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COMPARATIVE ANTIMICROBIAL EVALUATION OF CEPHALOSPORINS AND QUINOLONES IN COMMON PAEDIATRIC INFECTIONS

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ABSTRACT

More than 90% of world's children are born each year in the developing world. Each year 12.9 million children die. Twenty eight percent of death are caused by pneumonia, 23% by diarrheal disease and 16% by vaccine-preventable diseases. Thirty-five thousand die each day, most from common and preventable problems. Health and illness are the result of a complex dynamic of environmental, social, political and economic factors. Bacterial resistance to antimicrobial agents is a continuing serious problem in the treatment of infections. Although this problem was recognized shortly after the commercial introduction of antimicrobial agents, it means that resistance is now emerging at a more rapid rate than ever before. To start with, during the present study an effort has been made to accomplish this task, 84 clinical isolates of *Staphylococcus aureus, Escherichia coli* and *Pseudomonas aeruginosa* were collected from different hospitals in Karachi. An *in vitro* study of these isolates was carried out by Agar dilution method using eleven antimicrobial agents and their combination (Lorian, 1991). Among Cephalosporins, third generation Cephalosporin, Cefotaxime was highly effective against Gram positive and Gram negative bacteria. Cefotaxime was active against *Staphylococcus aureus, Escherichia coli* and *Pseudomonas aeruginosa.* 1.19% isolates of *Staphylococcus aureus,* 19% isolates of *Escherichia coli* and 10% isolates of *Pseudomonas aeruginosa* were resistant against Cefotaxime. In Quinolone group, Ofloxacin was highly active against *Staphylococcus aureus, Escherichia coli* and *Pseudomonas aeruginosa.* Whereas 28% isolates of *Staphylococcus aureus*, 26% isolates of *Escherichia coli* and 11% isolates of *Pseudomonas aeruginosa* were resistant to Ofloxacin. Twenty six percent isolates of *Staphylococcus aureus* and 58% isolates *Escherichia coli* were resistant against Ciprofloxacin.

INTRODUCTION

Pediatric bacterial infections are very rapidly growing in developing countries of the world. In Pakistan due to lack of education and socio economical condition 75% population is being in rural areas. Even in city like Karachi, there is lack of hygienic conditions and mostly contaminated water is being consumed.

In recent years, pediatrics has enlarged its scope to include perinatology and adolescent medicine has placed increasing emphasis on prevention and early recognition of disease and has acknowledged and importance and interpendency of the behavioral, sociologic, economic and political aspects of child health care (Behrman *et al.,* 1998).

Pediatric infection vary widely among the nations of the world depending on a number of

factors which are after interrelated. These factor include:

- The prevalence of ecology of infections agent and their host.
- Climate and geography.
- Agricultural resources and practices.

The bacterial infection of the new born, infant and child should be defined those as they are used here:

- The neonates -- Birth to 1 month
- The infant -- 1 month to 1 year
- Early childhood -- 1 year to *5* year
- Late childhood -- 6 year through 12 year

Most pediatrician in the developed countries, especially the USA and Canada, are primary care practitioners who direct their efforts to keeping neonates, infants and children well. This is done through illness prevention, early detection and treatment of disease. Most pediatrics infection don't require hospitalization and those that do most after are managed by pediatrics sub specialist practicing in tertiary care hospitals pediatrics is a specially bound by age and not by system. (Behrman *et al.,* 1998).

Objectives of the Present Study:

- To evaluate the type of organism involved in common pediatric infections in Karachi.
- To evaluate / Study the resistance pattern of pediatric clinical isolate using Cephalosporins and Quinolones.

EXPERIMENTAL

Agar Dilution Susceptibility Test:

To determine the MIC for one or more bacterial isolates, the study drug may be incorporated into a liquefied agar medium (45-50^{o}C), which is then mixed, poured into petri dishes and allowed to solidify (Barry, 1976; Snyder *et al.,* 1976). A series of petri plates are prepared with increasing concentration of the drug and with the aid of a multiple inoculum replicator (Steers *et al.,* 1959) as many as 11 different strains can be spot inoculated on to each plate. After overnight incubation, the MIC end point is read as the lowest concentration that completely inhibits growth, disregarding a single colony or faint haze or growth (Barry, 1976, Ericson, 1971 and Washington, 1985).

