Treatment of paediatric malaria during a period of drug transition to artemether-lumefantrine in Zambia: cross sectional study

Dejan Zurovac, Mickey Ndhlovu, Alexander K Rowe, Davidson H Hamer, Donald M Thea, Robert W Snow

Malaria Public Health and Epidemiology Group, Centre for Geographic Medicine, KEMRI/Wellcome Trust Collaborative Programme, PO box 43640, 00100 GPO, Nairobi, Kenya

Dejan Zurovac *clinical research officer*

Chainama Hills College Hospital of Health Sciences, Lusaka, Zambia

Mickey Ndhlovu *clinical research officer*

Malaria Branch, Division of Parasitic Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, GA 30341, USA

Alexander K Rowe *medical epidemiologist*

Center for International Health and Development, Boston University School of Public Health, Boston, MA 02118, USA

Davidson H Hamer *associate professor*

Donald M Thea *professor*

Malaria Public Health and Epidemiology Group, Centre for Geographic Medicine, KEMRI/Wellcome Trust Collaborative Programme

Robert W Snow *professor*

Correspondence to: D Zurovac dzurovac@wtnairobi.mimcom.net

BMJ 2005;331:734–7

Abstract

Objective To evaluate treatment practices for uncomplicated malaria after the policy change from chloroquine to sulfadoxine-pyrimethamine and to artemether-lumefantrine in Zambia.

Design Cross sectional survey.

Setting Outpatient departments of all government and mission facilities in four districts in Zambia.

Participants 944 children with uncomplicated malaria seen by 103 health workers at 94 health facilities.

Main outcome measures Antimalarial prescriptions in accordance with national guidelines and influence of factors on health workers' decision to prescribe artemether-lumefantrine.

Results Artemether-lumefantrine, sulfadoxine-pyrimethamine, and chloroquine were available, respectively, at 48 (51%), 94 (100%), and 71 (76%) of the 94 facilities. Of 944 children with uncomplicated malaria, only one child (0.1%) received chloroquine. Among children weighing less than 10 kg, sulfadoxine-pyrimethamine was commonly prescribed in accordance with guidelines (439/550, 79.8%). Among the children weighing 10 kg or more, sulfadoxine-pyrimethamine was commonly prescribed (266/394, 68%), whereas recommended artemether-lumefantrine was prescribed for only 42/394 (11%) children. Among children weighing 10 kg or more seen at facilities where artemether-lumefantrine was available, the same pattern was observed: artemether-lumefantrine was prescribed for only 42/192 (22%) children and sulfadoxine-pyrimethamine remained the drug of choice (103/192, 54%). Programmatic activities such as in-service training and provision of job aids did not seem to influence the prescribing of artemether-lumefantrine.

Conclusion Although the use of chloroquine for uncomplicated malaria was succesfully discontinued in Zambia, the change of drug policy towards artemether-lumefantrine does not necessarily translate into adequate use of this drug at the point of care.

Introduction

By 2002 in Zambia overwhelming evidence showed that chloroquine was failing to cure over 50% of patients by day 14,[1–3] and by 2003, pyrimethamine with sulfadoxine was failing in 8-33% of patients.[3 4] In December 2002, the Zambian Ministry of Health announced that chloroquine would be replaced as the first line therapy for uncomplicated malaria by artemether-lumefantrine for patients weighing 10 kg or more and by sulfadoxine-pyrimethamine in children weighing less than 10 kg. It was also specified that when artemether-lumefantrine was not yet available, sulfadoxine-pyrimethamine would be first line treatment for all categories of patients.[5]

We describe treatment practices in Zambian children during the transition from chloroquine to artemether-lumefantrine and to sulfadoxine-pyrimethamine and examine the factors influencing the prescribing of artemether-lumefantrine.

Methods

We purposively selected four districts representing the major malaria ecologies of Zambia: Chingola, Kalomo, Chipata, and Samfya. The government decided on a phased introduction of artemether-lumefantrine, beginning in February 2003 with seven districts and expanding to 28 districts by the end of 2003. The surveyed districts were part of these 28 districts. Kalomo was one of the seven early implementation districts.

Survey design and data collection

We carried out a cross sectional cluster survey at all government and mission facilities in each district between 28 January and 19 March 2004. A cluster was defined as all sick children seen at a health facility during one day. We observed health workers' outpatient case management practices for children aged less than 5 years. The consultations were observed over one day at each facility. After the health worker and caretaker (usually the child's mother) provided informed consent, a surveyor enrolled all children presenting to the outpatient departments.

