ORIGINAL ARTICLE

The Efficacy of Sulphate Quinine Compared to Fansidar in Treating Falciparum Malaria in Children 6 Months - 7 Years Old.

by

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Abstract

From January 1989 until February 1990, 65 children suffering from falciparum malaria without complication at the Department of Child Health Medical School Sam Ratulangi University/Gunung Wenang Hospital Manado were randomly allocated into two groups. The first group was treated with sulphate quinine based on the dose of 30 mg/kg bw/day in three divided doses and the other one was treated with single dose fansidar (sulphadoxine-pyrimethamine) based on the dose of sulphadoxine 20-30 mg/kg bw/day. The grouptreated with quinine showed much shorter duration of parasitemia compared with the group treated with fansidar.

Fever subsided more rapidly in children treated with quinine compared with those treated with fansidar.

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Introduction

In tropical countries like Indonesia malaria is still a public health problem and it is one of the communicable diseases that has priority in eradication.

At the end of 1950 chloroquine resistant plasmodium falciparum was recovered (occurred) in Southern Asia including Indonesia; it was reported since 1973 and it was spread to almost all of the Indonesian islands (Lestadi et al., 1983 ; Rampengan and Rampengan, 1989; WHO, 1984).

The combination of sulphadoxine and pyrimethamine was extensively used as an alternative drug for the treatment of chloroquine resistant falciparum malaria and its use became significant in the early 1980. By 1982 there were reports of increasing failure of treatment in Asia, South America, East Africa and in Indonesia it was reported by Hutapea (1979) in Jayapura Irian Jaya (cited by Adjung et al., 1984). Rampengan and Rampengan (1988) in Manado Sulawesi Utara found that 13.5% out of 37 patients were resistant to Fansidar.

Quinine was found in 1820 as antimalaria drug and it has been used widely in Europe and England. In 1946 chloroquine was found and it became more famous when it was used successfully in malaria eradication program in 1959 replacing quinine as an antimalaria drug (Adhyatma, 1986).

The present study sought to compare the effect of fansidar and quinine on falciparum malaria in children.

Materials and Methods

This is a prospective study on 65 children with uncomplicated falciparum malaria, carried out at the Department of Child Health Medical School Sam Ratulangi University/Gunung Wenang General Hospital Manado from January 1989 until February 1990. The age ranged from 6 months to seven years old.

The patients were randomly allocated into two groups. The first group was treated with sulphate quinine with the dose of 30 mg/kg bw/day in three divided doses for 7 days while the second group was treated with a single dose of a combination of sulphadoxine and pyrimethamine with the dose of sulphadoxine 20-30 mg/kg/day or pyrimethamine 1-1.5 mg/kg/day.

The diagnosis was based on the clinical symptoms and signs and microscopic parasitological examination of thick blood films stained with Giemsa. Blood film for falciparum was examined every day for 8 consecutive days from the day of admission (day 1) until day 8 with guidelines for interpretation as follows: Negative (−) means no parasite (trophozoid) on 100 fields. Positive (+) means 1-10 trophozoids on 100 fields. Positive (+ +) means 11-100 trophozoids on 100 fields. Positive (+ + +) means : -10 trophozoids on one field and positive (+ + + +) means 11-100 trophozoids on 1 field.

Resistance test was based on the criteria of resistance as established by WHO: Standard field test or 7 days test. When there was resistance (R II) in group I then it was treated with fansidar and when there was resistance (R II) in group II then it was treated with sulphate quinine following the schedules above.

Result

This study was conducted on 65 children with uncomplicated falciparum malaria with the age ranging from 6 months to 7 years old, they were randomly divided into two groups. Characteristics of the two study groups were similar. The difference of duration of fever before treatment of the two groups were not statistically significant.

Table 1 : *Characteristics of two study groups*

	Sulphate Quinine (group I)	Fansidar (group II)
No. of patients	33	32
Sex; male; female	13 : 20	17 : 15
Age (years) *	3 ± 1.8	3.5 ± 1.8
Duration of fever before admission**	5.4 ± 3.2	4.6 ± 3.3

* $p > 0.05$
** $p > 0.05$

Concerning the clinical manifestations on admission there were no differences between the two groups (Table 2). Laboratory results such as hemoglobin, white blood cells and platelets were not significantly different ($p > 0.05$).

