



Drug Utilization Evaluation of Antibiotics in Burn Patients at a Referral Teaching Hospital

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Received: 2022-01-14, Revised: 2022-04-24, Accepted: 2022-04-26, Published: 2022-06-31

ARTICLE INFO

Article type:

Original article

Keywords:

Drug Utilization,

Evaluation;

Anti-Bacterial Agents;

Burns

ABSTRACT

Background: Nowadays, due to the irrational and excessive use of antibiotics, antimicrobial resistance has become one of the main concerns of the medical community. Patients with burns are more prone to infections due to the loss of the skin's defense barrier and a weakened immune system. Therefore, proper antibiotic treatment is essential in these patients. In the present study, the rational use of antibiotics in the burn hospital of Imam Mousa Kazem in Isfahan was evaluated.

Methods: This prospective cross-sectional descriptive study was performed on 102 hospitalized patients over 9 months (from January to September 2020). Adult burn patients who received at least one antibiotic were included in the study. All required information, including demographic data, the prescribed antibiotic, basis of administration (empiric vs. culture-based), dose and duration of use, microbial culture test, and treatment outcome were recorded in the data collection form by referring to patients' medical profile and the hospital computer system. Judgments about the accuracy of the indication, dose, and duration of treatment, as well as the need for dose adjustment in renal or hepatic impairment were made using related guidelines and references.

Results: Among the 196 antibiotic prescriptions, cefepime (40.3%) was the most frequently used antibiotic, followed by vancomycin (17.9%) and meropenem (16.8%). Most prescriptions were empirical, while the antibiotics were administered based on the microbial culture results only in two cases (1.9%). The indication of use was correct in 52.6% of prescriptions (n = 103), of which 74.8% (n = 77) had correct dose. In addition, in 47 cases (45.6%), the duration of antibiotic therapy was correct. 6.8% of the patients died, 10.75 discharged with the patient's personal consent, and the rest of them discharged in good condition.

Conclusion: Prescribing antibiotics in Imam Mousa Kazem Hospital is associated with many errors in various aspects, including indication, dose, de-escalation, and duration of treatment.

J Pharm Care 2022; 10(2): 63-68.

► Please cite this paper as:

Soltani R, Sajjadi Sh, Shirani K, Minaiyan M, Saghafi F. Drug Utilization Evaluation of Antibiotics in Burn Patients at a Referral Teaching Hospital. J Pharm Care 2022; 10(2): 63-68.

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Introduction

Drug utilization evaluation (DUE) is a criteria-based study of medical evaluations, which is designed to evaluate appropriate medicine use in different aspects, such as indication of use, dose, and duration of drug administration, interactions, and other concurrent or past treatments (1, 2). The main purpose of DUE studies is to assess the rationality of drug use (3). It also can help healthcare providers to reduce the cost of treatment (4).

Burn injuries have serious effects on victim wellness in both emotional and physical aspects (5). Factors such as loss of skin as the first barrier against microorganism's entry, weak immune system, long hospitalizations, and also invasive procedures, which are necessary to be taken in burn injuries, make burn victims more susceptible to microbial infections (6). The primary cause of morbidity after burn injuries is infection; therefore, a proper treatment with antibiotics is necessary for these situations (7). Antibiotics are responsible for a significant amount of treatment costs for patients, hospitals, and the government (8).

Inappropriate use of antibiotics leads to antibiotic resistance, and it also causes 700,000 deaths annually over the world (9). It is challenging to treat infections caused by resistant pathogens with usual antibiotics and in their regular doses. Hence, there is a need to change the antibiotic or increase the dose in such cases, which may cause more cost or toxicity (10).

According to the abundance of burn traumas and their subsequent infections, the economic burden of antibiotics on the health system, and also a limitation of antibiotics resources (11, 12), we decided to conduct this DUE study to evaluate the antibiotic utilization in a referral burn hospital of Isfahan, Iran.

