Research Paper

Volume : 5 | Issue : 6 | June 2016 • ISSN No 2277 - 8179 | IF : 3.508 | IC Value : 69.48

To Study Antidepressant-Like Activity of Escitalopram oxalate in Rats.

Medical Science

KEYWORDS : Escitalopram, Antidepressants, Forced swim test

Dhara M. Jadav , Pharmacology & Toxicology, Gujarat Forensic Sciences University, Gandhinagar, Gujarat, India

ABSTRACT

Depression is a multifactorial disease, commonly occurring due to deficit of norepinephrine, dopamine and serotonin. Escitalopram oxalate, inhibits the CNS neuronal uptake of serotonin, is used in treatment of depression. Imipramine inhibits the reuptake of norepinephrine , Fluoxetine inhibits the reuptake of serotonin in the synaptic cleft and selegeline inhibits the reuptake of dopamine. This study was done to explore the antidepressant activity of Escitalopram in combination with Fluoxetine, Imipramine, Selegeline in rats by forced swim test. 54 rats were grouped randomly, of 6 rats in each group. Twenty four hours following the pretest session, they were given distilled water, escitalopram (5 mg/kg, 10mg/kg) and then combination of all antidepressants together (5 mg/kg, 10mg/kg) intraperitoneally. After 30 minutes of drug administration, they were made to swim individually in the cylindrical transparent jar with a water column of 30 cm for 6 minutes. Escitalopram in combination with (Fluoxetine, Imipramine, Selegeline) showed significant (p value <0.05) reduction in immobility time with increase in dosage. Escitalopram + Fluoxetine (10mg/kg) showed significant antidepressant activity compared to escitalopram with other antidepressants. Escitalopram+(Fluoxetine,Imipramine, Selegeline) together could be helpful in patients with depression.

INTRODUCTION

Depression is a disorder of mood, affecting 10-15 percent of people at some part of their lives [1]. It is defined as depressed mood on daily basis for a minimum duration of 2 weeks. It can affect people of any age, but the incidence increases with age. It is twice more common in females than in males [2]. It could occur due to genetic predisposition, neurotransmitter dysfunction or due to chronic illness [3]. In about 15 percent of people with depression suicidal thoughts are more common [4]. It has gained importance due to its high prevalence and its capacity to derail the quality of life. Depression is found to be the most common mental disturbance in almost half of patients with chronic pain, affecting their day to day activities [5]. Hence it is important to treat depression to have a better living. The commonly involved neurotransmitters in depression are noradrenaline and serotonin. The management of depression is a multistep process and antidepressant drugs are the treatment of choice. Common among them are the TCA (Tricyclic Antidepressants) and SSRI (Selective Serotonin Reuptake Inhibitor) which will inhibit the reuptake and increases the availability of the neurotransmitters in the synaptic cleft. Thus they enhance the synaptic transmission and afford relief from depression. The TCA's produce more side effects such as anticholinergic symptoms, drowsiness, restlessness, weight gain, sedation and sexual dysfunction, due to which the SSRI's are preferred now [3].

The Antidepressant effect was studied in rats as an experimental animal model. The forced swim test of rats is one of the models, whose predictive validity is well established. In this the rats were made to swim individually in a cylindrical tank (25cm X 10 cm) containing water of 15 cm height for a period of 6 minutes. The rats were observed for immobility in that 6 minute session. The duration of immobility reflects the state of depression in the animal. Drugs which cause reduction in the immobility time are said to possess anti depressant property [6].

Thus this study was done to evaluate the effect of Escitalopram oxalate in combination with other antidepressant drugs (Fluoxetine, Imipramine, Selegeline).

MATERIALS AND METHODS:

Subjects:

Albino rats of both sex were used in our study. All rats were 14-20 weeks old and weighed around 200-250 g. They were housed in groups of 6 mice in a cage. Food and water were provided ad libitum. The test was done during 11 a.m. to 2 p.m. Each experimental group consisted of six randomly grouped rats. All testing were conducted within the guidelines of CPSCEA. Utmost care was taken to ensure that all the animals were treated humanely.

Apparatus:

The experiment was carried out in a cylindrical transparent jar of height 25 cm and diameter 10 cm, which contained water to a height of 15 cm at 250C. The water was changed after each 6 minute session, and the activity was recorded by a video camera for further analysis.

