TREATMENT OF FALCIPARUM MALARIA WITH A SINGLE DOSE OF MEFLOQUINE

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INTRODUCTION

Mefloquine hydrochloride is a new anti-malarial drug used in the prophylaxis and treatment of falciparum malaria. It is an analog of quinine and WR 30,090 and has been used in the treatment of human volunteers infected with both chloroquine-sensitive and resistant strains of p. falciparum (1)

This drug is an odorless, slightly bitter, white powder and stable as neat powder or a formulated capsule for at least 3 months at room temperature, at least 3 months at 45°C. and at least 2 months at 60°C (2)

REVIEW OF LITERATURE

The drug was found to be safe and effective when tested in a series of drug trials carried on in non human primates.

A double blind dose tolerance test from 5 mg to 500 mg single oral dose was performed on 24 male volunteers (2). There were no clinical symptoms and no abnormal clinical findings. There was no phototoxicity reported and the results of the electrocardiograms and liver function tests were normal. Side effects were absent in those receiving less than 600 mgm mefloquine as a single oral dose but when the dose ranged from 600 mgm – 1500 mgm 3 out of 4 patients reported nausea within the first several hours after administration.

Mefloquine has been shown to be a safe and effective single dose antimalarial in a hospital study of chloroquine-resistant falciparum malaria (3). Segal et al (4) tested the efficacy and toxicity of WR 33063, a phenanthrene methanol derivative, and quinine sulphate in Prachinburi Provincial Hospital, Northern Thailand. The area was endemic for chloroquine-resistant falciparum malaria. A daily dose of 1.8 g of WR 33063 in divided doses for 6 days cured 23 of 25 patients and a daily dose of 1.95 g of quinine sulfate in divided doses for 6 days cured 21 of 22 patients. There was no hematologic and biochemical abnormalities during or following treatment with either drug (4).

Pearlman et al (5) studied the effect of various dosages of mefloquine hydrochloride (WR 142, 490) and sulfadoxine-pyrimethamine, in the suppression of malaria in Northeastern Thailand highly endemic for both chloroquine-resistant plasmodium falciparum and for P. vivax. Both preparations were effective in greatly reducing the incidence of falciparum infections. Mefloquine was more active in suppressing vivax parasitaemia than sulfadoxine-pyrimethamine; however, this combination remains the commercially available choice where both parasites occur and P. falciparum is resistant to chloroquine (5).

In Malaysia Fansidar has been found thus far to be the most effective antimalarial in adults that could produce a redical cure in a single dose when given to patients suffering from falciparum malaria. Unfortunately this does not hold true in about 10% of children who in our series have shown resistance to a single dose of Fansidar administered for the treatment of their falciparum infections (6). Some of the commonly used antimalarials are are also effective in single dosage but only in a rather small percentage of cases. Single dose therapy has an added advantage over a multiple dose regime and, with this in view, a preliminary trial was commenced using mefloquine. The aim of this project was to study the effects of the drug in the suppression of parasitaemia and fever in patients suffering from falciparum malaria.

No previous information is available on the side effects of mefloquine in the local population in west Malaysia as the drug has only just become available for research purposes.

It was therefore decided to reduce this dose to 10 mgm per kilogram body weight in our series, after one patient who was given 20 mgm/kg body weight complained of nausea, dizziness and abdominal pain.

MATERIALS AND METHODS

Patients under study were from the Gombak Hospital, Selangor, and the Police Field Force, Kuala Lumpur. Most of the patients at Gombak Hospital were aborigines from jungle-fringe settlements or deep jungle areas of West Malaysia where malaria is endemic. Some of the patients had a previous history of malaria. Members of the police also operated in jungle areas, and probably contracted malaria there. They were usually advised to take malaria prophylaxis, but the regularity with which these drugs were taken is not known.

Those admitted to hospital were suffering from acute symptoms. Thick blood films were examined before treatment, and almost daily thereafter for 7 days. In addition, blood pictures were studied before and after treatment. Glucose-6-phosphate dehydrogenase deficiency screening was carried out in each case, the Fluoreascent Screening Test being used. Temperature was monitored daily, and liver and spleen examinations were carried out at the time of the blood examination and at regular intervals thereafter.

Patients were requested to attend the malaria clinic at the hospital regularly for clinical examination, administration of drugs, examination of blood films and other routine tests. Follow up was carried out for up to 28 days, or longer where possible. However some left the study before the normal 28 day follow up period was completed.

The treatment schedule was a single dose of mefloquine consisting of 10 mgm per kilogram body weight, the drug being given under the supervision of a doctor. Thick blood films stained with 10% Giemsa were examined and parasite density calculated on the total white cell count.

