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Evaluation of the use of cephalosporin antibiotics in pediatrics

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ABSTRACT

The purpose of this study is to rationalize the use of cephalosporins in various common bacterial infections like infections of upper and lower respiratory tract, urinary tract, gastro- intestinal tract and of soft tissues in pediatrics (age range: neonate – 10 yrs). A retrospective study was carried out at multiple hospitals in the premises of Karachi. Not less than 150 prescriptions from pediatric ward were collected over a period of a month to evaluate the prescriptions for their rational approach. The prescriptions included in the study were from qualified doctors. Results showed that out of total prescriptions containing antimicrobial therapy collected from pediatric wards, 88.1% prescriptions contained cephalosporins, among which 1st generation cephalosporin 3.93%, 2nd generation cephalosporin 10.23% and 3rd generations cephalosporins 75% were observed. There is an urgent need to develop standards of antimicrobial drug prescriptions to avoid drug resistance.

INTRODUCTION

The cephalosporin antibiotics have become a major part of the antibiotic formulary for hospitals in affluent countries. They are prescribed for a wide variety of infections every day. Their undoubted popularity relies upon lesser allergenic and toxicity risks as well as a broad spectrum of activity (Dancer, 2001).

Cephalosporins are the most frequently prescribed class of antibiotics they are structurally and pharmacologically related to penicillin. Like penicillin cephalosporins have a beta-lactam ring structure that interferes with synthesis of the bacterial cell wall and are so named bactericidal. Cephalosporin compounds were first isolated from cultures of "cephalosporium Acremonium" from a sewer in Sardinia in 1948 by Italian scientist "Guiseooe Brotzu" (Jawetts et al, 2004). Cephalosporins are classified by generation. In general, lower-generation cephalosporins have more gram-positive activity and higher-generation cephalosporins more gram-negative activity. The fourth-generation drug cefepime is the exception, with gram-positive activity equivalent to first-generation and gram-negative activity equivalent to third-generation cephalosporins (Harrison et al, 2008). Third generation cephalosporins are less active against gram positive cocci.

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They are much more active against enterobacters and multiple resistant bacteria. A major advantage of third generations cephalosporins are active against gram negative rods. Third generation cephalosporins are useful in the management of hospital acquired infections like bacterimia and pneumonia (Jawetts et al, 2004).

In defense of the cephalosporin antibiotics, they provide useful activity against a number of common pathogens, and their low toxicity reassures clinicians and obviates the need for serum levels (Dancer, 2001; Neu, 1990). In general , the use of cephalosporins, even those extra ordinary potent under laboratory conditions, has resulted in the anticipated improvements in morbidity or mortality rates of common infectious syndromes, such as the pneumonias, meningitis, serious infections in cancer patients, complicated skin and soft tissue infections, urogenital infections, infective endocarditis, serious bone and joint infections and Salmonella infections in children. The introduction of new broad spectrum cephalosporins has improved the possibility of effectively treating infections with gram negative bacteria. High clinical and bacteriological success rates have been achieved with cefotaxime, moxalactam, ceftriaxone, ceftazidime, it soon became apparent however the use of this highly beta-lactamase stable antibiotic may also lead to rapid emergence of resistance bacterial strains in species such as enterobacter cloacae, pseudomonas auriginosa, serratia, citrobacter freundii.

A feature common to these entire micro-organism is the presence of an inducible chromosomal beta-lactamase which probably plays a major role in development of resistance. Cross resistance to all cephalosporins is the rule but in some cases susceptibility to aminoglycoside also decreased. In contrast to the large number of microbiological studies there are only few reports dealing with the clinical consequences of development of resistance.

Extensive cephalosporin class restriction significantly reduced nosocomial, plasmid-mediated, cephalosporin-resistant Klebsiella infection and colonization (James et al, 1998). Since 2008, there have been several outbreaks of cephalosporin-resistant Salmonella linked to animal products, with the most recent being Salmonella Hadar associated with the consumption of frozen turkey patties.

In addition, data from the Centers for Disease Control and Prevention show that approximately three percent of the estimated one million human Salmonella cases occurring in the United States annually are resistant to cephalosporin antibiotics. Treatment failures, including deaths, have already been reported among persons with cephalosporin-resistant Salmonella infections who were treated with cephalosporins.

