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Original Research Article

Drug utilization pattern in ICU in a tertiary health care institution

Karishma Adhikari*, Swopna Phukan

Department of Pharmacology, Gauhati Medical College and Hospital, Guwahati, Assam, India

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***Correspondence to:**
Dr. Karishma Adhikari,
Email: karismaadhikari@gmail.com

ABSTRACT

Background: The objective of the study was to evaluate the current prescription pattern of drug utilization so as to find out drug use indicators such as utilization of drugs per prescription that can reflect possibilities of drug interaction and patient compliance and to suggest measures for rational prescriptions in patients admitted in Intensive Care Unit for various medical and surgical indications.
Methods: It was a retrospective, observational hospital based study which was done for 1 year after obtaining permission from the Institutional Human Ethics Committee. The prescriptions of both genders and of any age groups suffering from any medical or surgical indication who were admitted in Intensive Care Unit were included. The parameters assessed were demographic profile of the patient, most common diagnosis, number of days of ICU stay, ICU outcome, number of drugs/prescription, most common group and route of drugs.
Results: Data collected from 560 prescriptions were analyzed using appropriate statistical method and 66% patients were male. Most common age group was 41-60(40%). Cerebrovascular accident (22.9%) was the most common diagnosis followed by septicaemia (20.7%). Average no. of days of ICU stay was 6.22 days/patient. ICU mortality rate was 58.6% which was the most common outcome. At an average 15.8 drugs were prescribed per patient. Antibiotics and proton pump inhibitors were the most commonly prescribed drugs in 100% prescriptions, ceftriaxone (37.1%) being the most common antibiotic. Most common route of drug administration was intravenous route (65%).
Conclusions: Prescribing guideline is required to reduce the prevalent poly-pharmacy and to promote appropriate use of antimicrobials based on the culture and sensitivity report.

Keywords: Drug utilization, Intensive care unit, Rational prescriptions

INTRODUCTION

Measurement of drug use in health facilities not only describes drug use patterns and the behaviour of prescribers but also helps in the identification of polypharmacy and the problems associated with it.[1] Along with that rational drug prescribing which is defined as the use of the least number of drugs to obtain the best possible effect in the shortest period and at a reasonable cost is also an important aspect to be taken into account.[2]

In the absence of a clear, comprehensive and rational drug policy, the production of pharmaceutical preparations in India is grossly distorted. Thus, Indian markets are flooded with over 70,000 formulations, compared to roughly 350 preparations listed on the WHO Essential Drugs List.[3] Irrational prescriptions of drugs is of common occurrence in clinical practice.[4] Important reasons being lack of knowledge about drugs, unethical drug promotions and irrational prescribing habits of clinicians. Irrational prescriptions of drugs can lead to unproductive and risky treatment and possess a major risk of present day medical practice.

Monitoring of prescriptions and drug utilization studies can identify the problems and provide feedback to

prescribers so as to create an awareness about irrational use of drugs.[5] So Drug Utilization Research which is defined by WHO in 1977 as "the marketing, distribution, prescription, and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences" is an essential part of pharmaco-epidemiology which can provide insights into both the aspects of drug use and rational drug prescribing like pattern of use, quality of use, determinants of use and outcomes of use.[6,7]

In order to compare drug utilization among different countries and even among health institutions within a country, the utilization has to be expressed in internationally accepted units. The Defined Daily Dose (DDD) is a statistical measure of drug consumption which was developed to overcome objections against traditional units of measurement of drug consumption.

