Research Article

A Prospective Drug Utilization Study and Pharmacoeconomic Analysis of Critically Ill Patients in Acute Medical Care Unit of a Tertiary Care Hospital

Juveria Samreen[1*], Anupama Koneru[1], K. Abedullah Khan[2], Atiba Sahar[1] and G. Satish Reddy[3]

[1] Department of Pharmacology, Sultan-ul-Uloom College of Pharmacy, Banjara Hills, Hyderabad - 500034, Telangana, India.

[2]Department of Pharmacy Practice, Sultan-ul-Uloom College of Pharmacy, Banjara Hills, Hyderabad - 500034, Telangana, India.

[3]Prime Hospital, Ameerpet, Hyderabad - 500016, Telngana, India.

ABSTRACT

Objective: Drug utilization in the in-patient setting can provide mechanisms to assess drug prescribing trends, efficiency and cost-effectiveness of hospital formularies and examine sub-populations, such as children, for which prescribing habits are different from adults. The aim of this study is to evaluate drug utilization in patients of acute medical care unit and perform a pharmacoeconomic analysis study. **Materials and Methods:** This prospective study was conducted for a period of six months from November 2014 to April 2015. A total of 166 patients were included in the study. Altogether, 3,372 drugs were prescribed, of 132 different types. The drugs were categorized on the basis of Anatomical Therapeutic Chemical classification (ATC) code. The average number of drugs per prescription, cost per prescription, cost per treatment and the prescribing pattern was assessed. The Defined Daily Dose (DDD)/100 bed-days was calculated to quantify drug consumption. Cost of each drug was taken from Current Index of Medical Specialties (CIMS) to determine the cost burden on the patients. **Results:** Pantoprazole was the most used drug (9.72%), followed by ondansetron (4.83%), ceftriaxone (3.94%), paracetamol (4.06%), atorvastatin (1.95%) and phenytoin (1.66%). Ceftriaxone was the commonly used antimicrobial in the study period. Reteplase was the costliest drug prescribed of all the drug types. The average number of drugs per prescription was **7.77 ±0.7**. The mean cost per prescription was **Rs. 1501±1010** and the mean cost per treatment was **Rs. 4056.4±3073.4**. The average duration of hospital stay for a patient was **4.7±3.8 days**. The total DDD/100 bed-days was found to be 4.6. **Conclusion:** Polypharmacy and irrational use of medicines were found to be the common problems.

Keywords: Drug utilization, pharmacoeconomics, polypharmacy, prospective study, morbidity.

INTRODUCTION

Acute medical care unit is a branch of healthcare, wherein the patient receives short-term treatment for an urgent medical condition and later transferred to higher dependency unit. However, the problems, practices, and issues of the acute medical care around the globe are indistinguishable[1].

A sound knowledge and skill is a primary requirement in prescription writing. Though the health care providers face difficulty in understanding, selecting, and initiating drug treatment for patients, it reflects their ability of clinical judgment. Irrational drug prescribing and use of drugs may result in unproductive treatment and prolongation of the hospital stay or increased costs or both. In developing countries like India, the funds for healthcare are limited[2]. Therefore, drugs should be prescribed rationally to make the best possible use of the limited funds available.

Moreover, due to the presence of multiple co-morbidities, requiring polypharmacy, the incidence of adverse drug reactions (ADRs) and potential drug interactions is very high. Therefore, continuous evaluation of utilization of drugs is necessary to ensure proper use of medications[3].

To examine the clinical and pharmacoeconomic effectiveness of drug therapy in patients, drug utilization studies can be used as a potential tool.

World Health Organization (WHO) defines drug utilization study as, the marketing, distribution, prescription and use of drugs in a society with special emphasis on the resulting medical, social and economic consequences[2].

The drug utilization pattern can be studied by determining the **Daily Defined Dose (DDD)** of a drug. The assumed average maintenance dose of a drug per day used for its main indication is called daily defined dose (DDD) [4, 5].

In the present study, we have evaluated the drug utilization pattern in terms of defined daily dose (DDD) of each drug and pharmacoeconomic analysis of medical in-patients of acute medical care unit is performed.

