Implementation of artemether-lumefantrine treatment policy for malaria at health facilities in Tanzania

V Mugoyela¹
O Minzi²
¹Department of Medicinal Chemistry, ²Unit of Pharmacology and Therapeutics, School of Pharmacy, Muhimbili University of Health and Allied Sciences, Dar Es Salaam, Tanzania

Background: The purpose of this study was to compare knowledge on the part of health workers in public and private health facilities about prescribing and dispensing of an artemether-lumefantrine combination, 3 years after moving from sulfadoxine-pyrimethamine to artemether-lumefantrine as a first-line treatment for nonsevere malaria in Tanzania.

Methods: A cross-sectional survey of a convenience sample of 306 dispensaries and pharmacies was conducted in Dar Es Salaam and the Coast region of Tanzania. Of these, 122 were community pharmacies, 143 were private dispensaries, and 41 were public dispensaries. Specific outcome measures were health workers’ knowledge of the new malaria treatment guidelines, recommended doses of artemether-lumefantrine, and food requirements.

Results: A total of 489 health workers were included in the study. The respondents were prescribers in private dispensaries, public dispensaries, and community pharmacies. Participants included medical officers (3.7%), clinical officers (38%), pharmacists (5.7%), and pharmaceutical technicians (3.9%). Nearly all workers in the public dispensaries and about 50% of workers in private dispensaries and community pharmacies were aware of recommended first-line malaria treatment. The difference in the proportion of health workers with adequate knowledge about the new recommended antimalarial medicine in public and private dispensaries was statistically significant \((P < 0.0001)\). There was a higher proportion of workers in public dispensaries who had adequate knowledge about doses of artemether-lumefantrine for adults compared with workers in private dispensaries \((P = 0.001)\). Only 58.0% of respondents were able to state correctly the recommended doses in private dispensaries as compared with 77.0% in public dispensaries.

Knowledge about the requirement for a concomitant fatty meal was not significantly different between workers in public and private dispensaries \((P = 0.280)\) or between those working in public dispensaries and pharmacies \((P = 0.622)\).

Conclusion: Knowledge about the use of artemether-lumefantrine was higher among health workers in public dispensaries than in their counterparts from private health care settings. The training organized by the Ministry of Health for workers in public health facilities in Tanzania contributed to such differences.

Keywords: knowledge, public dispensaries, private dispensaries, pharmacies

Introduction
Countries severely hit by malaria changed their national drug policies and introduced artemether-lumefantrine as first-line therapy for nonsevere \(Plasmodium falciparum\) malaria in 2006.¹-⁵ Since the introduction of artemisinin-based combination therapy for malaria, substantial progress has been made in delivering these products to patients through the public health system, basically by the funding from the Global Fund, the US President’s Malaria Initiative, and the World Bank in many African countries.⁶
Currently, the artemether-lumefantrine combination is the treatment of choice for nonsevere and uncomplicated malaria. Because of its considerably high price and concomitant food requirement, implementation of artemether-lumefantrine has encountered competition with some suboptimal nonartemether therapies like sulfadoxine-pyrimethamine. In developing countries like Tanzania, patients who seek treatment in private facilities cannot easily afford artemisinin-based combination therapy, so resort to cheaper less effective monotherapies. In Tanzania, apart from artemether-lumefantrine, other artemisinin-based combinations and antimalarial drugs for monotherapy are widely available and easily accessed in private health facilities. These include Duo-cotecxin tablets (Zhejiang Holley Nanhui Pharmaceutical Co Ltd, Jiaxing, China), Artequin tablets (Artepharm Co, Ltd, Guangzhou, China), Co-Malafin tablets (Shelys Pharmaceuticals Ltd, Dar Es Salaam, Tanzania), Amobin tablets (Regal Pharmaceuticals Ltd, Nairobi, Kenya), Ekelfin tablets (Elys Chemical Industries Ltd, Nairobi, Kenya), Fansidar tablets (Roche, Basel, Switzerland), and Halfan tablets and/or syrup (GlaxoSmithKline, Essone, France). Quinine injection and tablets are available in all private and public health facilities. Nonetheless, amodiaquine and sulfadoxine-pyrimethamine tablets and/or syrup are still present in both public and private health outlets.

Today, despite substantial funding by donors and government partners to support the implementation of these new treatment policies, very little is known about the extent to which health workers have implemented these changes in some countries. Policy implementation is a long process and can take several years to produce effective change. The steps involved include sensitization of health providers and the community, training of providers, issuing of directives (in terms of time limit) with regards to phasing out old medicines and full use of the newly introduced one, and directives on stocking, rational prescribing, and dispensing of the required medicines. Until now, published reports on health workers’ adherence to artemisinin-based combination treatment polices are only available for few countries. This study aimed at assessing the implementation of artemether-lumefantrine treatment in Tanzania by measuring knowledge among health workers about artemether-lumefantrine as a first-line malaria treatment, the correct doses, and the need for concomitant food intake 3 years after a policy change in this country.