Preparation of Antimicrobial Plates:

- Dilutions of antimicrobial agents are prepared in sterile double distilled water or other appropriate diluents at a concentration 10 times that desired in the final test (Barry, 1976 and Washington, 1985).
- The Agar medium is then prepared in flask or tubes and allowed to cool in a 50^{o}C water bath.
- Sufficient volumes are prepared to fill each 9 cm petri plates with 20 to 25 ml of Agar.
- The diluted antimicrobial solutions are added to the melted and cooled medium in a ratio of 1 part antimicrobial agent to 9 part medium (2 ml of drug to 18 ml of Agar for each petri plate).
- The medium is then mixed by gently inverting the tube or flask several times. The contents are then poured into the appropriate number of petri plates.
- The plates are then set aside on a flat horizontal surface and allow to harden undisturbed.
- For reference the Agar plates should be prepared on the same day that the tests are to be performed. However for most other purposes, the antimicrobial plates can be refrigerated in a

sealed plastic bag for at least 1 week without a significant loss of antimicrobial activity (Ryan *et al.,* 1970).

Inoculation of Test Plates:

Apply an inoculum (1-2 ml) of each organism to the surface of each antimicrobial plates with the help of a replicating device containing 11 wire loops, one for the standard and 10 for the clinical isolates. The inoculum should be applied as a spot that covers a circle about 5-8 mm in a diameter and each spot should contain about 10^4 viable cells (Ericson, 1971, Barry, 1976 and NCCLS, 1990).

Incubation of Test Plates:

The inoculated plates are allowed to stand undisturbed until the spot of inoculum have absorbed completely. The plates are then inverted and allowed to incubate at 37^oC for 16 to 24 hours.

Examine plate for the presence or absence of growth. The lowest concentration of each antimicrobials that inhibit growth (ignore single colony or faint inoculum haze) is considered the MIC (Wentworth, 1987).

RESULTS AND DISCUSSION

Bacterial resistance to antimicrobial agents is a continuing serious problem in the treatment of infections. Although this problem was recognized shortly after the commercial introduction of antimicrobial agents, it means that resistance is now emerging at a more rapid rate than ever before.

Present study consists of 6 antimicrobial agents of Cephalosporins and Quinolones group used against 84 clinical isolates of *Staphylococcus aureus. Pseudomonas aeruginosa* and *Escherichia coli* respectively.

Cephalosporins:

First Generation Cephalosporins were moderately active against Gram positive bacteria and Gram negative bacteria (Katzung, 1992). Cephradine was poor active against *Staphylococcus aureus* and *Escherichia coli.* Present study shows that 47% isolates of *Staphylococcus aureus* and 38% isolates of *Escherichia coli* are resistant against Cephradine (Table 1).

Cefatrizine was also poor antimicrobial activity against *Staphylococcus aureus.* Presently 48% isolates of *Staphylococcus aureus* are resistant against Cafatrizine (Table 1).

Cefadroxil is another 1^{st} generation Cephalosporin having activity closely resembles to Cephalexin. In present study 54% isolates of *Staphylococcus aureus* are resistant against Cefadroxil (Table 1).

Third Generation Cephalosporins:

Cefotaxime was highly active against Gram positive and Gram negative bacteria (Neu *et al.,* l979). Garcia *et al.* in 1992 observed high activity of Cefotaxime against *Staphylococcus aureus.* During the present study Cefotaxime was found to be active against *Staphylococcus aureus, Escherichia coli* and *Pseudomonas aeruginosa.* 1.19% isolates of *Staphylococcus aureus,* 19% isolates of *Escherichia coli* and 10% isolates of *Pseudomonas aeruginosa* are resistant against Cefotaxime (Table 1).