Methods

This prospective descriptive cross-sectional study was performed in a 9-month period from January to September 2020 in the burn ward of Imam Moussa Kazem Burn Hospital, affiliated to Isfahan University of Medical Sciences (IUMS), located in Isfahan, Iran. In this study, adult patients (over 18 years old) hospitalized in the burn ward who had received at least one injectable antibiotic

were included the study. Patients who were transferred to the intensive care unit (ICU) during the study period were excluded from the study population. The required information of each patient was extracted from the patients' medical profile and the hospital's computerized information system (HIS). All patients who met the inclusion criteria during the study period were included. The required information was collected in a pre-prepared form by a general pharmacist under the supervision of a clinical pharmacist.

The collected data included demographic information; degree and percentage of burns, which classified as 1th degree (superficial thickness, affecting the epidermis only), 2th degree (range from superficial partial thickness to deep partial thickness), 3th degree (full thickness), and 4 (require surgery and, paradoxically, usually present with almost no pain) (11); burnt limb(s); a brief history of patient and laboratory results including microbial culture, sensitivity test results (if performed), and serum creatinine (to calculate creatinine clearance by Cockcroft-gault formula); wound conditions (infectious or non-infectious); prescribed antibiotics, accuracy of their indication (based on the infection status of the wound), and the basis for their prescription (empirical or culture-based). Furthermore, for antibiotics prescribed with correct indication, the dose (according to renal and hepatic function) and duration of use as well as concomitant antibiotics were recorded.

Judgment on the accuracy of drug indication, dose and duration of antimicrobial treatment, the need for dose adjustment in renal and/or hepatic dysfunction, and the accuracy of the concomitant antibiotics was made by an infectious diseases clinical pharmacist and an infectious diseases specialist physician based on the clinical appraisal as well as relevant guidelines and references (13-15). The collected data were analyzed by SPSS software version 24, and the information was presented as frequency distribution and percentage.

Results

During the study period, 102 patients met the inclusion criteria, of which 72.5% were male. The mean \pm standard deviation (SD) age of patients was 34.78 ± 12.66 years. Other patient's demographics profile and baseline clinical characteristics are shown in Table 1.

Table 1. Patients demographics profile and baseline clinical characteristics.

Parameters	Frequency	Percent
Sex		
Men	74	72.5
Women	28	27.5
Degree of burns		
1 and 2	1	1
2	19	18.6
2 and 3	70	68.6
3	9	8.8
1, 2, and 3	3	2.9
Burns location		
Legs	14	13.7
Hands	2	2.0
Head and neck	3	2.9
Legs and hands	10	9.8
Legs, Hands, and trunk	5	4.9
Hands, Heads, and neck	16	15.7
Trunk, head, and neck	1	1.0
Trunk and hands	5	4.9
Trunk and legs	10	9.8
Trunk, hands, head, and neck	13	12.7
Total body	9	8.8
Time to admission after burn		
<24 hr	68	66.9
24-48 hr	17	16.7
>48 hr	17	16.7

A total of 196 antibiotic prescriptions were evaluated. Out of 102 patients, 45 patients (44.1%) received only one antibiotic, while in 30 patients (29.4%), two antibiotics were prescribed concomitantly. Also, simultaneous administration of three and four antibiotics occurred in 19 (18.6%) and six (5.9%) patients, respectively, and in only two patients (2%), five antibiotics were administrated at the same time. As illustrated in Table 2, the most commonly prescribed antibiotic was cefepime ($n = 79$, 40.3%), while vancomycin ($n = 35$, 17.9%) and meropenem ($n = 33$,

16.8%) were the second and the third most commonly prescribed antibiotics, respectively, among patients.

Table 2. Frequencies of prescribed antibiotics in patients.

Antibiotic	Frequency	Percent
Cefepime	79	40.3
Vancomycin	35	17.9
Meropenem	33	16.8
Teicoplanin	20	10.2
Piperacillin/Tazobactam	3	1.5
Metronidazole	5	2.6
Levofloxacin	3	1.5
Colistimethate sodium	4	2
Ceftazidime	8	4.1
Clindamycin	4	2
Linezolid	1	0.5
Amikacin	1	0.5
Total	196	100

Out of 196 antibiotic prescriptions, 103 cases (52.6%) had the correct indication, whereas the remaining 93 cases (47.4%) were inappropriate. Also, 193 prescriptions (98.5%) were administered empirically, while only three (1.5%) were used based on microbial culture results.

