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DRUG UTILIZATION STUDY OF RESTRICTED ANTIBIOTICS IN INTENSIVE CARE UNITS OF MCGANN DISTRICT TEACHING HOSPITAL, SHIVAMOGGA, KARNATAKA.

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ABSTRACT **BACKGROUND:** Drug utilization studies have very important value since it can help us to interpret, assess and improve prescribing patterns for diseases and ways to use medicine. **OBJECTIVES:** The objective of the study was to assess the prescription pattern and evaluation of restricted antibiotics' usage in Intensive care units (ICUs) along with observation any adverse drug reactions. **MATERIALS AND METHODS:** After taking approval from Institutional Ethics Committee study was undertaken over a period of 6 months. A standard case record Performa was used to collect the demographic, clinical and drug prescription data of cases in the ICU who were prescribed restricted antibiotics. Its indication, dose, frequency and duration were entered. Data was analysed was done by using descriptive statistics. **RESULTS:** A total of 200 cases who were admitted in ICU's were evaluated with mean age of 58.6. Average duration of stay in ICU was 4.52 days. Pneumonia (46%), septicaemia (23%), febrile neutropenia (11%), intra-abdominal infections (8%) were common cases who were prescribed restricted antibiotics reported in ICU. Cephalosporins (52.22%) were commonly prescribed followed by Meropenem (19.4%) and Vancomycin (12.3%). Number of antimicrobials prescribed per patient was 1.54. In only 18% of the cases culture sensitivity test was performed. **CONCLUSION:** Optimum and appropriate use of antimicrobials has to be done in ICU to prevent multidrug resistance and to improve patients' morbidity and mortality. The restricted antibiotics must be used after obtaining microbiological report only. Proper hospital or institutional antibiotic policy must be implemented for continuous monitoring of antimicrobial use to improve antibiotic prescribing.

KEYWORDS : Restricted antibiotics, Drug utilization study, ATC/DDD classification, Infectious diseases.

INTRODUCTION

Infectious diseases contribute to most common cause of curable morbidity and mortality in the world. Discovery of antibiotics since 1928 has been a boon to treat and prevent infections. Antimicrobial agents are "Magic bullets" have become most commonly used drugs in all hospital either to prevent or treat infections and are responsible for significant decline in infection related morbidity and mortality.[1-2] Newer antimicrobial agents are being added to the list to overcome the antibiotic resistance, which has become a global problem.

Critically ill patients who are admitted to ICU are highly susceptible to infections due to decreased immunity and exposure to resistant microorganism. Also use of invasive procedures like intubation, catheterization, tracheostomy and central venous cannulisation predisposes the patient to nosocomial infections.[2] This predisposes the patients to high antimicrobial pressure. Judicious use of antimicrobial agents is very important in ICU to prevent treatment failure, drug interaction and adverse drug reactions.[3,4]

Drug utilization studies on antimicrobials are needed for detecting, monitoring, and fighting emergence of resistant bacteria.[4] Use of antimicrobials in ICU is very important since careful titration and monitoring of dosage regimen is required for ideal treatment outcome. The Anatomical Therapeutic Chemical (ATC) Classification/defined daily dose (DDD) system is used for drug utilization research in order to improve quality of drug use and is recommended by the World Health Organization (WHO) as the international standard for drug utilization studies.[5,6] Drug utilization studies of antimicrobials in ICU will ensure safety and efficacy of antibiotics to improve health status.

Irrational use, overuse or misuse of antimicrobials results in development of resistance and also contribute largely to the hospital expenditure.[7,8] Restriction on usage of antibiotics will help in reducing overall health cost along with adverse drug effects. Also, it helps in facilitating the emergence of multi drug resistance. The goal of restriction is to maintain a low resistance levels to certain drugs and increasing the treatment options available in near future.[7-9]

Our hospital, Mc Gann District Teaching Hospital, Shivamogga, India is a tertiary care centre. We have no baseline data on utilization of antimicrobials in ICU of our hospital. The study will be helpful in analyzing the usage of antibiotics and make any necessary changes in the prescription pattern. The aim of our study is to assess the utilization of restricted antibiotics in ICU to prevent emergence of antibiotic resistance and adverse events. Our objective is to assess the prescribing pattern of restricted antibiotic in ICU.

