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Research Article

MONITOR THE USE OF ANTIBIOTICS IN INTENSIVE CARE UNITS WITH SPECIAL FOCUS ON RESTRICTED ANTIBIOTICS IN TERTIARY CARE HOSPITAL OF INDIA

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ABSTRACT

Objective: The present study was to monitor the use of antibiotics with restricted antibiotics in intensive care units (ICUs). The aim of this study was to observe number of patients receiving antibiotic(s), to observe number of patient receiving restricted antibiotics(s), number of restricted antibiotic(s) forms filled in 48 hrs, observing number of instances where within three or more than three antibiotics given for more than 3 days, any adverse drug reaction and medication error related in ICUs.

Methods: The study was done prospectively in ICUs of a tertiary care hospital. 200 patients were selected from ICUs on a random basis. The duration study was 6.5 months. All adult patients admitted in ICUs who received an antibiotic therapy within 24 hrs of admission were included. Outpatient department patients and patient admitted in the wards were not included in the study.

Results: Among 200 patients, the total number of patients received antibiotic were 188 (94%), while 12 (6%) patients were not received. Among 188 patients, 51 patients received restricted antibiotics, i.e., 27.2% and 137 patients not received restricted antibiotic, i.e. 72.8%. Out of 188 patients received antibiotics including restricted antibiotics only 31 patients received three or more than three antibiotics for three or more than three days, which are 16.4% and 157 patients, not received three or more than three antibiotics for three or more than three days which were 83.6%. According to Antimicrobial Stewardship Program, physician prescribed restricted antibiotic must have to fill restricted antimicrobial form, among 51 patients, only 8 (15.6%) forms were received.

Keywords: Antibiotics, Restricted antibiotics, Outpatient department, Antimicrobial stewardship program, Intensive care units.

INTRODUCTION

Antibiotics are among the most widely used class of drugs in hospitals, and they are really important to be used optimally otherwise emerging resistant pathogens will interfere with treatment outcomes. It has been estimated that two-third of all patients receive at least one antibiotic during hospitalization, and the cost involved is therefore correspondingly high and up to 40% of a total hospital's drug expenditure may be devoted to the purchase of antibiotics [1].

Irrational use of antibiotics can be associated with a number of serious consequences to the patients and the community. Developing resistance has been worrisome early after these agents became available for widespread use. Drug use evaluation (DUE) for commonly used antibiotics not only will improve treatment efficacy but also in conserving cost and preventing unwanted adverse effects [2].

This widespread and indiscriminate use of antimicrobial agents inevitably has resulted in the emergence of antibiotic-resistant pathogens. This practice of indiscriminate prescribing of Antimicrobial agents also leads to ineffective and unsafe treatment, prolongation of illness, disease exacerbation, distress and harm to the patients. All these issues produced a great concern over the inappropriate and injudicious use of antimicrobial agents all over the world [3].

Multidrug resistance in common clinical pathogens is a growing problem, and widespread and indiscriminate use of broad spectrum anti-invectives is a major contributor. Unnecessary use of antimicrobials as well as inappropriate choice, dose, and duration of therapy drive selection of resistant bacteria. Restricting use of certain antibiotics to defined groups of patients and using narrow spectrum antibiotics wherever possible can slow or constrain the emergence of antibiotic resistance and prolong the effectiveness of existing antibiotics [4].

The judicious use of antibiotics is an important strategy for preserving efficacy in the treatment of infectious diseases. Infectious disease practitioners are poised to provide patient-specific recommendations for appropriate agents and to optimize dosage and duration of therapy. Antimicrobial stewardship programs (involving pharmacists, physicians, and other healthcare providers) are increasing in number as antibiotic resistance increases with a disproportionately small number of new agents being developed [5].

DUE is an effective tool for monitoring the appropriateness of the usage of various medications. It is an essential component of the pharmacy service provision, and clinical pharmacy practice [6].

