Research Article

Evaluation of drug utilization pattern of antimicrobials using ATC/DDD system in intensive care unit of a tertiary-care teaching hospital

Suhena R Patel[1], Amit M Shah[2], Rima B Shah[2], Jatin G Buch[2]

[1]M.B.B.S. student, GMERS Medical College, Gandhinagar, Gujarat, India..
[2]Department of Pharmacology, GMERS Medical College, Gandhinagar, Gujarat, India.
Correspondence to: Amit M Shah, E-mail: dr_amit84@yahoo.co.in

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Abstract

Background: Critically ill patients admitted to intensive care units (ICUs) are highly susceptible to infections because of predisposing illnesses and the use of invasive and surgical procedures and are, therefore, exposed to high antimicrobial pressure. Use of antimicrobials in the ICU must follow best clinical practice if the emergence of resistance to antimicrobials is to be minimized.

Objective: To evaluate the antimicrobial prescription patterns in the ICU.

Materials and Methods: A prospective observational study was undertaken from April 2014 to September 2014 in a tertiary-care teaching hospital. All the patients admitted in ICU were included in the study. Relevant data such as demographic parameters, clinical data, drug use, and antimicrobial use were collected every day till patients were discharged from ICU using their case record sheets. Antimicrobial use was analyzed using Anatomical Therapeutic Chemical (ATC) Classification/defined daily dose (DDD) system, and DDD/100 bed-days were calculated for antimicrobials.

Result: Totally, 123 patients admitted into the ICU were included in the study. This included 75 men and 48 women. The average age of the patients was 56.7 years (±SD = 19.9 years). Majority of the patients admitted to the ICU were from the medical specialty (96, 78.05%). One hundred thirteen patients (91.87%) were prescribed an antimicrobial with an average of 1.49 (±0.79) antimicrobials per prescription. Majority of the patients (107; 94.69%) were prescribed the antimicrobials prophylactically. Ceftriaxone (J01DD04) was the most commonly (69; 61.60) prescribed antimicrobial agent with DDD/100 bed-days value of 11.86, followed by amoxicillin + clavulanate (J01CR02) with DDD/100 bed-days value of 5.42.

Conclusion: The need for antimicrobial should be reviewed daily on every patient, always stopping at the earliest possible opportunity where the benefits of continuing are outweighed by the drawbacks—both to that patient and to the unit as a whole in terms of its microbial ecology.

KEY WORDS: Antimicrobials; intensive care unit (ICU); drug utilization; ATC/DDD classification

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Introduction

The discovery of antimicrobials is considered as the greatest medical achievements of the twentieth century. The antimicrobials contributed to a significant decline in infectious disease-related mortality.[1] Antimicrobials are effective in the control and cure of serious infections. It is being increasingly recognized that antimicrobial use is a double-edged sword. On one side, the availability of effective antimicrobials allows

immediate improvement of the infectious disease condition; on the other side, overuse/misuse can lead to adverse drug reactions (ADRs) and antimicrobial resistant.[2]

Critically ill patients admitted to intensive care units (ICUs) are highly susceptible to infections because of predisposing illnesses and the use of invasive and surgical procedures and are, therefore, exposed to high antimicrobial pressure.[3] Use of antimicrobials in the ICU must follow best clinical practice if the emergence of resistance to antimicrobials is to be minimized. Antimicrobial resistance is an important factor governing treatment success and mortality.[4] The problem of resistance is greater in ICUs than in other hospital wards.[5] Control of antimicrobial resistance—that is, detecting, monitoring, and fighting the emergence of resistant bacteria—is, therefore, especially important in the intensive care environment.

The Anatomical Therapeutic Chemical (ATC) Classification/defined daily dose (DDD) system is a tool for presenting drug utilization research in order to improve quality of drug use and is recommended by the World Health Organization (WHO) as the international standard for drug utilization studies.[6] The DDD is an artificially and arbitrarily created statistical measurement used for research purposes when comparing the utilization of drugs. The formal definition of the DDD is "the assumed average maintenance dose per day for a drug used for its main indication in adults." DDD are assigned only to drugs that have already been provided with an ATC code. These parameters can be very useful for evaluating drug utilization at every level of health-care system.

Our hospital, Civil Hospital, Gandhinagar, Gujarat, India, is a 750-bedded tertiary-care teaching institute. Many critically ill patients admitted to ICU of our hospital. But, there are no baseline data about the utilization pattern of antimicrobial agents in the ICU. This will be helpful in analyzing the rationality of antimicrobial use and to make necessary changes if needed. Thus, it will help in prevention of further emergence of antimicrobial resistance. So, the objective of this study was to find the antimicrobial prescription patterns in the ICU.

Materials and Methods

This was a prospective observational study carried out in the ICU of the Civil Hospital, a teaching hospital attached to GMERS Medical College, Gandhinagar, Gujarat, India, from April 2014 to September 2014. The study protocol was approved by Institutional Ethics Committee. All the patients participating in the study were explained clearly about the purpose and nature of the study in the language they understand, and written informed consent was taken before including them in the study.

