

ANTIMICROBIAL THERAPY IN *Plesiomonas shigelloides*-ASSOCIATED DIARRHEA IN THAI CHILDREN

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Abstract. A retrospective case-controlled study was performed in 36 Thai children with *Plesiomonas shigelloides* (*P. shigelloides*)-associated diarrhea admitted to the Department of Pediatrics, Faculty of Medicine, Siriraj Hospital, Mahidol University from August 1990 to December 1992. Nineteen cases received antibiotics while seventeen did not receive any. The two groups were comparable in age, sex, duration of fever, duration and severity of diarrhea and medical treatment. The antibiotics given were norfloxacin, wintomylon, colistin, gentamicin, ceftriaxone, co-trimoxazole and ampicillin. In our study, 100% of *P. shigelloides* isolates were susceptible to quinolones and cephalosporins, while only 9% were susceptible to ampicillin. Co-trimoxazole, gentamicin, netilmicin, chloramphenicol and nalidixic acid showed high susceptibility.

The duration of fever and diarrhea after treatment was not significantly different between treatment and control groups ($p > 0.05$). Therefore, we conclude that antibiotics did not change the duration of fever and diarrhea in Thai children with *P. shigelloides*-associated diarrhea.

INTRODUCTION

Plesiomonas shigelloides is an oxidase-positive, fermentative, gram negative rod belonging to the family Vibrionaceae that has recently been implicated as a cause of sporadic and epidemic diarrhea (Holmberg and Farmer, 1984; Kain and Kelly, 1989a). A case-controlled study involving 31 *P. shigelloides* isolates from across the United States provided additional support for the role of the organism as a cause of diarrhea (Holmberg *et al*, 1986). The prevalence of *P. shigelloides* in stools submitted for culture was found to be 0.5-16.9% overall in the US population (Reinhardt and George, 1985a; Cohen *et al*, 1984). Our previous study showed that the occurrence of *P. shigelloides*-associated diarrhea in Thai children was 1.6% (Visitsunthorn and Ehbawornwong, 1993). *P. shigelloides* was isolated from < 0.1% of asymptomatic individuals (Holmberg *et al*, 1986; Reinhardt and George, 1985). Antimicrobial therapy is controversial in the treatment of *P. shigelloides*-associated diarrhea because the clinical symptoms are mild and self-limiting, but it is essential for successful outcome with extraintestinal disease (Ingram *et al*, 1987). The aim of this study was to

evaluate the result of antimicrobial therapy in *P. shigelloides*-associated diarrhea.

MATERIAL AND METHODS

Patient population

The retrospective case-controlled study was performed in 36 Thai children with *P. shigelloides*-associated diarrhea who were admitted to Department of Pediatrics, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand from August 1990 to December 1992. All of the patients selected had positive *P. shigelloides* in stool culture as the only organism (*Salmonella*, *Shigella*, *Campylobacter*, *Vibrio* and parasites were also excluded). All of them received no antibiotics before admission. The patients were divided into 2 groups: group 1 (19 patients) received sensitive antibiotics during admission, and group 2 (17 patient) did not receive any antibiotics during admission. Characteristics such as age, sex, clinical features, duration of fever and diarrhea, severity of diarrhea, and stool appearance before admission were compared between the antibiotics treatment and the control groups.

The sensitivity of *P. shigelloides* from stool culture was studied. Then the course of fever and diarrhea after treatment was compared.

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Stool culture, identification of isolates and antimicrobial susceptibility test

Stool specimens in Cary-Blair transport media were inoculated onto differential and selective enteric agar media (MacConkey and Salmonella-Shigella agar). All plates were incubated at 35 to 37°C for 16-18 hours. After incubation, the suspected colonies were picked up to perform biochemical tests as described by Von Graevenitz and Altwegg (1991). *P. shigelloides*, a non-lactose fermenter, ferments glucose without gas formation. Therefore, triple sugar iron agar yields an alkaline slant and an acid butt with neither gas nor H₂S formation. The positive biochemical tests are oxidase, indole, nitrate reduction, lysine decarboxylase, ornithine decarboxylase, arginine dihydrolase and inositol fermentation. The negative biochemical tests are DNase and mannitol fermentation. Most strains are susceptible to vibriostatic compound 0/129 (2,4 diamino 6,7 diisopropylpteridine).