This study aims to-

1. Assess the prescribing trend of the physicians in Acute Medical Care Unit (AMCU).
2. Study drug utilization pattern in terms of daily defined dose (DDD).
3. Study cost effectiveness of the hospital formulary and its effect on the patients.

MATERIALS AND METHODS

This prospective study was conducted by establishing the inclusion and exclusion criteria, wherein prescriptions of subjects admitted in the AMCU were included and those with minor ailments, outpatient prescriptions and those under observation were excluded.

The demographic data and health status of the subject were also collected. The medications prescribed were then collected from the nursing head and entered into our medication chart. On the basis of the name with which the drug product was prescribed, the medications of each prescription were categorized into branded and generics drugs and also on the basis of Anatomical Therapeutic Chemical (ATC) Code.

The subjects were counselled for medication adherence, reporting of any adverse drug events, its management and health promotion strategies.

The prescriptions were then evaluated for the number of drugs, cost per prescription and their utilization was quantified using Daily Defined Dose (DDD).

Defined daily dose is the assumed average maintenance dose of a drug used for its main indication in adults. It is used as a tool to quantify drug consumption between different healthcare environments. In this study, the DDD was calculated for 100 bed-days. DDD/100 bed-days gives a picture of the prescribing pattern in the AMCU patients.

Evaluation of drug utilization was done by calculating the DDD/100 bed-days in patients using the following formula,

$$\text{DDD/100 bed-days} = \frac{\text{Total dose in the study period (mg)} \times 100}{\text{DDD of drug} \times \text{duration of study (days)} \times \text{bed strength} \times \text{bed occupancy rate}}$$

The bed occupancy rate was calculated using the following formula,

$$\text{Bed occupancy rate} = \frac{\text{Total no. of inpatient days} \times 100}{\text{Available beds} \times \text{No. of days in study period}}$$

No. of beds available = 10
Total no. of inpatient days = 810
No. of days in the study period = 180
Upon substituting the above values in the above equation, the bed occupancy rate was found to be 45.

The bed strength and bed occupancy rate were **10** and **45** respectively in the AMCU. Evaluation of drug usage by brand names and generic names, oral and parenteral routes and the proportion of fixed drug combinations were also included. Drugs falling under National[6] and WHO[7] Essential Medicine Lists (EML) were enlisted and the costliest drugs were also evaluated. However, the expenses of the laboratory investigations, bed charges and nursing charges were excluded.

Statistical analysis

The data was analyzed using Microsoft Excel 2010, Microsoft Corporation Pvt. Ltd, U.S.A. Most of the data is expressed as descriptive statistics. Descriptive statistical data is presented in the form of Mean ± Standard Deviation (S.D). However, the categorization involved expression in the form of numbers and their percentage.

RESULTS

Altogether, 166 subjects were admitted in the AMCU during the study period and a total of 810 prescriptions were dispensed in the department. Twelve subjects with minor complaints, who were kept for observation, were excluded from the study.

62.04% (103) of the total patients were males and the rest 37.95% (63) were females. 53.6% of the patients belonged to the age group of 40-60 years, followed by 25.9% belonging to 20-40 years and 19.9% belonging to patients greater than 60 years of age.

The five most common conditions for admission were, Cerebrovascular Accident (CVA), Ischemic Heart Disease (IHD), Hypertension (HTN), Diabetes Mellitus (DM) and Congestive Cardiac Failure (CCF). However, involvement of multiple systems was also seen in many patients.

Central nervous system was the most affected system (25.3%), followed by cardiovascular system (15.06%), renal system (13.85%), metabolic system (12.04%), others (11.44%), infectious diseases (10.84%), gastrointestinal problems (6.62%), respiratory system (2.4%), genitourinary system (1.2%) and hematological system (1.2%). Morbidity pattern of all the patients is represented in Figure 1.

A total of **3372** drugs were administered in all the cases, out of which 91.45% (3084) were branded drugs and 8.54% (288) of the drugs were generic.

The drugs were then categorized on the basis of route of administration. Seventeen hundred and ninety six drugs (53.26%) were administered through intravenous route, followed by 40.54% (1367) by oral route, 5.57% (188) by nasal route and 0.62% (21) by topical route, which is represented in the Figure 2.

