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DRUG UTILIZATION RESEARCH OF ANTIBIOTICS IN AN INTENSIVE CARE UNIT: A RETROSPECTIVE STUDY FROM A RURAL HEALTHCARE SETTING IN SOUTH INDIA

Clinical Research

Dr. Harish Handyal*	D.A, IDCCM, Chief Intensivist, RDT hospital, Bathalapalli, Anantapur- 515661 *Corresponding Author
Dr. Gopi Kumar	D.A, consultant Intensivist, RDT hospital, Bathalapalli Anantapur:515661
Polina Akhila Chowdary	Doctor of Pharmacy (Pharm D), RIPER College, Chiyyedu, Anantapur- 515721
Vennapusa Jayasree	Doctor of Pharmacy (Pharm D), RIPER College, Chiyyedu, Anantapur- 515721
Dr. Mohan Raj Rathinavelu	B. Pharm, Pharm. D, Assistant Professor, RIPER, Chiyyedu, Anantapur- 515721

ABSTRACT

Drug utilization study is an important tool to study the clinical use of drugs and its impact on healthcare System. Also contributes to the rational use of drugs by describing patterns of drug use and identifying interventions to improve drug use in intensive care.

***Aims and Objectives*:** To assess the utilization of antibiotics in a 7-bedded general intensive care unit of a 340 bedded rural hospital in south India.

***Methodology*:** A retrospective study was carried out, studying Medical records of patients admitted in ICU between January 2015 and December 2017. To determine the most commonly prescribed AMAs & find out the utilization of AMAs in ICU as measured by DDD/ 100 bed-days.

Results: A total of 720 inpatients case papers of ICU were screened, of which 322 (44.72%) patients were male and 398 (55.27%) were female. Total 400 (55.55%), 210 (29.16%), 14 (1.94%) and 96 (12.91%) patients were admitted with medical, surgical, orthopaedics and OBG indications respectively. Average number of drugs per prescription was found to be 3.725. Number of antimicrobials per patient was found to be 3. 066. Total drug utilization in ICU in terms of DDD/100 bed days was found to be 113.19%.

In conclusion: In our setting, antibiotics utilized were found to be rational & are comparable to those of previous studies. However, prescription protocols need to be further addressed to guide appropriate use of drugs in the ICU setting.

KEYWORDS

Anti-microbial agents (AMA), Anatomic therapeutic chemical (ATC), Fixed dose combination (FDC), Prescribed daily dose (PDC), Defined daily dose (DDD).

INTRODUCTION

A method to evaluate and improve drug use is by conducting Drug Utilization Studies (DUS). Drug Utilization is defined by the WHO as the marketing, distribution, prescription, and use of drugs in society with special emphasis on the resulting medical, social, and economic consequences [1]. The intensive care unit (ICU) 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 [2]. AMAs are the most frequently prescribed drugs in the ICU [3]. Due to this, the total AMA consumption in ICU is approximately ten times higher than the general hospital wards [4]. Study carried out by Weber et al, ICU drug costs accounted for 38.4% of the total drug costs and have increased at a rate greater than non-ICU drug costs (12% vs 6%)[5].Critically ill patients admitted to intensive care units (ICUs) are highly susceptible to infections because of predisposing illnesses and the use of invasive and surgical procedures and are, therefore, exposed to high antimicrobial pressure[6].Since patients admitted to the ICU receive multiple drugs with altered pharmacokinetic and pharmacodyanmic conditions and 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 results in incidence of poor treatment response and adverse reactions increase due to critical conditions of patients[7]. CCU 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. The ICU's are often considered as the epicentre of antimicrobial resistance and it is an important problem influencing patient outcome [8]. Till date, about 5000 antimicrobial agents (AMAs) have been discovered, out of which only around 100 are used clinically for treating infection [9]. Unfortunately, as the need for new AMA has grown over time, development of novel drugs has been slow in the recent years. It seems likely that in coming decade we will have to depend on the currently available class of drugs [10]. Because each antibiotic has different unit dose of daily administration, specific standardized method should be used in the evaluation of in-hospital antibiotic use.

