RESPONSE OF FALCIPARUM MALARIA TO A COMBINATION OF QUININE AND SULFADOXINE-PYRIMETHAMINE IN BOOMY COUNTY OF LIBERIA

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ABSTRACT

Objective: To document the response of Falciparum malaria to a combination of Quinine and sulfadoxine- Pyrimethamine in Boomy County of Liberia.

Study Design: Quasi-experimental study.

Place and duration of Study: Pak Level-II Hospital Tubmanburg, Boomy County Liberia over a period of one year (Jan 2006 – Dec 2006).

Patients and Methods: Employees of United Nations' Mission in Liberia (UNMIL) mostly Pakistani soldiers but also other nationals belonging to different countries; who presented with Falciparum malaria and treated with quinine were included in the study. Falciparum malaria was confirmed microscopically in each case and was treated with a seven day course of Quinine followed by a single dose of Fansidar (sulfadoxine- Pyrimethamine).

Results: A total of 69 patients were treated with Quinine; age range 20 to 50 years; 43 Pakistanis and 26 other nationals. All responded well to a combination of Quinine and sulfadoxine-Pyrimethamine. Fever settled within 72 hours in 91% of cases and parasite disappeared from the blood in 96% cases within 72 hours.

Conclusion: A combination of Quinine and sulfadoxine- Pyrimethamine is very effective in the treatment of Falciparum malaria. Majority of patients became asymptomatic within 72 hours.

Keywords: Falciparum malaria, Quinine, sulfadoxine- Pyrimethamine, Parasite Clearance Time, Fever Settling Time.

INTRODUCTION

Every year 300-400 million people suffer from malaria in the world out of which 2-3 million die due to its complications[1]. Plasmodium falciparum and P. vivax account for the vast majority of infections[2]. Falciparum malaria has the potential to rapidly progress and carries a substantial risk of death. Microscopy is the gold standard for the diagnosis of malaria. It can estimate parasite density and identify the parasite species. Falciparum malaria can also be diagnosed by rapid diagnostic tests (RDTs) which detect parasite-derived proteins[3]. However, quantification of parasite load, stage identification and monitoring of parasite clearance are not possible with these tests[4].

Multidrug resistant strains of P falciparum occur in Southeast Asia, South America, and sub- Saharan Africa. The treatment of Falciparum malaria depends on the likely pattern of susceptibility to antimalarial drugs and their cost and availability. For this reason, recommendations vary according to geographic region and should be under constant review[5]. World Health Organization recommends a follow-up period of 7, 14, and 28 days[6]. The timing of recurrent parasitemia (parasitologic failure) or disease (clinical failure) reflects the degree of resistance. Late recurrence may be confounded by reinfection[7].

Quinine monotherapy had been the traditional treatment of choice for chloroquine resistant falciparum malaria in most of the endemic countries. However, the combination of antimalarial drugs prevent development of drug resistance. A combination of Quinine with doxycycline or clindamycin for 5-7 days or Quinine for 5-7 days followed by a single dose of sulfadoxine-pyrimethamine combination has been recommended[8]. The treatment of choice for severe or complicated malaria has been intravenous quinine infusion[9]. The Artemisinin compounds (artemether and artesunate) give

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faster relief of fever and clearance of parasites than other antimalarial agents[10]. The Artemisinin based combination therapy (ACT) is very effective against the multidrug resistant falciparum malaria. Parenteral Artemisinin compounds can be more effective in treating severe malaria in selected situations. They can also be used in patients with contra-indications to quinine.

Resistance of P. Falciparum to mefloquine at the border regions between Thailand and Cambodia remains high11. Atovaquone-proguanil is better tolerated than the combination of quinine and tetracycline12. Atovaquone-proguanil has reported cure rates of 94% to 100% for P falciparum infections acquired in Southeast Asia, Africa, and South America [13]. There have been published cases of atovaquone-proguanil failure for the treatment of P falciparum malaria14.

Falciparum malaria is endemic in Liberia like other sub-Saharan African countries. So far very limited data are available on the efficacy of currently used antimalarial drugs and the current situation of drug resistance in Liberia. The aim of this study was to document the therapeutic efficacy of quinine plus sulfadoxine-pyrimethamine for the management of uncomplicated falciparum malaria in Boomy County of Liberia.

