SEVERE SHIGELLOSIS IN CHILDHOOD

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Abstract. A prospective study was performed on 20 bacteriologically proven pediatric cases of severe shigellosis admitted to the Department of Pediatrics, Chulalongkorn Hospital during March 1989 to March 1990. Fourteen patients were male and six were female. *Shigella* B was found in 85% and *Shigella* D in 15% of cases. The major indications for admission were convulsions and dehydration. Fifteen per cent of cases had underlying malignancies and 42.1% had malnutrition. Most patients had a peak of fever between 39.5 and 40.5°C, serum sodium between 128-144 mEq/l. Mild acidosis was detected in 45% and moderate acidosis in 30% of cases. There were no statistical differences in peak of fever and serum sodium between patients who had convulsion and who did not. Shigellemia was found in one case who also had underlying neuroblastoma. One patient died due to necrotizing enterocolitis, septic shock and renal failure. Most of the organisms found resisted to ampicillin and trimethoprim-sulfamethoxazole (TMP-SMX). However, TMP-SMX was prescribed in most immunocompetent patients and they recovered well. All of three patients with underlying malignancy responded well to ceftriaxone.

INTRODUCTION

Shigellosis has been a health problem in Thailand. There were 76,850 cases of dysentery reported in 1995. The incidence was 129.3 per 100,000 population which changed only a little bit since 1989. Majority of cases were caused by shigellosis and most of them were children (Division of Epidemiology, 1995). *Shigella* B is the most common serogroup found in Thai patients and usually causes more severe disease than *Shigella* D (Thisyakorn and Rienprayoon, 1992).

Despite the high prevalence, there have been only a few studies on clinical manifestations and laboratory findings of shigellosis. Selection of appropriate antimicrobial agent is also an interesting issue. There is tendency to use new fluoroquinolone as the first line drug in shigellosis, especially in areas where multiresistant strain of *Shigella* occurs commonly. However, there have been very few data reported about clinical response in patients treated with resisted antimicrobial agents. This study describes clinical manifestations, laboratory findings and response to treatment of severe shigellosis.

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MATERIALS AND METHODS

From March 1989 to March 1990, all children with severe shigellosis admitted to the Department of Pediatrics, Chulalongkorn Hospital were studied. The patients were classified as having severe shigellosis when they had fever, acute diarrhea and mucous bloody stool with positive stool culture for *Shigella* sp accompanied with the presence of extraintestinal manifestations such as convulsion, pneumonia, dehydration or compromised conditions, *eg* malignancies. History and physical examination were taken in all patients who fulfilled the criteria. Laboratory investigations included complete blood count, serum electrolytes, hemoculture, and stool culture. In patients who presented with convulsion, blood sugar and cerebrospinal fluid examinations were performed. Clinical course of all patients was followed until they were discharged from hospital or died.

RESULTS

There were 20 patients with severe shigellosis during the period of study. Their age and gender distribution are shown in Fig 1. The major indications for admission were convulsion and dehydration (Table 1). Malnutrition as assessed by weight

for age was seen in 42.1% (Table 2). Most patients had a peak body temperature between 39.5-40.5°C (Fig 2). Seventy-five per cent had acidosis (Table 3). Serum sodium ranged from normal to slightly below normal. Complete blood count in 17 patients without underlying malignancy showed anemia in 33.3%, leukocytosis 27.8% and neutrophilia 44.4%. Only one patient with underlying neuroblastoma had shigellemia due to *Shigella* group B.

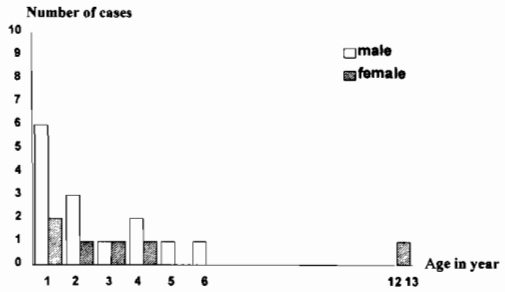

Fig 1–Age and gender distribution of patients with severe shigellosis.

