INTRODUCTION

Pain as a feeling or suffering is the most common symptom encountered in clinical practice all over the world. It is an unpleasant, sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage. NSAIDs and opioids are the most potent and commonly used group of established analgesic but their use is associated with a greater degree of adverse drug reactions. Since treatment of pain, especially the neuropathic pain, continues to be a challenge, a variety of drugs like Anticonvulsants, Gabapentin, Tricyclic Antidepressants have been evaluated from time to time as newer unconventional analgesic drugs. Some of these drugs are being empirically used, the rationality of their use for visceral tonic pain is still ill defined. They show variable effect on animal pain models (both phasic and tonic pain).

Evaluation of drugs in tonic pain models are uniformly standardized and well established and they have been in use for many years. So the present study was planned to verify the effects of Gabapentin with conventional analgesics in tonic visceral pain models of writhing test.

MATERIALS AND METHODS

Animals used
a) Adult Albino mice of either sex, weighing 18-30 g

Drugs

The following drugs were used to evaluate their antinociceptive effects in our study. The drugs were given per orally (p.o), 1 hour before the experimentation. The control group of 6 animals was run simultaneously and given saline double deionized water per orally (p.o). All the experiments were done at the same time in the morning hours on all days of experimentation.

Drug Doses

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
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<tbody>
<tr>
<td>Gabapentin</td>
<td>50mg/kg</td>
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<tr>
<td>Tramadol</td>
<td>10mg/kg</td>
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</table>

Commercial preparations of these drugs have been used. Gabapentin was suspended in 5% acacia & double deionized water. All drugs were administered per oral by gavage.

Procedures: For antinociceptive evaluation

Writhing test For the writhing test 0.55% acetic acid solution was prepared and injected i.p to the mice. Mice were placed individually into glass beakers and 5 minutes were allowed to elapse. The test drug was injected intraperitoneally to the mice. The mice were observed for a period of 10 min and the numbers of writhes were recorded for each animal for a period of 30 minutes. The animals reacted with a characteristic stretching behavior, which is called writhing. Treatment groups were compared with appropriate control groups using ‘student t-test’.
RESULTS

Writhing test

The Writhing test in mice which denotes inflammatory and visceral pain, revealed that tramadol (used as positive control) produced significant decrease in writhes in comparison with control (p < 0.01).

A significant reduction in number of writhes (p 0.05) was also found in the gabapentin pre-treatment group. (Table I)

<table>
<thead>
<tr>
<th>Group</th>
<th>Dose and Route of Administration of drugs</th>
<th>No. of Albino Mice</th>
<th>No. of Writhes</th>
<th>Mean ± SE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (NS)</td>
<td>0.09% p.o</td>
<td>6</td>
<td>40.00 ± 1.81</td>
<td></td>
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<tr>
<td>Tramadol</td>
<td>10 mg/kg p.o</td>
<td>6</td>
<td>32.33** ± 1.59</td>
<td></td>
</tr>
<tr>
<td>Gabapentin</td>
<td>50 mg/kg p.o</td>
<td>6</td>
<td>37.33* ± 1.48</td>
<td></td>
</tr>
</tbody>
</table>

**p < 0.01 vs. control values  *p <0.05 vs. control values

DISCUSSION

In the writhing test, tramadol showed significant analgesia, gabapentin also produced significant analgesic effect, though less in comparison to tramadol.

Writhing test in mice denotes inflammatory and visceral pain. Tramadol (used as positive controls) produced significant decrease in writhes in comparison with control (p < 0.01). Tramadol produced significant antinociceptive effect in writhing test as observed in a previous study whereby tramadol, 5 mg/kg & 10 mg/kg, i.p. produced a marked decrease in the number of writhes induced by acetic acid (1%v/v), suggesting a strong antinociceptive effect6. Further, in another study, tramadol 2.09 - 4.31 mg/kg, i.p. induced a dose dependent inhibition of the writhing response when administered to mice7.

Tramadol is an atypical opioid agent that also modulates the monoaminergic pathway8 and acts on central pathways of pain to modulate pain perception and reaction to pain. Its weak opioid agonist activity is mainly due to its active metabolite i.e. o-desmethyl tramadol. Earlier studies with Tramadol 10 mg/kg, i.e. have produced significant analgesic activity in hot plate and paw pressure test and p-phenyl benzoquinone induced writhing test9. Further, Tramadol, 1.7 mg/kg, p.o. & 19.5 mg/kg, s.c. produced dose related antinociception in rat in the 'air induced abdominal constriction’ & ‘hot plate’ tests respectively10, which further establishes the strong antinociceptive influence of tramadol in animal models of visceral and phasic pain a good candidate for positive control in present study.

In writhing test, in present study, Gabapentin pre-treatment also produced significant decrease (p>0.05) in number of writhes. In an earlier study, Gabapentin in a dose of 100 mg/kg, i.p. & 70 mg/kg, i.p. reduced acetic acid (0.6% & 0.75% v/v respectively) induced nociception9,10.

The very fact that Gabapentin showed significant pain relief in writhing test indicates that Gabapentin is a useful drug for neuropathic as well as inflammatory pain where central sensitization assumes a key role. Gabapentin which is a structural analogue of GABA and acts by binding to a subunit of voltage gated Calcium channel.
channel in the brain reverses not only the central component of pain but also its peripheral component by suppressing ectopic discharges in the peripheral nerves as has been documented earlier, where GABA<sub>A</sub> and GABA<sub>B</sub> receptor agonists inhibit Pain due to substance P while GABA<sub>A</sub> agonists decrease NMDA induced nociception<sup>11,12</sup>. In an another study the significant effect of Gabapentin (p>0.05) in Writhing model also throws light on peripheral mechanisms involved in antinociceptive effect of Gabapentin<sup>9</sup>.

To conclude, Gabapentin can act as an antinociceptive agent by in different kinds of pain than one and makes it an interesting drug for further evaluation and research for painful conditions unresponsive to conventional drugs and also for breaking the vicious cycle of Chronic pain that self perpetuates in neuropathic pain syndromes.

REFERENCES