

Imported quinine resistant *Plasmodium falciparum* malaria in Sri Lanka

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(Index words: Artemisinin, malaria contracted in Nigeria)

Introduction

Chloroquine still remains the first line drug for treatment of uncomplicated *Plasmodium falciparum* malaria in Sri Lanka. Sulfadoxine-pyrimethamine (S-P, Fansidar) is used as the main second line drug. Quinine is the drug of choice for complicated *P. falciparum* malaria.

Chloroquine resistant *P. falciparum* malaria in Sri Lanka was first reported from Dambulla in 1984 [1], and its spread has been identified and reported by the Anti-Malaria Campaign [2]. Resistance to chloroquine and sulfadoxine-pyrimethamine (S-P) has been infrequently reported in Sri Lanka in 1994 [3,4] and in 1996 [5]. More recently, chloroquine resistant *P. falciparum* malaria has been reported among the security forces personnel in the Mannar district [6].

Quinine resistant *P. falciparum* malaria has not yet been reported in Sri Lanka. Rare cases of RII and RIII resistance (failure to clear or failure to reduce parasitaemia in the first 7 days) to quinine have been documented in Thailand, Vietnam, tropical Africa and the Amazon region [7–9]. We report here for the first time, imported quinine resistant *P. falciparum* malaria encountered in Sri Lanka.

Case report

A 52-year old Sri Lankan gem cutter from Ratnapura, employed in Joss, Nigeria, returned to Sri Lanka via Dubai in May 2003, during the height of the SARS (severe acute respiratory syndrome) epidemic. Along the way, he developed high fever with chills, cough, vomiting and a confusional state, and was admitted to the Infectious Disease Hospital (IDH) at Angoda, with a suspicion of SARS.

At the IDH, the diagnosis of *P. falciparum* malaria was made on blood film examination. He was given a loading dose of quinine 20 mg/kg body weight by infusion over 4 hours followed by quinine 10 mg/kg 6-hourly thereafter. However, he developed respiratory distress, became more drowsy and was transferred to Sri Jaywardenepura General Hospital (SJGH).

On admission to the intensive care unit at SJGH, blood gas examination warranted immediate positive pressure ventilation. The Glasgow coma scale was 4. He was febrile, unconscious and jaundiced. There was no neck stiffness. The pupils were normal. Funduscopy was normal and

there were no retinal haemorrhages. The muscle tone was increased in all four limbs with generalised hyperreflexia. The liver was palpable. The diagnosis of *Plasmodium falciparum* malaria (PF) complicated by cerebral malaria and multi-organ failure was made.

Quinine infusion was continued with clarithromycin and ticarcillin-clavulanic acid 3.2 g intravenous 6-hourly for 7 days. In all, he received 5 days of quinine therapy in the recommended dose, intravenously. However, he remained febrile and daily blood films remained positive for asexual stage of *P. falciparum*. This indicated lack of responsiveness to quinine or quinine resistance.

The Anti-Malaria Campaign was contacted, and they advised artemisinin therapy. Artemisinin was administered two tablets twice daily up to 5 days. After 24 hours of starting artemesene, the temperature subsided and asexual parasitaemia disappeared.

He improved dramatically thereafter. Subsequently, he was given mefloquine 1500 mg in two equal divided doses 8 hours apart.

Discussion

Fortunately, quinine resistant *P. falciparum* malaria acquired in Sri Lanka has not yet been reported. This is probably due to the restricted use of the drug, since it is not a popular drug for importation by the pharmaceutical trade. However, quinine resistant *P. falciparum* can be encountered in people returning to Sri Lanka from the African continent or from south-east Asia. For complicated *P. falciparum* malaria acquired in Sri Lanka, intravenous quinine remains the first line drug.

The import of "Fansidar" is solely by the Anti-Malaria Campaign, and due to its restricted use, Fansidar resistant *P. falciparum* malaria is rare in Sri Lanka. Fansidar would not have been suitable for use in this patient who had severe and complicated *P. falciparum* malaria.

The minimum inhibitory concentration of quinine for *P. falciparum* in south-east Asia and tropical Africa has risen steadily. Thus, larger doses of quinine and combination with other drugs such as Fansidar, tetracycline and clindamycin are required for complete cure.

Analysis by molecular, genetic and biochemical approaches have shown that impaired uptake of chloroquine by the parasite vacuole is a common

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characteristic of resistant strains associated with certain recognised genetic mutations [8]. The mechanism of resistance to sulfonamides and sulfones involve mutations of dihydrofolate synthase (DHPS) [8]. The mechanisms of resistance to amino-alcohols (quinine, mefloquine and halofantrine) are still unclear [8].

As a result of increased international travel, overseas employment, tourism and globalisation, the chances of multi-drug resistant *P. falciparum* entering in Sri Lanka is likely. With the availability of the vector and the environmental conditions conducive to the growth of the parasite, the emergence of quinine resistant *P. falciparum* is imminent. Hence, the importance of quarantining exposed patients who return to Sri Lanka with features of malaria, and having a high degree of suspicion about existence of multi-drug resistant *P. falciparum* cannot be overemphasised.

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