METHODS

The study was done prospectively in the tertiary care hospital. The data were collected in the intensive care unit (ICU) which having a capacity of 191 beds. A total of 200 prescriptions were considered for the use of antibiotics in ICU. All 200 patients were selected from ICUs on the random basis. Prescription auditing and monitoring antibiotic usage are an on-going process in the hospital. The duration study was 6.5 months. All adult patients admitted in ICUs who received an antibiotic therapy within 24 hrs of admission were included. Outpatient department patients were excluded from the study and patients who visited the emergency department and patient admitted in the wards were not included in the study. The study was aimed to monitor the use antibiotics including restricted antibiotics prescribed to the patient admitted in ICUs or transferred from ward to ICUs. The use of antibiotics including restricted antibiotics and degree of their resistance was monitored by the prescription audition and by monitoring of culture reports of the enrolled patients. Data were collected using a well-structured data collection performa. This form is designed by the Clinical Pharmacology Department

for auditing of patients who admitted in wards as well in ICUs of the hospitals. The form consists of patient's identification (name, his/her age, his/her sex, bed number, and in patient identification number), diagnosis, date of admission, number of antibiotic, and total number of drugs prescribed. ICUs patients who received antibiotic or restricted antibiotics or both were evaluated by the data collection form, i.e., restricted antibiotic form. The form consists of name and number of antibiotic, name and number of restricted antibiotic, form of restricted antibiotics filled within 48 hrs, 3 or more antibiotics prescribed for 3 or more days, medication error in ICU, adverse reaction in ICU, check whether culture (specimens) sent to laboratory, culture report is received or not and any escalation and de-escalation of antibiotics on the basis of lab report and culture. If patients received restricted antibiotics, then AMS restricted antibiotic form had been filled within 48 hrs which was further send to in patient pharmacy. The patients were followed until discharge. The discharge summary is also maintained containing information about the total duration of stay in the hospital.

Monitoring of culture reports of the enrolled patients was done on the 3rd day of the patient admission. On the 3rd day, all the specification, like patient identification, clinical parameters, and laboratory reports, are monitored in the same way as done on the 1st day. The basic difference was the monitoring of the culture reports of the specimen sent for the laboratory tests and the sepsis profile of the patient. It was done for the determining the presence of the pathogen, sensitiveness of the pathogen observed, and the degree of resistance of the patient to the antibiotics administered to the patient.

The patients were followed from the first day to the third or fifth day of treatment when the microbiological results were available. The clinical progress notes of the attending physicians were used to evaluate the clinical outcome on the follow-up day. Appropriateness of these restricted antibiotics was assessed according to the following criteria:

- First, justification of antibiotic prescribing as stated in the antibiotic order form (AOF)
- Second, appropriateness of dosage regimen which included route of administration, dosage, dosing interval as well as dosage adjustment in geriatrics, in patients with hepatic or renal function impairment
- Third, re-evaluation of the empirical treatment when the microbiological and susceptibility data were obtained. Discontinuation, continuation, changing of antimicrobial, or dosage regimens was recorded.

After receive of culture or specimen report or sepsis profile report, on the basis of culture reports, the physicians were escalated or de-escalated antibiotics. They also decide which antibiotic is to be continuing or stop; they also check whether the patient is sensitive to antibiotic or having resistances.

Culture includes

1. Blood culture
2. Urine culture
3. Body fluid culture
    a. Pus culture
    b. Sputum culture
    c. Endotracheal tube culture
    d. Tracheotomy tubes culture
    e. Vaginal fluid culture.

RESULTS

The present study was carried out in the ICUs of the tertiary care corporate hospital. In this study, 200 patients were monitored from the inpatient department of the hospital, i.e., ICUs.

Out of 200 patients monitored in the study, the overall population was found to be 66.5% male (133 in number) and 33.5% female (67 in number). In this study, various age group of person was enrolled. The age range of patient age was 15-95 years. Among them, mostly patients are admitted between 55 and 65 age range, i.e., 65 patients.

The usage pattern of medication in the tertiary care hospital was evaluated, and it was observed that the total number of drugs including antibiotics prescribed to 200 patients included in the study were 3021. The average number of drugs prescribed per patient during their stay in the hospital was 15. Among 3021 drugs, 353 are antibiotics including restricted antibiotics prescribed to the patients. The average number of antibiotic prescribed per patient during their stay in the hospital was 2.

The usage pattern of antibiotic along with restricted antibiotic in the tertiary care hospital was evaluated. It was observed that the total number of the patient received antibiotic were 188 (94%) while 12 (6%) patients were not prescribed. Among 188 patients, 27.2 % patient received restricted antibiotics, i.e. 51 and 72.8% patient not received restricted antibiotic, i.e. 137. An evaluation of the patients who had received antibiotics for 3 or more than 3 days was also done. Out of 188 patients received antibiotics including restricted antibiotics only 31 patients received three or more than three antibiotics for 3 or more than 3 days, which are 16.4% and 157 patients, not received three or more than three antibiotics for three or more than three days which were 83.6%. Antimicrobials were prescribed to 188 (94%) patients in antibiotic use pattern study. Out of these 188 patients, 353 antibiotics prescribed along with restricted antibiotic. In this study, total 15 categories of antimicrobials were used including restricted antibiotics., e.g., β lactum + extended spectrum penicillin acid along with cephalosporin was also widely used. Similarly, 51 patients received restricted antibiotic; there were 84 restricted antibiotics among them. In tertiary care hospital where the study was carried out, there were 12 antibiotics namely meropenem, imipenem, vancomycin, colistin, teicoplanin, tigecycline, caspofungin, anidulafungin, micafungin, amphotericin, linezolid included as restricted antibiotics. Meropenem was widely used.