Intravenous drug administration was the preferable route of drug administration.

One hundred and thirty two (132) different types of drugs were prescribed, which are enlisted in Table 1. Out of these, 32.6% (42) of drugs belonged to the National List of Essential Medicine (NLEM)-2011, whereas 25.8% (34) drugs belonged to WHO Essential Medicine List (WHO EML).

8.45% (285) of drugs prescribed belonged to Fixed Drug Combinations (FDCs) and 3.23% (109) were multivitamin preparations.

The drug groups commonly prescribed are described in Table 2. The proton-pump inhibitor-pantoprazole (9.72%) was the most commonly prescribed drug, followed by H_2 receptor antagonist-ondansetron (4.83%), third generation cephalosporin-ceftriaxone (3.94%), non-steroidal anti inflammatory drug-paracetamol (4.06%), statin-atorvastatin (1.95%) and anticonvulsant-phenytoin (1.66%).

Mutlivitamins (3.23%), cefoperazone+sulbactam (1.27%), piperacillin+tazobactam (1.21%), amoxicillin+potassiumclavulanate (0.68%) and paracetamol+aceclofenac (0.47%) were the five most commonly used fixed drug combinations. Pantoprazole and domperidone were the most commonly used drugs not included in WHO Essential Medicine List (WHO EML) -2013. Levitiracetam and meropenem were the most commonly used drugs not included in the National List of Essential Medicine-2011.

The usage of antiemetics, proton-pump inhibitors, antimicrobials and NSAIDs was very high in patients with central nervous system involvement when compared to patients with effects on other body system.

A total of 42 different types of antimicrobials were used in all the cases. The three most common antimicrobials prescribed were ceftriaxone, metronidazole and clarithromycin. Cefoperazone+sulbactam, piperacillin+tazobactam and amoxicillin+potassiumclavulanate were the most used antimicrobial fixed drug combinations. 63 patients underwent culture sensitivity test.

The average number of drugs prescribed per prescription was 7.8±3.4.The average cost per prescription was Rs. 1501±1010. The average cost per treatment was Rs. 4056.4±3073.4.

The total number of drugs prescribed per prescription, total cost of the treatment and the morbidity pattern is represented in the Table 3.

Moreover, reteplase, darbepoetin alfa, ferric carboxymaltose, meropenem and imipenem+cilastatin were the five most costliest drugs prescribed, represented in Table 4.

The drug utilization in terms of DDD/100 bed-days was found to be 4.6 mg. The DDD/100 bed-days of each drug is shown in the Table 5.

DISCUSSION

Drug utilization in the in-patient setting can serve as a source in determining the drug prescribing trends, efficiency and cost effectiveness of the formulary used by the hospital. We showed drug prescribing pattern in AMCU.

Our study has a male preponderance. The number of emergencies in the age group of 40-60 years was high (53.6%), followed by 20-40 years (25.9%) and above 60 years (19.9%). Our study had central nervous system (CNS) trauma as the most common emergency, with hemorrhagic/ischemic stroke being the most common cause of admission (72%). The incidence was higher in males (64.3%) when compared to females (35.7%).

The WHO recommends not more than 2 drugs per prescription on average. The average number of drugs per prescription is an indicator of the standard of prescribing in the hospital setting. In the present study, the average number of drugs per prescription is **7.8±3.4**, which is higher than the WHO recommended average[8]. Nevertheless, it is preferable to keep the mean number of drugs per prescription as low as possible, to reduce the cost of treatment and to minimize the adverse effects and drug interactions. Five or more drugs were prescribed in 97% of the patients.

Pantoprazole and ondansetron were the most commonly used drugs acting on the GI tract. Patients not on oral nutrition or those on NSAID therapy such as aspirin and corticosteroid therapy are at high risk of

developing gastric mucosal damage. However, "GI prophylaxis" is the most frequent rationale mentioned by the physicians behind prescribing pantoprazole without any indication. According to Jung and MacLaren, proton pump inhibitors (PPIs) are safe and efficacious inraising intra-gastric pH in critically ill-patients. This may keep them at bay from stomach bleeding caused due to stress-related mucosal damage[9]. However, a study suggests that, H_2 receptor antagonists are the apt first-line agents. Nevertheless, it is not surprising that PPIs have become first-line agents in offering relief to critically ill patients, despite insufficient substantiation[10].