Of the current standard methods, the method suggested by the World Health Organization (WHO) is the prominent. The ATC/DDD index is developed and interval updated by the WHO. The WHO Collaborating Centre for Drugs Statistics Methodology has standardized this with the ATC/DDD (Anatomical Therapeutic Chemical/Defined Daily Dose) index 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 [11]. The defined daily dose (DDD) concept was developed to overcome objections against traditional units of measurement of drug consumption. DDD is defined as the assumed average maintenance dose per day for a drug used for its main indication in adults. DDD provides a fixed unit of measurement independent of price and formulation.DDD 100 bed-days has been used internationally in the comparison of in-hospital and outpatient antibiotic use, and such data have been used to compare and to throw light on the national level of antibiotic use and resistance relationship [12]. Periodic evaluation of drug utilization in the CCU is necessary for optimization of health care system, proper use of resources and making prescription policy. In this context, the current study was designed to study the drug utilization patterns of AMAs and rationality of their use in the ICU of our 7 bedded general intensive care unit, that would help us to

- Determine the most commonly prescribed AMAs;
- To find out the utilization of AMAs in ICU as measured by DDD/ 100 bed-days (WHO / DDD).

AIMS AND OBJECTIVES: The retrospective study of six-month duration was designed to assess the utilization of antibiotics in a 7-bedded general intensive care unit of a 340-bedded secondary referral hospital in south India.

MATERIALS AND METHODS

Study site: Seven bedded, Intensive care unit of Rural Development

Trust (RDT) Hospital, Bathalapalli, Ananthapuram, Andhra Pradesh, India

Study duration: Six Months (August 2018-January2019)
Study design: Retrospective study

Study criteria:
A retrospective study was planned to be carried after the permission from Institutional Review Board, Medical records of patients admitted in ICU between January 2015 and December 2017 were collected from the medical record section.

Study Procedure: The study was performed in III Phases:
- Phase I (1 Month)
- Preparation and submission of a detailed profoma (including critical evaluated biomedical literatures which reflects the objectives and necessity of study, patient data collection form) to the Institutional Review Board (IRB) for the approval.
- After IRB clearance, the permission from concerned hospital authority and the head of departments were obtained.

Phase II (4 Month) – Data Collection and Analysis
- Data Collection;
- A structured process was followed in collection of data. The data was collected from MRD from January 2015 to December 2017.
- Data were analysed for
- Demographic variables; indication of admission in ICU and systems involved, duration of ICU stay, total number of drugs prescribed per patient, proportion of common group and particular drugs used, the total number of antimicrobials used per patient, use of fixed dose combinations (FDCs); use of oral and parenteral formulations; organisms isolated and their antimicrobial sensitivity and outcome of the patient.
- The drugs were classified according to the Anatomical Therapeutic Chemical classification based on their chemical, pharmacological and therapeutic properties. The utilization was measured in DDD/100 bed days. (WHO Collaborating Centre for Drug Statistics Methodology, 2002)[13].
- DDD/100 bed days were calculated using the following equation:

$$\text{DDD/100 bed-days} = \frac{\text{No. of units administered in a given period (mg)} \times 100}{\text{DDD (mg)} \times \text{number of days} \times \text{number of beds} \times \text{occupancy index}}$$

- Prescribed daily dose was calculated using the following equation [14]:

$$\text{Prescribed daily dose} = \frac{\text{Total amount of drug}}{\text{Duration of hospital stay}}$$

Phase III (1 Month)
- Analysis and synthesis of results and interpretations.
- Drawing conclusion, along with limitations if any.
- Preparation and submission of project book.
- **Statistical Analysis:** Descriptive analysis, Excel spreadsheet.

RESULTS:
In department of Intensive Care Unit of a secondary referral healthcare settings 720 prescriptions were handled, data of which were collected from January 2015 to December 2017 and documented in the patient profile form (data collection form).

A total of 720 inpatients case papers of ICU were screened.102 (14.16%) patients were below > 20 years; 334 (46.38%) patients were between 21- 40 years and 206 (28.61%), patients were between 41-60years and 78 (10.83%) patients are above of > 60 years' age. A total 322 (44.72%) patients were male and 398 (55.27%) were female. Total 400 (55.55%), 210 (29.16%) and 14 (1.94%) and 96 (13.33%) patients were admitted with medical, surgical, orthopaedics and OBG indications respectively.