It is defined by the World Health Organization (WHO) as the assumed average maintenance dose per day for a drug used for its main indication.[8,9]

Drug utilization figures should ideally be presented as DDD/100 bed-days which provide a rough estimate of drug consumption in hospital inpatients.[8,9] and was calculated in this study using the following equation: [10]

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

Intensive Care Unit (ICU) patients are a heterogeneous group, who often suffer from severe illness, multiple organs dysfunction and coexisting medical disorders. Since most of the patients in the ICUs are critically ill and often suffer from multiple complications, polypharmacy becomes unavoidable.[10] It will lead to increase in incidence of poor treatment response and adverse reactions. ICU services use higher economic resources due to frequent use of high priced drugs and antimicrobial agents. Due to availability of limited funds in developing countries, drugs should be prescribed rationally so that the available funds can be utilized optimally.[11]

Hence this study is to be undertaken to find out the drug utilization pattern and use this information to predict the various drug use indicators and suggest some measures for rational prescriptions in patients admitted in Intensive Care Unit for various medical and surgical indications.

METHODS

The study was carried out in the Intensive Care Unit (General ICU) of Gauhati Medical College and Hospital, Guwahati for a period of 12 months (1st June 2015-31st May 2016) after getting the permission from the Institutional Human Ethics Committee vide letter no.MC/02/2015/208, dated 05-12-2015 and Head of the department, Intensive Care Unit, Gauhati Medical College and Hospital, Guwahati.

This was a retrospective, observational hospital-based study. We have not performed any activity on the patients but only data have been collected. The present study included patients of any age group and both the sexes (male/female) who were admitted in Intensive Care Unit (General ICU) for various medical and surgical conditions. Patient suffering from any medical or surgical indication who were not admitted in Intensive Care Unit (General ICU) were excluded from the study.

A total of 560 prescriptions were collected, analysed and classified during the study period. The prescriptions were collected daily, right from the day of admission till the time of discharge of the patient and following parameters were observed. Confidentiality of the data obtained from the patient case sheets was maintained throughout the study. The data obtained from the analysis of 560 prescriptions was further condensed was subjected to statistical analysis. The overall information generated was presented in the result section.

RESULTS

In this study more than 66% patients were male in this ICU which was higher than study by Biswal et al.[12] The probable reasons may be the sociological factors in this part of the country. In the Indian scenario it is noticed that female populations are reluctant to utilize health care faculties even if they are critically ill (Figure 1).

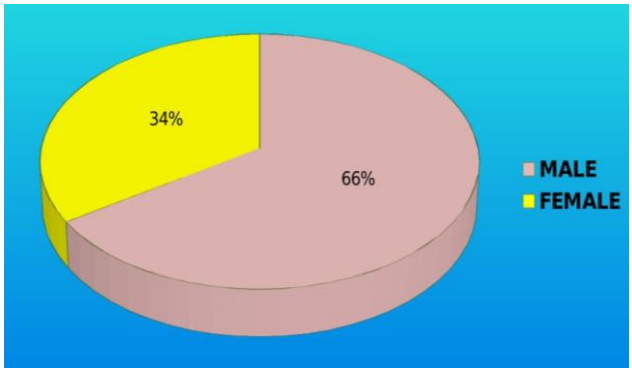

Figure 1: Gender wise distribution of the patients (n=560).

Majority of the patients (40%) in both male and female gender belongs to the age group 41-60 years in this study which was lower to study by Prakash et al, where more than 60% patients were in the same group (Table 1).[13]

Majority of the patients admitted in ICU were suffered from cerebrovascular accident (22.9%) in this study which was marginally followed by septicemia (20.07%) due to various causes which was in contrast to previous studies of Shankar et al, and Poudel et al, which had reported cancer, cardiovascular emergencies and chronic obstructive pulmonary disease as the major cause of admission (Table 2).[6,14,17]

Table 1: Age distribution of the patients (n=560).

Age group (In years)	No. of patients (gender wise distribution)		Total no. of patients	Percentage of patients (%)
	Male	Female		
<20	0	12	12	2.1
21-40	116	36	152	27.1
41-60	144	80	**224**	**40.0**
61-80	104	52	156	27.9
>80	4	12	16	2.9

Table 2: Most common diagnosis in general ICU (n=560).

