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Original Article

A STUDY EVALUATING APPROPRIATENESS OF UTILIZATION PATTERN OF ANTIMICROBIALS IN PATIENTS ADMITTED IN MEDICAL INTENSIVE CARE UNIT OF TERTIARY CARE TEACHING RURAL HOSPITAL

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ABSTRACT

Objectives: To evaluate the appropriateness of utilization pattern of antimicrobials in the intensive care unit of a tertiary care teaching rural hospital.

Methods: This prospective and observational study was carried out in 500 patients admitted to the intensive care unit (ICU) who was prescribed antimicrobial agents, between October 2011 and May 2013. All patients were followed up throughout their stay. A study was carried out to study the appropriateness of utilization pattern of antimicrobials in the medical ICU.

Results: The dosage form of the prescribed antimicrobial was most appropriate. Most common route of drug administration was intravenous and it was most appropriate. Dose of drugs chosen was acceptable and the frequency of administration of antimicrobials was also acceptable. However, in 47 patients change of antimicrobials following initial empirical therapy was done without CST which was inappropriate. The appropriateness score calculated using structured, semi scientific, arbitrary 20 point appropriateness scale, was 15.48. The score, 15.48, fell in the category of appropriate use and the use of antimicrobials was found to be appropriate.

Conclusion: To prevent antimicrobial resistance, rational use of antimicrobials is a must. The concept of prescribing antimicrobial drugs for every patient should be abolished. Antimicrobial policy should be developed and it must be ensured that it is implemented. Antimicrobial stewardship should also be implemented to prevent the emergence of resistance.

Keywords: Antimicrobials, Utilization pattern of antimicorbials, Intensive care unit, Rationale for use of antimicrobial.

INTRODUCTION

Intensive Care Unit (ICU) is a special ward of the hospital providing management to critically ill patients round the clock [1]. Patients are admitted in the ICU for various health problems such as cardiac diseases, shock, respiratory diseases, stroke, multiple traumas, including head injuries, and others [1, 2]. Infectious diseases, as defined by the World Health Organization (WHO), are those diseases that are caused by pathogenic microorganisms, such as bacteria, viruses, parasites or fungi; the diseases can be spread, directly or indirectly, from one person to another [3]. The ICU is an epicenter of infections. The intensive unit patients are vulnerable to infections, as they have decreased immunity and increased exposure to infections due to the use of invasive procedures like endotracheal intubation, mechanical ventilation, vascular access, and others that distort the anatomical integrity of the protective barriers of patients.

Antimicrobials are agents that destroy microorganisms capable of causing diseases. Antimicrobials are used and misused widely since their discovery for treatment and prevention of various disease conditions. Antimicrobials are most widely used for the treatment of different infections like those of the respiratory tract, urinary tract, soft-tissue, intra-abdominal infection, and others, and for prophylaxis of various diseases like rheumatic fever, meningococcal meningitis, and others. In most of these cases, antimicrobial agents are used empirically without culture sensitivity test [4, 5].

Antimicrobials are used inappropriately in 50% of the cases, as reported by the WHO in 2004 [6]. Inappropriate use of antimicrobials includes wrong choice of antimicrobial, use in case of wrong indications, and incorrect dosage or duration of treatment [7]. As a result of this, resistance has emerged to various antimicrobials and has led to the development of resistant strains of organisms that can cause severe life threatening infections [8]. The problem of superbug nosocomial infections in the ICU adds to the woes of infections in ICUs.

Inappropriate drug use may be in the form of overprescription (prescribing drugs when none are needed clinically), omission (when required drugs for certain conditions are not prescribed), the use of inappropriate dosages (too high or too low), incorrect duration (too short or too long), incorrect selection (mismatch between organisms), unnecessary expense (the selection of newer and more expensive drugs when older, cheaper drugs are clinically adequate), unnecessary risk (use of injections or intravenous antibiotics when oral forms would be suitable) [9]. In patient's context, the appropriate use of a drug implies the prescription of a well documented drug at an optimal dose, together with the correct information; and these drugs should be available at an affordable price [10].

Various guidelines have been framed by the WHO to check the use of antimicrobials and thus prevent the emergence of bacterial resistance. Using the WHO guidelines as reference, several national guidelines have also been developed. Along with these guidelines, WHO has also provided the list of essential medicines to guide the prescriber about the use of medicines in a cost effective manner [11, 12].

