

Treatment of the Acute Attack of Malaria Caused by
Plasmodium vivax: 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. vivax* in naturally infected humans.

BACKGROUND : Vivax malaria appears to be on the increase in Thailand. Standard therapy of *P. vivax* infections in Thailand consists of 1500 mg of chloroquine administered over the course of three days. Other therapy includes a combination of Sulfadoxine and Pyrimethamine (Fansidar). Fansidar is being used in increasing amounts for the therapy of vivax and falciparum infections in hospitals, clinics, and as self-treatment.

The new antimalarial, Mefloquine hydrochloride, has been shown to be useful in the therapy of the acute attack of vivax malaria (1). It is also useful in *P. falciparum* infections (2). Primaquine is gametocytocidal against the sexual forms of both *P. vivax* and *P. falciparum* in very small doses.

METHODS : This study has been carried out in two malaria - endemic areas in Thailand. The project was initiated at the Phrabuddabat Hospital, in Saraburi Province and later moved to the Phraya Paholpolpayuhasena Hospital, the Kanchanaburi Provincial Hospital. Most recently, the study has moved back to the Phrabuddabat Hospital. Patients were admitted from either the out-patient department of the hospital or the National Malaria Eradication Project detection center. Admission criteria of study subjects were:

1. Males at least 18 years of age.
2. Willingness to volunteer for hospitalization and follow-up. The procedure was carefully explained to the patient, and he was asked to sign a statement of understanding and agreement.

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3. Uncomplicated disease of mild to moderate severity.
4. Asexual parasite count between 1,000 and 100,000/cu.mm.
5. Initially, gametocytes had to be present on the initial thick film; however, this requirement was dropped during the study.

Patients were randomly assigned to one of the following therapeutic regimens, all of which were given orally:

1. Mefloquine hydrochloride, single dose, 1,500 mg.
2. Fansidar, single dose: a) two tablets, b) three tablets.
3. Chloroquine 1,500 mg. total dose given over three days.
4. Chloroquine 1,500 mg. as above plus primaquine 15 mg. daily for five days.
5. Pyrimethamine in dosages ranging between 50 and 150 mg. 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 the WHO criteria originally conceived to evaluate chloroquine resistance: "S" indicated clearance of asexual parasitemia and maintenance of a negative blood film for 28 days after therapy. "RI" refers to initial clearance of parasitemia followed by recrudescence within 28 days after treatment, "RII" indicates initial reduction in the level of parasitemia, but failure to clear in seven days, "RIII" indicates no reduction in parasitemia following treatment.

RESULTS : One hundred and five patients have been studied to date. No new patients were added to the pyrimethamine group. In the five comparable groups, the results are unchanged from those previously reported (3). The fever and parasite clearance times for all groups except Fansidar 2 tablets, were similar. The Fansidar 2 tablet group had significantly prolonged fever clearance times. We again conclude that Fansidar is ineffective treatment for vivax malaria and as such, will not be used for the treatment of vivax malaria in further studies. Mefloquine continues to be very effective in the elimination of parasites and fever.

The routine hematologic and biochemical parameters showed no significant difference between the various treatment groups.

There were no reported treatment failures in the Mefloquine or in either chloroquine group. However, in the Fansidar 2 and 3 tablet groups, treatment failures were noted and found to be of the RI and RII types (Table 2).

The calculated cure rate of 90% for Fansidar, (3 tablets), is based on a small number of patients in that group and may not be borne out in subsequent studies.

Because of its proven safety and efficacy, chloroquine remains the drug of choice for the treatment of vivax malaria. Mefloquine appears to be equally

Table 1. Therapy of the Acute Attack of Vivax 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	31	6,832	40 (N-21)	50	0
Fansidar (2 tabs)	12	7,478	64 (N-11)	80 (N-8)	4
Fansidar (3 tabs)	11	7,342	49	92 (N-10)	1*
Chloroquine	26	10,760	42 (N-20)	51	0
Chloroquine	25	8,516	43 (N-18)	42	0

* Failure to clear parasitemia within 7 days of the initiation of treatment and to remain clear for 28 days. The number of patients shown in parenthesis, varied because some records were incomplete.

Fever and parasite clearance times for RII resistance types were not included in the computation of mean values. Patients without fever were not included in computation of mean fever clearance time.

effective; however, the drug is not yet available commercially, Fansidar should not be used in vivax malaria.

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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.
3. AFRIMS Annual Progress Report, October 1977 to September 1978, pp 142-144.

Table 2. Results of Treatment of Vivax Malaria

Regimen	Total	Resistance Patterns				Cure rate
		RI	RII	RIII	S	
Mefloquine	31				31	100%
Fansidar (2 tabs)	12		4		8	66%
Fansidar (3 tabs)	11		1		10	90%
Chloroquine	26				26	100%
Chloroquine + primaquine	25				25	100%