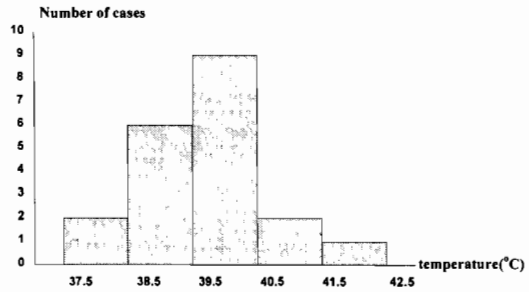

Fig 2–Peak body temperature in patients with severe shigellosis.

In eight patients who presented with convulsion, all were under 6 years old. None of them had hypoglycemia nor abnormality in cerebrospinal fluid examination. Their body temperature on admission and serum sodium values were not significantly different from the 12 patients without convulsions.

Stool cultures showed 85% *Shigella* B and 15% *Shigella* D, their susceptibility to antimicrobials were shown in Table 4. In 17 immunocompetent patients, five were treated with ampicillin, 10 with TMP-SMX and 2 with the other medications, their response were shown in Table 5. There was no difference in fever clearance time between patients with *in vitro* antimicrobial sensitive or resistant organisms who recovered from first line antimicrobial therapy. In two patients who did not respond to ampicillin, one died from necrotizing enterocolitis, the other recovered after norfloxacin was given. In one patient who did not respond to TMP-SMX, ceftriaxone was given and the patient recovered well.

The patient who died was a 3-month-old boy, who presented with abdominal distension, fever, mucous bloody diarrhea and convulsions. The

Table 1

Causes of hospital admission in severe shigellosis.

Causes of admission	Number of cases (%)
Convulsion	8(40)
Dehydration (moderate or severe)	6(30)
Pneumonia	3(15)
Acute lymphoblastic leukemia	2(10)
Neuroblastoma	1(5)

Table 2

Nutritional status of the patients with severe shigellosis.

Nutritional status	Number of cases (%)
Normal	11(57.89)
First degree malnutrition	4(21.05)
Second degree malnutrition	3(15.79)
Third degree malnutrition	1(5.26)

Table 3

Serum bicarbonate level in patients with severe shigellosis.

Serum bicarbonate (mEq/l)	Number of cases (%)
20-25 (normal)	5(25)
16-20 (mild acidosis)	9(45)
11-15 (moderate acidosis)	6(30)

Table 4

In vitro sensitivity pattern of isolated *Shigella*.

Drug	*Shigella* B (17 cases)			*Shigella* D (3 cases)		
	sensitive	resist	% sensitive	sensitive	resist	% sensitive
Ampicillin	2	14	12.5	2	1	66.67
Amikacin	17	0	100	3	0	100
Cefoperazone	17	0	100	3	0	100
Cefotaxime	17	0	100	3	0	100
Ceftazidime	17	0	100	3	0	100
Ceftriaxone	17	0	100	3	0	100
Chloramphenicol	2	6	25	1	1	50
Ciprofloxacin	17	0	100	3	0	100
Gentamicin	17	0	100	3	0	100
Imipenem	9	0	100	2	0	100
Netilmicin	8	0	100	1	0	100
Pefloxacin	17	0	100	3	0	100
TMP-SMX*	5	11	31.25	1	2	33.3

* Abbreviation : TMP-SMX = Trimethoprim-sulfamethoxazole

Table 5

Outcome of therapy.

Drug used	Recover	Not recover	% recovery
Ampicillin (*in vitro* sensitive)	2	0	100
Ampicillin (*in vitro* resist)	1	2	33.33
TMP - SMX (*in vitro* sensitive)	3	0	100
TMP-SMX (*in vitro* resist)	6	1	85.71

cerebrospinal fluid findings were normal. Initial therapy included parenteral ampicillin and gentamicin along with symptomatic and supportive treatment. Clindamycin was added on the following day. On the third hospital day, the abdomen became markedly distend and exploratory laparotomy disclosed an inflamed bowel. Stool culture grew *Shigella* B which was sensitive to TMP-SMX and resistant to ampicillin, hemoculture was negative. He finally died from overwhelming sepsis.

