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A STUDY OF DRUG UTILIZATION PATTERN IN MEDICAL CRITICAL CARE UNIT OF A TERTIARY CARE TEACHING HOSPITAL

General Medicine

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ABSTRACT

BACKGROUND: Chronic disease and life threatening disorders among CCU patients have resulted in medicating them with drugs from different pharmacological classes, which is further complicated by the altered physiology and multi-organ system failure.
OBJECTIVE : To evaluate the drug utilization pattern in patients admitted in Medical Critical Care Unit (MCCU).
MATERIALS AND METHODS: This was an observational study carried out in Medical Critical Care Unit at a tertiary care teaching hospital. The data were entered in pre tested case record form and analysed for demographic details, clinical management and prescribing pattern. The DDD per 100 bed days was calculated.
RESULTS: A total of 400 patients were evaluated consisting 70% male patients. Average duration of stay was 7.38 ± 0.34 (mean ± SE) days. Most common causes for admission to the ICU were intraparenchymal haemorrhage (18%), cerebrovascular stroke (15%) and chronic obstructive pulmonary disease (15%). An average number of drugs per patient was 15.14 ± 0.19 (mean ± SE). Commonly prescribed drug group was the antimicrobial agents (AMAs) in which metronidazole has highest DDD/100 bed days of 11.08. Other commonly prescribed groups were drugs affecting blood and gastrointestinal drugs. It was observed that out of 400 patients, 223 (56%) patients were discharged and 177 (44%) patients were expired.
CONCLUSION: The polypharmacy was present and antimicrobials were highest prescribed drug in our MCCU. The prescribers should be making aware about risks of polypharmacy.

KEYWORDS

INTRODUCTION:

Drug utilization research was defined by WHO(1977) as the study of marketing, distribution, prescription, and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences[1]. Drug utilization research help in identification of clinical use of drugs in populations and its impact on healthcare system [1]. Critical Care Unit (CCU) is highly specified and sophisticated area of hospital which is specifically designed, staffed, located, furnished, equipped and dedicated to management of critically sick patient[2]. Patients with varied demographic characteristics, admission criteria and heterogeneous group are admitted to CCU and are usually associated with co-morbid illnesses[3]. Chronic disease and life threatening disorders among CCU patients have resulted in medicating them with drugs from different pharmacological classes, which is further complicated by the altered physiology and multi-organ system failure [4]. Critical illness and associated co morbid conditions alter the absorption, distribution, metabolism, excretion and plasma concentrations of drugs. This in turn alters the pharmacodynamic responses which results in such therapeutic, supra therapeutic or toxic effects of drugs [5]. Hence, instituting rational pharmacotherapy is the need of the hour for saving the life of critically-ill patients while irrational drug use may be life threatening. In India there are various studies are conducted in Critical Care Unit (CCU) settings. However, very few studies had been conducted with aim of determining ATC classification/calculating DDD. Hence the present study was undertaken to determine drug utilization pattern, ATC classification/ calculating DDD in the CCU settings of tertiary care teaching hospital.

MATERIALAND METHODS

Our study was continuous, longitudinal, prospective and observational conducted at tertiary care teaching hospital during October 2018 to October 2020. Study approval was taken from Institutional Ethics Committee of Civil Hospital, Ahmedabad (CHA) (Ref No. EC/ Approval/13/2019). During the study period, the investigator visited Medical Critical Care Unit (MCCU) every day between 9 to 12 am. Adult patients above 18 years of age and of either gender who were admitted in Medical Critical Care Unit at Civil Hospital and willing to participate in study were enrolled. Consent was obtained from the patients and / or relatives. The information was obtained from the 400 patients and /or his/ her case papers admitted in MCCU. Data were collected for age, gender, diagnosis, duration of CCU stay, laboratory investigations and treatment provided during the stay in CCU. The sample size was decided according to previous studies [6,7,8].

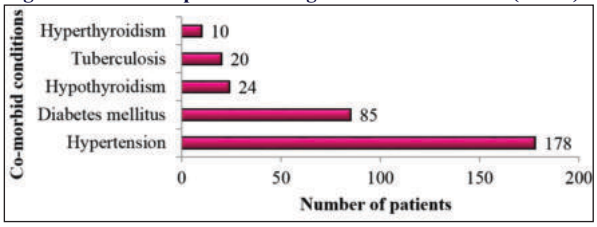
Recorded information of patients was entered in Microsoft Excel Worksheet and data were analyzed as follows: Demographic details, Clinical diagnosis, Outcome of patients, WHO core prescribing indicators, use of fixed dose combinations. The drugs were classified according to the Anatomical Therapeutic Chemical classification based on their chemical, pharmacological and therapeutic properties. The drug utilization was measured in DDD/100 bed-days. DDD/100 bed-days were calculated using the following equation:

