Global Health
AN ONLINE JOURNAL FOR THE DIGITAL AGE


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ASSESS THE APPROPRIATENESS OF RESTRICTED ANTIBIOTICS IN CRITICAL CARE UNIT WITH THE IMPORTANCE OF EMPIRICAL THERAPY AND ASSISTED RE-EVALUATION BY CLINICAL PHARMACIST

Introduction

Among hospitalized patient's restricted antibiotics are the most frequently prescribed drugs especially in Intensive Care Units (ICU) and surgical department as empirical therapy in India. Programs designed to make the antibiotic prescriptions effective in the health care institutions are an important element in the quality of care, infection control and cost containment[1]. Antibiotic misuse or over-use may increase the emergence of resistant bacteria and as a result increase the selection pressure on physicians who tend to prescribe newer broad spectrum agents for excessive period of time [2]. There are several factors which contribute to antibiotic resistance including misuse and irrational use by both physicians and patients, once resistance is established, it cannot be reversed [3]. Antibiotic resistance occurs when the antibiotic loses the ability to control or kill bacterial growth, in other words when the antibiotics becomes resistant and continues to multiply even in the presence of antibiotics in its therapeutic level [4]. Developing new antibiotics is not a solution for this. In order to help physicians in reducing the intensity of the problem it's the responsibility of the healthcare team to develop a good prescribing pattern. In developing countries, countries, the most important factor is inappropriate use of antibiotics, resulting from unregulated marketing of antibiotics and higher frequency of specific infectious diseases[3]. By providing the Continuing Education programs (CE) in the health care institution it is possible to prevent irrational use of restricted antibiotic in prescribing.

The authors of one major study concluded that 62% of hospital patients were receiving restricted antibiotics when they did not have definite evidence of infection like (LRTI, Sepsis or Nosocomial infection). The administration of antibiotics was considered to have been irrational in 66% of the cases reviewed and as questionable in another 22%. The use of these drugs is now often monitored, and several types of control programs have been either proposed or implemented in an attempt to modify patterns of use. Cooperation between the pharmacy and medical staffs has been highly effective in the areas of antibiotic use review, antimicrobial sensitivity monitoring and nosocomial infection control.

The Global Antibiotic Resistance Partnership (GARP) was launched in order to develop actionable policy recommendations especially suited to low income countries.[8] WHO has recommended multifaceted strategies to improve hospital prescribing pattern of antibiotics, such as:

- Establish infection control programs based on current best practice, with the responsibility for effective management of antimicrobial resistance in hospitals and ensure that all hospitals have access to such a program.
- Establish effective hospital therapeutics committees with the responsibility for overseeing antimicrobial use in hospitals.

- Develop and regularly update guidelines for antimicrobial treatment and prophylaxis, and hospital antimicrobial formularies.
- Monitor antimicrobial usage, including the quantity and patterns of use, and feedback results to prescribers[9].

The main cause of morbidity and mortality in hospitalized patients are nosocomial infection. The resistance to antibiotic is occurring more frequently and more rapidly all over the world, with Gram-positive bacteria and Gram negative bacilli being important causes of hospital-acquired infections [6]. The surgical antibiotic prophylaxis is used to prevent infections at surgical site. Antibiotics find a major use in surgical prophylaxis and have been regularly used to eradicate endogenous microorganisms and to prevent post-operative infectious complications manipulated during the procedure[7].

Objective

To optimize restricted antibiotic use in treatment and prophylaxis of infections among hospitalized patients in order to improve clinical outcomes by adopting the rational use of antibiotics in the critical care units at the tertiary care hospital.

Methods

This was a prospective observational study at a tertiary care center. The patient demographics and all medically relevant information was noted in a predefined data collection form. Alternatively, these case charts were analyzed. The changes and the daily notes in the case sheets were followed until the patient is discharged. The prescription guidelines, tertiary resources, Micromedex, Medscape and references books were used as tool to review the prescription and case charts. The patient demographic data was stored confidentially and was subjected to further analysis using appropriate software.

Inclusive criteria

All patients admitted in HICU suffering from infective illness and are being given antibiotic therapy.

Exclusive criteria:

i. All patients admitted to paediatric ICU and wards, NICU, obstetrics and gynaecology ward, private ward and patients in out-patient department.
ii. Patients not receiving antibiotics.

Source of data

Inpatient case sheets, Inpatient medication charts, Physician progress notes, Nurse's notes, Laboratory investigation charts.

