Section: Pharmacology

Original Research Article

EVALUATION OF ANTIMICROBIAL AGENTS' PRESCRIPTION PATTERN IN ADULT MEDICAL INTENSIVE CARE UNIT AT TERTIARY CARE TEACHING HOSPITAL IN SOUTHERN RAJASTHAN: AN OBSERVATIONAL STUDY

Ruchi Tantia[1], Meena Atray[2], Apurva Agrawal[3], Pratik Tantia[4]

[1]Assistant Professor, Department of Pharmacology, Ananta Institute of Medical Sciences & Research Centre, Rajsamand, India.
[2]Senior Professor, Department of Pharmacology, RNT Medical College, Udaipur, India.
[3]Professor, Department of Pharmacology, RNT Medical College, Udaipur, India.
[4]Professor, Department of Anaesthesiology, Ananta Institute of Medical Sciences & Research Centre, Rajsamand, India.

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Corresponding Author:
Dr. Pratik Tantia,
Professor, Department of Anaesthesiology, Ananta Institute of Medical Sciences & Research Centre, Rajsamand, India.
Email: dr.tantia@gmail.com

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ABSTRACT

Background: Antimicrobial agents are used extensively in Intensive care units and if used inappropriately, can lead to increase in morbidity, mortality and cost of the treatment. Our Institute is a tertiary care teaching Hospital. Therefore, it becomes important to know about the extent and pattern of Antimicrobial agents' use and their relation to the other parameters like comorbidities and outcome of the patients

Materials and Methods: This observational study was conducted in MICU at tertiary care teaching hospital in Southern Rajasthan for a period of 4 months.

Results: Out of 316 patients, 122 (38.6%) were females and 194 (61.3%) were males with a male to female ratio of 1:0.62. Hypertension was the most common co-morbidity in studied patients (81;42.6%), followed by Diabetes (55;28.9%), CAD (29;15.3%) and COPD (26; 13.7%). 291 (92.08%) patients were prescribed AMA and a total of 692 AMA prescriptions were studied. Five most commonly prescribed AMA were Ceftriaxone (27.31%) followed by Piperacillin+ Tazobactam (9.39%), Azithromycin (6.79%), Metronidazole (6.36%) and Artesunate (5.63%). The mean number of AMA prescribed in the patients during ICU stay was 2.00 ± 1.44.

Conclusion: Excessive use of Antimicrobial agent's was observed that could lead to the emergence of resistance. There is an urgent need to create awareness about Antimicrobial stewardship programme and make policies to contain the problem of Antimicrobial resistance (AMR).

Keywords: Antimicrobial agents, Prescription pattern, Antimicrobial resistance, Drug utilization study.

INTRODUCTION

Antimicrobial agents are among the most widely prescribed medications for the Infectious diseases which are a significant cause of morbidity and mortality worldwide. But the situation gets worsened when infection is due to a resistant organism.[1,2] Though antibiotic resistance is a natural phenomenon that occurs when microbes are exposed to antibiotics, but inappropriate choices, dosing schedules, poor adherence to treatment guidelines also contribute significantly to Antimicrobial resistance (AMR).[3-5] AMR and no replacement options due to paucity in the development of newer antibiotics have created serious public health problem globally as well as in India.

Intensive care units (ICU) receive critically ill patients either from Emergency Department or from general hospital wards when they become critically ill. Severe and life-threatening infections are common among them. Most infections being bacterial or fungal require antimicrobial therapy for clinical improvement. So, AMAs have become

cornerstone of therapy in the ICU. But AMAs are often not optimally administered. The indiscriminate and extensive use of AMAs in ICUs has been observed with increase in the risk of multidrug resistant infections.[6]

India is reported to be largest consumer of AMAs.[7,8] Various hospitals in India are reporting high levels of resistance to Fluoroquinolones, carbapenems and polymyxins.[7,9,10] This trend of AMR in India to the last resort AMAs is quite alarming.[7,11]

To know the pattern of AMA usage in our institute, tertiary care teaching hospital in Southern Rajasthan, this study was conducted. This would be of great help in the formation of guiding policies for AMA use in Future.

