ORIGINAL ARTICLE

Thiamphenicol in the Treatment of Cholera in Children.*

by

HAROEN NOERASID; EKO SUJANTO; ISMOEDIJANTO; DJOKO SOEJONO; I.G.G. DJELANTIK and SURATA

(From the Department of Child Health, School of Medicine, University of Airlangga/Dr. Soetomo Hospital Surabaya)

Abstract

A study has been performed to measure the efficacy of thiamphenicol by comparing it with tetracycline as a standard drug. Eighty bacteriologically confirmed cholera patients were included in this study.

Among them, 41 patients were treated with thiamphenicol while the other 39 with tetracycline.

Stool volume, duration of diarrhea and duration of hospitalisation were higher in the thiamphenicol group. And the volume of intravenous and oral fluid therapy were less in the tetracycline group.

Positive bacteriologic examinations of the second samples (taken on the second day of hospitalisation) of the thiamphenicol group were 41,46% as compared with 17,94% of the tetracycline group. But almost all of the third samples of both groups were negative.

Clinical success rate of thiamphenicol was 95,12% and tetracycline was 100%. Thiamphenicol appeared to be effective against cholera in children.

* Presented at the VIth meeting of Gastroenterology in Manado, August 1980.
Received 20th Jan. 1981.

Introduction

Diarrheal disease is one of the leading causes of morbidity and mortality in children, especially in developing countries (Lindenbaum et al., 1967).

It is estimated that 17% of the total mortality-rate and 60% of the mortality-rate of the under fives in Indonesia are caused by diarrhea.

The incidence of diarrhea is more than 400 in 1000 people, and 70 — 80% are under fives.

Of the watery diarrheal diseases, cholera is the most severe. It is characterised by a sudden onset of profuse "rice water stool" diarrhea, it may also be accompanied by vomiting, and only within a few hours the patient may fall into a severe dehydration state or even shock (Lindenbaum et al., 1967; Lindenbaum et al., 1966).

The primary treatment of cholera is rehydration and maintenance of proper fluid and electrolyte balance by means of fluid therapy, intravenously as well as orally (Gutman and Drutz, 1969).

The additional antibiotic therapy has been proved to shorten the duration and volume of diarrhea, thereby reducing the volume of fluid therapy needed (Lindenbaum et al., 1967).

Several antibiotics have been tested and among them tetracycline seemed to be the first choice, while chloramphenicol, furalaxine and streptomycine are the next alternatives (Kagan, 1974; Kobari et al.,

Anyhow recent reports indicate increasing data of resistant vibrio strains to either drugs (Kagan, 1974; Karchmer et al., 1970).

Thiamphenicol is a relatively new synthetic antibiotic which much resembles chloramphenicol in structure and pharmacologic action, but has much less toxic effect to the bone-marrow and achieves a higher concentration in the intestines due to the enterohepatic circulation.

Thiamphenicol has been reported effective against cholera in vitro (Bonang and Santoso, 1977).

It has been reported that the use of tetracycline is recently decreasing due to some side effects such as : resistance of microorganism, allergic reactions, hepatic toxicity, phototoxicity of the skin, renal azotemia, hematologic effects, staining and dysgenesis of teeth, bulging of fontanel etc. (Lindenbaum et al., 1966).

Many pediatricians seem to be also reluctant to prescribe tetracycline because of those above mentioned side effects.

The purpose of this study is to figure out the efficacy of the thiamphenicol by comparing it with the standard drug tetracycline in the treatment of cholera.

Material and methods

Patients aged 2 years or older admitted to the Department of Child Health, Dr. Soetomo Hospital, from January 1, 1980 until June 30, 1980, with confirmed bacteriologically cholera and had not taken any medication, were included in this study.

Duration of diarrhea and vomiting, frequency and nature of stool before admission were recorded in the anamnesis.

On admission physical examination was performed to determine the degree of dehydration and other concomitant diseases.

Patients with diseases or complications other than those directly related to cholera were excluded.

Bacteriologic examinations of stool were done three times. The first sample was taken just before antibiotic therapy had been given and the other samples were taken on the next two consecutive days.

Femoral blood was collected in a heparinised syringe for determination of blood pH and electrolytes. The first sample was taken just before the fluid therapy was started and the second sample on the third day of hospitalisation.

The patients were then immediately put on intravenous combined with oral fluid therapy as soon as possible.

Thiamphenicol 50 — 100 mg/kg B.W./day or Tetracycline 30 — 50 mg/kg B.W./day was given at random for a five-day course.

The time from the beginning of antibiotic therapy to the last diarrhea, stool volume, volume of intravenous and oral fluid therapy used were recorded.

