TREATMENT OF FALCIPARUM MALARIA WITH INTRA MUSCULAR QUININE IN A RURAL AREA OF THAILAND

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INTRODUCTION

In Thailand, malaria is endemic in rural forested foothill areas. The conventional treatment of severe falciparum malaria, especially with cerebral symptoms or vomiting, is to give 600 mg of quinine dihydrochloride (490 mg base) in 500 ml of normal saline solution intravenously over 2 hours every 8 hours until the patient can take the drug orally. Intravenous quinine treatment is quite expensive and needs closed observation by health personnel. In the endemic areas, patients with malaria are usually from low socio-economic groups and the number and availability of health personnel is limited.

Intramuscular injection of quinine is usually not recommended because it may cause muscle necrosis and absorption is considered to be unreliable. However, in the treatment of severe falciparum malaria in areas where intravenous quinine is not feasible, intramuscular administration of quinine is recommended (W.H.O. 1980). In Thailand, this practice is followed in certain malaria endemic areas where people are poor and the number of health personnel is very limited.

This study was carried out to assess the efficacy and absorption of intramuscular quinine in the treatment of falciparum malaria in a rural district hospital in Thailand.

MATERIALS AND METHODS

The study was carried out in 32 adult cases (20 males and 12 females, age ranging from 17-55 years) of falciparum malaria with nausea and vomiting in Chomboeng Crown Prince Hospital, Ratchaburi Province, 150 km. southwest of Bangkok, during April-December 1981. In this rural district hospital, all cases over 15 years of age were treated with adult dose of quinine (490 mg base) regardless of body weight. The patients were treated with 600 mg of quinine dihydrochloride (from Government Pharmaceutical Organization) intramuscularly every 8 hours until nausea and vomiting subsided and the drug could be given orally. Quinine was given 8 hourly for 7 days.

Thick and thin blood films for malaria parasites were taken before treatment and then on day 3 (D3), day 5 (D5), and day 7 (D7) after treatment was started.

In 13 cases, serum concentrations of quinine were measured prior to the first injection of quinine, then 4 hours and 8 hours later. In a further 6 cases, the determinations were carried out prior to the first injection and 4 hours later only.

Quinine concentrations were measured by the benzene extraction method of Cramer and Isaksson (1965).

In addition to parasitological examination, all patients were observed clinically for at

least 7 days. If the patients became clinically worse intravenous quinine was substituted for the intramuscular route.

RESULTS

Parasites were cleared from the blood by D_3 in 26 cases, and by D_7 in 4 cases. Fever was cleared in a mean of 2.8 days after the treatment. In the other two cases, intravenous quinine was given instead of intramuscular quinine on D_2 and D_3 respectively because of clinical deterioration and parasitaemia was cleared within seven days in both cases.

Table 1 shows the serum quinine concentrations of 19 patients (14 males and 5 females).

Table 1

Serum quinine concentrations prior to intramuscular injection of 600 mg of quinine dihydrochloride (490 mg base), and then 4 hours and 8 hours later.

Patient No.	Serum quinine n mol/ml		
	prior to	4 hours	8 hours
1	0	14.63	14.63
2	0	20.41	18.37
3	0	22.11	20.75
4	26.25	37.76	36.06
5	0	17.67	-
6	2.38	18.03	15.65
7	8.33	21.99	27.32
8	23.98	37.31	35.61
9	0	30.65	13.99
10	0	18.99	22.65
11	0	33.31	28.31
12	0	22.32	28.31
13	0	26.98	28.98
14	11.99	14.66	-
15	0	10.66	-
16	0	22.65	-
17	0	15.66	-
18	0	18.32	-
19	0	16.65	-

In 5 patients, quinine was already present in the blood prior to the injection of the first dose of quinine. In the other 14 patients, it was found that the mean serum quinine concentration 4 hours after the injection was 19.43 n mol/ml. The mean serum quinine concentration after 8 hours was 22.0 n mol/ml in the 8 patients studied.

There were no complications of intramuscular quinine. During hospitalization for at least 7 days, there were no inflammation at the injection sites except for slight tenderness in some cases.

DISCUSSION

The results shows that quinine was still effective in the treatment of falciparum malaria in rural areas of Thailand. Parasite and fever clearance of all patients occurred within 7 days (S or RI). No cases of RII or RIII resistance were observed. Since the study period for each patient was only 7 days, it was not possible to assess the resistance of the parasite at RI level.

Serum quinine concentration at 4 hours of 19.43 n mol/ml and at 8 hours of 22.0 n mol/ml were higher than the mean minimum inhibitory concentration (MIC) of quinine of 14.89 n mol/ml quoted in 1979 (Chongsuphajaisiddhi *et al.*, 1981). However, the MIC for quinine of falciparum malaria parasites has risen considerably in recent years and the mean value in 1981 was 21.65 n mol/ml (Tan Chongsuphajaisiddhi, pers. commun.). This is similar to the mean serum quinine level of 22.0 n mol/ml observed 8 hours after intramuscular injection. However, serum quinine concentrations after subsequent doses should be higher than those after the first dose.

Therapeutic serum quinine concentrations can be attained following intramuscular injection of quinine. Furthermore, the complications associated with this route of administration are minimal.

SUMMARY

The study was carried out in 32 adult cases of falciparum malaria who had nausea and vomiting. All patients were admitted in Chomboeng Crown Prince Hospital, Ratchaburi Province, during April-December 1981. Patients were treated with 600 mg of quinine dihydrochloride intramuscularly every 8 hours until nausea and vomiting subsided and the drug could be given orally. Quinine was given 8 hourly for 7 days. Parasites were cleared from the blood by D_3 in 26 cases, and by D_5 in 4 cases. Fever was cleared in a mean of 2.8 days after the treatment. In the other 2 cases, intravenous quinine was given instead of intramuscular quinine on D_2 and D_3 respectively and parasitaemia was cleared within D_7 in both cases.

In 13 cases, serum quinine concentrations were measured prior to the first injection of quinine, then 4 hours, and 8 hours later. In other 6 cases, the measurements were carried out prior to the first injection and 4 hours later only. In 5 patients, quinine was present in the baseline blood sample. In the other 14 patients, mean serum quinine concentration at 4 hours was 19.43 n mol/ml. The mean serum quinine concentration at 8 hours in 8 patients was 22.0 n mol/ml.

Therapeutic serum concentrations can be attained by intramuscular injection of quinine.

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