Barriers to prompt and effective treatment of malaria in northern Sri Lanka

B. Reilley[1], R. Abeyasinghe[2] and M. Vincent Pakianathar[1]

1 *Medecins sans Frontieres, Colombo, Sri Lanka*
2 *Anti-Malaria Campaign (AMC), Colombo, Sri Lanka*

Summary

BACKGROUND For the past 18 years, northern Sri Lanka has been affected by armed ethnic conflict. This has had a heavy impact on displacement of civilians, health delivery services, number of health professionals in the area and infrastructure. The north of Sri Lanka has a severe malaria burden, with less than 5% of the national population suffering 34% of reported cases. Health care providers investigated treatment-seeking behaviour and levels of treatment failure believed to be the result of lack of adherence to treatment.

METHODS Pre- and post-treatment interviews with patients seeking treatment in the outpatient department (OPD) and focus groups.

RESULTS A total of 271 persons completed interviews: 54.4% sought treatment within 2 days of the onset of symptoms, and 91.9% self-treated with drugs with prior to seeking treatment, mainly with paracetamol. Self-treatment was associated with delaying treatment (RR 3.55, CI 1.23–10.24, $P = 0.002$). In post-treatment interviews, self-reported default was 26.1%. The main reasons for not taking the entire regimen were side-effects (57.6%) and disappearance of symptoms (16.7%). Focus groups indicated some lack of confidence in chloroquine treatment and prophylaxis, and scant enthusiasm for prevention methods.

CONCLUSIONS A number of factors contribute to a lack of access and a lower quality of care for malaria: lack of medical staff and facilities because of the fighting; lack of confidence in treatment, and perception of malaria as a routine illness. Prevention efforts need to take into account certain beliefs and practices to be successful.

keywords malaria, conflict, treatment-seeking behaviour, treatment access, prevention

correspondence Brigg Reilley, 721 Valley Drive, Manhattan Beach, CA 90266, USA. Tel./fax: +1 310 937 4770; E-mail: briggr@hotmail.com

Introduction

For the past 18 years, the northeast of Sri Lanka has experienced an armed conflict between the Sri Lankan armed forces and the separatist Liberation Tigers of Tamil Eelam (LTTE). So far more than 60 000 deaths are attributed to the conflict, and hundreds of thousands have been internally displaced within Sri Lanka or have fled abroad. Although front lines are subject to change, at the time of writing much of the north was under LTTE control. Using humanitarian convoys through an established aid corridor, the government continues to supply these areas with essential drugs, medical supplies and salaries for medical workers. The government seeks to supply only what is necessary for the civilian population, so that no surplus might be used by the LTTE. Hence, only the minimum is supplied, sometimes resulting in shortages of medical supplies. Distribution of supplies and salaries to the northern districts can be delayed by months.

The population of the LTTE-controlled region is estimated at 371 154 (Government Agents Situation Report April 2000), many of whom are internally displaced persons (IDPs). The IDPs are mainly former residents of the Jaffna peninsula who fled fighting in 1995–1997. The district hospitals in Kilinochchi and Mullaitivu, as well as other health units, have been destroyed in heavy fighting. Because of the conflict, many medical professionals have fled the area, and there is a severe shortage of qualified

staff. Persons in the region continue to move and resettle because of conflict-related reasons, such as an area being cleared of mines or a change in front lines.

Background

Malaria has been a major health problem in Sri Lanka for decades, as the disease's unstable nature on the island has caused several major epidemics. The prevalent parasite species are *Plasmodium vivax* (PV) (75% of reported infections) and *Plasmodium falciparum* (PF) (25% of infections). Most infections occur in the dry zone of the country, which also includes the districts in armed conflict.

