ORIGINAL ARTICLE

Comparative Efficacy Study of Combination Fansidar-Sulphate Quinine and Fansidar-HCl Tetracycline in Falciparum Malaria in Children Above 7 Years Old

by

K. SILITONGA and T.H. RAMPENGAN

(From the Department of Child Health Medical School Sam Ratulangi University, Manado - Indonesia)

Abstract

The objective of this study is to compare the results of treatment of children with falciparum malaria with the combinations of fansidar-sulphate quinine and fansidar-chlortetracycline as an alternative treatment of chloroquine resistant falciparum malaria.

This study was carried out prospectively on 45 cases with the age equal or above 7 years, who had been admitted in the Pediatric Department, Gunung Wenang Hospital Manado during the period of January 1989 - December 1989. Twenty three cases had been treated with fansidar - sulphate quinine and 22 cases with fansidar - chlortetracycline, all of them underwent blood examinations for malaria for 7 consecutive days (day 0-8).

Asexual parasitemia and fever in the fansidar - sulphate quinine group significantly disappeared more rapidly than in the fansidar - chlortetracycline group ($p<0.03$ and <0.005). There occurred neither drug resistance nor serious side effect in both groups.

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Introduction

It has been reported that chloroquine and fansidar resistant plasmodium falciparum was found in Indonesia. (Verdager et al., 1976; Dakung et al., 1978; Hoffman et al., 1985; Pribadi et al., 1985). In Manado, the incidence of fansidar resistant plasmodium falciparum was about 13.5% (Rampengan and Rampengan, 1988) and that of chloroquine resistant about 28.6% (Rampengan and Rampengan, 1989).

The combination of quinine and sulfadoxine pyrimethamine has been the mainstay of anti malarial treatment of falciparum malaria in Southeast Asia. Quinine followed by a single dose of fansidar is the most effective treatment of chloroquine resistant falciparum malaria (Hall et al., 1975).

In adult patients the combination of quinine and tetracycline has been found to give very high cure rates (Colwell and Hickman, 1973), but the results of the treatment using a combination of fansidar and tetracycline has never been reported yet. Since tetracycline can not be used in children under 7 years old, the authors tested the effectiveness of fansidar - quinine to compare with fansidar - tetracycline in children of 7 years old or more.

Materials and Methods

A prospective study was done on 45 children with uncomplicated falciparum malaria.

The study was carried out in the Department of Child Health, Medical School Sam Ratulangi University/Gunung Wenang General Hospital in Manado, during January 1989 - December 1989. There were 33 males and 12 females, ranging in age from 7 to 13 years.

The diagnosis was based on clinical symptoms and signs and microscopic parasitological examination of thick blood films with Giemsa stain. Blood film for falciparum malaria were examined every day for 8 consecutive days from day 1 (on admission) until day 8, with guidelines for interpretation as follows: negative means no parasite (trofozoid) on 100 fields; positive (+) means 1 - 10 trofozoids on 100 fields; positive (+ +) means 11-100 trofozoids on 100 fields; positive (+ + +) means 1-10 trofozoids on one field; positive (+ + + +) means 11-100 trofozoids on one microscopic field.

The criteria of resistance as established by WHO: Standard field test or 7 days test. The patients were divided into two groups with 2 treatment schedules:

Group 1 : 23 patients, treated with pyrimethamine-sulphadoxine with pyrimethamine 1 mg/kg bw single dose and sulphate quinine 30 mg/kg bw, divided into three dosis for 7 days.

Group 2 : 22 patients, treated with pyrimethamine - sulphadoxine with pyrimethamine 1 mg/kg bw single dose and HCl tetracycline 50 mg/kg bw, divided into three dosis for 7 days.

Parasites and fever clearance were determined in days. Any complaints about the side effects of the drugs were recorded. The means values were used for analysis of the data.

Results

A total of 45 subjects (23 assigned to receive fansidar-sulphate quinine and 22 fansidar-HCl tetracycline). Most of the patients presented chills. As observed in table 1 the distribution of age, sex, and clinical features, were similar in both groups.