Table 1
Population distribution of MIC of different Cephalosporin
for 84 *Staphylococcus aureus*

Cefadroxil

Conc (mg/l)	1	2	4	8	16	32	% Resistant
RES	84	81	78	58	55	49	54.76
SEN	0	3	3	20	3	4	

Cefatrizine

Conc (mg/l)	0.25	0.5	1	2	4	8	% Resistant
RES	84	83	80	64	58	52	48.8
SEN	0	1	13	16	6	6	

Cefotaxime

Conc (mg/l)	1	2	4	8	16	32	% Resistant
RES	61	43	29	26	13	1	1.19
SEN	23	18	14	3	13	12	

Cephradine

Conc (mg/l)	1	2	4	8	16	32	% Resistant
RES	84	78	63	53	47	40	47.61
SEN	0	6	15	10	6	7	

Population distribution of MIC of different Cephalosporin
for 84 *Escherichia coli*

Cefotaxime

Conc (mg/l)	0.06	0.13	0.25	0.5	1	2	% Resistant
RES	70	59	51	48	33	16	19.04
SEN	14	11	8	3	15	17	

Cephradine

Conc (mg/l)	16	32	64	128	256	512	% Resistant
RES	84	63	45	34	32	29	48.8
SEN	0	21	18	11	2	3	

Population distribution of MIC of different Cephalosporin
for 84 *Pseudomonas aeruginossa*

Cefotaxime

Conc (mg/l)	8	16	32	64	128	256	% Resistant
RES	62	47	36	33	21	9	10.71
SEN	22	15	11	3	11	12	

Table contd…

Population distribution of MIC of different Quinolones
for 84 *Staphylococcus aureus*

Ofloxacin

Conc (mg/l)	0.5	1	2	4	8	16	% Resistant
RES	81	78	63	49	36	24	28.57
SEN	3	3	15	14	13	12	

Ciprofloxacin

Conc (mg/l)	0.5	1	2	4	8	16	% Resistant
RES	82	78	61	49	33	22	26.19
SEN	2	4	17	12	16	11	

Population distribution of MIC of different Quinolones
for 84 *Escherichia coli*

Ofloxacin

Conc (mg/l)	0.13	0.25	0.5	1	2	4	% Resistant
RES	79	71	59	47	29	21	26.29
SEN	5	8	12	11	18	8	

Ciprofloxacin

Conc (mg/l)	0.13	0.25	0.5	1	2	4	% Resistant
RES	83	78	61	48	30	21	58.33
SEN	1	5	17	13	18	9	

Population distribution of MIC of different Quinolones
for 84 *Pseudomonas aeruginosa*

Ofloxacin

Conc (mg/l)	1	2	4	8	16	32	% Resistant
RES	82	73	66	61	40	12	11.9
SEN	2	9	9	5	21	28	

RES: Indicates the number of resistant strains at particular concentration.
SEN: Indicates the number of sensitive strains at particular concentration.

Quinolones:

The resistant pattern against Ofloxacin and Ciprofloxacin belonging to Quinolone groups are presented in Table 1. Akpede *et al.* in 1995 showed that *Staphylococcus aureus* were sensitive to Ofloxacin. Goldblatt *et al.* in 1998 showed that *Staphylococcus aureus* and *Pseudomonas aeruginosa* were highly sensitive to Ofloxacin in children.

Iroha *et al.* in 1998 investigated more than hundred neonates with conjunctivitis. Pathogens predominately isolated were *Staphylococcus aureus* and *Pseudomonas aeruginosa.* His result

showed that both the organism were highly susceptible to Ofloxacin. Kakar *et al.* in 1999 investigated one hundred cases of pyodermas in children. *Staphylococcus aureus* were isolated from pyoderma lesions.

Result showed that *Staphylococcus aureus* were highly susceptible to Ofloxacin (98.4%) and Ciprofloxacin (85.9%). Ofloxacin was highly active against *Staphylococcus aureus, Escherichia coli* and *Pseudomonas aeruginosa.* Present study shows that 28% isolates of *Staphylococcus aureus* (Table 1) 26% isolates of *Escherichia coli* and 11% isolates of *Pseudomonas aeruginosa* are resistant against Ofloxacin (Table 1). Ciprofloxacin is also included in Quinolone group. Present study shows that 26% isolates of *Staphylococcus aureus* (Table 1) and 58% isolates *Escherichia coli* are resistant against Ciprofloxacin.

It is expected that the present work will be a milestone in the treatment and bring new idea in the field of Pediatric that will enable the Pediatricians, Physicians, Doctors and Pharmacists for the treatment of common pediatric bacterial infections and to select the most appropriate antibiotic for patient resulting in least side effects.

Further it is expected that the antibiotic guide-line (WHO) must be followed by the health care persons.

Finally suboptimal use of antibiotic and self-medication should be prohibited by the Health Ministry.

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