Malaria Treatment in Severe Malnutrition in Angola

By Amador Gomez and Elisa Domínguez

Amador Gomez is Technical Director of Acción Contra el Hambre (ACH). Previously he spent several years working on nutrition and medical programmes in Angola, Somalia, Guinea, Nicaragua and Colombia.

Elisa Domínguez is currently the Medical and Nutritional Coordinator of ACH in Angola, and has worked with ACH on nutrition and medical programmes in Liberia, Guinea and Malí.

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This field article outlines the results of a preliminary study carried out by ACH in Angola, which showed poor response rates to standard TFC protocols for managing malaria.

Registration at Ganda TFC

Acción Contra el Hambre (ACH) has been working in Angola for the past 10 years in the health, nutrition, food security, and water and sanitation sectors. The teams have been implementing emergency programmes, treating moderate and severe malnutrition in therapeutic and supplementary feeding centres. At the therapeutic feeding centres (TFCs), malnourished children usually receive a large combination of drugs following the systematic medical protocol for associated diseases. Systematic treatment for malaria is included, in accordance with the Angolan national protocol where chloroquine is the treatment of choice.

This approach concurs with the view that "malaria treatment during nutritional rehabilitation of famine victims should include malaria prophylaxis and careful surveillance." However, the use of mass drug administration and presumptive treatment has a big impact on development of resistance (see box). Furthermore, in our TFCs we observed deterioration in the programme outcome indicators (% mortality, weight gain, and length of stay). Despite several evaluations of the procedures and quality of care, the indicators remained sub-optimal. This led us to carry out a preliminary study in two TFCs in Angola, to evaluate the efficacy of the Angolan national protocol of treatment of malaria in severe malnutrition.
Methodology

The preliminary study was carried out at the TFCs of Ganda (Province of Benguela) and Caconda (Province of Huila). The TFC files from all patients aged between 6 and 59 months with suspicion of malaria were included in the study and analysed. Since no blood tests were done, it was not possible to differentiate between Plasmodium falciparum and other species that are not involved in resistance.

The period of study covered TFC admissions during the months of July, August and September 2003. Severely malnourished children received medical and nutritional treatments following standard protocols, using the specified drugs and doses when malaria was suspected (see table 1).

Malnutrition and malaria

Malnutrition is a significant cause of mortality and morbidity in complex emergencies, and is associated with an increased risk of a poor outcome from severe malaria. In turn, malaria is one of the leading causes of death among children under five years, a leading cause of low birth weight among infants, and contributes to high maternal mortality.

It has long been acknowledged that populations residing in malarial areas generally live under conditions that lead to poor nutritional status. The groups at highest risk for the adverse effects of malaria - children and pregnant women - are also most affected by poor nutrition. Despite some areas of uncertainty regarding links and interactions between malaria and severe malnutrition there is growing evidence that malnutrition is an important risk factor for increased clinical malaria attack and higher likelihood of malaria mortality (and complications) in humans.

The WHO recognise that malaria will continue to be one of the main problems of health in the coming years. This is not helped by new drugs development constantly being overtaken by emerging resistances, with a future risk of inefficiency of all treatment available. Different factors are implicated in the increasing resistance. First, the use of drugs in monotherapy in endemic areas. Since many anti-malarial drugs are closely related chemically, development of resistance to one can facilitate development of resistance to others. Secondly, factors that undermine the immune system (malnutrition, HIV) decrease the body's capacity to clear the parasite residuum after treatment, increasing the parasite's survival and thus facilitating development of resistance. Drug pressure in endemic areas, i.e. the use of mass drug administration, and presumptive treatment (increasing the number of people treated unnecessarily, with selective pressure on circulating parasites) further facilitate resistance.

In countries where mono-therapy (e.g. chloroquine, sulphadoxinepyrimethamine) is used for first and second line of treatment, but where the efficacy of these drugs has been compromised by resistance, WHO/Roll Back
Malaria recommended the use of drug combinations that include an artemisinin derivative\(^2\). The use of a combination therapy of drugs with low level of resistance is likely to be effective in many settings, and can be used in the treatment of both uncomplicated and severe malaria.