RESULTS

There were 16 cases under study, the majority of whom were aborigines. Eight were males and eight were females. The majority of cases were children between the ages of 12 months and 6 years.

The response of the parasites to mefloquine as shown by clearance of trophozoites is demonstrated in Table 1. On average, trophozoites disappeared from the perip heral blood 2 to 3 days. after mefloquine was administered. Among the 16 cases, one showed blood films positive for gametocytes on Day 0. In three of these gametocytes had cleared on Day 1, and in another three cases gametocytes cleared only after several days.

Three patients became positive for P.vivax on day 22, day 28, and 31 respectively. This showed that mefloquine may not be effective in the suppression of P. vivax infections and as such alternative treatment was administered.

It was observed that 10 out of the 16 patients were afebrile at commencement of treatment. One patient had fever persisting which may either be due to diarrhea or pasrasitaemia. Two patients with a temperature of 98.8°F were considered to be febrile.

There were 8 patients who did not have a complete follow-up for 28 days as they were anxious to return home.

DISCUSSION

The majority of patients under study were aborigines. They live in jungle settlements where malaria is endemic and malaria eradication is a difficult task for various reasons. The younger age groups suffered acute symptoms to a greater extent. This is probably because acquisition of immunity against malaria increases with age, and they had not reached this status yet. Among those from the Police Field Force, a few were perhaps non-immunes, and their entry into endemic jungle areas enhanced the possibility of infection.

Trophozoite clearance after a single dose of mefloquine took between 2 to 3 days on the average. the longest time being 5 days. This was consistent with the findings of Trenholme et al (1) who had similar results after a single dose of mefloquine. No recrudescence of parasites were observed within the follow-up period of 28 days. In the work of Doberstyn et al (3) none of the patients followed for up to 60 days developed new P. falciparum parasitaemia.

In cases 9, 10 and 15 the films became positive for P. vivax on day 22, 28 and 31 respectively. Alternative treatment was then given to these patients.

Another interesting festure in these cases was the absence of fever in 10 out of 16 patients. Most of those who presented with fever did not show the typical

textbook pattern: fever subsided on a average of 2 days after the single dose therapy.

By and large the single dose of mefloquine was effective in clearing the blood of gametocytes, although in 3 cases these persisted for periods up to 8 days, 10 days and 13 respectively.

The drug appears to be effective in producing radical cures in falciparum malaria.

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CLINICAL DETAILS OF PATIENTS.
TABLE: 1

Name	Sex	Age (Yrs)	Parasitaemia per mm before treatment		Parasitaemia per mm on Day 1.		No. of days trophozoites and gametocytes persisted.		No. of days for fever to subside.	Reappearance of parasite before Day 28	No. of days patient was followed up
			Troph.	Gamet	Troph.	Gamet	Troph.	Gamet			
A.S.	M	29	1,840.	800	2,160	1,360	2	10	3	Nil	19
S.A.	F	3	4,800	0	680	0	3	—	2	Nil	15
M.K.	M	10	1,040	0	0	0	1	—	afebrile on Day 0	Nil	11
R.C.	M	2 mths	2,640	40	not	done	4	1	afebrile on Day 0	Nil	25
J.A.	F	3	161,700	0	1,640	0	2	—	fever persisting diarrhea present	Nil	7
G.A.	M	1 yr. 9 mths	5,200	0	22,880	0	5	—	2	Nil	9
B.B.C	M	1	2,360	40	240	0	2	1	afebrile on Day 0	Nil	24
A.B.C	F	3	240	80	0	0	1	1	afebrile on Day 0	Nil	24
A.W.	F	6	1,720	0		0	2	—	Temperature 98.8°F subsided in 6 hours.	Positive for P.vivax on	
J.S.	M	11 mths	3,280	320	80	240	3	8	afebrile on Day 0	positive for P.vivax on Day 28	28
A.O.	F	2	296,400	0	2,800	0	2	—	Temperature of 98.8°F Subsided in 4 hours	Nil	30
A.O.	M	8	480	0	280	0	5	—	Afebrile on Day 0	Nil	27
H.C.	F	30	400	0	400	0	1	—	Afebrile on Day 0	Nil	12
R.Y.K.	M	3	2,000	0	1,320.	0	2	Gameto-Cytes appeared on day 2 and cleared On Day 13	Afebrile on Day 0	Nil	31
A.O.	F	5 mths	8,200	80	320	980	2	13	Afebrile on Day 0	positive for P.vivax on Day 31	31
A.O.	F	3	2,480	0	960	0	2	—	Afebrile on Day 0	Nil	31