This study was conducted to evaluate the appropriateness of utilization pattern of antimicrobials in the intensive care unit of a tertiary care hospital.

MATERIALS AND METHODS

This prospective, observational and non-interventional study was carried out in the medical Intensive Care Unit of Dhiraj Hospital, Piparia, Vadodara, in serially admitted patients over a period of 20 months starting from October 2011 to May 2013. The study was commenced only after taking approval from the Institutional Ethics Committee.

The sample size was obtained by using the formula, $n = 4*(pq/l^2)$, where p = population proportion of positive character, q=1-p and L = allowable error, based on the following assumptions: 95% confidence level with a 4.5% margin of error. The calculated minimum sample size was inflated by 10% to account for non-response & dropouts.

A total of 500 patients, admitted in the medical ICU, were enrolled in the study. The medical ICU was visited daily. Patients' diagnoses, drug charts, medical and nursing notes, and culture sensitivity report (if done) were noted. Data was collected to study the appropriateness of utilization pattern of antimicrobial agents in the medical ICU.

Patients' information such as age, gender, brief medical history, diagnosis, information about drugs like name (brand/ingredient and manufacturer), dosage form, dose, routes and duration of therapy, and start and stop dates were recorded. Information regarding culture sensitivity testing was also recorded. Whenever the antimicrobial was changed, the information about the new antimicrobial started was recorded separately.

Inclusion criteria for the study were adult patients of either gender, above 18 years of age, admitted in medical Intensive Care Units (ICU) of Dhiraj Hospital who was prescribed antimicrobials. Those patients who were less than 18 years of age and who were not willing to participate were excluded from the study.

The diagnosis made by the physician and the drugs selected by the physician, for the initial empirical management, was not taken into consideration in evaluating the appropriateness. The dosage form of antimicrobials administered, route of drug administration, dose and frequency of administration and change of antimicrobials following the initial empirical therapy was analyzed for evaluating appropriateness.

The appropriateness of the dosage form, route of administration, dose and frequency of administration was evaluated based on the diagnosis/indication, while the appropriateness of change of antimicrobials was evaluated based on culture sensitivity testing. The dose of the drug was considered as appropriate when it fell in the dose range for a particular indication; other factors such as renal/hepatic disease that also has an influence on the dose were not considered in evaluating the appropriateness in the present study. Duration of the therapy was not included in assessing the appropriateness as multiple co-morbid conditions are present in the patients admitted in the ICU and the presence of co-morbidities greatly influence the length of stay in ICU and the duration of antimicrobial therapy. Also, there are no fixed guidelines for the duration of therapy in patients in ICU or patients with multiple co-morbid conditions.

Appropriateness of antimicrobials used was assessed using structured, semi scientific, arbitrary 20 point appropriateness scale as under (table 1).

After assigning the score, in the scale of 0 to 20, for each drug, the appropriateness was categorized as under:

- ≥ 18-20 as most appropriate use,
- ≥14-<18 as appropriate use and
- <14 as inappropriate use.

All data obtained were analyzed using the Microsoft Excel software. Descriptive analysis was performed on all the variables to obtain the frequency and percentage.

RESULTS

Five hundred patients were enrolled in the study; of these, 308 (61.6%) were males and 192 (38.4%) were females. The mean age of the patients admitted in the ICU was 51.54±10.04 years, and the majority of them belonged to the 51 to 60 years age groups. Patients were admitted in the ICU due to respiratory conditions (30%), road traffic accidents (16%), cardiovascular accidents (13%), poisonings (4%), metabolic disorders (13%), epileptics (1%) and various severe life threatening infections (23%).

Out of 500 patients enrolled, 280 patients were transferred to the ward, mortality was seen in 175 patients and 45 patients were lost to follow up, thus the data were analyzed for 455 patients (table 2, fig. 1).

