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CASE STUDY

Prescribing Patterns of Antibiotics and Sensitivity Patterns of Microorganisms towards Different Antibiotics in Multidisipinary Health Care Hospital.

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ABSTRACT

Information about antibiotic use and resistance patterns of common microorganisms are lacking in hospitals in India. Excessive and inappropriate use of an antibiotic contributes to the development of bacterial resistance. This study was carried out to collect relevant demographic information, antibiotic prescribing patterns and the common organisms isolated including their antibiotic sensitivity patterns. The study of prescribing patterns seeks to monitor, evaluate and suggest modifications in practitioners prescribing habits so as to make medical care rational and cost effective. Antibiotic resistance is becoming a problem in the internal medicine ward. Formulation of a policy for hospital antibiotic use and an educational programme especially for junior doctors is required.

Key Words: Antibiotic Resistance, Culture Sensitivity, Prescription Pattern.

INTRODUCTION

Quality of life can be improved by enhancing standards of medical treatment at all levels of the health care delivery system. Setting standards and assessing the quality of care through performance review should become part of everyday clinical practice[1].The study of prescribing patterns seeks to monitor, evaluate and suggest modifications in practitioners prescribing habits so as to make medical care rational and cost effective. Information about antibiotic use patterns is necessary for a constructive approach to problems that arise from the multiple antibiotics available [2]. In developing countries the cost of health care is a matter of major concern [3]. This is especially true for India, a developing country in South Asia. Excessive and inappropriate use of antibiotics in hospitals, health care facilities and the community contributes to the development of bacterial resistance. In India reports on antibiotic utilization at an institutional level include both cross-sectional [3] and longitudinal studies [4, 5] of prescribing patterns.

Antimicrobial resistance is an issue of great significance for public health at the global level. Considered as wonder drugs, antibiotics are often prescribed inappropriately and inadequately and have thus become one of the highly abused agents [6]. Antibiotics represent a significant portion of overall health-care costs from 20 to 50% of total hospital drug expenditures. Over half of all hospitalized patients are treated with antibiotics, and it has been estimated that 50% of all antibiotics prescribed are either the wrong drug, the wrong dose, or are taken for the wrong duration. In addition to its potential to increase mortality, antibiotic resistance increases costs by increasing the length of stay in the hospital. Slowing the spread of resistance requires changes in the pattern of antibiotic use. Much of this increase can be traced to the spread of antibiotic resistance among pathogenic bacteria. Antibiotic resistance is particularly pronounced in nosocomial infections [6, 7].

The Center of Disease Control, Appropriate antibiotic prescribing is defined as “Prescribing antibiotics only when they are likely to be beneficial to the patient, selecting agents that will target the likely pathogens and using these agents at the correct dose and for the proper duration”. The ATC (anatomic-therapeutic-

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chemical) classification assigns code letters and numbers to drugs [8, 9].

RATIONALITY FOR CONDUCTING STUDY

- To collect relevant demographic information and information on duration of hospitalization of patients admitted to the internal medicine ward and prescribed antibiotics during the study.
- To obtain information on the antibiotic prescribing pattern and the disease conditions for which antibiotics were prescribed.
- To obtain information on the common organisms isolated during culture and sensitivity testing and their antibiotic sensitivity patterns.
- To apply the ATC classification to the commonly used antibiotics.
- To obtain Phrmacoeconomics aspects (mean ± SD cost) of most commonly used antibiotics.

MATERIALS AND METHODS

The study was carried out over six month's period at the Saifee hospital, Charni road, Mumbai. Patients admitted to the internal medicine ward who were prescribed antibiotics were included in the study and were identified manually. This may have the potential for bias and errors. Quantitative estimation of the bias has not been carried out in this study. Computerization of the Medical Records Department is in progress and there is a proposal for storing the hospital records in a computerized format. This may help in reducing any potential bias.