The war has disrupted organized vector control activities in the area and limited accessibility to treatment facilities. These two factors, coupled with the displacement of large populations, have resulted in increased man–vector contact. In 1982, prior to the start of the conflict, 3001 cases of malaria were reported from the districts of Kilinochchi, Mullaitivu and Mannar, consisting of 2803 PV (93.4%) and 198 PF infections (6.6%). The 3001 cases represented 7.8% of the total 38 566 malaria cases reported from the island in 1982. In 2000, a total of 72 425 malaria infections were reported from the Kilinochchi and Mullaitivu districts alone, comprising 42 008 PV (58.0%) and 30 417 PF infections (42.0%). The burden of malaria in this area is severe, with an estimated population of less than 5% of Sri Lanka suffering 34.5% of national case burden.

Malaria is a leading cause of mortality in Mallavi, a principal town in Mullaitivu district. According to records from Mallavi Peripheral Health Unit, of 832 deaths recorded from 1997 to 2000, 143 (17.2%) involved malaria. The toll is highest in the rainy season, with 56% of malaria-related deaths since 1997 occurring between December and February.

National protocol for malaria in adults for PV infection is 3 days chloroquine (4 : 4 : 2) followed by 5 days primaquine in malaria-endemic areas, while 14 days is recommended for areas of low endemicity. For PF infections, it is 3 days chloroquine followed by 1 day primaquine. Fansidar plus primaquine is the second-line regimen. If these treatments fail, or are contra-indicated, quinine is administered. *De facto*, a modified protocol is used in the region, treating both PF and PV infections with 5 days chloroquine (4 : 4 : 2 : 2 : 2) and 5 days primaquine. Second-line treatment is often another regimen of chloroquine and 14 days of primaquine. Alternatively, the person is admitted to the hospital for treatment with quinine. Fansidar is very rarely used. Pregnant women receive malaria prophylaxis (2/weekly chloroquine). All care in government facilities, including the cost of medications, is free of charge.

In Mallavi, the outpatient department (OPD) has two full-time doctors who provide a combined total of about 10 000 consultations per month, and one microscopist working full time on OPD blood slides. A diagnosis is made on clinical grounds if symptoms are assessed to be evident malaria and patient flow is too heavy for the laboratory to cope. If the slide is positive, the patient goes to the Anti-Malaria Campaign (AMC) desk in the same building and receives antimalarial drugs. These are wrapped together in newspaper and verbal instructions given on how to take them, such as taking the drugs with food. The AMC advises them to return on the seventh day after treatment for a check-up if the diagnosis is PF.

Health professionals in Mallavi frequently noted possible treatment failure in patients diagnosed with malaria, believed to be attributable to lack of treatment adherence. To better understand treatment-seeking behaviour and treatment adherence, we conducted quantitative and qualitative research, examining prevention measures but not focusing on them (see annex). A therapeutic efficacy study to measure drug resistance is pending.

Prompt and effective care is paramount in treatment of malaria, and informal treatment or self-medication often leads to delays in seeking medical care (Miguel *et al.* 1998). In Sri Lanka, adults sought treatment quicker when qualified care was made more readily available (Konradsen *et al.* 2000). Self-treatment is a frequent reaction to suspected malaria (Mniyka *et al.* 1995; Ruebush *et al.* 1995; McCombie 1996). Compliance, or treatment adherence, an important element for a successful treatment outcome, has been documented to be under 50% in some communities (Denis 1998). Simpler drug regimens (Fungladda *et al.* 1998) and blister packs (Qingjun *et al.* 1998) can improve adherence. Reasons for non-adherence include adverse reactions and forgetting to take the drugs (Fungladda 1998; Yepez *et al.* 2000).

Methods

The AMC field office recorded total blood slides tested/ confirmed, malaria episodes treated, number of pregnant women, and number of children 5 years or younger. Private sources of malaria treatment in Mallavi filled out a simple tally sheet for the number of malaria treatments dispensed. The four private sources comprised two pharmacies, a private clinic that confirms all suspected malaria by blood slide, and one pharmacy with limited slide confirmation capability.

