Cephalosporin resistance: Challenges in providing appropriate and effective treatment protocols

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ABSTRACT

Empiric therapy is designed to target the microbes that are likely to exist. Appropriate choice of empiric therapy, helps limit the antibiotic consumption and decreases morbidity and mortality. Cephalosporins have often been the mainstay of these protocols. In the present study, overall resistance to antibiotics was 48.69%. Resistance to fourth generation cephalosporins ran parallel to that of third generation cephalosporins. Temporary stoppage or limiting the use of cephalosporins is indicated.

Key words: *Cephalosporins, Resistance, ESBl*

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INTRODUCTION

Antimicrobial drug resistance cannot be taken for granted as they are increasingly attaining the status of non-renewable resources.[1] Since, the time of their introduction; Cephalosporins have been popular as both empiric and definitive therapy due to their wide spectrum of action against microbes. The rise in resistance to these antimicrobials in recent years is of concern. Variables predicting 3GC resistance are surgery, Intensive Care Unit (ICU) stay, receipt of beta lactams/inhibitors, ureidopenicillins, 3GC[2], all of which are routine in the health care systems and protocols. Besides the possibility of treatment failures, exposure to betalactums is known to increase the synthesis of Extended spectrum beta lactamase (ESBL) and AmpC beta lactamases.[3] Perhaps it is time to review the utility of cephalosporins in order to prevent further spread of multidrug resistant bacterial clones.

MATERIALS AND METHODS

The present study aimed to find the extent of resistance to various classes of antimicrobials among Escherichia coli (E coli) and *Klebsiella pneumoniae* and to also find the ESBL and Amp C producers among them. 100 each of E coli and *Klebsiella pneumonia*, isolated from routine samples like pus, urine and blood during January 2010 to June 2010 were included in the study. The study involved testing of antimicrobial susceptibility as per standard methods to routinely used antimicrobials like ampicillin, amikacin, fluroquinolones (ciprofloxacin, levofloxacin and gatifloxacin), 1st,2nd,3rd,4th generation cephalosporins, piperacillin/ tazobactum.[Table 1] ESBL was detected by phenotypic disc diffusion test with ceftazidime and ceftazidime/clavulanic acid, AmpC was detected by cefoxitin disc diffusion screening test method.

RESULTS

Overall 51.69% of E coli and 45.65% of Klebsiellae were found to be resistant to various antibiotics. Contrary to our expectation Klebsiellae were found to fare better that E coli in terms of resistance. Average resistance to cephalosporins was 58.57% among E.coli and 49.57% among Klebsiella.[Table 1] Surprisingly, not only the third but even the fourth generation cephalosporins have attained considerable resistance. Resistance to fourth generation cephalosporins was only marginally lower 42.25% in comparison to 53% among the third generation cephalosporins.

Table: 1

Antibiotics	E. Coli N=100	Klebsiella N=100	Total N=200
Ampicillin	92	89	181(90.5%
Amikacin	25	23	48(24%)
Ciprofloxacin	52	41	93(46.51%)
Gatifloxacin	8	3	11(5.5%)
Levofloxacin	33	35	68(34%)
Co trimoxazole	52	63	115(57.5%)
Cefazolin	71	62	133(66.5%)
Cefuroxime	68	62	130(65%)
Cefotaxime	60	52	112(56%)
Ceftriaxone	59	41	100(50%)
Ceftazidime	58	48	106(53%)
Cepirome	48	39	87(43.5%)
Cefepime	46	36	82(41%)
ESBL	41	40	81(40.5%)
Amp C	36	34	70(35%)

E. Coli: Escherichia coli, ESBL: Extended Spectrum Beta Lactamase, Amp C: Amp C beta lactamase

DISCUSSION

The results raise questions regarding the use of cephalosporins as there is approximately a 50% possibility of treatment failure if used as empirical therapy. In contrast the overall resistance to aminoglycosides was lower i.e 24%. Although average resistance to fluroquinolones (ciprofloxacin, gatifloxacin, and levofloxacin) was also low 28.66%, much of this could be attributed to exceptionally low resistance to gatifloxacin 5.5%. Otherwise resistance to ciprofloxacin was quite high 46.5%. [Table 1]

The European Antimicrobial Resistance surveillance have described resistance against 3GC in E coli as the most dynamic expansion of multidrug resistant pathogens. [4]

The increase in resistance demonstrates the dangerous spiral of spread of resistance and antibiotic use. It also indicates a rise in ESBL producing bacteria. [1] In the present study, 81(40.5%) of the isolates were ESBL and 70(35%) were Amp C beta lactamase producers. ESBLs and AmpC beta lactamases were more often found among Ecoli %, compared to Klebsiella %. [Table 1]

The rapid and disturbing spread of ESBL, Amp C enzymes and quinolone resistance is forcing increased reliance on carbapenams with resistance to these slowly accumulating via the spread of metallo, KPC, OXA 48 beta lactamases. [5]