The age and sex of the patients, clinical diagnosis, duration of hospitalization, antibiotic information (name, dose and frequency) and the results of culture and sensitivity testing were entered into the Case report form. The antibiotics prescribed for parenteral use and indications for their use were also analyzed separately. Antibiotics were used for bacteriologic ally proven infection (BPI) or non-bacteriologic ally proven infection (non-BPI). Details of antibiotic use in BPI were noted.

The mean cost of commonly prescribed 15 antibiotics during the hospital stay and on discharge from the hospital was noted. The cost of antibiotics prescribed during the hospital stay was determined using the price list supplied by the hospital pharmacy. For collection of data, retrospective analysis method *i.e.* analysis of previous record and prospective analysis method were used.

SELECTION CRITERIA

Inclusion criteria: Bacteriologic proven infection: The patient's lab data shows positive reports against microorganism.

Exclusion criteria: Non-Bacteriologic proven infection: The patient's lab data shows negative reports against microorganism or whose sensitivity not analyzed and antibiotics that patient had been prescribed prior to admission.

SPECIMEN COLLECTIONS: - Freshly voided specimen after due precautions were collected by ways,

1. Urine in sterilized bottles
2. Pus through disposable diagnostic swabs
3. Tracheal secretion in sterilized disposable syringes
4. Sputum in sterilized bottles
5. Blood in nutrient broth medium

Specimen were processed in clinical laboratory and, for identification of pathogenic bacteria and their sensitivity, standard techniques were used. Culture and sensitivity testing was carried out in 177 patients (84.6%) out of 209 patients.

MICROSCOPIC EXAMINATION OF SPECIMEN

Before culturing the specimen, it was carefully examined microscopically for pus cells and bacteria.

Urine: About 10 ml of urine was taken in a test tube, centrifuged at 2500 rpm for 6 minutes to obtain deposits. Supernatant was poured off and deposits were transferred onto a clean slide and covered with a glass cover slip. The slides were examined microscopically under 10 and 40 power magnifications for the presence of WBCs, RBCs, epithelial cells, crystals and parasites/bacteria/yeast cells.

Sputum: Sputum was examined microscopically before culturing. Sputum was taken with a wire loop on a clean glass slide and was examined microscopically under 10x, 40x and 100x lens magnification. Pathogens present were identified and cultured for antibiotic susceptibility.

Blood and pus swab: Blood and swab were not examined microscopically but, for, identification of bacteria, specimen were cultured in blood agar. The cultured media were sterilized, and then

Table 1: Case Report form

Case Report Form
Saifee Hospital, Charni Road, Mumbai

I.P. No. Age: Sex: M/F
Date of admission: Diagnosis:
Date of discharge:
Antibiotic information-

S.NO	Name	ROA	Dose	Frequency	Duration
Antibiotics prescribed on discharge					

Aerobic Culture and Sensitivity
Specimen: Date of Specimen received:
Date of Reporting: Culture Report:
Gram's stain:
Antibiotic sensitivity pattern-

Amikacin		Ceftazidime		Piperacillin+Tozabacu		penicillin	
Amoxacillin+clav.aci		Ceftriaxone		Piperacillin		Cefpodoxime	
Levofloxacin		Chloramphenicol		Teicoplanin		Gentamycin	
Ampicillin+Sulbactu		Imipenam		Ciprofloxacin		Gatifloxacin	
Linezolid		Meropenem		Azithromycin		Tobramycin	
Ampicillin		Netilmicin		Clandamycin		Vancomycin	
Cefepime		Erythromycin		Oxacillin/Methicillin		Ofloxacin	
Cefazolin		Moxifloxacin		Ticarcilllin +Clav.acid		Polymyxin B	
Cefoperazone+sulbact		Tetracycline		Nitrofurantion		Ticarcillin	
Cephotaxime		Nalidixic acid		Cotrimoxazole		Minocycline	
Cefuroxime		Doxycycline					

R: Resistant S: Sensitive M: Moderate

cooled to 50^0C Pin water bath and poured in Petri dishes. The specimen were then inoculated onto these media and incubated at 37^0C Temperatures for 24 hr.