Table 1: Structured, semi scientific, arbitrary 20 point appropriateness scale

	Appropriateness of use of drugs	Score
(a)	Dosage form	
	Appropriate (appropriate for disease & condition of patient)	2
	Inappropriate	0
(b)	Route of administration-	
	Appropriate (appropriate for disease & condition of patient)	3
	Inappropriate	0
(c)	Dose-	
	Most appropriate (within the recommended dose range)	5
	Acceptable (outside of recommended dose range but within 25% on either end of ideal dose range)	3
	Inappropriate (outside 25% of either end of ideal dose range)	0
(d)	Frequency of administration	
	Most appropriate (within the recommended frequency range)	5
	Acceptable (outside of recommended frequency range but within 25% on either end of ideal frequency range)	3
	Inappropriate (outside 25% of either end of ideal frequency range)	0
(e)	Change of antimicrobial therapy	
	Most appropriate (based on culture sensitivity test reporting)	5
	Inappropriate (without culture sensitivity test)	0
	Total Maximum Points	20

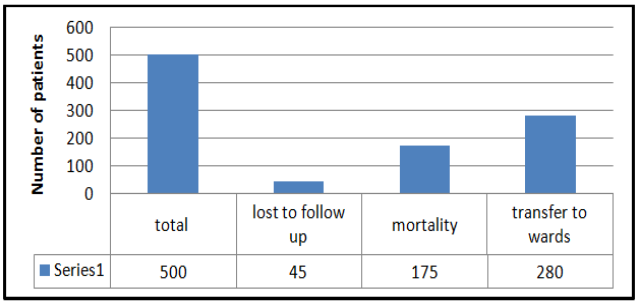

Fig. 1: Outcome of patients admitted in the intensive care unit

Table 2: Outcome of patients admitted to the intensive care unit

Outcome	Transfer to ward	Mortality (Case fatality rate)	Lost to follow up
ICU (n=500)%	280 (56%)	175 (35%)	45

Around 5 to 14 drugs were administered in each patient with a mean of 11.48±1.64 drugs. Of these, around 3 to 5 drugs were antimicrobial agents. The average number of antimicrobials prescribed were 4.12±1.49, which was 30.56% of the total drugs prescribed (fig. 2).

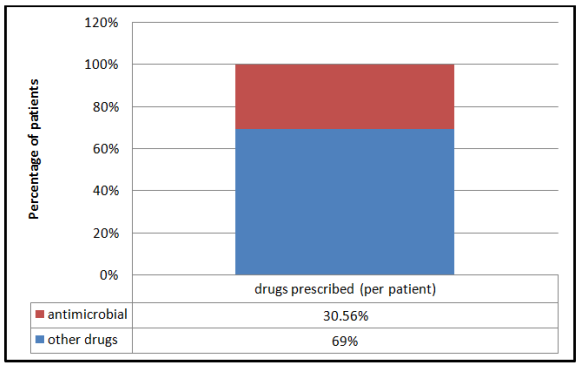

Fig. 2: Total number of drugs prescribed versus antimicrobials prescribed

Most commonly preferred dosage form was parenteral (94%) while most common route of antimicrobial administration was intravenous route (>90%) as compared to other route(s) (table 3, fig. 3).

Table 3: Percentage of drugs given using various routes

Route	Percentage of drugs given
Intravenous	91%
Subcutaneous	2%
Intramuscular	1%
Oral	2%
Topical	4%

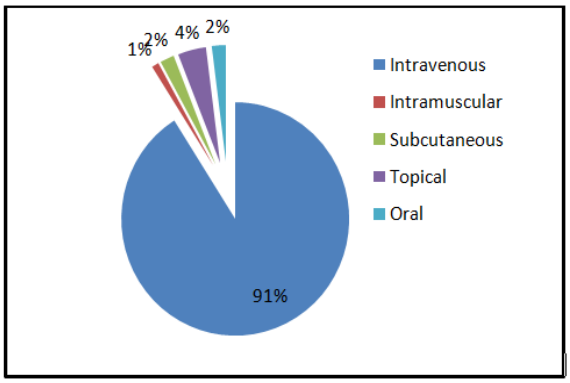

Fig. 3: Percentage of drugs given using various routes

Average duration of stay in the ICU was 9.5±1.25 days, while the average number of days for which antimicrobial agents were prescribed were 7.25±1.53 days, which were 76.32% of the average duration of stay in the ICU.

Antimicrobials were started empirically in all the patients. This was followed by a culture sensitivity test (CST), which was carried out in 283 patients out of 455 patients. Of these 283 patients, change in antimicrobial was done in 160 patients after CST report. Of the 172 patients in whom CST was not done, change of antimicrobial was done in 47 patients, which included the use of restricted higher antimicrobials like piperacillin+tazobactam, ceftazidime, cefepime, prulifloxacin, amikacin, meropenem, vancomycin. Change of antimicrobials following CST was statistically significant ($p<0.005$) by chi square test when compared to group in whom antimicrobials were changed without CST (table 4, fig. 4).

