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Research Article

STUDY OF PRESCRIBING PATTERN OF ANTIMICROBIAL AGENTS IN MEDICINE INTENSIVE CARE UNIT OF A TERTIARY CARE HOSPITAL

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ABSTRACT

Objective: The objective of the study was to assess the current use of antimicrobial agents (AMAs) and to assess prescription writing as per the WHO guidelines in the medicine intensive care unit (MICU).

Methods: The present study was conducted on admitted patients in MICU of a tertiary care hospital. The demographic and clinical treatment data of patients were collected in specially designed pro forma from the case record form.

Results: Of 400 patients enrolled in the study, 55.50% were male and 44.50% were female. A common indication of AMAs use was infection (61.75%), symptomatic (21.50%), and prophylactic (10.50%) use. In 65% patients, antimicrobial therapy was considered to be rational. The majority of patients have good recovery (61%). Polypharmacy was seen in 89.75% of patients. The average number of drugs prescribed per patient was 8.84±2.55. 1.90±1.20 was average number of AMAs per patient. Commonest AMAs prescribed are ceftriaxone (27.64%), metronidazole, and amoxicillin+clavulanic acid.

Conclusion: This study visibly highlights the practice of polypharmacy, low uses of generic drugs, high usage of antibiotic, and injection. Cephalosporins are the most prescribed AMAs in the ICUs. Remedy of this situation requires regulation, education, awareness, compliance with protocol, and guidelines of AMAs use.

Keywords: Antimicrobial agents, Prescription, Drug utilization, Intensive care unit.

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INTRODUCTION

Antibiotics are the substances that kill or inhibit the growth of microorganisms and are used for the treatment or prevention of different types of local and systemic infections [1]. Antibiotics help in reducing the burden of mortality and morbidity caused by infectious diseases [2]. Most of the patients in medicine intensive care unit (MICU) often suffer from severe illnesses, multiple organ dysfunction, and coexisting medical disorders. In such situation, multiple drugs are prescribed routinely. A major portion of drugs prescribed to the patients admitted in MICU consist of antimicrobial agents (AMAs) [3].

Unnecessary poly-pharmacy, high use of drugs with unproven efficacy, and irrational antibiotic usage are some of the recognized drug prescription issues in developing countries. These problems lead to increased health-care utilization, morbidity, mortality, adverse drug events, and drug resistance [4]. Inappropriate antibiotic prescribing is a grave danger worldwide, as many organisms have become resistant to commonly used antibiotics [2,5]. Although there are guidelines and appeal by Government and professional medical societies to decrease antibiotic prescribing for inappropriate indications, there has been a slight improvement in prescribing patterns [6,7]. Furthermore, information regarding antibiotic prescribing trends that can direct stewardship efforts remains sparse in developing countries.

A physician needs to possess a skill of prescribing drugs. This skill requires to be assessed and refined time to time. It reflects the physician's knowledge of medicine, his accuracy in diagnosis and attitude toward choosing the rational treatment [8]. The study of prescribing patterns will provide baseline data to suggest modifications in guidelines of prescription writing and antibiotic stewardship program. This may help in a great deal to reduce bacterial resistance.

With this state of affairs of antimicrobials, we planned to conduct a study with the aim to assess the prescribing pattern of AMAs in MICU of a teaching hospital in Central India. The primary objectives are to assess the current use of AMAs in the MICU and to assess prescription writing as per the WHO guidelines.

METHODS

The present study was conducted on admitted patients in MICU of a tertiary care hospital. The study was conducted after obtaining due approval from the Institute Ethics Committee. Informed consent was obtained from each patient or relatives of the patient admitted in MICU. The demographic and clinical treatment data of 400 patients were collected in specially designed pro forma from the case record form. Baseline demographic variables were recorded. The prescription data of all patients at admission into the MICU were noted with regard to antibiotic prescription and the class of antibiotics. The antibiotic prescription pattern was analyzed until the patient was discharged from MICU.

Inclusion criteria

The following criteria were included in the study:

- Patients admitted in MICU
- Patients or relatives willing to give written informed consent.

Exclusion criteria

The following criteria were excluded from the study:

- Patients not ready to give written informed consent.
- Patients not willing to be followed up, if required.
- Incomplete data and patients who stayed for <24 h in MICU.

Indication for the antimicrobial use

The following groups were essentially defined by the physician according to the way they treated the patients [9,10].