Antimicrobial susceptibility tests were performed with various antimicrobial agents (listed in Table 2) using the Kirby-Bauer disk diffusion method (Bauer *et al.*, 1966).

Statistical analysis

The results were analysed by chi-square and a *p* value < 0.05 was considered statistically significant.

RESULTS

Characteristics of the two groups of patients are shown in Table 1. The two groups were comparable in age, sex, duration of fever and diarrhea, severity of diarrhea, and the routine treatment other than antibiotics such as intravenous fluid, electrolyte solution, diluted formula etc. The percent susceptibility of *P. shigelloides* from stool culture to antibiotics is shown in Table 2. Quinolone group (ofloxacin, norfloxacin, perflaxacin and ciprofloxacin), cephalosporin group (cefazolin, cefamandole, cefotaxime, ceftriaxone, cefoperazone and ceftazidime), colistin, aztreonam and sulbactam/ampicillin showed 100% susceptibility while ampicillin and tetracycline showed only 9% and 39% susceptibility against *P. shigelloides* isolated from feces. Co-trimoxazole, the common drug used in the out-patient unit, showed 82% sus-

Table 1

Characteristics of control and treatment groups of patients with *P. shigelloides*-associated diarrhea on admission.

	With antibiotic	Without antibiotic
No. patients	19	17
Age (Months)	0.07-120	2-160
mean age	19.8	20.3
Sex		
male : female	10 : 9	9 : 8
Duration of fever (days)	0-3	0-2
mean	0.94 ± 0.82	0.94 ± 0.87
Duration of diarrhea (days)	1-13	1-5
mean	3.15	3
No. bowel movements per day	12.8 ± 9	13 ± 9
No. patients with vomiting	9	7
No. patients with dehydration		
moderate	7	5
mild	8	8
No. patients with acidosis	3	6
No. patients with WC in stool	5	5
No. patients with fever	11	8

Table 2

Percent susceptibility of *P. shigelloides* from stool culture to antibiotics.

Antibiotics	% Susceptible
Ampicillin	9
Aztreonam	100
Sulbactam/Ampicillin	100
Chloramphenicol	91
Tetracycline	39
Co-trimoxazole	82
Colistin	100
Nalidixic acid	91
Ofloxacin	100
Norfloxacin	100
Pefloxacin	100
Ciprofloxacin	100
Neomycin	57
Kanamycin	46
Gentamicin	96
Amikacin	78
Netilmicin	94
Cefazolin	100
Cefamandole	100
Cefotaxime	100
Ceftriaxone	100
Cefoperazone	100
Ceftazidime	100

ceptibility, and gentamicin and netilmicin showed 96% and 93% susceptibility respectively. Chloramphenicol and nalidixic acid both showed 91% susceptibility.

Antibiotics used in 19 group 1 children with *P. shigelloides*-associated diarrhea were oral colistin, nalidixic acid, norfloxacin, co-trimoxazole and injected gentamicin, ceftriaxone and ampicillin. The sensitive antibiotics were started on admission day and the duration of antibiotics used was 2 to 7 days. The duration of fever after treatment did not differ significantly between the antibiotic and non-antibiotic groups (1.1 vs 1.05 days, $p > 0.05$) (Table 3). The duration of diarrhea after treatment was also not significantly different (2.68 vs 2.65 days, $p > 0.05$). Total durations of fever and diarrhea between the two groups were also not significantly different ($p > 0.05$). Stool culture was repeated before discharge in 5 patients, 2 in the antibiotic and 3 in non-antibiotic group. The results were all negative.

DISCUSSION

P. shigelloides-associated diarrhea is not uncommon in the Thai population. The occurrence in Thai adults has been found to be 5.6% and in children, 1.6% (Visitsunthorn and Ekbawornwong, 1993). Children with *P. shigelloides*-associated diarrhea usually have mild or moderate clinical symptoms except in patients who have extra-intestinal manifestations (eg septicemia, meningitis) especially in newborn or immunocompromised hosts (Brenden *et al*, 1988; McNeeley *et al*, 1984). Antibiotic treatment of *P. shigelloides*-associated diarrhea is still controversial. Some reports show that most cases are mild and self-limiting so that antibiotic treatment is not required (Reinhardt and George, 1985a; Cohen *et al*, 1984; McNeeley *et al*, 1984). One previous study,

Table 3

Comparison duration of fever and diarrhea between the patients that received and did not receive antibiotics.

