

DRUG UTILIZATION STUDY IN TRAUMA INTENSIVE CARE UNIT

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ABSTRACT

Objective: Trauma is defined as major public health problem worldwide and associated with significant morbidity and mortality both in developed and developing countries and to study prescription pattern in TICU among head trauma patients.

Methods: The study was conducted in Trauma Intensive Care Unit of Department of Surgery in a Tertiary Care Hospital. This was a prospective, observational study done at a Tertiary Care Teaching Hospital. A total of 637 patients enrolled in the present study with fulfilling inclusion and exclusion criteria. Patient's data recorded in case report form and analyzed to study the prescription pattern.

Results: A total of 637 cases were enrolled in this study. Trauma was more common in 499 (78.34%) male followed by 138 (21.66%) female. The average duration of stay in TICU was 3.62 ± 1.38 days. In this study, mortality rate in study was 17.27%. In the current study, the total numbers of drugs prescribed per prescription in TICU are most commonly between 5 and 8 (55.26%) drugs followed by between 9 and 12 drugs were 37.83%. The present study states that the most common prescribed drugs used were ranitidine (100%) followed by ondansetron (89.64%). Among antimicrobials cephalosporins were most commonly used ceftriaxone (31.08%) and cefotaxime (27.63%).

Conclusions: The aim of study is monitoring and evaluation of the prescribers as well as recommends necessary modifications to achieve rational medical care. Study outcomes suggesting that admission to TICU is more in middle age group with mean age of 40.2 years. Average numbers of drugs prescribed were 8.76 drugs per patients which shows the trends of polypharmacy in the prescriptions.

Keywords: Trauma, TICU, Head injury, Antibiotic.

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INTRODUCTION

Drug utilization study consists of monitoring and evaluation of the drug prescribing patterns and suggests necessary modifications in prescribing practices, to achieve rational therapeutic practice as well as cost effective healthcare [1].

Trauma is defined as major public health problem worldwide and associated with significant morbidity and mortality both in developed and developing countries [2]. Major or severe trauma poses diagnostic and therapeutic challenges to trauma, orthopedic, and general surgeons practicing in developing countries [3].

Traumatic injury leads to sudden onset and severity of physical injury which require immediate medical/surgical attention. Traumatic injuries are the result of blunt, penetrating, and burn mechanisms [4,5].

The trauma intensive care unit (TICU) is a setting where most patients with serious diseases are admitted. Therefore, a large number of drugs are employed to save these patients and that make them susceptible to medication errors and adverse drug reactions [6].

Antimicrobials are the most commonly used drugs in trauma intensive care unit patients. As a consumption of antimicrobial rises, resistance to antimicrobial becomes major threat to public health. Other commonly used drugs include analgesics, antiepileptics, diuretics, H₂-antagonists, vasoactive drugs, inotropes, and antacids. The analgesic, sedative, and neuromuscular blockade medications used in the trauma intensive care unit not only are expensive; if used inappropriately, they can result in serious complications [7-9].

The present study aims to identify drug utilization and to analyze prevailing prescription trends in the trauma intensive care unit in a tertiary care teaching hospital.

METHODS

The study was conducted in Trauma Intensive Care Unit of Department of Surgery in a Tertiary Care Teaching Hospital. This was a prospective, observational study done at a Tertiary Care Teaching Hospital.

Patients admitted in trauma intensive care unit and fulfilling the inclusion/exclusion criteria and ready to give a written informed consent were included in this study. Data collected were of age, duration in TICU, final diagnosis, drugs prescribed and clinical outcome of patients from case papers. All patients admitted in Trauma ICU during January 2018 to June 2019 willing to participate in study were selected.

A total of 637 patients were included in the study. Enrolment details subjects fulfilling the inclusion/exclusion criteria and giving a written informed consent are enrolled in the study. On enrolment, a number is assigned to each and the following details are enquired and recorded in the case report form (CRF). All the details of the treatment taken by the patient were recorded.

