

LETTER TO THE EDITOR

EFFECT OF GLIBENCLAMIDE IN GABAPENTIN ANTINOCICEPTION

Sir,

(Received on August 7, 2000)

Gabapentin an antiepileptic agent is shown to possess antinociceptive effect in chronic inflammatory pain models (1, 2) and has been tried to treat chronic neuropathic pain (3). Although gabapentin structurally resembles gamma-amino butyric acid (GABA) it acts differently and does not involve GABA receptors. Recently the role of various ion channels including the potassium channels in the perception and modulation of pain processing has been emphasized (4). Potassium channels play a pivotal role in the control of neuronal excitability, action potentials, and neurotransmitter release, the processes necessary for pain transmission and modulation (5). Potassium channel openers have been shown to possess antinociceptive activity (6). The present study was carried out to evaluate the role of potassium channels in the antinociceptive action of gabapentin.

Healthy male albino rats of wistar strain (wt. 200-250 gm) were divided into six groups of six animals each. The animals received drugs as follows: group 1 (saline 2 ml/kg, s.c.); group 2 (gabapentin 30 mg/kg, s.c.); group 3 (morphine 3 mg/kg, s.c.); group 4 (glibenclamide 0.5 mg/kg, i.p.); group 5 (glibenclamide 0.5 mg/kg, i.p followed 10 min by gabapentin 30 mg/kg, s.c.); group 6 (glibenclamide 0.5 mg/kg, i.p followed 10 min by morphine 3 mg/kg, s.c.). Drugs were

dissolved in saline. Formalin test was used to assess analgesic activity and pain score was calculated according to the weighted score technique of Dubuisson and Dennis (7).

Pain scores were expressed as mean \pm SEM. ANOVA followed by Wilcoxon rank sign test was applied for the statistical analysis and $P < 0.05$ was considered as significant.

Gabapentin (30 mg/kg, s.c.) produced analgesia and decreased pain score for control (2.4 ± 0.49) to (1.19 ± 0.19) and (1.17 ± 0.26) respectively $P < 0.05$. Glibenclamide alone did not alter the pain score (2.21 ± 0.54) as compared to control. Pretreatment with glibenclamide decreased the effect of

TABLE I: Effect of glibenclamide on the gabapentin and morphine induced antinociception.

Drugs	Pain score
Saline (2 ml/kg, s.c)	2.4 \pm 0.49
Morphine (3 mg/kg, s.c)	1.17 \pm 0.26*
Gabapentin (30 mg/kg, s.c.)	1.19 \pm 0.19*
Glibenclamide (0.5 mg/kg, i.p.)	2.21 \pm 0.54
Glibenclamide + Morphine (0.5 mg/kg, i.p.) (3 mg/kg, s.c.)	2.01 \pm 0.42*
Glibenclamide + Gabapentin (0.5 mg/kg, i.p.) (30 mg/kg, s.c)	1.31 \pm 0.33

* $P < 0.05$; n = 6

morphine (pain score 2.01 ± 0.42 , $P < 0.05$) whereas it failed to alter the gabapentin action (pain score 1.31 ± 0.33) (Table I).

Potassium channels role in antinociceptive action of opiates has been proposed (8). The opening of potassium channel due to opiate receptor stimulation results in neural hyperpolarization (9). In present study, gabapentin and morphine

decreased the pain score in rats injected with formation. Pretreatment with glibenclamide (potassium channel blocker) attenuated the action of morphine whereas it did not modify the gabapentin effect. Aim of this study was to find out the involvement of K^+ channels in gabapentin antinociception. Results of the study suggest that K^+ channels are not involved in antinociceptive effect of gabapentin.

R. K. DIXIT AND V. K. BHARGAVA*

Department of Pharmacology,
PGIMER, Chandigarh - 160 012

REFERENCES

1. 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: 1513-1522.
2. Dixit R, Bhargava VK, Kaur N. Antinociceptive effect of gabapentin in the formation test. *Methods Find Exp Clin Pharmacol* 1999; 21(7): 481-482.
3. Backonia M, Beydoun A, Edward KR, et al. Gabapentin for symptomatic treatment of painful neuropathy in-patients with diabetes mellitus. *JAMA* 1998; 280(21): 1831-1836.
4. Eglon RM, Hunter JC, Dray A. Ions in the fire: recent ion-channel research and approaches to pain therapy. *Trends Pharmacol Sci* 1999; 20: 337-342.
5. Aronson JK. Potassium channels in nervous tissue. *Biochem Pharmacol* 1992; 43: 11-14.
6. Welch SP, Dunlow LD. Antinociceptive activity of intrathecally administered potassium channel openers and opioid agonists: a common mechanism of action? *J Pharmacol Exp Ther* 1993; 267: 390-399.
7. Dubuisson D, Dennis SG. The formation test: a quantitative study of the analgesic effect of morphine, meperidine, and brain stem stimulation in rats and cats. *Pain* 1977; 4: 161-174.
8. Dickenson AH. Mechanisms of the analgesic actions of opiates and opioids. *Br Med Bull* 1991; 47: 690-702.
9. Ocana M, Del Pozo E, Baeyens JM. ATP dependent K channels blockers antagonize morphine but not U-504884, induced antinociception. *Eur J Pharmacol* 1993; 230: 203-207.

*Corresponding Author