Asian Journal of Pharmaceutical and Clinical Research
Vol. 4, Issue 2, 2011 ISSN - 0974-2441

Research Article

DRUG UTILIZATION STUDY OF ANTIMICROBIAL AGENTS IN MEDICAL INTENSIVE CARE UNIT OF A TERTIARY CARE HOSPITAL

LISHA JENNY JOHN[1*], PADMINI DEVI[2], JENNY JOHN[3], SHOBA GUIDO[2]

Department of Pharmacology, Gulf Medical University, UAE, Department of Pharmacology, St. Johnâ€™s Medical College, India, Department of Paediatrics, Gulf Medical College Hospital, Gulf Medical University, UAE, Email: drlishaj@yahoo.com

ABSTRACT

Background: Patients admitted to the Intensive care unit receive multiple medications from a variety of pharmacological classes due to various life threatening illnesses. This study was conducted to assess the patterns of antimicrobial agents and to suggest necessary modifications in prescribing practices to achieve rational therapeutic practices. The present study aims to study the prescribing patterns of drugs and rationality of antimicrobial drug use in the medical ICU of a tertiary care hospital.

Methods: A prospective observational study was carried out at the 15 bedded medical ICU of St. John's Medical College Hospital, Bangalore from October 15th 2006 to September 15th 2007. The relevant data on drug prescription of each patient was collected from the inpatient case record. Drugs were classified into different groups based on WHO-ATC classification. The demographic data, disease data and the utilization of different classes of antimicrobial agents as well as individual drugs were analyzed.

Results: Of the 902 patients admitted in the medical ICU during the study period, 728(81%) consecutive patients were included for the analysis. Male to female ratio was 1.9. The mean for age was 49.21±15.84 years. Extensive polypharmacy (100%) was noticed. The average number of drugs per patient (prescription) was 11.6± 2.09. Cephalosporins 505 (69.3%) and aminoglycosides 263(35%) were the commonly prescribed antimicrobial drug class. Cefoperazone (J01DD12) 218 (30%), amikacin 211(28.9%), metronidazole 208(28.6%) were the commonly prescribed antimicrobial drug class. A total of 228 perscriptions (31.3%) contained two antimicrobial prescription and (187) 25.7 % contained 3 drugs. Cefoperazone + sulbactam (J01DD62) 224(30.8%) was the most common FDC noticed.

Conclusion: A wide spectrum of clinical disorders was noticed. Overall extensive poly-pharmacy and poly-pharmacy among antimicrobial agents was noticed.

Keywords: Drug utilization, Anti-microbial agents, Intensive care unit, Polypharmacy.

INTRODUCTION

Patients admitted to the Intensive care unit (ICU) are seriously ill and often suffer from chronic critical illnesses. These patients receive multiple medications from a variety of pharmacological classes due to life threatening illnesses[1]. They are a unique group of population with diverse disease processes, existing or impending multi organ failure and potentially altered pharmacokinetic and pharmacodynamic characteristics onto which pharmacotherapy is added.

Drug therapy in critically ill is therefore complicated. The judicious use of these medications can be lifesaving. The routine use of conventional drug dosage regimens may expose a substantial portion of ICU patients to drug related problems such as treatment failure, drug interactions and high risk of adverse drug reactions. Careful titration of dosage regimens becomes imperative to ensure the ideal treatment outcome[2].

Antimicrobial agents are one of the frequently utilized drug classes in an ICU setting. Patients with critical illnesses are at higher risk of developing nosocomial infections and antibiotics are the most powerful and useful tools to manage these infections. Extensive and indiscriminate use of antimicrobial agents has been documented in ICUs in previous published reports[3-4].

The widespread use of broad spectrum antibiotics has lead to the emergence of several resistant strains of microbes. These contribute significantly towards rise in the escalating health care costs and patient morbidity and mortality [3-4]. Therefore monitoring and evaluation of prescribing patterns of antimicrobial agents are one of the recommended strategies to contain and control resistance also to improve the prescribing practices.

Drug utilization study is a component of medical audit that does monitoring and evaluation of the drug prescribing patterns and suggests necessary modifications in prescribing practices to achieve rational therapeutic practice as well as cost effective health care[5].

It also improves the standards of medical treatment at all levels of health care and answers several relevant questions with regard to the current prescribing trends.