IDENTIFICATION OF BACTERIA

Bacteria were identified by Gram Staining Technique. Gram positive and gram negative bacteria were separated by gram staining technique.

Morphology: The colonies of Gram positive bacteria were small, dry and rough while the colonies of Gram negative bacteria were large in appearance and moist.

Biochemical Identification: Biochemically, bacteria were identified by means of citrate utilization, triple sugar iron agar test (for identification of Gram negative rods), coagulation test (for differentiation of pathogenic and non-pathogenic strains of *Staphylococcus*) and oxidase test (for identification of Gram negative *bacilli*).

Antibiotic Sensitivity Test: Bacteria were then tested for their ability to grow in the presence of different antibiotics. The test required cultured organisms, nutrient medium and antibiotic discs. Nutrient agar was basically used to maintain the culture of control organisms. Nutrient broth contained beef extract, peptone and distilled water. The depth of medium was kept 5 mm with pH 7.4. The Petri dishes having nutrient media were kept at 4^0C and the plates were kept in incubator at 37^0 C for 20 minutes to dry off the vapors. About 5 colonies of similar morphology were taken by using a sterile wire loop and suspended in 5 ml nutrient broth. The broth was left for 10 minutes after inoculation. The prepared culture was then poured uniformly onto the surface of agar plates and left for 4 minutes.

INTERPRETATION OF RESULTS

After 24 hours of incubation, the plates were examined for the presence of growth inhibition which is indicated by a clear zone surrounding each disc. The susceptibility of organisms was determined, using National Committee Control for Laboratory Standard (NCCLS) recommendations and expressed the results in mm. Accordingly, the results were recorded in investigation form as Sensitive (S), Intermediate (I) and resistant (R) respectively.

RESULTS

Two hundred and nine (209) out of the 721 patients admitted to internal medicine ward during study period. Out of total 209 patients, 119(56.9%) were male and 90(43%) were female. antibiotics prescribed in 209 patients. The table no. 2 shows different age groups of patients. The highest no. of patients i.e. 40 were in age group 61-70 and lowest no. of patient's i.e.02 were in age group 0-10.

Culture and sensitivity testing was carried out in 177 patients (84.6%) The results were negative in 46 patients. 131 patients normal flora were grown. 108 patients had single specimen, 19 patients had two specimens and 04 patients had three specimens sent for culture and sensitivity testing. Total 204 samples were sent for testing and 158 organisms were isolated. Most frequent specimen were Urine, Tracheal secretion, Pus, Sputum, Blood, Throat swab, Wound swab, Cath tip and others.

Table 2: Number of antibiotics prescribed during hospital stay:

No. of Antibiotics prescribed	No. of patients
1	19
2	54
3	64
4	32
5	24
6	9
7	5
8	3

MAJOR SENSITIVE ANALYSIS

Urine: Highly sensitive microorganism was *E-coli (n=17)* & towards this highly sensitive antibiotic Ceftriaxone (94.1%) and Highly resistant antibiotics were Amoxicillin+clav.acid & Meropenam (82.4%).

Tracheal secretion: Highly sensitive microorganism was *K.pneumoniae* (n=8) & towards this highly sensitive antibiotics were Cefepime (87.5%), pipracillin+tazobactum (87.5%), Ceftazidime (87.5%) and Highly resistant antibiotics was Cefotaxime (87.5%)

Sputum: Highly sensitive microorganism was *K.pneumoniae* (n=7) & towards this highly sensitive antibiotics were pipracillin+tazobactum (100%), ciprofloxacin (100%) and Highly resistant antibiotics was Cefotaxime (71.5%).

Pus: Highly sensitive microorganism was *P. aeurigenosa* (n=10) & towards this highly sensitive antibiotics were pipracillin+tazobactum (80%) and Highly resistant antibiotic was Amoxicillin+ clav.acid (90%).

