THE EFFECT OF MEFLOQUINE-SULFADOXINE-PYRIMETHAMINE *VS* QUININE ON PATIENTS WITH COMPLICATED FALCIPARUM MALARIA

PE THAN MYINT and TIN SHWE

Clinical Research Unit, Department of Medical Research,
Ministry of Health, No. 5 Zafar Shah Road, Dagon P.O., Rangoon, Burma.

INTRODUCTION

Mefloquine is effective against chloroquine and quinine resistant malaria. Although clinical trials were started in 1972 it has only relatively recently been introduced into clinical practice (Harinasuta *et al.*, 1982). Mefloquine resistance has already been reported from several countries before wide scale use of the drug. In an attempt to delay the area of drug resistance mefloquine has been combined with sulfadoxine pyrimethamine (MSP). This combination has previously used for cases of uncomplicated falciparum malaria, and quinine has been used in severe infections. With increasing use of this drug, it is inevitable that patients with severe infections will be treated (WHO, 1986). We have therefore prospectively studied patients in this group.

MATERIALS AND METHODS

The study was conducted during 1985-1986 at Tharawaddy Division on the western side of the Pegu Mountain range, 128 km north of Rangoon where malaria is hyperendemic and where chloroquine and sulfadoxine pyrimethamine resistance have been reported. Sixty-six patients with falciparum malaria, and one of more of the following complications were included in the study:

More than 2% of red cells infected with malaria parasites (asexual count over 100,000/c.mm of blood); patients with high fever temperature 105°F and above; anaemia, haematocrit less than 30%; blood urea more than 50 mg/dl and clinically detectable jaundice.

Patients with impaired level of consciousness, pregnancy and children under 12 yrs. age were not included in the study. The Wilson and Edison test for chloroquine, Lelijveld and Kortman test for 4 aminoquinolines, Mayer Tanret urine test for quinine, Lignin test for sulphonamides were tested as a screen for ingestion of antimalarial drugs before admission to hospital.

Written consent to participate in the study was obtained in every case. Patients admitted to the Tharawaddy Civil Hospital were paired according to age group, sex and complications. The following treatments were given to alternate patients. (a) Mefloquine 750 mg sulfadoxine 1500 mg and pyrimethamine 75 mg given as a single oral dose. (b) Quinine 10 mg/kg body weight 8 hourly for 7 days. The initial dose was given by intravenous infusion.

All patients were admitted to hospital for seven days. Routine laboratory biochemical examinations and an ECG were also done.

Body temperature was recorded every six hours for 24 hours and 12 hourly thereafter until it was normal. Thick and thin blood films were taken every 6 hours until no asexual forms were present in the peripheral blood for 24 hours, and then repeated daily up to day 7 and again on days 14, 21 and 28.

RESULTS

Sixty-six patients included in the study were as follows:

	MSP Group	Quinine Group
High parasite count (> 100,000/c.mm)	19	20
Anaemia (PCV < 30%)	14	10
Clinical jaundice	11	8
Raised blood urea > 50 mg/dl	4	5
Hyperpyrexia > 105° F	1	1
More than one complication	16	10

The MSP group consisted of 31 males and 2 females. Their mean weight was 46.6 ± 8.2 kg and mean age was 24 ± 7 years and the initial mean asexual parasite count was GM 238,000 ± 247,000/c.mm.

The quinine group consisted of 22 males and 9 females. Their mean weight was 43.6 ± 6.8 kg mean age was 32 ± 15 yrs and the initial mean asexual parasite count was GM 233,000 ± 232,000/c.mm.

The weight age and initial parasite count between the two groups were comparable. Comparison by students 't' test showed no significant difference ($p > 0.3$) between the groups.

Four patients in the MSP group and 6 patients in the quinine treated group needed blood transfusion as their PCV fell below 20% during the first few days of admission to hospital.

