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Comparative Study of the *in vivo* Response of Malaria Parasites to Chloroquine among the Urban and Rural Dwellers in Sokoto State, Nigeria

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The *in vivo* response of malaria parasites to chloroquine among the urban and rural dwellers in Sokoto state, Nigeria has been studied. A total of seventy-eight patients with acute uncomplicated malaria were selected for the study from two distinct centres representing the urban and rural dwellers of the state. All the treated cases from the rural centre (Umaruma) responded well; both the clinical features of the disease and the parasites in the blood cleared within three days of initiating treatment and there was no relapse after twenty-one days follow up. But 19.8% (5) of the patients from the urban centre showed resistance at R1 level to chloroquine. This study therefore concluded that, chloroquine is more effective for the treatment of malaria in the rural than the urban dwellers possibly because of the rampant abuse of the drug by the later group.

Key words: Chloroquine, malaria parasites resistance, treatment, umaruma

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INTRODUCTION

Malaria has continued to be an increasingly important health problem particularly in sub-Saharan Africa[1]. 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 20-50% of all consultations in health centres and is the greatest cause of mortality in hospitals[2].

In Nigeria, malaria is directly responsible for over 100,000 deaths of children every year and one quarter of an average Nigeria family income is spent on the treatment of malaria[3]. Chloroquine is the most commonly used first line drug against malaria in the continent of Africa. However, this enviable position of chloroquine is being threatened by the emergence of some species of malaria parasites resistant to chloroquine[4]. *In vitro* and *in vivo* resistance of *P. falciparum* to chlororquine have been confirmed in western Kenya, Ghana, Cameroon, Republic of Benin and Nigeria. Olatunde[5] and Ekanem[5] reported cases of therapeutic failures of chloroquine in Nigeria. Since then, reported cases of chloroquine resistant malarial parasites has been increasing especially in the eastern and middle belt areas of Nigeria[7].

Sokoto State is found in the northwestern part of Nigeria. It is a malaria endemic area being inhabited by a semi-immune population. A sensitivity study of *P. falciparum* to chloroquine in Sokoto State conducted by Osisanya *et al.*[8] indicated no resistance to the drug. But Eleuze[9] recorded a mild *in vitro* resistance to chloroquine.

The World Health Organisation has emphasised the need to continuously monitor how the parasite population in an area respond to a drug and what factors and their variation may be associated with a variation in drug response[10]. The focus of the present study was to assess the sensitivity level of the malarial parasites to chloroquine among the urban and rural dwellers in Sokoto State.

MATERIALS AND METHODS

This study was conducted independently and simultaneously at two distinct centres selected to represent the urban and rural dwellers in Sokoto State of Nigeria, between the months of June-September, 2003. Patients attending the outpatients units of the Specialist Hospital in the state capital and a rural health centre at Umaruma, a community about 15 km from the town centre were selected for this study. The modality of the study was approved by a committee of experts in the College of Health Sciences, Usmanu Danfodiyo University, Sokoto. The modality was explained to each patient and only those that consented were selected for the study. The required characteristics for selection were adults between the ages of 18-60 years residing in the areas of study with clinical features suggestive of malaria. Patients found to have evidence of recent therapy with chloroquine in urine samples using Dill-Glazko method[11] and whole blood samples dried on filter paper[12] were excluded. Also excluded from the study were pregnant women and patients with chronic debilitating disorders.

Immediate thick blood films were made from finger pricks 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. Each selected patient was treated orally with 25 mg chloroquine base (Maladrin, PZ, Lagos, Nig.) per kilogram body weight over three days (10 mg kg^{-1} on days 0 and 1 and then 5 mg kg^{-1} on day 2), two tablets of paracetamol were given under close supervision for at least 30 min each time after swallowing the tablets to ensure that it was not vomited. Where vomiting occurred, the dosage was immediately repeated. Blood smears were repeated on days 1, 2, 3, 7, 14 and 21 and screened for malarial parasites.

RESULTS

At the Specialist Hospital Sokoto centre (urban) out of the 117 patients diagnosed clinically as having acute malaria during the study period, twenty-three patients (19.7%) were excluded for various reasons that would have interfered with the results (Table 1). Eleven patients refused to give their consents and out of the remaining 83 patients, whose blood were screened for malarial parasites, only 37 were positive giving a percentage positivity of 44.6%. The parasitaemia range at day 0 before the commencement of the therapy was (650-85,000 μL^{-1}), while all the enrolled patients were seen on days 1 and 2 after the commencement of the treatment, only 27 (72.9%) reported for the last follow up on day 21. All the patients (37) did show clinical and parasitological response from day 1 but five had a resurgence of symptoms and/or malarial parasites in their blood smears within seven to fourteen days post drug therapy.