Study Procedure

The study was conducted adhering the below given procedure.

i. Study involves analysing the antibiotics prescribed in HICU.
ii. The appropriateness of the antibiotics prescribed was assessed with the help of Antibiotic policy of Bangalore Baptist Hospital.

Results

The demographic details of antibiotic use have been shown in Table 1.

Table 1: The demographic details of the patient and their antibiotics use with culture sensitivity reports

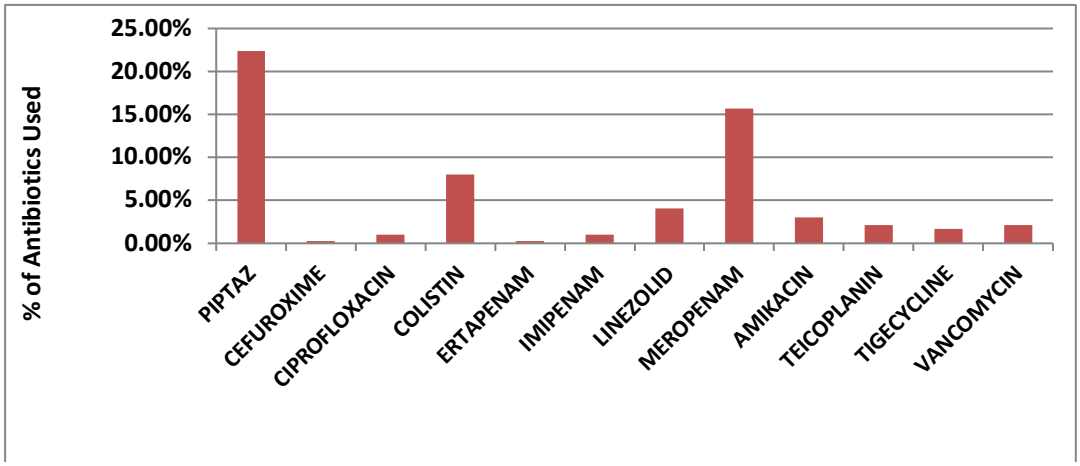
Gender	**N=290**	
Males	176	61%

Females	114	39.3 %
Total Antibiotics	764	263.4%
used	455	157%
Restricted	**N=774**	
Antibiotics used	171	60%
Commonly used	120	41%
Antibiotics	61	21%
Piperacilin	31	4%
Tazobactum	23	3%
Meropenam	16	2%
Colistin	162	2%
Linezolid	13	1.7%
Amikacin	8	1%
Teicoplanin	8	1%
Vancomycin	**N=350**	
Tigecycline	206	59%
Imepenem	144	41%
Ciprofloxacin	**N=290**	
Total no of	235	81%
Cultures sent	27	9.3%
Positive	28	9.6%
Negative	**N=333**	
Origin of infection	68	19.4%
Community	32	9.1%
Acquired	27	7.7%
Health care	25	7.1%
associated	22	6.2%
Hospital Acquired	13	3.7%
Common Isolated	3	0.8%
Organisms	143	41%
Klebsialla sp	**N=194**	
E.coli	22	6.2%
CONS*	6	1.7%
Acinetobacter sp	86	24.5%
S aureus	80	22.85%
P aeroginoses	**N=290**	
Candida sp	193	66.5%
No growth	48	16.5%
MDRO*	49	17%
MRSA*		
CRO*		
CRO+ESBL*		
ESBL*		
Final Status		
Alive		
Death		
LAMA*		

* CONS-Coagulase Negative Staphylococcus; MDRO-Multidrug Resistant Organism; MRSA- Methicillin-resistant staphylococcus aureus; CRO- Carbapenem resistant organism ; CRO+ESBL- Carbapenem resistant organism+ Extended spectrum beta-lactamase ; ESBL- Extended spectrum beta-lactamase ; LAMA- Left against medical advice.

The restricted antibiotics should only be prescribed or supplied after the approval of consulted microbiologist. The pharmacists are informed to first confirm from the microbiologist or the formulary for the indication before dispensing the restricted antibiotics. The most commonly used restricted antibiotics were found to be Piperacilin Tazobactum which was seen in 22.3% of the patients followed by Meropenam which was used in 15.7% of the patients and Colistin was seen in 8% of the patients. The indications for the use of the restricted antibiotics were as urinary tract infection (UTI), Nosocomial infections, Shock / Severe Sepsis, Skin or wound related infections, Unknown cause of infection, lower respiratory tract infection (LRTI). The figure 1 shows the most commonly used restricted antibiotics that is piperacilin Tazobactum followed by Meropenam and then Colistin and the least used was Cefuroxime.

