A comparative clinical trial of artemether and quinine in Cerebral Malaria

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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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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 \textit{P. falciparum} infections.\textsuperscript{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 \textit{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 comatose 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 features of study population (n=50)

<table>
<thead>
<tr>
<th>Patients</th>
<th>Group A Quinine group</th>
<th>Group B Artemether group</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total No</td>
<td>25</td>
<td>25</td>
<td>50</td>
</tr>
<tr>
<td>Male/Female</td>
<td>14/11</td>
<td>13/12</td>
<td>27/23</td>
</tr>
</tbody>
</table>

Age

<table>
<thead>
<tr>
<th>Male</th>
<th>Range: 20-50 Years</th>
<th>Mean: 29 Years</th>
<th>Range: 20-50 Years</th>
<th>Mean: 29 Years</th>
<th>Total: 20-50 Years</th>
<th>Mean: 29 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>Range: 18-35 Years</td>
<td>Mean: 24 Years</td>
<td>Range: 18-35 Years</td>
<td>Mean: 24 Years</td>
<td>Total: 18-35 Years</td>
<td>Mean: 24 Years</td>
</tr>
</tbody>
</table>

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

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

* 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\(^\text{10}\) and further studies confirmed these results.\(^\text{11}\) Our study is comparable and almost equivalent to the study conducted earlier in Pakistan.\(^\text{12}\)

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**

2. 2.