Table 1 : *Clinical features of the studied group*

Characteristic	% subject Group 1 n = 23	Group 2 n = 22
Age (years)		
7 - 10	56.52	50
>10	43.48	50
Sex		
male	78.26	68.18
female	21.74	31.82
Headache	60.86	63.63
Chills	82.60	81.81
Nausea and vomiting	62.21	63.36
Pallor	34.78	27.27
Liver enlargement	65.21	59.09
Spleen enlargement	60.80	68.18
Jaundice	8.70	9.09

On hospitalization, the means of temperature, hemoglobine, asexual parasites and duration of fever before admission were similar in both groups (Table 2).

Table 2 : *Mean temperature, hemoglobine, asexual parasite and duration of fever of the studied groups*

	Group 1	Group 2
Mean temp. (°C)	38.3	38.4
Range	37–40	37–40
Mean Hb (gm%)	11.01	11.27
Range	6.8 – 14.2	7–15
Mean asexual parasite	+ +	+ +
Range	+ + – + + + +	+ – + + + +
Mean fever (days)	4.52	4.77
Range (days)	1–8	1–8

Table 3 shows the mean parasite and fever clearance of children after receiving fansidar-sulphate quinine and fansidar-HCl tetracycline. The rapidity of the parasites and fever clearance in group 1 was more than in group 2, and the difference was statistically significant.

Table 3 : *The mean parasite and fever clearance of the studied groups.*

Clearance	Group 1	Group 2	P value
Parasites (days)	0.91 ± 0.60	1.27 ± 0.81	<0.03
Fever (days)	1.54 ± 0.70	2.41 ± 0.86	< 0.005

No resistance (R II or more) in the both studied groups was found, so was also no serious side effects encountered in the both studied groups; only one patient in group 1 presented delirium.

Table 4 : *Side effects of treatment*

Side effects	Group 1	Group 2
Nausea and vomiting	4	3
Malaise	–	1
Delirium	1	–

Discussion

This study was done on 45 children; consisting of 33 males and 12 females. Since tetracycline can not be used in children under 7 years old, the age of the patients chosen in this study ranged from 7 to 13 years.

The clinical features, mean temperature, hemoglobine, asexual parasite and duration of fever, were similar in both groups.

Quinine is believed to intercalate with DNA, but is probably bound to more than one site (Wernsdorfer and Kouznetsov, 1980). Quinine and chloroquine are active only against the blood stages of parasite malaria or blood schizontocides (Warhust, 1987). Quinine is rapidly and almost completely absorbed from the intestine and peak plasma concentrations are reached 3-4 hours after oral dose (Sabachorn et al., 1982; WHO, 1984).

Pyrimethamine inhibits dihydro-folate-reductase; sulfonamide competes with PABA and inhibits dihydropteroate synthetase thus the biosynthesis of nucleotides. The anti metabolites are active on all growing stages of malaria parasites but these agents act too slowly (Warhust, 1987).

Chlortetracycline have been shown to have some activity against the growing liver stages and marked activity against blood stages of plasmodium falciparum. Antibiotic of the above type is considered to be effective against protein synthesis on bacterial ribosomes, and it seems likely that they affect the mitochondria of malaria parasites which presumably have the type of ribosome. The effect of treatment takes approximately 48 hours to manifest (Warhust, 1987). Hall et al. (1975) reported that the children with plasmodium falciparum resistant to chloroquine, who were then treated by quinine following a single dose of fansidar, produced sensitivity of about 96% with no resistance II.

In Thailand, 62% of children with plasmodium falciparum who received quinine and sulphadoxine – pyrimethamine, were cured with no resistance II (Chongsuphajaisiddhi et al., 1983).

Children with plasmodium falciparum resistant to the combination of sulphadoxine-pyrimethamine who were then treated with a seven day tetracycline were cured of their infection. However, the clearance of fever and asexual parasitemia was slow with tetracycline (Verdager, 1976).

In this study it was found that asexual parasites and fever clearance in children who received fansidar-quinine were more

effective than fansidar-tetracycline (p value <0.03 and <0.005). No resistance II or more in the both group was found.

Quinine causes typical mild side effect such as nausea and tinnitus. Serious side effects such as coma or convulsions are more common in children than in adults. Fansidar, often causes fever and less often urticarial rashes.

Hall et al. (1975) reported no serious side effects on any of 392 patients who received quinine fansidar regimen.

In this study there were no serious side effects in both groups only one in the fansidar-quinine group presented delirium.

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