The objective of this study was to assess the prescribing patterns of anti microbial drugs and rationality of drug use in the medical ICU of a tertiary care hospital.

MATERIALS AND METHODS

A prospective observational study was carried out at St. John's Medical College Hospital tertiary care, a teaching hospital with super speciality services from October 15th 2006 to September 15th 2007. The study was approved by the institutional ethics committee.

All inpatients admitted to the medical ICU during the study period were included as the study population. Patients who get transferred to other specialty ICUs from medical ICU within 24 hours of admission were excluded from the study population.

Permission to collect the data and accompany physicians on ward rounds in the medical ICU was taken from the head of medical ICU before starting the study. The relevant data was collected while accompanying the clinicians 6 days in a week and also from the inpatient medical records.

We have reviewed all the prescriptions and the details were collected during that particular hospital stay. To evaluate the drug prescribing pattern a specially designed proforma containing relevant details such as demographics (age, sex and outcome of the patient), clinical data (Clinical diagnosis and associated co-morbid conditions, length of ICU stay), and drug data was used.

Drugs prescribed (generic/brand name), dosage, route, frequency of administration were collected as per proforma.

Statistical analysis: The data was subjected to descriptive analysis using Microsoft Excel. Drugs were classified into different groups based on WHO-ATC classification[6]. Utilization of different classes of drugs as well as individual drugs was analyzed and presented as percentage.

Table 1: Top five drug classes prescribed among patients in the medical ICU

Sl. No.	Drug Class	Number of prescription (n=728)	Percentage of prescriptions
1	Anti-peptic ulcer agents	709	97
2	Antimicrobials	439	83
3	Ionotropes	340	46.5
4	Anti-hypertensives	315	43
5	Anti-diabetic agents including Insulin	314	43

Table 2: Prescribing frequency of systemic anti-infectious agents among patients in the medical ICU

ATCclass	Drug class	Drug$	ATC code	No (%) of prescriptions (n=728)
J01 – Antibacterials for systemic use				
J01D	Cephalosporins and other beta lactums	Cefoperazone	J01DD12	218(30)
		Ceftriaxone	J01DD04	173(23.8)
		Cefazolin	J01DB04	47(6.5)
		Meropenem	J01DH02	35(4.8)
		Cefotaxime	J01DD01	34(4.7)
		Ceftazidime	J01DD02	17(2.2)
		Cefuroxime	J01DC02	8(1.0)
		Cefipime	J01DE01	8(1.0)
J01G	Aminoglycosides	Amikacin	J01GB06	211(28.9)
		Gentamycin	J01GB03	41(5.6)
		Neomycin	J01GB05	8(1.0)
		Netilmycin	J01GB07	3(0.4)
J01X	Other anti-bacterials	Metronidazole	J01XD01	208(28.6)
		Vancomycin	J01XA01	59(8)
		Linezolid	J01XX08	8(1.0)
J01A	Tetracyclines	Doxycycline	J01AA02	93(12.7)
		Tetracycline	J01AA01	1(0.2)
J01M	Quinolones	Levofloxacin	J01MA12	34(4.7)
		Ciprofloxacin	J01MA02	31(4.3)
		Ofloxacin	J01MA01	7(0.9)
J01F	Macrolides and Lincosamides	Clarithromycin	J01FA09	34(4.7)
		Clindamycin	J01FF01	28(3.8)
J01E	Sulfonamides	Cotrimoxazole	J01EE01	28(3.8)
J01C	Penicillins	Crystalline Penicillin	J01CE01	28(3.8)
		Ampicillin	J01CA01	4(0.5)
		Benzyl Penicillin	J01CE01	3(0.4)
		Cloxacillin	J01CF02	2(0.3)
J02 – Antimycotics for systemic use				
J02C	Triazole derivatives	Fluconazole	J02AC01	35(4.8)
J02A	Antibiotics	Amphotericin	J02AA01	24(3.3)
J04 – Antimycobacterials				
J04A	Drugs for treatment of Tuberculosis	Rifampicin	J04AB02	28(3.8)
		Pyrazinamide	J04AK01	28(3.8)
		Ethambutol	J04AK02	28(3.8)
		Isoniazid	J04AC01	21(2.9)
J05 – Antivirals for systemic use				
J05A	Agents affecting theVirus directly	Acyclovir	J05AB01	12(1.6)
		Lamivudine	J05AF05	6(0.8)
		Indinavir	J05AE02	3(0.4)
		Nevirapine	J05AG01	2(0.3)
		Zidovudine	J05AF01	2(0.3)