The presence of co resistance to other antimicrobials further complicates the treatment leaving very few choices. Among the ESBL positive E coli, more than 80% and > 40% are reported to be resistant to fluroquinolones and gentamicin.[6] In the present study too, despite the relative lower resistance to amikacin and fluroquinolones in general, co resistance to these antibiotics was considerably more among the ESBL producers. For instance, of the 81 ESBL producers, 48.14% of them were resistant to amikac in and 59.25% to fluroquinolones among which, highest resistance was noted to ciprofloxacin 93.82% and lowest to gatifloxacin 11.11%.[Table 1] It is now common to see enterobacteraceae susceptible only to carbapenems, tigecycline and polymyxin.[7]

Furthermore, ESBL producing, quinolone resistant E coli are also seeping into the community which is of concern in treating common infections like UTI that are no longer easy to treat with oral agents. [5]

Although development of newer antimicrobials appears to be an urgent need, they will only be useful for a short time as the microbes quickly adapt for survival thus highlighting the importance of other ways of resistance reduction. Besides the infection control measures, the prevention of emergence of resistance entails several strategies viz: decrease in antibiotic consumption, antibiotic cycling, new dosing strategies, combination of two classes of antibiotics. [8]

In recent years in the west, carbapenams, quinolones and third and fourth generation cephalosporin use has increased and aminoglycoside consumption has decreased substantially.[1] An informal review in our hospital predictably revealed that 3GC were extensively used. An Indian study in 2007 reported that ceftriaxone and amikacin are the commonly prescribed antibiotics.[9] The choice and the amount of antibiotic consumption is largely subjective and is often unchecked and unregulated. In case of antibiotic cycling, there is a more or less general agreement that the over use of one group of antibiotics selecting for similar resistance genes should be avoided.[8]

Considering all these factors, it is probably time to look beyond cephalosporins as they are burdened with various beta lactamases that undermine their effectiveness. This is especially true for empirical therapy. Nevertheless, presuming a bleak future in antibiotic therapy may be exaggerated. The picture is more mixed, improving against some pathogens but worsening against others. [5] As the options for infections with multidrug resistant GNB and KPC producing organisms are limited, besides tigecycline, old antibiotics like aminoglycosideds, fosfomycin, colstin and rifampin will have to be reemployed. [1]

Interventional studies are needed to determine whether replacing 3GC with fluroquinolones will be effective in reducing cephalosporin resistance and also the effect of such interventions on flouroquinolone resistance.[2]

CONCLUSION

Rsistance to 4th generation Cephalosporins runs parallel to that of third generation cephalosporins, which probably is a wake up call and indicates the temporary stoppage or reduction in cephalosporin use. The multi drug resistance appears to be driven by the ESBLs and AmpC beta lactamases. Switching over to quinolones, aminoglycosides and tigecycline depending on the infection to be treated, appears to be prudent at present. However continuous monitoring and detection in the microbiology laboratory is indicated.

The study also highlights the need for Indian data on antibiotic consumption and intervention studies so as to revise the therapeutic and prophylactic treatment strategies more scientifically.

REFERENCES

1. Meyer E, Schwab F, Schroeren B, Gastmeier P.Dramatic increase of third-generatin cephalosporin- resistant E. coli in German intensive care units: secular trends in antibiotic drug use and bacterial resistance, 2001-2008. Critical care 2010, 14: R113
2. Schwaber MJ, Cosgrove SE, Gold HS, Kaye KS, Carmeli Y. Fluoroquinoloes protective against cephalosporin resistance in gram negative nosocomial pathogens. Emerg Infect Dis, 2004 Jan; 10(1):94-99
3. Kaye KS, Cosgrove SE, Harris A, Eliopoulos GM, Carmeli Y. Risk Factors for Emergence of Resistance to Broad-Spectrum Cephalosporins among Enterobacter Spp. Antimicrob Agent and Chemotherap , Sept 2001;45(9):2628-2630.
4. European Antimicrobial Resistance Surveillance System annual report 2008 [http://WWW.rivm.nl/ears/Images/EARSS 2008_final_tem 61-65020.pdf]
5. Livermore DM. Has the era of untreatable infections arrived? J of Antimicrob Chemotherapy, 2009; 64(S 1):i29-i36
6. Livermore DM, Hope R, Brick G et al. Non Susceptibility trends among Enterobacteriaceae from bacteraemias in the UK and Ireland, 2001-2006. J Antimicrob Chemother 2008; 62(Suppl2):ii41-54
7. Livermore DM. Introduction: the challenge of multi resistance. Int J Antimicrob Agents 2007; 29(Suppl 3):S1-7.
8. Wagenlehner Flrian ME, Naber KG. Treatment of Bacterial Urinary Tract Infections: Present and Future. Europian Urology 2006; 49:235-244
9. Salman MT, Akram MF, Rahman S, Khan FA, Hasan MA, Khan SW. Drug prescribing pattern in surgical wards of a teaching hospital I North India. Ind J of Pract Doc 2008;5(2):5-6.

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