MATERIALS AND METHODS

Study design and Setting

This observational study was conducted at MICU, MB Hospital, Udaipur, a tertiary care teaching hospital in southern Rajasthan.

Sample size and Study Duration

The study was conducted for a period of 4 months from September 2021 to January 2022. A sample of 316 patients was selected. The sample size was calculated using prevalence from previous studies.[12-14]

The study was approved by Institutional Ethics Committee (RNT/Stat./IEC/2021/ 482).

Inclusion Criteria

- All patients (both male and female) above 18 years admitted to MICU.
- Patients or relatives willing to give informed consent.

Exclusion Criteria

- All those patients who were shifted to other ICUs or wards or declared dead within 24 hours of admission to the MICU.
- Incomplete patient data

All male and female patients (above 18 years) admitted to MICU and fulfilling inclusion criteria were included in the study. Before collecting the information about patient, the purpose of study was explained to the patients (if possible) and their relatives. Only after taking informed consent from the patient or relatives, data was collected.

Data like age, gender, diagnosis, investigations, comorbidities were taken from Case record sheet (CRS) of the Patient. Data related to AMA was also obtained from CRS. Patients (if possible) or relatives were interviewed daily for the relevant information till their discharge from MICU.

"Antimicrobial Prescription" means start of one AMA. For example, if a clinician wrote a prescription for amoxicillin-clavulanate and amikacin. The patient was considered to have received two prescriptions of AMA.

Fixed dose combinations of AMA where second component has not been assigned ATC code were considered one AMA. For example, amoxicillin-clavulanate was considered to be one AMA as clavulanate has no unique ATC code.

Number of AMAs means the total number of AMA that were prescribed during the stay in the ICU.

Statistical Analysis

The study data was collected and entered in the Microsoft excel sheet and statistically analysed. Descriptive statistics was used. For quantitative data mean and standard deviation were calculated and z-test was used. For qualitative data, Percentage was calculated and chi-square test was used. P value < 0.05 was considered as statistically significant.

RESULTS

A total of 316 patients aged 18 years and above admitted to Medical ICU for various indications were studied. Out of 316 patients, 122 (38.6%) were females and 194 (61.3%) were males with a male to female ratio of 1:0.62. Admissions to the MICU were common in the age group 51-65 years (33.2%) followed by <35 years (25%), >66 years (21.8%) and 35-50 years (19.9%). [Table 1]

Table 1: Age-Group Wise Distribution of Cases

S.No.	Age group (Years)	No. of males (n=194)	No. of females (n=122)	Total (n=316)
1.	≤35	42(21.6%)	37(30.3%)	79(25%)
2.	36-50	46(23.7%)	17(13.9%)	63(19.9%)
3.	51-65	68(35.0%)	37(30.3%)	105(33.2%)
4.	≥66	38(19.5%)	31(25.4%)	69(21.8%)

$\chi 2 = 7.513$, p= 0.057 (not significant)

The most common indications for MICU admission have been shown in the Figure:1 Various Co-morbidities were found in MICU patients. Hypertension was the most common co-morbidity in studied patients (81;42.6%), followed by Diabetes (55;28.9%), CAD (29;15.3%) and COPD (26; 13.7%) [Figure: 2]. Among 316 patients, 291 (92.08%) were prescribed AMA and a total of 692 AMA prescriptions were studied. Five most commonly prescribed AMA were Ceftriaxone (27.31%) followed by Piperacillin+ tazobactam (9.39%), Azithromycin (6.79%), Metronidazole (6.36%) and Artesunate (5.63%). [Figure: 3]