Four teams each comprising three surveyors collected the data. A surveyor observed the consultations and recorded the carrying out of clinical tasks, the child's main problems, and the duration and timing of consultations. The caretakers were interviewed before leaving the facility and information was collected on the child's age, history of fever, and type of visit (initial or follow-up consultation). Information was collected from patient held records about diagnostic procedures requested and results reported, drugs prescribed, and if the child was treated as an outpatient or referred for admission to hospital. The child was weighed and his or her axillary temperature measured. The health workers were interviewed to collect information on their personal characteristics, work experience, and exposure to guidelines, training, and supervision. The health facility was assessed for availability of antimalarial drugs and malaria treatment wall charts.

This is an abridged version; the full version is on bmj.com

Table 1 Antimalarial treatments for children with uncomplicated malaria according to bodyweight in four districts in Zambia

	Bodyweight <10 kg		Bodyweight ≥10 kg		Total	
Health facilities	**No (%)**	**95% CI**	**No (%)**	**95% CI**	**No (%)**	**95% CI**
All facilities:	n=550		n=394		n=944	
Sulfadoxine-pyrimethamine	439 (79.8)	73.8 to 85.9	266 (67.5)	58.8 to 76.2	705 (74.7)	68.4 to 81.0
Artemether-lumefantrine	6 (1.1)	0 to 2.6	42 (10.7)	5.4 to 16.0	48 (5.1)	2.6 to 7.5
Quinine	14 (2.6)	0.8 to 4.3	19 (4.8)	2.0 to 7.6	33 (3.5)	1.8 to 5.2
Chloroquine	1 (0.2)	0 to 0.5	0	NA	1 (0.1)	0 to 0.3
No antimalarial prescribed	90 (16.4)	10.7 to 22.0	67 (17.0)	11.7 to 22.3	157 (16.6)	11.9 to 21.4
Facilities with artemether-lumefantrine in stock:	**n=262**		**n=192**		**n=454**	
Sulfadoxine-pyrimethamine	189 (72.1)	61.1 to 83.1	103 (53.7)	39.7 to 67.6	292 (64.3)	53.2 to 75.4
Artemether-lumefantrine	6 (2.3)	0 to 5.7	42 (21.9)	12.4 to 31.3	48 (10.6)	6.1 to 15.1
Quinine	9 (3.4)	0.3 to 6.6	6 (3.1)	0.4 to 5.9	15 (3.3)	1.0 to 5.6
No antimalarial prescribed	58 (22.1)	11.8 to 32.5	41 (21.4)	12.7 to 30.0	99 (21.8)	13.0 to 30.6

Definitions

Our definitions reflect recommendations from the Zambian national guideline on the diagnosis and treatment of malaria.[5] According to the guideline any child with fever or a history of fever in the absence of signs of severe malaria is presumed to have uncomplicated malaria. The guideline is ambiguous on the interpretation of malaria smear results and states that the "presence of signs and symptoms of disease with negative blood smear does not preclude the diagnosis of malaria." We defined a case of uncomplicated malaria as a child presenting to a health facility for an initial visit with a history of fever during the present illness or with an axillary temperature of 37.5°C or more, and treated as an outpatient in the absence of a routine negative blood slide result. We excluded from the analysis children with negative blood slide results to prevent health worker practices from being judged as incorrect owing to the ambiguity of the guideline. Recommended treatment for uncomplicated malaria was defined as a prescription for artemether-lumefantrine for children weighing 10 kg or more and a prescription for sulfadoxine-pyrimethamine for children weighing less than 10 kg.

Statistical analysis

We estimated the precision of proportions (95% confidence intervals) accounting for the cluster sampling design by using "health facility day" as the primary sampling unit.

To identify predictors of prescriptions for artemether-lumefantrine in children weighing 10 kg or more with uncomplicated malaria, we used logistic regression modelling accounting for correlated nature of data.[6] We restricted the analysis to children with an antimalarial drug prescribed at facilities with available artemether-lumefantrine because we were interested in factors that influenced the selection of this drug. In the univariate analysis, we estimated the odds ratio, P value, and 95% confidence interval for the association between health workers' choice to prescribe artemether-lumefantrine and the factors associated with health facilities and health workers. We tested duration and timing of consultation, starting time of the consultation, child's age, whether the child was weighed, whether the temperature was measured, the child's temperature, and the child's main problem. We evaluated 11 logical two way statistical interactions either between factors of programmatic importance such as in-service training or between the child's main problems.

