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RESEARCH ARTICLE

COMPARATIVE EFFICACY OF GABAPENTIN A CONVENTIONAL ANTICONVULSANT WITH CONVENTIONAL ANALGESIC TRAMADOL IN VISCERAL PAIN MODEL OF RODENTS

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ABSTRACT

Carabmazepine is an established drug for trigeminal neuralgia while gabapentin has been tried in postoperative pain but its effectiveness in visceral pain and when compared to conventional analgesics needs to be evaluated.The present study was planned to study the analgesic effects of gabapentin in animal pain model of visceral nociception like writhing test and to compare it with conventional analgesic tramadol. This study has been carried out for evaluation of role of gabapentin in visceral nociception in mice . In the writhing test, a significant reduction in number of writhes have been observed in pretreated groups of mice reflects antinociceptive efficacy of gabapentin in acetic acid induced visceral nociception

Key Words- writhing test, visceral nociception, tramadol, gabapentin

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[1].

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[1]). 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

Gabapentin[2]	50mg/kg
Tramadol[3,4]	10mg/kg

Commercial preparations of these drugs have been used. Tramadol was dissolved in saline as it is water soluble. Gabapantin was suspended in 5 % acacia & double deionized water. All drugs were administered per oral by gavage.

Procedures: For antinociceptive evaluation[5]

Writhing test For the writhing test 0.55% acetic acid solution was prepared and injected i.p to the mice [3]. 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[6]. 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)

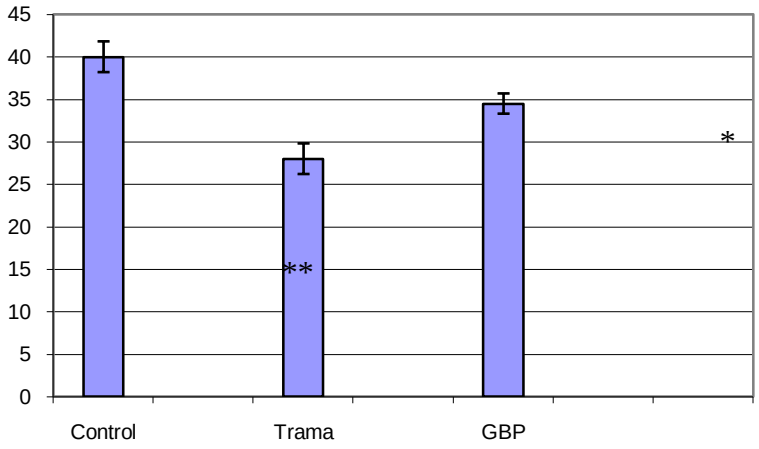
Table 1:

Writhing test: Pain was induced by injection of 0.55% acetic acid (0.55% given as .01ml/gm i.p) in the peritoneal cavity of mice. Both test and control drugs was administered 1 hr before giving acetic acid (i.p) in mice, abdominal contractions (writhes) were recorded after 5 min of injected acetic acid till 30 min.

Animals were divided into four groups of six animals each

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

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



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

Fig I: Effects of drugs on acetic acid (0.55% given as .01ml/gm i.p) induced visceral nociception in albino mice

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 effect[6]. 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 mice[7].

Tramadol is an atypical opioid agent that also modulates the monoaminergic pathway[8] 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.v. have produced significant analgesic activity in hot plate and paw pressure test and p-phenyl benzoquinone induced writhing test[3]. 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 respectively[4], 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 nociception[9,10].

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 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 $GABA_A$ and $GABA_B$ receptor agonists inhibit Pain due to substance P while GABAA agonists decrease NMDA induced nociception[11,12]. 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[9].

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

1. Abrol s, Kansal S, Agarwal A,Agarwal R,Goel T. Antinociceptive evaluation of anticonvulsant gabapentin with a conventional nonopioid analgesic in phasic and tonic animal model of acute and chronic pain.Int J Basic Clin Pharmacol, 2014 Aug;3(4):623-26.
2. Field MJ, Oles RJ, Lewis AS, McCleary S, Hughes J, Singh L. Gabapentin (neurontin) and s-(+)-3-isobutylgaba represent a novel class of selective antihyperalgesic agents. Br J Pharmacol, 1997;121:1513-22
3. Assi D, Azim A, Rahman A, Mahran S. Analgesic effects of tramadol-diclofenac combination and their interaction with psycostimulant drugs in mice and rats. Eur J Pharmacol, 1996;312:132-8.
4. Raffa RB, Friderichs E, Reimann W, Shank RP, Codd EE, Vaught JL. Opioid and nonopioid components independently contribute to the mechanism of action of tramadol, an atypical opioid analgesic. J Pharmacol Exp Ther, 1992; 260: 275-85.
5. Vogel HG, Vogel WGH, editors, Drug discovery and evaluation-pharmacological assays. 2nd ed. New York: Verlog Springer publication;1996.
6. Jha PK, Mazumdar B, Bhatt JD. Analgesic activity of venlafaxine and its interactions with tramadol, celecoxib and amlodipine in mice. Ind J Pharmacol 2006; 38: 181-4.
7. Christian D, Miranda HF, Raquel P, Mases A, Eulalia P. Synergistic interaction between dexamethasone and tramadol in a murine model of acute visceral pain. Fundamental Clin Pharmacol 2007; 21: 515-20.
8. Miranda HF, Pelissier T, Pinardi G. Involvement of adrenergic, serotonergic and opioid mechanisms in tramadol –induced antinociception in mice. Analgesia 1999; 4: 1-7.
9. Feng Y, Cui M, Willis WD. Gabapentin markedly reduces acetic acid induced visceral nociception. Anesthesiology 2003; 98: 131-9.
10. Petrovic RMS, Tomic MA, Vuckovic SM, Paranos S, Ugresic ND, Prostran MS, et al. The antinociceptive effects of anticonvulsants in a mouse visceral pain model. Anesth Analg 2008; 106: 1897-903.
11. Heughan CE, Sawynok J. The interaction between gabapentin and amitryptyline in the rat formalin test after systemic administration. Anesth Analg 2002; 94: 975-80.
12. Field MJ, Hughes J, Singh L. Further evidence for the role of the alpha2 delta subunit of voltage dependent calcium channels in models of neuropathic pain. Br J Pharmacol 2000; 13: 282-6.

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