Use of ondansetron is off-label, as it is not recommended anywhere except chemotherapy/radiotherapy-induced vomiting and post-operative nausea or vomiting[11]. Ondansetron was shown to prolong QT_c interval. However, Patanwala et al., suggested that ondansetron was found to be relatively safe and efficacious in relieving nausea and vomiting than droperidol, promethazine, prochlorperazine and metoclopramide in patients receiving emergency care[12].

Majority of the patients were inappropriately prescribed ondansetron and pantoprazole without any approved indication. Reducing inappropriate prescribing of GI drugs in the patients minimizes potential for adverse events and fosters controllable cost expenditure.

Unfortunately, 91.45% of drugs were prescribed by brand names. The physicians prefer writing trade names of drugs against generic names. Prescribing by brand names suggests promotional strategies by pharmaceutical companies. On the contrary, prescribing by generic names would reduce/eliminate the likelihood of duplication of drugs. It will help the hospital pharmacies to have a better control over the inventory. Hospital pharmacies can purchase drugs in bulk, as the number of brands will be less. Moreover, this will reduce the confusion among the pharmacists while dispensing medications. Prescribing by generic names will also reduce the cost burden of the patients.

The average cost of drugs per prescription was Rs. **1501±1010**, which is higher than two studies led by Shankar et al [2, 3]. Increased cost could be due to increased number of antimicrobials used against the previous studies.

Overestimation of severity of illness is presumed to be the main reason for such emperical use of antimicrobials. Use of culture specific antimicrobials should be promoted to reduce the chances of drug resistance. Moreover, reduced prescribing of antimicrobials would reduce the economic burden on the patients.

Of the total types of drugs used, less than 50% of the drugs were from National List of Essential Medicine (NLEM) and WHO Essential Medicine List (WHO EML). This reflects poor adherence in the Indian setup. Being a tertiary care hospital, use of generic drugs and drugs from essential drug lists should be practiced and promoted.

The mean DDD/100 bed-days was found to be **4.6**, which is lower than the previous study[11].

CONCLUSION

In the entire study duration, usage of pantoprazole and ondansetron were found to be high. However, use of these drugs was not justified in all the cases. This may contribute to increased cost on the patients. Rational use of these drugs needs to be evaluated. Polypharmacy was prevalent and was the main form of irrational prescribing. Prescribing patterns were need based rather than following the WHO criteria for rational use of drugs. To provide optimal, low-cost and effective medicines to the patients, it should be made mandatory for the prescribers to attend Continuing Medical Education (CME) to update their knowledge on WHO criteria for rational use of drugs. Additionally, hospital authorities should take stringent measures to minimize the influence of pharmaceutical companies and their representatives on the drug prescription. Patient counselling was found to be beneficial, as the patients adhered to the prescription. Improved medication adherence and immediate reporting of the adverse event may reduce the risk of complications and minimize the financial burden in the long run.

ACKNOWLEDGEMENT

I extend my sincere gratitude to the mentors for their constant guidance, without whom this work would've been unsuccessful. I also thank the hospital staff for providing case papers for this study.

Table 1: Types of Drugs Used

Indications	Names of drugs used
Cardiovascular diseases	
Arrhythmias,Hypertension, Angina Pectoris, Myocardial Infarction, Congestive Cardiac Failure, dysslipidemia, anemia	Amlodipine,Nifedipine,Nimodipine,Dobutamine,Dopamine,Noradrenaline, Furosemide,Torasemide,Metoprolol,Atenolol,Carvedilol,Ramipril,Perindopril, Amiodarone,Losartan,Telmisartan,Clonidine,Prazosin,Isosorbidedinitrate,Heparin, Digoxin, Atorvastatin, Folic acid, Ferrouos sulphate
Cerebrovascular diseases	
Anxiety,Epilepsy, Psychosis, Depression,Epilepsy prophylaxis, Peripheral neuropathy, Cognitive enhancement	Diazepam,Alprazolam,Lorazepam,Propanolol,Phenytoin,Gabapentin,Midazolam, Levitiracetam,Sodium valproate, Lamotrigine, Haloperidol, Sertraline, Pregabalin, Piracetam, Citicoline, Modafinil

