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Research Article

Evaluation of Drug Use in Intensive Care Unit of a Tertiary Care Teaching Hospital-A Prospective Observational Study

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Abstract

Context: Irrational drug use is a common problem worldwide and Intensive Care Unit (ICU) is one of the places where irrational drug use is very common. Because most of the patients in the ICUs are critically ill and often suffer from multiple complications, polypharmacy becomes unavoidable. Because of this in ICU the cost of hospitalization and treatment are high.

Purpose: The objectives of the present study were to evaluate the use of various drugs in the ICU and to assess the rationality of the drugs used in ICU.

Methods: All the new patients of age 18 years and above presenting to casualty and admitted to Intensive Care Unit (ICU) and willing to give consent were taken into the study. Demographic data, date of admission, chief complaints, provisional diagnosis, co-morbid illnesses and Adverse Drug Reactions (ADR), prescription given to the patient including the drug prescribed, dose, frequency, dosage form, route of drug administration and duration of the treatment was noted on the case record form. Rationality of each prescription was assessed using Phadke's criteria. Cost of the drugs was calculated using hospital drug list (hospital supplied) and patients' drug bills (for drugs prescribed from outside).

Results: Total 237 (118 Females, 119 Males) were enrolled with Mean ± SD of 49.51 ± 16.25 years. Total 1452 drugs were prescribed to the study population with 6.13 ± 1.54 mean number of drugs per patient. Out of 237 prescriptions, 104 were rational, 125 were semi-rational and 8 were irrational in nature. Average cost per patient was 8,803.93 INR and average cost per patient per day was 1,824.54 INR.

Conclusion: Both rational as well as irrational prescribing of drugs was found in our study. On comparing various parameters between two subgroups i.e. rational vs irrational prescription groups and found that there was a statistically significant difference in no. of Adverse Drug Reactions (ADR), no. of Anti-Microbial Agents (AMA) used and cost per patient.

Keywords: *Adverse Drug Reaction; Drug Utilization Study; Intensive Care Unit; Polypharmacy; Rational Drug Prescribing*

Introduction

Drug use evaluation, sometimes referred to as drug utilization review, is a system of continuous, systematic, criteria-based drug evaluation that ensures the appropriate use of drugs. It is a method of obtaining information to identify problems related to drug use and also provides a means of correcting the problem and contributes to rational drug therapy [1].

Intensive Care Unit (ICU) is highly specified and sophisticated area of a hospital which is specifically designed, staffed, located, furnished and equipped, dedicated to management of critically sick patient, injuries or complications [2]. Irrational drug use is a common problem worldwide and ICU is one of the places where irrational drug use is very common. Because most of the patients in the ICUs are critically ill and often suffer from multiple complications, polypharmacy becomes unavoidable [3]. Various studies have been done in India and have acknowledged the problem of irrational drug use and polypharmacy ICUs. Because of this in ICU the cost of hospitalization and treatment are high. Hence evaluation of drug use is important in ICU.

According to the comparison held by Weber., *et al*. 38% of the total drug costs are accounted for the ICU and these costs have increased at greater rate against non-ICU drug costs. Furthermore, the cost of hospitalization and drug treatment in the ICU are also high [4]. Since patients admitted to the ICU receive multiple drugs, the majority of these drugs are empirically prescribed and mainly based on physician previous experience resulting in the lack of quantitative precision of drugs usage. For example, some European reviews have indicated that over 50% of all neonatal ICU patients received off-label or an unlicensed prescription [5]. Several studies correlated multiple factors with mortality and duration of hospitalization in the ICU. Bobek., *et al*. showed that the number of medication classes was a significant independent factor associated with the length of stay in the ICU [6]. A study by Hartmann., *et al*. reported that antibiotic therapy correlates with hospital mortality in patients staying for more than 24 hrs in a surgical ICU [7].

Even with the presence of drug use guidelines and policies in the ICU, it might be difficult to apply them due to the patient-specific disease state and physician medication preferences. To improve therapeutic practices in such a case, it was found that the application of simple techniques of drug utilization was useful and inexpensive. Therefore, utilization trends and costs of drugs prescribed in the ICU need to be urgently addressed.