Total number of patients received antibiotic were 188, among them, 51 (27.2%) patient were received restricted antibiotic. Out of 51 patients, 49 (96%) patients specimen were sent, while the specimen of 2 (4%) patients were not sent because as they were expire. Reports all the 49 patients were received. Among these 49 (96%) patients, 24 (48%) patients had positive culture reports and 25 (52%) patients' culture reports were sterile or negative. 16 (32%) patients where escalation/de-escalation was done on the basis of culture report, while 33 (68%) patients continued same treatment. There were total 33 microorganisms isolated from 24 patients while 25 patients showing no growth means there culture report is sterile or negative. 17 were Gram-negative bacteria while 10 were Gram-positive bacteria and 6 was yeast microorganism responsible for fungal infections. The percentage of *Staphylococcus* species was more among all the isolated species, i.e. 31% while *Acinetobacter* species and *Candida* species were 27% and 18%, respectively. Pseudomonas was 9%, distribution of both *Klebsiella* and *Escherichia* species is 6% each, and the distribution of *Proteus* species was very less distribution among all the species, i.e., 3%.

Total numbers of patients received restricted antibiotics were 51. According to antimicrobial stewardship program, physician prescribed restricted antibiotic must have to fill restricted antimicrobial form, with proper justification for that antibiotic. Among 51 patients, only 8 (15.6%) forms were received. It means compliance is not following.

Out of 200 patients 77.5% patient discharge (155 in number), 8.5% patient expired (17 in number), 14% patient went leave against medical advice, and request discharged, respectively (28 in number). The mortality rate of the hospital (ICUs) was 8.5%.

DISCUSSION

From above results, it was observed that out of 200 patients enrolled in the study, 133 (66.5%) was male while remaining 67 (33.5%) was female, and it means that the population of male was greater than female. Age of patients varies between 15 years and 95 years, but 65 patients (32.5%) were between 55 years and 65 years. A total of

200 cases were evaluated with a mean age of 58.35 years while in the previous study the mean age was 50.3 years [7] and 44.62 years [8].

The average duration of ICUs stay was 8.99 days (ranges between 2 and 27) which is more as compared to the previous study, i.e., 4 days [9], 4.15 days [**7**] and 6 days [8].

The various study reported the use of antibiotics was 64% and 56%, respectively [10,11], while in some developing countries such as Nepal, Pakistan, and Indonesia were evaluated and antibiotics use of 61%, 76%, and 45% was reported, respectively [12].Among 200 patients, 188 patients received antibiotics, i.e., 94% while 12 patients not received antibiotics, i.e., 6%. It means that the use antibiotics seem to be high in ICUs of the hospital. Although there are no gold standards for the extent of use antibiotics in ICUs setting, the use of antibiotics must be restricted.

188 patients received antibiotics among them 51 (27%) received restricted antibiotics and 137 (72.8%) patients not received restricted antibiotics. Patients enrolled in the study were admitted in ICUs, some of them admitted for three or more than 3 days, and some of the patients admitted with serious infection/trauma/shock, according to their clinical condition physician prescribed three or more antibiotic on the basis of symptoms. Among 188 patients, only 31 patients received three or more antibiotic for three or more than 3 days, i.e., 16.4%. A recent study reported that 51 patients (25.5%) who received three or more than three antibiotics during their stay in the ICUs [13].

Total number of drugs received by the patients (200) is 3021 including antibiotics, then the average number drug received by the each patient is 15; it means that the use of drugs in ICUs is not significant as compared to 2.8, 3.5, 7.73, 13.54, and 14.6, respectively, reported in previous studies [7-9,14,15].

β lactums + extended spectrum pencillin (piperacillin + tazobactum and amoxcillin + clavulanic acid), cephalosporin, carbapenems, aminoglycoside, floroquinolones, macloride, antiamoebics, glycopeptide were widely used as similar to the previous study [16-20].