MATERIALS AND METHODS

Study Design

This was prospective observational study carried out in the ICUs of Mc Gann teaching District Hospital, Shivamogga, India from July 2016 to January 2017. Study was initiated after obtaining permission from the Institution Ethical Committee with reference number SIMS/IEC/296/2017-18. A written informed consent was taken from the relatives/guardians of the patient or the patient, they were explained clearly and in detail the nature and the purpose of the study.

Selection Criteria Of Patient

Inclusion Criteria:

1.Adult patients above 18 years of age and of either gender who were admitted in medical, or surgical Intensive Care Units.
2.Those patients or their relatives who gave consent and were willing to participate in this study.

Exclusion Criteria:

1.OPD patients and patient in casualty wards
2.Patient discharged against medical advice
3.Lactating and pregnant women
4.Patient who transferred out or expired within 24 hours of admission.

Method Of Data Collection

A detailed history and demographic data of the patient was noted down. Data was collected using well structured case record forms. A total of 200 prescription was reviewed for data collection as per case record forms. Number of restricted antimicrobial agents prescribed in the order of preference, dose of the drug, dosage form, route of administration, frequency of administration was noted. Clinical and laboratory relevance in use of the restricted antibiotics was assessed. The antimicrobial agents given along with restricted antibiotics was also noted. Antibiotics prescribed at the time of discharge were also taken in account. Laboratory parameters were also assessed regularly to find any variations. Culture and sensitivity reports were analyzed for the rationality of the antibiotic usage. All patients were followed up until the discharge of ICU.

Data Analysis-

Data was analyzed by assigning ATC code to antimicrobial use and calculation of DDD/100 bed day. The restricted antimicrobials were

classified using the ATC Classification system, and drug utilization was measured as DDD/100 bed-days. The DDD per 100 bed-days was calculated by the formula:

$$\text{DDD/100 bed days} = \frac{\text{Number of units administered in a given period x 100}}{\text{DDD x No.of days x no.beds x occupancy index}}$$

STATISTICALANALYSIS

The data was tabulated analyzed statistically by using appropriate software. Data were expressed as absolute numbers with or without percentages, as means with standard deviation or as medians with ranges.

RESULTS

In the study we collected data from 200 patients case record sheet out of that 123 were male and 77 were female. Average age of patients was 58.6 (±16.8). Diagnosis of cases admitted in ICU were respiratory tract infections, gastrointestinal tract, poisoning, skin and subcutaneous tissue infections, urinary tract infections, Septicaemia, Meningitis and other central nervous systems (CNS) infections and Others.

Out of 200 patients 113 patients were prescribed restricted antibiotics (56.5%). In all, the number of patients who were prescribed antimicrobials other than restricted antibiotics were 183(91.5%). On an average the antibiotic prescribed per patient was found to be 1.54±0.71. The distribution of antimicrobial use according to the type of use showed therapeutic prescriptions (76.8%) more than prophylactic prescriptions. Frequent diseases where restricted antibiotics were prescribed are pneumonia, septicaemia and febrile neutropenia.