Blood: Highly sensitive microorganism was *Staph.aureus* (n=7) & towards this highly sensitive antibiotics were pipracillin+tazobactum (85.7%) and Highly resistant antibiotic was Netilmicin (42.8%).

Table 3: Culture and Sensitivity Testing:

Total No. of Patients	Sensitivity Done		Sensitivity Not Done
209	177		32
	Normal flora grown	Normal flora not grown	
	131	46	

Table 4: Common conditions for which antibiotics were prescribed

Disease	No. of patients	Antibiotics prescribed (percentage)
Urinary tract infection(UTI)	34	124(23.3)
Chronic obstructive pulmonary disease(COPD)	19	73(13.7)
Pleural effusion	O8	32(6)
Cellulites	06	21(3.9)
Lower respiratory tract infection(LRTI)	05	13(2.4)
Other diseases	137	269(50.5)
Total diseases	209	100%

Table 5: Frequency of most commonly prescribed antibiotics during study.

Name of antibiotic	ATC code	Number of prescriptions (percentage)
Pipracillin+tazobactum	J01CR05	49(9.2)
Amoxacillin+Clav.acid	J01CR02	49(9.2)
Amikacin	J01GB06	48(9.0)
Cefuroxime	J01DC02	47(8.8)
Metronidazole	J01XD01	38(7.1)
Ceftriaxone	J01DD04	30(5.6)
Meropenem	J01DH02	26(4.8)
Cefoperazone+sulbactum	J01DD62	18(3.3)
Ciprofloxacin	J01MA02	17(3.1)
Levofloxacin	J01MA12	16(3.0)
Doxycycline	J01AA02	13(2.4)
Cefipime	J01DE01	12(2.2)
Ceftazidime	J01DD02	10(1.8)
Linezolid	J01XX08	10(1.8)
Netilmicin	J01GB07	8(1.5)
Others	-	141(26.5)
Total	-	532

Table No.6: Major sensitivity analysis:

Specimen	Highly sensitive Microorganism	highly sensitive antibiotics	Highly resistant antibiotic
Urine	*E-coli (n=17)*	Ceftriaxone (94.1%)	Amoxicillin +clav.acid & Meropenam (82.4%)
Tracheal secretion	*K.pneumoniae* (n=8)	Cefepime, pipracillin+ tazobactum, Ceftazidime (87.5%)	Cefotaxime (87.5%)
Sputum	*K.pneumoniae* (n=7)	Pipracillin +tazobactum, ciprofloxacin (100%)	Cefotaxime (71.5%)
Pus	*P. aeurigenosa* (n=10)	Pipracillin +tazobactum (80%)	Amoxicillin + clav.acid (90%)
Blood	*Staph.aureus* (n=7)	Pipracillin +tazobactum (85.7%)	Netilmicin (42.8%)

Mean± SD cost of Antibiotics: The Mean ± SD cost of most commonly prescribed 15 antibiotics during hospital stay was **338.76 ± 320.76 INR.**

DISCUSSION

Antibiotic resistance among pathogenic microorganisms is a matter of worldwide concern. Selective pressure by antimicrobial drugs is by far the most important driving force for the development of such resistance. Antibiotics are among the most commonly prescribed drugs in hospitals and in developed countries around 30% of the hospitalized patients are treated with these drugs [11]. The present study documents that 28.9% of the patients were prescribed antibiotics. This is very similar to the reports from developed countries [12]. Antibiotic prescription was studied over 6 months, the major disadvantage being that seasonal variations in antibiotic prescribing could not be taken into consideration over this short period.

The number of samples which were sent for culture and sensitivity testing were small which may also affect the validity of the conclusions drawn about antibiotic resistance. Among patients admitted to the internal medicine ward, there was a preponderance of those the age of 41-80 years. This factor may have influenced antibiotic prescribing as older patients are more likely to be sick and to have more serious illnesses. The Mean duration of hospitalization was 15.9 days and median duration of hospitalization was 21 days. The majority of patients were hospitalized for a time period between 4 to 18 days.

