drugs must be considered [1,4-9].

Antimicrobial resistance and excessive antimicrobial use are important issues in Turkey. The total annual expenditure for antimicrobials in Turkey in 2002 was 24% of all drug spending. Conversely, some studies revealed that the quality of antimicrobial use in Turkey is not satisfactory. A new restriction on antimicrobials was implemented as a method to improve antimicrobial drug use by May 2003. After May 2003, the reimbursement of wide-spectrum antimicrobials was cut, unless it was approved by an Infectious Diseases Physician (IDP) [10].

We evaluated antimicrobial practices at Dicle University Hospital (DUH) with an observational approach. This study evaluated the necessity and quality of antimicrobial drug prescribing. In the

present study, we aimed to assess the quality of antimicrobial use and to determine the factors related to correct use of antimicrobials in patients.

Methodology

Dicle University Hospital (DUH) is a referral hospital in the centre of Diyarbakir city. The hospital is the largest teaching hospital, with 1146 beds, in southeast Turkey. The hospital comprises departments covering all major specialties. In 2006, a total of 42,843 patients were hospitalized. The occupation rate of hospital beds was 64% in 2006.

Study design

From a prospective approach, the administration of antimicrobials was examined in all inpatients at the hospital, for which they were prescribed during the study days, 4 May 2006 and 4 October 2006. The epidemiological and medical data of all hospitalized patients was reviewed during the study days. The indication of antimicrobial use, the substance prescribed, the duration of treatment, the dosage, the route and intervals of antimicrobial administration were also recorded. The evaluation of the necessity of antimicrobials from a prospective approach was carried out through a point scoring system as a quality indicator; prophylactic use of antimicrobials was recorded on the same form, but this data will be evaluated elsewhere. The data was collected by a research team from the Department of Infectious Diseases and all cases were evaluated by specialists from the same department. The final decision on antimicrobial use was given by IDPs (S.H. and M.F.G). The appropriateness of antimicrobial treatment was evaluated using modified Kunin's criteria [6].

The following categories were used:

I. The use of antimicrobial therapy is necessary; the protocol (choice, route, duration, and dosage) is appropriate. This decision may have been supported with a microbiology report.

II. The use of antimicrobial therapy is necessary, but a different antimicrobial (less expensive, less toxic, or another combination) is preferred.

III. The use of antimicrobial therapy is necessary, but a different antimicrobial dose, interval, duration or route of administration is preferred.

IV. Disagreement with the use of antimicrobial therapy; administration is unjustified. Category I indicates "appropriate therapy," Categories II and III indicate that there was some major deficiency in the choice or use of antimicrobials. Category IV indicates

unnecessary antimicrobial use. The evaluation and categorization of antimicrobial treatment was carried out based on the literature and clinical experiences of the authors [6-9,11-22].

Possible influencing factors on the quality of antimicrobial use were examined. At this stage, the cases in Category I were entered into the model as appropriate antimicrobial use and the others were labeled inappropriate.

Statistical analyses

The quality of antimicrobial use was evaluated for association with the following predictor variables: type of department (surgical or medical), type of health insurance, primary hospitalization reason (emergency, elective surgical, medical, infections), severity of the disease, fever ($>38^{\circ}\text{C}$), existence of a leukocyte increase, neutrophily ($>70\%$), existence of a C-reactive protein test, increasing erythrocyte sedimentation rate (ESR) ($>30\text{ mm/h}$) and decision-maker for antimicrobial use (resident from same department, academic from same department, IDP). The data was analyzed using SPSS version 10.0 (SPSS Inc, Chicago, IL). The χ^2 test and independent sample t-tests were used to assess the strength of the association between variables. Multiple logistic regression modeling was performed to identify predictor variables that influenced the quality of antimicrobial use.