The data obtained were then analyzed in Microsoft excel and GraphPad Prism version 7. Continuous data are expressed as mean \pm SD. Descriptive statistics such as frequencies and percentages were calculated for categorical variables. For continuous variables, means and standard deviations (\pm SD) were reported. Data so collected were tabulated and analyzed accordingly.

Objectives

The objective of the study was to study prescription pattern in Trauma Intensive Care Unit among head trauma patients.

Inclusion criteria

The following criteria were included in the study:

1. Patients admitted in trauma ICU Tertiary Care Teaching hospital:
 - a. Diagnosed as RTA with head injury, chest injury.
 - b. Diagnosed head injury because of self-fall.
 - c. Blunt trauma associated with head injury.
2. Patient or relatives are willing to give informed consent

Exclusion criteria

The following criteria were excluded from the study:

1. Patients admitted in trauma ICU with other causes.
2. Patient or relatives not willing to give informed consent.

The study was conducted after obtaining permission from the Institutional Ethics Committee (IEC). All the data collected as a part of this study were kept strictly confidential and used for the purpose of this study only.

Steps taken by us to maintain confidentiality were: (1) Identification of patients by the hospital number only, (2) case records to be accessed by the principal investigator only, and (3) patient details not to be divulged to any party.

Follow-up Schedule till the patient is discharged or transferred from TICU. Withdrawal/discontinuation Criteria: Those patients who did not wish to continue to participate in the study were withdrawn from the study. Those patients who were noncompliant were discontinued from the study.

OBSERVATIONS AND RESULTS

The study was carried out at Tertiary Care Teaching Hospital in Trauma Intensive Care unit. It was a prospective, observational study.

Total prescriptions of 637 patients were analyzed.

Detailed information about baseline demographic characteristics and treatment received by the patient was studied. Observations of the study are presented in the form of different tables and figures.

From TICU total 637 prescriptions were analyzed. The male and female distribution in these 637 patients was as follows. Out of 637 patients, 499 (78.34%) were male, while 138 (21.66%) were female (Table 1).

Patients were further categorized into different age groups ranging as follows: The mean age of the patients admitted in TICU was 40.20±10.84 years. The mean age of male patients was 38.99±9.56 years. The mean age of female patients was 44.57±13.74 years. Majority of the belonged to the age group between 31–40 years and 41–50 years of age (Table 2).

A total of 220 patients were of 31–40 years of age out of 198 were male, while 22 were female. 175 patients were from 41 to 50 years of age from which 161 were male, while 14 were female (Table 3).

The average duration of stay in TICU was Mean±SD 3.62 ± 1.38 days. Duration of stay in TICU 3-4 days in 352 number of patients i.e.55.26% followed by duration of stay in TICU 5-6 day in 153 number of patients i.e. 24.03% followed by duration of stay in TICU 1-2 days in 110 number of patients i.e.17.27% (Table 4 and Fig. 1).

In details of outcome of patients in TICU, 483 number of patients (75.82%) were transferred to ward, followed by 110 number of patients (17.27%) expired followed by 44 number of patients (6.91%) were given DAMA (Table 5).

A total of 637 patients from TICU received 5579 drugs, number of drugs prescribed per patient being 8.76±1.56 (mean±standard deviation). The most common drugs used were ranitidine (100%), antimicrobial agents (100%), and ondansetron (89.64%). Among antimicrobials cephalosporin was most commonly used, ceftriaxone (31.08%), cefotaxime (27.63%), and cefoperazone+sulbactam (6.91%). Other antimicrobials most commonly used were metronidazole

(44.90%), amoxicillin+potassium clavulanate (27.47%), and piperacillin+tazobactam (6.91%). Total 29 different types of drugs were prescribed for patients of head injury and chest trauma (Table 6).

