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Original Article

Levels of Adherence to Coartem© In the Routine Treatment of Uncomplicated Malaria in Children Aged Below Five Years, in Kenya

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Abstract

Background: This study sought to determine the level of adherence to Coartem© in the routine treatment of uncomplicated malaria among children under the age of five years in Nyando district, Kenya.

Methods: Seventy-three children below the age of five years with microscopically confirmed uncomplicated *Plasmodium falciparum* malaria and prescribed Coartem® during the normal outpatient department hours were included into the study on 27th of April to 15th of May 2009. Adherence was assessed through a semi-structured interviewer administered questionnaire; pill count and blister pack recovery. Patients were then classified into three categories of adherence. Patients who had tablets remaining in the blister pack were classified as definitely non-adherent. Those who had blister pack missing or empty and the caretaker did not report administering all the doses at the correct time and amount were considered probably non-adherent or as probably adherent when the caretaker reported administering all doses at the correct time and amount.

Results: Nine (14.5%) patients were definitely non-adherent, 6 (9.7%) probably non-adherent and 47 (75.8%) probably adherent. The most significantly left tablet was the sixth doses ($P = 0.029$).

Conclusion: Caretakers should be made much aware that non-adherence might not only be dangerous to child's health but also dramatically increase the financial cost for public-health services.

Keywords: Children, Artemisinin, Therapies, Antimalaria, Non-adherence

Introduction

Early diagnosis coupled with effective treatment of malaria is vital in controlling malaria episodes. There is a consensus that Artemisinin Combination Therapies (ACTs) are efficacious in the treatment of malaria (1). ACTs are efficacious, effective and tolerant (2- 4). Kenya adopted Artemisinin Lumefantrine (AL) as its first-line ACT malaria treatment in April 2004. The same year, the Government of Kenya also began distributing free AL branded Coartem® in the public formal sector (5).

However, making efficacious malaria therapies available is not enough to reduce malaria episodes. What is required is optimal malaria treatment as even the most efficacious antimalarial drug if not used correctly may fail to cure malaria. There are a number of factors that inhibit access and use of antimalarials in real life settings. Complicated drug schedules and limited understanding of how or why to adhere to recommended antimalarial drug is a major hindrance to malaria therapy (6-9).

Adverse effects, poor instructions, poor provider-patient relationship, loss of drugs, forgetting to take a drug, patient's disagreement with the need for treatment, perceived ineffectiveness of the medicine, the inability to pay for treatment (10, 11) and perceived feeling of recovery from an illness (12) are just but a few documented reasons for non-adherence. The need of a caretaker most often a parent compounds the issue of adherence in children (1).

With a view of scaling down malaria, the Kenyan Government permitted the sale of ACTs over the counter in 2011 (5). However, there are limited adherence to ACT's studies in particular Coartem© which is widely used in the public formal sector. This study therefore, sought to determine the level of adherence to Coartem© in the routine treatment of uncomplicated malaria among children under the age of five years in Nyando district of Kenya.

Materials and Methods

Study Area

In this cross sectional survey, Nyando District Hospital, in Nyanza province was chosen for this evaluation because of its central location and high usage. Nyanza Province is an area of year-round malaria transmission. Malaria is a major health problem accounting for approximately two-thirds of all Out-Patient Department (OPD) consultations in the health facility. *Plasmodium falciparum* is present in more than 95% of all malaria infections (5). Each day over 100 new patients flock the hospital, yet just one doctor, 15 nurses and four clinical officers are on hand to cover all shifts. The lean workforce means that patients often have to wait for long periods to get attention. Old, faulty, and limited technology and poor facilities compound the shortage of the health care staff.

Sample Specification

Study Population

Children below the age of five years with microscopically confirmed uncomplicated *P. falciparum* malaria and prescribed Coartem® during the normal OPD hours on 27th of April to 15th of May 2009 comprised the study subjects. Assuming an adherence of 80%, a precision of 10%, a type 1 error of 5% and a 20% loss to follow-up, 73 patients were randomly recruited into the study.

Inclusion and Exclusion Criteria

Patients included in the study were residence of Nyando district aged 12-59 months, no household member participating in the study, reported fever within the last 48 hours or axillary temperature $\geq$ 37.5°C on presentation at the clinic and weighed $\geq$ 10 kg. Patients who had signs of complicated malaria manifested by microscopically confirmed high parasitemia levels (> 100,000 parasites/µl), inability to sit or stand, altered consciousness lethargy or coma, breathing difficulties, severe anemia (hemoglobin concentration $\leq$ 5 g/dl), recent history of convulsions, inability to drink or breast-feed or persistent vomiting were excluded from the study.

Laboratory Procedures

A capillary blood smear for microscopic examination was collected. The blood was stained with Giemsa and read for species and parasitemia by an experienced technician. Parasitemia were calculated against 200–500 leukocytes according to the formula: parasitemia (/µl) = number of parasites x 8,000/number of leukocytes (13). A slide was considered negative after 200 high-power fields had been examined.

Measurement of Outcome

Patients were classified as adherent, probably non-adherent and definitely non-adherent based on the findings from the blister pack check and questionnaire. Patients were classified as 'adherent' if their caretakers followed exactly the medication instructions when administering the standard 3-day course of Coartem® (10.0 – 14.9 kg: 1 tablet per dose; 15.0 – 24.9 kg: 2 tablets; Novartis Pharma AG, Basel, Switzerland).

Patients who had tablets remaining in the blister pack were classified as definitely non-adherent irrespective of whether they gave correct or incorrect account on how they administered the medicine. Those who had blister pack missing or empty

and the caretaker did not report administering all the doses at the correct time and amount were considered as probably non-adherent or as probably adherent when the caretaker reported administering all doses at the correct time and amount.