Results

In the surveillance study, the first surveillance was started on 4 May 2006 and the second started on 4 October 2006. In total, 1,350 inpatients were evaluated, with 461 of them (34.1%) using antimicrobial for treatment and 187 (13.9%) for prophylaxis. The occupancy rate of the hospital was 58.9% during the study days. In total, 648 patients were using antimicrobials (48.0%). Antimicrobial use for prophylaxis was very rare in medical departments but more common in surgical departments (0.3% vs. 28.2%, respectively). In total, 364 of 656 (55.4%) patients were using antimicrobials in surgical departments and 284 of 694 (40.9%) patients in internal departments ($p=0.0016$). Antimicrobial use for treatment was more common in medical departments (282 patients, 40.6%) than in surgical departments (179 patients, 27.3%) ($p<0.001$). The route of antimicrobial use was intravenous in 556 cases (73.5%), oral in 198 cases (26.1%) and intramuscular in three cases (0.4%).

Assessment of antimicrobial use in the treatment group

The mean age of patients was 31.5 (\pm 25.4) (range 0-80 years), and 255 (55.3%) of them were male. In the treatment group, the most common reason for hospitalization was (non-infectious) internal disease (174 patients, 37.7%) (Table 1). The most common reason for antimicrobial use was community-acquired infection (267 patients, 57.9%) (Table 2). The most common infectious diseases were: pneumonia (94 patients, 20.4%), skin and soft tissue infections (43 patients, 9.11% and urinary tract infections (36 patients, 7.9%). The most commonly used antimicrobials were ceftriaxone (124 cases, 26.9%), ampicilline-sulbactam (59 cases, 12.8%) cefazoline (45 cases, 9.8%), and meropenem (45 cases, 9.8%). Antimicrobial treatment was arranged according to positive culture results in 39 patients (8.5.0%).

The decision for antimicrobial treatment was made by responsible academics from the same department in 347 cases (75.3%), by resident physicians in 24 cases (5.2%), and by infectious diseases physicians/consultants in 78 cases (16.9%). In 12 cases (2.6%), responsible academics/physicians added one or more antimicrobials after IDP consultations. All of these 12 cases had been treated with unnecessary antimicrobials. The mean number of antimicrobials was 1.8 per patient in the treatment group.

Assessment of antimicrobial use

Antimicrobial use was found necessary in 355 patients (77.0%) in the treatment group. In 243 (52.7%) patients, all steps of antimicrobial use were found appropriate (Category I). In 74 patients (16.1%), antimicrobials were needed, but the choice of antimicrobial treatment was inappropriate (Category II). In 53 patients (11.5%), the inappropriateness was having used two antimicrobials that had similar spectrums, and in 21 patients (4.6%) the spectrum of antimicrobials was broader than the spectrum needed. In 40 patients (8.7%), the antimicrobial treatment was necessary, but the treatment was not acceptable (Category III). In these patients, the following types of inappropriateness were found: narrower spectrum than needed (24 cases, 5.2%), not given the necessary combination (6 patients, 1.3%), wrong choice and wrong dosage (5 patients, 1.1%), unnecessary toxic antimicrobials (3 patients, 0.7%), and wrong choice and wrong interval (2 patients, 0.4%). There was no indication to use antimicrobials in 106 patients (23.0%) (Category IV).

The related factors of quality of antimicrobial use

The factors related to appropriate antimicrobial use were evaluated. In the univariate analyses, primary hospitalization reason, critical situation upon admission, fever, clinical manifestation of infection at admission, existence of a leukocyte increase, neutrophil elevation, existence of a C-reactive protein test and decision-maker for antimicrobial use were found significant factors in appropriate antimicrobial use (Table 3).

In the multivariate analyses, clinical manifestation of infection at the beginning (OR=3.8; CI=1.9-5.4; $p<0.001$), existence of a leukocyte increase (OR=3.3; CI=1.2-9.2; $p<0.001$) and antimicrobial decision made by an IDP (OR=7.4; CI=3.5-15.3; $p<0.001$) were considered significantly positive factors for appropriate antimicrobial use. Hospitalization with a medical reason other than infection (OR=0.5; IR=0.3-0.7; $p=0.001$) was found as a significant negative factor for appropriate antimicrobial use.

