

SULFADOXINE-PYRIMETHAMINE RESISTANT FALCIPARUM MALARIA IN THAI CHILDREN

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INTRODUCTION

After the emergence of chloroquine resistant falciparum malaria in Thailand in 1962 (Harinasuta *et al.*, 1963), sulfadoxine/ pyrimethamine (SP) combination has been one of the main antimalarials for the treatment of falciparum malaria in Southeast Asia. When the drug was introduced into Thailand, a single dose gave a high cure rate. In adult malaria patients, 1000 mg sulfadoxine/50mg pyrimethamine gave a cure rate of 89.5% (Harinasuta *et al.*, 1967), 82% (Segal *et al.*, 1975); while Doberstyn *et al.*, (1976) attained a cure rate of 85% with a higher dose, 1500mg sulfadoxine/75 mg pyrimethamine. During 1971-1977, in children with falciparum malaria in Bangkok, the cure rate of 76.7% was obtained with a single dose, proportional to 1000 mg sulfadoxine/50mg pyrimethamine adult dose (Chongsuphajasiddhi *et al.*, 1979).

There has been a sharp decline in the effectiveness of SP in the treatment of falciparum malaria in adult patients. In falciparum malaria patients admitted to the Hospital for Tropical Diseases in Bangkok, the cure rates obtained with 1000mg sulfadoxine/50mg pyrimethamine were only 32% during January 1978-April 1979 and 14% during April 1979-March 1980, (Bunnag *et al.*, 1981). In a study carried out in Kanchanaburi Provincial Hospital, 120 kilometres west of Bangkok, during July 1979 to March 1980, 1000mg sulfadoxine/50mg pyrimethamine cleared parasitaemia within 7 days in only 25.6% of falciparum malaria patients (Chongsuphajasiddhi *et al.*, 1980).

This study was carried out to assess the efficacy of sulfadoxine/pyrimethamine in the treatment of uncomplicated falciparum malaria in Thai children.

MATERIALS AND METHODS

The study was carried out in 68 children with uncomplicated falciparum malaria in the Hospital for Tropical Diseases in Bangkok during April and December 1980. There were 43 males and 25 females, ranging in age from one to twelve years with an average of 6.9 years.

Diagnosis was based on clinical symptoms and signs and parasitological examination of thick and thin blood films stained with Field's and Wright's respectively. Asexual erythrocytic parasites were counted 12 hourly during parasitaemia and then daily throughout the 28 day follow up period. The details of study methods are described elsewhere (Chongsuphajasiddhi *et al.*, 1979).

The patients were randomly divided into three groups with 3 treatment schedules:

- Group 1 : Twenty seven patients, 19 males and 8 females, were treated with a single dose of sulfadoxine 20 mg per kg body wt and pyrimethamine 1.0 mg per kg body wt.
- Group 2 : Eighteen patients, 12 males and 6 females, were treated with a single dose of sulfadoxine 30 mg per kg body wt, and pyrimethamine 1.5 mg per kg. body wt.

Group 3 : Twenty three patients, 12 male and 11 females, were treated with quinine 10mg base per kg body wt, 8 hourly for 5 days, and sulfadoxine 20 mg per kg body wt, and pyrimethamine 1.0 mg per kg body wt single dose given with the last dose of quinine.

The drugs were given orally in crushed form, 'Fansidar' tablet containing 500 mg sulfadoxine and 25 mg pyrimethamine, quinine sulphate tablet containing 250 mg quinine base.

All patients were observed clinically and parasitologically to determine whether treatment failure (RI, RII, RIII) was apparent or, in the absence of these features, whether the patient remained clear of parasites for at

least 28 days after the start of the treatment (cured: S) (WHO, 1967). Any complaints about any side effects of the drugs were recorded by the nursing staff. Supportive measures and symptomatic treatment were given to the patients during hospitalization.

Case with treatment failure were retreated with quinine 10 mg base per kg body weight eight hourly for 14 days.

RESULTS

The pretreatment temperatures, packed cell volumes (PCV) and asexual parasite counts of the children with falciparum treated with sulfadoxine/pyrimethamine and quinine are shown in Table 1. The response of the studied groups to the treatment is shown in Table 2.

Table 1

Children with falciparum malaria treated with sulfadoxine/pyrimethamine and quinine.

Group	Treatment	No. treated	Sex M F		Mean Temp.(°C)	Mean PCV	Mean asexual parasite count per c. mm.
1	Sulfadoxine 20 mg per kg. body wt + pyrimethamine 1.0 mg base per kg body wt	27	19	8	39.2 (37.0-40.5)	0.27 (0.13-0.37)	33,687 (2,332-132,000)
2	Sulfadoxine 30 mg per kg. body wt + pyrimethamine 1.5 mg base per kg body wt	18	12	8	39.2 (38.0-40.6)	0.27 (0.14-0.41)	21,917 (419-113,333)
3	Quinine 10 mg base per kg body wt 8 hourly for 5 days + sulfadoxine 20 mg per kg. body wt + pyrimethamine 1.0 mg base per kg body wt	23	12	11	39.7 (38.2-41.0)	0.28 (0.15-0.37)	76,125 (2,556-311,778)

Range of individual measurements shown in parenthesis.