Table1. Patient Demographics

Sl. no	Indication for ICU Admission	Age (in years)				Gender	
		< 20	21-40	41-60	> 60	Male	Female
1	Medical	68	186	114	32	196	204
2	Surgical	16	70	85	39	121	89
3	Orthopaedic	2	3	4	5	5	9
4	OBG	16	75	3	2	0	96
Total		102	334	206	78	322	398

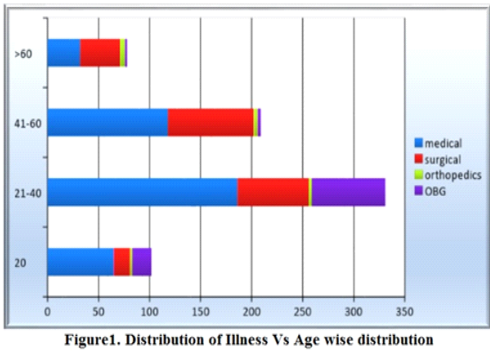

Figure1. Distribution of Illness Vs Age wise distribution

Based on age groups the age group of 21 to 40 years are mostly admitted into ICU. Results of which are thoroughly assessed and summarized in Table 1. Patient demographics and Figure:1. Distribution of illness. A total of 2266 drugs were prescribed in all patients.

Table 2: Pattern of Drug Use as per the ATC / DDD Classification

S. no	Drug Use Indicators	Results
1.	Average number of drugs per prescription	3.725
2.	Average number of antimicrobial drugs per prescription	3.066
3	Percentage of drugs containing antimicrobial FDCs	56.6%
4	Percentage of prescriptions with an oral drug prescribed	47.5%

The antimicrobials and inotropes were used in 1795 (79.2%) and 471 (20.78%) patients respectively. The pattern of drug use as per the ATC/DDD classification (Table: 2) shows average number of antimicrobials prescribed per patient was 3.066, average no of drugs per prescription was found to be 3.725, the percentage of drugs containing antimicrobial FDCs was found to be 56.6% and among the FDCs Piperacillin Tazobactam is the drug that was mostly used and the percentage was found to be 12.7%. Among all the Antibiotic Utilization in Intensive Care Unit, Ceftriaxone was found to be mostly used which accounts for 14.7% followed by Piperacillin Tazobactum12.7%.

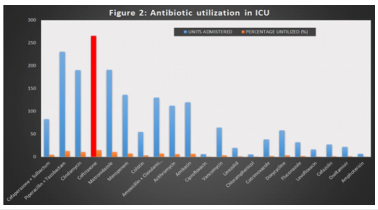

Table 3: Pattern of antibiotics utilization as per the WHO ATC / DDD Classification (Year 2015-17) n = 720

Sl. No	Antibiotics	ATC Code	WHO DDD (gm)	PDD	DDD/100 Bed Days	PDD/ DDD
1	Cefaperazone + Sulbactum	J01DD62	4	4.15	3.96	1.03
2	Piperacillin + Tazobactam	J01CR05	14	16.5	15.5	1.18
3	Clindamycin	J01FF01	1.8	1.79	9.83	0.99
4	Ceftriaxone	J01DD04	2	2.1	11.2	1.06
5	Metronidazole	G01AF01	1.5	1.40	8.24	0.93
6	Meropenem	J01DH02	2	2.45	18.1	1.22
7	Colistin	J01XB01	3	3.65	9.37	1.21
8	Amoxicillin +Clavulanic acid	JO1CRO2	3	3.3	6.7	1.1
9	Azithromycin	JO1FA10	0.5	0.56	6.12	1.13
10	Amikacin	JO1GB06	1	0.7	3.87	0.7
11	Vancomycin	A07AA09	2	1.9	4.92	0.95
12	Vancomycin	JO1XX08	1.2	0.99	0.14	0.82
13	Chloramphenicol	J01BA01	3	2.07	0.31	0.69
14	Cotrimoxazole	JOIEE01	1.92	1.11	1.84	0.57
15	Doxycycline	JO1AA02	0.1	0.11	3.59	1.16
16	Fluconazole	JO2AC01	0.2	0.23	4.08	1.16
17	Levofloxacin	J01MA12	0.5	0.58	2.84	1.17
18	Cefazolin	J01DB04	3	1.72	0.53	0.57
19	Oseltamvir	J05AH02	0.15	0.15	1.6	1
20	Amphotericin	J02AA01	0.035	0.02	0.0003	0.76
21	Ciprofloxacin	JO1MAO2	0.5	0.4	0.321	0.8

