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ORIGINAL ARTICLE

Antibiotic use and cost in a teaching hospital in İstanbul

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ABSTRACT

Objectives: The aims of this study were to determine the usage patterns and the cost of antibiotics, along with the evaluation of the effects of infectious diseases (ID) specialists on appropriate antimicrobial use in hospitalized patients.

Materials and methods: A one-day, cross-sectional study was conducted in a major tertiary hospital and data on the use of antibiotics were collected by using a standard form. The appropriateness of the antibiotic usage was evaluated using the Council for Appropriate and Rational Antibiotic Therapy (CARAT) criteria; and the consumption and daily cost of antibiotics were determined.

Results: On the study day, antibiotics were prescribed in 199 (35.6%) of 553 hospitalized patients, in 109 (32.9%) on the surgical and 90 patients (40.5%) on the medical wards. The total empirical antibiotic use was more frequent (49.7%) than prophylactic (29.1%) and culture-based therapy (21.2%). In 44 patients (22.1%) the antibiotics were used inappropriately; any of these antibiotics needed the approval of ID specialist. The inappropriate usage was more common in prophylactic therapy (46.5%) than empirical (16.1%) and specific antibiotic administration (2.3%). ID consultation rates were significantly higher in the appropriate antibiotic administrations (69.6%) than in the inappropriate group [(6.8%, $p<0.0001$), odds ratio (OR) 10.2, confidence intervals (CI) =3.0–3.7]. The total one-day cost of antibiotic therapy in our hospital was US $3350.6, and the total daily cost for hospital infection was $2137.1. The mean daily cost per patient was $2.1 for prophylaxis, $10.7 for community-acquired infections and $54.7 for hospital infections ($p<0.001$, OR 9.8, CI 4.7–20.7).

Conclusion: This study showed that antibiotic prescription rates are high, surgical prophylaxis is still a major problem in our hospital, ID approval is effective for appropriate use of antibiotics, and the antibiotic cost of hospital infections is an important part of extra costs. *J Microbiol Infect Dis 2011;1(3):128-133*

Key words: Antibiotics, rational use, cost

İstanbul'da bir eğitim hastanesinde antibiyotik kullanımı ve maliyeti

ÖZET

Amaç: Bu çalışmanın amacı hastanemizde yatan hastalarda antibiyotik kullanım oranlarını, maliyetini ve enfeksiyon hastalıkları konsültasyonunun uygun antibiyotik kullanımına etkisini değerlendirmektir.

Gereç ve yöntem: Antibiyotik kısıtlama politikası uygulanan bir eğitim hastanesinde bir günlük nokta prevalans araştırması ile antibiyotik kullanımına ait veriler toplandı. Antibiyotik kullanım kalitesi, Council for Appropriate and Rational Antibiotic Therapy (CARAT) kriterlerine göre değerlendirilmiş ve günlük antibiyotik tüketimi ve maliyeti belirlenmiştir.

Bulgular: Çalışma günü hastanede yatan toplam 553 yatan hastanın 199'u (% 35,9) antibiyotik kullanmaktaydı. Cerrahi kliniklerde yatan hastalardan 109'u (% 32,9) dahili kliniklerde, 90'ı (% 40,5) antibiyotik kullanmaktaydı. Antibiyotik kullanmı 141 hastada (% 70,8) tedavi amaçlı (% 49,7 ampirik, % 21,2 kültüre dayalı) iken 58 hastada proflaktik (% 29,1) amaçlıydı. Kırkdört hastada (% 22,1) uygunsuz antibiyotik kullanımı saptandı. Uygunsuz kullanılan antibiyotiklerin hepsi enfeksiyon hastalıkları uzmanı (EHU) onayı gerektirmeyen antibiyotikler idi. Uygunsuz kullanım oranı proflaktik olanlarda % 46,5) ampirik olanlarda %16,1 ve kültüre dayalı tedavide % 2,3 idi. Enfeksiyon hastalıkları uzmanı konsültasyonu istenme oranı uygun antibiyotik uygulanan hastalarda uygun olmayanlara göre anlamlı şekilde yüksekti (% 69,6'a karşılık % 6,8, $p<0,0001$, tahmini rölatif risk (OR)=10,2), güven aralığı (CI):3.0–3.7). Hastanemizde bir günlük toplam antibiyotik kullanım maliyeti 3350.6 dolar, hastane enfeksiyonları için bir günlük antibiyotik maliyeti 2137.1 dolar idi. Hasta başına