COPD, LRTI and UTI were the most frequent clinical conditions for which an antibiotic was prescribed. The morbidity Profile of antibiotic use broadly corresponds to that observed in an Indian study.[12] In another study from Israel, antibiotics were most commonly used in respiratory tract infection and UTI followed by sepsis and intra-abdominal infections. However, the authors had looked at the entire hospital patient population [13]. The antibiotics most frequently prescribed together were Amoxacillin+clav.acid, Piperacillin+tazobactum, Cefoperazone+sulbactum. Two or Three

antibiotics were prescribed to patients in whom the antibiotics were changed either after reviewing the culture and sensitivity results or due to lack of improvement in the clinical condition. Four or more antibiotics were started together in seriously ill patients.

Eighty four Percent (84.7%) of the patients were prescribed antibiotics by the parenteral route. In a study reported from South India [14], 36% of antibiotics were prescribed by the parenteral route. In the israeli study[13], 64% of antibiotics were prescribed parenterally. Parenteral antibiotics in the study were prescribed for a median duration of 5 days. The duration of use of parenteral antibiotics was increased and the patients not switched over earlier to oral antibiotics. In our hospital the use of parentral antibiotics was very high which leads to increase the cost of medicines and bacterial resistance towards various antibiotics were developed in patients.

In Canada a route conversion program on the prescribing of antimicrobials succeeded in reducing the frequency of use of parenteral antibiotics [15]. Parenteral antibiotics are costly and the cost of drugs is a major factor influencing treatment in a developing country like India. In our hospital, patients are usually discharged once the antibiotics are changed from the parenteral to the oral route.

Early switchover to oral antibiotics may be more difficult for rural patients as they may have difficulty in accessing medical care in case of problems. The patients are generally unwilling to stay in the hospital after injectable drugs have been stopped. Economic considerations may be partly responsible for the desire to continue further treatment at home. The patients can be educated about the need for remaining under observation in the hospital even after the stoppage of parenteral drugs, thus a programme similar to the one in the Canadian study could be implemented in our hospital for cost-effective use of parenteral antibiotics.

Antibiotics were used for BPI in 131 patients. Two hundred and nine (209) patient antibiotics were prescribed. In BPI the patient's lab data shows positive reports against microorganism. In 15 patients the antibiotic was changed after reviewing the sensitivity report. In 8 patients though the organism was resistant to the antibiotic, the patient improved clinically and the use of the antibiotic was continued. Delay in receiving the sensitivity reports was a problem encountered and may have delayed switching over the patient to the sensitive antibiotic. Steps which could be taken to quicken the report availability are:

a) Immediate transport and processing of the specimen after collection.

b) Constant monitoring of the culture systems to detect growth.

c) Identification of the organism and antibiotic sensitivity testing (AST) to be done at 16hr.

d) Reading of the AST to be taken 16 hr after putting the antibiotic disc.

e) Immediate dispatch, collection and interpretation of the results.

In our hospital due to logistical problems these steps cannot be followed strictly within the specified time period, hence the results are delayed by about 12 to 24 hr.