DDD/100 bed-days = Number of units administered in a given period × 100
DDD of drug × study duration (days) × bed strength × Avg. bed occupancy rate

RESULTS

A total of 400 patients who met the inclusion, exclusion criteria were studied. The mean age of the patients observed in this study was 52.20 ± 0.80 (mean ± SE) years with a range of 19 to 87 years. Maximum number of patients (101) belonged to the age group of 61- 70 years that includes 69 male and 32 female patients. Out of 400 patients, 280 (70%) were males and 120 (30%) were females. Male to female ratio was 2.33:1. Out of 400 patients enrolled, 306 (76.5%) patients were having co-morbid conditions. Most common was hypertension which was present in 178 (44.5%) patients followed by diabetes mellitus 85 (21%), hypothyroidism 24 (6%) and tuberculosis 20 (5%). In some patients there are more than one co-morbid condition was present (Figure 1).

Figure 1: Number of patients having co- morbid conditions (n=306)



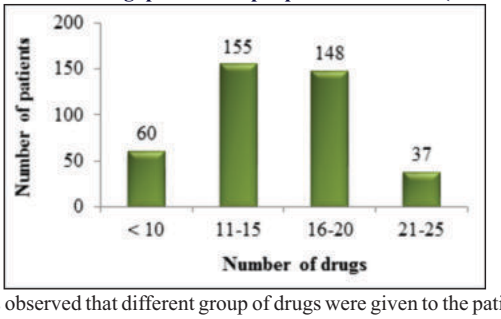
Patients admitted in medical CCU were diagnosed on the basis of clinical examination, laboratory, radiological and other investigations by subject expert. Most common diagnosis was intaparenchymal haemorrhage (18%) followed by cerebrovascular stroke (CV stroke) (15%), chronic obstructive pulmonary disease (COPD) (15%), lower respiratory tract infection (LRTI) (11%), guillain- barre syndrome (GBS) (8%) (Table 1).

Table 1: Diagnosis of patients admitted in medical CCU (MCCU) (n=400)

Sr No.	Diagnosis	Number of patients (n=400)
1	Intaparenchymal haemorrhage (IPH)	71 (18%)
2	Cerebrovascular stroke (CV stroke)	61 (15%)
3	Chronic obstructive pulmonary disease (COPD)	61 (15%)
4	Lower respiratory tract infection (LRTI)	44 (11%)
5	Guillain- barre syndrome (GBS)	32 (8%)
6	Acute kidney injury (AKI)	11 (2.7%)
7	Chronic kidney disease (CKD)	11 (2.7%)
8	Diabetic ketoacidosis (DKA)	10 (2.5%)
9	Epilepsy	10 (2.5%)
10	Organophosphorus (OP) poisoning	10 (2.5%)
11	Septicaemia	10 (2.5%)
12	Ischemic heart disease (IHD)	10 (2.5%)
13	Hepatic encephalopathy	9 (2.2%)
14	Alcoholic liver disease	8 (2%)
15	Cirrhosis of liver	5 (1.2%)
16	Left ventricular failure (LVF)	5 (1.2%)
17	Metabolic encephalopathy	5 (1.2%)
18	Dengue	5 (1.2%)
19	Snakebite	5 (1.2%)
20	Encephalitis	5 (1.2%)
21	Rheumatic heart disease (RHD)	4 (1%)
22	Subdural haemorrhage (SDH)	4 (1%)
23	Transverse myelitis	2 (0.5%)
24	Neuroleptic malignant syndrome	1 (0.2%)
25	Anaphylactic shock	1 (0.2%)

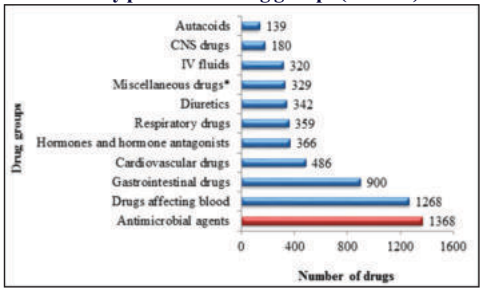
It was observed that out of 400 patients, more than 200 patients were stayed for less than five days in MCCU. Average duration of stay was 7.38 ± 0.34 (mean ± SE) days. Total 6057 drugs were prescribed in 400 patients. The mean number of drugs prescribed was 15.14 ± 0.19 (mean ± SE). In 155 patients, 11 to 15 drugs were prescribed while in 60 patients, less than ten drugs were prescribed (Figure 2). These 6057 drugs were administered by mainly five route of administration. Most common route of administration was intravenous (65.6%) followed by oral (29.6%), Inhalation (3.8%), Subcutaneous (0.5%) and Intramuscular 12 (0.2%) (Figure 2).