Treatment-seeking behaviour and adherence to treatment was assessed by an interview of patients. From 27 November 2000 to 31 January 2001, two interviewers spoke with selected malaria patients in the OPD of Mallavi

Peripheral Unit. Priorities for being interviewed were as follows: (1) all PF patients, (2) random selection of PV patients and (3) random selection of unconfirmed patients. After the AMC dispensed the antimalarial drugs, the person was referred to an investigator who conducted the interview in a private setting. Participants were given a ticket and asked to come back in 5 days. Those who did not return were followed up at their home address by bicycle or motorbike. All individuals admitted as inpatients for malaria were asked about their treatment-seeking. Data were analysed using EPI INFO 6.0, and variables checked for association using standard chi-square with level of significance at $P = 0.05$.

The 5-day chloroquine protocol was followed, rather than the 3-day national protocol. The 5-day regimen has been in use for several years in this locality, and changing to a 3-day protocol for the purpose of the study was thought to result in patients feeling they were receiving suboptimal care.

Focus groups were conducted in the towns of Puthukkudiyiruppu and Chemmalai. Discussions were held with health care workers, teachers, urban women, and rural women. Groups were asked about febrile disease, recognizing malaria and aspects of treatment and prevention.

Results

Government and private treatments

In the period December 2000 to January 2001, the Mallavi OPD dispensed drugs for 3587 malaria episodes. Of these, 1254 (35.5%) were confirmed by blood smear as 1227 (97.8%) PV and 27 (2.2%) PF infections. Of confirmed cases, 630 (50.2%) were male and 212 (16.9%) aged 5 years or younger. Forty-four persons (3.5%) were admitted as inpatients and 45 (3.6%) patients were pregnant women. One 19-year-old man with unconfirmed blood slide died from suspected cerebral malaria.

The private sites where malaria treatment can be obtained recorded 952 episodes treated during the same period. In total, private sites, pharmacies and Mallavi OPD dispensed 4606 treatments, of which the private sites' share was 20.1%. A set of 14 chloroquine and 10 primaquine tablets cost about 45 rupees at a pharmacy. The same drug regimen with medical consultation and blood slide confirmation cost about 130 rupees.

Treatment-seeking behaviour and adherence at the OPD

We interviewed 271 people, 242 (89.3%) PV, 19 (7.0%) PF and 10 (3.7%) unconfirmed cases. The respondents were 55.6% female, with a mean age of 22.6 years (range

8 months to 80 years). Of the adults (≥ 18 years), 91.4% had completed secondary school. Thirty participants (18.8%) were 5 years old or younger.

The mean distance from the patient's residence to the OPD was 5.8 km (range 1–75 km); 54.6% of patients resided within 3 km of the OPD and 90.6% within 10 km. Patients from further away tended to be visiting or travelling through Mallavi.

The number of days ill before seeking treatment ranged from 0.5 to 30, with 54.4% coming to the OPD within 2 days of feeling ill and 84.1% within 4 days. Although 80.1% went directly to the OPD, 12.2% had first consulted a family member or friend and 7.7% had consulted a pharmacist. Most patients (91.9%) had taken drugs for their symptoms prior to coming to the OPD, mainly paracetamol (95.6%), chloroquine (8.1%), aspirin (4.0%), and penicillin (2.0%). Sources of the drugs were a general shop (52.0%), home stock (36.3%), the pharmacy (10.9%) and a friend or family member (0.8%).

All patients received appropriate doses of chloroquine and primaquine (unless primaquine was contra-indicated as a result of young age or pregnancy); 91.3% also received additional drugs from the OPD, namely paracetamol (74.0%), phenergan (73.2%), aspirin (19.0%), penicillin (8.1%) and tetracycline (3.3%). Nearly all patients had had malaria before, with 94.4% stating that they had taken the chloroquine + primaquine regimen. About 64.7% considered the drugs very effective.

Variables were examined for association with delayed seeking of treatment. Delay was defined as coming to the OPD more than 2 days after the onset of symptoms. The most significant factor for delay was taking drugs prior to coming to the OPD (RR 3.55, CI 1.23–10.24, $P = 0.002$); there was no association with distance to OPD: 38.3% of those living within 1 km delayed treatment.