Total number of antibiotics received by the patients (188) is 353, and then average number antibiotic received by the each patient is 2 which less compared to previous studies, i.e., 2.09 [21] and 2.50 [8].

Meropenem is widely used, teicoplanin, imipenem, linezolid, and micafungin is less used while vancomycin, caspofungin, anidulafungin, amphotericin, tigecycline, and doripenem are not used [22,23].

Among 188 patients, 51 patients received restricted antibiotics; total number of restricted antibiotics received by the patients is 84 among them 25 (49%) patients received one restricted antibiotic, 22 (43%) patients received two restricted antibiotic while 3 (6%) patients received three antibiotic and remaining 1 (2%) patient received four restricted antibiotic [19].

Total number of patients who received restricted antibiotics was 51, the specimen of 49 patients sent for culture while 2 patients got expired. Among 49 patients, 49 patients received their culture reports, 24 patients with positive culture report while 25 with sterile or negative report. Total 33 microorganisms were isolated from 24 patients. The culture reports of 24 patients showed that the percentage of *Staphylococcus* species is more among all the isolated species, i.e., 31% while *Acinetobacter* species and *Candida* species is 27% and 18%, respectively. *Pseudomonas* is 9%, distribution of both *Klebsiella* and *Escherichia* species is 6% each, and the distribution of *Proteus* species is very less distribution among all the species, i.e., 3% and the specimen was taken from both blood/urine and body culture. The most common isolated organisms in our study are *Staphylococcus aureus* [24] which is similar to the previous study while other studies had reported *Pseudomonas* **[**22,25**]** and *Escherichia coli* [9,26].

Among 200 patient, 155 (77.5%) patients were discharged while 28 (14%) patients went LAMA/on request discharge, and 17 (8.5%) patients got expire, on basis of 200 patients who were admitted in ICUs, we can say that the mortality rate of hospital (ICUs) is 8.5% less as compared to previous study, i.e., 10.4% [7**]** and 15.4% [9].

Medication error can cause due to the negligence of treating staff, lack of knowledge. Due to the medication error, the cost of treatment has been increased. Among 200 patients, only 2 patients in which medication error had been occurred, i.e., only 1%. It means the quality of treatment in tertiary care hospital is very good.

Adverse drug reaction (ADR) can be developed in any patient it may be severe or may be normal. The development of ADR depends from person to person. There were total 4 patients who developed ADR, and the percentage of the development of ADR was 2% [27,28].

The result depicts that the antibiotics prescribed empirically to the patients admitted in ICU, which are chosen according to provisional diagnosis and the escalation/de-escalation of treatment was done on the basis of culture reports. Our results are comparable with several other previous DUE studies [6].

CONCLUSION

The present study monitored the use of antibiotics with a special focus on restricted antibiotics in the tertiary care corporate hospital with special reference to the use of antibiotics in ICU was observed. Antibiotics are commonly prescribed to most ICU patients at the time of admission. Antibiotics continue to be widely prescribed in critically ill patients and form a significant proportion of the total drugs consumed in the ICU. Based on the results, we conclude the use antibiotics seem to be high in ICUs of the hospital. Antibiotic use during the audit appeared inappropriate, and the average number of drugs along antibiotics prescribed per patient is very high, i.e., 15. The duration of ICUs stay is also very high.

The use of high number of drugs is a common problem. Drugs prescribing policy should be framed. The number of drugs prescribed by generic names was low in the ICUs and effort must be made to encourage prescribing by generic names. Clinicians practicing in the ICUs must develop standard operating procedures for more effective drug therapy. They should promote infection control practices and rational antibiotic utilization aimed at minimization of antibiotic resistance.

Prescribing guideline is required to reduce the prevalent poly-pharmacy and to promote appropriate use of antimicrobial drugs based on the culture and sensitivity report. The high utilization rates during the stay in ICUs are a matter of great concern and need to be improved by the use of guidelines and surveillance. A committee should be involved in the ICUs to monitor the prescription pattern of drugs regularly. Low levels of bacterial resistance were detected during the audit and all the antibiotics prescribed according to the culture report of patients.

AMS program is partially followed by the hospital, the incidence of filling AMS form or restricted AOF is not up to mark. Antimicrobial Stewardship program has been closely monitored. Education of the prescriber is the cornerstone of any successful antibiotic stewardship program, and teaching of guidelines and clinical pathways will aid in improving antimicrobial prescribing behavior to a large extent.

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