Table 1: Age and Sex distribution

AGE	Male	Female	Total
18 - 35	20	11	31
36 - 55	32	28	60
56 - 75	62	32	94
76 - 95	9	6	15
TOTAL	123	77	200
Mean ± SD			58.6 ± 16.8

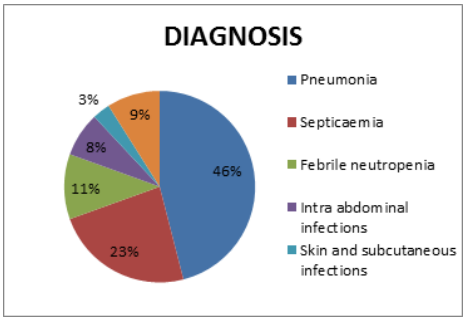

Figure 1: Percentage Of Patients Prescribed With Restricted Antibiotics

Cefepime was most commonly (34.51%) prescribed restricted antimicrobial agent, followed by Meropenem (19.4%), Cefoperazone/Sulbactam (13.27%), and Vancomycin (12.38%). The prescribed antimicrobials were given ATC code, and their number of DDDs was calculated according to the WHO formula as mentioned in Materials and Methods section. These results are shown in Table no 2. Average duration of prescribed antimicrobials was 4.52 days (±2.13 days) in ICU.

Table 2- Analysis Of Use Of Antimicrobials According To ATC/DDD System

ANTIMICROBIAL AGENT	A T C CODE	WHO DDD	N O . O F PATIENTS	UNITS	DDD/100 B E D DAYS
Cefepime	J01DE 01	4g	39	234	29.25
Meropenem	J01DH 02	2g	22	33	8.25
Cefoperazone/Sulbactam	J01DD 62	4g	15	60	7.5
Vancomycin	J01XA 01	2g	13	28	7
Piperacillin/Tazobactam	J01CR 05	4g	11	44	1.5
Ceftazidime	J01DD 02	4g	5	12.5	1.56
Amikacin	J01GB 06	1g	3	1.5	0.75
Ciprofloxacin (IV)	J 0 1 M A02	0.5g	2	1.6	1.6
Aztreonam	J01DF 01	0.225 g	2	6	0.75
Amphotericin B	J02AA 01	0.35g	1	1.2	1.6

Clinical specimen was sent for cultures and sensitivity testing in 36 cases which yielded bacteria in 32 of 36 episodes of suspected bacterial infection. Microorganisms isolated from specimens of 36 episodes were multi drug resistant and were susceptible only to the restricted drugs. However, there were 6 cases, where antibiotics were changed according to the sensitivity data, and 2 cases that the antibiotics were continued despite the microbiological results showing that the pathogens were resistant to the drugs being used. In seven cases, pathogens were susceptible to first or second generation of Cephalosporins but patients were treated with Cefepime which would indicate an overuse of this drug. Among cultured negative specimens (4 cases) the antibiotics were continued in most cases, which were due to the clinical improvement.

Table 3 - Frequency Of Prescription Of Other Antimicrobials That Were Prescribed Concurrently

Antimicrobials concurrently used	Number/%
Cetriaxone	160 (87.43%)
Cefotaxime	34 (18.57%)
Gentamycin	27 (14.7%)
Metronidazole	18 (9.8%)
Ofloxacin	17 (9.2%)
Penicillin	12 (6.5%)
Sulfamethoxozole/Trimethoprim	11 (6.01%)
Erythromycin	10 (5.4%)
Amoxicillin/clavulunate	10 (5.4%)
Clindamycin	7 (3.8%)
Tetracycline	6 (3.2%)
Others	11 (6.01%)

Table 4 - Frequency Of Culture And Sensitivity Testing Before Prescribing Restricted Antibiotics.

Data	Number	Percentage
Use of restricted antibiotic after Culture and Sensitivity	36	31.85%
Use of restricted antibiotic without Culture and Sensitivity testing	77	42.07%

DISCUSSION

The present study on restricted antibiotics prescribed at the Intensive Care Unit of Mc Gann Teaching District Hospital, for a period of 6 months included prescriptions from 200 case record forms.

Male preponderance (61.5%) is observed and male: female is in accordance with the previous reports.[12] The average age in the study is - (58.6%) more than the previous reportings.[13]

The study indicated that restricted antibiotics were frequently prescribed empirically (42.07% or 77/113) at the initial treatment. This is because patients admitted were in critical condition and required urgent intervention. On the basis of clinical experience due to increased prevalence of multidrug resistant pathogens physician/surgeons preferred the use of broad-spectrum antibiotics in the initial treatment. On the account of risk-benefit ratio and clinical improvement of the patient the decision favoured the early treatment with restricted antibiotics. Also, the high incidence of multidrug resistant bacteria supported the use.

