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Research Article

PHARMACOLOGICAL EVALUATION OF ANTIDEPRESSANT ACTIVITY OF CLONIDINE IN MICE MODEL

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ABSTRACT

Objectives: Present study was designed to investigate the anti depressant activity of the clonidine.

Methods: Anti-depressant activity evaluated by forced swim test, tail suspension test and open field test. Healthy albino mice (6-7 week old) weighing 20-40 grams were used. Potency of the test sample was compared with the standard fluoxetine drug.

Results: Results showed that the administration of the clonidine produced adiminution of immobility time (a posture thought to reflect a state of ''behavior despair'' in which animals have given up the hope to escape) of mice exposed to the both forced swimming and tail suspension tests. In the present study, clonidine (150 mg/kg, ip) administered to mice, produced significant antidepressant-like effect in both TST and FST and efficacy was found to be comparable to fluoxetine (20 mg/kg, ip).

Conclusion: Further studies would be necessary to evaluate the contribution of clonidine for the observed antidepressant activity as it still remains to be determined for the side effects.

Keywords: Clonidine, Fluoxetine, Diazepam, Open Field Test, Forced Swim Test, Tail Suspension Test.

INTRODUCTION

Depression is characterized primarily by changes of mood, rather than by thought disturbances. Depressive disorders are common; approximately 15% of the population experiences a depressive episode at some point of life. It may range from a very mild condition to severe depression, accompanied by hallucinations and delusions. Two types of depressive illness can be distinguished, namely unipolar depression, in which the mood swings are always in the same direction, and bipolar affective disorder, in which depressive episodes alternate with mania [1]. An antidepressant is a psychiatric medication used to alleviate mood disorders, such as major depression and dysthymia and anxiety disorders such asocial. The main types of antidepressant drugs are TCA, selective serotonin reuptake inhibitors (SSRI), MAOI and atypical antidepressants. Lithium is used as mood stabilizer in manic-depressive illness (bipolar depression). The Selective serotonin reuptake inhibitors (SSRIs) are the class of antidepressants commonly used as the first line treatment for depression because they have a favorable side-effect profile and low toxicity. The atypical antidepressants act like the TCA, but have a different chemical structure [2, 3]. Study drug, clonidine resembles pharmacological features of typical antidepressants. Therefore we undertook the study to evaluate the anti depressant action of clonidine [4].

MATERIALS AND METHODOLOGY

Animal

Healthy albino mice (6-7 week old), 20-40gms. Animals were housed in hygienic cages and fed with standard pellet diet, water *ad libitum* & overnight before the day of experiment. Room temp: 27degree Celsius. The protocol was approved and carried out after the permission of Institutional Animal Ethics Committee [5].

Investigational drugs and dosage preparations:

Clonidine 150 mg (Boehringer Ingelheim Ltd.) was purchased from the hospital pharmacy counter. The appropriate body weight adjusted doses of groups: Group I as control was given normal saline (0.1 ml/10gm). Group II as clonidine (150 mg/kg) and Group III as fluoxetine (20 mg/kg, ip) or diazepam (10mg/kg). Clonidine, fluoxetine and Diazepam were dissolved in normal saline.

Forced Swimming Test

In experimental room white neon ceiling lights (standard lighting) used. Fresh water was filled in transparent cylinder. On day 1, at least 60 min before the beginning of the habituation session, marked the animals and randomly assigned them to a drug treatment. All animals within a cage received the same treatment[6]. Weighed animals individually, then placed rat in cylinders for 15 min (habituation session). No scoring of immobility was performed during the habituation session [7].

On the test day, administered the test substance 30 min (for intra peritoneal) prior to the session. Tested animals by placing in cylinder containing fresh water and observed their behavior for 6min. Scored the duration of immobility by summing the total time spent immobile[8,9] (i.e.; the time not spent actively exploring the cylinder or trying to escape from it. Included within the time spend immobile are the short periods of slight activity where the animals just make those movements necessary to maintain their heads above water).

