Original Article

A comparative clinical trial of artemether and quinine in Cerebral Malaria

Sheraz Jamal Khan, Syed Munib

From Department of Medicine,
Gomal Medical College, Dera Ismail Khan
Correspondance: Dr Sheraz Jamal Khan

Received: July 6, 2005 Accepted: August 26, 2005

ABSTRACT

Objective: To compare artemether and quinine as treatment for cerebral malaria in hospitalized adult patients

Patients and Methods: Fifty cases of cerebral malaria who fulfilled the diagnostic criteria of WHO were placed at random into two groups of 25 patients in each group. These groups were named Group A and group B. Group A patients were treated with Quinine infusion and group B patients were treated with Artemether intramuscularly. Clinical features, temperature and laboratory detection of Falciparum were noted every twelve hours. Side effects were also noted and 12 hourly blood sugar was taken from all patients.

Results: In group A, twenty (80%) patients recovered completely and five (20%) died, while in group B, 21 (84%) patients recovered and four (16%) died. Only one patient (4%) in quinine group developed hypoglycemia at 12 hours. Mean disappearance time of Plasmodium from the blood of Group A was 36 hours and in group B, it as 24 hours. Mean time for regaining full consciousness with orientation in time space and person and no neurological deficit was 36 hours in both groups.

Conclusion: Quinine and artemether are equally effective in cerebral malaria. The side effects with Quinine seem to be negligible in this study. (Rawal Med J 2005;30:62-64).

Keywords: Cerebral malaria, artemether, quinine

INTRODUCTION

Worldwide, an estimated 300–500 million people contract malaria each year, resulting in 1.5–2.7 million deaths annually.[1] The most dreaded manifestation of Falciparum Malaria is cerebral malaria which, if untreated, has a very high mortality. The situation is further complicated by the widespread drug resistance which is quickly emerging to even the new drugs.[2] The strict definition of cerebral malaria requires the presence of Plasmodium falciparum parasitemia with a Glasgow Coma Scale score of 9 or less, and other causes ruled out.[3] In 1990, the World Health Organization (WHO) established criteria for severe malaria which was revised in 2000.[4] Severe malaria can lead to cerebral malaria and complications can develop rapidly and progress to death within hours or days.[5] In various studies, risk factors for severe malaria and death include age greater than 65 years, female sex (especially when associated with pregnancy), nonimmune

status, coexisting medical conditions, no antimalarial prophylaxis, delay in treatment, and severity of the illness at admission, such as coma, acute renal failure, shock, pulmonary edema, coagulation disorders.[6]

Intravenous quinine is currently the most widely used agent for the treatment of severe falciparum malaria. Both quinine and quinidine have narrow therapeutic windows and severe toxicities can result.[7] Although artemisinin derivatives clear parasites from blood about 20% faster than quinine dihydrochloride, improved survival was observed only in regions of South East Asia with recognized quinine resistance.[8] However, recovery from coma may be delayed and the incidence of seizures was higher than with quinine dihydrochloride. At present, artemisinin derivatives are recommended for treatment of quinine-resistant *P. falciparum* infections.[9] The aim of this study was to compare the efficacy of quinine and artemether, the two most frequently used drugs for cerebral malaria due to Plasmodium falciparum.

PATIENTS AND METHODS

This study was conducted at DHQ Teaching Hospital Dera Ismail Khan from January 2004 to December 2004. Only Falciparum positive cases who were deeply comatosed and fulfilled the criteria of WHO for cerebral malaria (unarousable coma, asexual Falciparum parasitemia and no other demonstrable cause of coma) were included in this study. Fifty cases of cerebral malaria were enrolled in the study at random during the one year time. The clinical features of all of these patients were equivalent. Pretreatment evaluation included a detailed physical examination, routine hematological and biochemistry analysis, chest radiography and a lumbar puncture with CSF examination.

Patients were assigned two groups of 25 patients in each group. These were named group A and group B. Group A patients were treated with Quinine dihydrochloride infusion in the dosage of 600mg in 500ml of 10% Dextrose water every 8 hours for at least seven days and group B patients were treated with Artemether in the dosage of 80mg intramuscular twice daily on the first day and then 80mg once daily for the remaining six days. Clinical features as well as temperature and laboratory detection of Falciparum was noted every twelve hours. Side effects were also noted and 12 hourly blood sugar was taken from all patients.

RESULTS

The demographic and baseline characteristics are shown in table 1. Nine (18%) of the patients died while the remaining 41(82%) completed the study. In group A, 20 (80%) patients recovered completely and five patients (20%) died, while in group B, 21(84%) patients recovered and four (16%) patients died. Only one (4%) patient in quinine group developed hypoglycemia at 12 hours but no other major side effects were noted.