Discussion

Many studies have shown that more than one-third of antimicrobials prescribed for hospitalized patients are not necessary [7-9,20,21,26]. Antimicrobial stewardship programs constitute a basis for prevention strategies to control the emergence and spread of antimicrobial-resistant pathogens in hospitals alongside effective infection control and prevention measures. Antimicrobial resistance has become one of the most difficult problems in medical treatment in the world. Many studies have been implemented to evaluate and control resistance processes. Unfortunately, none of them have discovered a clear solution to stop the resistance. Most of them have focused on the quantity of antimicrobial use [6,11].

The quality of antimicrobial use in hospital settings has been evaluated in few studies. The quality of antimicrobial use may be primarily evaluated based on the following criteria: reasonable indication, correct drug choice with maximal efficacy, minimal toxicity at the lowest cost, correct dosage interval and correct route. The acceptable indication should be supplemented with a suitable antimicrobial treatment course [7,8]. This study has concentrated on issues of the quality of antimicrobial drug use for hospitalized patients and possible influential factors of appropriate antimicrobial use. In this study, Kunin's criteria were modified and used in a simpler way [6-9].

Table 1: Reasons for hospitalization of 461 patients

Hospitalization reasons	No. of patients (%)
Medical disorders (non-infectious)	174 (37.7)
Community acquired infections	119 (26.8)
Elective surgical intervention	41 (8.9)
Emergent surgical intervention	35 (7.6)
Multiple disorders	33 (7.2)
Medical + surgical reasons	30 (6.5)
Nosocomial infections	20 (4.3)
Burn	9 (2.0)
Total	461 (100)

Table 2: Indications of antibiotic use of 461 patients

Reasons for antibiotic use	No. of patients (%)
Community acquired infections (empirical)	237 (51.4)
Nosocomial infections (empirical)	77 (16.7)
Nosocomial infections (microbiologic evidence)	39 (8.5)
Community acquired infections (microbiologic evidence)	30 (6.5)
Community acquired + Nosocomial infections	3 (0.7)
Unknown	75 (16.3)
Total	461 (100)

Table 3 - Univariate analyses of related factors with appropriate antimicrobial use

Variables	Appropriate	Inappropriate	OR	% 95 CI	P value
Departments (Surgical)	78/243	84/218	0.747	0.509-1.097	0.137
Type of insurance					
<i>Low income group (government support)</i>	140/243	119/218	1.119	0.773-1.620	0.552
<i>Workers/professional</i>	64/243	69/218	0.766	0.511-1.148	0.196
<i>Governmental workers</i>	21/243	18/218	1.045	0.541-2.019	0.895
<i>Other</i>	16/243	10/218	1.458	0.647-3.286	0.360
Primary hospitalization reason					
<i>Emergent surgical</i>	26/243	17/218	1.416	0.746-2.687	0.286
<i>Elective surgical</i>	25/243	36/218	0.576	0.333-.996	0.046
<i>Non-infectious</i>	97/243	136/218	0.396	0.272-.578	<0.001
<i>Infectious</i>	123/243	59/218	2.774	1.875-4.103	<0.001
Critical situations upon admission	123/243	44/218	4.040	2.665-6.126	<0.001
Fever (>38 °C)	122/237	58/206	2.707	1.821-4.024	<0.001
Clinical manifestation of infections	214/242	117/218	6.707	4.144-10.855	<0.001
Leukocyte increase	235/243	193/218	4.001	1.681-9.523	0.001
PMNL (>70%)	147/235	92/198	1.855	1.259-2.733	0.002
CRP measurement	165/243	121/218	1.682	1.149-2.463	0.007
ESR increased (>30 mm/h)	77/126	49/101	1.668	0.982-2.832	0.058
Decision maker of treatment:					
<i>Resident from department</i>	13/243	13/218	0.886	0.402-1.956	0.765
<i>Academic from department</i>	151/243	193/218	0.361	0.236-0.551	<0.001
<i>IDP</i>	78/243	10/218	9.798	4.916-19.525	<0.001

Antimicrobials consist of a significant part of drugs prescribed in hospital settings. In Turkey, in contrast with many other countries, antimicrobials are the drugs that are used first [5,26,27]. The proportion of antimicrobial use reported in hospitalized patients in Croatia was 15% (Department of Medicine), 44.5% in Thailand (university hospital), (30.6% in Turkey (multi-central) and 88.8% in China [7,27-29]. In our study, the proportion was 48%. These proportions could be related to different variables, such as the patients' characteristics. Some studies reported that antimicrobial use was more common in surgical departments than in medical departments. This was concordant with our study when prophylactic antimicrobial uses were included [28,30].