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günlük antibiyotik maliyeti proflaksi için 2,1 dolar iken; toplum kaynaklı enfeksiyonlar için 10,7 dolar, hastane enfeksiyonları için 54,7 dolar olarak bulundu (p<0,0001, OR:9,8, CI:4,7–20.7).

Sonuç: Bu çalışma göstermektedir ki, hastanemizde antibiyotik kullanım oranları yüksek olup, cerrahi proflaksi hala önemli bir sorundur, hastane enfeksiyonları antibiyotik kullanım maliyetinin en önemli kısmını oluşturmaktadır ve enfeksiyon hastalıkları uzmanı onamı uygun antibiyotik kullanımında etkilidir.

Anahtar kelimeler: Antibiyotikler, uygun kullanım, maliyet.

INTRODUCTION

Rational antimicrobial use is important not only for the effectiveness of the treatment but also to prevent the spread of antimicrobial resistance and to decrease undesirable side effects and high costs.[1] However, in hospitalized patients, antibiotics are the most frequently prescribed drugs; and antimicrobial use has been reported to be irrational in 9–64% of inpatients.[2] Antibiotics also constitute 19.9% of the Turkish drug market.[3] and inappropriate antibiotic use percentages range between 8.6-60% in Turkey.[4-8] In 2003, an antibiotic restriction policy was implemented by Turkish Ministry of Health to decrease the antibiotic usage and especially the economic burden of antibiotics. According to this regulation, most of the parenteral and extended- spectrum antibiotics should be prescribed by the infectious diseases (ID) specialists.

The aim of this study was to determine the usage patterns of antibiotics, costs of antibiotic therapy, and to evaluate effect of ID specialists on appropriate antimicrobial use in hospitalized patients in a major tertiary hospital.

MATERIALS AND METHODS

This cross-sectional observational study was conducted in Haydarpaşa Numune Hospital, a 750-bed training hospital in Istanbul, Turkey. The hospital has all major clinics, including medical and surgical subspecialties, and medical and surgical intensive care units.

A nationwide antibiotic restriction regulation (NARP) was released by the Ministry of Health in 2003 in Turkey. According to this policy, carbapenems, glycopeptids, piperacillin-tazobactam, cefoperazone-sulbactam required the ID specialist approval. Third and fourth-generation cephalosporins, netilmicin, amikacin and parenteral quinolones could be prescribed by all specialists, but after 72 hours of treatment, ID specialist approval was also required. After its publication date, the restriction policy was initiated at our hospital.

On May 15, 2011, each hospitalized patient at the medical and surgical wards was visited by two ID specialists. Data concerning patients and antibiotic therapy were recorded for those patients who received antibiotics for any reason, using a standard form. They were reevaluated by the same ID specialists after 3–5 days, and the patient's clinical and laboratory data (which were recorded before and after five days of the study day) were reviewed by the hospital wide computer system and nursing records to exactly evaluate the appropriateness of antibiotic therapy on the study day. The appropriateness of the antibiotic usage was evaluated using the Council for Appropriate and Rational Antibiotic Therapy (CARAT) criteria.[9] These criteria included establishment of a need to justify use of antibiotics (e.g., colonization versus disease), evidence-based results, therapeutic benefits, safety, optimal drug, optimal duration, and cost-effectiveness. Because this study was a one-day cross-sectional one, the duration of therapy could not be evaluated exactly. The universal guides were also accepted as references for the diagnosis of infections and appropriate therapeutic recommendations.[10] The cost of antibiotic therapy was calculated in United States dollars. The statistical program GraphPad Prism 5.0, Fisher's Exact test, and chi-square test were used for the statistical analysis, and a rate of $p < 0.05$ was considered to be statistically significant.

