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Original Research Article

Drug Utilization Pattern of Antimicrobial Agents in the Medical and Surgical Intensive Care Unit: A Study from Western Gujarat

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Abstract

Background: Drug utilization research plays an important role in clinical practice as it forms the basis for amendments in the drug dispensing policies at local and national levels.

Objective: To study the drug utilization pattern of antimicrobial agents among patients attending the medical and surgical Intensive care units of a tertiary care teaching hospital.

Material and Method: A longitudinal, prospective and observational study was carried out to determine the utilization pattern of antimicrobial agents in 16 bedded medical and surgical ICUs at tertiary care hospitals from June 2017 to May 2018 over 12 months. Individual case papers with antimicrobial prescriptions were studied, and the prescribing pattern was analyzed using the World Health Organization (WHO) basic drug indicators.

Results: A total of 622 patients with a mean age group of 46 years were analyzed, out of which 391(62.8%) were male, and 231(37.1%) were female. The mean duration of stay was *4.2* days. The most common cause of admission was post-operative (23.9%), followed by accidental trauma (13.8%) and organophosphorus poisoning (9.8%). The average number of drugs per encounter was 2.3 in our study. In our study, 39.4% of patients were expired, while 54.5% were shifted to a ward. The most common drug prescribed was metronidazole (22.4%), followed by ceftriaxone (20.6%), while the most common class of antimicrobial agents was cephalosporin drugs (27.5%). In a single drug prescription, cefotaxime was the most commonly prescribed drug (7.7%), followed by ceftriaxone (6.6%). In this study, 63.9% of drugs were prescribed by generic names and 36.1% by brand names. About 98.1% of drugs were prescribed via the parenteral route followed by the oral route (1.9%). In our study average, antimicrobial drug cost per patient was Rs. 2091.54, and the most common FDC prescribed was amoxicillin with clavulanic acid (12.6%), followed by piperacillin with tazobactam (4.21%).

Conclusion: The present study in medical and surgical ICUs can provide a framework for continuous prescription audits in ICUs at the regional and national levels. This will provide the database to predict future trends and cost-effective use of existing antimicrobial agents. This will help develop standard operating procedures (SOPs) for ICU clinicians to rationalize prescribing antimicrobial agents.

Introduction

Drug utilization research plays an important role in clinical practice as it forms the basis for amendments in the drug dispensing policies at local and national levels. [1] Patients with severe illness and life-threatening diseases admitted to the Intensive care unit (ICU) require multidrug therapy from different pharmacological classes. [2] Drug therapy is complicated in ICU patients due to having mixed types of infections and contributes to a substantial portion of routine prescriptions. The irrational use of broad-spectrum antimicrobial agents results in the emergence of resistant microbes, drug interactions, treatment failure and a high risk of adverse effects. [3] The resistant strains indirectly impact the health care cost of patients' duration and severity of infections. Therefore, evaluating the drug utilization pattern of antimicrobial agents is important to guide local and national prescription protocol in health care facilities. This will improve the prescription pattern of drugs and helps to control resistance. [4] So, it was planned to undertake a prospective drug utilization study to guide the quality of care provided by health care professionals.

The study aimed to observe and evaluate the current drug utilization pattern of antimicrobial agents among patients attending the medical and surgical Intensive care units with life-threatening disease conditions in tertiary care teaching hospitals.

Material and method

This longitudinal, prospective and observational study was carried out to determine the utilization pattern of antimicrobial agents in the Medical and surgical ICU at Guru Gobindsing Government hospital, Jamnagar, a tertiary care teaching hospital, from June 2017 to May 2018 over 12 months. Patients were enrolled as per inclusion criteria: adult patients above 18 years of age and of either gender who were admitted **to** medical or surgical, Intensive Care Units (ICU), patients who were prescribed antimicrobial agents, patients or their relatives who gave consent and were willing to participate in this study. Patients under 18 years of age who were not willing to participate in the study were excluded. Study approval was taken from the Institutional Ethics Committee of Guru Gobindsing Government Hospital, Jamnagar.

The data was collected from the sources like admission case papers, lab reports and therapy charts in predesigned case record form (CRF). The intensive care unit has issued a protocol for empirical use of antibiotics in commonly encountered disease conditions. The patient's demographic details and diagnosis and drug therapy data were collected. Enrolled patients were followed up every day until their ICU hospitalization or mortality occurred. Information about adding or changing antimicrobial agents and any adverse drug reactions (ADR) were collected during the follow-up visit. The prescription patterns were analyzed using World Health Organization (WHO) basic drug indicators. The average cost of AMAs was calculated by multiplying the cost per unit dosage and the dose number used in each patient.