PATIENTS AND METHODS

This is a Quasi-experimental study conducted at Pak Level-II Hospital Tubmanburg in Boomy County of Liberia from January 2006 to December 2006. All the patients suffering from falciparum malaria and treated with a combination of Quinine and sulfadoxine-pyrimethamine were included in this study. The patients included employees of United Nations' Mission in Liberia (UNMIL), mostly Pakistani soldiers but also other nationals belonging to different countries. Most of the UNMIL employees used to take mefloquine or Doxycycline for malaria prophylaxis.

All the patients suffering from falciparum malaria confirmed on microscopy and hospitalized for the initiation of treatment under direct observation were included in this study. Those patients were excluded from the study who received empirical therapy for malaria or received outdoor Quinine treatment or got discharged before their three consecutive blood smears were negative or got other antimalarial drugs. Patients having concomitant Lassa fever were also not included in the study.

A detailed history was taken at presentation and physical examination was done. Falciparum malaria was confirmed by microscopic examination of blood smears. Other baseline investigations included Complete blood counts (CBC), Urinalysis, blood sugar, Liver function tests (LFTs) and Renal function tests (RFTs). A baseline parasite density (percentage of infected erythrocytes on a thin film) was determined and Quinine was started. Patients having persistent vomiting or looking very ill were started intravenous Quinine infusion. The parasite density was determined 12 hourly till three consecutive blood smears were negative. The Fever Settling Time (FST) and the Parasite Clearance Time (PCT) of the patient was determined. Patients remained in hospital until they were afebrile for at least 72 hours and their three consecutive blood smears were negative for malaria parasites. Those discharged were given drugs in outdoor and were reviewed clinically and parasitologically after completion of the course of antimalarial drugs. The study endpoints included clinical recovery and parasitological cure 7 days after initiating treatment.

All patients received treatment with 600 mg of Quinine sulphate oral 8 hourly for 7 days followed by a single dose of 3 tablets of Fansidar (sulfadoxine 500 mg co-formulated with pyrimethamine 25mg) [15]. Some patients received intravenous Quinine infusion 600 mg 8 hourly to start with but were started on oral Quinine as soon as was possible. After successful treatment the patients were advised to take malaria prophylaxis (weekly mefloquine or daily doxycycline) regularly. They were asked to report immediately if they developed recurrent fever.

RESULTS

A total of 69 patients were included in the study; 66 were males, 3 were females; forty

three patients were Pakistanis and 26 were other nationals. Age was between 20 to 50 years. In 63 (91%) patients fever settled within 72 hours (range 24-168 hours) (Table-1), while parasite was cleared from blood within 72 hours in 66 (96%) patients (range 36 to 96 hours) (Table-2). In 42 (61%) patients fever settled before the clearance of the parasite while in18 (26%) the parasite cleared earlier than fever settled. In only 9 (13%) FST corresponded to PCT. 44 (64%) patients had a parasite density of <1% (range 0.01-2.5%) at presentation. There was no direct correlation between parasite density at presentation, fever settling time and parasite clearance time as every patient had his own characteristic response (Table-3). Patient with lowest parasite density at presentation (0.01%) had FST of 72 hours and PCT of 36 hours whereas the patient having the highest density at presentation (2.5%) had FST of 72 hours and PCT of 96 hours. The patient having longest fever (FST168 hours) had a density of 0.05% at presentation and PCT of 48 hours.

All the patients had parasitologic and clinical cure within the first week of treatment. No patient reported back with recurrent fever after completion of treatment. Of the 69 treated patients, 20 reported nausea, 13 dizziness, 4 vomiting and 3 tinnitus. However, these symptoms were well tolerated and did not require discontinuation of Quinine. No allergic reactions attributable to Fansidar were observed in the study group.