In our study therapeutic indication (76.8%) dominated over the prophylactic use of restricted antibiotics in contrast to previous study by Vishwanathan et al.[14]

The most common indication where the restricted antibiotics were used were pneumonia which is in contrast to previous studies, which had reported cancer, cardiovascular emergencies and chronic obstructive pulmonary disease. The emergence of multidrug resistant bacteria is due to serious and dangerous infections encountered in the ICU with lowering immunity of the patient or to the emergence of nosocomial infections.

The use of restricted antibiotics in the ICU under our study was (56.5%) 113/200, which shows the high usage more than recommended by WHO. The restricted antimicrobial use without the microbiological reports was in high proportion. But this high usage may be explained due to high incidence of complicated pneumonia and septicaemia in the ICU. Similar studies showed the used of restricted antibiotics was 49% which is little lower than in our study. Many other multispecialty hospitals have shown the utilization of these antibiotics 62% which is more than our study. However, AFMC, Pune shows 10% use of the restricted antibiotics where the programme for improvement of these antimicrobials is going on.[15]

Cefepime was most common restricted antibiotic used in our study (DDD/100 - 29.5). This may be attributed to its wide spectrum of antibacterial activity and excellent action on gram-negative organisms. This is high use of Cefepime compared to international standards.[10] This is an alarm for our prescribers to reduce the use of this Cephalosporin and use it only after culture and sensitivity testing. Also, the DDD in our study was high because the dose adjustment was not done in any patient with renal impairment. Cefepime is most abused restricted antibiotic in the ICU of our hospital. This warrants an urgent education program for physicians/surgeons to improve antibiotic prescribing.

The ATC/DDD system is very effective tool for comparison of drugs. The DDD calculated in our study serves as a baseline data for comparison in future studies.[11] This will help in comparison the trends over years or after introduction of antibiotic usage reforms implemented. These data can also be used in comparing other academic research and reports.

The average duration of ICU stays (4.15 days) is similar to Shankar et al. (2005) and Shrishyla et al.[12,16] Concurrent antimicrobials used in our study were Cephalosporins (94.30%), Gentamycin (14.67%) and Metronidazole were the other most commonly prescribed antimicrobials similar to previous studies. Our study showed lower utilization of antibiotic sensitivity (18%) testing than Shrishyla et al and other studies.[16] There is requirement of continuous antimicrobial auditing programme to curtail the use of both restricted and concurrent antibiotics.

Limitations -

More diverse number of patients can be included with larger sample size. We had not interfered in the prescription when irrational/overuse was seen. A randomised controlled study can be conducted by adopting antibiotic order forms and hence improve the study design.

The aim of our study was to improve antibiotic prescribing. The measures to improve the antibiotic usage that can be taken in our hospital are by implementing prescribing guideline, close monitoring of the prescriptions, introduction of antibiotic order forms before dispensing restricted antibiotics and cooperation from all the hospital staff. The selection of initial appropriate antibiotic regimen is important for reducing the mortality.

CONCLUSION

The optimum use of antimicrobial agents in intensive care unit is crucial, due the seriousness of the infection and the emergence of the resistance. There is need to increase the utilization of antibiotic sensitivity testing for the better selection of antimicrobials and to reduce the mortality rate. Continuou monitoring of antimicrobials is required and to evaluate the risk benefit ratio of the use of higher restricted antibiotics. Avoiding the use of restricted antibiotics helps to improve sensitivity to various antibiotics and the morbidity and mortality of the patients and also helps in reduction in development of antibiotic resistance. Proper Hospital Antimicrobial policy is required to reduce the prevalent abuse and to promote appropriate use of antimicrobial drugs based on the culture and sensitivity report.

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