

Treatment of the Acute Attack of Malaria Caused by
Plasmodium falciparum : A Comparison of
Mefloquine with Standard Therapy

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OBJECTIVE : To determine the effect of several therapeutic regimens upon sexual and asexual parasitemia with *P. falciparum* in naturally infected humans.

BACKGROUND : Falciparum malaria in Thailand is now considered, for all practical purposes, resistant to chloroquine. As a result, treatment is either with quinine and/or a combination of Sulfadoxine-Pyrimethamine (Fansidar). Other treatment regimens using combinations of tetracycline, quinine and/or sulfamethoxazole-trimethoprim are occasionally employed, but are inferior in clearing parasites.

Quinine continues to be the standard drug given for *P. falciparum*; its efficacy is well known. A few scattered reports of slow response to quinine do continue to cause concern (1). Fansidar's efficacy in falciparum malaria has been proven, with radical cure rates ranging from 80-90% (2). Apparently there is little difference in cure rates between two or three tablet dose regimens in infected adult Thais. Mefloquine hydrochloride, developed by the US Army Antimalarial Drug Development Program, has been shown to be 94% curative in a single oral dose (3).

METHODS : This study is being carried out as a companion effort to that dealing with the treatment of acute vivax malaria, the results of which are reported elsewhere in this Annual Report. The conditions and methods of patient selection and laboratory studies are described in that report. Patients were randomly assigned to one of the following oral therapeutic regimens:

1. Mefloquine hydrochloride, single dose 1,500 mg.
2. Fansidar, single: a) two tablets, b) three tablets.

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3. Quinine, 650 mg. every 8 hrs. for 7 days.
4. Quinine, 650 mg. every 8 hrs. for 7 days plus primaquine, 15 mg. for 5 days.

Patients were normally retained in the hospital until clearance of parasitemia and clinical symptoms. They were followed weekly for 28 days, and at their final visit, they were given primaquine 15 mg. daily for 14 days.

Treatment results were evaluated according to WHO criteria originally conceived to evaluate chloroquine resistance and are described in an accompanying report.

RESULTS : One hundred and nine patients have been studied to date. It is apparent from Table 1 that Mefloquine is at least as good as quinine alone and quinine with primaquine when comparing fever clearance times and parasite clearance times. These data suggest however, that Fansidar in the two tablet dose is slower than the other modes of therapy in clearing fever.

In Table 1, treatment failures are defined as failure to clear parasites in seven days and to remain clear for 28 days. In this regard, there were no treatment failures with Mefloquine but Fansidar in both doses and quinine with and without primaquine showed a total of 7 treatment failures. The resistance patterns were equally divided between RI and RII types (Table 2).

Parasitemia detected before day 28 may have been due to reinfection rather than recrudescence as some of these patients returned to malarious regions.

Of the commercially available drugs, quinine continues to be the drug of choice for the treatment of moderate to severe falciparum malaria. The results reported here, show Fansidar, in either the 2 or 3 tablet dose, to be less effective but still an acceptable form of treatment. Previous reports have shown that a combination of 3 days of quinine followed by a single 3 tablet dose of Fansidar, to be 96% curative (3). Mefloquine continues to be the most effective mode of treatment in experimental studies when treating patients with mild to moderate malaria who do not require parenteral medication,

Routine hematological and biochemical parameters have not reflected any ill effects of the different modes of therapy. We have seen no new side effects of mefloquine.

The effects of the therapy regimens on the sexual parasitemias will be addressed elsewhere in this Annual Report.

REFERENCES :

1. Suvit Sangarlangkarn, Suphat Noepatimanondh, Personal Communication.
2. Doberstyn, E.B., Phintuyothin, P., Noeypatimanondh, S., Teerakiartkamjorn, C.: Single Dose Therapy of Falciparum Malaria with Mefloquine or Pyrimethamine-Sulfadoxine. Bulletin of the World Health Organization, 57(2):275-279, 1979.

Table 1. Therapy of the Acute Attack of *Falciparum Malaria*

Therapy	Number of Patients	Mean Initial Asexual Parasite count/mm ³	Mean Fever Clearance Time in Hours	Mean Parasite Clearance Time in Hours	Number of Treatment Failures*
Mefloquine	25	33,299	60 (N-22)	72	0
Fansidar (2 tabs)	20	22,232	80 (N-16)	71 (N-18)	4
Fansidar (3 tabs)	22	24,729	55 (N-19)	68 (N-19)	4
Quinine	21	22,413	57 (N-21)	69 (N-21)	2
Quinine + primaquine	21	30,415	72 (N-20)	78 (N-20)	2

* Failure to clear parasitemia within 7 days of the initiation of treatment and remain clear for 28 days. Fever and parasite clearance times for RII resistance types were not included in the computation of mean values.

The number of patients shown in parenthesis, varied because some records were incomplete.

3. Hall, A.P. et al.: Sequential Treatment with Quinine and Mefloquine or Quinine and Pyrimethamine-Sulfadoxine for Falciparum Malaria. British Medical Journal. 1(6077):1626-1628, 1977.

Table 2. Results of Treatment of Falciparum Malaria

Regimen	Total	Resistance Patterns				Cure Rate
		RI	RII	RIII	S	
Mefloquine	25				25	100%
Fansidar (2 tabs)	20	2	2		16	80%
Fansidar (3 tabs)	22	2	2		18	81%
Quinine	21	2			19	90%
Quinine + primaquine	21	1	1		19	90%