Current Opinion

Time to switch from quinine

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Since 2006, following publication of the South East Asian Quinine verus Artesunate Malaria Trial (SEAQUAMAT) [1] involving 1461 patients, mainly adults, WHO recommends parenteral artesunate (for IV or IM use) as first choice treatment in areas of low-malaria transmission. The African Quinine versus Artesunate Malaria Trial (AQUAMAT) has now proved that parenteral artesunate is superior to quinine also in children with severe malaria [2]. The AQUAMAT trial represents the largest trial on hospitalized patients with severe malaria ever completed, with 5425 patients, equally divided in two treatment groups exposed to artesunate and quinine, respectively. Two thirds of the patients in each group were treated via intravenous route, while the remaining one third received their treatment by intramuscular administration. The overall case fatality rate was 22.5% lower in the artesunate group compared to the quinine group; moreover, the clinical profile was superior in the artesunate group. Based on this evidence, WHO revised guidelines for the treatment of Malaria [3], placing parenteral artesunate as first choice treatment for all malaria endemic areas. This evidence is further confirmed by a recent Cochrane meta-analysis that found an overall mortality reduction of 39% among adults and 24% among children treated with artesunate compared to quinine [4]. It is interesting to note that one of the early randomized controlled trials conducted in Africa to compare an artemisinin with quinine was reported from Sudan in 2002 [5]. A total of 77 children with cerebral malaria were randomly allocated to receive either artemether or quinine. The response to artemether was found to be slightly better than that of quinine, but the differences between the two groups were not statistically significant. The outcome in terms of cure rate, neurological sequalae and case fatality was also comparable. The findings are in line with the current WHO guidelines which regards quinine and artemether as comparable alternatives to artesunate.

Quinine is still the main anti-malarial treatment used for the management of severe malaria in the majority of endemic countries, and will continue to be used in many settings, as the availability of parenteral artesunate is still limited. Quinine requires multiple daily dose administrations, may induce hypoglycemia

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especially in pregnant women, and is associated with side effects. WHO has prequalified artesunate manufactured by Guilin Pharmaceutical Co. Ltd, Guangxi, China. This is the first injectable artemisinin-based formulation manufactured in China which has been prequalified. It is expected that following the change in the recommendations by WHO the demand for IV artesunate will progressively increase.

Some countries would prefer to have their own evidence before changing national treatment policies. While it is understandable that health professionals may want to make an evaluation in their own context, it is clear that the available evidence points to superiority of parenteral artesunate compared to quinine in severe malaria. Operational research is encouraged to guide implementation of the new policy. In rare condition like severe malaria recruitment of large numbers of cases requires multicentre and perhaps multicountry involvement as in SEAQUAMAT and AQUAMAT studies. Moreover, based on the international ethical guidelines [6] it could be unethical to delay implementation of the new guidelines and subject patients to further drug effectiveness trials.

By 2004 there was a general consensus among international experts about the need to switch from chloroquine as first-line treatment against falciparum malaria to the extent that organizations providing chloroquine for endemic countries were accused of medical malpractice in a famous letter published in The Lancet [7]. This lead to drastic revisions of the malaria treatment policies and practices of WHO and the Global Fund. In spite of the earlier and overwhelming evidence of chloroquine resistance in Sudan, the change of the first-line treatment was implemented as late as 2004-2006 [8]. The health consequences of this lag before switching to an effective treatment for a potentially fatal disease are obvious. We hope that the lesson has been learnt.

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