The commonly prescribed fixed dose combinations were of multi-vitamin (44.90%) followed by amoxicillin+clavulanic acid (27.47%), followed by piperacillin+tazobactam(6.91%), followed by

Table 1: Gender distribution in TICU

Gender	Number of patients	Percentage
Male	499	78.34
Female	138	21.66
Total	637	100.0

Table 2: Age distribution in TICU

Age group	Number	Percentage
21–30	132	20.72
31–40	220	34.54
41–50	175	27.47
51–60	88	13.81
61–70	22	3.45
Total	637	100.0

Table 3: Age distribution with gender in TICU

Age in years	Gender		Total
	Male	Female	
21–30	88	44	132
31–40	198	22	220
41–50	161	14	175
51–60	44	44	88
61–70	8	14	22
Total	499	138	637
Mean±SD	38.99±9.56	44.57±13.74	±10.84

Table 4: Duration of stay in TICU

No. of Days	No. of Patients	Percentage
1-2	110	17.27
3-4	352	55.26
5-6	153	24.02
7-8	22	3.45
Total	637	100.00
Mean±SD	3.62±1.38	

Table 5: Outcome of patients in TICU

Outcome	Number of patients	Percentage
Transferred toward	483	75.82
Expired	110	17.27
DAMA	44	6.91
Total	637	100.00

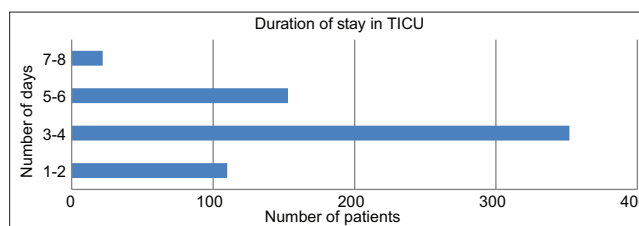


Fig. 1: Duration of stay in TICU

Table 6: Various drugs used in TICU

S. No.	Drugs	Number of prescriptions	Percentage	ATC code
1.	Ranitidine	637	100.00	A02BA02
2.	Ondansetron	571	89.64	A04AA01
3.	Phenytoin	549	86.19	N03AB02
4.	Diclofenac	439	68.92	D11AX18
5.	Multivitamin infusion	287	45.05	A11A
6.	Metronidazole	286	44.90	J01XD01
7.	Tramadol	286	44.90	N02AX02
8.	Mannitol	264	41.44	B05BC01
9.	Paracetamol	242	37.99	N02BE01
10.	Ceftriaxone	198	31.08	J01DD04
11.	Cefotaxime	176	27.63	J01DD01
12.	Vitamin K	176	27.63	B02BA
13.	Amoxicillin+potassium clavulanate	175	27.47	J01CR02
14.	Tranexamic acid	175	27.47	B02AA02
15.	Furosemide	154	24.18	C03CA01
16.	Vitamin B complex	154	24.18	A11EA
17.	Ethamsylate	153	24.02	B02BX01
18.	Doxofylline	88	13.81	R03DA11
19.	Hydrocortisone	88	13.81	C05AA01
20.	Levetiracetam	88	13.81	N03AX14
21.	Theophylline	88	13.81	R03DA04
22.	Serratiopeptidase	66	10.36	B06AA12
23.	Thiamine	65	10.20	A11DA01
24.	Cefoperazone+ sulbactam	44	6.91	J01DD62
25.	Piperacillin+ tazobactam	44	6.91	J01CR05
26.	Iron and folic acid	22	3.45	B03AD
27.	Phenobarbitone	22	3.45	N03AA02
28.	Potassium solution	22	3.45	B05XA01
29.	Risperidone	21	3.30	N05AX08

cefoperazone+sulbactam (6.91%), and followed by iron+folic acid (3.45%) (Table 7 and Fig. 2).

The total number of drugs prescribed per prescription in TICU was most commonly between 5 and 8 (55.26%) drugs, between 9 and 12 were 37.83% followed by between 13 and 16 were 6.91% (Table 8).

Average number of drugs prescribed per encounter in TICU was 8.76±1.56. Percentage of encounters with injection in TICU was 64.98%. Percentage of drugs from National list of essential medicine in TICU was 85.03%. Percentage of drugs from the WHO essential medicine list in TICU was 74.01% (Table 9).

