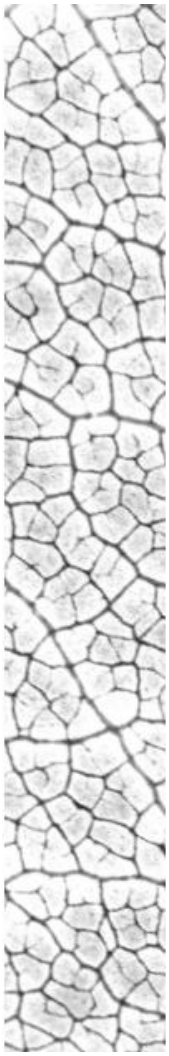

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Physiological dysfunctions in rats resulted from paroxetine

Wissam Sajid Hashim [1*], Ihab Abbas Taher [2], Sarah Aboodi Muhammad Ali [3]

[1] Ass. Prof., College of Medicine, Al-Muthanna University, IRAQ
[2] Lecturer, College of Medicine, Al-Muthanna University, IRAQ
[3] Ass. Lecturer, College of Veterinary Medicine, Al-Muthanna University, IRAQ
*Corresponding author: dr.w80@mu.edu.iq

Abstract

Objective: The aim of performing this study was to reveal the anticipated effects of paroxetine on rats' sperm parameters.

Materials and Methods: Twenty four adult male rats of 200-225 grams weight were adopted. Rats were randomly allocated into three groups; Control, Paroxetine 40mg, and Paroxetine 80mg. The experiment period was one month. The control group rats were dosed with distilled water. Paroxetine 40mg were dosed with 40 mg paroxetine hydrochloride and the Paroxetine 80mg group were dosed with 80 mg paroxetine hydrochloride. All groups were dosed orally and daily for one month.

Results: The results revealed that paroxetine causes significant decrease in sperm count and significant increase in dead and abnormal sperms when it was offered to rats as 40 mg/kg and it causes more significant bad effects when it was offered as 80 mg/ kg comparing among the treatment groups and with the control at (P≤0.05).

Conclusions: Paroxetine does effect rats' sperm count and sperm availability and morphology.

Keywords: paroxetine, SSRIs, sperm, rat

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INTRODUCTION

Anti-epileptic and anti-depressant medications are widely prescribed worldwide nowadays. This is due to the vast range of mental, neurological, behavioral and psychological disorders. The anti-depressant and anti-epileptic medications fall into many classes and groups such as the selective serotonin reuptake inhibitors (SSRIs), sodium channel blockers, GABA receptor agonists, GABA reuptake inhibitors, GABA transaminase inhibitors, Glutamate blockers, Serotonin and norepinephrine reuptake inhibitors (SNRIs), Tricyclic antidepressants, Monoamine oxidase inhibitors (MAOIs) and many others (Ritter et al.). The previously mentioned medications were compromised in many studies by many researchers to find out their anticipated side effects on both humans and animals. In this study, we try to spotlight the effects of paroxetine on the sperm parameters of laboratory rats. Paroxetine is one of the anti-depressant medications belonging to the family of SSRIs (Goodman 2017).

MATERIALS AND METHODS

Animals of the study

Twenty four adult male rats (*Rattus norvegicus*), weighting about 200-225g were bought from the Iraqi Center for Genetics and Cancer Research in Baghdad. The animals were housed in standard opened cages made of plastic with a stainless steel roof. The animals were allocated randomly on a pattern of four rats in each cage. The temperature of the room was set on 24±1C° and the lighting was fit on a pattern of 12 hours dark/light cycle by the use of automatic set fluorescent light tubes. The animals lived two weeks of acclimatization prior to the experiment. All the experiment conditions were complied with and applied according to the Institutional and National Guide for the Care and Use of Laboratory Animals (Albus 2012). Animals were fed a standard rat diet recommended by the subcommittee on laboratory animal nutrition (1995) along the experiment period, which continued for one month (Subcommittee, 1995). Rats were given free access to food and water *ad libitum* along the period of experiment.

Experimental Design

1- Control group: Eight male rats were daily dosed orally with 2ml of distilled water for one month.