Indication in general ICU	% Of patients
CVA	22.90%
Septicemia	20.70%
Surgical	7.90%
Head injury	7.10%
Carcinoma	6.40%
Gynaecological	5%
Lung infection	4.30%
Copd/cardiogenic shock	12.10%
Brain infection	3.60%
Others	10.00%

It has also been observed in this study that while CVA, septicemia, head injuries were more common in males; Carcinoma, cardiogenic shock was more common in females. In contrast to our study, one study done in Bhopal found that in all disease condition male patients' outnumbered female patients.[15]

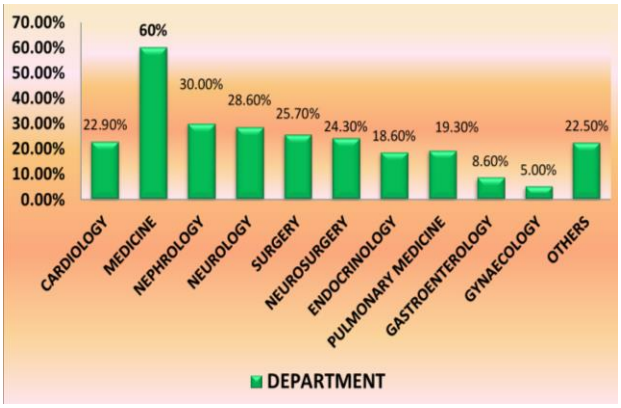

Figure 2: Distribution of the patients in different specialities.

Total 53.5% patients were having more than one illness in this study, which was slightly less than another published report of Patel et al, who reported it as 57.18 and Shankar et al, (Table 3).[16,17] Involvement of multiple system leading to complications can be a major reason behind intervention by multiple departments and hence prescription of different medications, thus leading to untoward actions of polypharmacy. Maximum no. of cases was intervened by medicine department in this study accounting around 60% patients followed by nephrology, neurology, cardiology and almost every department (Figure 2). Hence determination of department wise distribution of the patients is essential to have rough view over the prescription pattern.

Table 3: System wise distribution of the patients (n=560).

System wise involvement	Total no. of patients	Percentage of patients
1 System	260	46.5%
2 Systems	144	25.7%
3 Systems	88	15.7%
> 4 Systems	68	12.1%

There is a need for optimizing an efficient distribution and use of ICU resources. For that purpose, there are many measures to assess ICU resource utilization like ICU LOS and the duration of mechanical ventilation, as this is one of the most common procedures in the ICU. Prolonged ICU stay can adversely affect the health status by increasing the risk of infection, complications, and possibly, mortality. It was found in this study that average length of ICU stay was 6.22±5.09 days which was more than Shankar et al, but less than Prakash et al.[13,17] In a study from the United States, the mean LOS of the patients was 5.2±9.8 days. Our mean LOS was more than that reported in the American study but since the illness pattern, treatment protocols and economic conditions may be different, comparison can be difficult. Around 49.3% patients were on mechanical ventilation with an average no. of days as 3.17±2.76 days. Hence a large proportion of patients in ICU were on ventilator support and this may be one of the reasons for higher average length of stay in this study (Table 4).

Table 4: Parameters regarding ICU stay in general ICU.

Parameters	Results (n=560)
Average no. of days on mechanical ventilation	3.17±2.76 days**
Average length of stay (LOS)	6.22±5.09days**
ICU mortality rate (%)	58.6% (328)

Table 5: Outcome of patients in general ICU (n=560).

Outcome of the patients	Patients IN general ICU
Died	58.60%
Discharge against medical advice	21.40%
Leave against medical advice	9.30%
Improved	7.10%
Discharge on request	2.90%
Referred to higher centre	0.70%

The overall reported ICU mortality in this study was 58.6% which was higher than previously published reports of 33% in Smythe et al, and 15.1% in Shankar et al. (Table 5).[17,18] This is due to the fact that most of the patient died of septicemia which is again because of antimicrobial resistance leading to antimicrobial failure (Figure 3).