RESULTS

In the study day, the number of inpatients was 553, 331 of them (59.9%) were hospitalized in surgical wards and 222 (40.1%) in medical wards. On the study day, antibiotics were prescribed in 199 (35.6%) of 553 hospitalized patients, in 109 patients (32.9%) on the surgical and 90 patients (40.5%) in the medical wards. Antibiotics were used in 141 (70.8%) patients for treatment (em-

pirical or culture-based) and in 58 (29.1%) for surgical prophylaxis.

The total empirical antibiotic use was more frequent (49.7%) than prophylactic (29.1%) (p=0.003, OR 2.4, CI 1.3–4.3) and culture-based use (21.2%) (p < 0.0001, OR 3.7, CI 2.0–6.9).

The most frequently prescribed antibiotics in the hospital were ampicillin-sulbactam (16.9%), first-generation cephalosporins (16.6%), third-generation cephalosporins (15.1%). The most commonly used antibiotic was ampicillin-sulbactam in medical wards and cefazolin in surgical wards. The data are shown in detail in Table 1.

In 44 patients (22.1%) the antibiotics were used inappropriately; any of these antibiotics needed the approval of ID specialist. Inappropriate antibiotic use rate was higher in patients hospitalized on surgical wards (29.3%) than on medical wards (13.3%, p=0.087, OR 2.7, CI 1.3–5.6). Inappropriate use was observed in 27 of 58 (46.5%) prophylactic administration, in 16 of 99 (16.2%) empirical, and 1 of 42 (2.3%) culture-based administrations, respectively. The most frequent causes of inappropriate use of antibiotics were improper administration time for prophylaxis and excessive length of treatment (34.0%), unnecessary or unsuitable combination (13.6%), and the absence of a valid indication (11.3%).

Appropriate use rate was found for 286 of 320 (87.0%) restricted antibiotics and 185 of 310 (59.6%) unrestricted antibiotics (p<0.001, OR 0.2, CI 0.1–0.4). ID consultation rates were significantly higher in the appropriate antibiotic administrations than in the inappropriate ones (p<0.001, OR=10.2, CI=3.0–33.7). The appropriate and inappropriate prescription of prophylactic, empirically and culture-based therapies and the ID consultation rates in hospitalized patients receiving antibiotics are presented in Table 2.

The total one-day cost of antibiotic therapy in our hospital was $3350.6, and the total daily cost for hospital infection was $2137.1. The mean daily cost per patient was $2.1 for prophylaxis, while it was $10.7 for community-acquired infections and $54.7 for hospital infections (p<0.001, OR 9.8, CI 4.7–20.7). The mean daily cost per patient was $10.3 in surgical wards and $24.7 in medical wards (p<0.001, OR 3.0, CI 1.3-6.6). Daily antibiotic usage cost in hospitalized patients is demonstrated in Table 3.

Table 1. Antibiotic usage rates

Antimicrobials	Medical Wards, n (%)	Surgical Wards, n (%)	Total, n (%)
Ampicillin-sulbactam	60 (19.3)	48 (14.5)	108 (16.9)
Cefazolin	6 (1.9)	100 (30.3)	106 (16.6)
Ceftriaxone and Cefotaxime	50 (16.1)	47 (14.3)	97 (15.1)
Metronidazole	43 (13.8)	36 (10.9)	79 (12.4)
Imipenem-cilastatine and Meropenem	48 (15.4)	28 (8.5)	76 (11.9)
Piperacillin-tazobactam	27 (8.7)	22 (6.9)	49 (7.7)
Teicoplanin and Vancomycin	18 (5.8)	13 (3.9)	31 (4.8)
Cefoperazone-sulbactam	18 (5.8)	4 (1.2)	22 (3.4)
Ciprofloxacin and Levofloxacin	11 ((3.5)	4 (1.2)	15 (2.3)
Clindamycine	5 (1.6)	8 (2.4)	13 (2.0)
Linezolide	8 (2.6)	4 (1.2)	12 (1.9)
Gentamicin and Amikacin	0 (0)	10 (3.0)	10 (1.5)
Colistin	6 (1.9)		6 (0.9)
Clarithromycin	4 (1.3)		4 (0.6)
Tigecycline	2 (0.6)	2 (0.6)	4 (0.6)
Daptomycine	3 (0.9)		3 (0.4)
Other antibiotics	1 (0.3)	3 (0.9)	4 (0.6)
Total	310 (100.0)	329 (100.0)	639 (100.0)

