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## **Research Article**

# Drug utilization pattern in an intensive care unit setting in Eastern India

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#### ABSTRACT

**Background:** The intensive care unit (ICU) is a setting where a large number of drugs are administered to patients, most of them critically ill and suffering from multiple complications, making the costs of hospitalization and drug treatment high. There is a dearth of information on drug utilization in ICUs in Eastern India. The present study was undertaken to evaluate the drug utilization pattern in an ICU setting in Eastern India. The objective was to monitor, evaluate, and suggest modifications in the prescribing pattern of ICU drugs.

**Methods:** A retrospective analysis of the case records of patients admitted to the ICU of a multispecialty hospital in Eastern India during the time period from January 2015 to June 2015 was carried out. The demographic profile of the patients, drug utilization pattern and defined daily dose (DDD)/100 bed-days of the commonly used drugs in the ICU were studied.

**Results:** A total of 275 patients were evaluated consisting 61% male patients. Most common causes for admission to the ICU were a cerebrovascular accident, chronic kidney disease, and road traffic accident. An average number of drugs per patient was 10.5. Commonly prescribed drug classes were the antimicrobial agents (AMAs) in 96% patients followed by gastrointestinal drugs. Ceftriaxone was the most commonly used AMA (41.5% patients), having a drug consumption of 35.1 DDD/100 bed-days during the study period.

**Conclusions:** An antibiotic use policy should be framed and followed to curb the excessive use of AMAs. Formation of a multidisciplinary team to oversee drug use will be helpful to make the drug utilization in the ICU rational.

**Keywords:** Drug utilization, Intensive care unit, Antimicrobial agents, Defined daily dose

#### **INTRODUCTION**

Drug utilization is defined as "the marketing, distribution, prescription, and use of drugs in a society with special emphasis on the resulting medical and social consequences."<sup>1</sup> It is an important tool to study the clinical use of drugs in populations and its impact on the health care system.<sup>2</sup> In developing countries, where limited funds are available for healthcare, it becomes necessary to prescribe drugs rationally so as to utilize the funds optimally. Irrational prescription of drugs leads to unproductive and risky treatment, posing a major risk to present day medical practice.<sup>3</sup>

The intensive care unit (ICU) is a setting where a large number of drugs are administered to patients, most of them critically ill and suffering from multiple complications, making the costs of hospitalization and drug treatment high. Antibiotics are the most frequently prescribed drugs among hospitalized patients especially in ICU settings.<sup>4</sup> Widespread use of antibiotics, crowding of patients, presence of invasive medical devices favor the emergence, and spread of resistant organisms, which substantially raises already rising health care costs and increases patient morbidity and mortality.<sup>5</sup> Keeping all these factors in mind, the study of prescribing pattern of drugs in an ICU should be undertaken to monitor, evaluate, and suggest modifications in practitioner's prescribing habits so as to make medical care rational and cost-effective.<sup>4</sup>

In order to compare drug utilization among different countries and institutions within a country, the utilization has to be expressed in internationally accepted units. The defined daily dose (DDD) concept was developed to overcome objections against traditional units of measurement of drug consumption. The DDD is defined as the assumed average maintenance dose per day for a drug used for its main indication in adults. The DDD provides a fixed unit of measurement independent of price and formulation.<sup>6</sup> For hospital inpatients, DDD/100 bed-days provide a rough estimate of drug consumption.

There is the dearth of information on drug utilization in ICUs in Eastern India. The present study was undertaken to study the demographic profile of the patients, drug utilization pattern and measure drug consumption in DDD/100 bed-days of the commonly used drugs in the ICU of a multispecialty hospital in Eastern India.

#### **METHODS**

A retrospective analysis of the case records of all patients admitted to the ICU of a multispecialty hospital in Eastern India with 18 beds during the time period from January 2015 to June 2015 was carried out. The demographic and clinical treatment data of 275 patients were collected in the following format:

- Age and sex of the patient
- Diagnosis of patients
- Drugs prescribed
- Average number of drugs per patient
- Number of drugs prescribed by parenteral route
- Number of patients receiving antimicrobial agents (AMAs)
- Use of AMAs for:
  - Ø Bacteriologically proven infection (BPI)
  - Ø Non-BPI (NBPI)
  - Ø Prophylaxis.
- Percentage of AMAs prescribed in order of preference
- Dose and route of AMAs
- Average number of AMAs per patient
- Number of AMAs received by the patients
- Percentage of patients who were prescribed intravenous fluids and inotropic agents
- Percentage of patients who underwent nebulization and were given blood products
- DDD/100 bed-days of most commonly prescribed drugs. Most commonly used drugs were classified according to the anatomical therapeutic chemical (ATC) classification system, and drug utilization was measured in DDD/100 bed-days.<sup>6</sup>