Table 3: Prescribing pattern of fixed drug combinations among patients in the medical ICU

Fixed drug combination	ATC code	Number (%) of Prescriptions (n=728)	% out of total number of antimicobial FDCs (n=361)
Cefoperazone + sulbactam	J01DD62	224(30.8)	62
Amoxicillin+clavulanic acid	J01CR02	58(8)	16
Piperacillin + tazobactam	J01CR05	33(4.2)	8.3
Suphamethoxazole+trimethoprin	J01EE01	28(3.8)	7.9
Isoniazid+rifampicin+pyrazinamide+ethambutol	J04AM06	21(2.9)	5.8
Total		361 (5)	100

RESULTS

The total number of admissions in the medical ICU during the study period was 902 among which 728(81%) consecutive patients who got hospitalized were included for the analysis. Data on the remaining 128 patients were excluded for the analysis due to various reasons such as patients were shifted out of the medical ICU within 24 hours and thus did not receive active treatment in the medical ICU, incomplete charts, patients admitted due to lack of bed availability in another unit. Male to female ratio was 1.9. The mean for age was 49.21±15.84 years with a range of 18-91 years. The mean age among males was 49.2±15.7 years and among females 49.6±16 years. Patients above 55 years constituted 40.6% of the study population. The mean length of stay in the medical ICU was 6.22±3.3 days.

Out of 728 patients, the common clinical diagnoses included sepsis, acute renal failure, multi organ dysfunction syndrome, acute respiratory distress syndrome, pneumonia and lower respiratory tract infections. Among the 728 patients studied, 473 (65%) patients had ≥5 co-morbid conditions. The most common co-morbid conditions found were hypertension 221 (30.4%), diabetes mellitus in 201(27.6%), ischemic heart disease 74(10.5). Hypertension and diabetes were coexistent in 168 (23%) patients.

The total number of 8444 drugs prescribed among the 728 patients and the average number of drugs per patient (prescription) was 11.6±2 drugs. The mean number of drugs received by male and female patients where 11.7±2.2 and 11.4±1.9 respectively. It was observed that the maximum number of drugs prescribed to a single patient was 23. All the patients 728 (100%) received more than five drugs. Prescription by brand name was noticed in 70% of the prescription.

Anti-peptic ulcer drugs 709(97%), anti-microbial agents 679(83%), inotropes 340(46.5%) were the commonly utilized drug classes in the medical ICU. The utilization of top five drug classes in the medical ICU is listed in table 1.

Polypharmacy among various drug classes was observed. It was maximum 69% in antimicrobials, 41% among antihypertensives, 38% in corticosteroids, 32% in bronchodilators, and 20% in inotropes. Among antimicrobial agents, two antimicrobials were prescribed in 228 (31.3%), three and four in 187 (25.7%) and 89 (12.2%) respectively, ≥ 5 antimicrobial were prescribed in 30 (9.5%) patients as explained in Figure 1.

Cephalosporins 505(69.3%) and aminoglycosides 263 (35%) were the commonly prescribed antimicrobial drug classes (other than penicillins) (J01D class), and cefoperazone (J01DD12) 218(30%) was the commonest cephalosporin. Prescribing frequency of anti-infectious agents among patients in the medical ICU is detailed in Table 2. A total of 361 antimicrobial fixed drug combinations (FDC) were noticed among 728 patients. Cefoperazone+sulbactam (J01DD62) 224(30.8%) was the most common FDC noticed. Prescribing frequency of different antimicrobial FDCs is shown in Table 3.

Among 728 patients admitted to the medical ICU, 483 (65.6%) patients improved, 43(5%) patient's discharged at request, and 34 patients (3.8%) discharged against medical advice and 204 (28%) patients died.

DISCUSSION

The clinical setting in the medical ICU warrants the use of drugs from various drug classes. Rational prescription of drugs is essential for better patient care. The first step in any intervention programme to improve drug utilization is to assess the extent of existing problem in prescribing. The objective of our study was to evaluate the drug utilization patterns among patients admitted to the medical ICU of a tertiary care hospital.