Patients of all ages and both genders who were admitted in ICU during study duration and willing to give informed consent were included in the study.

Collection of Data

The study was conducted for patients meeting inclusion criteria. All patients was visited daily during their hospital stay and interviewed. Every patient was followed up till he/she was discharged from ICU, and their case record sheets were reviewed for gathering necessary information as per case record form. Patients' history, clinical presentation, diagnosis, and drug treatment, especially antimicrobial use, were recorded in a structured case record form.

Format of Analysis

Data of all the patients were analyzed for following parameters: (1) patient's demographic details and (2) analysis of antimicrobial use: (i) type of antimicrobial use; (ii) number of antimicrobials prescribed; (iii) prescribed antimicrobial agent; and (iv) assigning ATC code to the antimicrobial use and calculation of DDD/100 bed-days.

Assigning ATC code to the antimicrobial use and calculation of DDD/100 bed-days

The most commonly used antimicrobials were classified using the ATC Classification system, and drug utilization was measured as DDD/100 bed-days. In the ATC Classification system, the drugs were divided into different groups according to the organ or system on which they act and their chemical, pharmacological, and therapeutic properties.[6] The DDD per 100 bed-days was calculated by the formula:

$$\text{DDD/100 bed-days} = \frac{\text{No. of units administered in a given period} \times 10}{\text{DDD} \times \text{number of days} \times \text{number of beds} \times \text{occupancy index}}$$

$$\text{where Occupancy index} = \frac{\text{Total inpatient service days for a period} \times 100}{\text{Total inpatient bed count} \times \text{number of days in the period}}$$

Statistical Analysis

The data were subjected to statistical analysis using SPSS software package. Data were expressed as absolute numbers with or without percentages, as means with standard deviation or as medians with ranges. Frequency comparisons were performed by χ^2-test. A probability value less than 0.05 was considered to denote statistical significance.

Result

Totally, 123 patients admitted into the ICU during the study period were included in the study. Of these 123 patients, 75 were men and 48 women. The average age of the patients was 56.7 years (±19.9 years). Majority of the patients admitted to the ICU were from the medical specialty (96, 78.05%) [Tables 1 and 2].

A total of 846 drugs were prescribed in total 123 patients with an average of 6.87 drugs per prescription. One hundred

thirteen patients (91.87%) were prescribed an antimicrobial. In all, 183 antimicrobials, at an average of 1.49 (±0.79) antimicrobials/prescriptions were ordered, and antimicrobials constituted 21.63% of the total drugs prescribed [Figure 1].

On analyzing the type of antimicrobials use, it was found that majority of the patients (107; 94.69%) were prescribed the antimicrobials prophylactically. Only six patients showed confirmed diagnosis of infectious disease and were prescribed antimicrobials empirically at the time of admission in ICU, and it was changed to definitive antimicrobial therapy based on culture and sensitivity report in three patients only [Table 3].

Ceftriaxone was most commonly (69; 61.60%) prescribed antimicrobial agent, followed by amoxicillin + clavulanate (28; 24.78%), cefotaxime (23; 20.35%), and metronidazole (19; 16.81%). The prescribed antimicrobials were given ATC code, and their number of DDDs was calculated according to the WHO formula as mentioned in Materials and Methods section. These results are shown in Table 4. Average duration of prescribed antimicrobials was 4.25 days (±2.31 days) in ICU.

Discussion

One of the most important sources of nosocomial infections are the ICUs.[7] The high chances of getting infections and high prevalence of infections lead to heavy consumption of antimicrobial agents in this set up, around 10 times than in general wards.[8]

In this study, totally, 123 patients admitted into the ICU were included with men predominance. The average age of the patients was 56.7 years (±19.9 years) in this study. In a similar Indian study, the average age of the patients was 49 years.[9] A similar finding was observed in a study on drug use patterns from an ICU in Iran.[10] So, the middle age group was the most common affected age group in all three studies. Majority of the patients admitted to the ICU were from the medical specialty (96, 78.05%). This finding is supported by the study done by Williams et al.[9]

The average drugs prescribed per prescription in this study was 6.87. This finding was comparable with the other data reported in literature, ranging from 5.1 to 12.[9,11,12] The number of drugs per prescription is an important index of a prescription audit. In our study, 113 (91.87%) patients were prescribed an antimicrobial, and an average of 1.49 antimicrobials per prescription was ordered. These findings were similar to that described in other studies.[9,13] In our study, most patients (55%) received one antimicrobials. A study in a Danish university hospital ICU reported that the majority of their patients were on one antimicrobial.[14] It is recommended that the number of drugs per prescription should be kept as low as possible to minimize the risk of drug interactions, development of bacterial resistance, and hospital and patients costs.[15]

With regard to antimicrobial prophylaxis, a majority of the patients (107; 94.69%) were prescribed the antimicrobials prophylactically in this study. Many guidelines are available for antimicrobial prophylaxis in surgical patients, and there is

Table 1: Distribution of the patients according to different age groups

Age groups (years)	No. of patients (%)
11–20	2 (1.62)
21–30	16 (13.00)
31–40	16 (13.00)
41–50	11 (8.94)
51–60	20 (16.26)
61–70	28 (22.76)
71–80	15 (12.20)
81–90	15 (12.20)
Total	123 (100.00)
Mean ± SD	56.7 ± 19.9
Min–Max	18–90

Table 2: Distribution of the patients according to gender

Gender	No. of patients (%)
M	75 (60.98)
F	48 (39.02)
Total	123 (100.00)

M:F—1.6:1.