**Methods and materials**

This was a prospective, cross-sectional, descriptive study conducted in community pharmacies and public and private dispensaries in Dar Es Salaam and the Coast region of Tanzania. The study took place in public and private health facilities because people in the community receive treatment from both of these facilities. For effective treatment of malaria with first-line medicine after a policy change, it is important for all health providers to have some level of awareness and knowledge about correct doses, irrespective of the nature of the health settings. The regions used in this survey were selected due to their similar geographical locations and climatic conditions. The regions are situated along the coast of the Indian Ocean, and the local people have similar outdoor activities. The study took place between January 2009 and June 2009, and data were collected from both public and private health settings. A total of 489 health workers were included from three settings, ie, private pharmacies, and public and private dispensaries. The public and private dispensaries are all at the same level, hence there were no variations in staff qualifications or levels of care. The inclusion criteria for dispensers was whether the dispensary was private or public and whether it was accessible. Only pharmacy staff who consented to participate in the study were included. Both prescribers and dispensers were interviewed in public and private dispensaries. Only the dispensers were interviewed in the private pharmacies.

**Data collection**

Data were collected using structured questionnaires (see Appendix) and assessed knowledge among health workers about first-line malaria treatment, including the dosage regimen for artemether-lumefantrine in the different age groups and the need for concomitant food intake. The first set of questions investigated the qualifications of the participants, the category/level of each health facility, and awareness of first-line malaria treatment among respondents. Other questions assessed knowledge of the dosage regimen for the different age groups. Because of the requirement for fat ingestion to improve the bioavailability of artemether-lumefantrine, there were questions assessing the knowledge of participants about this. Another set of questions asked whether participants received any kind of training concerning current first-line and second-line malaria medicines. Examples of the last two questions included “Have you ever been given any formal training/health education on the use of artemether-lumefantrine?” and “In your opinion, what is currently the second-line drug for nonsevere malaria in Tanzania?” These questions were basically meant to determine whether participants received training on the current malaria treatment guidelines.
Data analysis
Data collected were coded and analyzed using the Statistical Package for Social Sciences, Version 15.0 software (SPSS Inc, Chicago, IL). Descriptive statistics were used to measure the relative frequencies of variables. Distribution of prevalence was analyzed using cross-tabulation and Chi-square tests.

Results
This study took place 3 years after implementation of the new artemether-lumefantrine treatment policy in Tanzania. In total, 489 health workers were interviewed (Table 1), comprising clinical officers (38.0%), nurse assistants (38.6%), pharmacists (5.7%), and medical officers (3.7%). Of the three different types of health facilities assessed, 39.8% were community pharmacies, 46.7% were private dispensaries, and 13.4% were public dispensaries. Only 18.8% of respondents had received any formal training on how to use artemether-lumefantrine since its introduction as a first line-treatment for malaria.

Awareness of new malaria treatment policy
Table 2 shows the proportion of health providers with knowledge of first-line antimalarial drug treatment for nonsevere malaria after the changes in the treatment guidelines. Almost all (96.6%) respondents in public dispensaries knew about correct first-line malaria treatment as compared with their counterparts in private health settings, ie, private dispensaries and pharmacies (P < 0.0001). Similarly, more health workers (86.2%) in public dispensaries were able to cite quinine tablets/intramuscular injections correctly as second-line malaria treatment than their colleagues in either private dispensaries or community pharmacies (P < 0.0001). The difference in awareness of first-line and second-line treatment among health workers in public and private health settings was highly statistically significant. In private dispensaries, less than 50% of respondents could mention the recommended first-line malaria medicine. In community pharmacy, only 40% of all respondents were able to mention correctly the second-line malaria medicine, ie, quinine.

Knowledge about doses
Table 3 shows the proportion of health workers in public dispensaries who were able to state the correct artemether-lumefantrine doses in comparison with workers in private settings. Of the participants in public dispensaries, 77.0% were able to state correctly the recommended doses for adults as compared with 58.0% and 60.6% in private dispensaries and community pharmacies, respectively. This difference was statistically significant (P < 0.001). There was a statistically significant difference between public dispensaries and private dispensaries as well as community pharmacies on knowledge about the doses in children from different age groups (Table 3). This was evident from the results, whereby 73.5% of participants in public dispensaries mentioned the correct doses for children with body weight of 5–14 kg, while less than 50% of participants in the private settings were able to do so (P < 0.0001).