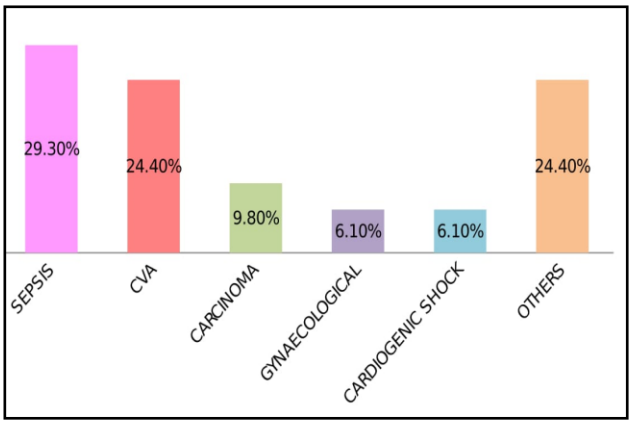

Figure 3: Common indication for ICU mortality.

The average number of drugs per prescription is an important index of a prescription audit. 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 costs.[17] Poly pharmacy is defined as concomitant use of five or more drugs and it could enhance drug interaction. In this study, 560 patients were enrolled who received 8848 drugs and 1748 antibiotics during their stay in the ICU. The average number of drugs prescribed per patient was 15.8±5.6, antibiotics constituted 19.80% of the total drug prescribed. However, the average number of drugs prescribed per patient was higher than Shankar et al.[6,17] and Smythe et al.[18] This can be due to multiple co-morbid condition leading to higher length of stay in ICU and consequently multiple medications (Table 6).

Table 6: Basic data regarding drug usage in ICU.

Basic data	General ICU
Total no. of drugs	8848
Total no. of patients taking the drugs in ICU	560
Average no. of drugs per prescription	15.8±5.6 drugs/prescription
Total no. of category of drugs	205
Total no. of antibiotics	1748
No. of drugs with generic name	4032
No. of drugs with brand name	4816
No. of Fixed Dose Combination	1384
Maximum no. of drugs in a single prescription	35
Minimum no. of drugs in a single prescription	06

In spite of various benefits like low cost of drug therapy, increased patient adherence and equivalent therapeutic benefits as brand name alternatives, generic prescribing is not a common practice in India.[19-21] In this study, around 54.4% drugs were prescribed by brand names, mainly includes pantoprazole, metronidazole, salbutamol-ipratropium and furosemide which is higher than Patel et al, around 15.6% drugs were prescribed as FDC and 62.6% of drugs prescribed were from the National List of Essential Medicines (Table 7).[16,19,20,22]

Table 7: Fixed dose combinations in ICU.

Fixed dose combinations	No. prescribed (n=1384)
Salbutamol+Ipratropium	328
Multivitamin (oral and with IVF)	308
Piperacillin-Tazobactum	200
Imipenum-Cilastin	76
Ceftriaxone-salbactum	60
Pentazocin-promethazine	36
Atorvastatin-aspirin	36
Others	340

Drug use indicators are important parameters given by WHO to determine the extent of rationality followed while prescribing medications (Table 8).

Table 8: Drug use indicators (prescribing indicators) by WHO.

Prescribing indicators	General ICU
Average no. of drugs per prescription	15.8±5.6 drugs
Percentage of prescriptions with an antibiotic prescribed	100%
Percentage of drugs prescribed by generic name	45.6%
Percentage of prescriptions with an injection prescribed	98.6%
Percentage of drugs prescribed from essential drug list	62.6%

Approximately 65% of drugs were prescribed as an injectable in 98.6% of prescriptions, mostly antibiotics, pantoprazole, inotropes, mannitol infusion, furosemide etc. However, use of parenteral drugs (65%) is higher than Shankar et al, (52.8%) but lower than Patel et al, (86.57%).[6,16,17] The high percentage of injectables was quite explainable since this was an inpatient study with patients mostly having acute and serious illnesses. Injectable drugs are associated with problems of administration and medication errors (Table 9).[23]

Antimicrobial drugs (19.8%), antipeptic ulcer drugs (6%) and inotropes (5.2%) were the commonly utilized groups similar to John et al.[24] However, cardiovascular drugs were the commonly used therapeutic class in Biswal et al, and Smythe et al (Table 10).[12,18]

Table 9: Formulations of drugs used in ICU.