1. If clinical and/or laboratory data gave evidence of infection, the infection was considered as the indication
2. If there was no evidence of infection and the agent was employed to prevent infection (e.g., catheterization), the therapy was considered as prophylactic
3. If no evidence of prophylaxis could be found and records showed the same symptoms being treated, for example, antimicrobial use in the treatment of fever in the absence of specifically suspected infection, the indication was considered as symptomatic.

Rationality [9,10]

a. If the antimicrobial use and its dose, route of administration, frequency, and duration of use were considered appropriate for infection, the therapy was considered rational
b. If the antimicrobial was used without indication, prophylaxis under circumstances of unproven efficacy or by clearly inappropriate route, dose, or preparation for that indication, therapy was considered irrational
c. When insufficient clinical or laboratory data were present to help the therapy to be classified as clearly rational or irrational, for example, the patient of congestive heart failure having cough but do not know that cough is due to CHF or infection then treatment with AMA considered questionable, therapy was considered questionable.

Statistical analysis

Data were analyzed using descriptive statistics. Statistical software Graph Pad Prism was used for the analysis of data and Microsoft Word and Excel to generate graphs and tables.

RESULTS

During the study period total, 400 patients were enrolled, consisting 222 (55.50%) male and 178 (44.50%) females patient. 1.25 was male to female ratio. Middle age male was the most common age group among all admitted patients. Patients above 40 years were 293 (73.25%). The mean age of patients was 52.01±15.33 years (Table 1).

As shown in Fig. 1, the indication for antimicrobial use in which common indication was infection (61.75%) followed by prophylactic use (21.50%) and symptomatic use (10.50%). Fig. 2 shows the evaluation of antimicrobial therapy according to its use, wherein 65.00% patients the antimicrobial therapy was considered rational, in 23.75% patients, therapy was irrational, while in 11.25% patients, it was questionable. In this study, a good prognosis was seen in 61% of patients and mortality rate was found to be 13.50%. The majority of the prescriptions were properly signed (52.25%) followed by improperly signed (28%) and absence of signature (19.75%).

As depicted in Table 2, 2.89.75% of patients received more than five drugs per day, 66.75% patients received 6–10 drugs per day, and 23% received 11–15 drugs. It was observed that the maximum number of drugs prescribed to a single patient was 15. The average number of drugs prescribed per patient was 8.84±2.55. Fig. 3 depicts 158 (39.50%) patients received only one AMA, 24.25% received two AMAs, and 30.50% received 3–6 AMAs. The average number of AMAs per patient was 1.90±1.20. Only 20.20% of AMAs were prescribed by generic name while majority by brand name. The most common dosage form used for AMA was injection (76.08%) followed by tablet (19.35%) and nebulization (4.57%).

The commonly prescribed antimicrobial drug classes were cephalosporins (31.13%) and penicillins (18.03%). Ceftriaxone (27.64%) was the commonest AMA followed by metronidazole (17.79%) to be prescribed. Prescribing frequency of AMAs among patients in the MICU has been detailed in Table 3. A total of 175 (20.03%) antimicrobial fixed drug combinations (FDC) were used among 400 patients. Amoxicillin+clavulanic acid (11.30%) was the most common FDC noticed. The number of patients who were prescribed antimicrobial FDCs is shown in Table 4.

DISCUSSION

A prescription by a doctor may be taken as a reflection of the doctor's attitude toward the disease and the role of the drug in treatment. It provides valuable insight into the nature of the health-care delivery system of the country [11]. Quality-of-life can be raised by enhancing standards of medical treatment at all levels. Setting regulations and assessing the quality of health care through performance review and audits should become a part of everyday clinical practice [12].