Tail Suspension Test

This protocol describes, that immobility is induced by suspending the mice by the tail. After initially trying to escape by engaging in vigorous movements, mice rapidly become immobile. Equipped the environmental room with the white neon ceiling lights (standard lighting). With the tail suspension apparatus, 6 mice are tested separately. Weighed the mice and administered the test substance 30 min (for intra peritoneal) prior to the test and placed the mice back in their home cages. The different treatments administered to individual animals in fixed rotations to ensure a regular distribution of the different treatments over time. Wrapped adhesive tape around the animal's tail in the constraint position three quarters of the distance from the base of the tail. Suspended the animals by passing the suspension hook to the adhesive tape. So that the animal hanged with its tail in a straight line [10,11]. Measured the duration of immobility continuously for 6 min.

Open Field Test

The open field test was carried out on dark grey floor subdivided into 25 equals parts in a wooden box (100cm× 100cm × 30cm), and the treatment was given to the animals & 30 min later, the animals were individually placed in the corner square of the open field. This

test was used to evaluate the exploratory activity of the animal [12, 13]. The following parameters were observed for 5min:

- Activity in the centre (number of central squares crossed).
- Spontaneous ambulation (number of squares crossed at periphery).
- Rearing (No. of times the animal stands on the rear paws).

STATISTICAL ANALYSIS

The results of FST, TST and OFT were expressed as mean + /- SEM. Statistical analysis for the FST, TST and OFT were statistically analyzed by using ANOVA (two way classification analysis).

RESULTS & DISCUSSION

Modern day life style leads to numerous stress conditions, among which anxiety and depression are general and widely prevalent senile neurological disorders. The widely used animal models for assessing antidepressant like activity in small animals are forced swimming test, tail suspension test and open field test. It was expected that immobility occurs in these tests will reflect a state of behavioural despair or unable to adapt the stress as seen in human.

The results of forced swim test and tail suspension test of clonidine revealed that the mobility time was significantly decreased and the effect was comparable well with standard drug dose.

The administration of the clonidine produced adiminution of immobility time (a posture thought to reflect a state of ''behavior despair'' in which animals have given up the hope to escape) of mice exposed to the both forced swimming and tail suspension tests. In the present study, clonidine (150 mg/kg, ip) administered to mice, produced significant antidepressant-like effect in both TST and FST and efficacy was found to be comparable to fluoxetine (20 mg/kg, ip). It has been established that the shortening of immobility time in the forced swimming test (table 1) and the tail suspension test (table 2) showed significant effect. It depends mainly on the enhancement of central 5-HT and catecholamine neuro transmission [14 &15].

The effects produced by clonidine and DZP (1.0mg/kg) upon the open field test demonstrated that it does not modify the spontaneous locomotor activity of mice, which indicates that the clonidine exerts antidepressant effects[16] without modifying significantly this parameter (table 3). Therefore, it is probable that these effects are not related to the stimulation of general motor activity.

Table 1: Forced Swim Test

S. No.	Control	Fluoxetine	Clonidine
1.	27	16	25
2.	62	11	32
3.	42	33	37
4.	77	30	40
5.	38	24	29
6.	69	08	43

Values are mean ±SEM, n=6, $p<0.05$ vs control

Table 2: Tail Suspension Test

S. No.	Control	Fluoxetine	Clonidine
1.	87	93	79
2.	91	98	86
3.	79	98	89
4.	101	107	95
5.	105	125	99
6.	112	131	105

Values are mean ±SEM, n=6, $p<0.05$ vs control

Table 3: **Open Field Test**

S. No.	Control	Diazepam	Clonidine
1.	52	22	41
2.	55	36	47
3.	68	41	59
4.	79	29	67
5.	70	58	61
6.	77	64	73

Values are mean ±SEM, n=6, $p<0.05$ vs control

CONCLUSION

From the above consideration we can conclude that the clonidine have the antidepressant activity which is comparable with the standard. However, further studies would be necessary to evaluate the contribution of clonidine.

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