Analgesic Activity Of Artesunate By Central Mechanism In Experimental Animal - Model

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ABSTRACT

The present study was undertaken to assess the central analgesic effect of Artesunate in Swiss albino mice. The analgesic action in acute pain model was studied by the tail flick method. Thirty six swiss albino mice were divided into three groups of twelve animals (six males and six females) each and maintained under ideal laboratory conditions. Group I was taken as control and group II treated with Pentazocine (50mg/kg intraperitonially) and group III was treated with Artesunate (36.4mg/kg intraperitonially). In the present study, the effect of artesunate alone for its central analgesic activity has been evaluated. It was observed that Artesunate possess a significant (p<0.001) central analgesic activity. The central analgesic activity of Artesunate can be due to rise in the pain threshold and thus increase the capacity to tolerate pain as its activity has been compared with pentazocine.

KEYWORDS: Analgesic, Artesunate, central analgesic activity, Pain

INTRODUCTION

Malaria is a leading cause of mortality and morbidity in developing areas of the world. The treatment of multi-drug resistant Plasmodium falciparum malaria has posed great challenge to medicine [1].

Artemisinin and its derivatives (artesunate, Artemether, Arteether, & Hydroartemisinin), obtained from Artemesia annua have been used against multidrug- resistant strains of P.falciparum with good tolerability and lack of significant adverse effects. Artesunate, one of the most widely used artemisinin compounds, is a water soluble hemisuccinate derivative given parenterally either by intravenous or intramuscular injection [2]. Artesunate at lower dosage levels in animals had no significant systemic pharmacological effects, i.e. artesunate had a relatively high selectivity as an antimalarial. However, at higher dosage levels there was an appearance of sedative effect, lowered movement of synchronism, elevation of tolerated lack of oxygen, lowered body temperature, analgesia, muscle relaxation, tremor, convulsions, depressed respiration and heart beat, lowered blood pressure, and depressed activity of the gastrointestinal tract[3].

An analgesic (also known as a painkiller) is any member of the group of drugs used to relieve pain
Analgesic drugs act in various ways on the peripheral and central nervous systems; they are distinct from anesthetics, which reversibly eliminate sensation [4]. The analgesic action of artesunate by peripheral mechanism has been already studied [5].

The present study was undertaken with the objective to investigate the analgesic activity of artesunate by central mechanism in experimental animal model.

**MATERIALS AND METHODS:**

Animal ethical committee approval was obtained from Yenepoya University before conducting the experiments.

**ANIMALS:** Swiss albino mice weight 25-30 g, 12 in each group (6 males & 6 females). Animals were acclimatized under standard laboratory condition and were kept in 12hr day and night cycle before the start of the experiment. Animals were handled carefully according to Committee for the purpose of Control and Supervision of Experiments on Animals (CPCSEA) guidelines.

**DRUGS—**

i. Inj. Pentazocine

ii. Inj. Artesunate, Supplied by Yenepoya Medical College Hospital Pharmacy, Mangalore

**Analytic activity**

Analgesic activity of Artesunate was studied by tail flick method. Before the study, Swiss albino mice were screened for sensitivity test by placing the tip of the tail on the radiant heat source. Any animals that held to withdraw its tail in 5 second were rejected from the study. The selected animals were divided into three groups of 12 (6 + 6) mice each (Table 1). Each animal of the groups received distilled water orally, standard drug and test drug intraperitonially. Analgesia was assessed with a tail flick apparatus (Analgesiometer). The basal reaction time was measured initially and another set of four measures were taken as 15, 30, 45 and 60 minutes interval and the reaction of the animals considered as the post – drug reaction time. A cut-off period of 10 sec was observed to prevent tissue damage of the tail of the animals [6] [7].

**Statistical analysis**

All the values were statistically analyzed by one-way analysis of variance (ANOVA) followed by Tukey-Kramer multiple comparison test. All values are expressed as mean ± SEM. P <0.05 was considered to be significant.

**RESULTS**

Artesunate group shows a considerable analgesic activity in comparison with the control mice group (Table 2). Analgesic activity of Artesunate treated group is comparable to Pentazocine treated group.

**Table 1:** Shows division of selected animals into 3 groups of six mice each, the dose for each group and the number of days to be housed.

<table>
<thead>
<tr>
<th>Group</th>
<th>Drug</th>
<th>Animals</th>
<th>Male</th>
<th>Female</th>
<th>No. of days animals were housed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>Distilled Water (p.o)</td>
<td>Swiss albino mice</td>
<td>6</td>
<td>6</td>
<td>10</td>
</tr>
<tr>
<td>Group II</td>
<td>Pentazocine (50mg/kg i.p)</td>
<td>Swiss albino mice</td>
<td>6</td>
<td>6</td>
<td>10</td>
</tr>
<tr>
<td>Group III</td>
<td>Artesunate (36.4mg/kg i.p)</td>
<td>Swiss albino mice</td>
<td>6</td>
<td>6</td>
<td>10</td>
</tr>
</tbody>
</table>
Table 2: Shows analgesic activity of artesunate by tail flick method

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Withdrawal of tail in seconds</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (DW) (p.o)</td>
<td>2.666±3.985</td>
<td>--</td>
</tr>
<tr>
<td>Artesunate (A1) (36.4 mg/kg, i.p)</td>
<td>12±0.7385</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>Pentazocine (50mg/kg, i.p)</td>
<td>13.5±2.87</td>
<td>p&lt; 0.001</td>
</tr>
</tbody>
</table>

n = 12, p.o – Per oral, I.P – Intraperitonial, DW-Distilled water.

DISCUSSION

Malaria is an important tropical mosquito-borne infectious disease. Headache is an important presentation in malaria, either cerebral type or not. The cytokine is believed to be an important factor leading to headache in acute malaria [8]

In one of the studies both lamivudine and artesunate were evaluated for peripherally mediated analgesia. Artesunate demonstrated significant analgesic property (p<0.05) compared to vehicle control in the acetic acid induced writhing reflex model in mice. The effect exhibited was inhibited in the presence of lamivudine, although the mechanism by which this occurred is not currently known. Inhibition of acetic acid induced writhing has been used to evaluate peripherally mediated analgesia [9] [10] and thus it was shown that artesunate possesses peripherally mediated analgesia although centrally acting drugs have been known to inhibit acetic acid induced writhing.

In our study there is a significant increase in the reaction time for tail flick method indicated the analgesic effect of artesunate and may elucidate the involvement of central mechanism in analgesic action. Analgesic effect mediated through central mechanism indicates the involvement of endogenous opioid peptides and biogenic amines like 5HT [11] [12]. From the results of the present study it can be inferred that apart from peripheral analgesic activity, Artesunate also possess analgesic activity by central mechanism in the dose of 36.4mg/kg intraperitonially.

CONCLUSION:

The results of the present study shows that Artesunate possess analgesic activity by central mechanism, and require further studies to establish its exact mechanism of action as well as its therapeutic value as an analgesic especially in malarial patients who is presenting with headache.

REFERENCES:


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