Table 2

Response of children with falciparum malaria to sulfadoxine/pyrimethamine and quinine.

Group	Treatment	No. treated	No. cured:S	No. failure	Resistance		
					RI	RII	RIII
1	Sulfadoxine 20 mg per kg body wt + pyrimethamine 1.0 mg base per kg body wt.	27	2 (7.4%)	25 (92.6%)	4 (14.8%)	17 (63.0%)	4 (14.8%)
2	Sulfadoxine 30 mg per kg body wt + pyrimethamine 1.5 mg base per kg body wt.	18	2 (11.1%)	16 (88.9%)	7 (38.9%)	7 (38.9%)	2 (11.1%)
3	Quinine 10 mg base per kg. body wt. 8 hourly for 5 days + sulfadoxine 20 mg per kg. body wt + pyrimethamine 1.0 mg base per kg body wt.	23	13 (56.5%)	10 (43.5%)	10 (43.5%)	-	-

DISCUSSION

There is no statistical significance between the cure rate of 7.4% in group I treated with the sulfadoxine/pyrimethamine at the dose proportional to 1000 mg sulfadoxine/50 mg pyrimethamine in adult and 11.1% in group 2 with the dose proportional to 1500 mg sulfadoxine/75 mg pyrimethamine in adult.

The study showed that the efficacy of the sulfadoxine/pyrimethamine in the treatment of falciparum in children in Thailand in 1980 was much lower than during 1971-1977 when a cure rate of 76.7% was obtained (Chongsuphajaisiddhi *et al.*, 1979).

The findings were similar to the results of other investigators where low cure rates (S) of 14% and 17% were obtained with 1000 mg sulfadoxine/50 mg pyrimethamine and 1500 mg sulfadoxine/75 mg pyrimethamine respectively in adult patients during April 1979 and March 1980 (Bunnag *et al.*, 1981) and the initial response cure rate (S + RI) of 25.6% in adult patients in Kanchanaburi during July 1979 and March 1980 (Chongsuphajaisiddhi *et al.*, 1980).

The cure rate with the combination of quinine and sulfadoxine/pyrimethamine (56.5%) is also lower than the cure rate of 90.6% obtained during 1971-1977. Bunnag *et al.*, (1981) obtained a cure rate of 40% with quinine sulphate 10 grains 8 hourly for 5 days plus 1000 mg sulfadoxine/50 mg pyrimethamine in adult falciparum malaria patients in Bangkok during 1979-1980.

In 1975, a cure rate of 92% was obtained in adult malaria patients in Trad Province with regimen up to 18 doses of quinine 540 mg base 8 hourly plus 1500 mg sulfadoxine/75 mg pyrimethamine (Hall *et al.*, 1975).

It is apparent that the sensitivity of falciparum malaria to the sulfadoxine/pyrimethamine alone or with quinine is decreasing in Thailand. The sensitivity of falciparum to quinine has also been decreasing (Chongsuphajaisiddhi *et al.*, 1981). The study supports the notion that the clinical response of falciparum malaria in children to treatment is relatively poorer than in adults (Chongsuphajaisiddhi *et al.*, 1979).

SUMMARY

Sixty-eight children with uncomplicated falciparum malaria admitted to the Hospital for Tropical Diseases in Bangkok during April-December 1980 were randomly divided into 3 groups and given 3 regimens. Group 1 of 27 cases were treated with a single dose of sulfadoxine 20 mg per kg body wt and pyrimethamine 1.0 mg per kg body wt. Two cases (7.4%) were cured (S) while 4 cases (14.8%) showed RI failure, 17 cases (63.0%) RII failure and 4 cases (14.8%) RIII failure. In Group 2, 18 cases were treated with a single dose of sulfadoxine 30 mg per kg body wt and pyrimethamine 1.5 mg per kg body wt. Two cases (11.1%) were cured (S), while 7 cases (38.9%) showed RI failure, 7 cases (38.9%) RII failure and 2 cases (11.1%) RIII failure. In Group 3, 23 cases were treated with quinine 10 mg base per kg body wt 8 hourly for 5 days plus sulfadoxine 20 mg per kg body wt and pyrimethamine 1.0 mg per kg body wt, single dose given with the last dose of quinine. Thirteen cases (56.5%) were cured (S), while 10 cases (43.5%) showed RI failure.

This study shows that the sensitivity of *P. falciparum* malaria to sulfadoxine/pyrimethamine alone or with quinine is decreasing in Thailand.

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