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In vivo Response of Malarial Parasites to Mefloquine in an Urban Clinic in Sokoto State, Nigeria

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Abstract: The *in vivo* response of malarial parasites to mefloquine was studied. A total of seventy one patients with acute uncomplicated malaria were selected for study. All the treated cases (100%) responded well and both the clinical features and malarial parasites in the blood cleared within seventy two hours after initiating treatment. About seventy five percent of the patients who recovered, were follow up after fourteen days and confirmed to be symptoms and parasites free. This study suggested that mefloquine is effective and well tolerated for the treatment of malaria within the study area.

Key words: Mefloquine, *Plasmodium falciparum*, parasite, malaria and chloroquine

Introduction

Despite all the global actions and rhetorics about the treatment, prevention and control of malaria, the disease has continued to be the number one killer especially among infants and a major public health problem in Sub Saharan Africa. There are more than 200 million cases each year with an estimated one to two million deaths annually, mostly in children less than five years of age. It represents twenty to fifty percent of all the consultations in health centres and is the greatest cause of mortality in hospitals (Amadou *et al.*, 2001).

In Nigeria, malaria is directly responsible for over 100,000 deaths of children every year and one quarters of an average Nigerian family income is spent on the treatment of malaria (Afolabi, 2001). Chloroquine is the most commonly used first line drug against malaria in the continent. However, the spread of chloroquine resistance has been reported in most areas in Africa (Nicholas, 1999). In Rwanda for instance, in 1985 only thirty one percent of the patients showed some grade of resistance to chloroquine whilst in 1987 the resistance had doubled to sixty-five percent (Bhatt *et al.*, 1997). *In vitro* and *in vivo* resistance of *P. falciparum* to chloroquine have been confirmed in Western Kenya, Ghana, Cameron, Republic of Benin and Nigeria. The reported cases of chloroquine resistant malarial parasites has been increasing especially in the eastern and middle belt areas of Nigeria (Bisseru, 1995).

In view of the very high incidence of malaria in Nigeria and rapid spread of resistance to most of the commonly available antimalarials, it is critically important to test the newer and hopefully more effective drugs. The World Health Organization has emphasized the need to continuously monitor how the parasite population in an area respond to a drug and what factors and factor variation that may be associated with a variation in drug response (Anonymous, 1984).

The increase in resistance to chloroquine has lead to change in the prescription of antimalaria drugs especially among the elite population. Currently, the most commonly used prophylactic antimalarial drug in Kenya, South Africa and other countries where chloroquine resistant *falciparum* malaria exist is mefloquine. Mefloquine is also widely used for the treatment of acute malaria where multidrug resistant *falciparum* malaria occurs and even high dose of mefloquine is used in some areas (Bhatt *et al.*, 1997). In Nigeria, mefloquine is sparingly used as an alternative drug in the treatment of malaria. This is partly because, mefloquine is scarce in the market and there is little or no information about its clinical trial within the country. Mefloquine like several other antimalarial drugs is a distant derivative of quinine. Their common feature is the bicycle conjugated quinoline ring system. Although the mechanism of action is not fully understood, mefloquine is thought to bind with high affinity to erythrocyte membrane and may thus possibly block the invasion of uninfected erythrocytes by merozoites. It appears that the action of mefloquine is linked to the breakdown of haemoglobin by the Plasmodia leading to their destruction by lethal membrane damage. The mode of action of quinine, chloroquine and mefloquine are very similar in many respects but unlike the first two compounds, mefloquine does not intercalate the deoxyribonuclic acid (DNA). Mefloquine is a blood schizontocidal drug for *Plasmodium falciparum* malaria. It also exerts a gametocidal effect on *Plasmodium malariae, P. ovale* and *P. vivax* but not on the mature gametocytes of *P. falciparum.* There is no effect on exoerythrocytic hepatic forms and sporozoites (Okpako, 1993).

The main aim of this study is to ascertain the efficacy or otherwise of mefloquine in the chemotherapy of malaria and also its tolerableness by the patients after oral administration. The results of this study will add to the available information on this drug and this will enable its users to make informed decision.