Table 4: Change of antimicrobial agent

	Total	Number of patients in which antimicrobials were changed
CST done	283	160
CST not done	172	47

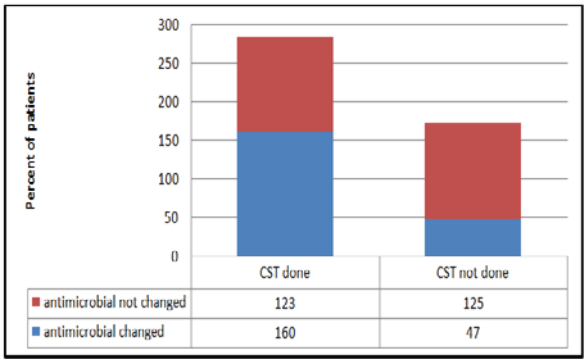

Fig. 4: Change of antimicrobial agents

It was found that the dosage form of the prescribed antimicrobials was most appropriate, most common route of drug administration was intravenous and it was most appropriate, doses of the antimicrobials chosen were acceptable, frequency of administration of antimicrobials was also acceptable; however, in 47 patients change of antimicrobials following initial empirical therapy was done without CST which was inappropriate. The appropriateness score calculated using structured, semi scientific, arbitrary 20 point appropriateness scale, was 15.48. This score of 15.48 fell in the category of appropriate use. Thus, the use of antimicrobials was found to be appropriate.

DISCUSSION

Rational drug therapy is essential not only to decrease the emergence of resistance but also to decrease the burden of the cost of therapy for the patients and also to decrease the occurrence of adverse events. In our set up, the dosage form of the prescribed antimicrobial was parenteral which was the most appropriate, although it was higher compared to a study carried out in Israel where 64% of antimicrobials were prescribed parenterally [13]. Most common route of drug administration was intravenous, more than 90% of the cases, and it was the most appropriate route. This was done to achieve the rapid onset of drug action as the patients are admitted in ICU due to critical condition, where rapid action of the drug is required [14].

Doses of drugs chosen were acceptable; frequency of administration of antimicrobials was also acceptable. However, in 47 patients change of antimicrobials following initial empirical therapy was done without CST which was inappropriate. Change of antimicrobials without CST report contributes to the development of the resistance and also adds to cost burden of the patient. If the antimicrobial that is changed without CST is not effective against the causative organism, it will add to the cost burden of the patient and will cause toxic effects without offering any benefits.

There will be failure of therapy and prolongation of stay in the ICU, which in itself has drastic outcomes due to increased chances of nosocomial infection and also increases the cost of therapy as evidenced by studies carried out in Geneva, Switzerland and Chicago [15, 16]. Also, there may be a possibility that restricted higher antimicrobials may be started without CST and the organism might be sensitive to other lower antimicrobials, this will contribute to the emergence of resistance. When costly higher antimicrobials are started cost of the therapy increases. Thus, it was found that the use of antimicrobials in our set up was appropriate.

CONCLUSION

To prevent antimicrobial resistance, rationale use of antimicrobials is a must. The concept of antimicrobial for every patient should be eradicated. Antimicrobial policy should be developed and it must be ensured that it is implemented. Antimicrobial policy should be developed for every unit, ward, including ICU, operation theatre and regular monitoring should be done to ensure that antimicrobial policy is strictly implemented. Emphasis should be made on the use of drugs from the essential medicines list, and such list should be readily available in the ICU. Rotation therapy of antimicrobials should be followed to deal with the problem of resistance, restricting the drug formulary can also help in reducing antimicrobial resistance.

Empirical therapy should be used only in an emergency and should be guided by the antimicrobial policy of the hospital, common causative organisms of nosocomial infection and local resistance pattern. These steps will ensure rational prescribing of antimicrobial agents and also decrease the risk of development of resistance to antimicrobial agents. The hospital staff should regularly be made aware of recent updates, changing patterns of resistance, and availability of new antimicrobials.

The presence of a clinical pharmacologist in every ICU setup will ensure rational use of antimicrobials in a cost effective manner. The antimicrobial stewardship program is a must for every hospital and it should seek to achieve optimal clinical outcomes related to antimicrobial use, minimize toxicity and other adverse events, reduce the costs of health care for infections, and limit the selection for antimicrobial resistant strains.

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CONFLICT OF INTERESTS

Declared None

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