Results

We observed 1423 consultations among children aged less than 5 years seen by 103 health workers at 94 health facilities. Most health workers were nurses (52%) or clinical officers (29%; see bmj.com). Most facilities were rural health centres (83%), and most were government run (92%). We analysed 1350 of 1423 consultations; we failed to interview 73 caretakers (5.1%). Of these 1350 consultations, 944 children met our definition of uncomplicated malaria. Of the 944 children with uncomplicated malaria, 550 (58.3%) weighed less than 10 kg; of these 550 children, 17 (3.1%) had received sulfadoxine-pyrimethamine at home before coming to the facility.

Antimalarial treatments for children with uncomplicated malaria

Table 1 shows the antimalarial treatments for 944 children with uncomplicated malaria. In children weighing less than 10 kg, national treatment recommendations were commonly followed: sulfadoxine-pyrimethamine was prescribed for 79.8% (439/550), only one child received chloroquine, and artemether-lumefantrine was rarely (6/550, 1.1%) prescribed. Of children weighing 10 kg or more, sulfadoxine-pyrimethamine was often used for treatment (266/394, 68%), no children were treated with chloroquine, and only 11% (42/394) of children were treated with artemether-lumefantrine. Overall, 16.6% (157/944) of children left the facility with no antimalarial prescription.

We found no significant difference in artemether-lumefantrine use between Kalomo, the early implementation district, and the other three districts. In Kalomo, artemether-lumefantrine was prescribed for 10% (9/92) of children weighing 10 kg or more compared with 13% (23/180) in Chipata, 7% (6/88) in Samfya, and 12% (4/34) in Chingola.

At facilities where artemether-lumefantrine was available on the day of the survey, the drug was prescribed by health workers for only 22% (42/192) of children weighing 10 kg or more, and sulfadoxine-pyrimethamine continued to be a preferred drug in this weight group (103/192, 54%; table 1). Furthermore, health workers prescribed artemether-lumefantrine for only 18% (9/49) of children weighing 10 kg or more in Kalomo compared with 23% (33/143) in the other districts.

Table 2 Univariate analysis of association between factors of programmatic importance and prescription of artemether-lumefantrine in children with uncomplicated malaria

Factor	No of consultations	No (%) prescribed artemether-lumefantrine	Odds ratio (95% CI)	P value
Health worker received in-service training on artemether-lumefantrine:				
Yes	24	6 (25)	0.89 (0.24 to 3.30)	0.866
No	127	36 (28)	1.0	
Artemether-lumefantrine wall chart in consultation room:				
Yes	45	12 (27)	0.81 (0.28 to 2.36)	0.705
No	106	30 (28)	1.0	
Health worker had national malaria guideline:				
Yes	93	30 (32)	1.69 (0.41 to 4.21)	0.323
No	58	12 (21)	1.0	

Readiness to deliver artemether-lumefantrine

Of 103 health workers, 62 (60%) had received in-service training that included the management of malaria (see bmj.com). Only 26 (25%), however, had received training in artemether-lumefantrine, more commonly in Kalomo (12/25, 48%) than in Chipata (3/36, 7%), Samfya (10/25, 37%), or Chingola (1/10, 10%). Yet 60 (58%) health workers possessed the national malaria guideline. Weighing scales were available in 92 of the 94 facilities (98%) whereas wall charts showing dosages for artemether-lumefantrine were displayed in 19 (20%), more commonly in Kalomo (9/24, 38%). Artemether-lumefantrine was available in 48 (51%) facilities, with a higher availability in Kalomo (15/24, 63%) and Chingola (7/9, 78%) than in Chipata (16/36, 44%) and Samfya (10/25, 40%). Conversely, sulfadoxine-pyrimethamine was universally available, and oral quinine and chloroquine were available at 74 (79%) and 71 (76%) facilities, respectively.

