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STUDY ON ANTIDEPRESSANT ACTIVITY OF TAPENTADOL

Pharmacology

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ABSTRACT

AIMS: To evaluate the antidepressant activity of tapentadol in Swiss albino mice. MATERIALS AND METHODS: Thirty inbred male albino mice weighing 20-25 grams were selected from central animal house. They were divided into five groups of six animals each. The control group I received normal saline 10 ml/kg intraperitoneally, standard group II received fluoxetine (20 mg / kg, intraperitoneally) and test groups III, IV, V received tapentadol in graded doses 10mg/kg, 20g/kg and 40 mg /kg intraperitoneally. Antidepressant activity was assessed by using Forced swim test. The results were tabulated and analysed with suitable statistical method. RESULT: Tapentadol showed statistically significant antidepressant activity at all the three test doses ($P < 0.05$). The results were comparable to that produced by standard drug fluoxetine. CONCLUSION: Tapentadol have antidepressant activity which is comparable to fluoxetine. Further, studies are essential to prove the anti-depressant effect of Tapentadol in human.

KEYWORDS

Antidepressant, Fluoxetine, Tapentadol, Forced swim test, Mice.

1.INTRODUCTION:

Depression is a common mental disorder which presents with depressed mood, loss of interest or pleasure, feelings of guilt or low self-worth, disturbed sleep or appetite, low energy, and poor concentration. Depression is a disorder of public health importance, in terms of its prevalence and suffering, dysfunction, morbidity, and economic burden. It's more common in women than men. According to global burden of disease study conducted by the world health organisation unipolar major depression ranked fourth among all diseases in term of disability adjusted life years and was projected to rank second by the year 2020[1]. The prevalence of depression is 7.9 to 8.9 per thousand population in India and the prevalence rate were nearly twice in the urban areas of India[2].

Depression is most commonly associated with chronic medical illness, between 20 to 30 % of cardiac patient's manifest as depressive disorder[1]. Pain is the cardinal symptom of somatic disease. In conditions where pain is unremitting, despite attempts to avoid the offending stimuli can lead to affective disorders like depression and anxiety. There is a close relation between chronic pain and depression. The prevalence of depression in chronic pain among general population ranges from 22 to 78 % worldwide[3]

Tapentadol is a new molecular entity that is structurally similar to tramadol and thus shares a number of its molecular and pharmacological features. Tapentadol is a centrally acting FDA approved analgesic for the treatment of moderate to severe acute pain. Tapentadol is a newer analgesic with modest μ-opioid receptor affinity and significant norepinephrine reuptake inhibiting action[4]. It has an opioid and non-opioid activity in a single compound. It is a weak opioid receptor agonist and also produces analgesia by inhibiting reuptake of norepinephrine and serotonin. Tapentadol due to the dual mechanism of action as an opioid agonist and norepinephrine reuptake inhibitor, there is potential for off label use in depression associated with chronic pain.

2.AIM :

Study was aimed to evaluate the antidepressant activity of tapentadol in Swiss albino mice.

3. MATERIALS AND METHODS:

Study centre:

Study was carried out in Central animal house, Madurai Medical College, Madurai, after getting clearance from the Institutional Animal Ethics Committee

Study design:

Thirty inbred male albino mice weighing around 25- 30 grams from central animal house, Madurai medical college were divided into five groups and each group comprised of six mice. They were housed as six per cage and they had free access to food and water. They were maintained in room temperature and 12 hour light dark cycle. Mice were allowed to adapt to their surroundings for one week before the experimentation. All the experimental procedures were carried out between 10.30 and 13.00 hours. Group I served as Control and received normal saline, Group II served as Standard and received fluoxetine 20 mg /kg , Group III, ,IV,V served as test groups and received tapentadol (10 ,20 and 40 mg /kg) respectively.All doses were administered intraperitonelly under strict aseptic precautions.

Drugs: Tapentadol (Lucynta , Lupin laboratories limited) ,fluoxetine (Flutop , Bogs India pvt limited) were used in the study and distilled water was used as solvent .

Methodology:

Forced swim test was conducted in all five groups of animals forty minutes after drug administration. Animals were kept in the test room for at least 1 hour for habituation. All mice were forced to swim individually in a glass jar (25x12x25 cm3) containing fresh water of 15 cm height and maintained at room temperature in which mice cannot touch the bottom of the tank or escape. After initial period of vigorous activity the animal assumed an immobile posture, mouse is considered to be immobile when it remained floating in water without struggling making only minimum movements of its limb necessary to keep its head above water. Total duration of immobility was recorded for next 4 minutes in a total of 6 minutes trial. The tests were conducted in a dim light room and each mouse was used only once.

Statistical analysis:

The results were expressed as Mean ± SD. The data was analysed by one-way ANOVA (F) followed by post hoc comparisons using the Dunnett's test for multiple comparison. P values < 0.05 was considered statistically significant.

Table 1: Period of Immobility – Forced Swim Test

Group	Treatment	N	Mean ± S.D
I control	Normal saline	6	188.33 ± 7.1
II standard	C.flouoxetine 20 mg /kg	6	70.83 ± 4.6*
III test group	Tapentadol 10 mg/kg	6	172.33 ± 3.2*
IV test group	Tapentadol 20 mg /kg	6	150 ± 3.5*
V test group	Tapentadol 40 mg /kg	6	132.67 ± 3.5*

*p value < 0.05 significant

4. RESULTS AND DISCUSSION

In this study it was found that there was statically significant difference in the immobility period existed between the groups and the control by

doing a one way ANOVA ($p < 0.05$). Post hoc comparisons was done using the Dunnett's test which showed that there was a statistically significant ($p<0.05$) decrease in the immobility period in the test groups III, IV, V when compared to control group.

Anti-depressant activity was evaluated in our study using forced swim test. It is based on the principle of behaviour despair. Mice were forced to swim in a cylinder with no escape, animal becomes immobile after an initial struggling phase. The total duration of immobility was measured for a period of four minutes. Immobility period reflects despair reaction. Anti-depressants decrease the immobility period. Forced swim test is the most commonly used behaviour model to test antidepressant activity[5]. From this study it was found that all the three test doses of tapentadol produced significant anti-depressant activity compared to control. Tapentadol at dose of 40 mg/kg produced more significant antidepressant activity when compared to control animal. The findings also agree with the study done by Ramnath Royal et al, which showed that tapentadol produced significant antidepressant activity in Swiss albino mice[6]. Tapentadol with dual action acting on both μ opioid receptors and norepinephrine reuptake inhibition causes spinal inhibition of pain and due to this action, it was used as analgesic agent for the treatment of mild to severe acute pain and due to its norepinephrine reuptake inhibition there may be antidepressant effect. Further studies are needed to prove the antidepressant effect in various animal models for depression so that tapentadol can be used for depression associated with chronic medical illness.

5. CONCLUSION:

The present study demonstrates that tapentadol can produce significant antidepressant activity and we recommend further testing in various models of depression to prove its effect so that it can be used in depression associated with chronic pain.

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