Journal of Pharmaceutical and Scientific Innovation
www.jpsionline.com
Research Article

# ANALGESIC EVALUATION OF NOVEL ANTICONVULSANT WITH A CONVENTIONAL ANALGESIC IN DUAL PAIN MODEL OF RAT

Dhanesh Kumar[1], Saurabh Kansal[2]*, Priti Saxena[3], Kalpana Chauhan[4], Abhishek Aggarwal[5]
[1]Department of General Surgery, Subharti Medical College, Meerut, U.P., India
[2]Department of Pharmacology, Subharti Medical College, Meerut, U.P., India
[3]Department of Anatomy, Subharti Medical College, Meerut, U.P., India
[4]Department of Microbiology, Subharti Medical College, Meerut, U.P., India
[5]Department of Ophthalmology, Venkateshwara Institute of Medical Sciences, Gajraula, U.P., India
*Corresponding Author Email: kansalsaurabh513@gmail.com
**DOI: 10.7897/2277-4572.033150**
Published by Moksha Publishing House. Website www.mokshaph.com


Received on: 05/05/14 Revised on: 10/06/14 Accepted on: 20/06/14

**ABSTRACT**
Gabapentin and carbamazepine like anti epileptics are being used now a days to treat a number of diseases associated with neuropathic pain. The aim of this study is to observe whether novel anticonvulsants are able to produce analgesic response in pain conditions of acute and chronic type. This study observed the analgesic effect of lamotrigine in rats by biphasic nociceptive pain model of formalin test and compared its potency with a conventional opioid analgesic tramadol. Per oral administration of lamotrigine produced no significant effect on early phase response of formalin test but significantly suppressed the late phase response. We conclude that lamotrigine has antinociceptive effect in chronic inflammatory pain as seen by its effect on late phase of formalin test while tramadol has antinociceptive effect both on acute and chronic inflammatory pain.
**Keywords:** Lamotrigine, nociception, formalin test, tramadol

## INTRODUCTION

The principal objective of the treatment of pain is to remove or abolish the cause of pain. But it is not always possible to do so; analgesics are used for the symptomatic treatment of pain. Pain 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 drugs in treatment of pain, but their use is associated with a greater degree of adverse drug reactions and abuse liability[2]. Recently, Gabapentin and Carbamazepine like anticonvulsants are being widely used for postoperative pain and trigeminal neuralgia.[3] Other anticonvulsants are also being tried as newer nonconventional analgesic drugs that are expanding day by day. There is no comparable data available, whereby these drugs could be compared. So the aim of this study is to examine the antinociceptive effects of lamotrigine in dual pain model of rat and compared its antinociceptive effects with conventional analgesic tramadol.

## MATERIALS AND METHODS

Animal used: Adult albino rats of either sex, wt 150-200 g have been utilized for these experiments.
Ethical clearance no. HIHTPHARMA/I-1/2006/338

### Drugs

The following drugs have been used to evaluate their antinociceptive effects in each group of 6 animals, given per oral 1 h before the experimentations. There has been a control group of 6 animals, run simultaneously, and given saline/vehicle p.o. as per the experiment. All the experiment was done at the same time in the morning hours on all days of experimentation.

| | |
|---|---|
| Lamotrigine | 50 mg/kg[4,5] |
| Tramadol | 10 mg/kg[6,7] |

Commercial preparations of these drugs have been used. Lamotrigine and control drug tramadoL has been dissolved in saline as they are water soluble. Both drugs were administered p.o. by gavage in a volume of 1.0 ml/kg in rats.[8]

### Procedure for antinociceptive evaluation

### Formalin Test

The formalin test was used as the dual model of acute and chronic inflammatory pain. Formalin has been characterized by the occurrence of two characteristic phases of increased pain sensitivity in rats. The first phase was of 0-15 minutes and phase second phase was of 45-75 minutes. Rat was administered 0.05 ml of 10 % formalin into the dorsal portion of the front paw. The test drugs was administered orally and scored according to a pain scale. Pain has been quantified by counting the incidence of spontaneous flinches, shakes and jerks of the formalin injected paw. Number of leg raising [LR], licking and biting [LB] were measured for the two phases as end points. Analgesic response or protection has been indicated if both paws are resting on floor with no obvious favoring of injected paw. Treatment group was compared with appropriate control groups using "student t test".[9]

