Original Article / Özgün Araştırma

Meandros Med Dent J
doi:10.4274/meandros.galenos.2023.76993
Meandros Med Dent J 2023;24(4):298-302
298

A Cross-sectional View of Rational Antibiotic Use

Akılcı Antibiyotik Kullanımına Kesitsel Bir Bakış

Güliz Uyar Güleç, Gözde Çetinkaya

Aydın Adnan Menderes University Faculty of Medicine, Department of Infectious Diseases and Clinical Microbiology, Aydın, Turkey

Abstract

Objective: Antimicrobial resistance is an issue that threatens human health worldwide. One of the main factors responsible for the formation of resistance is the irrational use of antibiotics. The inappropriate use of antibiotics has many direct and indirect effects. Ceftriaxone and quinolones are the leading antibiotics associated with this condition, which is known as collateral damage. In this study, we aimed to evaluate the consultations requested regarding the use of these antibiotics in a cross-sectional manner.

Materials and Methods: Ceftriaxone and parenteral quinolone consultations from adult patients hospitalized in our hospital between 01.01.2022 and 30.06.2022 were included in the study. Demographic data and consultation results of the patients were retrospectively evaluated.

Results: A total of 560 consultations from 538 patients were evaluated, of which 40.7% were women. Three hundred forty-seven patients (64.5%) were followed in internal clinics. The most requested antibiotic was ceftriaxone (73.6%). There was no diagnosis of infection in 82 (15.2%), and antibiotics were continued postoperatively in 75 (13.9%) patients. The rate of patients who were not cultured before treatment was 45.4%, while the rate of patients who were diagnosed with infection but were not cultured was 36.6%. Pre-treatment culture rate was lower and antibiotic withdrawal rate was higher in surgical units than in internal units.

Conclusion: Resistance can be slowed down by the sensitivity of not only infectious disease specialists but also all physicians prescribing antibiotics, the use of antibiotic stewardship programs and local guides, and education. Scientific studies should be continued to generate local and national data.

Keywords: Antimicrobial resistance, infectious diseases consultation, third generation cephalosporin, fluoroquinolone

Öz

Amaç: Antimikrobiyal direnç tüm dünyada insan sağlığını tehdit eden bir konudur. Direnç oluşumunda başlıca sorumlu faktörlerden biri irrasyonel antibiyotik kullanımıdır. Antibiyotiğin uygunsuz kullanımı doğrudan ve dolaylı olarak birçok etkiye neden olmaktadır. Kollateral hasar olarak adlandırılan bu durumla ilişkili antibiyotiklerin başında seftriakson ve kinolonlar gelmektedir. Bu çalışmada bu antibiyotiklerin kullanımı ile ilgili istenen konsültasyonların kesitsel olarak değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntemler: Hastanemizde 01.01.2022-30.06.2022 tarihleri arasında yatan erişkin hastalardan gelen seftriakson ve parenteral kinolon konsültasyonları çalışmaya dahil edildi. Hastaların demografik verileri ve konsültasyon sonuçları retrospektif olarak değerlendirildi.

Bulgular: Beş yüz otuz sekiz hastadan toplam 560 konsültasyon değerlendirildi. Hastaların %40,7'si kadındı. Üç yüz kırk yedi hasta (%64,5) dahili kliniklerde takip edilmekteydi. En çok talep edilen antibiyotik seftriaksondu (%73,6). Seksen iki (%15,2) hastada enfeksiyon tanısı yoktu, 75 (%13,9) hastada ise postoperatif antibiyotik tedavisi devam ediyordu. Tedavi öncesinde kültür alınmayan hastaların oranı %45,4, enfeksiyon tanısı olup kültür yapılmayan hastaların oranı ise %36,6 olarak belirlendi. Cerrahi birimlerde dahili birimlere göre tedavi öncesi kültür alma oranı düşük, antibiyotiğin kesilme oranı daha yüksekti.

Sonuç: Sadece enfeksiyon hastalıkları uzmanları değil antibiyotik reçete eden tüm hekimlerin direnç konusunda hassas olması, antibiyotik yönetişim programlarının ve lokal rehberlerin kullanılması ve eğitim ile direnç yavaşlatılabilir. Yerel ve ulusal verilerin oluşturulması için bilimsel çalışmalara devam edilmelidir.