After fluid therapy had been stopped, daily diet consisting of porridge and meat was given.

Results

Among the total 95 patients included in this study, 80 (84,21%) showed positive vibrio cholerae in one or more stool bacteriologic examinations.

From 80 patients, 41 (51,25%) and 39 (48,75%) belonged to thiamphenicol and tetracycline group respectively.

All patients were in severe dehydration state on admission. Age and sex distribution of either groups are listed in table 1.

Table 2 indicated that age, body weight and duration of illness before admission in both groups did not differ significantly from each other.

Clinical success rate is described in table 3.

All patients belonging to the tetracycline-group showed improvements directly after therapy was started.

While from 41 patients of the thiamphenicol-group, 2 patients did not respond to the therapy and even several times fell into shock.

Therefore on the 3rd day, therapy was changed to tetracycline and showed much improvements thereafter.

TABLE 1: *Age and sex distribution of Thiamphenicol and Tetracycline groups*

Age (years)	Thiamphenicol group		Tetracycline group		Total
	Male	Female	Male	Female	
2 — 3	—	1	2	1	4
3 — 4	5	4	4	6	19
4 — 5	7	2	6	4	19
5 — 6	4	2	4	2	12
6 — 7	—	1	1	2	4
7 — 8	3	—	—	2	5
8 — 9	3	4	1	2	10
9 — 10	—	—	—	1	1
10 — 11	3	2	1	—	6
Total	25	16	19	20	80

TABLE 2: *Mean and range (in parenthesis) of age, body weight and duration of illness before admission in Thiamphenicol and Tetracycline groups*

	Thiamphenicol group	Tetracycline group	P	
Age (years)	5,32 (2 — 11)	4,53 (2 — 11)	$P > 0,1$	not significant
Body weight (kg)	13,93 (8 — 23,5)	12,41 (9 — 20)	$P > 0,1$	not significant
Duration of illness before admission (hours)	13,8 (3 — 36)	13,1 (3 — 36)	$P > 0,1$	not significant

TABLE 3: *Success rate of Thiamphenicol and Tetracycline*

	Thiamphenicol	Tetracycline
Number of patients	41	39
Number of patients recovered	39	39
Success rate	95,12%	100%

The first bacteriologic examinations showed positive results in 80 patients.

The second bacteriologic examinations showed positive results in 17 patients (41,46%) of the thiamphenicol group as compared with 7 patients (17,95%) of the tetracycline group, as shown in Table 4.

The greater part of the results of the third bacteriologic examinations became negative which did not differ in either groups.

TABLE 4: *Positive bacteriologic examinations of stools of Thiamphenicol and Tetracycline groups*

	Thiamphenicol group	Tetracycline group
Number of patients	41	39
1st bact. examination	41 (100 %)	39 (100 %)
2nd bact. examination	17 (41,46%)	7 (17,95%)

Table 5 indicated the stool volume and the volume of intravenous and oral fluid therapy used. Table 6 showed the duration of diarrhea after treatment had been started and the duration of hospitalisation.

These tables showed several significant differences between the two groups. The thiamphenicol group had higher stool and fluid therapy volume (intravenous and oral) and longer duration of hospitalisation and diarrhea, compared with the tetracycline group.

TABLE 5 : *Mean and range (in parenthesis) of volume of stool, intravenous and oral fluid therapy in Thiamphenicol and tetracycline groups*

	Tetracycline group	Thiamphenicol group	P
Stool volume (L)	1,92 (0,50 — 8 50)	3,05 (0,20 — 5,50)	$P < 0,01$
Intravenous fluid therapy (L)	2,13 (1.25 — 8,40)	2,96 (1,35 — 5,00)	$P < 0,01$
Oral fluid therapy (L)	1,48 (0,20 — 4,80)	1,62 (0,15 — 3,50)	$P < 0,01$

TABLE 6 : *Mean and range (in parenthesis) of duration of hospitalisation and diarrhea after treatment had been started in thiamphenicol and tetracycline groups*

	Tetracycline group	Thiamphenicol group	P
Duration of hospitalisation (days)	3,6 (4 — 11)	5,1 (3 — 6)	$P < 0 1$
Duration of diarrhea after treatment (hours)	19,2 (10 — 48)	25,0 (6 — 48)	$P < 0 1$

TABLE 7: *Mean and range (in parenthesis) of pH and electrolytes of blood, before fluid therapy and on the third day of hospitalisation of Thiamphenicol and Tetracycline groups*

