Chemotherapy for Cerebral Malaria

*[Van Hensbroek MB, Onyiorah E, Jaffar S, Schneider G, Palmer A, Frenkel*J, *et al. A trial of artemether or quinine in children with cerebral malaria. N EnglJMed 1996, 335: 69-75].*

Cerebral malaria is the most serious complication of *Plasmodium falciparum* infection. Quinine remains the drug of choice since wide spread chloroquine resistance has been recorded. The mortality rate is still 10 to 30%, so there is an urgent need for more effective drugs which can easily be administered even at rural health centers.

hi this study which was conducted in Gambia, West Africa (a highly endemic area for malaria), intramuscular artemether and intramuscular quinine were compared in an open, randomized trial in patients suffering from cerebral malaria. These children who were 1 to 9 years of age were unconscious when brought to the hospital. Patients were considered for study if they had Blantyre coma score of 2 or less and sexual forms of *Plasmodium falciparum* were identified on a thick blood film. Those who regained consciousness after correcting hypoglycemia were excluded from the study. Patients were randomly assigned to artemether group or quinine group and received antimalarial regimen as shown in *Table I.* The end points of study were death in hospital, and residual neurological sequelae that persisted on long term follow up. The secondary end points were rates of clearance of parasite and fever, length of time to recovery from coma, and neurological sequelae at discharge and 1 month after admission.

A total of 576 children were randomly allocated to receive either artemether or quinine. Fifty nine (20.5%) of the 288 children treated with artemether died in hospital as compared to 62 (21.5%) of the 288 children treated with quinine. Among the 418 children analyzed at approximately five months, neurological sequelae were present in 7 (3.5%) of 209 artemether treated survivors and 11 (5.3%) of 209 quinine treated survivors. These differences were not statistically significant. No difference could be observed in any of the secondary end points. However, there were fewer local reactions at the injection site with

TABLE I-*Antimalarial Regimens for Artemether Group and Quinine Group.*

Artemether		
Initial	-	3.2 mg/kg
Afterwards	-	1.6 mg/kg daily for 4 days (Intramuscular in anterior thigh)
Quinine		
Initial	-	20 mg/kg
Afterwards	-	10 mg/kg 12 hourly for 5 days (Intramuscular in the anterior thigh, when patient was able to swallow, oral tablets were given).
On Follow up for Prophylaxis		
(After child regained consciousness) Treatment for both groups. Pyrimethamine 1.25 mg/kg and sulfadoxine 25 mg/kg (oral).		

artemether than with quinine. The authors concluded that artemether is as effective as quinine in the treatment of cerebral malaria in children.

Comments

Malaria is endemic in almost all parts of India. Every year about 2 million new cases are reported by the National Malaria Eradication Programme(l). *Plasmodium falcipafum* is highly pathogenic and is the cause of almost all deaths due to malaria. Cerebral malaria is the most serious complication of falciparum malaria. Loss of consciousness can occur with frightening rapidity and some children are already in deep coma by the time they reach hospital. Convulsions are frequent and status epilepticus may occur(2). Quinine so far remains drug of choice for cerebral malaria and ideally needs to given by intravenous infusion-a procedure that is often difficult to practice in young children in the setting of rural health centres. According to the World Health Organization (WHO), intramuscular route is equally effective in all respects on the cost of few local complications in the form of abscess formation(3). The present study again establishes the efficacy of intramuscular route of administration.

Artemether and artesunate are two derivatives of traditional Chinese antimalarial drug Qinghaosu (artemisinin). These derivatives are most rapidly acting and potent of all antimalarial drugs. These compound have activity against all malarial parasites including multidrug resistant strains. These drugs are presently indicated for the treatment of severe malaria caused by parasites with suspected resistance to quinine(4). It is apparent from this study that artemether is as effective as quinine in. treating cerebral malaria in children. It is simple to administer and had no apparent local or systemic side effects. Artemether is currently being evaluated in India at the Central Drug Research Institute, Lucknow and is likely to be available soon for our patients. Unfortunately, both artemether and quinine are relatively inefficient for eradicating the malarial infection in the body. In this study also, a large number of children who were free of parasitemia had parasites in their blood at one month follow up. So, the authors suggested that there is a need to provide continuous prophylaxis with pyrimethamine and sulfadoxine.

Hypoglycemia is particularly common in young children, in those with convulsions or hyperparasitemia and in patients with profound coma. It is easily overlooked clinically because the manifestations may be similar to those of cerebral malaria. Quinine is a potent stimulator of the secretion of insulin by pancreatic beta cells and is associated with an increased risk of hypoglycemia. In the present study also it was observed that quinine did contribute to hypoglycemia in a proportion of children with cerebral malaria. In an unconscious patient, glucose should regularly be given to present starvation hypoglycemia. It is most

conveniently provided as 5% dextrose in water infusion. If hypoglycemia occurs, it should be treated with an intravenous injection of 50% glucose (upto 1.0 ml/ kg) followed by slow intravenous infusion of 10% glucose to prevent recurrence of hypoglycemia(5).

Another important complication in children with cerebral malaria is convulsions, which may occur in more than 50% of patients. In this study, the artemether group had significantly increased incidence of convulsions, probably due to its potential neurotoxicity(6). A slow intravenous injection of diazepam (0.15 mg/kg body weight) or intramuscular injection of paraldehyde (0.1 ml/kg of body weight with a glass syringe) will usually control convulsions. Paraldehyde is specially suited at primary health centers because of absence of serious systemic side effects and a simple method of administration. The use of a single intramuscular injection of phenobarbital sodium, 10-15 mg/kg of body weight on admission, may reduce the incidence of convulsions(7).

A proportion of children (about 10%) who survive cerebral malaria have neurological sequelae which persist into the convalescent period. Sequelae may take the form of hemiparesis, cerebellar ataxia, cortical blindness, severe hypotonia, mental retardation, generalized spasticity, or aphasia(8).

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