Data Management and Analysis

The three categories of adherence were presented as proportions in percentages. Adherence was measured on day 3 through a semi-structured questionnaire, a pill count and a blister pack recovery where possible. Secondary outcomes were the number of doses taken correctly and number of tablets remaining in the blister pack (where applicable).

Analysis was performed by SPSS version 17. Association between adherence and variables was analysed by Chi-square test. All the variables that were significant at 95 % CI ($P \leq 0.05$) were entered into logistic regression model to test for linear relationship.

Ethical Approval and Informed Consent

The study was given ethical approval by Institutional Research and Ethics Committee (IREC) of Moi University and Moi Teaching and Referral Hospital (MTRH).

Results

General Characteristics of the Samples

A total of 73 (15.6%) patients out of the 469 children screened were recruited into the study. These were 30 (41.1%) male and 43 (58.9%) female patients. The vast majority of these patients had pure *P. falciparum* (90.3%), fever on presentation at the health facility (85.5%), low parasitemia (< 500 parasites/µl) levels (69.4%) and body weights of 10.0 – 14.9 kg (75.8%). (Table 1)

Of the 73 patients recruited, eight (11.0%) could not be traced for home visit leaving data for 65 home visit interviews. Among the 65 patients who completed the follow-up visit, three had incomplete data for analysis of adherence due to failure of the caretakers to give analyzable information on the timing of the doses or the number of tablets taken per dose and were thus excluded from the analysis.

Table 1: General characteristics of the sample

Characteristics of the sample	Percent
Sex	
Male	41.1
Female	58.9
Diagnosis	
Pure *P. falciparum*	90.3
Additional diagnosis	9.7
Presence of fever at examination	
Fever	85.5
Reported fever within the last 48 hours	15.5
Parasitemia levels	
Low (<500 parasites/µl)	69.4
Medium (500 – 100,000 parasites/µl)	30.6
Body weights	
10.0 – 14.9 kg	75.8
15.0 – 24.9 kg	24.2

Level of Adherence

Of the 62 children, nine (14.5%) had tablets remaining in the blister pack, and were thus classified as definitely non-adherent; six (9.7%) reported taking the regimen in a non-adherent manner and were thus classified as probably non-adherent; 47 (75.8%) reported taking the regimen in an adherent manner and were therefore classified as probably adherent (Table 2).

Table 2: Classification of adherence

Categories of Adherence	Number of Patients	Percent
Probably Non-Adherent	6	9.7
Definitely Non-Adherent	9	14.5
Probably Adherent	47	75.8

The most significantly left tablet was the sixth doses ($P = 0.029$). The caretakers of patients who had tablets remaining in the blister packs were asked to specify why they did not administer the full treatment course. These reasons were significantly varied depending on the number of the missed dose(s) ($P = 0.029$). One caretaker (11.1%) did not give one dose because the child did not like the medicine, five (55.6%) discontinued the

treatment prematurely by a dose because the patients' condition had improved, two (22.2%) gave the patient few tablets with two doses and one (11.1%) could not give any reason for not administering a dose (Table 3).

Table 3: Caretaker's reasons for failing to administer a full dose by missed doses

Reasons for failing to administer a full dose	Total n (%)
The child did not like the medicine	1 (11.1)
Did not give any reason	1 (11.1)
Gave an under dose with one or more doses	2 (22.2)
The patient's condition had improved	5 (55.6)

None of these reasons however were influenced by the caretakers level of education ($P = 0.825$), caretaker relation to the child ($P = 0.145$), number of children cared for by the caretaker ($P = 0.549$), household size ($P = 0.825$) or the sex of the patient ($P = 0.687$). Apparently, only one caretaker who did not give a reason for not administering a full dose admitted to have shared the medicine meant for the study participant with a sick member of the family ($P = 0.021$).

Discusions

Adherence to antimalarial medications is an important component of malaria control although measuring it is difficult as the available measurement techniques have drawbacks (14). In this study, adherence was assessed using self-report measurements that had been standardized, validated, and well accepted in the adherence literature (15).

The study reported encouraging high levels of adherence than in Zambia (16); southern Sudan (17) and Uganda (13) but lower levels than that in Uganda (12). In Zambia and southern Sudan, the studies were conducted in complex settings in refugee and internally displaced populations, whereas, in a stable semi-urban area with high educational level in Uganda (13). These were not easily comparable to this study site in an unstable typical African rural setting with low level of education.

Many patients were reported to be definitely non-adherent, an indication that the prevalent form of non-adherence was not the way in which Coartem® was administered with regard to time and number of tablets but rather the failure to complete tablets (18, 19). This calls for improved caretakers counseling on the importance of giving the patient full dose when administering the drug.

Admittedly, self-report and tablet counts alone are imperfect measures of adherence. These methods are vulnerable to overestimates of adherence and under-estimates of non-adherence. Interviews had been shown to identify 80% of the true non-adherence as assed by pill count (14).

However, interviews are not equally sensitive for all subgroups of patients (20). Therefore, a pharmacological assessment of lumefantrine-plasma concentrations would have been more robust in this study. Nevertheless, there is a significant difference in the concentration of lumefantrine levels between the adherent and non-adherent groups (13).

Conclusions

The adherence levels reported in this study were encouraging. However, there is a need for study to be conducted outside a health facility to ascertain whether the same adherence levels could be obtained.

Ethical considerations

Ethical issues (Including plagiarism, Informed Consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc) have been completely observed by the authors.

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