## RESULT

In the first phase of leg raising [LR] formalin test, tramadol produced significant decrease in leg raising [$p < 0.05$], of experimental antiepileptic drug produced no any significant effect on leg raising in comparison to control values (Table 1). In the first phase of licking and biting [LB], positive control tramadol again produced significant decrease [$p < 0.02$] than control values while lamotrigine had no effect. In the second phase of leg raising [LR] tramadol and lamotrigine produced significant decrease [$p < 0.05$] as compared to control. In the licking and biting episodes of second phase also tramadol and lamotrigine exert significant

effect [p < 0.02] in comparison to control in licking and biting and leg raising response. Decrease observed in licking and biting [LB] with tramadol was more [p = 0.001] as compared to control values than with experimental antiepileptic drug [p < 0.02] versus control values.

**Table l: Analgesic Effects of Experimental Drug Lamotrigine and positive controls Tramadol on Rats in Formalin Test**

| Group | No of Albino Rats | Dose and Route of Administration of drugs | Raising Foot [Mean ± SE] | | Licking and Biting [Mean ± SE] | |
|---|---|---|---|---|---|---|
| | | | First Phase | Second Phase | First Phase | Second Phase |
| Control | 6 | 0.09 % p.o. | 12.9 ± 1.8 | 5.9 ± 0.2 | 25.0 ± 4.0 | 18.6 ± 1.8 |
| Tramadol | 6 | 5 mg/kg p.o. | 5.3 ± 2.2* | 2.8 ± 1.3** | 7.9 ± 1.2** | 6.1 ± 0.5*** |
| Lamotrigine | 6 | 50 mg/kg p.o. | 12.9 ± 3.6 | 3.1 ± 0.3* | 20.7 ± 3.0 | 7.9 ± 0.7** |

*p < 0.05 vs control values, **p < 0.02 vs control values, ***p = 0.001 vs control values

## DISCUSSION

The present study was done to evaluate the antinociceptive effect of the novel newer antiepileptic lamotrigine on biphasic animal pain models i.e. phasic pain model [tail flick by radiant heat method] and tonic inflammatory pain model [formalin test] with the help of conventional analgesic drugs i.e. tramadol which was used as positive control in rats. Tramadol 10 mg/kg, p.o. produced significant analgesic effect in both phase 1 and 2 of formalin test in present study. In an earlier study, tramadol 10 mg/kg, i.v. produced significant analgesic effect in formalin test when given alone or in combination of NSAIDs[10]. In another study, tramadol, 0.5-2.0 mg/kg, i.p. [intraperitoneal] produced dose dependent significant analgesic effect in both phase 1 and phase 2 of formalin test in mice[11]. In the present study in formalin test, lamotrigine produced significant effect in second phase but not in first phase of formalin test. In a previous study, lamotrigine [4-265 nmol, i. t. (intrathecal)] dose dependently inhibited only the second phase [ED 50 = 28 nmol, i. t.] but not first phase.[12] In yet another study, lamotrigine [50-400 microgram, s.c.] significantly reduced number of flinches during phase 2 while significant effect on phase 1 was observed only at a very high dose of 400 microgram s.c.[13] The first and second phase of formalin test are generally believed to reflect excitation of peripheral afferent nociceptors and central sensitization, respectively[14]

## CONCLUSION

Evaluation of antinociception in acute and chronic pain was done with the help of standard method of formalin test in albino rats. The test drug lamotrigine did not produce any significant effect on phase 1 denoting acute pain while in 2 phase which denotes prolonged inflammatory pain, lamotrigine produced significant antinociceptive effect. Based on the present study we concluded that newer anticonvulsant lamotrigine, has antinociceptive effect in chronic inflammatory pain model but does not affect acute nociception in animals, so the novel anticonvulsant lamotrigine could be effective in clinical conditions associated with chronic inflammatory pain in humans also.