Table 3: Purpose of the use of antimicrobials in the patients (*N* = 113)

Purpose	No. of patients (%)
Prophylaxis	
• Surgical	6 (5.31)
• Non-surgical	101 (89.38)
• Total	107 (94.69)
Therapeutic	
• Empirical	6 (5.31)
• Definitive	3 (2.65)

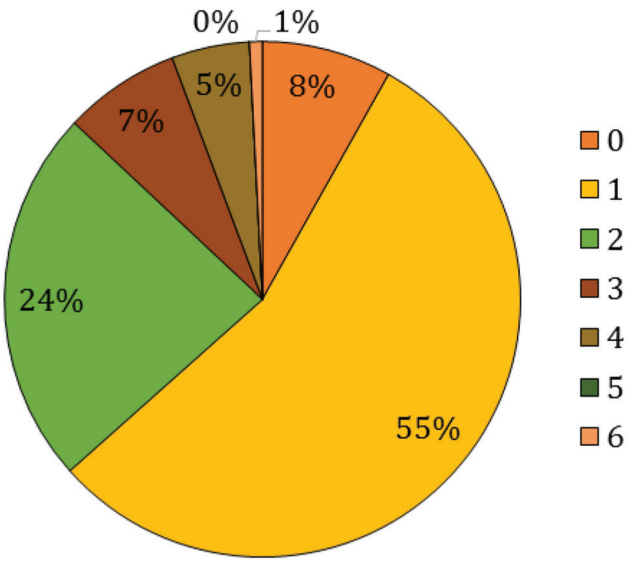

Figure 1: Number of antimicrobials prescribed (mean ± SD: 1.5 ± 0.8).

Table 4: Analysis of use of antimicrobials according to ATC/DDD system

Antimicrobial agent	ATC Code	WHO DDD (g)[6]	No. of patients (%), *N* = 113	Units	DDD/100 bed days
Ceftriaxone	J01DD04	2	69 (61.60)	205	11.86
Amoxicillin + clavulanate	J01CR02	3	28 (24.78)	140.6	5.42
Cefotaxime	J01DD01	4	23 (20.35)	104	3.01
Metronidazole	J01XD01	1.5	19 (16.81)	54	4.17
Levofloxacin	J01MA12	0.5	13 (11.50)	25	5.79
Amikacin	J01GB06	1	12 (10.61)	22	2.55
Cefoperazone + sulbactam	J01DD62	4	9 (7.97)	80	2.31
Cefixime	J01DD08	0.4	4 (3.54)	8	2.31
Cefoperazone	J01DD62	4	2 (1.77)	10	0.29
Ciprofloxacin	J01MA02	0.5	1 (0.88)	3	0.69

ATC, Anatomical Therapeutic Chemical Classification; DDD, defined daily dose.

an agreement in recommending cefazolin as first choice.[16,17] But, in our study, none of the patients were prescribed cefazolin. Concerning prophylaxis in nonsurgical patients, after excluding a few specific conditions such as neutropenia, the only two indications for which there is evidence are selective digestive decontamination and ventilator-associated pneumonia prophylaxis but limited to certain situations. We observed that lengthy treatment (4.25 days), mainly with inappropriate antimicrobials (third-generation cephalosporin in 61.6% of cases), in too many patients (89.38% of non-surgical patients without sepsis). Prophylaxis in nonsurgical patients is not supported by any randomized clinical trial and is not recommended by any scientific society. This practice influenced by the idea that low bacterial growth could protect against infections.

The DDD system is most frequently used in academic articles and reports and a tool for national and international comparison of drug consumption. The number of DDDs for prescribed antimicrobials in our study was calculated, which can serve as a baseline data for comparison in future studies that could be done in similar set up to identify the trends in drug consumption over years. These data can also be used for comparison of drug consumption in different parts of this country and for international comparisons. In this study, number of DDDs for ceftriaxone was 11.86, and it suggests the more consumption of ceftriaxone in our setup when compared with international standards.[6]

Antimicrobial resistance is rapidly increasing globally; therefore, suitable policy and actions are urgently needed to combat it. The first step in combating inappropriate use of antimicrobials is to measure access and use of antimicrobial in order to quantify the scale of the problem and to have a baseline data to compare and evaluate the impact of any intervention. So, this study will helpful in this regard.

Conclusion

Optimization of antimicrobial therapy in the ICU is difficult but important and is not going to get any easier with increasing problems of multiresistance. The need for antimicrobial should be reviewed daily on every patient, always stopping at the earliest possible opportunity where the benefits of continuing are outweighed by the drawbacks—both to that patient and to the unit as a whole in terms of its microbial ecology.

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