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# Efficacy of artemisinin derivatives in treating severe malaria in children: A systematic review and meta-analysis

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## ABSTRACT

### Background

Evidence shows that the efficacy of intravenous quinine, which is the mainstay for treating severe malaria in children, is decreasing. Artemisinin derivatives are the potential replacement for quinine. Their efficacy compared to quinine in treating severe malaria in children is not well known.

### Objective

To assess the efficacy of parenteral artemisinin derivatives versus parenteral quinine in treating severe malaria in children.

### Search strategy

The Cochrane Central Register of Controlled Trials (The Cochrane Library Issue 4, 2005), MEDLINE (1966 to October 2005), EMBASE (1980 to October 2005), and LILACS (1982 to October 2005) were searched. Malaria researchers and a pharmaceutical company were contacted. In addition, conference proceedings were also searched.

### Selection criteria

Randomised controlled studies comparing parenteral artemisinin derivatives with parenteral quinine in treating severe malaria in children. All trials had to report mortality as an outcome.

### Data collection

After data were extracted, two individuals independently assessed the trial quality. In addition, information on adverse effects from the studies was also collected.

**Main results**

Eleven trials were selected (1455 subjects), nine of them from Africa and the rest from Asia. Allocation concealment was adequate in seven trials (1238 subjects). Overall there was no difference in mortality between artemisinin derivatives and quinine (Risk Ratio= 0.89, 95% confidence interval 0.71 to 1.1). There was no difference in mortality between adequately concealed and inadequately concealed /unconcealed trials (Risk Ratio = 0.93, 95% confidence interval 0.74 to 1.16 and Risk Ratio=0.66, 95% confidence interval 0.36 to 1.22). In Parasite Clearance Time (PCT), though there was no statistical difference between the two groups there was a tendency towards favouring the artemisinin derivatives (weighted mean difference among studies which reported PCT as mean was -4.76 with 95% confidence interval -9.68 to 0.17 and all three studies which reported PCT as median showed that artemisinin derivatives cleared parasites faster than quinine, each had $p<0.001$). However; when only trials with adequate concealment were considered this potential advantage disappeared. In exploring heterogeneity for PCT, it was shown that study settings (Asia versus Africa) might have been a cause for heterogeneity. The artemisinin derivatives resolved coma faster than quinine (weighted mean difference=-5.32, 95%CI: -8.06 to -2.59), but when only trials with adequate concealment were considered this difference disappeared. Other secondary outcomes i.e. Fever clearance time, Incidence of neurological sequelae, and $28^{th}$ day cure rate showed no significant difference between artemisinin derivatives and quinine. There was no enough data to make meaningful comparison of adverse effects between the two groups.

**Conclusions**

The available evidence suggests that parenteral artemisinin derivatives are as efficacious as quinine in preventing mortality from severe malaria in children.