Rational (appropriate) prescribing is that which bases the choice of a drug on its effectiveness, safety and convenience relative to other drugs in a particular patient and takes cost into account only when the above criteria for choice have been satisfied [8]. Evidence indicates that high prevalence of inappropriate prescribing of medicines in elderly people is associated with increased morbidity and mortality, increased cost of treatment and decreased quality of life. Inappropriate prescribing has therefore become a significant public health issue worldwide. Hence effective optimization strategies are needed to improve prescribing of medicines in older patients. There are no definite standardized criteria for assessing rationality of doctors' prescription. Different investigators have analyzed prescriptions with their own different indicators. In our study, we have used Phadke's criteria for assessing the rationality of the prescriptions [9].

Most of the studies done in the past were retrospective in nature but ours was a prospective one. Studying drug prescribing pattern in the ICU is critically important in guiding prescription practices, and therefore, will help in ensuring an optimal outcome and containing costs. Keeping this background in mind we conducted this study which is first of its kind at our setup.

Objective of the Study

The objectives of the present study were to evaluate the use of various drugs in the ICU and to assess the rationality of the drugs used in ICU using Phadke's criteria.

Materials and Methods

Study design

This prospective cross-sectional study was a collaboration of the Department of Pharmacology and the Emergency Medicine Department at Smt. N.H.L Municipal Medical College and V.S General Hospital, Ahmedabad, India and carried over for the period of 12 months from June 2017 to May 2018.

Inclusion criteria

1. All the new patients of age 18 years and above presenting to casualty and admitted to Intensive Care Unit (ICU).
2. Patients who are willing to give their consent.

Exclusion criteria

1. Moribund patients.

Ethical aspects

The protocol, Performa, Case Record Form and Inform consent form were reviewed by the Institutional Review Board (IRB). The study was started after written approval from IRB and written Inform Consent Form of participants in vernacular language. Confidentiality of all data was maintained.

Data collection

All the new patients of age 18 years and above presenting to casualty and admitted to Intensive Care Unit (ICU) were enrolled in the study after explaining the aim of the study and obtaining a written consent in vernacular language.

Demographic data like initials, age and sex were recorded on the case record form. After which the date of admission, chief complaints, provisional diagnosis, co-morbid illnesses and Adverse Drug Reactions (ADR) were noted. The prescription given to the patient including the drug prescribed, dose, frequency, dosage form, route of drug administration and duration of the treatment was noted on the case record form.

Rationality of each prescription was assessed using Phadke's criteria. Harrison's Principles of Internal Medicine, 19th edition and Goodman and Gilman's The Pharmacological Basis of Therapeutics, 12th edition were considered as standard reference textbooks for the same.

Cost of the drugs was calculated using hospital drug list (hospital supplied) and patients' drug bills (for drugs prescribed from outside).

Statistical analysis

Statistical analysis was carried out using Statistical Package for the Social Sciences (IBM® SPSS) Version 23 and Microsoft Excel 2016.

The data were analysed for:

- Demographic pattern
- Presenting symptoms
- Diagnoses
- Co-morbid conditions
- Prescription pattern
- Rationality
- Cost
- Mean and SD were used to describe numerical variables and frequency (%) was used for categorical variables
- Unpaired t test and Fischer's exact test were used
- P value < 0.05 was considered statistically significant.

Results

Demographic pattern

Total 237 (118 Females, 119 Males) were enrolled with Mean ± SD of 49.51 ± 16.25 years. Female: Male was 0.99. The most common age group was of 51 - 60 years.

Presenting symptoms

Following table shows the most common presenting symptoms in our study population (Table 1).

Presenting symptoms	N = 237
	Present no (%)
Altered sensorium	89 (38)
Breathlessness	84 (35)
Chest pain	68 (29)
Nausea/Vomiting	49 (21)
Giddiness	47 (20)
Fever	37 (16)
Abdominal pain	36 (15)

Table 1: *Presenting symptoms.*

Apart from these, out of 237 patients enrolled, 199 (84%) patients had no other presenting symptom other than mentioned above, 18 (8%) patients presented with muscular weakness, 10 (4%) patients presented with convulsions, 5 (2%) patients each presented with diarrhoea and road traffic accidents.