Knowledge about food requirements
Table 4 shows the level of knowledge about the food requirement during malaria treatment with artemether-lumefantrine. As many as 63.8% of participants in public dispensaries, 51.9% in private dispensaries, and 70.4% in community pharmacies responded correctly. However, very few providers in public and private settings knew that a fatty meal was

Table 1 Characteristics of health facilities and health workers

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health facility category (n = 306)</td>
<td></td>
</tr>
<tr>
<td>Community pharmacies</td>
<td>122 (39.8%)</td>
</tr>
<tr>
<td>Private dispensaries</td>
<td>143 (46.7%)</td>
</tr>
<tr>
<td>Public dispensaries</td>
<td>41 (13.4%)</td>
</tr>
<tr>
<td>Health workers qualifications (n = 489)</td>
<td></td>
</tr>
<tr>
<td>Clinical officers</td>
<td>186 (38.0%)</td>
</tr>
<tr>
<td>Medical officers</td>
<td>18 (3.7%)</td>
</tr>
<tr>
<td>Nurse assistants</td>
<td>189 (38.6)</td>
</tr>
<tr>
<td>Pharmaceutical technician</td>
<td>19 (3.9%)</td>
</tr>
<tr>
<td>Pharmacists</td>
<td>28 (5.7%)</td>
</tr>
<tr>
<td>Registered nurses</td>
<td>49 (10.0%)</td>
</tr>
</tbody>
</table>

Table 2 Knowledge of the new malaria treatment policy in health workers in different facilities

<table>
<thead>
<tr>
<th>Health facility</th>
<th>Public dispenser (n = 117)</th>
<th>Private dispenser (n = 244)</th>
<th>Community pharmacy (n = 119)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>First-line treatment with AL</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Able to tell correctly</td>
<td>113 (96.6%)</td>
<td>111 (45.5%)</td>
<td>62 (52.1%)</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>Second-line treatment (quinine)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Able to tell correctly</td>
<td>100 (86.2%)</td>
<td>149 (61.6%)</td>
<td>46 (40.0%)</td>
<td>&lt;0.0001*</td>
</tr>
</tbody>
</table>

Note: *Highly statistically significant.
Abbreviation: AL, artemether-lumefantrine.
Table 3 Knowledge of artemether-lumefantrine doses in health workers according to body weight

<table>
<thead>
<tr>
<th>Dose</th>
<th>Public dispensary</th>
<th>Private dispensary</th>
<th>Community pharmacy</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult &gt;35 kg</td>
<td>n = 113</td>
<td>n = 212</td>
<td>n = 104</td>
<td></td>
</tr>
<tr>
<td>dose correctly</td>
<td>87 (77.0%)</td>
<td>123 (58.0%)</td>
<td>–</td>
<td>= 0.001**</td>
</tr>
<tr>
<td>Stated dose correctly</td>
<td>87 (77.0%)</td>
<td>–</td>
<td>63 (60.6%)</td>
<td>= 0.009***</td>
</tr>
<tr>
<td>All children ≥5 kg</td>
<td>n = 113</td>
<td>n = 206</td>
<td>n = 99</td>
<td></td>
</tr>
<tr>
<td>3 months to 3 years (5–14 kg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stated dose correctly</td>
<td>83 (73.5%)</td>
<td>98 (47.6%)</td>
<td>–</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>Stated dose correctly</td>
<td>83 (73.5%)</td>
<td>–</td>
<td>44 (44.4%)</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>3–8 years (1–24 kg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stated dose correctly</td>
<td>83 (73.5%)</td>
<td>98 (47.6%)</td>
<td>–</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>Stated dose correctly</td>
<td>83 (73.5%)</td>
<td>–</td>
<td>41 (41.4%)</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>8–12 years (25–35 kg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stated dose correctly</td>
<td>83 (73.5%)</td>
<td>99 (48.1%)</td>
<td>–</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>Stated dose correctly</td>
<td>83 (73.5%)</td>
<td>–</td>
<td>42 (42.4%)</td>
<td>&lt;0.0001*</td>
</tr>
</tbody>
</table>

Notes: **Highly statistically significant; ***statistically significant.