DISCUSSION

Trauma is the leading cause of death worldwide for individuals younger than 65 years [10]. In India, the available trauma care services are restricted to major cities, thus resulting in an increased incidence of deaths from traffic accidents [11-13].

In the present study, out of 637 patients (Table 1), 499 (78.34%) were male, while 138 (21.66%) were female. As suggested by data from various sources, there is male dominance in road traffic accidents [14]. Pirie *et al.* studied Utilization profile of the trauma intensive care unit at the Role 3 Multinational Medical Unit at Kandahar Airfield between May 1 and October 15, 2009. In this study 95% of patients were male [15]. A study by Pang *et al.* in a 748-bed tertiary-care facility and regional level trauma center also gives similar results with 60% male population [16]. These findings are similar to our observations.

The mean age of the patients in present study (Table 2) was 40.20±10.84 years. S. Gopala Krishnan studied Public Health Perspective

Table 7: Commonly used fixed dose combinations in TICU

Fixed dose combinations	Number of prescriptions	Percentage
Multivitamin Infusion	286	44.90
Amoxicillin+potassiumclavulanate	175	27.47
Cefoperazone+sulbactam	44	6.91
Piperacillin+tazobactam	44	6.91
Iron and folic acid	22	3.45

Table 8: Total number of drugs per prescription in TICU

Total number of drugs	Number of prescriptions	Percentage
5-8	352	55.26
9-12	241	37.83
13-16	44	6.91
Total	637	100.00

Table 9: The WHO core indicators

S. No.	Core indicator	Percentage
1	Total number of drugs prescribed	100% (5579)
2	Average number of drugs per prescription	8.76% (5579/637)
3	Total encounters having injectable formulations	64.98% (3652/5579)
3	Drugs mentioned in NLEM 2015	85.03% (4744/5579)
4	Drugs mentioned in the WHO model list of essential medicines 2019	74.01% (4129/5579)

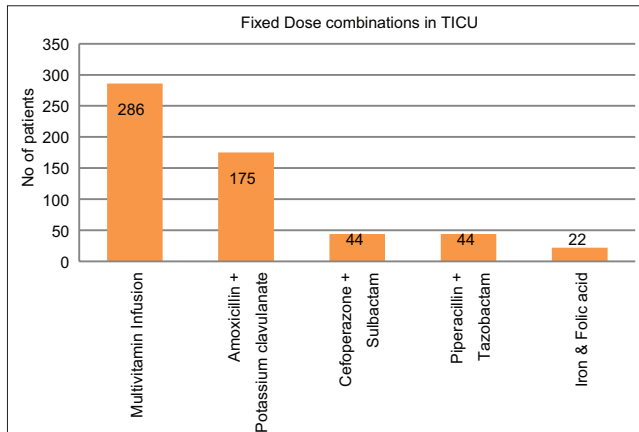


Fig. 2: Commonly used fixed dose combinations in TICU

of Road Traffic Accidents in developing countries. His findings suggest more than half of all RTA deaths among young adults between 15 and 44 years of age which is similar to finding of our study [14].

The average duration of stay in TICU (Table 4 and Fig. 1) was 3.62±1.38 days. A study by Böhmer *et al.* gives following key points regarding duration of stay of trauma patients in ICU [17].

- Treatment regimens, as well as secondary effects and complications of trauma and intensive care treatment, prolong ICU Length of Stay (LOS) more than the mechanism of trauma or pre-trauma patient conditions.
- The most prominent epidemiological parameter to prolong ICU stay was patient’s age.
- Secondary effects that influenced the prolongation of ICU LOS most were renal failure, Sepsis, and respiratory failure.

- Successful prevention of complicated courses of illness could significantly abbreviate the ICU stay in trauma patients.

Mortality rate in our study (Table 5) was 17.27% which is approximately similar to those reported in other studies by Brattström *et al.*, Sardinha *et al.*, Chalya *et al.*, and Ulvik *et al.* which typically vary between 10.4%, 19.0%, and 32.7%, respectively [3,18-20].