Materials and Methods

Patients attending the out patient unit of Kofar Rini Clinic in Sokoto State of Nigeria between the months of June – October 2001 were selected for this study. The required characteristics for selection were adults between the ages of 18-55 years with clinical features of malaria. Patients who have received any form of antimalarial drugs in the last two weeks, pregnant women and those with recurrent serious illnesses were excluded. Immediate thick blood films were made from finger prick of selected patients. The films were stained with Gimsa stain and later screened for malarial parasites. Only positive cases were included in the final study. Five hundred milligrams of mefloquine (Lariam) Swisspharma Nigeria Limited with two tablets of paracetamol were given orally to the patients in the clinic and they were observed for at least 30 minutes after taking the drug to ensure that it was not vomited. The remaining 500 mg with another two tablets of paracetamol were repeated after 8 h and the patients were sent home and asked to report back on 2nd, 3rd and 14th days. Repeated finger pricks were performed on each visit and thick blood films produced and screened for malarial parasites. Observed side effects by the patients from the drug were also recorded.

Results

A total of 172 patients were diagnosed clinically as having acute malaria during the study period. While five of the patients were excluded because of various reasons that would have interfered with the study, seven refused to participate when their consent were being sought. Out of the remaining 160 patients whose blood were screened for malarial parasites, 71 were positive giving a percentage positivity of 44.4%. While all the patients reported for follow up on the 2nd and 3rd days; only 53 (74.7%) came for the last visit on 14th day. The patients were from the ages of 18-55 years, 29 of them were males and 42 were females. Their

Table 1: Clinical data of patients who participated in the study

Description	Values
Number of patients	71
Age range (years)	18-55
Weight range (kg)	48-85
Parasite density (mm^3)	
- Below 10,000	20.0
- 10,000-20,000	43.0
- 20,000 and above	8.0
Common presenting symptoms	
- Fever and headache only	71.0
- Fever, headache, lost of appetite with joint pain	63.0
- Fever, headache, lost of appetite, weakness, general body pains with vomiting	13.00
Common side effects	
- Nausea	11.00
- Nausea and Dizziness	3.0
- Dizziness	5.0

Table 2: Number of patients with malarial parasites and clinical features after treatment with Mefloquine

Days	Numbers of patients positive for malarial parasite	Number of patients with clinical features
1	71	71
2	18	26
3	0	0
14	0	0

weights ranged from 48-85 kg. All the patients had shown clinical improvement, 24 h after the drug administration. The blood films were all negative for malarial parasite, 72 hours after the treatment giving a mean parasite clearance time of about 30 hours. Eighty three percent of the patients had no side effects after taking the drug, the remaining 17% complained of dizziness and nausea.

Discussion

In this study, the screening of one hundred and seventy two patients attending the out patient unit of an urban clinic in Sokoto State of Nigeria over a period of five months (June–October) in 2001 provided a suitable number of acute malarial cases (71) confirmed with positive malarial parasites in the blood films. The chosen months covered the rainy season which is always associated with the peak incidence of malarial transmission in this area. The remaining 89 patients diagnosed clinically as having malaria but showed no detectable parasitemia. The absence of parasitemia in the peripheral blood may have been due to the inappropriate self medication or fluctuating parasitemia especially in light infections. The 44.4% positively recorded is an increase over the 41% of Eleuze (1987) obtained in children below the age of ten years within the same area. However, the previous study lasted for only two months and only cases positive for *P. falciparum* were selected. A mean parasite density of 18,500 mm^{-3} of blood recorded is significantly lower than 31,000 mm^{-3} which Eleuze (1987) had.

Mefloquine completely treats the clinical features of malaria in all the patients within 24 h. The thick blood film for the patients became negative after 72 hours and remained so after 14 days follow up. This result is similar to what Bhatt *et al.* (1997) reported after the clinical trial of mefloquine against *P. falciparum* in a Kenyan hospital. In that study, it was possible to follow up all the participated patients after two weeks because the study was community based, the individual home of patients were known therefore those who did not turn up were traced. In present study, 74.7% of patients returned after 14 days and the remaining 25.3% who did not turn up could not be traced because the patients were selected from the out patient unit of an urban clinic and their homes were not known. The 100% efficacy rate recorded by mefloquine in the treatment of malaria infection within the Sokoto urban is very significant. This might be because, mefloquine is expensive as compared with chloroquine, scarce in the market and thus is not easily abused by the patients. In fact, none of the patients who participated in the study had ever taken mefloquine for malaria treatment. The drug was well tolerated because only 27% of the patients complained of minor side effects like nausea and dizziness.

This study therefore concludes that mefloquine is 100% effective *in vivo* against malarial parasite within the study area.

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