Table 4 Knowledge of food requirement during artemether-lumefantrine therapy in health workers

<table>
<thead>
<tr>
<th>Knowledge of food requirement</th>
<th>Public dispensary</th>
<th>Private dispensary</th>
<th>Community pharmacy</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>before taking AL</td>
<td>n = 116</td>
<td>n = 231</td>
<td>n = 115</td>
<td></td>
</tr>
<tr>
<td>Said “yes” food is needed while taking AL</td>
<td>74 (63.8%)</td>
<td>119 (51.9%)</td>
<td>–</td>
<td>= 0.030**</td>
</tr>
<tr>
<td>Said “yes” food is needed while taking AL</td>
<td>74 (63.8%)</td>
<td>–</td>
<td>81 (70.4%)</td>
<td>= 0.283***</td>
</tr>
<tr>
<td>Knowledge of type of food needed</td>
<td>n = 73</td>
<td>n = 119</td>
<td>n = 79</td>
<td></td>
</tr>
<tr>
<td>Stated “milk and/or fatty meal”</td>
<td>23 (31.5%)</td>
<td>29 (24.4%)</td>
<td>–</td>
<td>= 0.280***</td>
</tr>
<tr>
<td>Stated “milk and/or fatty meal”</td>
<td>23 (31.5%)</td>
<td>–</td>
<td>22 (27.8%)</td>
<td>= 0.622***</td>
</tr>
</tbody>
</table>

Notes: **Statistically significant; ***not statistically significant.

Abbreviation: AL, artemether-lumefantrine.

important for improving drug absorption (Table 4). The difference in responses amongst the health workers in public and private dispensaries on knowledge about the need for food during treatment with artemether-lumefantrine was not statistically significant (P = 0.030). The results compare the knowledge of participants in public dispensaries and community pharmacies about the food requirement before artemether-lumefantrine intake and indicates that there was no statistically significant difference (P = 0.622).

Discussion

This study compared knowledge on implementation of artemether-lumefantrine policy in malaria treatment in Tanzania between health workers in public and private health care facilities.

The changes in policy from sulfadoxine-pyrimethamine to artemether-lumefantrine as a first-line antimalarial drug was officially announced at the end of 2006. Within 6 months, Minzi et al conducted a survey to assess if dispensers in private pharmacies had received any training on the implementation of the treatment policy changes from chloroquine to sulfadoxine-pyrimethamine and from sulfadoxine-pyrimethamine to artemether-lumefantrine and showed that none of the participants were either involved in the preparation of the guidelines or trained on their implementation.25 The present study was conducted 3 years later and compared knowledge among health workers in public and private health settings about implementation of the artemether-lumefantrine treatment policy in uncomplicated P. falciparum malaria.

Our results indicated that only 18.8% of the interviewed health workers had received formal training on how to prescribe and/or dispense artemether-lumefantrine. This proportion is less than half that reported from Kenya where 46% of health workers received inservice training on artemether-lumefantrine.17 However, there is still a lot to be desired with regard to how preparation and implementation of new treatment guidelines is being handled in developing countries. Probably the best solution to increase the number of trained personnel
and reach nonqualified health workers is through training at least one health worker from each drug outlet who could in turn train colleagues in the workplace. Another approach is to provide adequate sensitization in the country before the policy is implemented.26,27 This study provides information on the qualifications of respondents (Table 1) whereby pharmaceutical personnel comprised only 9.6% and qualified prescribers (medical and clinical officers) comprised 41.7%. These are the health workers who are supposed to comprise the majority of dispensers in community pharmacies and prescribers in public and private dispensaries, respectively. It has been previously reported by Mugoyela and Ally that dispensers lack sound knowledge on good pharmacy practice because of their training background and lack of regular access to health information provided by the regulatory body and other sources.28 This trend of an inadequate training background has been observed among prescribers and dispensers in the current study. In our study, we investigated awareness of health workers about first-line and second-line malaria treatments. The results show a highly statistically significant difference in awareness between workers in public and private settings. Almost all (96.6%) participants in public dispensaries and less than 50% in private dispensaries and community pharmacies stated the first-line and second-line malaria treatment correctly. A very important observation made from these results is that the new treatment policy was prescribed mainly in public settings. In addition, the procurement of artemether-lumefantrin was included in the “WHO Model List of Essential Medicines” for adults and children, and Novartis, the manufacturer of artemether-lumefantrin (Coartem®), and the World Health Organization in 2001 signed a memorandum of understanding to ensure that artemether-lumefantrin was available at cost price in malaria-endemic areas.7 Indeed, in developing countries, global subsidy plays an important role in supplying artemether-lumefantrin in public health care facilities.29,30 Therefore, priority was given by the Ministries of Health to training health workers in public hospitals and dispensaries in various countries where artemether-lumefantrin is available.