Figure 2: No. of drugs prescribed per patient in MCCU (n=400)



It was observed that different group of drugs were given to the patients admitted in MCCU to treat their life threatening diseases as well as co-morbidities. Commonly used drug groups include antimicrobial agents followed by drugs affecting blood and related organs. Other drug groups used were gastrointestinal drugs, cardiovascular drugs, hormone and hormone antagonists, respiratory drugs, diuretics, intravenous (IV) fluids, central nervous system (CNS) drugs and autacoids (Figure 3).

Figure 3: Commonly prescribed drug groups (n=6057)



* Miscellaneous drugs include immune globulins, antisera, antidotes, antirheumatoid drugs, nutritional supplements and enzymes.

There were two antimicrobial agents were prescribed in 86 (21.5%) patients and more than two antimicrobial agents were prescribed in 257 (64.2%) patients. The average no. of antimicrobials was 3.42 ± 1.81 (mean ± SD) in MCCU. Out of 6057 total drugs, 3392 (56%) drugs were prescribed by generic name. All the patients were given antibiotics and injections. There were 85% of drugs were prescribed from national list of essential medicines (NLEM), 2015.

Total 543 fixed dose combinations were prescribed in 317 (79.25%) patients. More than one fixed dose combination was given to 166 (41.50%) patients. The most commonly prescribed fixed dose combination was piperacillin- tazobactam (34.0%) followed by salbutamol - ipratropium (21.7%), multivitamin (19.8%), cefoperazone-sulbactam (6.6%), amoxicillin- clavulanic acid (6.4%), theofylline + etofylline (4.23%),HRZE (combination of isoniazid, rifampicin, pyrazinamide and ethambutol) (3.6%), cough mixtures (2.94%) and laxatives (0.8%).

Table 2: Analysis of DDD/100 bed days of various drug groups

Drugs	Total (n= 5201)	DDD by WHO	Prescribed dose	DDD/100 bed days	ATC code
Antimicrobial agents					
Metronidazole	250	1.5 g	2579 g	11.08	J01XD01
Piperacillin-tazobactam	184	14 g	14035.25 g	6.46	J01CR05
Ceftriaxone	177	2 g	1969 g	6.34	J01DD04
Azithromycin	102	0.5 g	258.5 g	3.33	J01FA10
Meropenem	65	2 g	1009 g	3.25	J01DH02
Cefoperazone-sulbactam	36	4 g	776 g	1.25	J01DD62
Amoxicillin-clavulanic acid	35	3 g	563.55 g	1.21	J01CR02
Vancomycin	45	2 g	340 g	1.09	J01XA01
Linezolid	25	2 g	174 g	0.56	J01XX08
Levofloxacin	14	0.5 g	38.37 g	0.49	J01MA12
Cefotaxime	5	4 g	179.5 g	0.28	J01DD01
Drugs affecting blood and related organs					
Atorvastatin	215	20 mg	53440 mg	17.22	C10AA05
Aspirin	139	75 mg	99150 mg	8.5	B01AC06
Clopidogrel	79	75 mg	34875 mg	2.99	B01AC04
Gastrointestinal drugs					
Pantoprazole	376	40 mg	212880 mg	34.30	A02BC02
Ondansetron	365	16 mg	61492 mg	24.77	A04AA01
Cardiovascular drugs					
Amlodipine	103	5 mg	4790 mg	6.17	C08CA01
Noradrenaline	108	6 mg	3830 mg	4.11	C01CA03
Enalapril	49	10mg	2630 mg	1.69	C09BA02
Telmisartan	15	40 mg	9160 mg	1.47	C09CA07
Metoprolol	79	0.15 g	28.97 g	1.24	C07AB02
Dopamine	28	0.5 g	61.2 g	0.78	C01CA04
Dobutamine	10	0.5g	24 g	0.30	C01CA07
Diltiazem	15	0.24 g	10.74 g	0.28	C08DB01
Hormones and hormone antagonists					
Dexamethasone	34	1.5 mg	4060 mg	17.44	H02AB02
Budesonide	71	1.5 mg	1001mg	4.30	A07EA06
Diuretics					
Furosemide	134	40 mg	33488 mg	5.39	C03CA01
Spironolactone	22	75 mg	5075 mg	0.43	C03DA01
Central nervous system drugs					
Valproate	127	1.5 g	888.5 g	3.81	A12CA01
Tramadol	12	0.3 g	24.8g	0.53	N02AX02
Phenytoin	7	0.3 g	14.7g	0.31	N03AB02
Autacoids					
Paracetamol	122	3 g	732.65 g	1.57	N02BE01