According to Table 3, cefepime with 28 correct prescriptions followed by meropenem and vancomycin with 22 (21.4%) and 21 times (20.4%), respectively, were the most correctly prescribed antibiotics.

Table 3. Frequencies of correctly prescribed antibiotics.

Antibiotic	Frequency	Percent
Cefepime	28	27.2
Meropenem	22	21.4
Vancomycin	21	20.4
Teicoplanin	17	16.5
Ceftazidime	7	6.8
Piperacillin/tazobactam	3	2.9
Colomycin	2	1.9
Clindamycin	2	1.9
Linezolid	1	1
Total	103	100

Out of 103 prescriptions that were correct in terms of indication, 101 (98.1%) were empirical, and 2 (1.9%) were based on microbial culture results. In addition, in 77 (74.8%) and 26 (25.2%) cases, the prescribed dose was correct and incorrect, respectively. The mean duration of antibiotic use for correctly prescribed antibiotics was 4.28 ± 2.68 days. The duration of use was correct in 47 cases (45.6%). Notably, of 56 cases of incorrect duration, 7 (6.8%) and 11 (10.7%) cases were due to patient death and early discharge with the patient's individual consent, respectively.

In four cases (3.9%), the prescribed antibiotic required dose adjustment due to renal impairment, of which, three cases (75%) were correctly adjusted, while in none of the prescriptions, the dose need to be adjusted due to hepatic impairment. In 76 of the antibiotic prescriptions with the right indication, the prescribed antibiotic was accompanied by at least one other antibiotic, of which 67 cases (88.2%) were accompanied by the correct antibiotic, while it was incorrect in nine cases (11.8%). Also, in 18 patients, three concurrent antibiotics were prescribed that in 10 of which (55.6%), the third antibiotic was correct, whereas it was incorrect in eight patients (44.4%). Moreover, in only one patient, the fourth antibiotic was added to the treatment; however, the accompaniment was not valid. 6.8% of the patients died, 10.75 discharged with the patient's personal consent, and the rest of the them discharged in good condition.

Discussion

The results of the current study indicated that prescribing antibiotics is accompanied by a high level of errors, mostly in terms of indication, in burn wards of a university-related referral hospital.

Similar studies have been done in Iran and other countries. During a study conducted in 2007 at Masih Daneshvari Hospital in Tehran, the drugs used for patients admitted to the ICU were evaluated. The most commonly used antibiotics in that ward were cefuroxime (30.1%), ceftriaxone (29.2%), clindamycin (24.7%), and cefazolin (23%) (16). In our study, the most commonly used antibiotics were cefepime (40.3%), vancomycin (17.9%), and meropenem (16.8%). Therefore, our center has more usage of extended-spectrum antibiotics. This could be associated with a higher risk of antimicrobial resistance.

The pattern of drug use was assessed in 100 burn patients in a hospital in India. At least one antibiotic was prescribed for all patients. The most prescribed antibiotics were ceftazidime (13.1%), gentamicin (10.%), and metronidazole (8.5%). One to four antibiotics were prescribed for each

patient and in most cases, the treatment was performed experimentally (17). In our study, cefepime, vancomycin, and meropenem were the most commonly prescribed. The number of antibiotics was 1-5 and similar treatments were mostly performed experimentally.

The results of another observational study on vancomycin utilization evaluation in Imam Reza Hospital of Mashhad indicated vancomycin was administered in about 30% of patients who were hospitalized in the burn ward. 6.8% of patients received vancomycin without an antibiogram test and the dose of vancomycin was incorrect in 41% of orders (18). Khalighi et al., evaluated antibiotic susceptibility pattern *Pseudomonas* spp. isolated from burn unit of Payambar e Azam Hospital of Bandar Abbas, which the results indicated high antibiotic resistance. They found 46.15, 15.38, 46.15, 23.08, 15.38, 15.38 and 38.46% of the tested isolates were resistant to ciprofloxacin, imipenem, piperacillin, ceftazidime, respectively (19).