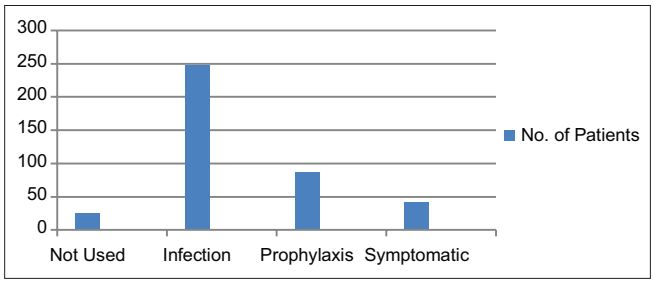

Fig. 1: Indication for antimicrobial use

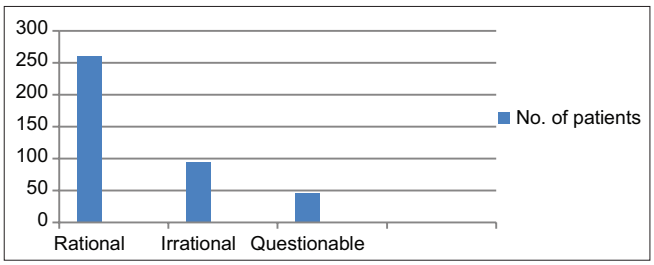

Fig. 2: Evaluation of antimicrobial therapy according to use

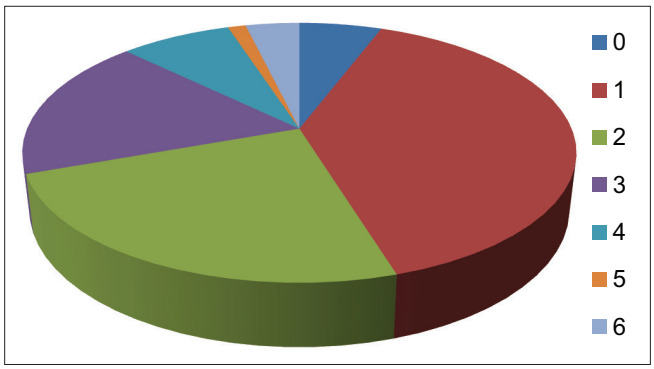

Fig. 3: Total number of antimicrobial agents per patient

Table 1: Age- and sex-wise distribution of the patients

Parameters	No. of patients	Percentage
Age (years)		
11–20	08	2.00
21–30	33	8.25
31–40	66	16.50
41–50	74	18.50
51-60	92	23.00
61–70	84	21.00
71–80	30	07.50
81–90	13	03.25
Sex		
Male	222	55.50
Female	178	44.50

Table 2: Total number of drugs prescribed per patients

S. No.	Total No. of drugs prescribed	No. of patients	Percentage of patients
1.	1	00	00
2.	2	3	00.75
3.	3	2	00.50
4.	4	8	02.00
5.	5	28	07.00
6.	6	43	10.75
7.	7	48	12.00
8.	8	51	12.75
9.	9	43	10.75
10.	10	82	20.50
11.	11	31	07.75
12.	12	38	09.50
13.	13	10	02.50
14.	14	3	00.75
15.	15	10	02.50

Table 3: Commonly prescribed antimicrobial agents

S. No.	Name of drug	No. of patients	Percentage
1.	Ceftriaxone	230	27.64
2.	Metronidazole	148	17.79
3.	Amoxicillin+Clavulanic acid	94	11.30
4.	Ofloxacin	61	7.33
5.	Azithromycin	53	6.37
6.	Piperacillin+Tazobactam	47	5.64
7.	Levofloxacin	30	3.60
8.	Cefixime	29	3.48
9.	Doxycycline	23	2.76
10.	Artesunate	21	2.52
11.	Ofloxacin+Ornidazole	19	2.28
12.	Meropenem	18	2.16
13.	Rifaximine	16	1.92
14.	Ceftriaxone+Sulbactam	15	1.80
15.	Amikacin	13	1.56
16.	Amoxicillin	09	1.08
17.	Acyclovir	3	0.36
18.	Chloroquine	2	0.24
19.	Moxifloxacin	1	0.12

Table 4. Number of patients prescribed antimicrobial drugs in fixed-dose combination

S. No.	Antimicrobial agents in fixed-dose combinations	No. of patients	Percentage
1.	Amoxicillin+Clavulanic acid	94	11.3
2.	Piperacillin+Tazobactam	47	5.65
3.	Ofloxacin+Ornidazole	19	2.28
4.	Ceftriaxone+Sulbactam	15	1.80

In our study, male to female ratio was 1.25, whereas in studies conducted by John *et al*. [13] and Naikwadi *et al*. [14], it was 1.9 and 1.4, respectively. Similar male preponderance has been shown in previous studies [15,16]. In contrast, a study done by Smythe *et al*. [17] showed an equal proportion of male and female admitted to the MICU. The difference in gender distribution was due to differences in admissions in MICU in an Indian setting. The probable reason for such a finding could be the higher male to female ratio in the central India. In the Indian scenario, it is noticed that female populations, especially the lower socioeconomic status, are reluctant to utilize health-care facilities, even if they are critically ill.