In antimicrobial group, metronidazole has highest DDD/100 bed days followed by pipracillin-tazobactam and ceftriaxone. In drug affecting blood, atorvastatin has highest DDD/100 bed days. In gastrointestinal drugs, pantoprazole has highest DDD/100 bed days. In cardiovascular

drugs, amlodipine has highest DDD/100 bed days. The detailed analysis of total prescribed dose, DDD/100 bed days and ATC code of various groups is shown in Table 2.

DISCUSSION

WHO recommends that drug utilization studies should be conducted using, the Anatomical Therapeutic Chemical [ATC] classification system and the Defined Daily Dose [DDD] as a measuring unit. The purpose of the ATC\DDD system is to serve as a tool for drug utilization re-searches in order to improve the quality of drug use [9]. Access to standardized and validated information on drug use is essential to allow audit of patterns of drug utilization, identification of problems and monitoring of the outcomes of educational or other interventions.

We evaluated 400 cases admitted in medical CCU of a tertiary care hospital. The comparison of demographic variables of our study with the other studies mentioned in Table 3. The possible reason for the differences in demographic variables is due to different inclusion- exclusion criteria, presence of co-morbidities, and prevalence of non-communicable diseases across geographical areas. The mean duration of stay was 7.38 ± 0.34 (mean ± SE) days. In our study, total 208 patients were stayed for less than five days and 198 patients were stayed for more than five days in CCU. The mean duration of stay in study conducted at Bhavnagar was 4.15 days while it was 4.5 ± 3.5 days in Oman [6,8]. The possible explanation for these finding is because of different patient profile and presence of co-morbidities in patient admitted in CCU. The severity of illness during admission to CCU influences the overall length of stay; there are many occasions where even after recovering from the initial critical illness, it may be necessary to retain patients in the CCU for a longer time to provide supportive therapy [10].

Length of stay in the CCU is considered to be one of the most important factors which determine the outcome of patient admitted in CCU[11]. It has been shown consistently that longer stays in CCU correlates closely with worse outcome of the patient [12,13,14,15].

Total 6057 drugs were prescribed in 400 patients. The mean number of drugs prescribed was 15.14 + 3.90 (mean + SD). The mean number of drugs prescribed in our study was higher compared to other studies [6,7,8].

These findings suggest that Polypharmacy is present in all studies. The reason for polypharmacy is because of clinical condition of patients admitted in CCU with co-morbidities. Polypharmacy is associated with adverse outcomes including mortality, drug- drug interactions, adverse drug reactions, and increased length of stay in hospital. The risk of adverse effects increases with increasing numbers of medications [16]. The prescriber should be making aware about these disadvantages of polypharmacy.

Table 3: Comparison of our study with other studies

Sr. No.	Type of variables	Present study	Bhavnagar study (Patel MK et al.,2013)[6]	Eastern India study (Patanaik SK et al.,2015) [7]	Oman study (Al-zakwani et al.,2017) [8]
1	**Sample size**	400 patients	397 patients	275 patients	138 patients
2	**Study duration**	October 2018 to October 2020	January 2008 and December 2010	180-day	1st June 2013 to 31st October 2013
3	**Mean age (Years)**	52.20±0.80 (mean ± SE)	44.62 years (95% CI: 42.56-46.69)	54.3	46±19 (mean ± SD)
4	**Sex ratio**	2.33:1	1.62:1	1.54:1	1.76:1
5	**Common Co-morbidities**	Hypertension (44.5%), Diabetes mellitus (21%)	-	Hypertension (27.6%), diabetes mellitus (16%)	-
6	**Common Clinical diagnosis**	Intraparenchymal haemorrhage (18%), cerebrovascular stroke (CV stroke) (15%), chronic obstructive - pulmonary disease (COPD) (15%)	Septicaemia (35.37%), head injury (32.39%), complicated acute abdomen (25.35%)	Cerebrovascular accident (20.5%), chronic kidney disease (17.3%), road traffic accidents with multiple injuries (13%)	Trauma (22%), cardiovascular diseases (15%), gastrointestinal diseases (13%)
7	**Duration of stay**	7.38 ± 0.34 (mean ± SE) days	4.15 days	-	4.5 ± 3.5 (mean ± SD) days
8	**Outcome of patients**	Mortality (44%)	Mortality (71.58%)	-	Mortality (25%)
9	**Mean number of drugs**	15.14 ± 3.90 (mean ± SD)	13.54 (95% CI: 13.05-14.04)	10.5	8.0±4.6
10	**Route of administrat-ion**	Parenteral route (70.1%), oral route (29.6%).	Parenteral route (86.57%)	Parenteral route (63.3%)	Parenteral route (66%), enteral route (26%)
11	**Common drug groups**	Antimicrobials (22.58%), drugs affecting blood (20.93%), gastrointestinal drugs (14.85%)	Antimicrobi-als (15.65%), inotopes (12.16%), gastrointestinal drugs (10.58%)	Antimicrobials (21.69%), gastrointestinal drugs (16.86%), vitamins calcium and protein supplements (9.92%)	Antimicrobials (25.1%), gastrointestinal (20.4%), drugs affecting blood (10.4%)

