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Investigation of the Efficacy of Home-Based Oral Chloroquine Treatment among Under-Five Children with *Plasmodium falciparum* Malaria in Some Parts of Jos, Plateau State, Nigeria

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Abstract

Background: Nigeria is currently a malaria endemic country with an estimated 76% of her population at risk of contracting malaria [1]. According to a study in Nigeria, the first line of action mothers took when their children under 5 years have malaria showed that over 50% of them used non-prescription drugs they have at home or bought from pharmacy stores. And 60% of the most commonly used drugs for malaria treatment were chloroquine [2]. Many recent studies have demonstrated re-emergence of chloroquine-sensitive *P. falciparum*, suggesting a possible role in future malaria control [3]. **Objective:** The aim of this study was to investigate the effect of home-based oral chloroquine treatment among children under 5 years with *Plasmodium falciparum* malaria attending Jos University Teaching Hospital and OLA Hospital in Jos Metropolis. **Method:** This is a cross-sectional study of 93 malaria and non-malaria children. Malaria diagnosis was carried out using microscopical examination of Leishman's stained thick and thin blood films, *P. falciparum* parasitemia was assessed by standard microscopy techniques and complete blood count was done using Beckman Coulter Analyzer. **Results:** The body temperature on admission was significantly lower ($p < 0.05$) in the control group (36.80˚C ± 0.07˚C) than in the three malaria groups. The mean body temperature of chloroquine treated children with malaria was significantly lower ($p < 0.05$) than that of children presenting with severe malaria. Parasitaemia was significantly lower ($p < 0.05$) in the pre admission chloroquine treated group (18.13% ± 0.49%) than in the non-treated simple malaria group (34.35% ± 2.75%) and severe malaria group (43.57% ± 5.49%), respec-

tively. The average number of days before the cases were reported in the hospital was 4.80 days. The haemoglobin concentration of 7.23 ± 1.01 g/dl obtained for non-treated malaria patients indicates a mild anaemia, whereas the haemoglobin concentration values of 9.60 ± 0.51 g/dl and 10.52 ± 0.16 g/dl obtained for chloroquine treated children and control children respectively show that the two groups of children were not anaemic and the values obtained were within the normal range. **Conclusion:** The results obtained in this study demonstrate that there was significant positive impact of chloroquine treatment on *Plasmodium falciparum* parasitemia and degree of anemia in children under 5 years with *Plasmodium falciparum* in Jos Metropolis.

Keywords

Malaria, Chloroquine, Children, Parasitemia, *Plasmodium falciparum*, Anemia, Nigeria

1. Introduction

Over the years, malaria has remained one of the leading causes of death in Nigeria [4]. In 2019, Nigeria contributed about 27% of the malaria cases and 24% of the malaria deaths worldwide [5] [6] [7]. A larger proportion of the malaria cases that resulted in mortality likely occurred among children less than 5 years old [8] [9] [10] [11]. The actions mothers take in the management of children with malaria are important in minimizing the malaria burden. Home-based oral chloroquine treatment of malaria in children was reported to be the most popular practice among mothers in Nigeria [2]. Treatment failure of chloroquine in the home management of childhood malaria has been associated with non-compliance to correct dosing and incomplete treatment [12].

In Nigeria chloroquine was banned as a first line treatment drug for malaria in 2005 [13], as chloroquine use was discontinued from the treatment of *Plasmodium falciparum* infection in almost all endemic regions because of global spread of resistant parasites. But since the first report in Malawi, numerous epidemiological studies have demonstrated that the discontinuance led to re-emergence of chloroquine-susceptible *P. falciparum* [14].

2. Materials and Methods

2.1. Study Design

The study was design to investigate the effect of first aid, home-based oral chloroquine treatment within 24 hours prior to hospital presentation, on *P. falciparum* infection in children under the age of 5 years. To this effect, the work was aimed to determine changes in the levels of parasitemia, red blood cell count, haemoglobin concentration and haematocrit in the home-based oral chloroquine-treated children, as compared to the non-treated simple malaria children and non-treated children with severe malaria. To achieve these study objectives,

P. falciparum parasite count and assay for red blood cells count were carried out.

The working interval of within 24 hours period between the home-based oral chloroquine administration and hospital presentation is an average time interval recorded in the study area for the transfer of the malaria child from home to the hospital in situations where immediate medical attention or access to medical facility is not possible.