The DDD/100 bed-days was calculated using the following formula:

 $DDD / 100 \text{ bed-days} = \frac{\text{study period(mg)} \times 100}{DDD (mg) \times \text{ period of study} \times \text{bed strength} \times \text{average bed occupancy}}$ 

Our study was carried out for a time period of 180-day. There were 18 beds in the ICU, and the average occupancy index was 0.7.

#### Statistical analysis

After collection of data, it was doubled entered in Microsoft Excel sheet and verified. A clean datasheet was generated and copied into SPSS sheet (SPSS version 16.0). After this, the whole analysis was done in SPSS (version 16.0).

#### RESULTS

During the study period, total 275 patients were evaluated consisting 167 (61%) male patients and 108 (39%) female patients. The mean age of patients was 54.3 years. 173 (63%) patients were aged more than 40 years. The most common diagnosis which warranted admission to ICU was cerebrovascular accident (20.5%), followed by chronic kidney disease (17.3%), road traffic accidents with multiple injuries (13%), and multiorgan dysfunction syndrome (MODS) (10.8%) (Figure 1). MODS included cases of septicemia and suspected/diagnosed malarial patients. 76 (27.6%) patients admitted to the ICU were hypertensives and 44 (16%) were known diabetics.

A total of 2881 drugs were prescribed during the stay in the ICU. An average number of drugs prescribed per patient was 10.5. Parenteral drugs prescribed accounted for 63.3% of the total drugs. The most commonly prescribed drug classes were the AMAs followed by the gastrointestinal drugs, vitamins calcium and protein supplements, diuretics, and steroids (Table 1).



Figure 1: Common causes of admission to intensive care unit.

# Table 1: Prescription pattern of different drugs in<br/>the ICU during the study period.

Drugs prescription	Number	Percentage
	of drugs	of patients
Antimicrobial agents	625	
Gastrointestinal drugs	486	
Pantoprazole	133	48.4
Rabeprazole	86	31.3
S-omeprazole	76	27.6
Ranitidine	10	3.6
Ondansetron	124	45.1
Sucralfate	19	6.9
Lactulose	28	10.2
Ursodiol	10	3.6
Vitamins, calcium, and	286	
protein supplements		
Diuretics	209	
Furosemide	67	24.4
Furosemide+triamterene	56	17.5
Torsemide	48	20.4
Mannitol	38	13.8
Steroids	190	
Fluticasone	75	27.3
Methylprednisolone	48	17.5
Dexamethasone	47	17.1
Prednisolone	10	3.6
Deflazacort	10	3.6
Antihypertensive drugs	179	
Nifedipine	67	24.4
Clonidine	56	20.4
S-amlodipine	27	9.8
Ramipril	19	6.9
Nebidilol	10	3.6
Pressor agents and	174	
emergency drugs		
Adrenaline, noradrenaline	67	24.4
Dopamine	38	13.8
Mephenteramine	11	3.6
Isoprenaline	10	4.0
Atropine	38	13.8
Octreotide	10	3.6
Bronchodilators	142	
Theophylline combinations	75	27.7
Levosalbutamol	67	24.4
Analgesic antipyretic drugs	116	
Low dose aspirin	39	14.2
Paracetamol	38	13.8
Drotaverine	19	6.9
Pentazocine	10	3.6
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Table 1: (Continued...).

Drugs prescription	Number of drugs	Percentage of patients
Diclofenac	10	3.6
Antiepileptic drugs	93	
Fosphenytoin	57	20.7
Phenytoin	18	6.5
Carbamazepine	18	6.5
Antipsychotic- antidepressant drugs	81	
Haloperidol	10	3.6
Quetiapine	10	3.6
Escitalopram	61	22.2
Topical clotrimazole	65	23.6
Sedative-hypnotic drugs	48	
Lorazepam	29	10.5
Alprazolam	10	3.6
Midazolam	9	3.3
Cognition enhancer piracetam	48	17.5
Antihistamines	47	
Promethazine	28	10.2
Levocetirizine	19	6.9
Human insulin	44	16.0
Lipid lowering agents	29	10.5
Digoxin	19	6.9
Total drugs	2881	

ICU: Intensive care unit

About 97% patients were given intravenous fluids during the period in the ICU, 95 (34.5%) patients underwent nebulization while 38 (13.8%) patients were prescribed dopamine. Blood products were used in 26 patients.