Commonly used drug groups in our study, include antimicrobial agents (22.58%) followed by drugs affecting blood and related organs (20.93%). Our findings are similar to study conducted at Bhavnagar, eastern India and Oman as mentioned in table 3.[6,7,8]

In our study, metronidazole was highest prescribed drug followed by piperacillin- tazobactam and ceftriaxone. Metronidazole account for 18.27% of antimicrobial usage in our study while it was 10.92% in study conducted by Shelat[17]. The higher use of metronidazole in our study may be due to anaerobic infection is very common in CCU setting [18,19]. In our study, two antimicrobial agents were prescribed in 86 (21.5%) patients and more than two antimicrobial agents were prescribed in 257 (64.2%) patients. The average no. of antimicrobials prescribed per patient was 3.42 + 1.81 (mean + SD). In our study, second most common drug group prescribed was drugs affecting blood and related organs. Most common prescribed drug in this group was atorvastatin followed by aspirin. In present study, atorvastatin account for 3.54% of total drug use while in study conducted at Bhavnagar it was 0.44% [6]. The most common prescribed drug from gastrointestinal group was pantoprazole (6.20%) followed by ondansetron (6.02%). The variation in drug group prescribing among different studies is due to dissimilarity in indication of admission, presence of co morbidities and duration of stay in intensive care unit.

As compared to study conducted at Oman and Chandigarh, we have higher number of drugs prescribed from essential medicine list. Ideally, 100% of drugs should be prescribed by generic name and as far as possible from essential medicine list. The advantage of prescribing generic drug is low cost and easy availability while the advantage of prescribing from essential medicine list is that these drugs have established efficacy and safety [20,21].

In our study, total 543 fixed dose combinations were prescribed to 317 (79.25%) patients. More than one fixed dose combination was given to 166 (41.50%) patients. Increased prescription of FDCs lead to development of ADRs, drug- drug interactions and increased cost of treatment. [22]

The DDD/100 bed days provides an estimate of the therapeutic

intensity and estimates that percentages of the inpatient receive one DDD every day. This indicator is quite useful for benchmarking in and between hospitals. In our study, from antimicrobial group, metronidazole (11.08) has highest DDD/100 bed days followed by piperacillin- tazobactam (6.46) and ceftriaxone (6.34) while in study conducted at Bhavnagar has DDD/100 bed days of metronidazole was 10.97 and of ceftriaxone was 7.41. In drugs affecting blood, a DDD/100 bed day of atorvastatin was 17.22 and of aspirin was 8.5. In gastrointestinal drugs, pantoprazole has highest (34.30) DDD/100 bed days while in study conducted at eastern India, DDD/100 bed days of pantoprazole was 48.9. In cardiovascular drugs, amlodipine has highest (6.17) DDD/100 bed days followed by noradrenaline (4.11). In central nervous system, valproate has highest (3.81) DDD/100 bed days while in diuretics, furosemide has highest (5.39) DDD/100 bed days. In study conducted by shelat et al, DDD/100 bed days of furosemide was 5.54. The variation in values of DDD/100 bed days can be explained by disparity in sample size, duration of study, types of patients admitted and categories of drug used among different studies.

LIMITATIONS

Like other studies this study also has its own limitations, for example we have collected data from adult patients admitted in medical critical care unit only. We have not done rationality assessment of prescription as well as culture sensitivity analysis and cost analysis. Also majority of data collection was over by March 2020 and there was different hospital set up for COVID 19 patients, hence these patients were not included in the study.

CONCLUSION

We can say that polypharmacy was present and antimicrobials were highest prescribed drug in our CCU. Each CCU should have their own antibiogram and guidelines on use of antimicrobial agents and it should be updated regularly. The prescribers should be making aware about risks of polypharmacy.

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