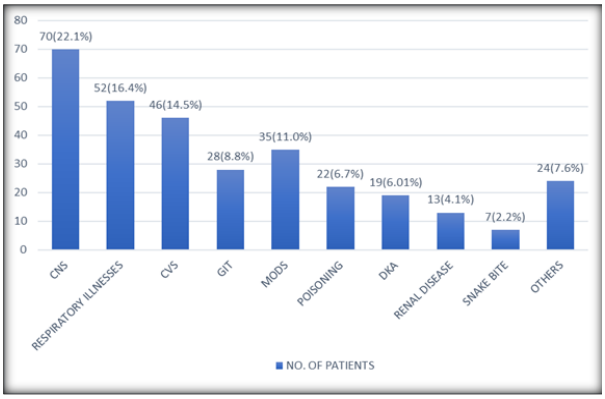

Figure 1: Indications for MICU admission

[Others include Guillain barre syndrome, Dengue fever, Scrub typhus, Puerperal sepsis, malaria]

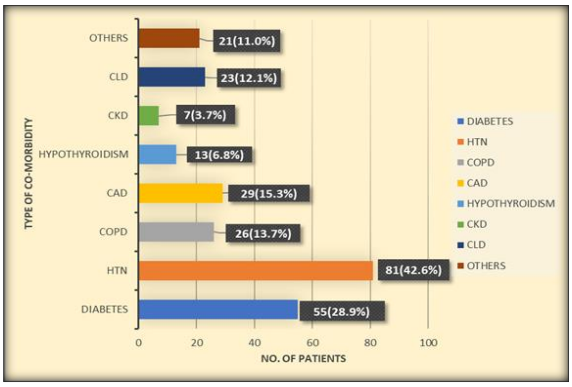

Figure 2: Distribution of Co-Morbidities

*Total percentage is more than 100 as many patients are having more than one comorbidity

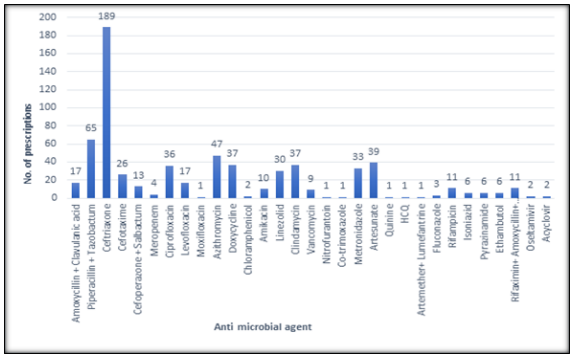

Figure: 3 Prescription frequency of Individual AMA

*291 patients received AMA therapy.

Total no. of AMA prescribed to the patients during MICU stay was also studied. [Table: 2]
The number of AMA prescribed to the patients and the number of comorbidities in them was studied. The mean number of AMA prescribed in the patients having one comorbidity was 2.00 ± 1.44 and 2.21 ± 1.41 in the patients having 2 comorbidities [Table: 3]. This difference in the mean no. of AMA prescribed in patients with comorbidities was not found to be significant. (p=0.43).

Table 2: Number of AMA prescribed in MICU

S.No.	No. of AMA's	No. of Patients(%) (n=291)
2	1	105(36.1)
3	2	81(27.8)
4	3	51(17.5)
5	4	27(9.3)
6	5	12(4.1)
7	≥6	15(5.1)

Table 3: AMA use Vs Number of Comorbidities

S.No.	No. of Comorbidities	AMA (Mean ± SD)
1.	1	*2.00± 1.44
2.	2	*2.21± 1.41
3.	≥ 3	2.16± 1.43

*p= 0.43 (not significant)
The mean ± SD and median of duration of AMA therapy was 5.56 ± 4.68 and 4 respectively.
Length of stay in MICU ranged from 1 to 34 days with an average of 5.7 ± 4.98 days.
Out of 316 patients, 145 got improved (45.8%). This included the patients discharged and shifted to other wards. 131 patients (41.4%) expired during their stay in the ICU and 40 patients (12.6%) went LAMA.
Outcomes in the various age groups was studied. Maximum improvement (50.6%) was seen in the age group of <35 years. Total mortality during the study period was 41.4% with maximum mortality of 40.9% in the age group 51-65 years. [Figure: 4]