The demographic results of patients admitted to the medical ICU over a period of 12 months revealed male preponderance with a mean age of around 50 years similar to a study carried out in Nepal in 2005[5]. In contrast, Smythe et al. study showed equal number of male and female patients admitted to the medical ICU with a mean age of 65 years[1]. Previous Indian study also documented male predominance which suggests that more males are admitted to the ICU in an Indian setting[8]. The probable reasons for this finding could be the male to female ratio is higher in the state of Karnataka. In the Indian scenario it is noticed that female populations are reluctant to utilize health care faculties even if they are critically ill and especially by the lower socio economic strata.

A wide spectrum of clinical diagnoses was observed including sepsis, renal failure, acute respiratory distress syndrome, multi organ dysfunction. Debilitating condition of the patients due to underlying disease, invasive diagnostic and therapeutic procedures and prolonged utilization of life support equipment predispose these patients to infections. Nina et al had reported that ICU contributes 20-30% of the nosocomial infections in the hospital[9]. Sepsis could have been the major contributor to the development of ARF observed in the study.

It was observed that 65.5% patients admitted to the medical ICU had more than five comorbid conditions with hypertension (30.4%), diabetes mellitus (27.6%), and IHD (10.5%) as the major comorbid conditions. 'Comorbidity' increases the total burden of the illness in a patient and also contributes to clinical outcomes as well as to economic outcomes[11].

The mean number of drugs received by patients in the present study (11.6±2 drugs) was comparable to Smythe et al study[1] (12±7.6 drugs) but higher compared to report from Nepal in 2005 which recorded a mean of 5.1±2.7 drugs[7]. It was noticed that most of the antimicrobial agents were prescribed by brand name (70%) which requires revision of current prescribing practice. Extensive polypharmacy (100%) that is more than five drugs were prescribed in all the patients. Polypharmacy is defined as concomitant use of five or more drugs and it could enhance drug interactions and drug related problems[12]. It is difficult to treat patients in the ICU with multiple co-morbidities with less number of drugs as they require drugs for treatment of specific condition as well as for prophylaxis, but it is also essential to keep a balance between the number of drugs and effective pharmacotherapy.

In contradiction to previous reports by Smythe et al[1] and Biswal et al.[8] who documented cardiovascular drugs and antimicrobials as the commonest therapeutic class, antipeptic ulcer drugs (97%) were most commonly utilized drug class in our study. In an ICU setup aggressive prophylactic and therapeutic utilization of antipeptic ulcer agents can be explained by the higher occurrence rate of stress induced ulcers among the critically ill patients.

High antimicrobial prescribing frequency was observed in our study inconsistent with earlier studies from Nepal and Turkey[7,14] which documented 30% and 57.5%. More than one antimicrobial agent was prescribed among (69%) of the prescriptions. This could be expected since sepsis, multi organ dysfunction, acute respiratory distress, pneumonia and lower respiratory tract infections was prevalent among the patients of the present study necessitating therapeutic as well as prophylactic utilization of antimicrobials. Antimicrobial protocol and guidelines; formulary based antimicrobial restrictions[15] can be used to improve rational usage of antimicrobials. A multidisciplinary approach can be adopted in the ICU set up involving intensive care specialist; infectious disease control specialist, pharmacists and microbiologists can work together for more rational antimicrobial pharmacotherapy.

Higher utilization of cephalosporins (J01DA) (69.3%) and aminoglycosides (35%) was noticed (table 2), similar to Usluer G et.al study[14] but, differed from Shankar et al[7] in which penicillins were the commonest antimicrobial drug class prescribed. Cephalosporins are commonly prescribed due to their relatively lower toxicity and broader spectrum activity. Cephalosporins often used in combination with aminoglycosides due synergistic activity and broader coverage of organisms for several serious gram negative infections. Among the antimicrobial agents cefoperazone

(30%), amikacin 211(28.9%) and metronidazole 208(28.6%) were the most commonly prescribed antimicrobial agent. Usluer et al[14] reported cefazolin and Biswal S et al[8] documented metronidazole as the commonly prescribed antimicrobial agent in their studies. Cefoperazone + sulbactam combination (J01DD62) (30.8%) was the most preferred fixed drug combination in contrast to amoxicillin + clavulanic acid noticed in Biswal et al[8] study. Since Biswal et al[8] study was carried in a government setup the findings differed from the present study which was carried out in a private institution. In our study, utilization of newer antimicrobial drugs were noticed such as meropenem and imipenem (carbapenems), clarithromycin (macrolides) linezolid (oxazolidinones), clindamycin (lincosamides), levofloxacin (quinolones), and vancomycin (glycopeptides).

