IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 14, Issue 6 Ver. VIII (Jun. 2015), PP 82-85
www.iosrjournals.org

Correlation between Antimicrobial Consumption and Antimicrobial Resistance in A Tertiary Care Hospital

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Abstract:
Introduction: *Antibiotics are given for patients posted for surgery as a precautionary measure. They may cause resistance in the hospital microbial flora leading to resistant nosocomial infections.*
Aim: *This study is aimed at finding the relation between the antimicrobials used in a hospital and the resistance patterns observed in the organisms isolated.*
Materials &Methods: *The study was conducted in a tertiary care hospital using cefotaxime- sulbactam as routine antimicrobial cover. 60 isolates of Gram negative bacilli were isolated from post-operative patients, from various samples like pus, urine and blood. They were identified and tested for resistance against ceftazidime, cefepime, cefotaxime + sulbactam, cephalexin, gentamycin, amikacin, imipenem, norfloxacin, ciprofloxacin.*
Results: *91% of the isolates were resistant to ceftazidime. 75% were resistant to cefotaxime –sulbactam. 6% were found to be resistant to Imipenem. 87% of the pus samples were resistant to cefotaxime-sulbactam. All the isolates resistant to cefotaxime-sulbactam were found to be resistant to ceftazidime. 25% were resistant to aminoglycosides and 12% resistant to fluoroquinolones.*
Conclusions: *Routine use of extended spectrum cephalosporins can cause increased resistance to β-lactams and aminoglycosides. Continuous surveillance regarding the antibiotic usage and resistance patterns should be done. Stringent regulations should be put in hospitals regarding the antibiotic precautionary measures.*
Keywords: *Antibiotic resistance , Cefotaxime-sulbactam, Gram negative bacilli , Prophylaxis , Nosocomial infections*

I. Introduction

The hospital flora are continually exposed to high amounts of antibiotics thus favoring resistant strains. Continuous use of antimicrobials is implicated as one of the reasons for the development of antimicrobial resistance.[1]This may be due to either a single drug or many drugs. Thus multi drug resistant strains are isolated from hospital environment.

In addition, lots of patients coming to hospital would have taken antibiotic course either from a primary care physician or a pharmacist or over the counter. This exposes the invading organism to various types of antibiotics and thus multi drug resistant strains develop.

Gram Negative bacilli like Klebsiella, Pseudomonas, E. coli, Acinetobacterspp. etc are the leading cause of nosocomial infections.[2]The incidence of infections caused by the antimicrobial resistant strains has increased in the recent years. It is presumed that the antimicrobial resistant strains cause greater mortality, longer hospitalization and higher costs than the infections caused by the susceptible strains.[3] Resistance develops far faster in Gram negative bacteria than Gram positive bacteria.This is due to the presence of mobile genes on plasmids that can readily spread through bacterial populations.[4]

The present study was conducted in a hospital which uses Cefotaxime – Sulbactam as antibiotic cover for the patients posted for surgery . The study was aimed at finding the antimicrobial resistance pattern of the Gram Negative Bacilli isolated from the postoperative patients with nosocomial infections and to correlate it with the routine antibiotic usage.

II. Materials & Methods

The study was conducted in a tertiary care hospital which uses Cefotaxime – Sulbactam combination as antibiotic cover to prevent nosocomial infections. The surgical patients were given the drug 1 day prior to the surgery and continued till 3 – 5 days after the surgery in a dose of 500mg BD. Any nosocomial infections in postoperative patients are treated with Amikacin,or Linazolid . 60 isolates of various Gram negative Bacilli were obtained from various samples (n=70) like pus, urine and blood from the post operative patients . They were identified by various biochemical tests. Then they were subjected to Modified Kirby Bauer's Disc diffusion test with the following antimicrobials , Ceftazidime, Cefepime, Cefotzime + Sulbactam, Cefalexin, Gentamycin,

Amikacin, Imipenem, Ciprofloxacin and Ofloxacin. The resistant isolates were identified according to CLSI guidelines. Negative controls used were Escherichia coli ATCC 25922 and Pseudomonas aeruginosa ATCC 27853.

III. III. Results

A total number of 60 isolates of various Gram Negative bacilli were obtained from a tertiary care hospital from post operative patients.

TABLE 1 : Sex wise distribution of the isolates

Sample	Male	Female	Total
Pus	29	14	43
Urine	15	5	20
Blood	7	0	7
Total	51	19	70

TABLE 2 : Organisms isolated from various samples

Organism	Pus	Urine	Blood
Klebsiella pneumonia	12	8	0
Escherichia coli	12	6	0
Pseudomonas aeruginosa	9	4	3
Proteus species	4	0	0
Acinetobacterspp.	2	0	0
Total	39	18	3

TABLE 3 : Resistance of isolates to various drugs tested

Drug Tested	Resistant	Sensitive	Total
Ceftazidime	55 (91%)	5	60
Cefepime	49 (81%)	11	60
Cefotaxime + Sulbactam	45 (75%)	15	60
Cefalexin	29 (48%)	31	60
Gentamycin	16 (26%)	44	60
Amikacin	13 (21%)	47	60
Ciprofloxacin	7 (11%)	53	60
Imipenem	4 (6%)	54	60
Ofloxacin	3 (5%)	57	60