Drugs:

The drugs used in this study were, Escitalopram Oxalate, Imipramine, Selegeline, Fluoxetine , PURCHASED FROM Macleods Pharmaceuticals Limited (Valsad, Gujarat).. They were all dissolved in distilled water and given intraperitoneally. Control group received only distilled water i.p.

Study Design: It was a randomized, controlled experimental study, conducted in the Department of Pharmacology, GUJARAT FORENSIC SCIENCES UNIVERSITY.

EVALUATION OF ANTIDEPRESSANT ACTIVITY USING FORCED SWIM TEST

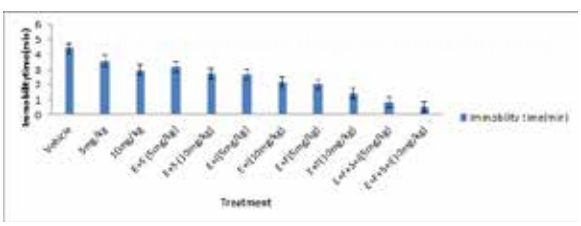
Each animal was subjected for two sessions of treatment, i.e. pretest and test session [7]. In the pretest session, the mice were made to swim inside the cylinder for a period of 6 minutes, without administration of any drug. After 24 hours, the same rats were given the respective drug and after 30 minutes of drug administration they were made to swim again in the tank for 6 minutes. In this test session, the swimming activity of each mouse was observed and recorded with a video camera [8]. Following the swimming session, the animals were removed out of the beaker, dried with towel and placed in a dry cage for 1 hour, before returning to their home cage. The water in the beaker was changed after each session. The activity of the rats in the initial 2 minutes was discarded and period of immobility in the last 4 minutes was measured. The observation of immobility is made in such a way that there can be little and finer movements, for the rats to keep its head above the surface of water. This state of immobility provides the state of depression of the animal [5]. The drugs with antidepressant property, decreases the duration of immobility and vice versa. The test results obtained from the standard and test groups are then compared and analyzed.

RESULTS AND DISCUSSION

COMPARISON OF 4 ANTIDEPRESSANTS TOGETHER WITH CONTROLLED

Comparison between different antidepressant drugs at 2 different dose was performed statistically by using one way annova and it was found that escitalopram is most effective in combination with fluoxetine at a dose of 10mg/kg and combination of escitalopram oxalate in combination with all the 3 antidepressants together i.e imipramine , fluoxetine , selegeline produces effective results at 10mg/kg dose.

	Vehicle	E 5 mg/kg	E 10 mg / kg	E+S (5 mg/kg)	E+S (10 mg/kg)	E+I (5 mg/kg)	E+I (10 mg/kg)		E+F (10 mg/kg)
Immobility time (min)	4.50	3.9	2.9	3.2	2.6	2.7	2.4	2.0	1.2
	4.20	3.8	2.9	3.5	2.8	2.9	1.9	2.2	1.6
	4.60	3.1	3.0	2.9	2.9	2.5	2.2	1.9	1.5
MEAN	4.43	3.60	2.98	3.20		2.70	2.16		1.43
SE of Mean	0.14	0.30	0.02	0.21		0.14	0.17		0.14



[Figure 1.1 Effect of escitalopram in combination with fluoxetine, imipramine, selegeline on rats]

In graph data are expressed as Mean + SEM followed by one way annova. As a result of statistical analysis p value was found less than 0.05 (p value 0.004) which indicates that result was significant.

CONCLUSION

From this study it can be concluded that Albino rats offer several advantages that make them an attractive in vivo model for different diseases. First of all they show a high genetic, physiological and pharmacological similarity to humans. For instance, Albino rats exposed to different class of antidepressants shows decreased immobility time in forced swim test model. Here we use Albino rats and combination of different antidepressants (Escitalopram oxalate, Fluoxetine, Imipramine, Selegeline)

Results of this study shows that effect of Escitalopram oxalate in combination with Fluoxetine have satisfactory results compared to Escitalopram oxalate with other Antidepressants (Imipramine, Selegeline)

Whereas the combination of all the 3 drugs together (Fluoxetine, Imipramine, Selegeline) with Escitalopram oxalate produces significant results.

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