AMAs were prescribed in 264 (96%) patients. Antimicrobials were used for BPI in about 26% patients, for NBPI in 43% patients and for prophylaxis in 31% patients (Figure 2).

Ceftriaxone was the most commonly used AMA by 41.5% patients, followed by cefoperazone + sulbactum combination (23.3%) patients and amikacin (22.5%) patients. Other AMAs used were cefpodoxime, artesunate, teicoplanin, metronidazole, piperacillin + tazobactum, ofloxacin + ornidazole, and linezolid, cefepime + tazobactum (Table 2).

About 94% patients were administered AMAs by the parenteral route. The average number of AMAs per patient was determined to be 2.27.

The number of AMAs received by the patients. 31.8% of the patients receiving AMAs were prescribed 1 AMA; another 31.8% received 2 AMAs, 6% patients received 3 AMAs, 29.3% were given 4 AMAs, and 1.1% patients given 5-6 AMAs (Figure 3).

Antimicrobial prescribed	Number of patients	Percentage of patients
Ceftriaxone	114	41.5
Cefoperazone+sulbactum	64	23.3
Amikacin	62	22.5
Cefpodoxime	48	17.5
Artesunate	38	13.8
Teicoplanin	30	10.9
Metronidazole	29	10.5
Piperacillin+tazobactum	29	10.5
Ofloxacin+ornidazole	28	10.2
Linezolid	22	8.0
Cefepime+tazobactum	20	7.3
Cefexime	18	6.5
Imipenem+cilastin	18	6.5
Levofloxacin	18	6.5
Meropenam	18	6.5
Amoxicillin+clavulanic acid	17	6.2
Cefuroxime	11	4.0
Feropenam	11	4.0
Azithromycin	10	3.6
Clarithromycin	10	3.6
Ofloxacin	10	3.6

 Table 2: Prescription pattern of AMA's in the ICU during the study period.

ICU: Intensive care unit, AMA's: Antimicrobial agents

Table 3: ATC code and DDD/100 bed-days of the commonly prescribed drugs in the ICU.

Drugs	ATC code	DDD/100 bed-days
Pantoprazole	A02BC02	48.9
Ceftriaxone	J01DD04	35.1
Rabeprazole	A02BC07	26.8
Furosemide	C03CA01	23.7
Fluticasone	R01AD08	22.1
Ondansetron	A04AA01	19.9
Theophylline	R03DA54	18.6
combinations		
Nifedipine	C08CA05	17.4
Cefoperazone	J01DD12	16.98
Amikacin	J01CA01	16.2

ICU: Intensive care unit, ATC: Anatomical therapeutic chemical, DDD: Defined daily dose

The ATC codes and DDD/100 bed-days of the most commonly prescribed drugs are shown in Table 3.

#### DISCUSSION

The ICU is an identified, resource-intensive component of the health care services.



Figure 2: Indications for antimicrobial use



Figure 3: Number of antimicrobial agents received by the patients.

The present study was done in 275 individuals admitted to the ICU of a multispecialty hospital over a period of 6-month. The number of male patients admitted (167) was higher than the number of admitted female patients (108), similar to a previous study which documented male predominance in an ICU in an Indian setting.<sup>7</sup> The mean age of the patients admitted during the study period was 54.3-year, similar to a study carried out in Nepal<sup>8</sup> and in Iran.<sup>9</sup> In the present study, 63% patients were aged above 40 years, which is in accordance with an ICU study conducted in Central India,4 where 66% patients were aged above 40 years. The most common illnesses, warranting ICU admission in the study were cerebrovascular accident followed by chronic kidney disease and road traffic accident which differed slightly from a study in Nepal where the most common causes were chronic obstructive pulmonary disease, cerebrovascular accident, and myocardial infarction.<sup>1</sup> In our study, the average number of drugs prescribed in ICU was 10.5, in another study, it was 12.1±76.10 The average number of drugs in our study was less than or comparable to that reported in other studies.<sup>11,12</sup> The average number of drugs should be kept as low as possible to minimize the risk of drug interactions, development of bacterial resistance, and hospital costs.13

In ICU, patients are always in critical condition, so they receive most of the drugs by the parenteral route to combat the life-threatening situation. In this study, the parenteral therapy accounted for 63.3% for the total drugs prescribed,

nearly similar to a study which documented 52.8% of the drugs administered by a parenteral route in the ICU.

