

QUININE (Comment)

Should quinine be used if artesunate is available ?

Quinine has long been the mainstay for the treatment on falciparum malaria, especially in Africa – the continent where young children are most severely afflicted by this debilitating, and often lethal, disease. Quinine is cheap and widely available. Most parasites remain generally sensitive to this long-used drug and, in areas where some degree of partial resistance seems to be developing, further secondary oral treatment (as outlined in the recently updated quinine monograph) will almost always effect a complete cure.

When oral treatment is possible: Treatment with oral quinine remains a very widely used strategy, especially in Africa, and it is relatively cheap. However it has a relatively bitter taste and use will not effect a complete cure unless the full seven day course is taken exactly as recommended, and evidence from a recent controlled trial (Achan *et al.*, 2009) suggests that, unless oral treatment with can be reliably supervised, treatment with just three days of artemether with lumefantrine is *much* more likely to eliminate the risk of early relapse. In subsequent correspondence Dr Höglund pointed out that the bitter taste of the quinine salt or the poor solubility of some formulations (Amin and Kokwaro, 2008) might well explain why quinine was less effective in the present study (only curative in 64% v. 96% of the children). He pointed out that the ethyl carbonate salt of quinine is as therapeutically effective as the more commonly used hydrochloride sulphate salt, and has a much less bitter taste (Jamaludin *et al.*, 1988). Other correspondents pointed out that current guidelines (WHO, 2006) stress that treatment with quinine should always be supplemented where possible with a short course of clindamycin, doxycycline, mefloquine or pyrimethamine and sulfadoxine (Fansidar®), as has been shown many times in the last 35 years (Hall *et al.* 1975).

Tablets containing 20 mg of artemether with 120 mg of lumefantrine are now becoming more widely available in Africa. They are now also available across Europe under the trade name Riamet® in Europe (where they currently cost 1€ each) and in North America under the trade name Coartem®. A more child-friendly formulation (in the form of an easily dispersible tablet) was also used in one recently published study from sub-Saharan Africa (Abdulla *et al.*, 2008).

When the child is too ill for oral treatment to be reliably effective: Quinine given IM still remains the mainstay of treatment for children with severe malaria in many parts of Africa, although there is little doubt that IV treatment is a better (and certainly a less painful option), while a meta-analysis of 10 small trials in moderately ill children has suggested that rectal quinine (if made less acidic by adjustment to a pH of 4.5) may be as effective as IV quinine (Eisenhut and Omari, 2009). Parental artemether is slowly becoming more widely available in most countries, and a number of studies have already shown that, even if mortality remains much the same as after treatment with quinine (van Hensbroek *et al.*, 1996; Murphy *et al.*, 1996; Cao *et al.*, 1997; Taylor *et al.*, 1998; Olumese *et al.*, 1999; Satti *et al.*, 2002; Huda *et al.*, 2003; Aceng *et al.*, 2005; Dorndrop *et al.*, 2005) there is little doubt that, as in adults, IV artemether clears parasites from the blood stream more quickly than IV quinine. Indeed there is already growing evidence that, in adults IV artemether or artesunate is a better treatment option (Jones *et al.*, 2009). Nevertheless the first, still unmet, challenge for those working in much of the developing world is currently to get most really ill children seen much more quickly in some setting where *any* form of treatment can be started.

In that connection, one further recent very large trial has shown that, if it is going to take at six or more hours for the child to reach a centre where any reliable parenteral treatment with IM (or, where possible, IV) quinine can be started, the insertion of a single 100 mg artesunate suppository into the rectum prior to transfer can halve the risk of death or permanent disability due to cerebral malaria (Gomes *et al.*, for the Study 13 Research Group, 2009). It is, of course possible that rectal quinine might be almost equally effective in this situation (Barennes, *et al.*, 2006) but no formal trial of any such strategy has yet been done.

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