The mean age of the patients in MICU in this study was 52.01±15.33 years, which is similar to a study by John *et al*. [13] and a study conducted in Srishyla *et al*. [18] as 50 years. In contrast, a study by Naikwadi *et al*. found mean age to be 34.16±14.13 [14] while Mangrulkar *et al*. showed a mean age of >60 years (62.2±16.24 years) [19]. The relatively high mean age in our study was due to the fact that the majority of the patients in this study were admitted due to cardiac, renal, neuronal, or pulmonary problems which are usually encountered at a relatively older age.

It has been found that the common indication for the use of AMAs in this study was infection (61.75%) followed by prophylactic use (21.50%) and symptomatic use (10.50%). AMAs were not used in 6.25% of patients also. This is comparable to the result observed by Badar and Navale [9] wherein the indications were infection (64.9%), symptomatic use (24%), and prophylaxis (11%) and to a study by Pandiamunian and Somasundaram [20], i.e., infection (63.4%), prophylaxis (23.9%), and symptomatic (12.7%). In our study, evaluation of 65% of AMAs use was rational, 23.75% irrational, and 11.25% was questionable. These results are contradictory with a study by Badar and Navale [9], where 30.4% of AMAs evaluation was rational, 58.6% irrational, and 11% questionable.

In this study, a good prognosis was seen in 61% of patients and the mortality rate was found to be 13.50%. This is in accordance with the study done by Nikhilesh *et al*. [21] and a study done in Shankar *et al*. [22], wherein ICU mortality rate was found to be 12% and 15.4%, respectively. However, many Indian studies reported very high MICU mortality rate as around 35% [13,23].

The average number of drugs prescribed to a patient in our study was 8.84±2.55 which is comparable to a study conducted by Badar and Navale [9] and Pandiamunian and Somasundaram [20], wherein it was 7.5 and 10.4±2, respectively. The number is lesser than that was observed by John *et al*. (11.6±2 drugs) and Smythe *et al*. (12.1±7.6) [13,17] but is higher compared to a report from Nepal which recorded a mean of 5.1±2.7 drugs [22] and Alamchandani *et al*., wherein it was 4.12±1.49 [24].

Polypharmacy is defined as concomitant use of five or more drugs and it could enhance drug-drug interactions and drug-related problems. Polypharmacy was seen in around 96.75% patients. It is difficult to treat patients in the ICU with multiple comorbidities with less number of drugs as they require multiple drugs for the treatment of the specific condition as well as for prophylaxis. It is essential to keep a balance between the number of drugs and effective pharmacotherapy. The mean number of drugs per prescription should be as low as possible since higher numbers increase the risk of drug interaction, risk of bacterial resistance, noncompliance, and cost of the treatment [25,26].

In our study, patients received more than one AMA on a number of occasions (94.25%). As these patients were suffering from mixed infections, they received one AMA for Gram positive, other for Gram negative and third one for anaerobic infection. This multidrug therapy is useful in decreasing the prevalence of drug resistance and total drug duration. A high percentage of patients were prescribed at least one antibiotic which was in accordance with a study conducted by Badar and Navale. (83%), John *et al*. (83%), and Shankar *et al*. (92%) [9,13,22] but was contrary to some studies where lesser AMAs were used such as Naikwadi *et al*. (70.85%) and Curcio *et al*. (51%) [15,27]. The mean number of AMAs per patient was 1.90±1.20 which equals to that of studies conducted by Nikhilesh *et al*. (1.73) [21] and by Amit (1.74) [28].

In our study, drugs prescribed by generic name were only 20.20%, which are very much comparable to the study by John *et al*. (30%) and Pandiamunian and Somasundaram (29.21%) [13,20]. Contradictory to these results, 79.18% drugs were prescribed by generic name in a study by Admane *et al*. and 100% in Alharafsheh *et al*. [29,30] generic prescribing helps the hospital pharmacy to have better inventory control. Confusion among the pharmacists while dispensing, when prescribed by generic names, can also be reduced. Moreover, generic drugs are more cost-effective than the branded one [31].