The present study analyzed the antimicrobial drug utilization of a special population of patients admitted to the medical ICU of a super-specialty setting. The purpose of inpatient based prescription audit has advantage of minimizing the 'drop-outs' as patients had to purchase and take the prescribed drugs and limitation of the study was qualitative assessment of antimicrobial drug utilization was not performed.

CONCLUSION

In conclusion, a wide spectrum of clinical diagnoses and a variety of drugs were utilized from various drug classes. Overall, scope for improving rational use of antimicrobial agents exists. The present study on antimicrobial drug prescribing patterns in medical ICU can provide a framework for continuous prescription audit in the medical ICU. Longitudinal surveillance of antimicrobial drug use in medical ICU can be carried out to create a database to compare the future trends in utilization of antimicrobial agents. Pharmacoeconomic studies in the ICU can encourage cost effective antimicrobial drug therapy. This will help in rationalizing prescribing practices based on the feedback from these studies and practices between institutions, regions and countries can be compared.

ACKNOWLEDGEMENT

We acknowledge all faculty and staff of the medical intensive care unit of St. John's Medical College for the valuable help and support in this study.

REFERENCES

1. Smythe MA, Melendy S, Jahns B, et al. An exploratory analysis of medication utilization in a medical intensive care unit. Crit Care Med 1993; 21(9):319-23.
2. Townsend PL, Reynolds JR, Zaske DE. Applied Pharmacokinetics in the Intensive Care Unit. In, Irwin RS, Cerra FB, Rippe JM (ed). Irwin and Rippe's Intensive Care Medicine, 4th edition. Philadelphia, Lippincott-Raven Publishers, 1999; 1413.
3. Niederman MS. Appropriate use of antimicrobial agents: Challenges and strategies for improvement. Crit Care Med 2003; 31: 608- 16.
4. Pulcine C, Pradier C, Samat-Long C, Hyvernat H, et al. Factors associated with adherence to infectious diseases advice in two intensive care units. J Antimicrob Chemother 2006; 57: 546-50.
5. Srishyla MV, Krishnamurthy M, Nagarani MA, et al. Prescription audit in an Indian hospital setting using the DDD (Defined Daily Dose) concept. Indian J Pharmacol 1994; 26:23-8.
6. WHO Collaborating Centre for Drug Statistics Methodology: Anatomic- therapeutic-chemical classification of drugs (ATC) Classification index, 2005[cited 2010 Jan 15]. Available from URL: http://www.whocc.no/atcddd/.
7. Shankar PR, Partha P, Dubey AK, et al. Intensive care unit drug utilization in a teaching hospital in Nepal. Kathmandu Univ Med J 2005; 3(10):130-7.
8. Biswal S, Mishra P, Malhotra S, et al. Drug utilization pattern in the intensive care unit of a tertiary care hospital. J Clin Pharmacol 2006; 46:945-51.
9. Singh N, Yu VL. Rational empiric antibiotic prescription in the ICU. Chest 2000; 117:1496-9.
10. Bellomo R. Defining, quantifying, and classifying acute renal failure. Crit Care Clin 2005; 21:223-37.
11. de Rooij SE, Abu-Hanna A, Levi M, et al. Factors that predict outcome of intensive care treatment in very elderly patients: a review. Critical Care 2005; 9:307-14.
12. Viktil KK, Blix HS, Moger TA, et al. Polypharmacy as commonly defined is an indicator value in the assessment of drug-related problems. Br J Clin Pharmacol 2007; 63(2):187-95.
13. WHO Model list of essential drugs, 2007 [Cited 2007 Jan 20]. Available from URL: http://www.who.int/entity/medicines/publications/EssMedList15.pdf.
14. Usluer G, Ozgunes I, Leblebicioglu H. A multicenter point-prevalence study: antimicrobial prescription frequencies in hospitalized patients in turkey. Ann Clin Microbiol Antimicrob 2005; 4:16.
15. Fish DN, Ohlinger MJ. Antimicrobial resistance: factors and outcomes. Crit Care Clin 2006; 22:291-311.