MATERIALS AND METHODS

The study database was assembled from the records of patients (age range: neonates -12 years old) hospitalized at various hospital of Karachi, Pakistan. The retrospective analysis reported here in includes 6 months period from Nov2011 to Apr2012. It was found that most of the patients (children) were treated with broad-spectrum cephalosporins (ceftazidime, cefixime, ceftriaxone and cefotaxime). Clinical data was collected with the special considerations on the certain parameters including demographic details of patient (age and sex), infectious diseases (cardiovascular disease, skin infections, G.I.T and respiratory tract infections), and antimicrobial exposures of cephalosporin and details of antibiotic administration (the dosage form of drug, dosage, route of administration, dose intervals, and duration of therapy). The data collected was then keenly reviewed in order to promote rational use of cephalosporins and to prevent the problem of treatment failure.

RESULT

150 prescriptions were gathered from various hospitals and health care setups for patients having systemic infections. Among 150 prescriptions 88.1% of data contained cephalosporins as the treatment option in various infections as compare to penicillin 5.1%, macrolides 1.33%, aminoglycosides 44.5%, tetracyclines 0% and quinolones 1.96% in various systemic infection (upper respiratory tract infection, lower respiratory tract infection, CNS, UTI, GIT, and skin infections). It was found that the use of 3rd generation cephalosporin in these infections is 75% as compare to 3.93% 1st generation and 10.23% 2nd generation cephalosporin.

It has been reported that, penetration of some 3rd generation cephalosporin (cefotaxime, ceftriaxone and ceftazidime) into the CSF is adequate to effectively treat bacterial meningitis. The results (see Table 1) demonstrate that the % use of 1st generation cephalosporin in urinary tract infection is 2.36% and in GIT infection is 1.57% and the use of 2nd generation cephalosporin in CNS is 1.57% and in GIT its 8.66% .

By comparing this result with 3rd generation of cephalosporin the use of 3rd generation is much more than 1st and 2nd generation cephalosporin that is in upper respiratory tract infections 11.8%, in lower respiratory tract infection 26.7%, in CNS infections (meningitis) 14.9%, in UTI 3.29%, in GIT 16% and in skin infections 0.78% prescriptions were found in which 3rd generation cephalosporins were prescribed.

Table. 1: Comparative use of antibiotics in different systemic infections.

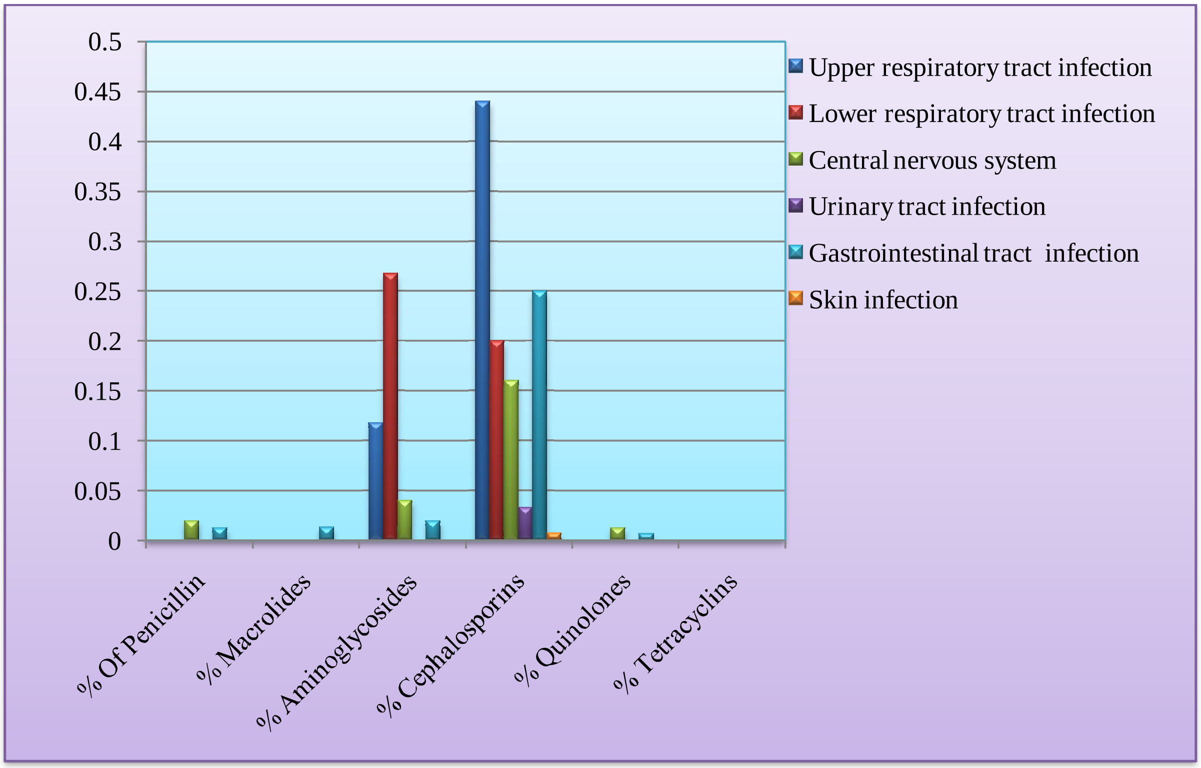
COMPARATIVE USE OF ANTIBIOTICS IN DIFFERENT SYSTEMIC INFECTIONS (n=150)