At the Umaruma Centre (rural), a total of 91 patients were diagnosed clinically as having acute malaria during the same period; out of which 43 (47.3%) were positive for malarial parasites and only two (4.7%) were prevented from participating in the study because of various health reasons (Table 1). The parasitaemia range at day 0 taken before the commencement of the chloroquine therapy

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

Description	Number	
	Urban	Rural
Number of patients screened	117	91
Number of positive cases	37	43
Number of patients excluded	23	2
Age range (years)	18-55	20-60
Weight range (kg)	48-85	50-76
Parasite density (mm^3)		
Below 1,000	3	4
2,000-10,000	18	7
11,000-20,000	11	9
Above 20,000	5	21

Table 2: Summary of *in vivo* response of malarial; parasites to chloroquine

Description	Urban (n=37)	Rural (n=41)
Mean parasite density (mm^3)		
Day 0	32,112 (100%)	53,199.8 (100%)
Day 1	8,413.3 (26.2%)	5,639.2 (10.06%)
Day 2	995.5 (3.1%)	601.2 (1.13%)
Day 3	0	0.0
Day 7-21	669.8 (5.2%)	0.0
Mean parasite clearance time (Days)	-	2.5

was (820-1110,000 μL^{-1}). Only four patients (9.8%) did not appear on the last day of the follow up (day 21). The patients, as indicated in Table 2, showed both pathological and clinical features remission within 24 h after the commencement of the therapy with chloroquine. No malarial parasites were seen in their blood smears within seven to twenty-one days after the therapy with the drug.

DISCUSSION

The screening of 208 patients attending the outpatients units of two health facilities in the urban and rural areas of Sokoto state over a four-month period in 2003 did provide adequate number (78) of malaria cases needed for this study. Similar surveys by Osisanya *et al.*[8] using primary schools and rural health facilities at Gwadabawa and Bodinga areas of the same Sokoto State provided a sufficient number (54) of malaria infections with suitable parasitic densities.

The 38.5% malarial parasite positivity obtained in this study is higher than 34.9% reported earlier by Eleuze[9] and 37.4% obtained by Hendrikse *et al.*[13]. However, it is lower than 47.8% reported by Salako *et al.*[14] in a longitudinal study over 6 years in which 6.132 were screened.

The pre-treatment parasite densities varied widely between (650-85,000 μL^{-1}) in patients in the urban centre and (820-110,000 μL^{-1}) among their rural counterparts (Table 1). This indicates a higher percentage of malarial parasite positivity (47.3 vs. 44.6%) and significantly higher mean parasite density (53,199.8 vs. 32.112 mm^3) ($p>0.01$) among the rural patients. This study has also shown that a higher number of patients [23 (19.7%)] were excluded from the study in the urban centre than in the rural centre [2 (4.7%)]. Most of these cases were excluded because of positive chloroquine in their urine samples. Chloroquine is over the counter (OTC) drug that is freely dispensed and abused by patients without prescriptions[15]. The higher literacy and financial levels as well as easy accessibility to the drug outlets by the urban dwellers has made them more prone to abusing the drug. Walker *et al.*[16] observed that 50% of patients diagnosed as having malaria in a teaching hospital in Nigeria had high plasma chloroquine levels before receiving treatment.

Among the 37 patients selected and treated with chloroquine at the urban centre, all the patients had shown clinical improvement within 24 h and the blood films were all negative at day 3 after the drug administration. But the clinical features and/or malarial parasites in the blood smears of 5 of the 37 patients resurged within 7-14 days. The resurgence of the clinical features and malarial parasites in the blood smears of 5 of the 37 patients within 7-14 days after the treatment with chloroquine is highly significant. All the 41 patients selected from the rural centre responded satisfactorily to chloroquine treatment without any resurgence in clinical features or parasites within the 21 days followed up. These findings suggest that while malarial parasites are still sensitive to chloroquine in Umaruma, a rural community in Sokoto State, the parasites have developed resistance at R1 level in about 19.7% of the 37 patients who participated in this study among the urban dwellers in the same state.

The present results differ from that of Osisanya *et al.*[8] and Eleuze[9] who reported no change in the sensitivity of malarial parasites to chloroquine therapy in both the urban and rural areas of Sokoto state. One of the predisposing factors to malaria parasites developing resistance to chloroquine is through the widespread use of inadequate dose of chloroquine in the treatment of malaria infection. A previous study reported that, about 60% of commercially available oral preparations of chloroquine in Sokoto urban contains less than the label concentrations of the drug[17]. Most urban dwellers in Sokoto, Nigeria do have easy access to the drug and thus may have abused chloroquine on slight suspicion of malaria.

The increased mean parasite clearance time (2.5 days) even among the chloroquine sensitive rural dwellers in Sokoto is still a point of concern. Osisanya *et al.*[8] reported 2.1 days and Elueze[9] reported 1.9 days. Increasing parasite clearance time may indicate a possible decreasing *in vivo* sensitivity of the malarial parasites to

chloroquine[14]. Resistance of malarial parasites to chloroquine is now widespread in many malarious areas of the world[18]. This study therefore concludes that while there exists a resistance (about 19.8%) by malarial parasites at R1 level to chloroquine therapy in the urban areas of Sokoto State, the drug is still effective in a selected rural community (Umaruma) in the state.

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