TABLE 4 : Multidrug resistance among the isolates

No. of drugs resistant	No. of Isolates
1 drug	2 (3.3%)
2 drugs	5 (8.3%)
3 drugs	9 (15%)
4 drugs	20 (33.3%)
5 drugs	12 (20%)
6 drugs	8 (13.3%)
7 drugs	4 (6.6%)
Total	60

TABLE 5 : Sample wise distribution of Cefotaxime + sulabctam resistant isolates

Sample	No. of Cefotaxime + sulbactam resistant isolates
Pus	34
Urine	11
Blood	0
Total	45

TABLE 6 : Antimicrobial susceptibility pattern of Cefotaxime + Sulbactam resistant isolates

Drug	Resistant	Susceptible
Ceftazidime	45	0
Cefepime	35	10
Cefalexin	23	22
Gentamycin	8	37
Amikacin	3	42
Imipenem	0	45
Ciprofloxacin	0	45
Ofloxacin	0	45

IV. Discussion

In the present study, the resistance observed for various drugs correlates with that observed in a nation-wide survey done by Global Antibiotic Resistance Partnership (GARP) – India Working Group.[5]

TABLE 7 : Comparison of resistance to various drugs

Drug	Current study	Average resistance
Ceftazidime	91%	80%
Cefepime	81%	80%
Cefotaxime + Sulbactam	75%	30%
Cefalexin	48%	50%
Gentamycin	26%	56%
Amikacin	21%	56%
Ciprofloxacin	11%	36%
Imipenem	6%	39%
Ofloxacin	5%	36%

There was increased resistance to Cefotaxime + Sulbactam (75%) in the current study than that compared to that observed in the GARP survey(30%). It may be attributed to the use of Cefotaxime + Sulbactam as the routine antimicrobial agent in the hospital. This correlates with the studies of Po-RenHsueh et al and Goossens H et al, where it was found that there is significant raise in the resistance to β-lactam drugs which are used for prolonged periods.[6,7.] The study by Po-RenHsueh et al was conducted over a period of 13 years during which the researchers found that there is not only significant change in the use of antibiotics in hospitals but also the resistance patterns as well.[6]

73.3% of the isolates were resistant to 4 or more drugs. All the isolates found resistant to Cefotaxime + Sulbactam were found to be resistant to 4 or more drugs. This correlates with the finding of Montraverset al.[8] They found that resistance was seen for many antibiotics when β-lactam antibiotics were used for empirical therapy. There was increased resistance to extended spectrum cephalosporins, carbapenems and aminoglycosides. This correlates with the study of Lai CC et al.[9] This may be attributed to the fact that prolonged use of β-lactams favor the propagation of Class I integrons which confer resistance to sulphonamides, Extended spectrum cephalosporins, aminoglycosides and carbapenems.[10]

There was no increased resistance to fluoroquinolones observed in the present study. This correlates with the study of Lai CC et al. They found out that consumption of extended spectrum cephalosporins is not associated with any increase in resistance to fluoroquinolones but consumption of flouroquinolones is positively associated with increased resistance to ceftazidime.[9]Some studies have found out reduced resistance to fluoroquinolones and they attributed this to the observation that fluoroquinolones are not generally prescribed as routine antibiotics. [11,12 and 13] This may also be contributing to the decreased resistance found in the current study to fluoroquinolones than other studies.

There were multiple risk factors favoring the development of multi-drug resistance in the current study. Continuous use of single antibiotic for empirical therapy has been implicated in development of multi-drug resistance in tertiary care hospitals.[14]Another important risk factor is inadequate antibiotic therapy. The patients coming to the tertiary care hospital are mostly treated inadequately prior to the admission in the hospital. Inadequate antibiotic treatment has been found to correlate positively with the development of multi drug resistance.[15 & 16]Use of another antibiotic to treat the resistant infections also contribute to the development of multi-drug resistance as the hospital microbial flora act as reservoir for resistant strains.[17] The time over which the antibiotic prescribed is also associated with the development of resistance. A study in Finland showed positive correlation with development of resistance for the empirical antimicrobial used in the hospital over a year.[18]

V. Conclusions

There was positive correlation between development of multi drug resistance and consumption of extended spectrum β-lactam antibiotics. Prolonged use of extended spectrum cephalosporins can cause increased resistance to many drugs like β-lactams, amino glycosides and sulphonamides. Multi-drug resistant Gram negative bacteria due to the production of extended spectrum beta lactamases have become very common in India.[18,19]

In India the infectious disease burden is highest in the world and a recent study showed the inappropriate and irrational use of antimicrobial agents against these diseases, which led to increase in development of antimicrobial resistance.[20]In order to tackle the growing problem of antimicrobial resistance many countries have formed surveillance committees, e.g. The European Surveillance of Antimicrobial Consumption (ESAC programme), collecting data from 35 countries, Global Antibiotic Resistance Partnership (GARP) with India, Kenya, Vietnam and Korea.[21,22]

In addition to that, the Directorate General of health services, India has issued "National policy for containment of antimicrobial resistance" to tackle the problem of increasing antimicrobial resistance in the country. It outlines strict policies for surveillance of antimicrobial resistance and inter departmental co-ordination. It is currently working on development of a national antibiotic policy and designing appropriate strategies to improve drug use and prevent the emergence of resistance.

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