## REFERENCES


1. Kansal S, Kalra J, Dhasmana DC, Singh M, Goutham C. The antinociceptive effects of orally administered novel antiepileptic in rat models of acute and chronic pain. Journal of Advance Research in Biological Sciences 2012; 4(4): 345-49.
2. Fields HL. Pain Free: Modern Drugs and Neuropathic Pain; 2014.
3. Maizes M, Mccarberg B. Antidepressant and antiepileptic drugs for chronic noncancer pain. Am Fam Physician 2005; 71: 483-90.
4. Hunter JC, Gogas KR, Hedley LR, Jacobson LO, Kassotakis L, Thompson J, *et al*. The effect of novel antiepileptic drugs in rat experimental models of acute and chronic pain. Eur J Pharmacol 1997; 324: 143-60. http://dx.doi.org/10.1016/S0014-2999(97)00070-8
5. Craig MN, Follenfant RL. Effect of lamotrigine in the acute and chronic hyperalgesia induced by PGE2 and in the chronic hyperalgesia in rats with streptozotocin induced diabetes. Pain 1995; 63: 33-7. http://dx.doi.org/10.1016/0304-3959(95)00016-L
6. Assi D, Azim A, Rahman A, Mahran S. Analgesic effects of tramadol-diclofenac combination and their interaction with sycostimulant drugs in mice and rats. Eur J Pharmacol 1996; 312: 132-8.
7. Raffa RB, Friderichs E, Reimann W, Shank RP, Codd EE, Vaught JL. Opioid and nonopioid Pandi PV, Nagappa AN. Effect of acute and chronic treatment of losartan potassium on tail flick response in mice. Ind J Pharmacol 2006; 38: 281-2. http://dx.doi.org/10.4103/0253-7613.27026
8. Carrie K, Jones SC. Efficacy of duloxitine, a potent and balanced serotonergic and noradrenergic reuptake inhibitor, in inflammatory and acute pain models in rodents. J Pharmacol Exp Ther 2005; 313: 726-32.
9. Vogel HG, Vogel WGH, editors, Drug discovery and evaluation-pharmacological assays. 2nded. New York: Verlog Springer publication; 1996. p. 702-03.
10. Chen Y, Suiy C, Paul HO. Isobolographic analysis of the analgesic interactions between ketamine and tramadol. J Pharma Pharmacol 2002; 54: 623-31. http://dx.doi.org/10.1211/0022357021778934
11. Laughlin TM, Jram KV, Wilcox GL, Birnbaum AK. Comparison of antiepileptic drugs tiagabine, lamotrigine and gabapentin in mouse models of acute, prolonged and chronic nociception. J Pharmacol Exp Ther 2002; 302: 1168-75. http://dx.doi.org/10.1124/jpet.302.3.1168
12. Arguelles CF, Lopez JE, Soto VG. Peripheral antinociceptive action of morphine and the synergistic interaction with lamotrigine. Anesthesiology 2002; 96: 921-5. http://dx.doi.org/10.1097/00000542-200204000-00020
13. Dickenson D, Sullivan AF. Peripheral origins and central modulation of subcutaneous formalin induced activity of rat dorsal horn neurons. Neurosci Lett 1987; 83: 207-11. http://dx.doi.org/10.1016/0304-3940(87)90242-4
14. Aggarwal M, Agarwal R, Agarwal A, Aggarwal G, Kansal S. Efficacy of a novel and potent antiepileptic in inflammatory and acute pain model in rodents. Indian J. Sci. Res 2013; 4(2): 45-48.


Source of support: Nil, Conflict of interest: None Declared


| QUICK RESPONSE CODE | ISSN (Online) : 2277 –4572 |
|---|---|
| | Website http://www.jpsionline.com |

**How to cite this article:**

Dhanesh Kumar, Saurabh Kansal, Priti Saxena, Kalpana Chauhan, Abhishek Aggarwal. Analgesic evaluation of novel anticonvulsant with a conventional analgesic in dual pain model of rat. J Pharm Sci Innov. 2014;3(3):260-261 http://dx.doi.org/10.7897/2277-4572.033150