Table 2. The appropriate prescription of prophylactic, empirically and culture-based therapy, and ID specialist consultation rates

Antibiotic use indications	Groups	Appropriate, n (%)	Inappropriate, n (%)	P
Prophylactic therapy (n=58)	Patients given prophylactic therapy	31 (53.4)	27 (46.5)	>0.05
	ID consultation	4 (12.9)	0 (0.0)	<0.001
Empirical therapy (n=99)	Patients given empirical therapy	83 (83.8)	16 (16.2)	<0.001
	ID consultation	63 (75.9)	3 (18.7)	<0.001
Culture-based therapy (n=42)	Patients given culture-based therapy	41 (97.6)	1 (2.3)	<0.001
	ID consultation	41 (100.0)	0 (0.0)	<0.001
Total (n=199)	Patients given antibiotics	155 (77.8)	44 (22.1)	<0.001
	IDS consultation	108 (69.6)	3 (6.8)	<0.001

ID: Infectious diseases

Table 3. Daily antibiotic usage cost in hospitalized patients

Reason of antibiotic use	Number of patients, n (%)	Total daily costs of antibiotics, US Dollar (%)	The daily cost per patient US Dollar
Prophylaxis	58 (29.1)	121.8 (3.6)	2.1
Hospital infection	39 (19.6)	2137.1 (63.8)	54.7
Community-acquired infection	102 (51.3)	1091.7 (32.6)	10,7
Total	199 (100.0)	3350.6 (100.0)	16.8

DISCUSSION

Although many methods have been developed by healthcare institutions targeting the improvement in antibiotic use, excessive and inappropriate antibiotic prescribing is still a major problem throughout the world. It has been reported that approximately 60% of all hospitalized patients in the United States receive an antibacterial drug during hospitalization and about 50% of this use is unnecessary or otherwise inappropriate.[1] Several strategies for antimicrobial stewardship have been suggested, such as education efforts of healthcare providers, formulary restriction and review, antibiotic order forms, feedback activities, and approval requirement from an ID specialist for drug prescription.[1,11–13]

In this study, antibiotic usage rate in hospitalized patients was found to be 35.6%. This frequency was reported between 16.6% and 51.8% in the other Turkish studies, and as high as 77.8% from a university hospital in China.[4–8,14] The antibiotic prescription ratio was higher in medical wards (40.5%) than surgical wards (32.9%). Likewise, various studies showed that a higher proportion of antibiotic use occurs in the medical wards.[4] In order of the frequency of prescription in our hospital, the three first-line antibiotics were ampicillin-sulbactam (16.9%), first-generation cephalosporins (16.6%), and third-generation cephalosporins (15.1%). In accordance with our data, Ozkurt et al. reported that the most commonly used antibiotics in a research hospital were ampicillin-sulbactam (15.0%), first- generation cephalosporins (14.7%), and nitroimidazoles (11.1%).[5]

The total empirical antibiotic use was more frequent (49.7%) than prophylactic (29.1%) and culture-based (21.2%) therapies. The appropriate use rate was highest in the patients given culture-based therapy. Inappropriate antibiotic usage rate was found to be 22.1% in our hospital, whereas it is reported as being 9 three 64% in the literature and most studies showed rates between 30% and 40%.[2] In this study, even though the antibiotic usage rate was lower in the surgical wards, inappropriate antibiotic use (29.3%) was more frequent in these units. Forty-six point five percent of surgical prophylaxis was inappropriate, while