Predictors of artemether-lumefantrine prescriptions

We examined 26 factors and 11 interaction terms that we hypothesised may have influenced the prescribing of artemether-lumefantrine in 151 children weighing 10 kg or more who were prescribed an antimalarial at facilities with artemether-lumefantrine. On univariate analysis, factors significantly associated with the outcome that a child received a prescription for artemether-lumefantrine were child aged 2 or more years (odds ratio 3.00, 95% confidence interval 1.29 to 6.97), consultation seven or more minutes (2.69, 1.26 to 5.76), and treatment provided at health centres compared with hospitals (8.69, 1.28 to 58.84). In-service training on artemether-lumefantrine, presence of artemether-lumefantrine wall charts, and possession of the guideline were not significantly associated with prescribing artemether-lumefantrine (table 2).

Discussion

The policy shift in Zambia in 2003 away from chloroquine as a first line therapy for uncomplicated malaria has been successfully implemented. Although the discontinuation of chloroquine was immediate, most clinicians opted for the more familiar sulfadoxine-pyrimethamine rather than the recently introduced artemether-lumefantrine. Although chloroquine was commonly in stock, it was almost never (0.1%) used. This result represents a major improvement in the management of paediatric malaria. However, 17% of children meeting the definition of uncomplicated malaria received no antimalarial. A possible explanation may be that the guideline based concept that equates all fevers with malaria is not accepted for children with another obvious cause of fever. Children were rarely prescribed (22%) artemether-lumefantrine at facilities with available stocks. Compared with the other three districts, use of artemether-lumefantrine was equally low in Kalomo, which was more ready to deliver artemether-lumefantrine, and had had experience with the drug.

Predictors of artemether-lumefantrine prescriptions

Provision of programmatic interventions such as in-service training did not seem to influence artemether-lumefantrine use. This was not surprising, and previous studies with a similar design suggested that in-service training improved treatment practices,[7] had no association with performance,[8 9] or had an effect only in subgroups of health workers.[10] One strategy that consistently failed to achieve improvements in most studies was the isolated dissemination of clinical guidelines,[11] and our observations concur with these findings.

Other factors might also be responsible for the low use of artemether-lumefantrine. The presence of a study observer could modify usual clinical practices (Hawthorn effect), however this effect is almost always in the direction of better performance.[12] Therefore although this bias may have led to an underestimation of chloroquine use, it is unlikely to explain the low use of artemether-lumefantrine. Our study was not designed to capture subtle health worker perceptions, but the reluctance to prescribe artemether-lumefantrine may reflect health worker concerns about drug potency, side effects, or concerns about the stock interruptions.

Deciding on a new drug policy is arguably the easy part of a complex process of policy change—the greatest challenge remains in changing clinical practices. Although a sustainable supply of expensive artemisinin based combination therapies is urgently needed across Africa, this must be accompanied by similar investments in effective interventions to ensure swift implementation and proper use of drugs at the point of care.

We thank the field teams, health workers, children, and caretakers; the data entry clerks Rodney Katango and Christine Mwape; Michael Macdonald, Mubiana Macwan'gi, Naawa

What is already known on this topic

Zambia was the first African country to change its antimalarial treatment policy to artemisinin based combination therapy (artemether-lumefantrine)

Changing clinical practice to support the change presents challenges

What this study adds

Most Zambian clinicians prescribe sulfadoxine-pyrimethamine rather than artemether-lumefantrine for children with uncomplicated malaria

Interventions such as in-service training did not seem to influence the choice of artemether-lumefantrine

Sipilanyambe, Pascalina Chanda, Mike English, and Jon Simon for comments on earlier drafts. RWS is a senior Wellcome Trust fellow (No 058992) and acknowledges the support of the Kenyan Medical Research Institute. This paper is published with the permission of the director of the Kenya Medical Research Institute.

Contributors: See bmj.com

Funding: Zambian-Boston University Malaria Project (Association of Schools of Public Health and Centers for Disease Control and Prevention cooperation agreement S1954-21-21) and the Wellcome Trust, United Kingdom.

Competing interests: DZ and RWS have received a fee for speaking at a meeting organised by Novartis Pharma, the manufacturer of artemether-lumefantrine.

Ethical approval: This study was approved by the Boston University institutional review board (2003-412B) and research ethics committee of the University of Zambia (federal wide assurance No IRB00001131).