Gastrointestinal (GI) diseases	
Hyperacidity, Gastroesophageal Reflux Disease (GERD), Peptic Ulcer, GI Prophylaxis, Diabetes Mellitus	Panatoprazole,Rabeprazole,Ranitidine,Ondansetron,Domperidone,Metoclopramide, Plain insulin, Insulin glargine
Infections	
Urinary Tract Infections, Respiratory Tract Infections(Pneumonia), Typhoid, Food Poisoning, Meningitis, Cellulitis, Malaria, Tuberculosis	Gentamicin,Ceftriaxone,Cefotaxime,Ciprofloxacin,Doxycycline,Linezolid, Meropenem,Amikacin,Streptomycin,Ofloxacin,Levofloxacin,Norfloxacin,Vancomycin, Azithromycin,Doxycycline,Artesunate,Arte-ether, Isoniazid, Ethambutol, Pyrazinamide

Table 2: Commonly Used Drug Groups

Morbidity	Anti-emetics	Proton-pump inhibitors	Antimicrobials	NSAID's
Cerebrovascular diseases	24	37	48	31
Cardiovascular diseases	3	14	12	9
Renal diseases	15	18	30	5
Metabolic disorders	9	18	24	6
Others	11	18	22	10
Infections	10	17	43	15
GI diseases	8	11	15	3
Respiratory diseases	3	3	4	-
Genitourinary disorders	2	2	3	2
Hematological disorders	1	2	2	1

Table 3: Morbidity Pattern, No. of Drugs and Treatment Cost

Morbidity	Percentage of patients (%)	No. of drugs/ prescription (Mean ± S.D)	Drug cost/ prescription(Rs.) (Mean ± S.D)	Total cost/treatment (Rs.) (Mean ± S.D)
Cerebrovascular diseases	25.3	8±3	926±778	5358±4000
Cardiovascular diseases	15.06	7.2±3.2	6304±1785	6876±3338
Renal diseases	13.85	8±3	3561±3060	9928±8300
Metabolic disorders	12.04	7.5±2.5	733±695	5702±3022
Others	11.44	8±3	1011±861	2879±2208
Infections	10.84	8±4	937±900	3895±3428
GI diseases	6.62	6±3	365±235	1025±837
Respiratory diseases	2.4	8±3.5	918±915	3960±3540
Genitourinary diseases	1.20	8.5±3.5	197±198	648±515
Hematological disorders	1.20	8.5±5	717±675	2093±1546

S.D. – Standard Deviation

Table 4: Five Costliest Drugs Used

S. No.	Brand Name	Generic Name	Price per Unit
1	Injection Retefuse (18 mg)	Reteplase	Rs. 29,750
2	Injection Cresp (200mcg/0.4ml)	Darbepoetin alfa	Rs. 10,570
3	Injection Ferinject 500 mg (10ml)	Ferric carboxymaltose	Rs. 2,900
4	Injection Meroza (1gm)	Meropenem	Rs. 2,630
5	Injection Cilaxter (500 mg)	Imipinem + Cilastatin	Rs. 2,350

Table 5: Drug Utilization in Terms of DDD/100 bed-days

S. No.	Drug	ATC Code	DDD/100 days	SNo.	Drug	ATC Code	DDD/100 days
1	Piracteam	N06BX03	0.06	29	Aceclofenac	M01AB16	0.0001
2	Phenytoin	N03AB02	0.02	30	Atorvastatin	C10AA05	0.12
3	Levitiracetam	N03AX14	0.02	31	Noradrenaline	C01CA03	0.03
4	Chlordiazepoxide	N05BA02	0.005	32	Dopamine	C01CA04	0.44