Follow-up interview

For the follow-up interview, 128 patients (47.2%) returned to the OPD, 132 (48.7%) were followed up by home visit and 11 (4.1%) were lost to follow-up. The time of follow-up ranged from 4 to 30 days after the malaria diagnosis (day 0); 51.4% were followed up by day 6 and 80.6% by day 10.

More than three-quarters (77.7%) attributed one or more side-effects to the antimalarial drugs, namely headache (42.3%), drowsiness/fatigue (26.7%), vomiting (22.2%), stomach ache/abdominal pain (9.9%), diarrhoea (7.4%), dizziness (4.5%) and rash (4.0%).

Non-adherence to treatment was defined as failing to take the full course of chloroquine or primaquine issued, or not taking the pills over a 5-day period. Sixty-eight of the

260 people followed up (26.1%) did not adhere to treatment; 82.3% of these did not take all primaquine tablets and 77.9% did not take all the chloroquine; 63.0% did not take the full regimens of either drug, and two persons consumed all tablets in less than 5 days. Table 1 lists the reasons for defaulting, the most common one being side-effects (57.6%).

Variables associated with non-adherence to treatment were examined. Neither the presence of side-effects nor any individual effect was significantly associated with non-adherence. No other demographic or treatment factor (i.e. age, receiving additional drugs, someone else responsible for treatment) was associated with non-adherence.

Focus groups

Malaria was generally acknowledged as the most common source of fever and a serious disease. It was always called by name and distinguished as normal malaria, 'brain' malaria and malaria with diarrhoea. The perceived severity of each type of malaria differed: 'brain' malaria was considered deadly, malaria with diarrhoea dangerous, and ''normal'' malaria about as perilous as a serious flu. Malaria is easily identified from experience with prior infection, based on the symptoms of fever with chills.

Treatment-seeking behaviour depended on transport and access to clinics, the patient's age and financial means. Treatment options were mainly government dispensaries and hospitals, private clinics and self-treatment from pharmacies or home stock. Self-treatment was cited frequently for adults, but generally participants said that for young children they would immediately seek proper medical care. The decision to self-treat depended on available transport to a clinic, and if they had the time to wait in the long queues at public clinics. Self-treatments were paracetamol for 2–3 days, or chloroquine, then seeking medical help if this did not alleviate the symptoms. Boiled coriander water was considered useful for symptom

relief. More affluent persons, mainly because of the time saved and the possibility that the government clinic may be out of drugs, used private clinics or doctors. In more rural areas, self-treatment, traditional healers, or a Sri Lankan Red Cross mobile clinic was used.

There were multiple motives for not taking any or all of the antimalarial drugs. The main reason was severe side-effects: chloroquine weakened the body, evidenced by a variety of symptoms such as vomiting, loss of appetite and hair loss, so it was thought wise to stop taking the drugs as soon as the malaria symptoms ceased. There was concern that chloroquine use for treatment or prophylaxis during pregnancy may do more harm than good. Examples cited included pregnant women who contracted malaria or had miscarried while on chloroquine prophylaxis. The toxic effects of the drug are well known, as local health units see cases of intentional overdose for abortion of an unwanted pregnancy or suicide.

Some people stopped treatment to save drugs for other family members, or because of the bitter taste of pills. Health care workers noted that sugar-coated chloroquine had been used a couple of years ago and was popular to the point of healthy children asking for extra tablets. Some participants showed a general lack of confidence in chloroquine and gave examples to illustrate that taking full treatment was no guarantee of health, citing acquaintances who had not taken all the pills did not get malaria for years afterwards, while others who took the full regimen experienced frequent attacks. Frustration was expressed at a lack of treatment options: if chloroquine failed, some patients said they were simply given more.