Table 2 : *The clinical manifestations on admission*

	Sulphate Quinine (group I)		Fansidar (group II)	
Fever	33	100%	32	100%
Convulsion	18	54%	15	47%
Chills	4	12%	3	9%
Vomiting	7	21%	7	22%
Anorexia	10	32%	15	47%
Hepatomegaly	21	63%	16	54%
Splenomegaly	19	57%	19	59%

Table 3 : *The laboratory results on admission*

	Sulphate Quinine (group I)		Fansidar (group II)	
Hemoglobin	11.1 ± 3.1		11.2 ± 2.7	
WBC (/mm^3) *	10.0 ± 3.5		9.0 ± 3.3	
Platelets	145.0 ± 52.7		150.0 ± 30.8	
Thick blood-film				
Ring +	22	(66%)	23	(72%)
Ring + +	4	(12%)	5	(16%)
Ring + + +	7	(21%)	4	(12%)

* $p > 0.05$

In the sulphate quinine group (I) there were no parasites in blood thick film after 3 days of treatment, compared with those in group two where the parasites were still positive after 7 days of treatment.

Table 4 : *Parasitemia features of two groups after receiving the regimen*

		Sulphate Quinine (group I)		Fansidar (group II)	
day	0	33	100%	32	100%
	1	17	50%	16	50%
	2	9	26%	12	37%
	3	4	11%	7	22%
	4	0	0%	3	9%
	5	0		3	9%
	6	0		3	9%
	7	0		2	6%
	8	0		2	6%

There were two patients in the fansidar group who still had parasites in the thick blood film after 7 days and it was thus categorized as R II.

Fever subsided more rapidly in children treated with sulphate quinine compared with children treated with fansidar ($p < 0.01$). Concerning the duration of parasitemia it also showed that the sulphate quinine group had much shorter duration than the fansidar group ($p < 0.05$), Table 5.

Table 5 : *The result of treatment with sulphate quinine and fansidar in 65 tropical malaria patients*

		Sulphate Quinine (group I)	Fansidar (group II)
Duration of fever	*	2.6 ± 0.8	3.2 ± 0.8
Duration of parasitemia	**	2.0 ± 1.0	2.6 ± 1.9

* $p < 0.01$

** $p < 0.05$

These differences were statistically significant.

Discussion

This study was done in 65 children consisting of 33 males and 32 females with the age ranging from 6 months to 7 years. The age of 6 months was considered in order to get more safety in using malaria drugs eventhough some authors said that fansidar could be safely used in infants older than 2 months (Adhyatma, 1986).

Characteristic of both groups i.e. clinical signs and symptoms and laboratory result were similar. All children had a history of fever of the same duration. Peripheral parasites in thick blood films before treatment were similar.

Though quinine has been replaced by chloroquine since 1946 it is still the most effective drug available for the treatment of falciparum malaria especially in severe cases. Quinine acts as antimalaria by inhibiting protein synthesis thus preventing cleavage of DNA (Adhyatma, 1986; Sabchareon et al., 1982). Quinine is rapidly and almost completely absorbed from the intestine and peak plasma concentrations are reached 3-4 hours after orally taken (WHO, 1984).

Reports of quinine resistance are still quite rare and the alleged quinine failures are mostly the result of a too short course of treatment and/or inadequate doses. There is a tendency of an increasing plasmodium falciparum resistant to quinine in Thailand, but in Indonesia until 1986 there has not been such kind of report (Adhyatma, 1986; Sabchareon et al., 1982; WHO 1984).

Fansidar (sulphadoxine-pyrimethamine) has been used as a substitute for chloroquine in the treatment of falciparum malaria and most studies emphasized its effect on the asexual form of plasmodium falciparum (Ittiravivongs et al., 1984). For preventive purposes fansidar is more effective than chloroquine and it is very commonly used in endemic areas with plasmodium falciparum resistant to chloroquine (Lestadi et al., 1983). The sulphadoxine- pyrimethamine combination does not, however, provide a 100% cure rate even in persons infected with fully sensitive parasites, because of individual abnormalities in sulfonamide metabolisme, disposition and elimination. There were reports of increasing failure rates from Burma and Malaysia in 1982 and also in Indonesia; Rampengan and Rampengan (1988) reported plasmodium falciparum resistant to fansidar in 13.5% out of 37 patients.

Chongsuphajaisiddhi et al., (1983) in his study found out that a combination between quinine and fansidar resulted in a sharp decline in the effectiveness in children and adults with falciparum malaria. Quinine alone would be successful if serum quinine levels could be maintained above the minimal inhibitory concentration (MIC) for 7 days. He also reported that there was no additional effect of fansidar when combined with quinine.

The present study showed that asexual parasites in the group treated with sulphate quinine vanished faster than in the group treated with fansidar ($p < 0.05$). Also that the fever subsided more quickly in the group treated with sulphate quinine ($p < 0.01$). Two patients out of 32 (6%) were resistant II (R II) to fansidar but succesfully treated with sulphate quinine for 7 days.

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