30 دورص تخفیف نوروزی ویژه کارگاه‌ها و فیلم‌های آموزشی

اصول تنظیم قراردادها

پروپوزال نویسی

آموزش مهارت های کاربردی در ندوین و چاپ مقاله
Levels of Adherence to Coartem© In the Routine Treatment of Uncomplicated Malaria in Children Aged Below Five Years, in Kenya

Jared Otieno OGOLLA 1, Samuel Omulando AYAYA 2, Christina Agatha OTIENO 3

1. Dept. of Public Health, School of Health Sciences, Mount Kenya University, Eldoret, Kenya
2. Dept. of Child Health and Paediatrics, School of Medicine, Moi University, Eldoret, Kenya
3. Dept. of Environmental Health, School of Public Health, Moi University, Eldoret, Kenya

*Corresponding Author: Tel: +254723340142 Email: jotienoogolla@gmail.com

(Received 20 Aug 2012; accepted 11 Jan 2013)

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 ≥ 37.5°C on presentation at the clinic and weighed ≥ 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 ≤ 5 g/dl), recent history of convulsions, inability to drink or breastfeed 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) (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 ($P = 0.021$).

### Discussions

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.

### Acknowledgement

We extend our gratitude to all the people who gave us support in many different ways. Our sincere gratitude goes to Institutional Review and Ethics Committee (IREC) of Moi University and Moi Teaching and Referral Hospital Eldoret, Kenya. We are also grateful to the commitment...
and hard work of the research team. Lastly, we remain grateful to the caretakers and children who took part in the study. The authors declare that there is no conflict of interest.

References

1. World Health Organization (WHO) (2001). Antimalarial Drug Combination Therapy. Report of a WHO Technical Consultation. WHO/CD5/RBM/ 2001: 35.

2. Nosten F, van Vugt M, Price R (2000). Effects of artesunate-mefloquine combination on incidence of *Plasmodium falciparum* malaria and mefloquine resistance in western Thailand: a prospective study. *Lancet*, 356: 297–302.

3. Von Seidlein L, Milligan P, Pinder M (2000). Efficacy of artesunate plus pyrimethamine–sulphadoxine for uncomplicated malaria in Gambian children: a double-blind, randomised, controlled trial. *Lancet*, 355: 352–357.

4. Dorsey G, Vlahos J, Kamya MR, Staedke SG, Rosenthal PJ (2003). Prevention of increasing rates of treatment failure by combining sulfadoxine-pyrimethamine with artesunate or amodiaquine for the sequential treatment of malaria. *J Infec Dis*, 188: 1231–1238.

5. Abdinasir A (2004). The difference between efficacy and effectiveness of antimalarial drugs in Kenya. *Trop Med Int Hyg*, 9 (7): 967 - 974.

6. Fungladda W, Honrado FR, Thimasarn K (1998). Compliance with artesunate and quinine + tetracycline treatment of uncomplicated falciparum malaria in Thailand. *Bal of the WHO*, 76 (1): 59–66.

7. Bloland PB, Kachur SP, Williams HA (2003). Trends in antimalarial drug deployment in sub-Saharan Africa. *J Exp Bio*, 206: 3761 – 3769.

8. Yepez MC, Zambrano D, Carrasco F, Yepez RF (2000). The factors associated with non-compliance with antimalarial treatment in Ecuadorian patients. *Rev Cub de Med Trop*, 52: 81–89.

9. Gomes M, Wayling S, Pang L (1998). Interventions to improve the use of antimalarials in South East Asia. *Bal of the WHO*, 76 (1): 9-19.

10. Haynes RB, Mc Donald H, Garg AX, Montague P (2002). Interventions for helping patients to follow prescriptions for medications. *The Cochrane Database of Syst Rev* 2002, Issue 1.

11. White NJ (1998). Why is it that antimalarial drug treatments do not always work? *Ann Trop Med Parasitol*, 92 (4): 449-58.

12. Fogg C, Bajunirwe F, Piola P (2004). Adherence to a six-dose regimen of artemether-Lumefantrine for treatment of uncomplicated *Plasmodium falciparum* malaria in Uganda. *Am J Trop Med Hyg*, 5: 525–530.

13. Pullar T (1991). Compliance with drug therapy. *Brit J Clin Pharm*, 32: 535 - 539.

14. Bosworth HB (2006). Medication treatment adherence. In: Patient treatment adherence, concepts, interventions, and measurement. Lawrence Erlbaum Associates, Mahwah New Jersey, pp. 147-94.

15. Depoortere E, Guthmann JP, Sipilanyambe N (2003). Adherence to the combination of sulfadoxine-pyrimethamine and artesunate in the Maheba Refugee Settlement, Zambia. *Trop Med Int Hyg*, 9: 62–67.

16. Depoortere E, Salvador ET, Stivanello E, Bisoffi Z, Guthmann JP (2004). Adherence to a combination of artemether and lumefantrine (Coartem®) in Kajo Keji, Southern Sudan. *Am J Trop Med Hyg*, 98: 635–637.

17. Nshakira N, Kristensen M, Ssali F, Whyte SR (2002). Appropriate treatment of malaria? Use of antimalarial drugs for children’s fevers in district medical units, drug shops and homes in eastern Uganda. *Trop Med Int Hyg*, 7: 309–316.

18. Chanda P, Sikaala CH, Kapelwa W, Moonga H, Njunju E, Macdonald M, Thea D, Hamer DH, Sipilanyambe N (2004). Assessment of the therapeutic efficacy of artemether-lumefantrine (Coartem®) and sulfadoxine-pyrimethamine (SP)-artesunate in Zambian children. *Soc Trop Med Hyg*, 53 (213): 7-11.

19. Rugemalila JB, Lwanga CL, Kilama WL (2006). Adherence to a combination of artesunate plus pyrimethamine with amodiaquine or sulfadoxine-pyrimethamine for the sequential treatment of uncomplicated *Plasmodium falciparum* malaria in Maheba Refugee Settlement, Zambia. *Trop Med Int Hyg*, 9: 62–67.

20. Sattabongkot J, Tsuboi T, Zollner GB, Sirichaisinthop J, Cui L (2004). *Plasmodium vivax* transmission: chances for control? *Trends Parasitol*, 20:192 - 198.
دوره تخفیف نوروزی ویژه کارگاه‌های و فیلم‌های آموزشی

- اصول تنظیم قراردادها
- پروپوزال نویسی
- آموزش مهارت های کاربردی در ندوین و چاپ مقاله