Anahtar Kelimeler: Antimikrobiyal direnç, enfeksiyon hastalıkları konsültasyonu, üçüncü kuşak sefalosporin, florokinolon

Address for Correspondence/Yazışma Adresi: Güliz Uyar Güleç, MD, Aydın Adnan Menderes University Faculty of Medicine, Department of Infectious Diseases and Clinical Microbiology, Aydın, Turkey
Phone: +90 256 444 12 56 **E-mail:** guliz.uyar@adu.edu.tr
ORCID ID: orcid.org/0000-0002-8565-1042

Received/Geliş Tarihi: 29.05.2023
Accepted/Kabul Tarihi: 07.09.2023

Introduction

Antimicrobial resistance (AMR) is defined as the ability of all microorganisms to resist the action of antimicrobial agents and to survive and grow even in the presence of drugs that previously affected them (1).

The increasing consumption of antibiotics in the healthcare and agriculture sectors has led to the emergence of microorganisms resistant to antibiotics all over the world. This trend is manifested in a high prevalence in a wide variety of microorganisms. This problem has become one of the biggest public health threats today, and World Health Organization estimates that 10 million deaths could occur by 2050 due to infections with resistant microorganisms (2). AMR causes to serious illness, treatment failures, need for treatment with second-generation drugs, prolonged hospital stays and, higher healthcare costs (3).

Inaccuracies in the use of antibiotics in general, difficulties in developing new antibiotics, easy travel routes and bacterial biological factors are contributing factors to AMR (1). Undesirable effects detected in bacterial ecology such as selection of resistant bacteria, colonization/infection with multi-resistant bacteria as a result of inappropriate or excessive use of antibiotics are defined as "collateral damage". The antibiotics most commonly associated with collateral damage are third-generation cephalosporins, fluoroquinolones, and carbapenems (4).

One of the rational antibiotic use methods in the fight against AMR is the policies to restrict the use of antibiotics. In our country, antibiotic prescribing rules were determined with the budget implementation instruction that came into force in 2003 (5). Infectious diseases specialists (IDS) were authorized to prescribe broad-spectrum antibacterials, antifungals and antivirals used in the hospital. Some group antibiotics including third-generation cephalosporins, fluoroquinolones can be prescribed by any specialist at the beginning of the treatment, but requiring IDS approval if it will be used more than 72 hours.

In this study, it was aimed to draw attention to the rational use of antibiotics evaluating the consultations in a period of six months requested from the internal and surgical clinics of Aydın Adnan Menderes University Hospital regarding the use of this group antibiotic.

Materials and Methods

Hospital Setting

The hospital where the study was conducted is a 997-bed tertiary hospital. There are nine internal medicine services and nine surgical services at the hospital. There are four internal, four surgical, one general and three pediatric intensive care units.

Antibiotic Prescription Policy

Within the IDS approval definitions;

1. Non-restriction antibiotics (e.g., ampicillin, cefazolin).

2. Antibiotics that can be prescribed by specialist physicians in outpatient treatment or by all physicians including general practitioners depending on the specialist physician's report, and by all physicians in inpatient treatment (e.g., ampicillin sulbactam, cefuroxime).

3. Antibiotics for which IDS is not required for prescription but if the same drug will be used for longer than 72 hours, IDS approval must be obtained within the first 72 hours at the latest (*the group of antibiotics evaluated in this study) (e.g., piperacillin, cefoperazone, cefotaxime, ceftriaxone, parenteral ciprofloxacin- levofloxacin- moxifloxacin).

4. Antibiotics that only IDS can prescribe. If there is no IDS, they can be prescribed by an internist or pediatrician. (e.g., piperacillin tazobactam, ceftazidime)

Data Collection

In the study, consultations requested for third group antibiotics at Aydın Adnan Menderes University Hospital between 01.01.2022 and 30.06.2022 were evaluated retrospectively. Cefotaxime, ceftriaxone, parenteral ciprofloxacin, levofloxacin and moxifloxacin are available in our hospital as third group antibiotics.

Of all patients' who used these group antibiotics for an average of 72 hours, demographic features, departments in which they were hospitalized (internal/surgical, clinic/intensive care), antibiotics used, infection diagnoses, doses and dose range, and whether or not microbiological culture was performed were recorded in the study form.

As a result of the consultations; the decision to continue antibiotics is made in patients with a diagnosis of infection for the initiation of antibiotics, appropriate cultures were taken at the beginning, and the antibiotic was administered at the correct dose and dose range. Treatment is discontinued in patients without a diagnosis of infection and no indication for antibiotic therapy and receiving unnecessary or prolonged prophylaxis. A decision can be made to change the treatment (escalation or deescalation) in patients who do not improve clinically or according to the susceptibility of microorganism grown in cultures taken before treatment. In some patients, additional tests, especially microbiologic evaluation may be recommended.