	Thiamphenicol group before treatment	3rd day hospitalisation	Tetracycline group before treatment	3rd day hospitalisation
Na mEq/l	128,17 (123,48 — 137,39)	134,16 (119,13 — 143,48)	126,67 (119,13 — 133,04)	133,90 (123,40 — 144,28)
K mEq/l	3,87 (2,62 — 4,95)	3,83 (2,87 — 5,38)	3,93 (3,23 — 4,95)	3,43 (2,15 — 4,46)
Cl mEq/l	98,00 (90 — 132)	110,6 (97 — 108)	97,34 (90 — 107)	106,17 (94 — 130)
CO_2 mol/l	16,9 (13,0 — 20,8)	22,3 (19,5 — 26,4)	18,8 (16,6 — 22,2)	21,8 (18,6 — 23,3)
pH	7,18 (7,09 — 7,24)	7,35 (7,30 — 7,40)	7,20 (7,06 — 7,25)	7,40 (7,39 — 7,43)

All blood pH and electrolytes examinations showed improvement on the 3rd day and did not differ significantly in both groups (Table 7).

Discussion

As observed in this study the volume of stool and fluid therapy was smaller in the Tetracycline group and so was the duration of diarrhea and hospitalisation also shorter.

This condition was almost the same as found by Lindenbaum, et al. (1967). Compared with Chloramphenicol and Streptomycin, Tetracycline was superior in reducing stool volume and duration of diarrhea especially in children.

In the other previous study Lindenbaum et al. (1966) found that antibiotic reduced the stool volume and shortened the duration of diarrhea in cholera.

Karchmer et al. (1970) and Kobari et al. (1970) found that tetracycline reduced the duration of vibrio excretion more than chloramphenicol and furazolidone (a nitrofuran derivative).

In our study, the second bacteriologic stool examinations were positive in 17,95% and 41,46% of the tetracycline and thiamphenicol group respectively. But almost all of the stool samples of the third examinations became negative.

There was no significant difference between the two groups. This evidence indicated that in reducing vibrio excre-

tion, thiamphenicol and tetracycline had almost the same potency.

Kobari et al. (1970) in a study in Manila found that with chloramphenicol the mean duration of culture positivity was 3,1 days in children.

Compared with our study, it seemed that thiamphenicol gave a shorter duration of vibrio excretion than chloramphenicol.

In that same study Kobari et al. (1970) also discovered many vibrio strains being resistant to chloramphenicol and streptomycin and a few of them were also resistant to tetracycline.

Karchmer et al. (1970) also reported an increasing evidence of tetracycline resistant vibrio strain, that alternative antimicrobial agents against cholera were worth to be investigated.

Unfortunately, due to technical difficulties, sensitivity tests were not performed in our study.

Lindenbaum et al. (1966, 1967) found that therapeutic failure of tetracycline was less than 1% and chloramphenicol was about 8%.

In our study, the success rate of tetracycline and thiamphenicol was 100% and 95,12% respectively.

Compared with chloramphenicol as found by Lindenbaum et al. (1966, 1967) there was evidence that the thiamphenicol success rate was higher.

Thiamphenicol appeared to be effective against cholera in children, it even might be more effective than chloramphenicol.

Acknowledgement

The authors wish to express their gratitude to "Zambon Chemical Pharmaceutical Laboratories" for the financial support and the Urfamycin and Tetracycline used for our study.

REFERENCES

1. BONANG, G. and SANTOSO, U.S. : The in vitro sensitivity of vibrio strains to thiamphenicol. Mod. Med. Asia 13 : 10 - 11 (1977).
2. GUTMAN, R.A. and DRUTZ, D.J : Double blind fluid therapy evaluation in Pediatric Cholera. Pediatr. 44 : 922 - 931 (1969).
3. KAGAN, B.M. : Antimicrobial Therapy, 2nd Ed. p. 95 - 104 (Saunders Philadelphia 1974).
4. KARCHMER, A.W.; CURLIN, G.T.; HUG, M.I. and HIRSCHORN, N. : Furazalidone in Pediatr. cholera. Bull. Wld. Hlth. Org. 43 : 373 - 378 (1970).
5. KOBARI, A.W.; TAKAKURA, I.; NAKATOMI, M.; SEGAWE, S. and HYLANGGO, C. : Antibiotic resistant strains of El Tor Vibrio in the Philippines and the use of Furalazine for chemotherapy. Bull. Wld. Hlth. Org. 43 : 365 - 371 (1970).
6. LINDENBAUM, J.; GORDON, R.S. Jr.; HIRSCHORN, N.; AKBAR, R.; GREENBURGH, W.B. and ISLAM, M.R. : Cholera in children. London 1 : 1066 (1966).
7. LINDENBAUM, J.; GREENBURGH, W.B. and ISLAM, M.R. : Antibiotic therapy of cholera in children. Bull. Wld. Hlth. Org. 37 : 529 - 538 (1967).