Prevention

Environmental interventions such as pesticide spraying, irrigation management, and improved quality of housing have been found to be effective in other parts of Sri Lanka. However, the applicability of such interventions in the northern region is limited. As areas become alternately accessible and inaccessible because of direct warfare and mining/de-mining activities, the population is somewhat mobile. Building materials and pesticides that are permitted to cross the front lines are extremely restricted to prevent their use by the LTTE for military purposes. Spraying is irregular and only done focally.

Bednet use was infrequent, with 73.1% never using a bednet, 10.7% rarely, 3.7% sometimes, and 12.5% always. Children $\leq$ 5 years had higher rates, with 43.8% reporting some bednet use. Five of the seven pregnant participants used a bed net.

In focus groups there was not much enthusiasm for prevention. Generally, personal interventions such as

Table 1 Follow-up, non-adherence to treatment, and reasons given

Follow-up interview completed	95.9% (260 of 271)
Did not take full treatment	26.2% (68 of 260)
Reasons for non-adherence (multiple answers possible)	
Side-effects ($n = 39$)	57.6%
Symptoms cured ($n = 11$)	16.7%
Forgot to take drugs ($n = 9$)	13.6%
Lack of food ($n = 6$)	8.3%
Save drugs for future illness ($n = 2$)	3.0%
Lost the drugs ($n = 1$)	1.5%
Drugs ineffective ($n = 1$)	1.5%

keeping the living area free of mosquito breeding areas and burning mosquito coils or neem leaves were not considered very effective. The subject of bednets was explored in greater detail. At about 700 rupees, cost is a significant barrier. However, some persons find bednets uncomfortable, and sleeping under them is too hot and stuffy. Getting in and out of bed at night, for example, to tend to small children, means the nets are often not re-closed when getting back into bed. A more significant obstacle is that bednets were not perceived to reduce the likelihood of getting malaria. The primary motive for bed net use appeared to be the comfort of keeping mosquitoes out rather than health reasons. However, it is common to buy small, semirigid bednets for children. These collapse like umbrellas when not in use, and cost about 300 rupees. Parents use these bednets for infants' health rather than comfort. However, the bednet bottom is uneven; thus gaps usually exist between the net and the bed/ground.

Discussion

This rainy season experienced the lowest number of cases of PF in years, attributed at least in part to the unusually low amount of rainfall. The Mallavi OPD serves mainly the town of Mallavi, so data from more remote households are under-represented. There is likely some observation bias; people who know they will be followed up are more likely to adhere to treatment. These considerations are believed to result in a possible overestimate of levels of adherence to treatment. Unconfirmed cases are also under-represented in this sample, and persons without confirmed malaria may have different adherence levels.

Focus groups provide qualitative data. These groups are not meant to find out how many persons engage in a certain behaviour or hold certain opinions, but to identify the kinds of behaviour and opinions that do exist and their possible reasons. The results of these discussions explore the range of knowledge, attitude and practices, but cannot be interpreted as being representative of a larger sample.

There are numerous barriers to prompt and effective care. Many of the factors that result in delayed or incomplete treatment are exacerbated by the ongoing conflict, while others are related to perceptions of chloroquine.

The quality of care is adversely affected by the increased demand for services with fewer resources. The time for an OPD consultation generally must be kept to less than 1 min. There are not enough microscopists to meet the need for blood slides. These factors hinder accurate diagnosis. A reliance on rapid clinical diagnosis can lead to use of chloroquine for non-malarial fevers, which in turn

can erode trust in the drug when it fails. Although Mallavi is usually well stocked (the OPD only lacked primaquine for 10 days in the year 2000), focus groups suggest that a lack of drugs is periodically a problem in delivering quality care. Improvements to the quality of care or access to care are extremely difficult during a civil war. Infrastructure improvements to bring the region to the level of the rest of Sri Lanka, such as more clinics, better roads, or increased transport service are not realistic goals now. Mobile clinics, such as those supplied by the Sri Lankan Red Cross, are one of the only possible interventions to address the access gap.