2.2. Home-Based Chloroquine-Treated Malaria Subjects, Chloroquine Dosage and Administration

In Nigeria chloroquine tablet is a non-prescription drug and could readily be bought over the counter in any pharmacy or patent medicine stores across the country.

The home-based chloroquine-treated malaria subjects are children that were positive for malaria parasite screening on hospital admission. Oral chloroquine was administered to the subjects at home by their mothers, following suspected malaria symptoms. The administration of chloroquine treatment was within 24 hours prior to hospital admission, malaria parasite screening and sample collection. The home-treated children have no history of any other medication in this particular episode of the sickness. An average dosage of 1 tablet, for oral administration, which contains 250 mg of Chloroquine phosphate, USP (equivalent to 150 mg base) in 24 hours was recorded from the mothers of chloroquine treated subjects. All the 16 home-based oral chloroquine treated patients recruited for this study, presents uncomplicated malaria on admission in the hospital. While, all patients presenting severe malaria on hospital admission did not receive any medication prior to sample collection in the hospital.

2.3. Study Area and Location

Jos metropolis, mainly, Jos North local Government area, is the study site. Its geographical coordinates are latitude: 9˚55'42"North and longitude: 8˚54'31"East.

2.4. Study Subjects

The study subjects were malaria positive children under the age of five years attending the Emergency Paediatrics Unit (EPU), Paediatrics Department, Jos University Teaching Hospital (JUTH), Jos and Our Lady of Apostle (OLA) hospital, Jos. The malaria-free, control children were healthy children of the same age range and attending the Child Welfare Center of the Department of Community Health and Paediatrics Outpatient Department (POPD) for immunization, both at JUTH. The malaria children were recruited consecutively and divided into groups.

2.5. Inclusion Criteria

The criteria used for the selection of children (under the age of 5 years) with severe malaria were: Fever and presence of *Plasmodium falciparum* in peripheral

blood (malaria parasite positive), and at least one of the following conditions; unconsciousness or coma, altered sensorium or inability to sit unaided, repeated convulsion in 24 hour period (meningitis was ruled out, via lumber puncture and Cerebrospinal fluid analysis [lumber puncture-sterile]), and no history of any medication in the particular episode of the sickness. Whereas selected children with simple, uncomplicated malaria were children with fever and presence of *Plasmodium falciparum* in blood, without symptoms of other sickness, and no history of any medication in the particular episode. The chloroquine-treated malaria group were children with defined malaria, but were administered oral chloroquine 24 hours prior to sample collection. The control group were children of the same age group range and living in same area, but without fever, negative to malaria parasite screening, and were not under any medication.

2.6. Study Population

Blood samples were collected from the various treatment groups. A total of 93 children were recruited for this study. 47 of these children were qualified for the selection of the control group and total children presenting malaria were 46 in number. 23 children of the 46 total malaria children (50%) presents non-treated uncomplicated malaria, while 7 children (15.22%) present non-treated severe malaria and 16 children (34.78%) were home-based oral chloroquine-treated malaria children. The control children were 23 males (48.94%) and 24 females (51.06%). While the total malaria children were 24 males (52.17%) and 22 females (47.83%). Sample size was determined using Krejcie and Morgan, (1970) table for determining sample size of finite population [15].

2.7. Clinical Examination of Subjects by Clinician and Data Collection

For the course of recruitment, each subject was examined by a clinician for anthropometric, demographic and other diagnostic indicators of malaria as well as malaria history. The child's age, sex and measurements of weight, height and temperature were recorded. The weight was measured using a bathroom scale, while height or length was measured using height board or length board respectively depending on whether the child can stand alone or not.

2.8. Sample Collection and Preparation

The selection and examination of children for this study and blood sample collection was carried out under the clinical supervision of a pediatrician. Blood samples were collected by the assistance of qualified medical professionals. 2 ml sample of venous blood was collected from each subject by venous puncture, using 5 ml syringe and needle. The collected blood was immediately dispensed into a Z5 tube containing an anticoagulant, Ethylene diamine tetra acetic acid (EDTA) solution. The tube was gently shaken and the portion kept at room temperature pending the haematological analysis, which was carried out within 6 hours of sample collection.

2.9. Malaria Diagnosis

The standard diagnosis of malaria by microscopic determination of Malaria Parasite in the thick and thin blood film on slide using Leishman's stain was carried out as described by Dace & Lewis [16], in all the recruited children. Malaria diagnosis was based on the presence of asexual stages of *P. falciparum* on the blood films. The determination of complete blood counts was done using Beckman Coulter Analyzer [17].