Antibiotics were used in non-BPI in 24.2% of the cases. In Western Nepal study of ICU patients 84.5% of the antibiotics were prescribed without bacteriological support [16]. In an Indian study 62% of prescriptions were therapeutic, of which 36% were therapeutic prescriptions without bacteriological support while 59% were on a bacteriological basis [17]. This shows that in our hospital antibiotics were prescribed mostly after culture and sensitivity testing. Pipracillin+tazobactum, Amoxacillin+clav.acid, Cefuroxime, Amikacin, Metronidazole, Ceftriaxone, Meropenem, Cefoperazone+sulbactum, Ciprofloxacin, Levofloxacin, Doxycycline, Cefipime, Ceftazidime, Linezolid, and Netilmicin were the 15 most commonly prescribed antibiotics. In many patients treatment was started with parenteral Pipracillin+tazobactum, Amoxacillin+clav.acid which later changed to oral amoxicillin and cefuroxime once the condition of the patient improved. The use of cephalosporin's i.e. Cefuroxime (8.8%), Ceftriaxone (5.6%), Cefoperazone +sulbactum (3.3%), Cefipime (2.2%), Ceftazidime (1.8%) total=21.7% in this study was less than that reported in the literature. while in the study carried out at a rural hospital, Ceftriaxone (19%) and cefuroxime (11.8%) together accounted for 30.8% of the total antibiotic days [18] which shows that comparatively less amount of cephalosporin's were used in this study. While this study was confined to the internal medicine ward. The isolated organisms are becoming resistant to the

commonly used antibiotics and cephalosporins may have to be prescribed in resistant cases. Cephalosporins are available in the hospital pharmacy but more data on sensitivity patterns is required before they can be more frequently prescribed. Total 204 samples were sent for culture and sensitivity testing and 158 organisms were isolated. The small number of specimens may, however, limit conclusions about antibiotic resistance. Carrying out the study for a longer period of time could partly overcome this lacuna. *E.coli, K.pneumoniae, P. aeurigenosa, Staph. aureus* were the commonest organisms isolated and were resistant to Amoxacillin+clav.acid, Ciprofloxacin, Cefuroxime and Netilmicin in a significant number of cases. Urine was the second most common specimen sent for culture and sensitivity testing. In a study reported from Trinidad [19], *E. coli* was the most frequent isolate from urine samples and was mostly resistant to tetracycline, trimethoprim and cotrimoxazole. The low number of samples in this study makes it difficult to draw firm conclusions but an increasing resistance of *E. coli* and *S. aureus* to commonly used antibiotics is observed.

As reported earlier, *E-coli*, K.pneumoniae, *P.aeurigenosa and Staph.aureus* were the five most prevalent species isolated from Internal Medicine Ward patients. The hospital Internal Medicine Ward is highly susceptible to *E-coli (n=27), P. aeurigenosa (n=26), K.pneumoniae (n=26), Staph.aureus (n=19), Candida albicans (n=2) acitobactor species (n=1) and streptococcus pneumonia* respectively. So from all this data it is interpreted that both gram positive and gram negative bacteria were highly susceptible to pipracillin+tazobactam (90.33%), Amikacin (75.65%),Cefuroxime(60.83%) and highly resistance to Ciprofloxacin(40.56%), Amoxicillin+clav.acid (40.42%).

CONCLUSION

Apropos study, Antibiotics which are mostly sensitive towards hospital acquired microorganisms must be keep always available. Parentral antibiotics (84.7%) prescribed leads to increase SD cost of total antibiotics prescribed during hospital stay and prepare guidelines to reduce them.

- There should be rational use of antibiotics.
- In many patients treatment was started with parenteral antibiotics which later changed to oral antibiotics once the condition of the patient improved.
- Decrease the prescribing of parental antibiotics and early switch to oral antibiotics is most important. An intravenous to oral antibiotic conversion program can be instituted.
- Quickening the availability of culture and sensitivity reports is most important
- Antibiotics should be prescribed not only depending on their sensitivity but also on their cost and availability.
- Formulation of a policy for hospital antibiotic use and an educational programme especially for junior doctors is required
- Variation between Antibiotics prescribed before culture report should be matched with Ideal Antibiotics guidelines.
- There should be a continuous monitoring of the presence of resistant microorganisms and avoidance of continued or overuse of any one antibiotic for a longer period of time.
- The low number of samples in my study makes it difficult to draw firm conclusions about sensitivity pattern of antibiotics towards different microorganisms
- Lastly, there is a need of research for alternative antibacterial agents which should have high efficiency against bacterial pathogens.

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