Total drug utilisation in ICU during the study period (2015-2017) was found to be 113.19%. The utilisation of Meropenem was 18.10%, Piperacillin Tazobactam 15.53(%) Various Drug utilisation of antibiotics were shown in Figure:2 (Antibiotic Utilisation in Intensive Care Unit) and Pattern of antibiotics utilization as per the WHO ATC / DDD Classification (Year 2015-17) is shown in Table:3.

DISCUSSION

The present study evaluated drug utilization patterns in the ICU at RDT Hospital. ICU is a setting where seriously ill patients who often suffer from multiple organ dysfunctions are administered. Therefore, the number of prescribed drugs and the cost of treatment and hospitalization are usually high. Periodic studies on drug utilization are useful to meet the needs of assessing drug prescribing trends and optimizing pharmacotherapy. We evaluated 720 cases admitted in 7 bedded ICU of a tertiary care hospital. The Patients were admitted for Medical and Surgical indications, Orthopaedics and OBG Indications for admission in Intensive Care Unit. The demographic data of 720 patients admitted to the ICU during the three years' study period revealed that the 322(44.72%) were male and 398(55.27%) were females. This finding were compared with *Mahendra K Patel et.al*., (2013)[15] and the demographic findings were more female compared to this study.

FDCs were also commonly prescribed. This had also been observed in previous studies carried out *Lohani SP et al., (*2006)[16]. this study noted the use of a FDC of amoxicillin and clavulanic acid. In Our Study Piperacillin Tazobactam was mostly used. The use of total number of drugs and parenteral formulations may be comparable with the general condition of the admitted patients in different ICU settings.

More critical patients were admitted in our ICU. Antimicrobial drugs (79.02%), and inotropes (20.78%) were the commonly utilized groups lesser to *John et al.,* (2011) [17]. Cephalosporin's, metronidazole and penicillins were the most commonly prescribed antimicrobials in other studies previous studies. However, Meropenem, and piperacillin + Tazobactam were the most utilized antimicrobials similar to the *ShankarPR et al*., (2010)[18], Crucio *DJ et al*., (2009)[8]studies.

The average number of drugs in our study was 3.25 less than to that reported in Aparna *Wiliiams et al*., (2011) [7] other studies. The average number of drugs should be kept as low as possible to minimize the risk of drug interactions, development of bacterial resistance and hospital costs.

The DDD/100 bed days was found to be in our hospital was found to be 113.19. According to *HamdiSözen et al*., (2013) [19] Study the DDD/100 bed day's consumption was found to be 87.8%. These values are higher than the values in our study. The utilisation of Meropenem was 18.10%, Piperacillin tazobactum15.53(%), Ceftraixone11.20(%), Clindamycin 9.83%, Colistin9.374%, Metronidazole8.24%, Amoxicillin clavulunate 6.7%, Azithromycin 6.12%. In the individual analysis of antimicrobial agents utilized at hospital in the period of this study, the most consumed were Meropenem and Piperacillin Tazobactam. The Meropenem consumption has decreased from 20.35 DDDs/ 100 patients-day in the year of 2015 to 14.18DDDs/100 patients-day in the year of 2017. Blood Tissue culture and sputum were the most common specimens sent for culture and sensitivity testing. Testing was done in 26.3% of patients compared to 24.8% reported in *Shankar PR et al*., (2003) [20]. The organisms isolated were sensitive to the commonly used antibiotics.

CONCLUSION

In conclusion, antibiotics utilized were found to be rational but further studies are recommended on periodic basis for preparation of quality standard antibiotics guidelines. Study also highlights the need for improving the prescribing pattern to guide appropriate use of drugs in a rural Critical care setting. Therefore, intensivists should be sensitized regarding rational pharmacotherapy; restricting drugs to essential bare minimum and judicious use of antibiotics.

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