	With antibiotic	Without antibiotic
Fever after admission (days)	0-4	0-6
mean	1.1 ± 1.48	1.05 ± 1.55
Diarrhea after admission (days)	1-7	1-5
mean	2.68 ± 1.48	2.65 ± 1.53
Total duration of fever (days)	0-6	0-7
mean	2.33 ± 1.33	2.20 ± 1.11
Total duration of diarrhea (days)	2-15	2-10
mean	5.83 ± 2.05	5.65 ± 2.16

however, showed that appropriate antimicrobial agents resulted in a significantly shorter clinical course of intestinal disease (Kain and Kelly, 1989a). Eighty-eight percent of the group that received appropriate antibiotic recovered from diarrhea within 2 weeks but only 24% of the group that did not receive antibiotics did so (Kain and Kelly, 1989a). Another study concluded that some patients with severe symptomatic *P. shigelloides*-associated diarrhea might benefit from antibiotic therapy (Reinhardt and George, 1985b). Some authors have treated patients with co-trimoxazole with resolution of diarrhea and clearing of *P. shigelloides* from the gastrointestinal tract (Davis *et al*, 1978a, b).

Our study showed that antibiotic treatment did not change the duration of diarrhea or fever in *P. shigelloides*-associated diarrhea in Thai children. The cases in our study had mild to moderate diarrhea without extraintestinal manifestation, so the antibiotics did not change the course of the disease. Stool culture 1-2 weeks after admission showed negative result with or without antibiotic therapy. This was supported by previous reports which showed that spontaneous cure usually occurs within a week accompanied by a return of normal bowel flora (McNeeley *et al*, 1984), but there was a possibility of continued excretion of the organism up to 2 weeks or more following the onset of diarrhea. However, prolonged carrier states were not observed (Bhat *et al*, 1974).

In our study quinolone and cephalosporin groups showed 100% susceptibility while ampicillin showed only 9%. The former reports have stated that the organism showed a varied pattern of sensitivity to antibiotics (Davis *et al*, 1978a; Bhat *et al*, 1974; Geizer *et al*, 1966). Twenty-five years ago *P. shigelloides* was sensitive to nearly all antibiotics, but 10 years later it was resistant to penicillin, ampicillin and carbenicillin (Reinhardt and George, 1985b; Davis *et al*, 1978a). Most papers, however, have shown that the organism was highly sensitive to quinolone and cephalosporin groups (Kain and Kelly, 1989b; O'Hare *et al*, 1985; Yeh and Tsai, 1991; Sifuentes-Osornio *et al*, 1989; Von Graevenitz and Bucher, 1982), while showing low susceptibility to penicillin, erythromycin, ampicillin, vancomycin and clindamycin (Kain and Kelly, 1989b; Yeh and Tsai, 1991; Carlson *et al*, 1983; Richard *et al*, 1978; Rahim *et al*, 1992) and higher susceptibility to netilmicin and chloramphenicol (Kain and Kelly, 1989b; O'Hare, 1985). Some antibiotics such as trimetoprim, doxy-

cycline and tetracycline indicate various susceptibility patterns (Kain and Kelly, 1989b; Sifuentes-Osornio *et al*, 1989; Carlson *et al*, 1983). Cotrimoxazole, which showed very high susceptibility, up to 100%, in most of the studies (Kain and Kelly 1989b; Sifuentes-Osornio *et al*, 1989; Carlson *et al*, 1983; Rahim *et al*, 1992), showed 82% susceptibility in our study. Variability in sensitivity of *P. shigelloides* to antibiotics may be due to regional differences in the strains studied (Reinhardt and George, 1985b).

In conclusion, antibiotics did not significantly change the course of diarrhea or fever in *P. shigelloides*-associated diarrhea in Thai children who had acute, mild or moderate episodes. Antibiotics should be given only in cases that have prolonged or serious diarrhea, serious underlying disease or evidence of extra-intestinal manifestation. Oral antibiotics such as norfloxacin and co-trimoxazole and parenteral antibiotics such as cephalosporin, ciprofloxacin and netilmicin showed high susceptibility *in vitro* against *P. shigelloides* isolated from feces.

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