In MICU, patients are always in critical condition, so they frequently receive drugs by the parental route to combat the emerging life-threatening situation. The most common dosage form used for AMA was injection (76.08%), which is similar to a study by Pandiamunian and Somasundaram (72.56%) [20].

In our study, cephalosporins (31.13%) and penicillins (18.03%) were the commonly prescribed antimicrobial drug classes. Similar results were observed by Pandiamunian and Somasundaram [20], i.e., cephalosporins (35.6%) and penicillins (21.3%), whereas in a study by Jokandan and Jha [32], a different trend in the use of AMA was seen, i.e., cephalosporins (22.03%), quinolone (15.57%), antifungals (14.36%), aminoglycosides (11.59%), and penicillin (10.76%).

Among the AMAs in our study, ceftriaxone was the commonest to be prescribed, followed by metronidazole, FDC of amoxicillin+clavulanic acid, ofloxacin, and azithromycin. Ceftriaxone was found to be used most commonly in some other studies also [9,33,34]. Usluer *et al*. [35] reported Biswal *et al*. [36] documented metronidazole as the most commonly prescribed AMA. Contradictory to above results ampicillin, amoxicillin, metronidazole, ciprofloxacin, and crystalline penicillin were the five most commonly prescribed AMAs in the study conducted by Shankar *et al*. [37] different trend in the use of AMA was seen in a study by John *et al*. [13] as cefoperazone (30%), amikacin (28.9%), and metronidazole (28.6%). Another study by Naikwadi *et al*. and Nikhilesh *et al*. showed AMA use pattern of ceftriaxone, FDC of piperacillin+tazobactam, and metronidazole [15,21]. Another study by Maharani *et al*. showed yet another AMAs usage pattern with cefotaxime (37.6%), metronidazole (19.9%), azithromycin (17.2%), and FDC of piperacillin+tazobactam (12.2%) to be the common antibiotics used in MICU settings [38].

Cephalosporins are commonly prescribed because of their comparatively lower toxicity and broader spectrum activity. For several serious Gram-negative infections, cephalosporins in combination with aminoglycosides are frequently used due to synergistic activity and broader coverage of organisms. Recent studies done in this decade in our country documented that third-generation cephalosporins are the most commonly prescribed AMAs in the ICUs as well as in the outpatient clinics in India [20].

In this study, among total antimicrobials prescribed, 21.03% were FDC and amoxicillin+clavulanic acid (11.30%) was the most common FDC noticed followed by piperacillin+tazobactam (5.65%) and ofloxacin+ornidazole (2.28%) which was in correspondence with a study conducted by Maharani *et al*., where most common combination used was amoxicillin+clavulanic, piperacillin+tazobactam, and amoxicillin+benzylpenicillin [38]. However, a study by John *et al*. [13] shows that cefoperazone+sulbactam combination was the most preferred FDC.

LIMITATIONS OF STUDY

There are certain limitations of this study as it was conducted in a single tertiary care setting and results cannot be generalized to the whole population in Central India. We looked at drug use patterns over a 4-month period only. The study was retrospective. Data on the scales used to grade the severity of illness of admitted patients such as acute physiology, age, and chronic health evaluation were not available in the case record. Hence, we were unable to correlate the drug prescribing patterns with the severity of patient illness.

CONCLUSION

This study clearly highlights the practice of polypharmacy, low uses of generic drugs, a very high usage of AMAs, injections, and cephalosporins being the most prescribed AMAs in the ICUs. Rational use of the drug is the foremost goal in writing a prescription. A multidisciplinary approach can be undertaken in the ICU set up. Pharmacists, microbiologists, infectious disease control specialists, and intensive care specialists can work together to lead a pathway for creating awareness and guidelines of rational antimicrobial pharmacotherapy. Future research should be aimed at determining the impact of incomplete prescriptions on a patient's health status and drug resistance. Remedy of this situation requires regulation, education, awareness, compliance to protocol, and guidelines of AMAs use. Overall, the scope for improving rational use of AMAs exists. The present study on antimicrobial drug prescribing patterns in MICU can provide a framework for continuous prescription audit.

AUTHORS' CONTRIBUTIONS

All the authors had contributed in conduct of the study and preparation of the manuscript.

CONFLICTS OF INTEREST

The authors declared no conflicts of interest regarding the research, authorship, and publication of this article.

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