The consultation decision was recorded in the study form. Consultations requested again from the same patient were recorded as re-consultations.

Patients with incomplete examination and follow-up processes, whose data could not be reached, and patients in the pediatric age group were excluded from the study. IDS approval consultations requested for antibiotics other than the specified group were not included in the study.

Statistical Analysis

Data was analyzed using IBM SPSS Statistics 22 (SPSS Inc, ABD). Chi-square tests were used for comparing the two groups. $P<0.05$ value was accepted as significant.

The study was approved by Aydın Adnan Menderes University Faculty of Medicine Non-interventional Clinical Research Ethics Committee (decision no: 31, date: 04.05.2023).

Results

During the 6-month study period, a total of 7,962 consultations, including repeated consultations from the same patient, were scanned from the hospital information system.

A total of 560 consultations, including 538 consultations and 22 re-consultations, which met the study criteria were included in the study. Of the 538 patients for whom consultation was requested, 219 were female (40.7%) and 319 were male (59.3%). The mean age was 68.81±16.4.

Three hundred and fourty-seven patients were followed in internal clinics and 191 patients were followed in surgical clinics. It was observed that the most requested antibiotic was ceftriaxone (73.6%). According to the consultation request, the patients were divided into four groups. While 371 (69%) patients had a diagnosis of infection, 82 (15.2%) patients did not have. There was a request to continue antibiotherapy for prophylactic purposes in 10 (1.9%) patients and postoperative antibiotic therapy in 75 (13.9%) patients. Among the patients who received postoperative treatment (n=75), it was decided to continue or revise the treatment due to infection (perforation, etc.) in 19 (25.4%) patients, and to discontinue the treatment in 56 (74.6%) patients.

No culture was sent before the start of antibiotic therapy in 244 of 538 patients (45.4%), while the rate of patients who were diagnosed with infection but were not cultured was 136/371 (36.6%). Cultures sent from other patients and pre-diagnosis/diagnoses of infection are shown in Table 1. As a result of the consultation, it was decided to discontinue the treatment in 202 (37.5%) patients, to continue in 283 (52.6%), and to revise antibiotics in 53 (9.9%) patients. Additional tests were requested from 46 (8.6%) patients. The numbers and percentages according to the units are given in Table 2. It was observed that antibiotics were used in the correct dose and dose range in all patients.

When the re-consultations were evaluated, antibiotics were not started in 11 patients because there was no infective focus. It was decided to continue antibiotics in 6 patients and to revise treatment in 5 patients.

Discussion

In this study, consultation data on the use of certain groups of antibiotics in a 6-month period were evaluated with a cross-sectional view. When the literature is reviewed, most of the studies on rational antibiotic use have been conducted using the one-day point prevalence method (6-8). It is reported that the rates of antibiotic use in hospitalized patients vary between 36.2% and 63.2% in studies reported from our country (9). In the point prevalence study evaluating the use of antibiotics in Latin American countries, the rate of antibiotic use was found to be 54.6% (10). In various studies from other countries, antibiotic use rates were reported as 46%, 32% and 14.1% (8,11,12).

In a multicenter study conducted in Korea, when a total of 10,948 therapeutic, surgical and medical prophylactic treatments were evaluated, the rate of inappropriateness was found to be 27.7% (12). In a systemic review and meta-analysis containing data from Turkey, the mean rate of inappropriate antibiotic prescribing was reported as 36%. The reasons for inappropriateness were listed as, use of similar antimicrobials together, failure to use antibiotics in the correct indication, administration of antibiotics at improper dose and dose range, inaccurate prophylaxis and, unnecessarily prolonged treatment cure (13). Accordingly, we can characterize antibiotherapy as inappropriate or suboptimal for our study in patients without a diagnosis of infection (15.2%) and in patients who started therapy as prophylaxis and continued unnecessarily postoperatively (74.6%).

In addition, in studies evaluating the use of antibiotics according to clinics, it is noteworthy that surgical departments use inappropriate antibiotics at a higher rate than internal departments. The most important reason for this is seen as inappropriate surgical prophylaxis of surgical

Table 1. Clinic, culture samples and infection diagnosis of the patients

Clinic	n (%)
Internal medicine service	286 (53.2)
Medical intensive care unit	61 (11.3)
Surgical service	161 (29.9)
Surgical intensive care unit	30 (5.6)
Culture sample	
Blood	75 (13.9)
Sputum	66 (12.3)
Urine	40 (7.4)
Wound/body fluid	32 (5.9)
Feces	6 (1.1)
More than one culture	73 (13.6)
Infection diagnosis	
Respiratory	187 (34.8)
Biliary tract	58 (10.8)
Gastrointestinal system	44 (8.2)
Urinary system	34 (6.3)
Soft tissue, surgical field	20 (3.7)
Sepsis	16 (3)
Other	12 (2.2)

departments. In our study, the rate of culture taking before treatment in patients with infection was lower (p>0.05) and the rate of discontinuation of the current treatment was higher (p<0.001) in surgical units compared to internal clinics (Table 2).