3. Statistical Analysis

The analysis of the data obtained was carried out using Statistical Package for Social Sciences (SPSS) version 21. Several statistical tools were employed, such as t-test of independence for comparison of two independent groups, and one way analysis of variance (ANOVA) was used to confirm the difference in means of several groups. As a prerequisite to statistical test, an assessment of the normality of data was carried out (using graphical method) as normal data is an underline assumption in parametric testing.

The result of test of normality shows that, the data obtained in this study were normally distributed. Therefore, t-test, ANOVA and Pearson correlation for parametric testing were employed. P-values less or equal to 0.05 ($p \leq 0.05$) was considered significant.

4. Results

As shown in Table 1, the mean age for the 93 subjects recruited for this study

Table 1. Measurements of body temperature and anthropometric indices in under-five children attending JUTH and OLA hospital in Jos Metropolis.

Treatment Group	Age (months)	Weight (kg)	Height (cm)	Temperature (˚C)
Control	12.47 ± 1.60	8.42 ± 0.40	71.27 ± 1.32	36.80 ± 0.07
	(47)	(47)	(47)	(47)
Choloroquine	23.69 ± 3.67[a*]	10.68 ± 0.80[a*]	81.96 ± 3.25[a*]	37.94 ± 0.30[a*]
Treated Malaria	(16)	(16)	(16)	(16)
Simple Malaria	27.22 ± 4.18[a*]	9.97 ± 0.97	83.69 ± 3.99[a*]	38.45 ± 0.25[a*]
without Treatment	(23)	(23)	(23)	(23)
Severe Malaria	19.00 ± 1.48	8.88 ± 0.44	75.71 ± 5.20	39.24 ± 0.47[ab*]
without treatment	(7)	(7)	(7)	(7)

Tabulated values are means $\bar{X}$ ± S.E.M for (n) subjects given in parenthesis. *The mean difference is significant at the $p < 0.05$ level, and **at $p < 0.01$ level. [a]comparing respective malaria infected group with control; [b]comparing untreated severe malaria group with chloroquine treated malaria group.

was 18.54 ± 1.59 (months) and their ages ranges from 2 months to 60 months. The mean age of the control children was 12.47 ± 1.60 (months); while the mean age of 23.69 ± 3.67, 27.22 ± 4.18 and 19.00 ± 1.48 (months) were recorded for the chloroquine treated children, non-treated simple malaria children and non-treated severe malaria children respectively. The younger control subjects were the malaria free children attending the child welfare center of the Department of Community Health for routine immunization, whereas the older children presenting with malaria were under 5 years attending the emergency paediatrics unit (EPU) where the samples were respectively taken.

The body temperature on admission was significantly lower ($p < 0.05$) in the control group (36.80˚C ± 0.07˚C) than in the three malaria groups. The mean body temperature of chloroquine treated children with malaria was significantly lower ($p < 0.05$) than that of children presenting with severe malaria.

The results of diagnostic screening of the under 5 years children for *P. falciparum* in the circulating blood are summarized on Table 2: Parasitaemia was significantly lower ($p < 0.05$) in the pre-admission chloroquine-treated group (18.13% ± 0.49%) than in the non-treated simple malaria group (34.35% ± 2.75%) and severe malaria group (43.57% ± 5.49%), respectively. However, there was no significant difference ($p > 0.05$) in parasitaemia of the untreated simple malaria and untreated severe malaria subjects.

There was no significant difference in duration of fever before hospital admission between the three treatment groups. The average number of days before the cases were reported in the hospital was 4.80 days.

As shown in Table 3, the mean value of red blood cell counts, haemoglobin concentration, and haematocrit for non-treated simple malaria children were significantly lower ($p < 0.05$) than that of the control children and chloroquine treated children. However, the corresponding values of red blood cell counts, haemoglobin concentration, and haematocrit for chloroquine treated malaria children were not significantly different from the values obtained for the control children.

Table 2. Parasitaemia and duration of fever in the under 5 years subjects presenting with malaria.

Treatment status	Parasitemia %	Duration of fever (day)
Chloroquine	18.13 ± 0.49	6.13 ± 1.45
Treated (pre Admission)	(16)	(16)
Simple Malaria	34.35 ± 2.75*	3.39 ± 0.66
Without Treatment	(23)	(23)
Severe malaria	43.57 ± 5.49*	6.42 ± 2.53
Without Treatment	(7)	(7)

Tabulated values are means $\bar{X}$ ± S.E.M for n subjects given in parenthesis. *The mean difference is significant at the $p < 0.05$ level comparing untreated malaria groups with chloroquine treated (pre admission).