for empirical therapy and culture-based therapy, the rates were 16.2 % and 2.3%, respectively. Improper antibiotic initiation time, long duration of therapy, and inappropriate antibiotic selection (especially third-generation cephalosporins and IV quinolons) were the main problems in surgical prophylaxis. From Switzerland, Cusini et al.[2] reported that 37% of therapeutic and only16.6% of prophylactic prescriptions were found to be inappropriate. However, in the other Turkish studies in which the data were parallel with our results, Tunger et al.[4] and Özkurt et al.[5] detected high inappropriate antibiotic usage rates in prophylaxis (37.5% and 50%, respectively), and these rates were higher than empiric and specific use. These results show that surgical prophylaxis still remains a problem in our country. Indeed, the national restriction policy did not cover either the use of antibiotics for surgical prophylaxis or the third-generation cephalosporins and quinolons in the early 72 hours of therapy; therefore, this policy was ineffective in surgical prophylaxis. We consider that local surgical prophylaxis guidelines and constant education programs for health-care workers would be useful for solving this issue.

In a recent study, Erdem et al.[15] reported that Turkey appears to be a perfect social laboratory to assess the perceptions of ID specialists and non-ID specialists about the consultations of infectious diseases. The authors evaluated the beneficial and problematic aspects of this enforced teamwork by using a nationwide survey, and they concluded that the consultation service provided by the ID specialists in Turkey is widely accepted among other clinicians. Obviously, just after the new antibiotic restriction policy, the number of ID specialists consultations increased dramatically, and in this study, we detected that ID consultation rates were significantly higher in the appropriate antibiotic administrations (69.6%) than the inappropriate ones (6.8%) ($p < 0.0001$). Byl et al.[16] showed that the rates of appropriate therapy were significantly higher in the patients cared for by the ID specialists than those treated by other physicians. In a study from Spain, the authors reported that the patients seen by ID consultants were more likely to receive appropriate empirical therapy (66% vs. 55%) and to have their antimicrobial therapy narrowed or otherwise adjusted after culture results became available (58% vs. 33%).[17] Erbay et al.[6] also demonstrated that an antibiotic prescription without an ID consultation was more likely to be inappropriate and antibiotics given empirically were less likely to be appropriate than those based on culture and susceptibility results.

Appropriate use rate was found to be 87.0% for restricted antibiotics and 59.6% for unrestricted antibiotics ($p<0.001$). In a multicenter study from Turkey, Hosoglu et al. showed that the Turkish government's new antibiotic restriction policy resulted in a significant reduction in the prescription of antimicrobials.[7] Ozkurt et al. reported that after restriction, the rate of appropriate use was 88.4% for restricted antibiotics versus 58.1% for unrestricted ones.[5]

The cost of antibiotics is an important issue in our country. The most prescribed drugs are anti-infective drugs (19.9% of all drugs) and the annual total drug and antibiotic cost per person was calculated as $130 and $26 in Turkey, respectively.[3] We found that the total one-day cost of antibiotic therapy in our hospital was $3350.6, and daily antibiotic cost per patient was $16.[8] The mean daily cost per patient of hospital infections was significantly higher than that of community-acquired infections ($p<0.001$). Inan et al. found that daily antimicrobial cost of hospital-acquired infection was $89.6 per patient in intensive care units.[18] In another study from Turkey, Naz et al. reported that the daily antibiotic cost was $13.8, but daily antibiotic cost for hospital infection was $25.[19] Actually, the exact costs of antibiotic therapy include complex factors such as nursing services, expenditures of intravenous administration, monitoring serum antibiotic levels, and antibiotic adverse effects. Therefore, we can assume the real cost of antimicrobial therapy is higher than those reported in these studies.

In conclusion, this study showed that the rate of inappropriate antibiotic use in our hospital was comparable to other studies. ID specialist approval and restriction policy is effective for rational use of antibiotics. However, antibiotic prescription rates are high, surgical prophylaxis is still a major problem, and hospital infections are an important part of extra costs in the hospital. We considered that other interventions such as national and local treatment and prophylaxis guidelines and ongoing postgraduate education should also be provided for all antibiotic prescribers.

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