5	Diazepam	N05BA01	0.001	33	Dobutamine	C01CA07	0.4
6	Oxcarbazepine	N03AF02	0.02	34	Amiodarone	C01BD01	0.25
7	Midazolam	N05CD08	0.01	35	Perindopril	C09AA04	0.12
8	Zolpidem	N05CF02	0.015	36	Amlodipine	C08CA01	0.12
9	Sodium valproate	N03AG01	0.002	37	Aspirin	N02BA01	0.003
10	Halperidol	N05AD01	0.001	38	Ramipril	C09AA05	0.05
11	Lorazepam	N05BA06	0.006	39	Clopidogrel	B01AC04	0.05
12	Gabapentin	N03AX12	0.001	40	Rosuvastatin	C10AA07	0.003
13	Modafinil	N06BA07	0.005	41	Metoprolol	C07AB02	0.001
14	Alprazolam	N05BA12	0.002	42	Atenolol	C07AB03	0.001
15	Ceftriaxone	J01DD04	0.001	43	Sildenafil	G04BE03	0.01
16	Amikacin	J01GB06	0.007	44	Furosemide	C03CA01	0.25
17	Gentamicin	J01GB03	0.001	45	Prazosin	C02CA01	0.185
18	Metronidazole	G01AF01	0.08	46	Torasemide	C03CA04	0.02
19	Ofloxacin	J01AM01	0.43	47	Nifedipine	C08CA05	0.01
20	Levofloxacin	J01AM12	0.13	48	Losartan	C09CA01	0.005
21	Clarithromycin	J01AF09	0.15	49	Telmisartan	C09CA07	0.05
22	Azithromycin	J01FA10	0.02	50	Nimodipine	C08CA06	0.001
23	Norfloxacin	J01MA06	0.004	51	Isosorbide dinitrate	C01DA08	0.002
24	Pantoprazole	A02BC02	0.4	52	Vancomycin	J01XA01	0.002
25	Ondansetron	A04AA01	0.6	53	Artesunate	P01BE03	0.02
26	Domperidone	A03FA03	0.002	54	Meropenem	J01DH02	0.03
27	Paracetamol	N02BE01	0.05	55	Linezolid	J01XX08	0.01
28	Diclofenac	M01AB05	0.05	56	Doxycycline	J01AA02	0.04

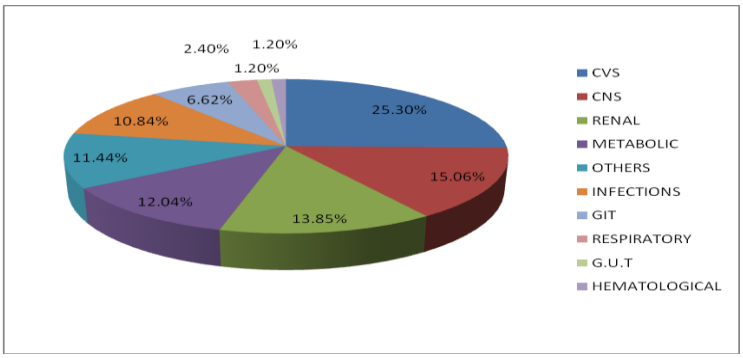

Fig. 1: Morbidity pattern of AMCU patients

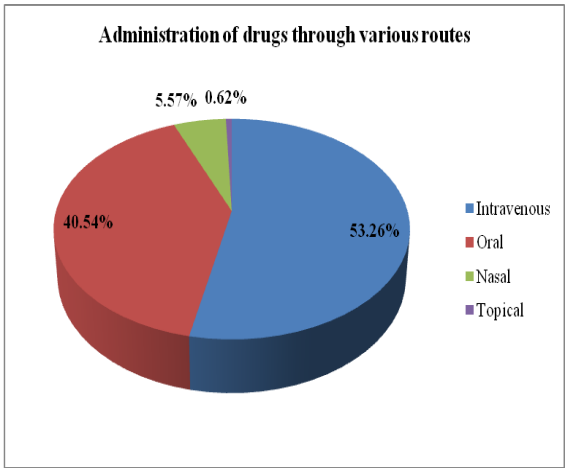

Fig. 2: Routes of administration of different drug

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