

LETTER TO THE EDITOR

ANTINOCICEPTIVE EFFECT OF GABAPENTIN IN RATS

Sir,

(Received on September 9, 1999)

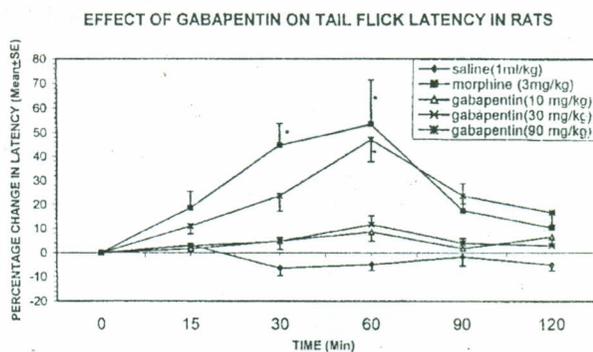
Gabapentin is an anti-epileptic agent structurally related to gamma-amino butyric acid (GABA). It has recently been shown to be effective in several neuropathic pain conditions (1). However, no study for its antinociceptive action has been reported in experimental model for acute pain. Present study was therefore conducted to study the antinociceptive effect of gabapentin in pain induced by thermal stimulation using tailflick latency method.

Healthy male albino rats of Wistar strain (200-250 gms) were divided into five group of 8 animals each. Animals were kept under standard laboratory conditions. The experiments were performed in a noise-free room at temperature ranging from 29-32 °C. Group 1 received saline (1 ml/kg, s.c.), group 2 received morphine (3 mg/kg, s.c.) and group 3,4,5 received gabapentin (Neurontin, Parke-Davis) 10 mg, 30 mg, 90 mg/kg s.c. respectively. The rat was placed on the tail flick apparatus, radiant heat was applied on the tail (about 5 centimetres from the tip) and latency of the tail flick responses were noted down for each rat at 0 (predrug), 15, 30, 60, 90 and 120 minutes after drug administration. A cut off time of 15 seconds was maintained to reduce tissue damage. All rats were subjected to rota-rod test before

and after gabapentin administration. Results were expressed as mean  $\pm$ SE. Statistical analysis was done by ANOVA followed by 't' test and  $P < 0.05$  was considered significant.

In the present study, gabapentin caused a dose dependent increase in the tail flick latency which was significant at 90 mg/kg dose level ( $P < 0.05$ ). The effect started after 15 minutes of administration of drug and was maximum at 60 minutes. This increase was comparable with that of 3 mg/kg morphine (Fig.1). Gabapentin in the doses employed produced no motor deficits on rota rod test.

Gabapentin although designed to mimic GABA, its mechanism of action remains elusive. GABA has been postulated as an inhibitory neuro transmitter in allodynic



(n=8) \*P < 0.05

Fig. 1

response at spinal level (2). Although Gabapentin does not bind to GABA receptors, some studies suggest that GABAergic inhibition may be involved in its antinociceptive action (3). Evidence suggest that NMDA mediated events and/or  $Ca^{2+}$  channel interactions could be involved in gabapentin induced activity (4). Recent studies suggest role of cholinergic, serotonergic, adrenergic gabaergic, and

opioidergic system in analgesic action of several drugs (5,6,7). Gabapentin may act through one or several of these mechanisms. Present study confirms the antinociceptive effect of gabapentin in experimental model of acute pain. Further studies are needed to ascertain the role of putative neurotransmitter in gabapentin modulated antinoceptive action.

RAKESH DIXIT, V. K. BHARGAVA AND NAVPREET KAUR

Department of Pharmacology,  
Postgraduate Institute of Medical Education and Research,  
Chandigarh - 160 012

#### REFERENCES

1. Rosner H, Rubin L, Kestenbaum A. Gabapentin adjunctive therapy in neuropathic pain states. *Clin J Pain* 1996;12:56-58.
2. Hao JX, Xu XJ, Yu YX, Seiger A, Wiesenfeld-Hallin Z. Baclofen reverses the hypersensitivity of dorsal horn wide dynamic range neurons to mechanical stimulation after transient spinal cord ischemia implications for a tonic GABAergic inhibitory control of myelinated fiber input. *J Neurophysiol* 1992; 68:(2) :392-396.
3. Taylor CP. Emerging perspectives on the mechanism of action of gabapentin. *Neurology* 1994;44 (suppl 5): S10-S16.
4. Taylor CP, Ge NS, Su TZ, Kocsis JD, Welty DF, Brown JP, Dooley DJ, Boden P, Singh L. A summary of mechanistic hypotheses of gabapentin pharmacology. *Epilepsy Res* 1998;29: 233-249.
5. Iwamoto ET, Marion L. Adrenergic, serotonergic and cholinergic components of nicotinic antinociception in rats. *J Pharmacol Exp Ther* 1993;265(2): 777-789.
6. Hwang JH, Yaksh TL. The effect of spinal GABA receptor agonists on tactile allodynia in a surgically induced neuropathic pain model in the rat. *Pain* 1997;70:15-22.
7. Gray AM, Spencer PSJ, Sewell RDE. The involvement of the opioidergic system in the antinociceptive mechanism of action of antidepressant compounds. *Br J Pharmacol* 1998;124:669-674.