1 National Malaria Control Centre. *National malaria situation analysis 2000.* www.cboh.gov.zm/documents/Copy%20of%20Final%20Malaria%20SA%20Document%202000.pdf (accessed 1 Aug 2005).
2 Hamer DH, MacLeod W, Addo-Yobo E, Duggan CP, Estrella B, Fawzi WW, et al. Age, temperature, and parasite density predict chloroquine treatment failure in children with uncomplicated falciparum malaria *Trans R Soc of Trop Med Hyg* 2003;97:422-8.
3 Bijl HM, Kager J, Koetsier DW, van der Werf TS. Chloroquine-and sulfadoxine-pyrimethamine-resistant falciparum malaria in vivo—a pilot study in rural Zambia. *Trop Med Int Health* 2000;5:692-5.
4 Chanda P, Sikaala CH, Kapelwa W, Moonga H, Njunju E, MacDonald M, et al. Decreasing efficacy of sulphadoxine-pyrimethamine (SP) in Zambian children. Proceedings of the 53rd annual meeting of the American Society of Tropical Medicine and Hygiene. Miami, USA. *Am J Trop Med Hyg* 2004;71(4) suppl:abstract 708.
5 Central Board of Health. *Guidelines for the diagnosis and treatment of malaria in Zambia.* A Production of the RBM Partnership in Zambia. Lusaka, Zambia: CBoH, 2003.
6 Horton NJ, Lipsitz SR. Review of software to fit generalized estimating equation regression models. *Am Stat* 1999;53:160-9.
7 Naimoli J. *Theoretical and empirical advances in research on the implementation of an integrated approach to managing childhood illness in outpatient facilities in developing countries.* [Doctoral dissertation.] Cambridge, MA: Harvard School of Public Health, 2001.
8 Rowe AK, Hamel MJ, Flanders WD, Doutizanga R, Ndoyo J, Deming MS. Predictors of correct treatment of children with fever seen at outpatient health facilities in the Central African Republic. *Am J Epidemiol* 2000;151:1029-35.
9 Rowe AK, Onikpo F, Lama M, Deming MS. Risk and protective factors for two types of error in the treatment of children with fever at outpatient health facilities in Benin. *Int J Epidemiol* 2003;32:296-303.
10 Zurovac D, Rowe AK, Ochola SA, Noor AM, Midia B, English M, et al. Predictors of the quality of health worker treatment practices for uncomplicated malaria at government health facilities in Kenya. *Int J Epidemiol* 2004;33:1080-91.
11 World Health Organization. *Interventions and strategies to improve the use of antimicrobials in developing countries.* WHO/CDS/CSR/DRS/2001.9. Geneva: WHO, 2001.
12 Rowe AK, Lama M, Onikpo F, Deming MS. Health worker perceptions of how being observed influences their practices during consultations with ill children. *Trop Doct* 2002;32:166-7.

Healer shopping in Africa: new evidence from rural-urban qualitative study of Ghanaian diabetes experiences

Ama de-Graft Aikins

Abstract

Objectives To provide counterevidence to existing literature on healer shopping in Africa through a systematic analysis of illness practices by Ghanaians with diabetes; to outline approaches towards improving patient centred health care and policy development regarding diabetes in Ghana.
Design Longitudinal qualitative study with individual interviews, group interviews, and ethnographies.
Settings Two urban towns (Accra, Tema) and two rural towns (Nkoranza and Kintampo) in Ghana.
Participants 26 urban people and 41 rural people with diabetes with diverse profiles (sex, age, education, socioeconomic status, diabetes status).
Results Six focus groups, 20 interviews, and three ethnographical studies were conducted to explore experiences and illness practices. Analysis identified four kinds of illness practice: biomedical management, spiritual action, cure seeking (passive and active), and medical inaction. Most participants privileged biomedicine over other health systems and emphasised biomedical management as ideal self care practice. However, the psychosocial impact of diabetes and the high cost of biomedical care drove cure seeking and medical inaction. Cure seeking constituted healer shopping between biomedicine, ethnomedicine, and faith healing; medical inaction constituted passive disengagement from medical management and active engagement with faith healing. Crucially, although spiritual causal theories of diabetes existed, they were secondary to dietary, lifestyle, and physiological theories and did not

Department of Social and Developmental Psychology, Faculty of Social and Political Sciences, University of Cambridge, Cambridge CB2 3RQ
Ama de-Graft Aikins
ESRC postdoctoral fellow
ada21@cam.ac.uk

BMJ 2005;331:737–42

ELPS *This is an abridged version; the full paper appears on bmj.com*