Table 1: Fever Settling Time

FST	No of Patients
24 hours	28 (41 %)
48 hours	17 (25 %)
72 hours	18 (26 %)
4 days (96 hours)	2 (3 %)
5 days (120 hours)	3 (4 %)
7 days (168 hours)	1 (1 %)

Table2: Parasite Clearance Time

PCT	No of Patients
36 hours	13 (19 %)
48 hours	30 (44%)
72 hours	23 (33 %)
96 hours	3 (4 %)

Table 3: Correlation of Parasite Density to FST and PCT

Parasite density at Presentation	No of Patients	FST (Range)	PCT (Range)
<1%	44 (64 %)	24 – 168 hours	36 – 72 hours
1 – 2%	22 (32 %)	24 – 120 hours	36 – 96 hours
>2%	3 (4 %)	48 – 72 hours	72 – 96 hours

DISCUSSION

Chloroquine-resistant Falciparum infections in most of Africa and some parts of Asia and South America usually respond to a single-dose combination of sulfadoxine and pyrimethamine. Unfortunately, resistance to sulfadoxine–pyrimethamine has developed in many areas particularly in South America and Southeast Asia. The rates of parasitologic failure with sulfadoxine–pyrimethamine in sub-Saharan Africa were relatively high (>50 percent) in southern regions and low (<5 percent) elsewhere. The rates of clinical treatment failure in sub-Saharan Africa were <5 percent in the west and 8 to 34 percent in the east and south[16]. Studies in Southeast Asia indicated that the rates of parasitologic failure at day 7 and day 28 were 36 percent and 49 percent, respectively[17]. Good efficacy (80 percent) persisted elsewhere; in southwestern Asia and on the Horn of Africa[18]. In southern Asia the failure rate of 18 percent by 28th day has been reported[19].

The combination of Quinine with a single dose of sulfadoxine-pyrimethamine for the treatment of P. falciparum malaria in areas with low levels of sulfadoxine-pyrimethamine resistance can be highly effective. This can be an affordable approach and can protect against the evolution of quinine resistance in poor communities. In our study sulfadoxine-pyrimethamine was given to the patients after 7 days of treatment with quinine and by that time parasitologic and clinical cure for Falciparum malaria was already achieved with quinine. So, in our case, we cannot comment on the efficacy of sulfadoxine - pyrimethamine on fever clearance time and parssite clearance time. However, the treated patients did not report

back again with recurrent fever during the study period.

The compliance with a seven day course of quinine is often poor because of its side effects. In Cambodian villages, the rate of compliance with the Quinine regimen was 11 to 20 percent[20]. In our patients a 7 day course of Quinine was well tolerated and the common adverse effects noted were nausea, dizziness, vomiting and tinnitus. None of our patients developed allergic reactions attributable to sulfadoxine-pyrimethamine.

When the patients of uncomplicated Falciparum malaria are treated with a combination of Quinine and sulfadoxine/pyrimethamine, compliance may be improved by shortening the course of Quinine from 7 days to 3 days followed by a single dose of sulfadoxine/pyrimethamine. Matsiegui et al[21] assessed the efficacy of a 3-day course of quinine plus a single dose of sulfadoxine/pyrimethamine for the treatment of uncomplicated falciparum malaria in 50 children in Gabon. Parasites were cleared after 66 hours and the fever after 46 hours. All patients evaluated by day 28 were negative for malaria parasites (100% efficacy rate). There was no adverse event attributable to the study drugs[21]. Athan et al. evaluated a 3-day course of quinine followed by a single dose of sulfadoxine-pyrimethamine in 133 hospitalised patients with uncomplicated falciparum malaria at South Africa. One hundred and thirty of 131 patients (99%) successfully followed up for 42 days demonstrated clinical and parasitological cure[22].

CONCLUSION

A very high efficacy can be reached using a 7-day course of quinine followed by a single dose of sulfadoxine/pyrimethamine for the treatment of falciparum malaria cases in our study area. This combination is effective, safe and well-tolerated and it can be an affordable alternative to ACT in poor communities. In Liberia in addition to falciparum malaria, Lassa fever is also endemic. The contribution of undiagnosed Lassa fever to mortality of the patient suffering from concomitant falciparum malaria is not known. Many cases of malaria may die because of undiagnosed Lassa fever instead of poor response to antimalarial drugs. This point needs to be clarified further.

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