Results

Of 622 patients, 391(62.8%) were male, and 231(37.1%) were female. Maximum patients belonged to the age group of 31-45 years 153(24.6%), followed by 46-60 years 144(23.1%) and 19-30 years-138(22.1%). The mean age in study subjects was 46.1±18.4 years, the mean age in males was 46.3±18.4, and in females was 45.8±18.4.

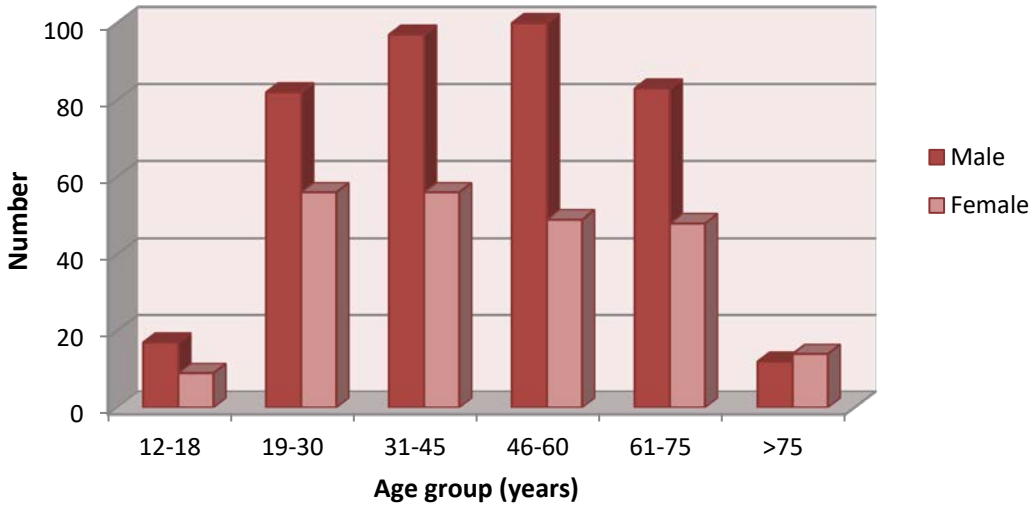

Figure 1: Age & Sex distribution

In the present study, most of the patients (48.5%) had a stay of 1-3 days. 38.7% of patients had a stay of between 4-6 days. The mean duration of stay was *4.2±3.5* days.

Most patients were suffering from post-operative complications 149(23.9%). Other common conditions were accidental injuries (13.8%), organophosphorus poisoning 61(9.8%), pneumonia (4.2%) and other 48.2%.

In this study, about 34.4% of the patients had received 2 antimicrobial drugs followed by 3 (28.5%) and 1(24.7%).

No of drugs	No patients out of 620 (100%)
1	154 (24.7%)
2	214 (34.4%)
3	177 (28.4%)
≥4	77 (12.4%)

The average number of drugs per encounter was 2.31±1.4 in our study, ranging from 1 to 7.

In our study, 245 (39.4%) patients were expired, while 307 (54.5%) were shifted to the ward.

OUTCOME	Number of patients
Expired	245 (39.4%)
Shifted to ward	339 (54.5%)
Refer to higher Centre	28 (4.5%)
Discharge against advice (DAMA)	8 (1.3%)
Discharge on Request	2 (0.32%)

The most common drug used was metronidazole (22.4%), followed by ceftriaxone (20.6%). In comparison, the most common class of antimicrobial agents was Cephalosporin drugs (27.5%), followed by Anti amoebic drugs (22.4%), Penicillin 242(17.6%), Fluoroquinolones 182(13.2%), Carbapenems 82(5.95%), Aminoglycosides 57(4.1%), Antimalarial 41(2.9%) and others 6.18%.

In a single drug prescription, cefotaxime was the most commonly prescribed drug 48(7.7%), followed by ceftriaxone 41(6.6%) and a fixed-dose combination (FDC) of amoxicillin and clavulanic acid 24(3.9%). In a two-drug combination,

metronidazole with ceftriaxone was the most commonly prescribed combination 41(6.6%), followed by metronidazole and FDC of amoxicillin and clavulanic acid 20(3.2%). In a three-drug combination, metronidazole, ceftriaxone and FDC of amoxicillin and clavulanic acid were the most commonly prescribed combinations 51(8.2%).

In this study, 921 drugs were prescribed by generic name and 521 by brand name. So, 63.9% of drugs were prescribed by generic name and 36.1% by brand name.

In our study, 1414(98.1%) drugs were prescribed via the parenteral route while 28(1.9%) via the oral route.