Table 3. Measurement of hematological indices of malaria in children under 5 years presenting with malaria in Jos metropolis.

Treatment group	RBC count ($\times 10^6/\mu L$)	Haemoglobin concentration (g/dl)	Haematocrit (%)
Control	4.38 ± 0.09	10.52 ± 0.16	33.96 ± 0.48
	(20)	(20)	(20)
Simple malaria	2.92 ± 0.39[a]*	7.23 ± 1.01[a]*	23.70 ± 3.37[a]*
Without Treatment	(6)	(6)	(6)
Chloroquine	4.01 ± 0.21[b]*	9.60 ± 0.51[b]*	30.97 ± 1.43[b]*
Treated malaria	(9)	(9)	(9)

Tabulated values are means ± S.E.M for n subjects given in parenthesis. *The mean difference is significant at the ($p < 0.05$) level; [a]The mean difference is significant ($p < 0.05$) compared to the control; [b]The mean difference is significant ($p < 0.05$) compared to untreated simple malaria group.

The haemoglobin concentration of 7.23 ± 1.01 g/dl obtained for non-treated malaria patients indicates a mild anaemia, whereas the haemoglobin concentration values of 9.60 ± 0.51 g/dl and 10.52 ± 0.16 g/dl obtained for chloroquine-treated children and control children respectively shows that the two groups of children were not anaemic and the values obtained were within the normal range.

5. Discussion

The high body temperature obtained in this study for all the malaria children is in agreement with the reports that malaria is always accompanied with fever [18] [19] [20], and the lower temperature obtained in chloroquine-treated children as compared to the non-treated severe malaria children demonstrate the positive effect of chloroquine within 24 hours of it administration. This suggests that early chloroquine treatment could possibly prevent hyperpyrexia in this group of children.

The parasitaemia value was significantly lower in the chloroquine treated children than in all the non-treated malaria children. This shows that chloroquine have a protective effect on the proliferation of the plasmodium parasite in the red blood cells, and thus, could prevent anemia in the chloroquine treated subjects. This result is in agreement with other earlier reports of studies from Nigeria and Mauritania respectively [21] [22]. The higher parasitaemia values obtained for the non-treated simple malaria children and severe malaria children were similar.

Duration of fever before hospital admission was statistically similar for all the groups. This could be interpreted as that; the severity of *P. falciparum* malaria in children under 5 years in Jos metropolis is not directly a function of the duration of fever before it was reported in the hospital.

The results of the red blood cells count and other indicators of anemia, shows

that early chloroquine treatment prevented incidence of anemia in the treated children as compared to all the non-treated children that were anemic. Mild anaemia was observed in the non-treated malaria children.

6. Conclusion

Home used of oral chloroquine in the treatment of *P. falciparum* malaria has been shown to be very effective in reducing the level of parasiteamia as well as degree of anemia in the studied children within the first 24 hours of administration. These beneficial effects of the chloroquine treatment are an indication of sensitivity of *P. falciparum* to chloroquine in Jos Metropolis. A similar observation of re-emergence of chloroquine-susceptible *P. falciparum* in Uganda and Malawi respectively has led to contemplation of re-introducing chloroquine for targeted uses in those countries [23]. Therefore, more evidence of *P. falciparum* sensitivity to chloroquine in other regions of Nigeria could open up possibilities of re-introduction of chloroquine as an option for malaria treatment or prevention. Rational use of oral chloroquine needs to be re-evaluated and encouraged in the treatment of children with *P. falciparum* malaria, in areas where immediate medical attention is remote or scarce.

7. Study Limitation

Many of the screened children have either or both of associated illness other than malaria and histories of non-chloroquine medications before hospital report and as such were not eligible for this study.

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Authors' Contribution

OAS conceptualized and designed the research work, UGA (Late) supervised the work, OSN co-supervised the work. TJ and SYG reviewed the manuscript. All authors partook in the analysis, interpretation of data obtained. All authors read and approved the final manuscript.

Ethics Approval and Consent to Participate

The research protocol for this study was approved by the Medical and Health Ethics Committee of Jos University Teaching Hospital, Jos and informed consent and assent was obtained from the parents.

Consent for Publication

Not applicable.

Funding

Not applicable.

Conflicts of Interest

All the authors hereby declare that we have no conflicting interests on this study.

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