Diagnoses

Left ventricular failure was the most common diagnosis followed by others (Figure 1).

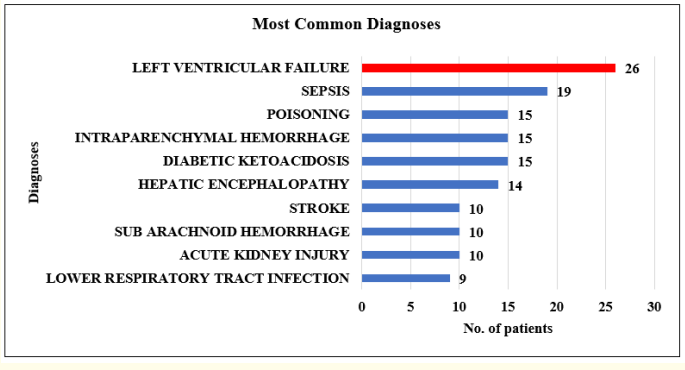

Figure 1: *Most common diagnoses.*

Co-morbid conditions

Out of 237 patients, Hypertension (111 patients) and Diabetes mellitus (48 patients) were the two most common co-morbid conditions present. Other co-morbid conditions are shown in figure 2.

Prescription pattern

Total 1452 drugs were prescribed to the study population with 6.13 ± 1.54 mean number of drugs per patient. Drugs were ranging from 4 to 11 drugs per patient with 6 drugs being most common (in 80 patients). Number of Fixed Dose Combinations (FDCs) prescribed was 44 (3%). Injection was the most common dosage form (1045, 72%) and intravenous was the most common route (996, 69%) of administration. Pantoprazole and Ondansetron (232 patients) were the most commonly prescribed drugs followed by others.

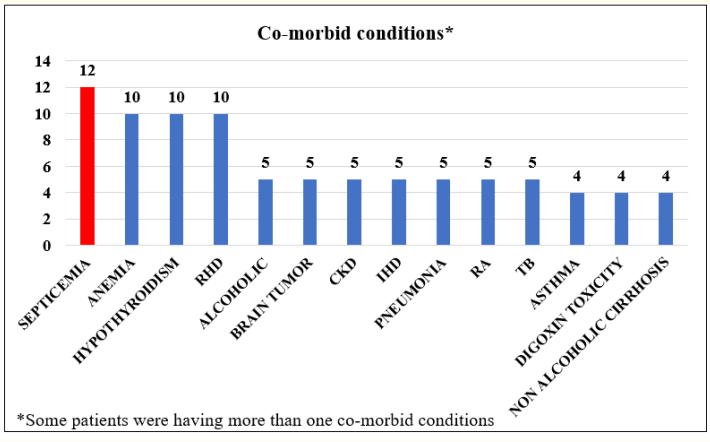

Figure 2: *Co-morbid conditions.*

Rationality of the prescription (Based on Phadke's criteria)

Out of 237 prescriptions, 104 were rational, 125 were semi-rational and 8 were irrational in nature. We have clubbed semi rational and irrational prescriptions into one and termed them collectively as irrational prescriptions for results and discussion purpose. So total 133(55%) were irrational and 104 (45%) were rational in nature.

Cost

We have considered 227 patients for cost analysis as five patients of Guillain-Barre Syndrome (GBS) and five patients of Septicaemia fell into outlier group as single drug cost was extremely expensive. The cost has been calculated in the Indian currency i.e. Indian National Rupees (INR). Total expenditure was 19,98,494.03 INR. Average cost per patient was 8,803.93 INR and average cost per patient per day was 1,824.54 INR. Following are the five costliest drugs prescribed in our study (Table 2).

Immunoglobulin	38000 INR
Octreotide	8246 INR
Tirofiban	5748 INR
Colistin	2439 INR
Teicoplanin	2100.99 INR

Table 2: *Five costliest drugs.*

Rational vs irrational prescriptions

We have done subgroup analysis of various parameters between rational and irrational prescriptions (Table 3).