Systemic Infections	*% Of Penicillin*	*% Macrolides*	*% Aminoglycosides*	*% Cephalosporins*	*% Quinolones*	*% Tetracyclin*
Upper respiratory tract infection	------	------	11.8%	14%	------	------
Lower respiratory tract infection	------	------	26.7%	20%	------	------
Central nervous system	2%	----	4%	16%	1.3%	-----
Urinary tract infection	----	----	----	3.33%	------	------
Gastrointestinal tract infection	1.3	1.33%	2%	25%	0.666%	----
Skin infection	-----	----	-----	0.78%	---	----

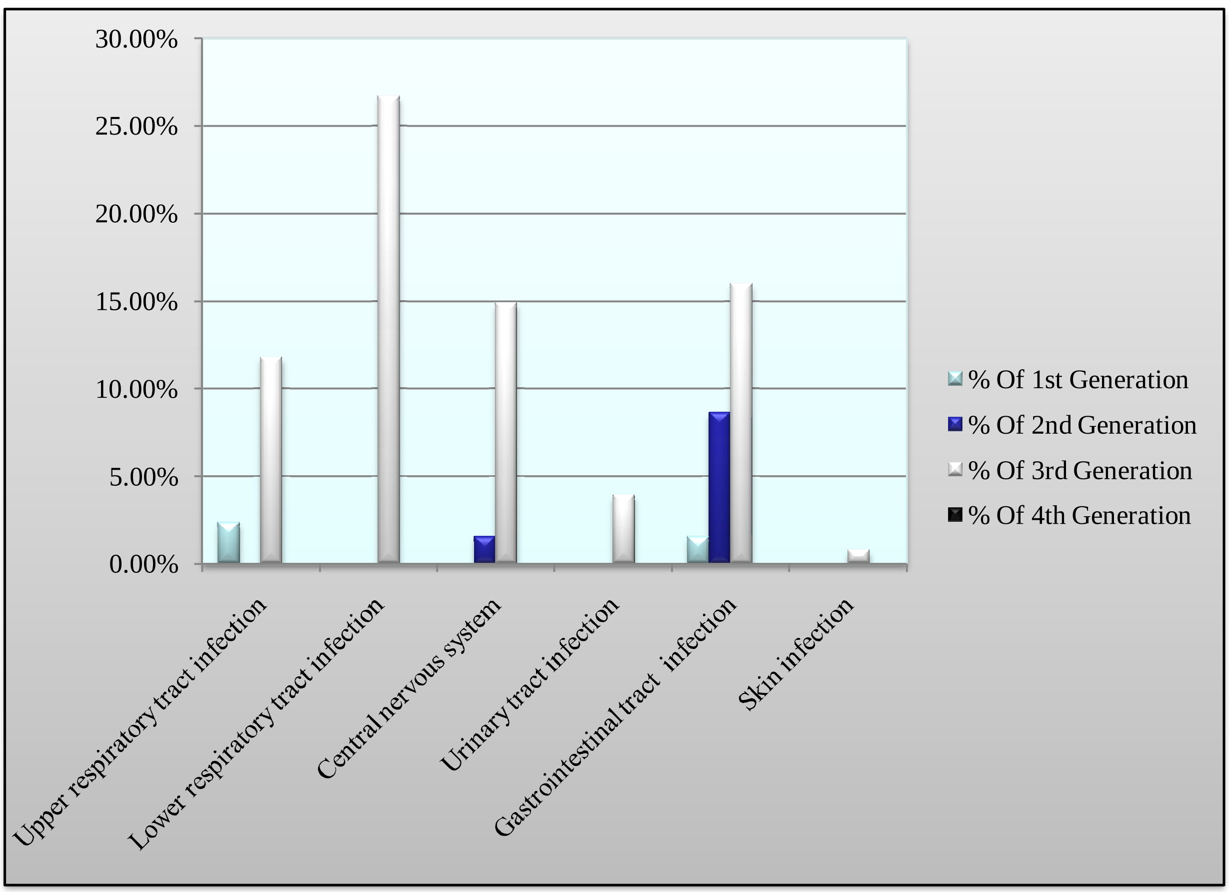
Table. 2: Use of different generations of cephalosporin in systemic infections.