In the current study (Table 8), the total number of drugs prescribed per prescription in TICU are most commonly between 5 and 8 (55.26%) drugs, between 9 and 12 were 37.83%, and between 13 and 16 were 6.91%. Average number of drugs prescribed per patient from present study was 8.76±1.56. In a study by Boucher *et al.*, the mean total number of drug orders per patient was 9.1 during an average stay of 6.6 days. They are also established positive correlation between age and total drug use, probably because of the prevalence of concomitant disease in the elderly, although patients aged 80-89 years received the least drugs of any age group [21]. Results of Boucher *et al.* are similar to our observations.

However, prescribing by the present study states (Table 6) that the most common drugs used were ranitidine (100%) and ondansetron (89.64%). Ranitidine is mostly used for prophylaxis of stress related gastritis; while ondansetron is used for symptomatic treatment of nausea and vomiting which is common association in trauma patients. Use of ondansetron is not recommended except in chemotherapy/radiotherapy induced vomiting and post-operative nausea or vomiting. However researchers like Patanwala *et al.* suggested that based on the comparative safety and efficacy of ondansetron with droperidol, promethazine, prochlorperazine, metoclopramide, ondansetron may be used as a first line agent for relief of nausea or vomiting for most patient populations in the emergency department [22].

Stress-related mucosal disease (SRMD) is an acute, erosive gastritis representing conditions ranging from stress-related injury to stress ulcers [23,24]. Several studies based on surgical and medical ICU patients suggest that as the number of risk factors increases, the frequency of clinically important bleeding increases [25]. Specifically, two risk factors have been found to be independent predictors of clinically important bleeding—coagulopathy and mechanical ventilation [26]. Initiation of acid suppression therapy (AST) for stress ulcer prophylaxis (SUP) in the ICU setting is well established H₂ blockers work by inhibiting histamine-stimulated acid secretion by reversible, competitive inhibition of H₂ receptors of the parietal cells [23,27]. Among the available H₂ blockers, cimetidine is the least potent, ranitidine is in the middle, and famotidine is the most potent. Considering potency and cost ranitidine are a commonly prescribed drug for stress ulcer prophylaxis.

Antimicrobials were next commonly used drugs. Among antimicrobials cephalosporins were most commonly used, ceftriaxone (31.08%), cefotaxime (27.63%), and cefoperazone+sulbactam (6.91%). Other antimicrobials most commonly used were metronidazole (44.90%), amoxicillin+potassium clavulanate (27.47%), and piperacillin+tazobactam (6.91%) (Table 6).

In a study by Boucher *et al.* antimicrobials were the most commonly prescribed drugs to trauma patients [28]. Antimicrobials are usually commonly prescribed drugs in intensive care units for prevention and management of various complications such as ventilator associated pneumonia, catheter associated infections, secondary wound infections, and sepsis [29].

Among antimicrobials cephalosporins were most commonly used, ceftriaxone (31.08%), cefotaxime (27.63%), and cefoperazone+sulbactam (6.91%). Other antimicrobials most commonly used were metronidazole (44.90%), amoxicillin+potassium clavulanate (27.47%), and piperacillin+tazobactam (6.91%) (Tables 6 and 7, Fig. 2). Studies done by Mamatha *et al.*, Rajendra Gupta, Drupad *et al.*, and John

et al., showed that Cephalosporin's, Metronidazole, and Penicillin's were the most commonly prescribed antimicrobial in ICU similar to present study [30-33]. However, in the study done by Shankar *et al.*, Penicillin's were the most common antimicrobial drug class prescribed [34].

Among second-line antimicrobials (Table 7 and Fig. 2), penicillin derivative Piperacillin + Tazobactam combination was prescribed. Reason for choosing the above drug is that it is wide variety of antimicrobial activity and is active against the organisms which have shown resistance to cephalosporin's. The combinations of antimicrobials covered Gram positive, Gram negative, and aerobic and anaerobic organisms.