The proportion of inappropriate antimicrobial use was reported in a wide range. The variation could be related to the evaluation methods for antimicrobial use. At the same time, the patients' characteristics are important. Some studies included only treatment purposes, but some of them included treatment and prophylactic purposes together. In this study, the duration of treatment was not evaluated because of the study design. A multi-centre study from Turkey reported that 61.5% of prescriptions were evaluated as clinically appropriate in patients receiving antimicrobials for treatment [27]. Another study reported 45.7% appropriate use in a hospital setting [30]. In this study, the appropriate proportion was found as 52.2%. These studies have revealed that at least half of antimicrobial prescriptions at Turkish hospitals could be regarded as inappropriate.

Prescription without antimicrobials is one of the most frequent characteristics of inappropriate treatments. In the present study, according to the prescribers' statements, 16.3% of the prescriptions had no reason for antimicrobial use. On the other hand, in our assessment, 23.0% of the antimicrobial use was unnecessary. Vlahović-Palčevski *et al.* reported the same proportion (23%) for unnecessary antimicrobial prescriptions in Croatia [9]. They reported that the main reason for inappropriate antimicrobial treatment was the wrong choice of antimicrobials (37%).

The quality of antimicrobial prescription is related to the accuracy of the diagnosis of the infection. A Norwegian study reported that bacteriological samples were obtained from 85% of the patients and compliance with the guidelines was >90%. Compliance was highest when the results of bacteriological samples were positive [31]. In Rijeka Hospital, 32% of the antimicrobial prescriptions were based on microbiology results [8]. In our study, only

8.5% of prescriptions were based on microbiological evidence. The majority of the prescriptions were arranged empirically. Physicians frequently chose broad-spectrum antimicrobials because of diagnostic uncertainty. Limited use of the microbiology laboratory in the decision for antimicrobial prescriptions could be a reason for the low quality of antimicrobial use. Improving adherence to local or major guidelines for antimicrobial prescription could be another effective approach to decrease inappropriate antimicrobial use.

In the multivariate analyses, clinical manifestation of infection at the beginning was a supporting factor for appropriate antimicrobial use. The existence of clinical manifestation makes it easier to accurately diagnose the infection. Effective use of laboratory methods other than microbiology (leukocytes, C-reactive protein) could be helpful for accurate diagnosis of infections. In particular, an increasing number of leukocytes/neutrophils could be a valuable marker for acute infections. In our study, the existence of a leukocyte increase was found as one of the related factors for appropriate antimicrobial prescriptions. These data indicate that some doctors do not use simple and basic laboratory tools for confirmation of infection.

The debate on the decision-makers for antimicrobials is ongoing. Many studies have indicated that IDPs with a multidisciplinary team approach play a critical role in controlling antimicrobial use in the hospital [12,26,32]. Our study confirmed these data, and showed that antimicrobial decisions made by an IDP were a significantly positive factor for appropriate antimicrobial use.

This study provided many new data on the behaviours of antimicrobial prescriptions in a Turkish university hospital. On the other hand, this study has some limitations. The study was organized and performed by infectious diseases physicians. This situation could be considered a risk for bias. A specialist from the public health department monitored the study to avoid such risks.

Conclusion

In conclusion, almost half of the hospitalized patients were prescribed antimicrobial drugs in this study. Nearly the same proportion of antimicrobial prescriptions for treatment was found as inappropriate. The quality of antimicrobial use could be improved with better clinical and laboratory diagnoses and consultation with infectious diseases specialists.

Further studies are needed to define the most efficient approaches to improve hospital antimicrobial drug use.

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