Kömür et al. (14) in their study to determine the appropriateness of surgical prophylaxis reported that they evaluated the prophylaxis in 49.1% of patients as inappropriate in various aspects. Starting time of the antibiotics, given prophylaxis at clean surgery, continuing prophylaxis at a prolonged time, type and dosage of the antibiotic, not giving prophylaxis when it's indicated, were reasons of incompliance (14).

In a multicenter point prevalence study in Ghana in which only surgical units were evaluated, the rate of antibiotic use in 540 patients was found to be as high as 70.7%. It was stated that surgical prophylaxis was used longer than recommended in 88.4% of the patients who received antibiotics (15). Although first generation cephalosporins, which are frequently used prophylactically, were not in the scope of our study, it was recommended to discontinue antibiotics in 56 patients (74.6%) whose postoperative treatment was continued. In our study, while the rate of culture in the appropriate indication was 56.4% in surgical units, it was emphasized that microbiological analysis was performed in only 3.7% of the patients in this study (15).

In our study, respiratory tract infections, primarily pneumonia, were found to be the most common diagnosis in patients with an infection diagnosis. In the meta-analysis containing data from our country, it was reported that third generation cephalosporins (36%) were the most commonly prescribed antibiotics, and respiratory tract infection (88%) was the most common infection diagnosis (13). In a study conducted in Kenya, it was reported that antibiotics were given most frequently with the diagnoses of soft tissue infection (18%), sepsis (17%) and pneumonia (15%), respectively (11). In another study conducted in internal medical wards, the most common possible infectious disease was pneumonia, following meningitis. Ceftriaxone was the most commonly used agent in patients receiving single or combined antibiotics (16).

In our study, the rate of patients who were not cultured before treatment was found 45.4% while the rate of patients who were diagnosed with infection but were not cultured was 36.6%. Taking the necessary cultures before antibiotic therapy significantly reduces inappropriate antibiotic use. In the cross-sectional study of Oğuz et al., (17) it was stated that 67% of 126 patients were asked to culture before treatment, and the rate of inappropriate antibiotic use was 24% in general. In another study, it was reported that culture samples were taken from 57.8% of the patients who were given antibiotics for treatment (7). Additional tests including culture examinations were recommended to 8.6% of the patients in our study. However, since our study group consisted of patients who had been taking antibiotics for an average of 3 days, it was thought that the sensitivity of the cultures taken afterwards might be low.

Conclusions

Although the rates of antibiotic use are variable, inappropriate use of antibiotics is a problem all over the world. Although not addressed in this study, the negative

Table 2. Antibiotics requested, pretreatment culture in infectious patients and consultation results according to the unit

Hospital unit	Surgical clinics (n=191)	%	Internal clinics (n=347)	%	p-value
Age	58.27±16.4	-	66.71±15.9	-	<0.001
Sex (female/male)	75/116	-	144/203	-	-
Requested antibiotic					<0.001
Ceftriaxone	174	91	222	63.9	
Ciprofloxacin	12	6.3	36	10.4	
Moxifloxacin	4	2.1	49	14.2	
Levofloxacin	1	0.6	40	11.5	
Pretreatment culture					0.146
No	38	43.6	98	34.5	
Yes	49	56.4	186	65.5	
Consultation decision					<0.001
Continuation of the antibiotic	73	38.2	210	60.5	
Discontinuation of the antibiotic	100	52.3	102	29.4	
Revision (escalation/de-escalation)	18	9.5	35	10.1	

effects of irrational antibiotic use on cost and resistance cannot be ignored. The size of the problem should be revealed by obtaining hospital and country data. The sensitivity of all physicians ordering antibiotics, especially in the use of unrestricted antibiotics, can only be achieved by knowing the extent of the problem. Antibiotic stewardship programs, education, local antibiotic guidelines and their active use are effective methods in the fight against resistance.

Acknowledgement

A special thank to the consultation team of the Infectious Diseases and Clinical Microbiology clinic.