AMAs were the most commonly prescribed drug class, these were prescribed in 96% patients which is very high as compared to an ICU study in Qatar, which reported use of antimicrobials in 74% of ICU patients.14 AMAs were indicated for BPI in 26% patients, for NBPI in 43% and for prophylaxis in 31% of the individuals who were prescribed AMAs. In a previous study, antibiotics were used for BPI and NBPI in 32.2% and 60.5% of the patients and for prophylaxis in 7.3% patients.<sup>1</sup> This indicates that the use of AMAs for the prophylaxis is very high in our study. Antibiotic utilization varies between ICUs and with time in a given ICU, this study was conducted over a 6-month period without taking into account the seasonal variations in drug utilization. The most common AMA prescribed was ceftriaxone 41.5%, this is in accordance with a similar study,14 whereas cefoperazone + sulbactum 23.3%, amikacin 22.5%, and cefpodoxime 17.5% were the other commonly prescribed AMAs. This is similar to an ICU study in Maharashtra which reported the use of cephalosporins and aminoglycosides in 65.33% and 27.5% of the individuals on AMA therapy,<sup>3</sup> but differed from another study in which the penicillins were the most common antimicrobial drug class prescribed.<sup>1</sup> Cephalosporins are commonly prescribed due to their relatively lower toxicity and broader-spectrum activity. About 94% of the AMAs were administered parenterally, and the average number of AMAs per patient was 2.27. About 31.8% patients received one AMA; another 31.8% received two AMAs, 6% were administered three AMAs, 29.3% were given four AMAs, and 5-6 AMAs were given to 1.1% patients. This is similar to a study where 77% of the ICU patients were given 1-3 AMAs, 23% were given 4-8 AMAs.<sup>4</sup> In our study, patients received more than one AMA on a number of occasions. As some of these patients were suffering from mixed infections, three or more AMAs to treat the Gram-positive, Gram-negative, and anaerobic infection were used. In many instances, patients received AMAs one after another when the first one was not effective after the culture sensitivity tests.

The DDD/100 bed-days of the antiulcer drugs, pantoprazole, and rabeprazole was 48.9 and 26.8 DDD/100 bed-days, respectively, which was higher than a study reporting 28.8 and 6.8 DDD/bed-days of ranitidine and omeprazole, respectively.<sup>1</sup> The antiulcer drugs are relatively safe drugs having minimum side effects. The utilization of ceftriaxone and cefoperazone was 35.1 and 16.9 DDD/100 bed-days which was higher than the use of third generation cephalosporins - 13.74 DDD/100 bed-days, which was comparable to 21.8 DDD/100 bed-days utilization in Nepal.<sup>1</sup>

In our study, almost all the parameters matched with the previous studies in various ICUs, except for the excessive use of the AMAs, which are prescribed in about 96% of the patients. ICUs are frequently associated with the emergence

and spread of bacterial resistance due to excessive use of broad-spectrum antibiotics and other multiple factors.<sup>15</sup> Bacterial resistance to antibiotics has emerged as an important factor influencing patient mortality and morbidity. So, measures should be taken to avoid the inappropriate use of antibiotics. Physicians must have a clear understanding of the therapeutic use of antibiotics; they must be aware of the prevalence of various pathogens and resistance patterns in their hospital and exercise good judgment in the selection of empirical antibiotic regimens. Management teams consisting infectious disease specialists, intensive care specialists, pharmacologists, pharmacists, and microbiologists may be helpful.

#### CONCLUSIONS

Our study had many limitations; we looked at the drug utilization pattern in the ICU over a 6-month study period, the study was retrospective and record based. We were unable to correlate the drug prescribing patterns with the severity of patient illness. However, it was seen that a variety of drugs from various drug classes were used for a wide spectrum of clinical diagnoses. This drug utilization study can provide a framework for continuous prescription audit in the ICU. The alarming increase in antimicrobial use and along with it, the increasing antibiotic resistance will lead to increasing morbidity, mortality, and treatment costs. An antibiotic use policy should be framed and followed to curb the excessive use of AMAs. It is the responsibility of the medical fraternity to contain the problem of drug resistance by judicious use of antimicrobials. Prescribing guidelines are required to reduce the prevalent poly-pharmacy and to make the drug utilization in the ICU rational as far as possible.

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