In another study, the use of antibiotics in hospitalized and non-hospitalized patients was evaluated in Zanjan, Iran. A total of 26 types of antibiotics were prescribed to patients. Cephalosporins, macrolides, and vancomycin as a glycopeptide antibiotic, were the three classes of drugs that accounted for 80% of the antibiotics usage. Among them, ceftriaxone (35.2%), cefazolin (15.8%), cephalexin (11.3%), and vancomycin (9.6%) were the most widely used. The indication and the dose of antibiotics were correct in 79% and 73.7% of cases, respectively. In 41.5%, the susceptibility test and microbial culture were requested by the physician, and among the patients in which the test was performed, 90.7% had the correct indication (20).

The results of a study that was performed in the ICU wards of Al-Zahra Hospital in Isfahan showed 63.9% of cases received two antibiotics simultaneously. In 22.2%, 11.1%, and 2.8% of cases, 3, 4, and 5 antibiotics were administered together, respectively (21). In the current study, the administration rates of 1, 2, 3, 4, and 5 antibiotics simultaneously were 44.1%, 29.4%, 18.6%, 5.9%, and 2%, respectively. This comparison shows that in the burn hospital, most treatments are done as single drug treatment, but in the intensive care unit of Al-Zahra Hospital, more treatment is done with two drugs or more, which can be due to higher microbial resistance in cases of nosocomial infections due to the longer hospitalization days of patients. In Al-Zahra Hospital, the method of administration of antibiotics was 75.8% experimentally and 24.2% according to the result of microbial culture. Among the antibiotics that were prescribed experimentally, 31.88% were prescribed after culture. Totally, 51.6% of cases had the correct

indication, and 58.5% had the right dose. 15.95% of the cases required renal dose adjustment (21).

In a DUE study conducted in 2014 in all five wards of Sina Hospital in Tabriz, 140 patients received one of cefepime or piperacillin/tazobactam during the 6-month study period were evaluated. Among these patients, only one case of cefepime (1.4%) and 36 cases of piperacillin/tazobactam (51.4%) were in the burn ward. The highest dose of piperacillin/tazobactam was prescribed in the burn ward. In general, the dose of piperacillin/tazobactam was correct in 90% of cases and incorrect in 10%, and in the case of treatment in 67.1%, the duration of treatment was correct in accordance with the guidelines. The highest pattern of incorrect administration (incorrect dose and treatment period) was seen in the infectious (46.4%) and burn wards (36.1%), respectively (22). Of the three cases of piperacillin/tazobactam administered in our hospital, all three had the correct indication.

Other studies have also been conducted in other parts of the world. In Saleem et al., study, which was performed in 2017 in Lahore, Pakistan, 43.4% of cases received single-drug therapy with antibiotics, and 56.6% received combination antibiotic therapy. Among the patients receiving antibiotics in different wards of the hospital, 29.7% had received the correct treatment, which was in accordance with the standards, and about two-thirds of the prescribed antibiotics did not have the correct indication. The most commonly prescribed antibiotics in the study population were cephalosporins (46.1%), followed by aminoglycosides (15.6%), penicillins (14%), and fluoroquinolones (9.5%). Overall, the most common antibiotics were ceftriaxone (21%), amikacin (15.2%), cefoperazone/sulbactam (11.4%), ciprofloxacin (6.4%), and metronidazole (5.9%). In 63.5% of cases, the indication, dose, or both were wrong (23).

Also, a study was conducted in 2014 in different wards of a teaching hospital in Oman. According to the results, in most cases, patients were treated with a combination of two antibiotics together. The most prescribed antibiotics were penicillins, cephalosporins, and macrolides, respectively. In general, piperacillin/tazobactam (22%), azithromycin (15%), meropenem (11%), and ceftriaxone (11%) were the most commonly prescribed. In 85% of the cases, sampling for microbial culture and antibiotic susceptibility testing were performed before using antibiotics. Only in 18% of the patients with available culture results, antibiotics were prescribed according to the test results (24).

In conclusion prescribing antibiotics in Imam Moussa Kazem Hospital is associated with many errors in various

aspects, including indication, dose, de-escalation, and duration of treatment. Therefore, considering the patterns of antibiotics utilization by educational programs could be pivotal.

Acknowledgments

We would like to commend the nursing personnel of Imam Moussa Kazem Burn Hospital for their cooperation and assistance.

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