The cost was calculated according to the minimum price of that drug in IDR drug triple I compendium 2018 Issue. Our study's average antimicrobial drug cost per patient was Rs. 2091.54 Rs.

Antimicrobial agents	ATC CODE	WHO DDD g	No of patients	PDD g
Metronidazole	J01XD01	1.5	308	1.5
Ceftriaxone	J01DD04	2	283	1.9
Amoxicillin+Clavulanic acid	J01CR02	3	173	3.6
Levofloxacin	J01MA12	0.5	116	0.5
Cefotaxime	J01DD01	4	83	2
Meropenem	J01DH02	2	82	2
Ciprofloxacin	J01MA02	0.5	60	1
Piperacillin + tazobactum	J01CR05	14	58	13.5
Linezolid	J01XX08	1.2	38	1.2
Amikacin	J01GB06	1	36	1
Artisunate	P01BE03	0.28	37	0.25
Azithromycin	J01FA10	0.5	18	1
Gentamycin	J01GB03	0.24	18	0.42
Clindamycin	J01FF01	1.8	17	1.16
Oseltamivir	J05AH02	0.15	10	0.3
Cefoperazone + sulbactam	J01DD62	4	9	3.2

In our study most common FDC prescribed was amoxicillin with clavulanic acid in 173(12.6%), followed by piperacillin with tazobactam in 58(4.21%)

Fixed drug combination	ATC code	No FDCs out of a total number of AMAs prescriptions (%)
Amoxicillin + clavulanic acid	J01CR02	173 (12.6%)
Piperacillin + tazobactum	J01CR05	58 (4.2%)
Cefoperazone + sulbactam	J01DD62	9 (1.4%)

Discussion

The intensive Care Unit (ICU) is a specialized hospital ward where patients' critical illnesses and life-threatening conditions are being monitored and treated. Numbers of drugs are prescribed to the patients admitted to ICU. Antimicrobial agents are prescribed to almost all patients admitted to ICU. There is a lack of data about the utilization pattern of antimicrobial agents at our set-up. Hence the present study was carried out to use antimicrobial agents in ICU.

Our study's demographic results revealed that the patient's mean age was 46.2±18.4 years, similar to a study in Punjab in 2011 with an average age of 49 years [5]. In another study by Lisha et al. 2011 which mean age was 49.2±15.8 years [6]. Similar reports from Malaysia and Nepal reported

mean age of the patient was 50.8 ± 21.8 years and 49 years, respectively [7]. The reason why in the age group of 45-59 years is that life-threatening diseases like cardiovascular diseases, respiratory infection, diabetes, cancer and traumatic injury are common and may require ICU admission [8].

The most common age group admitted in our study was 31-45 years 153(24.6%) In a study conducted by Naqvi et al. 2016 also shows the most common group was 15-30years with the highest rate of admission, 31.8%, while in a study by Pandiamunian et al. 2014 most common age group was 51-60 years which was 23% [9, 10].

In our study male to female ratio was 1.69:1, males were about 391(62.3%), and females were 231(37.1%), which is similar to males 70(63.6%) and females 40(36.4%) in the study carried out by Naqvi et al. 2016[9].

The majority of the patients admitted to ICU were due to post-operative complications 149(23.9%), accidental trauma 86(13.8%), Organophosphorus poisoning 61(9.8%) and pneumonia 26(4.2%). Patients with post-operative, traumatic injury or poisoning require basic life supports like mechanical ventilation and continuous vitals monitoring. Reason: Most patients are admitted post-operatively due to continuous monitoring of vital functions during post anaesthetic recovery and pain management [11]. While the other was having most common indication for admission was sepsis [9]. In another study in UAE, having sepsis was the most common condition for admission [6].

We observed 245(39.4%) patients expired, and 339(54.5%) patients were shifted to the ward. While in another study in Punjab by William et al. 2016 showed the result that 121(60.50%) were discharged and 79(39.50%) expired [5], and in another study in UAE, 204(28%) expired, 526(70.6%) improved [6].

In our study mean duration of stay in ICU was 4.23±3.5 days, and this may be due to more number of patients on a life support system which may prolong stay in ICU [12]; In the study by William et al. (2016) which was having an average duration of stay of 5.75 days and in another study at Mohali average duration of stay was 6.6 days [13].

It was observed that the average number of antimicrobial drugs prescribed per patient was 2.31±1.40 in ICU, similar to the study carried out by Gangwar et al. and Mahajan et al., where the average no. of the prescribed antimicrobial drug was 2.09 and 3.36 respectively[14,15]. In the ICU, polypharmacy was observed due to critical and morbid conditions [16].