Formulation of drugs	% Of drugs in ICU (n=8848 drugs)
Oral	2080 (23.5%)
Sublingual	28 (0.32%)
Intravenous	5752 (65%)
Subcutaneous	136 (1.5%)
Intramuscular	144 (1.6%)
Rectal	88 (0.9%)
Topical	104 (1.2%)
Inhalational	516 (5.8%)

Table 10: Most common category of drugs prescribed in ICU.

Category of drugs prescribed in ICU	% Of category of drugs prescribed in ICU (n=8848 drugs)
Antimicrobials	19.80%
Antiulcer drugs	6%
Laxative	3.30%
Antiepileptic drugs	3.60%
Analgesics	3.20%
Inotropes	5.20%
Antihypertensive	2.70%
Bronchodilator	5.30%
Diuretics	5.60%
Vitamin minerals	4.60%
Hormones	2%
Others (Antiemetics, steroids, probiotics, glycosides, hypnotics, anticoagulants etc)	38.7%

Ceftriaxone (37.1%) and metronidazole (36.4%) were the most commonly prescribed antimicrobials similar to John et al, but different from Shankar et al, where penicillin and quinolones were frequently used.[17,24] The selection of initial appropriate antibiotic combination regimen is important for reducing the high mortality due to septicemia (Table 11).[25]

Aggressive use of antipeptic ulcer drugs was to prevent stress induced ulcer. Atropine was used in patients for bradycardia in late stages of septic shock. Adrenaline was mainly used for cardiac resuscitation. Dopamine, dobutamine and noradrenaline were used in combination with intravenous fluids for the patients of septic and cardiogenic shock. Inotropes are mainly effective in early stages of shock.[26] The selection of individual inotropes is mainly empirical.

It was observed in this study that DDD/100 bed days was found to be highest for pantoprazole as it was the commonest individual drug found in this study. Among antibiotics metronidazole (34.9%) have the highest DDD/100 bed days as it was the 2nd most common antibiotic but with most frequent daily dosing. Patel et al, reported that DDD/100 bed days of ceftrixone was 7.41 which was lower compared to our study (Table 12).[16]

Table 11: Most common individual drug prescribed in ICU.

Common individual drugs	No. of patients (n=560)
Pantoprazole	504
Salbutamol+Ipratropium	328
Lactulose	288
Furosemide	280
Noradrenaline	240
Ceftriaxone	208
Mannitol	208
Metronidazole	204
Meropenem	200
Pipercilin-tazobactum	180
Atropine	164

Table 12: DDD/100 BED days of the most commonly used drugs.

Drugs	ATC code	Units prescribed	DDD (WHO)	DDD/ 100 BED days
Pantoprazole	A02BC02	3024	40mg	86.3
Furosemide	C03C A01	2800	40mg	79.9
Noradrenaline	C01CA03	2400	6mg	11.41
Atropine	A03BA01	164	1.5mg	3.12
Dopamine	C01CA04	100	0.5gm	1.14
Ceftriaxone	J01DD04	832	2gm	11.87
Linezolide	J01XX08	1872	2gm	13.36
Metronidazole	J01X D01	3060	1.5gm	34.9
Meropenem	J01DH02	1200	2gm	17.12

DISCUSSION

As we all know the intensive care unit (ICU) is a setting where multiple medications are prescribed to critically ill patients which will lead to increase in incidence of poor treatment response and adverse reactions.[10,11] Here comes the role of the pharmacologist in conducting different studies in different clinical set ups to find out the irrational drug prescription and to give the feedback to the clinicians so as to modify the prescribing pattern and adopt rational means of prescription. Hence studies conducted in different countries have acknowledged irrational drug use in the Intensive Care Units and recommended interventions to improve the drug use pattern. As most of the patients visit this centre, results from this area may reflect the prescribing pattern of whole state.