USE OF CEPHALOSPORINS IN DIFFERENT SYSTEMIC INFECTION (n=150)

Systemic Infections	*% Of 1st Generation*	*% Of 2nd Generation*	*% Of 3rd Generation*	*% Of 4th Generation*
Upper respiratory tract infection	2.36%	-	11.8%	-
Lower respiratory tract infection	-	-	26.7%	-
Central nervous system	-	1.57%	14.9%	-
Urinary tract infection	-	-	3.92%	-
Gastrointestinal tract infection	1.57%	8.66%	16%	-
Skin infection	-	-	0.78%	-



Graph. 1: Comparative use of antibiotics in different systemic infections.



Graph. 2: Use of different generations of cephalosporin in systemic infection.

DISSCUSION

The cephalosporins are now becoming a major part of hospitals formulary as it deals with wide variety of systemic infections, to treat skin and soft tissue infection as well as for surgical prophyllaxis (Beers et al, 2003). Our study was conducted to evaluate the use of cephalosporins in the treatment of various infections. As it is evident that various bacterial species produce resistance against the cephalosporins because of the presence of beta-lactam ring in their structure. There are scientific reports that extensive use of cephalosporins have led to decreased efficacy of these antibiotics by resistant bacterias. If cephalosporins are not effective in treating these diseases, doctors may have to use drugs that are not as effective or that have greater side effects (FDA, 2012).

Healthcare-associated infections due to third-generation cephalosporin-resistant Enterobacteriaceae (CRE) have become a major public health threat, especially in intensive care units (ICUs) (E. O'Neill et al, 2005). .

Resistance to third-generation cephalosporins occurring among patients with Gram-negative bacillary meningitis have been reported in the past. Although the mortality and treatment failure rates were low, the future occurrence of Gram-negative bacillary meningitis owing to organisms resistant to both cephalosporins and carbapenems is a cause of worry as there are few options for therapy (E. O'Neill et al, 2005). During 2001--2010, decreased gonococcal susceptibility to cephalosporins and reported treatment failures have been documented in Asia (Tapsall, et al, 2009). According to a recent report, the cephalosporin (cefixime, ceftriaxone) susceptibility among *Nisseria gonorrhoeae* isolates was decreased in the United States during 2000—2010 (Carlos,2011). The potential emergence of cephalosporin resistance is of particular concern. Vigilance of clinicians and enhanced surveillance by local and state health departments will be critical for early detection of treatment failures.

CONCLUSION

Our study reveals the facts & figures about cephalosporins' extensive use as the scientific reports have proved that extensive use of cephalosporins may lead to decrease the efficacy of other beta lactam ring antibiotics by forming bacterial resistance. It is an alarming sign for all health care professionals to take immediate action on this because resistance development against cephalosporins by resistant strains of *Enterobacter cloacae*, *Serratia marcescens*, *Klebsiella oxytoca*, *Pseudomonas aeruginosa*, *Citrobacter freundii* and others may lead to severe clinical consequences such as treatment failure, relapse or secondary infections may occur (Follath, et al, 1987).

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