Table 1. Demographic featuresof study population (n=50)

Patients	Group A Quinine group	Group B Artemether group	Total
Total No	25	25	50
Male/Female	14/11	13/12	27/23
Age			
Male			
Range:	20-50 Years	20-50 Years	20-50 Years
Mean:	29 Years	29 Years	29 Years
Female			
Range:	18-35 Years	18-35 Years	18-35 Years
Mean:	24 Years	24 Years	24 Years

Mean disappearance time of Plasmodium from the blood of group A was 36 hours and in group B, it was 24 hours. Mean time for regaining full consciousness with orientation in time space and person and no neurological deficit was 36 hours in groups (table 2). The patients who did not recover never gained consciousness and their coma worsened with time. One of these patients developed hypoglycemia during the 12 hours of treatment but later no hypoglycemia was found in him. The patients died during the first 48 hours of treatment. One of them died within twelve hour.

Table 2. Clinical and hematological response to quinine and artemether
:

Patients	Group A Quinine group	Group B Artemether group	Total
Number of patients	25(50%)	25(50%)	50(100%)
Number of patients recovered	20(80%)	21(84%)	41(82%)
Mean disappearance time of Plasmodium from the blood (in hours)	36 Hrs	24 Hrs	30 Hrs
Mean time for regaining full consciousness	36 Hrs	36 Hrs	36 Hrs
Deaths	5(20%)	4(16%)	9(18%)
Side Effects	1(4%)*	0(0%)	1(2%)*

* The side effect noted was hypoglycemia. This was the only side effect, which was monitored during the study.

DISCUSSION

Quinine is the standard drug used for the treatment of cerebral malaria. Artemether is a new product and claimed to be more effective in cerebral malaria. Both drugs showed comparable results in this study and is consistent with others published reports[10] and further studies confirmed these results.[11] Our study is comparable and almost equivalent to the study conducted earlier in Pakistan.[12]

Cerebral malaria treatment is considered equivalent to Quinine therapy and probably this concept has not changed over the years. It is fortunate that we have a comparable drug after so many years. It was a dangerous situation when Chloroquine resistance was reported from almost every part of the world and we were left with the only option of using quinine for cerebral malaria. Unfortunately enough no more than three drugs come in parenteral form for malaria and there are many situations in which oral therapy cannot be administered.

In conclusion, this study showed that Quinine and Artemether are excellent drugs and are comparable in their efficacy and both can be used in cerebral malaria with satisfactory results. These drugs, however, should mainly be reserved for cerebral malaria as their indiscriminate overuse can lead to resistance which will be a real dreaded situation as we are already left with only few drugs for malaria especially the dangerous cerebral malaria.

REFERENCES

1. White NJ: The assessment of antimalarial drug efficacy. Trends Parasitol 18: 865, 200
2. 2.

3. Hayton K, Su XZ. Genetic and biochemical aspects of drug resistance in malaria parasites. Curr Drug Targets Infect Dis 2004;4:1-10.

4. WHO. Management of severe and complicated malaria: a practical handbook. WHO, Geneva. 1991**.**

5. WHO. Severe falciparum malaria. Trans R Soc Trop Med Hyg 2000;94(suppl 1):S1–S90.

6. WHO. Severe and complicated malaria. Trans R Soc Trop Med Hyg 1990;84(suppl 2):S1–S65.

7. Bruneel F, Hocqueloux L, Alberti C, Wolff M, Chevret S, Bedos JP, et al. The clinical spectrum of severe imported falciparum malaria in the ICU: Report of 188 cases in adults. Am J Respir Crit Care Med 2003;167:684–689.

8. Bonington A, Davidson RN, Winstanley PA, Pasvol G. Fatal quinine cardiotoxicity in the treatment of falciparum malaria. Trans R Soc Trop Med Hyg 1996;90:305–307..

9. Pittler MH, Ernst E. Artemether for severe malaria: a meta-analysis of randomized clinical trials. Clin Infect Dis 1999;28:597–601.

10. Tran TH, Day NP, Nguyen HP, Nguyen TH, Tran TH, Pham PL, et al. A controlled trial of artemether or quinine in Vietnamese adults with severe falciparum malaria. N Engl J Med 1996;335:76–83.

11. 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 Engl J Med 1996;335:69-75.

12. Faiz MA, Rahman E, Hossain MA, Rahman MR, Yunus EB, Samad R, et al. A randomized controlled trial comparing artemether and quinine in the treatment of cerebral malaria in Bangladesh. Indian J Malariol. 2001;38:9-18.

13. Haider G, Chaudhry M A, Shah M A, Munir S M, Masroor Ahmed. Quinine compared to Artemether in adults with Cerebral Malaria JCPSP 2002;7:34-5.