Certain limitations of our study where authors looked at drug use patterns over a 12-month period only. The study was retrospective and data on the scales used to grade the severity of illness of admitted patients like APACHE were not available in the case record. So authors were unable to

correlate the drug prescribing patterns with the severity of patient illness.

Certain good prescribing practices have been observed in this study. For example, only 15.6% drugs were used as FDCs which decreases the chances of use of irrational FDC. Prescription of single drug formulations instead of FDCs may make better prescribing sense in terms of cost and safety. Generic prescribing and use of essential medicines are important parameters to evaluate the rational use of medicines (RUM). It was observed in this study around 45.6% drugs were prescribed by their generic names which mainly includes antibiotics, mannitol, lactulose and inotropes. Our study fares similar or better than other studies, in this regard. This is attributed to the fact that most drugs supplied by hospital pharmacy are generic products, which are likely to be chosen by prescribers. This practice suggests there were fewer gaps in communication between the hospital pharmacists and the prescribers regarding the list of available drugs. Essential drugs offer a cost-effective solution to many health problems in a developing country. Knowledge, availability and access to drugs in the NLEM promote rational therapeutics. Almost 5522 drugs (62.6%) were prescribed from NLEM which mainly includes antibiotics like levofloxacin, vancomycin, ceftriaxone; insulin, furosemide, mannitol, steroids like dexamethasone, inotropes like adrenaline etc.[16,19,20,22]

But except few good prescribing habits there were lots of loopholes and irrational practices in this study. Length of stay of ICU was 6.22±5.09 days which was quite higher than other studies which increases the complications and cost burden for the patients.[13,17] Also, the ICU mortality was around 58.6% which indicate multiple complications prevailing in this set up.[17,18] Another major reason can be low reporting of antibiotic culture and sensitivity which results into antibiotic failure and hence septicemia turned out to be the major cause of ICU mortality which was quite high as compared to other studies. Around 15.8±5.6 drugs/prescription were prescribed which indicates high degree of polypharmacy exist in this set up resulting in therapeutic failure, drug-drug interaction, adverse drug reaction and increase cost burden for the patients.[6,17,18] Also these cost burden issue was quite obvious by the fact that around 30% patients didn't complete their treatment but were discharged/absconded against medical advice. Lastly low data available in case sheets regarding reporting of antibiotic culture and sensitivity not only leads to increase in antibiotic resistance but also push the patient towards the negative consequences of injudicious use of antibiotics such as increase antibiotic failure and mortality.

CONCLUSION

So, to conclude with keeping in considerations the aims and objectives of this study, on evaluation of prescription pattern to find out drug utilization, we found that antimicrobials were the most frequently prescribed group of drugs whereas pantoprazole was the most frequently prescribed individual drug. Among antimicrobials ceftriaxone followed by metronidazole were the most commonly prescribed drugs.

Regarding the utilization of drugs per prescription (drug use indicator) it was found that multiple antimicrobials were prescribed per prescription mainly as intravenous preparations along with many other groups of drugs and hence there was high rate of polypharmacy (>15 drugs) prevailing in all prescriptions to treat multiple complications

So various measures for rational prescription can be use of broad spectrum antimicrobials instead of multiple antimicrobials per prescription, use of antibiotic culture and sensitivity in every case, avoiding polypharmacy by implementation of local antibiotic management programs, infectious disease specialist consultation, restricted authorization to prescribe antibiotics and preparation of antibiotic use policy for better patient compliance by reducing cost burden, therapeutic failure, adverse drug reactions, drug-drug interactions.

Hence to promote rational prescribing it is essential to conduct drug utilization studies and to use the data as feedback for educating and training the physicians as well as undergraduate students adequately regarding the need for rational prescribing.

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