Ethics

Ethics Committee Approval: The study was approved by Aydın Adnan Menderes University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee (decision no: 31, date: 04.05.2023).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: G.U.G., G.Ç., Concept: G.U.G., Design: G.U.G., Data Collection or Processing: G.U.G., G.Ç., Analysis or Interpretation: G.U.G., Literature Search: G.U.G., G.Ç., Writing: G.U.G., G.Ç.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Dadgostar P. Antimicrobial Resistance: Implications and Costs. Infect Drug Resist 2019; 12: 3903-10.
2. Pulingam T, Parumasivam T, Gazzali AM, Sulaiman AM, Chee JY, Lakshmanan M, et al. Antimicrobial resistance: Prevalence, economic burden, mechanisms of resistance and strategies to overcome. Eur J Pharm Sci 2022; 170: 106103
3. Antimicrobial Resistance Collaborators. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. Lancet 2022; 399: 629-655.
4. Şener B. Kollateral hasar ve antibiyotik direnci. ANKEM Derg 2012; 26: 288-92.
5. Ozkurt Z, Erol S, Kadanali A, Ertek M, Ozden K, Tasyaran MA. Changes in antibiotic use, cost and consumption after an antibiotic restriction policy applied by infectious disease specialists. Jpn J Infect Dis 2005; 58: 338-43.
6. Sağmak Tartar A, Denk A, Özden M, Çelik Kırık Y, Akbulut A, Demirdağ K. Investigation of the rationality of antibiotic use in the Fırat University Hospital: A point prevalence study. ANKEM Derg 2015; 29: 16-20.
7. Yilmaz GR, Bulut C, Yildiz F, Arslan S, Yetkin MA, Demiröz AP. Examining antibiotic use at an education and research hospital in Turkey: Point prevalence results. Turkish J Med Sci 2009; 39: 125-31.
8. Moulin E, Boillat-Blanco N, Zanetti G, Plüss-Suard C, de Vallière S, Senn L. Point prevalence study of antibiotic appropriateness and possibility of early discharge from hospital among patients treated with antibiotics in a Swiss University Hospital. Antimicrob Resist Infect Control 2022; 11: 66
9. Öztürk DB, Kaçmaz B, Torun Edis Ç, Erol Ö, Çalışkan O, Ecemiş K, et al. Kirikkale ilindeki iki hastanede yatan hastalarda antibiyotik kullanimi: bir günlük nokta prevalans çalişmasi. Kırıkkale Üniversitesi Tıp Fakültesi Derg 2019; 21: 90-4.
10. Levy Hara G, Rojas-Cortés R, Molina León HF, Dreser Mansilla A, Alfonso Orta I, Rizo-Amezquita JN, et al. Point prevalence survey of antibiotic use in hospitals in Latin American countries. J Antimicrob Chemother 2022; 77: 807-15.
11. Omulo S, Oluka M, Achieng L, Osoro E, Kinuthia R, Guantai A, et al. Point-prevalence survey of antibiotic use at three public referral hospitals in Kenya. PLoS One 2022; 17: e0270048.
12. Park SY, Moon SM, Kim B, Lee MJ, Park JY, Hwang S, et al. Appropriateness of antibiotic prescriptions during hospitalization and ambulatory care: a multicentre prevalence survey in Korea. J Glob Antimicrob Resist 2022;29:253-8
13. Selcuk A. The point prevalence and inappropriateness of antibiotic use at hospitals in Turkey: a systematic review and meta-analysis. J Chemother 2021; 33: 390-9
14. Kömür S, Ulu A, Kurtaran B, Türkoğlu BÖ, İnal AS, Kuşçu F, et al. Bir günlük nokta prevalans ile bakış: cerrahi profilaksi uygun mu? Mustafa Kemal Üniversitesi Tıp Derg 2016; 7: 11-5.
15. Bediako-Bowan AAA, Owusu E, Labi AK, Obeng-Nkrumah N, Sunkwa-Mills G, Bjerrum S, et al. Antibiotic use in surgical units of selected hospitals in Ghana: a multi-centre point prevalence survey. BMC Public Health 2019; 19: 797.
16. Anteneh DA, Kifle ZD, Mersha GB, Ayele TT. Appropriateness of Antibiotics Use and Associated Factors in Hospitalized Patients at University of Gondar Specialized Hospital, Amhara, Ethiopia: Prospective Follow-up Study. Inquiry 2021; 58: 469580211060744.
17. Oğuz E, Kurçer Z, Sırmatel F, Kurçer MA, Tavflan Ö, Yengin E. Harran Üniversitesi Tıp Fakültesi Araştırrma ve Uygulama Hastanesi'nde Yatan Hastalarda Antibiyotik Kullanımının Değerlendirilmesi. Klimik Dergisi 2006; 19: 46-48.