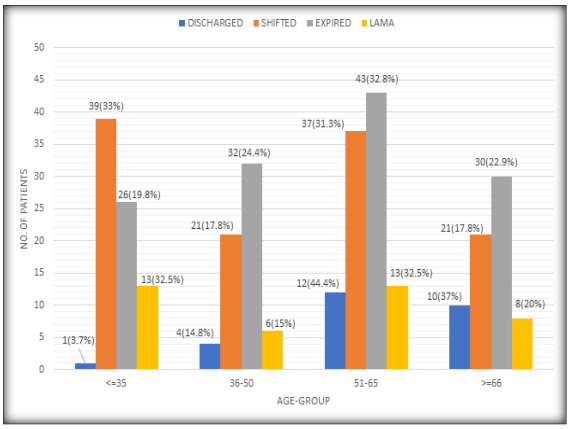

Figure 4: Age-group wise Outcome

DISCUSSION

The present study revealed that a greater number of male patients were admitted with male: female ratio of 1: 0.62 which is in accordance with the studies done by Suraj B et al. in 2019 at Gulbarga in Karnataka, Naikwadi et al in 2017 at Aurangabad in Maharashtra and Patanaik et al in 2015 at Bhubaneshwar in Odisha.[14-16] In the present study, maximum number of patients admitted in MICU were from the age group 51-65 years, both among males and females which is similar to the studies done by Anand et al, Satapathy et al , Suraj B et al, and Al-zakwani et al.[12,15-18] Naikwadi et al reported maximum number of admissions in 21-30 years age group in their study.[14] The reason for this finding could be the illness pattern among the study population.

Most common indications observed in the present study were related to Central Nervous System (CVA, encephalopathies and meningitis), Respiratory System and Cardio Vascular System. Multi Organ Dysfunction Syndrome (MODS), Gastro intestinal (GI) disorders, Organophosphorus (OP) poisoning, Diabetic Ketoacidosis (DKA) and snake bite were other indications. This finding was similar to the study done by Khirasaria et al(19) .Trauma was the most common indication reported by Satapathy et al and Al- zakwani.[17,18] OP poisoning was the most common indication observed by Naikwadi et al, done at Aurangabad.[10] This variation in the finding could be due to the different geographic regions of studies and the type of ICU they might have included their study. Hypertension was observed to be the most common co-morbidity in the present study followed by diabetes, CAD and COPD. This finding was consistent with the studies done by Anand et al, Naikwadi et al and Thomas et al done at Mangalore, Aurangabad, and Pune respectively.[12,14,20] In the present study Chronic liver disease(CLD) and Chronic obstructive pulmonary disease(COPD) were more commonly observed in males. This could be supported by the presence of risk factors like smoking and drinking alcohol which are more commonly seen in males.[21,22]

MICU is the setting of maximum AMA utilisation in any hospital; therefore, it becomes important to know the extent and pattern of AMA use. Total AMA utilization in our study was found to be 92.08%. AMA utilization was found to be 80.3%, 80.4%, 70.85% and 96% in the studies done by Debasis et al, Anand et al, Naikwadi et al and Patanaik et al in the year 2017, 2014, 2017 and 2015 respectively.[12-14,16] Average no. of AMA per patient in the present study was found to be 2.27±1.37 which is similar to the study done by Patanaik et al but higher than 1.71, 1.73 and 1.74 in the studies done by debasis et al, Anand et al and Amit GS et al respectively.[12,13,16] After comparing total AMA utilization (92.08%) and mean AMA utilization (2.27±1.37) with other studies it was observed that higher use of AMA (92.08%) was done in the present study which was also reported by Patanaik et al (96%). The difference found in the utilization of AMA in the various AMA utilization studies could be due to the differences in the indication of patients' admission, seasonal variation in the different regions of the country.