Table 3 shows a highly statistically significant difference in knowledge between health workers about adult doses in public dispensaries as compared with workers in private health settings. The majority of respondents (77.0%) in public dispensaries managed to state the adult doses correctly. Similarly, most of the health workers (73.5%) in public dispensaries stated doses for children correctly. In private health facilities, only 45% of respondents were able to state the pediatric doses correctly, although 60% managed to mention the right doses for adults. The high level of knowledge among health workers in public settings is partly the outcome of sensitization training by the Ministry of Health and reading of directions for use of the medicine on the labeling of packaged materials.22,25,31 It has been reported in the literature that incorrect weight-specific prescriptions of artemether-lumefantrin are rare, and blister packaging is likely to be a factor contributing to this level of knowledge.14,17 The six-dose regimen of artemether-lumefantrin has proven to be highly effective when given at hours 0, 8, 24, 36, 48, and 60 of the treatment course.7,32 For children, appropriate weight-adjusted doses are recommended, so children weighing ≥5/15 kg, ≥15/25 kg, and ≥25/35 kg should be given one, two, and three tablets, respectively, per time point.7,19

In our study, we used artemether-lumefantrin available in packs with a weight-specific number of tablets, including pictorial instructions on how to use the medicine. For ease of use and rapid policy dissemination, all health workers should undergo training. In most of the developing countries, during the change of policy to artemisinin-based combinations, only health workers in public health systems and very few in private health facilities were trained on how to dispense artemether-lumefantrin due to financial constrains.22,33 The outcome of lack of trained health workers responsible for handling the new introduced medicine as per guidelines could lead to administration of wrong doses and incorrect information being given to patients.

Oral absorption of artemether-lumefantrin is enhanced by concomitant consumption of fat-containing food,11,34 and it was recently reported that intake of soy milk enhances bioavailability of the drug.7,35 In our study, we found that the majority of respondents (>50%) in each health care facility stated that “food intake” is one of the necessary requirements for artemether-lumefantrin therapy (Table 4). However, the responses regarding type of food needed, ie, whether “milk or fatty meal”, was not statistically significant either between respondents in public and private dispensaries (P = 0.280) or between public dispensaries and community pharmacies (P = 0.622). Less than 50% respondents in each setting were able to mention this correctly. At the time we conducted this study, subsidized artemether-lumefantrin was only available in public health facilities. In the private health settings, other antimalarial medicines were available. For effective implementation of policy change for malaria treatment in developing countries, subsidized AL should be available both in public and private health facilities. Nonetheless, the availability of other malaria therapies should not be overlooked.

**Conclusion**

Knowledge about the use of artemether-lumefantrin was higher among health workers in public dispensaries than...
in their counterparts in private health settings. Training organized by Ministry of Health for workers in public health facilities in Tanzania contributed to this difference in awareness. For effective implementation of the new treatment guidelines, training should be given to health workers in both public and private settings.

Acknowledgments
The authors acknowledge the assistance of health district authorities for issuing permission letters to collect data from the public dispensaries. They also acknowledge the support provided by the community pharmacy owners and private dispensers during data collection. This study was funded by the Directorate of Research and Publication at Muhimbili University of Health and Allied Sciences, Dar es Salaam, Tanzania, through the Sida funding mechanism for small grants.

Disclosure
The authors report no conflicts of interest in this work.

References
### Appendix: Questionnaire used to interview health workers

1. Name of the interviewer __________
2. Serial number __________________
3. Name of the health facility __________
4. Category of the health facility (tick appropriately)
   - Public dispensary
   - Private dispensary
   - Community pharmacy
5. Qualifications of the respondent (tick)
   - Pharmacist
   - Medical officer
   - Nurse assistant
   - Pharmaceutical technician
   - Clinical officer
   - Pharmaceutical attendant
   - Registered nurse
   - Other (specify) __________
6. District name ______________
7. Do you know that there have been changes in the recommendations for treating malaria?
   - Tick YES or NO
8. If yes, do you know when it changed? ______________
9. Do you know which antimalarial drug is currently recommended for treating uncomplicated malaria?
10. What dose of artemether-lumefantrine tablets do you prescribe/dispense to malaria patients?
    - 3 months to 3 years (4–14 kg)
    - 3 to 8 years (15–24 kg)
    - 8 to 12 years (25–35 kg)
    - Adult > 35 kg
11. Is there any food requirement which should be fulfilled by a patient before taking artemether-lumefantrine?
    - YES or NO
12. If yes please state the type of food required?
    - YES or NO
    - If yes, mention how you know ______________
13. Have you ever been given any formal training/health education on the use of artemether-lumefantrine?
    - YES or NO
14. What is the second-line antimalarial drug in Tanzania? Name __________