At present study set up, antimicrobial agents are available according to Gujarat state Essential Medicine List, and the majority of antimicrobial agents were prescribed according to this state's Essential Medicine List. Out of 27 drugs, 23 (85.2%) drugs were prescribed according to the essential medicine list of WHO, 2017, while 22(81.5%) drugs were prescribed according to the National Essential Medicine List (EML) of India (2016) WHO reported that average 60% drugs prescribed from EML on a survey of 35 countries in the world which was lower compared to our study (WHO 2004). It indicates that prescribing pattern of AMAs in ICU is much more rational.

In ICU, 214(34.4%) patients received more than two antimicrobial agents. A Study by Vandana et al. showed that 216(45%) of patients received more than two antimicrobial agents (AMAs) [17]. A study from the German ICU reported that 7.2% were prescribed more than two antimicrobial agents [18]. Prescribing more than two antimicrobial agents may be due to the majority of the patients were admitted post operatively and thus the longer duration of stay in ICU for monitoring of vitals and complications.

In our study, 98.05% of antimicrobial agents were prescribed via the parenteral route in ICU, which was much higher than other administration routes. Similar findings were reported in a study by Bansal et al. 2014, was having 67% of drugs via the parenteral route [13], and a study carried out at a hospital in Israel suggested 64% of antimicrobials were prescribed parenterally [19]. Critical condition and operative patients are required for parenteral/IV treatment for immediate action to maintain vital function [17].

It was observed that above 921(63.8%) antimicrobial agents were prescribed generically in ICU. Antimicrobial agents were prescribed generically higher as compared to brand name prescriptions. In our study, 521(36.1%) antimicrobial agents were prescribed by brand name. In contrast to our study, a study conducted in Bangalore showed that 70% of antimicrobial agents were prescribed by brand name [20]. In another study by Lisha et al., prescription of 70% was with brand name [6]. The prescription by generic names decreases the unnecessary economic burden on patients from lower socioeconomic statuses.

In our study, all patients were started with Empirical antimicrobial therapy, similar to the study conducted by Williams et al., who reported that 95% of patients were empirically prescribed antimicrobial agents [5].

The most common group prescribed was Cephalosporins 379(27.54%) in our study, followed by Anti-amoebic 308(22.38%) and Penicillin group 242(17.58%), which was contrary to the study by Bansal et al. 2016 which shows maximum usage of cephalosporins 409(27%) followed penicillin group 15.3% and antiamoebic group12.6% [13]. The most common antimicrobial drug prescribed was metronidazole 308(22.38%), followed by ceftriaxone 283(20.56%) and Amoxicillin+Clavulanic acid 172(12.57%). At the same time, another study at Mohali also shows the AMA with maximum consumption was metronidazole (14.3%), followed by ceftriaxone (12.6%) and Artisunate (10.8%) [13]. As in ICU, most patients admitted after operative procedures and post-operative patients had a risk of developing gram-negative and anaerobic infection [21,22].

In our study, the most common FDC was Amoxicillin+Clavulanic acid in 173(12.6%) prescriptions. While in an investigation, the most common FDC was cefoperazone + sulbactam in 30.8% of prescriptions [6].

Our study's average cost per patient for antimicrobial drug usage is Rs. 2091.54. Another study from Uttarakhand revealed average cost per patient for the antimicrobial drug is Rs. 1995[5], While the same Rs 1995.05 per patient for antimicrobial drug usage is seen in the study by Williams et al. 2016 [14].

Antimicrobials are widely prescribed empirically and in the post-operative period to the patients admitted to ICU. Hence we recommended the following suggestions to improve rational prescribing of antimicrobial agents and to reduce the risk of development of resistance to antimicrobial agents: 1) Education of prescriber by encouraging attending seminars, medical workshops, conferences, Continuous Medical Education (CME) 2) Availability of drug formularies, EML and antimicrobial policy in every unit, ward including ICU, operation theatre and to every prescriber. 3) Strict monitoring of the implementation of antimicrobial policy. [23]

Conclusion

The medical and surgical ICUs comprise the majority of the drug-resistant microbiome for which a wide variety of antimicrobial agents are utilized to treat these infections. The emergence of drug resistance has become a challenging problem nowadays. It has been essential to

improving the rational use of antimicrobial agents. The present study in medical and surgical ICUs can provide a framework for continuous prescription audits in ICUs at the regional and national levels. This will provide the database to predict future trends and cost-effective use of existing antimicrobial agents. This will help develop standard operating procedures (SOPs) for ICU clinicians to rationalize prescribing antimicrobial agents.

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