### Table 1 Treatments and dosage used against malaria

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>chloroquine</td>
<td>CHQ 10mg/kg</td>
</tr>
<tr>
<td>quinine</td>
<td>QUI 30mg/kg</td>
</tr>
<tr>
<td>sulfadoxine+pyrimethamine (fansidar)</td>
<td>FAN 25mg/kg</td>
</tr>
<tr>
<td>chloroquine /eritromicine</td>
<td>CHQ/ERT 10mg/kg - 50mg/kg</td>
</tr>
</tbody>
</table>

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**Ganda TFC**

Eighty-one files were initially studied at Ganda TFC, of which 80% corresponded to children between 6 and 59 months old (see figure 1). We decided to include only those between 6 and 59 months in the study, since the other age groups were not adequately represented.

For the study group of 65 children aged between 6 and 59 months, the standard protocol was applied in 64 cases and chloroquine used as the first choice of treatment. One case was initially treated with fansidar without improvement and subsequently required a quinine perfusion.

Of the 64 cases treated with chloroquine, 62 failed to respond (97%), one case died (1.5%), and one case was cured (1.5%).

Of the 63 cases that failed to respond to firstline treatment (62 that failed to respond to chloroquine and 1 treated initially with fansidar, above), the majority (47 cases) were then treated with fansidar, which had a 45% cure rate (21 cases).

Of those 26 cases (55%) who did not respond to fansidar, subsequent treatment involved:

- quinine (20 cases). Of these, 13 were cured (65%), three defaulted (15%), and four cases failed.
- chloroquine + eritromicine (6 cases). Of these, two were cured (33%), and four who failed to respond
were treated with quinine (50% cured).

Fourteen cases who did not respond to initial chloroquine treatment were treated with quinine. Of these, the majority (10 cases, 71%) were cured. The 4 cases (29%) that did not respond were then treated with either a combined therapy of chloroquine and eritromicine (1 case cured), fansidar (1 case cured), 1 case re-treated with fansidar and then quinine, cured, and 1 case defaulted.

The remaining two non-responders to firstline chloroquine treatment received a combination therapy of chloroquine and erithromicine and were cured.

Examination in Ganda TFC

**Caconda TFC**

Thirty-five files were initially studied at the centre in Caconda. As in Ganda TFC, the majority (85%) comprised children between 6 and 59 months of age, and again, only this age group was included in the study (see figure 2).

For the 30 study children aged between 6 and 59 months, the standard protocol was applied and chloroquine used as first choice treatment.

Of the 30 cases treated with chloroquine, 18 failed to respond (60%), and 12 cases were cured (40%).

Of the 18 cases that failed to respond to chloroquine, two cases defaulted the TFC, and the remaining 16 cases were treated with fansidar. Of these, 10 were cured (63%) and 6 failed to respond (37%). These six cases were then treated with quinine where 3 defaulted, 2 were cured (67%), and 1 case failed (33%).

**Conclusions**

In this preliminary study we observed that most of the severely malnourished children aged between 6 and 59 months old, who were admitted at the TFCs of Ganda and Caconda, did not adequately respond to chloroquine treatment. While there was also a high degree of failure using fansidar, especially at the Ganda TFC, the profile of resistance differed between the two sites, and fansidar had a greater efficacy in Caconda compared to Ganda (63% versus 45% of patients cured). Treatment used as the third choice, quinine, presented a higher efficacy than chloroquine and fansidar in both TFCs. However, the number of cases treated in Caconda was too small to be representative, and the side-effects of this therapy (such as reducing appetite) need to be considered.
Given our results and the issue of resistance, we consider that combination therapy of drugs with low levels of resistance should be the first line of treatment for malaria. Since the absorption and bioavailability of several antimalarial drugs, including chloroquine and quinine, can be significantly impaired in patients with severe malnutrition\(^5\), increasing antimalarial drug bioavailability may reduce the risk of treatment failure due to poor drug absorption. Consequently, drugs with high bioavailability, such as artemisinin-based combinations, may be preferred.

A combination therapy with artesunate plus amodiaquine is now recommended by ACH in Angola, and is being implemented in both TFCs. A trial following this new treatment protocol will allow us to see how the management of severe malnutrition is influenced by malaria treatment in the TFC setting. Meanwhile, deeper study on malarial drug resistance in the malnourished is indicated, to detail more clearly the links between malaria and malnutrition.

For further information, contact Amador Gomez, Technical Director, Acción Contra el Hambre, Caracas 6, 1º 28010 Madrid, Spain. tel: +34 91 391 5300, fax: +34 91 391 5301, email: agomez@achesp.org


\(^2\)Report of the WHO Technical Consultation, Antimalarial Drug Combination Therapy, 13-17 November, 2001


\(^5\)Intestinal permeability-review, \texttt{http://www.ntmed.finers.edu.au/publications/inpress/kwashiorkor/chapter1.html}