All patients survived. The mean parasite clearance time was 56.0 ± 24.8 hours and fever clearence time was 44.8 ± 32.7 hours in the MSP group. The parasite clearance time was 76.5 ± 23.7 hours and fever clearance time was 47.1 ± 22.0 hours in the quinine treated group. Among patients treated with MSP the mean parasite clearance time was significantly shorter than those treated with quinine. There was no significantly difference in fever clearance time of the two groups of patients. (Table 1 and Fig. 1).

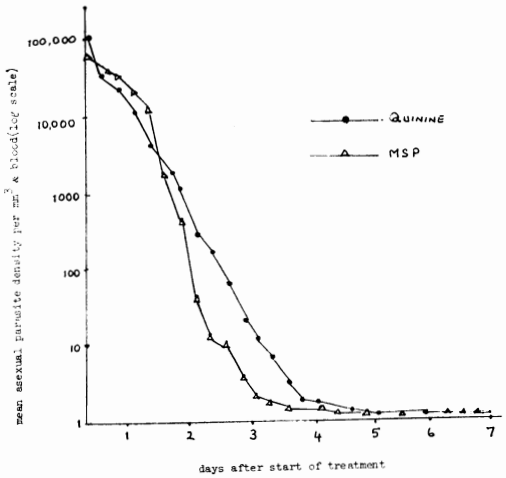

Fig. 1—Sensitivity of *P. falciparum* (Asexual forms) to Mefloquine / Sulfadoxine / Pyrimethamine triple combination and quinine at Tharawaddy, Burma, April-July 1986.

There were no serious clinical or electrocadiographic signs of drug toxicity in the MSP group. Follow up of the patients showed one patient with resistance at RII level and 5 patients with resistance at RI level, in MSP group. Among patients in quinine group 3 patients were resistant at RI level.

DISCUSSION

Although there are a number of reports on the use of mefloquine on malaria patients there are relatively few reports on the use of triple drug combination (MSP). A double blind trial carried out in Thailand reported that one out of 49 patients failed to respond to the drug. This patient vomitted shortly after treatment and the amount of drug absorbed might have been insufficient. A similar study performed at Brazil on 25 patients reported that asexual parasitaemia was cleared within 3.3 days without any recrudescence. All these reports were on patients with uncomplicated malaria (WHO, 1984).

In this study the patients had high parasitaemia yet the parasite clearance time of patients treated with MSP was shorter than those treated with quinine. However, if a patient vomits, the dose of drug absorbed would be inadequate and it must also be accepted that if no loading dose is used then quinine levels may be subtherapeutic in first 24 hours. Therefore parasite clearance could be delayed. The further advantage of MSP is the effectiveness with a single dose which saves a lot of time. Hence MSP may be a drug of choice and may be claimed as a drug better than quinine in terms of toxicity and tolerance in patients with high parasitaemia.

Falciparum malaria can present with severe gastrointestinal symptoms. Thus, oral single MSP can be a handicap in such a situation.

In this study among patients treated with MSP one patient had RII resistance (resistance of parasites on day 7 with further rise in the level of parasites till day 13 when the drug had to be changed). This case has been discussed in a separate paper. Hence, there can be patients with primary resistance to MSP from the area where the drug had never been used.

Li (1984) had found the addition of qinghaosu to mefloquine greatly increased the rate of parasite clearance with no additional side effects. Hence, studies on this line of management is needed to be considered for future research.

SUMMARY

Sixty-six patients with complicated falciparum malaria (defined as anaemia, hyperpyrexia, jaundice, or more than 2% of RBC parasitised) were studied. Patients with cerebral signs and symptoms were not included in the study. Patients were randomised in pairs to receive either mefloquine 750 mg, sulfadoxine 1500 mg and pyrimethamine 75 mg (MSP) single oral dose or quinine (10 mg/kg tds × 7 days oral therapy). All the patients were admitted in hospital for 7 days and were followed on days 14, 21 and 28.

All patients survived. The parasite clearance times in MSP treated patients were significantly shorter then those treated with quinine. There was no difference in fever clearance time in the two groups of patients. One patient was resistant to MSP at RII level and 5 patients were resistant at RI level. Among patients treated with quinine 3 patients were resistant at RI level.

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