Training other necessary professionals such as microscopists is a critical need. Even with training, however, keeping the needed positions filled is difficult. In 1999, nine microscopists were trained in the region, and by the end of 2000 only three were still in working in the government system. No government training is done in the LTTE-controlled area, and non-governmental training (in this case by an international NGO) does not carry government accreditation. NGO-trained individuals receive casual labourer wages from the government, which is insufficient to sustain them in the posts.

Finally, the tendency not to use second-line treatment is not well understood. Reasons given by health professionals as to why fansidar is rarely used included side-effects, lack of availability, and that patients disliked it. Quinine, unless contra-indicated, is used in most cases of apparent treatment failure. Increased use of second-line treatment would be preferable, but reasons for the non-use of fansidar needs to be better explored.

Delays in seeking treatment may be related to decreased access to care. The influx of IDPs has resulted in greater needs, while the destruction of some clinics and hospitals has reduced capacity. Queues at the OPD are often hours long, which discourages utilization of health services. The private sector plays a significant role in meeting the needs of persons with malaria, but its accessibility is limited because of fees. Reduced access also creates greater transport needs. Transport difficulties are directly attributable to the deterioration of infrastructure from the 18-year conflict. Road conditions are deplorable; as an example, the approximately 100 km route from Mallavi to the front lines to the south requires a minimum of 4 h in a 4×4 vehicle and is prone to flooding. Motorbikes have been converted to kerosene consumption because of lack of diesel, but kerosene is too expensive for most people. The few buses that operate are not adequate for demand and are in poor condition. Walking and bicycling are the main modes of transport. Malaria incidence and mortality is highest in the rainy season, when transport is most difficult.

Self-treatment, usually with paracetamol, was highly associated with delayed seeking of care and appears to be encouraged by reduced access, with long waiting times being an important deterrent to coming to the OPD. However, other factors are also involved. The perception of malaria as a routine illness promotes taking paracetamol to alleviate the fever as an easy and adequate first response. There is aversion to taking chloroquine because of doubts about its efficacy and safety. Although side-effects were the foremost reason for not completing the treatment course, other reasons for non-adherence are similar to those for self-treatment, such as perception of severity of malaria. When side-effects occur and symptoms have subsided, there is strong incentive to halt treatment. The link between adherence to treatment and severity of disease is difficult to determine from this sample, as cases of PF were few. Persons suffering from PF may have different levels of adherence.

There are serious caveats before starting a programme to improve adherence by making chloroquine more appealing by packaging or taste. It is not clear from these data if better packaging of chloroquine, such as blister packs, would be effective in improving adherence by simplifying the regimen and improving the image of the drug. Any intervention should be started with a closely monitored pilot to assess impact on adherence in the short and longer term. Making chloroquine more palatable by sugar coating can pose health risks such as the possibility of accidental overdose by children. One alarming finding is that several patients did not complete treatment because of a lack of food to take with the drugs, and suggests that food insecurity is an important problem for some families.

Public awareness campaigns are possible to encourage people to promptly seek medical care, to adherence to treatment and prevention. It is important to bear in mind that any public awareness campaign will have to be carefully researched and planned to be sure the behaviour it is advocating is appropriate to the situation. For example, encouraging persons to attend government clinics is problematic when the system already cannot cope with demand. A campaign to increase awareness of the need to take the full regimen of chloroquine for successful treatment is necessary. However, this will require addressing the numerous reasons why chloroquine is viewed with scepticism and would need to emphasize that malaria is a serious disease for which paracetamol alone is not an efficacious treatment. Increasing awareness of the need for proper care of vulnerable groups appears to be the most feasible. Danger of malaria in pregnancy and young children appears to be recognized. Encouraging good prevention, prompt treatment seeking and adherence to treatment in these target groups is a priority.

Quantitative (survey) and qualitative (focus group discussions) data served complementary roles in identifying and understanding the correlation between delay in treatment-seeking behaviour and self-treatment. Triangulation of these data sources reinforced and clarified the results of this research.

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