Reduction in raised intracranial pressure is mainstay of management of head injury cases. Osmotic agents (Mannitol) and diuretics (Furosemide) are often used for this purpose (Table 6). The proportion is more in Trauma ICU compared to Medicinal ICU as evident in a study by John *et al.* in MICU (23.69%) [33].

Older intravenous antiepileptic agents, such as phenytoin (86.19%) were preferred in this study. This finding was in concordance to an earlier study from India such as John *et al.* and Biswal *et al.* [32,35]. Phenytoin was used mainly for seizure prophylaxis and maintenance therapy. Newer antiepileptic agents can replace phenytoin, due to its saturation kinetics, drug interactions, and adverse effects. Newer agents, such as levetiracetam (13.81%), are also frequently used in this study. Phenobarbitone was used as a second line in 3.45% patients (Table 6).

Ethamsylate and Tranexamic acid were the drugs used for the management of acute bleeding in 24.02% and 27.47% patients, respectively. NSAIDs Diclofenac (68.92%) and Paracetamol (37.99%) and Opioid Analgesic Tramadol (44.90%) were the common analgesic drugs. Other drugs used were Thiamine, Vitamin B complex, Potassium solution, and Risperidone (Table 6).

CONCLUSIONS

The study of prescribing pattern is a component of medical audit that does monitoring and evaluation of the prescribers as well as recommends necessary modifications to achieve rational medical care. In this study prescribing pattern in Trauma Intensive Care unit in a tertiary care teaching hospital is studied.

Study outcomes from present study were suggesting that the risk of trauma and admission to TICU is more in middle age group with mean age of 40.2 years. The sex distribution clearly shows male predominance with 78.34% males in study population. Average numbers of drugs prescribed were 8.76 drugs per patients which show the trends of polypharmacy in the prescriptions. The prescribing pattern can be improved by reducing the number of drugs per prescription. All patients received antimicrobials (100%), ranitidine (100%), ondansetron (89.64%), and phenytoin (86.19%). Among antimicrobials β lactam antibiotics are commonly used.

- It was also observed that drug prescription by generic name is still low, which could be an economic burden on the patients and can be reduced by prescribing more generic drugs.
- Significant amount of drugs was prescribed from National List of Essential Medicines -2015 and WHO EML-2015, but this also could be increased by sensitizing physicians for the same.
- In conclusion, the present study provides valuable insight about the overall pattern of drugs used in Trauma ICU.
- Physicians should be motivated to use gastro protective agents rationally and rational use of antimicrobials to avoid polypharmacy.
- All required investigations and essential drugs should be made available 24x7 for the better drug utilization in government set up.
- The presence of a clinical pharmacologist in every trauma ICU setup will ensure rational use of all drugs in a cost effective manner. The antimicrobial stewardship program is a must for every hospital and it should seek to achieve optimal clinical outcomes related to antimicrobial use, minimize toxicity and other adverse events,

reduce the costs of healthcare for infections and limit the selection for antimicrobial resistant strains.

Limitations of the study

- This study was conducted at a single tertiary health-care center. Studies with data from multi-centric group of population in similar context would give additional information on this aspect.
- In our study, we have enrolled only head injury and chest injury patients.

Hence, this study results may not be generalized to other population in Trauma ICU.

- It was a quantitative type of drug prescribing pattern study with the WHO core prescribing indicators and therefore determining the quality of diagnosis and the appropriateness of treatment was beyond scope of prescribing indicators.
- In this study, the prescription data after the patients were transferred from Trauma ICU to other wards was not included.
- Defined daily dose was not calculated which would have given a more knowledge on drug utilization.
- The utilization of intravenous fluids and various drug interactions among the prescribed drugs was not accounted.
- Pharmacoeconomic calculation of expenditures was not done.

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CONFLICTS OF INTEREST

None declared.

ETHICAL APPROVAL

The study was approved by the Institutional Ethics Committee.

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