Discussion

Drug utilization studies are used typically as pointer to the prescribing behaviour. Our study was done in the ICU at our setup. Apart from drug utilization we have focused on rationality of the prescription and cost analysis as well in our study. Rationality of the prescription was assessed using Phadke's criteria.

Parameter	Rational (N = 104)	Irrational (N = 133)	p-value
Age	51.47 ± 14.49	47.97 ± 17.43	0.1003[a]
Gender			
Male	51	68	0.7941[b]
Female	53	65	
Co-morbid conditions			
LVF	17	9	0.0220[b]
IPH	10	5	0.1042[b]
Diabetes	9	39	<0.0001[b]
DKA	0	15	0.0002[b]
Prescription details			
Stay	5.07 ± 1.20	4.64 ± 1.64	0.0257[a]
No. of drugs	6.15 ± 1.07	6.11 ± 1.83	0.8432[a]
Phadke's	25.96 ± 1.03	20.06 ± 3.43	0.0001[a]
No. of AMAs	127	197	0.0490[b]
No. of FDCs	24	20	0.5227[b]
Cost[#]			
Total	7,02,624.19 INR	12,95,869.84 INR	0.0003[b]
Per patient	7474.72 ± 943.70 INR	9743.38 ± 3126.90 INR	0.0001[a]
Per patient per day	1474.30 ± 186.13 INR	2063.71 ± 673.90 INR	0.0001[a]
ADR			
No of ADRs	19	45	0.0081[b]

Table 3: *Rational vs irrational prescriptions.*

**LVF=Left Ventricular Failure, IPH=Intra Parenchymal Haemorrhage, DKA=Diabetic Keto-Acidosis, AMA=Anti-Microbial Agent, FDC= Fixed Dose Combination, ADR=Adverse Drug Reaction.*

a=Unpaired t-test, b=Fischer's exact test (p value less than 0.05 was considered statistically significant). #N=94 was considered for rational prescriptions. Five patients of Guillain-Barre Syndrome (GBS) and five patients of Septicaemia fall into outlier group as single drug cost was extremely expensive.

In our study patients with the age group of 51 - 60 yrs. were almost 30% of the total study population. This finding was similar to the study done by Shelat., *et al*. and study by Aly NY., *et al*. at Kuwait. In our study almost equal percentage of male and female patients were reported which is similar to studies done by Shelat., *et al*. Biswal., *et al*. and Smythe., *et al*. in which also they reported similar results [10-13].

In our study maximum number of cases presented with altered sensorium (38%) followed by breathlessness (35%), Chest pain (29%) and others. Our study was unique in this parameter because none of the similar studies done in past had measured this parameter. This helps in understanding the prescription pattern and how it is affected by the presenting symptoms.

Left Ventricular failure (LVF) was the most common diagnosis (26, 11%) followed by others. This is similar with the findings of studies done by Patel MK., *et al*. and Paudel R., *et al*. which also had cardiovascular conditions as most common diagnosis.

Out of the total 237 patients enrolled 20% were having diabetes and 47% were having hypertension as a co morbid condition. This can be explained by breathlessness and chest pain being the most common presenting symptoms and cardiovascular disorders being the most common diagnosis.

A total of 1144 prescriptions for 237 patients were included. Total 1452 drug formulations were given to patients. So, there were 4.82 prescriptions per patient. This is in contrast to the study done by Al-Zakwani., *et al*. in which 1098 prescriptions were included for 138 patients. So per patient prescriptions were much higher at 7.95 than our study [14].

In our study 6.13 ± 1.54 drugs were prescribed per patient in the ICU which was in contrast to the studies done by Shelat., *et al*. in which average more than 11 drugs were prescribed and to the study done by Smythe., *et al*. where mean number of drugs were 12.6 ± 7.6. Polypharmacy was common in ICU due to critical and comorbid illness. In the ICU only 10% of the study population were prescribed more than 2 antimicrobial agents which was lesser compared to the study done by Shelat., *et al.* in which above 75% patients were prescribed more than 2 antimicrobials and to a study by Pandiamunian J., *et al*. in which 17% patients were given more than 2 antimicrobials. Prescribing more than two antimicrobials may be due to critical illness and longer duration of stay [15,16].