Figure 1: Commonly used restricted antibiotics



In a Turkish study Sultana N et al. (2016) showed that the irrational antibiotic use in Ankara Numune Education and Research Hospital was 59.3%. Also the Antibiotic Control Committee implemented an antibiotic restriction policy in 1999, aiming to ensure the correct and restrictive use of broad-spectrum antibiotics, which resulted in reduction of inappropriate use of antibiotics down to 22.4%, according to a study published in 2005[2]. In contrast to that, this (research?) study focuses on the appropriateness of antibiotic use in critical care unit especially in HICU and ICU of the Hospital. The study expects the use of antibiotics to be in compliance with the antibiotic policy of the hospital and it was found that antibiotics were prescribed appropriately accordingly to policy of hospital in the concerned departments. With collective rate of noncompliance was found to be 18.3%.

Discussion

The present study was conducted in High and ICU each showing a large variability in diagnosis. Infection was considered as the indication for the prescription of Anti-Microbial Agents. Hansens et al (2008) reported that 74% of patients admitted to a medical intensive care unit were treated with antimicrobial medications. One study showed that 35.3% and 39% of the acute admitted patients had at least one antimicrobial exposure[4]. The study on gender categorization had revealed that the overall study population was predominantly male population. In a similar study conducted by Ravi Pathiyil Shankar et al (2011) also noted that majority of patients were males.

In a study, conducted by Venugopal D et al[10] (2016) it was found that cephalosporin's were most commonly prescribed for in-patients and penicillin's were prescribed for out- patients. The study found that the classes of antibiotics

mainly used in the HICU and ICU are Piperacilin & Tazobactum and Meropenam. In a study by Bosu et al (2010) a variation was seen in average percentages (which were 41%, 45%, 79% and 98%) of patients receiving at least one antibiotic, in different health centers. In this study patients received more than one AMA on number of occasions

As these patients were suffering from mixed infections they receive one AMA for gram positive, other for gram negative and 3rd one for anaerobic infection. Many patients received antibiotic treatment without subjecting the patient to culture sensitivity tests received alternative. In our study it was found that nearly 9 anti-microbial agents were given in HICU and ICU, during their stay in hospital.

Girish MB et al (2010) study revealed that 58% received two or more antimicrobials in combination and their mean duration of administration being 9.79+ 1.33 days. Even though the common organism causing acute gastroenteritis is Gram negative bacteria (E.coli), Metronidazole had been given along with Ciprofloxacin in the study. In the study it was observed that 77.61% of the prescriptions were empirical, 6.76% were directed and 18.48% were targeted.

The study can further be taken up to check for studying the resistance pattern in the hospital and further help in optimizing therapy making it a more targeted one. Take up continuing education program for the physicians. Pharmacists and other health care professionals can be informative and help in making the antibiotic prescribing rational and error free. The study can further take up pharmacoeconomics facts of antibiotic use in the hospital and can help in making a more economic pattern of antibiotic use. Use of restricted antibiotic order form can optimize utilization of restricted antibiotics and help making the use of antibiotic very systematic and prevent any kind of misuse. The form helps to keep a track of use of restricted antibiotic for a specific patient. This can ensure that rate of emergence of resistant bugs from these drugs are curbed.

Conclusion

A wide variety of diagnoses were observed with a large variety of drugs used to treatment. Though the overall use of antimicrobial agents in the hospital was found to be appropriate still there is a scope in improving the use of restricted antibiotic in the hospital. Poly pharmacy was seen commonly with the total number of antibiotics ranging from a minimum of 3 to a maximum of 9 antibiotics per patient throughout the three departments. Thorough efforts should be made to contain emergence of resistant species of bugs. Implementation of a restricted antibiotic order form will help in reducing as well as preventing misuse of restricted antibiotics.There should be a policy developed which states the use of fixed dose combination antibiotics. Regular education and updates regarding antibiotics and resistant bacterial species will be very helpful in making the antibiotic prescription rational.

Limitations

The study had following limitations:

- A large number of patients could have been included in the study.
- Patient expired during the study.
- Illegibility of the prescriptions.

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