Cephalosporins (n= 692,33%) were the most commonly utilized class of AMA in the present study followed by Penicillin+ β lactamase inhibitors (n=692, 11.8%). When individual AMA utilization was analyzed it was observed that 3rd generation Cephalosporin Ceftriaxone was the most commonly utilized AMA in most of the studies.[12,14,16,17,19,23] except in the study by Suraj et al where most commonly utilized AMA was Metronidazole (29.7%) and in the study by Debasis et al, Meropenem (25.56%) was reported to be most commonly utilized AMA.[13,15] Maximum use of CEFTRIAXONE might be explained by its broader spectrum and lower toxicity. Azithromycin (6.8%), Metronidazole (6.4%) and Artesunate (5.6%) were among commonly used AMA besides ceftriaxone and piperacillin + Tazobactam in the present study. This is in contrary to the results of study by Patra SK and Saxena S where carbapenems were used besides ceftriaxone and Piperacillin +Tazobactam. Meropenem (0.57%) and vancomycin (1.3%) were used less commonly in the present study. This is the positive finding from the present study as their use should be restricted only to resistant cases. The difference in AMA utilization in various studies might be due to different sensitivity pattern of microbes and the practising habits of clinicians.

Out of 291 patients in our study who received AMA, 105(36.1%) received one AMA, 81(27.8%) received 2 AMA, 51(17.5%) received 3 AMA, 27(9.3%) received 4 AMA, 12(4.1%) received 5 AMA and 15(5.1%) received 6 or more AMA during stay in MICU. This finding is similar to the study done by Patanaik et al.[16] In the present study patients were given more than one AMA due to mixed infections, to treat Gram positive, Gram negative and anaerobic infections. Another finding in the present study was that patients were given AMA one after another when the first one was not effective.

The duration of therapy in most of the patients was 4 days with a mean of 5.56±4.68 days which corresponds to the mean length of stay 5.7±4.98 days. Some patients stayed for about a month and AMA were also continued. Longer duration of AMA therapy might be due to the inadequate response of the patients to initial empirical therapy. It is noteworthy to state here that longer duration of AMA therapy predisposes the patients to infections by resistant microbes.[24]

The risk of various infections increases with the presence of comorbidities and so, the use of AMA. But the difference in the mean number of AMA prescribed in patients with one and multiple

comorbidities in the present study was not found to be significant (p=0.43). The higher utilization of AMA in the present study requires necessary and urgent steps to be taken for judicious use of AMA.

45.8% patients got improved (discharged and shifted to wards), 41.4% patients expired during their stay and 12.6% left against medical advice (LAMA). The mortality in our study is similar to the study by Khirasaria et al. Improvement rate was better in our study as compared to other study.[19] The outcome of LAMA patients and effectiveness of AMAs in them could not be assessed. Maximum number of improved cases (50.6%) were seen in the age group < 35 years. Younger patients with lesser number of comorbidities are immunocompetent which might be the reason of maximum improvement in this age group. Maximum no. of mortality occurred in the age group 51-65 years. It is noteworthy to state here that maximum number of patients having comorbidities also belonged to the age group 51-65 years which might be the reason of increased mortality.

Comparing the results of present study to the previously done studies, it was found that overall consumption of AMAs was much higher. In today's world, ICUs are associated with the emergence of Antimicrobial resistance due to excessive and inappropriate use of AMAs which can certainly influence mortality and morbidity. Therefore, various measures should be taken. For example, educating clinicians about the prevalence of microbes and resistance patterns, antimicrobial stewardship, minimising the time from sample collection to report generation so that appropriate AMAs could be started timely. The whole management should be sensitized about AMSP.

Strength of the Study

Being a tertiary care teaching hospital, patients of varied diagnosis and severity were admitted. As the treatment is free of cost the patients that were admitted, came from all the social and economic strata. The present study was first AMA utilization study of its kind in MICU in the institute where all the drugs were available free of cost.

Limitation of the Study

The present study was done on a limited number of patients. The severity of illness was not judged at the time of admission to MICU. Outcome of the LAMA patients could not be assessed. All the patients were considered fresh admission, readmissions were not taken into account. Bacterial resistance patterns were not studied.

CONCLUSION

Excessive use of antimicrobial agents' was observed that could lead to the emergence of resistance and hence increase in mortality and morbidity. There is an urgent need to educate about AMSP and implement the same. There is also an urgent requirement to form hospitals' own Antibiogram. This becomes the utmost responsibility of the management team to take action at the earliest to contain the problem of AMR.

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