Ceftriaxone was given to three patients with underlying hematologic malignancies including the one with shigellemia and all recovered well.

DISCUSSION

This study of severe shigellosis in Thai children showed the same pattern of age group and clinical features as a previous study (Thisyakorn and Rienprayoon, 1992). Malnutrition is a major associated problem in our patients, complete blood count is not helpful in diagnosis, serum sodium is found to be slightly low or normal, these findings are all concordant to the previous studies (Black *et al,* 1982; Donald and Winkler,1960; Jadhav *et al,* 1966). Up to 75% of patients had acidosis, this indicates the necessity of electrolyte and acid base studies in patients with severe shigellosis.

Concerning complications of shigellosis, convulsions occurred in 40% of our patients. Although it is believed that fever and *Shigella* toxin are the causes of convulsion, hyponatremia, hypoglycemia, and infection of central nervous system can also be the causes of convulsion (Avital *et al*, 1982; Donald *et al*, 1956). In our study, it is likely that the causes of convulsion are due to fever and/or *Shigella* toxin, since other causes have been excluded.

Shigellemia is a rare but well-recognized phenomenon. Positive blood cultures have been reported in association with all four serogroups. Some common clinical features associated with shigellemia are severe dehydration, malnutrition, pneumonia, seizure, skin petechiae and late secondary temperature elevation (Struelens *et al*, 1985). One of our patients who had shigellemia had compromised condition from neuroblastoma and he recovered well. It is not clear whether compromised hosts are in fact at greater risk from shigellemia than normal patients since shigellemia was seen in both compromised and normal hosts (Struelens *et al*, 1985).

Causes of death during shigellosis are varied and include septicemia, febrile convulsion, pneumonia, hemolytic-uremic syndrome and colonic perforation. Pathologic findings in fatal shigellosis showed that death resulting from severe and extensive colonic mucosal inflammatory destruction was often complicated by pneumonia and septicemia. It has been suggested that the patient potentially at greatest risk of death from *Shigella* sepsis is malnourished, afebrile and severely dehydrated; develops leukopenia and is infected by ampicillin resistant organisms (Butler *et al*, 1989; Thisyakorn, 1987). In one of our patients who died, the clinical features were compatible with necrotizing enterocolitis which is rare complication with high mortality (Thisyakorn,1987). In addition, the patient was infected with ampicillin resistant organism.

Concerning therapy of shigellosis, fluid loss is usually not great and is easily managed (Thisyakorn and Rienprayoon,1992; Jadhav *et al*, 1966). For the more severely ill patients, antimicrobials can shorten the duration of illness and rapid bacterio-logic cure can be achieved (Fontaine,1989; Thisyakorn,1987). The problem at present is to select an appropriate drug which has maximal cost-effectiveness. Resistance to the drugs in general use, including ampicillin and TMP-SMX, is an increasing problem (Thisyakorn and Rienprayoon,1992). The new fluoroquinolones appear to be highly active and clinically effective. Although they can cause cartilagenous damage in young animals, there are still no evidence of this side effect in children and they are now being widely prescribed for childhood shigellosis (Bhattacharya *et al*, 1992; Fontaine,1989; Salam and Bennish,1991). However, the cost of these drugs and an emerging incidence of fluoroquinolone-resistant bacteria due to widespread use are major issues of concern and these drugs should be reserved for severe infection not respond to other first line therapy. Bennish *et al* (1985) suggested usage of ampicillin or TMP-SMX as a first line drug for patients in poorly developed areas regardless of stool culture and sensitivity results; if treatment failure occur after 24-72 hours, another drug should be introduced. This study supports the above suggestion, 85.7% of our patients whose *in vitro* study showed resistance to TMP-SMX still recovered well after TMP-SMX therapy. However, in the otherwise well persons, shigellosis is usually a self-limited disease, and antimicrobial therapy is generally not necessary (Thisyakorn and Rienprayoon,1992). It is possible that some of our patients might have recovered spontaneously. It is also possible that *in vitro* bacterial sensitivity test by the disc diffusion method, which was used in our study, cannot accurately predict clinical response *in vivo*.

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