Drugs per patient ranged from 4 drugs to 11 drugs per patient. Highest number of patients (80, 33.75%) were prescribed 6 drugs. It is well known that elderly patients are suffering from multiple diseases and are prescribed a large number of drugs Polypharmacy increases the risk of drug-drug interactions. In our study total 44 (3.03%) fixed dose combinations (FDCs) were used which is much lower than the previous studies done. Study conducted in Rajasthan by Patidar K., *et al*. reported much higher proportion of Fixed Dose Combinations (FDCs) at around 19%.

Most commonly used dosage form was injection which is similar to the previous studies done in the ICU setup. It is required in emergency settings for the need of faster action, good bioavailability and predictable concentration of drugs. Most common route for administering the drug in our study was intravenous route followed by oral route. This finding is similar with the study done by Al-Zakwani., *et al*. Intravenous administration accounted for the majority of the parenteral drugs.

Pantoprazole and Ondansetron were the most commonly prescribed drugs in 232 (97.89%) patients followed by other drugs in our study which was similar to the previous study done by Barot., *et al*. In our study, these drugs were most commonly prescribed empirically. Patanwala., *et al*. suggested that based on the comparative safety and efficacy of ondansetron with similar agents, Ondansetron may be used as a first-line agent for relief of nausea or vomiting for most patient populations in the emergency department. The most frequently mentioned explanation for prescribing PPI without an indication was "GI prophylaxis". Majority of the patients were inappropriately prescribed ondansetron and pantoprazole without any approved indication, which was also reported by the earlier study. Ondansetron contributed to 20.64% and pantoprazole 12.61% of the total drug cost respectively. Reducing inappropriate prescribing of GI drugs in the patient minimizes potential for adverse events and fosters controllable cost expenditure [17]. In our study rationality of the prescription was assessed using Phadke's criteria. Majority of the previous studies have used WHO core prescribing indicators for rationality assessment. WHO core prescribing indicators are suitable only for outdoor patients and not for indoor patients hence we have not used it.

Average duration of stay was 4.82 days in our study which was lesser than the studies done by Shelat., *et al*. in which the duration was 9 days and Pandiamunian J., *et al*. in which the length of stay in ICU was 6 days. When we compared various parameters between the rational and irrational prescribing groups, there was a statistically significant difference in nos. of antimicrobial agents prescribed (127 in rational and 197 in irrational) ($p = 0.04$). As far as ADRs were concerned, 19 were reported in rational and 45 in irrational group ($p = 0.008$). In cost analysis, all the parameters i.e. total cost, cost per patient and cost per patient per day were different with high statistical significance ($p = 0.0003, 0.0001, 0.0001$) [18]. In our study average cost per patient was 8,803.93 INR, which was slightly higher as compared to the previous study done by Patel MK., *et al*. in which the average cost per patient was 3225.70 INR. This difference is mainly due to the longer duration of stay in our study and utilization of newer and advanced antimicrobial agents like Teicoplanin, Colistin and Meropenem. These antimicrobial agents are more effective as compared to the conventional agents and are being used in the patients resistant to the conventional antimicrobial agents. The downside is the cost of these antimicrobial agents which is significantly higher.

Conclusion

To conclude, both rational as well as irrational prescribing of drugs was found in our study as illustrated above; although most of the drug utilization was justified. Because most of the patients in the ICUs are critically ill and often suffer from multiple complications, poly-

pharmacy becomes unavoidable. This study also shows that irrational prescribing and polypharmacy is prevalent in ICU setup. The good thing about our study was - average drugs per prescription, number of FDCs used and average stay of the patients were well below than the similar studies done in the past. None of the previous studies done in the direction of "ICU drug utilization" has focused on the rationality part. Our study was unique because we have assessed rationality of the prescription and that also using proper tool i.e. Phadke's criteria which is devised specifically for this purpose. We also have compared various parameters between two subgroups i.e. rational vs irrational prescription groups and found that there was a statistically significant difference in no. of ADRs, no. of AMAs used and cost per patient.

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