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Table 1. Effect of paroxetine on rat sperm count and motility

GROUPS	Sperms count (× 10^6 / ml)	Individual movement (%)	Mass movement (%)
Control	a 180.3±2.91	a 80.2±0.50	a 80.3±2.5
Paroxetine (40 mg)	b 145.2±1.34	b 60.0±0.00	b 60.3±2.36
Paroxetine (80 mg)	C 52.4±3.19	c 15.00±0.00	c 8.0±0.0
LSD	3.8	0.07	0.04

Numbers represent the mean ± standard deviation. Letters refer to significant differences

Table 2. Effect of paroxetine on rat sperm availability

GROUPS	Alive sperms %	Dead sperms %	Abnormal sperms %
Control	a 70.4±1.91	c 16.4±1.00	c 7.0±1.63
Paroxetine (40 mg)	b 58.2±2.06	b 20.6±2.21	b 13.00±1.41
Paroxetine (80mg)	C 14.00±1.15	a 50.6±3.30	a 27.2±2.98
LSD	1.56	2.42	2.06

Numbers represent the mean ± standard deviation. Letters refer to significant differences

2- Paroxetine First treated group: Eight male rats were dosed orally (40mg/rat) of paroxetine daily for one month.

3- Paroxetine Second treated group: Eight male rats were dosed orally (80mg/rat) of paroxetine daily for one month. Paroxetine hydrochloride (Sigma-Aldrich) was dissolved in distilled water and dosed to the rats as 2ml containing the certain dose in both treated groups. Oral LD50 of paroxetine for rats = 350 mg/kg (Riva 2017). Oral dosing of all animal groups was done by the use of oral gavage.

Seminal Analysis

Sperm Concentration: The sperms were counted according to method of (Amiridis et al. 2012).

Abnormal Spermatozoa Percentage: The abnormal spermatozoa were counted according to the method of (Amiridis et al. 2012).

Analysis of data: One way ANOVA test was depended to obtain the least significant differences among the experimental groups using SPSS program version 20.

RESULTS

The results reveal that paroxetine causes significant decrease in total sperm count, individual motility and mass motility when it is offered to rats as 40 mg/kg for one month as compared with control group at (p≤0.05) as it is obvious in **Table 1**. The same table shows that when the dose of paroxetine is increased 80mg/kg, it causes further significant decrease in sperm count, individual and mass motility as compared with control and paroxetine 40mg group at (p≤0.05).

Considering the sperm availability, **Table 2** shows that paroxetine causes significant decrease in alive sperm with significant increase in dead sperm count and abnormal sperms when it was offered t rats as 40mg/kg as compared with control group at (p≤0.05). It is also clear from **Table 2** that when paroxetine is offered to rats as 80 mg/kg causes further significant decrease in alive sperm counts with significant increase in dead and abnormal sperms as compared with control and paroxetine 40mg group at (p≤0.05).

DISCUSSION

Anti-depressant medications were reported to be harmful on the health of humans and animals by many researchers and they were found to cause risk changes in behavior beside their effects on different body functions. Examples about these studies include the effect of SSRIs on behavior of rats (Amodeo et al. 2015), effect on behavior of fish (Kellkner 2017), effect on behavior of humans (Figneira et al. 1997; Walsh 2001), effect on noradrenaline and serotonin outflow in mice (David et al, 2003), effects on blood cells and lipids of rats (Hashim et al. 2020), effects on humoral and cellular components of blood of mice (Hanoon 2020; Al-Uboody et al. 2017), effects on functions of kidney and liver of mice (Al-Uboody et al. 2017) and other studies report the effect of antidepressant medications on fertility and sperms which agree with our findings in this study like the effect of antidepressants on the fertility of women (Casilla et al 2016), the effects of paroxetine on reproductive functions of rats (El-gaafarawi 2005), the paroxetine effects on human sperms (Tanrikut et al. 2010), the damaging effect of paroxetine and other anti-depressants on tissues of testes of rats (Erdemir et al. 2014) and the effects of antidepressants on human male fertility (Beeder, 2020). As it is obvious from our results, which agree with all the mentioned above studies, paroxetine causes bad effects on rat sperms aspects. These effects of paroxetine on sperms might be due to the base of mechanism of action of paroxetine where it causes fluency in neurotransmission of serotonin and the latter is paramount in regulation of the function of hypothalamic-pituitary-adrenal axis and finally affecting the gonadotrophins and sperm production mechanisms (Hendrick et al. 2000; Marrison et al. 2004). The over released serotonin which is caused by paroxetine stimulate the serotonin receptors in different body organs including the testes and epididymis and this excessive stimulation might lead to abnormalities in sperm count and availability (Jimenez et al. 2007; Syed et al. 1999; Fujinoki 2011).

CONCLUSION

Paroxetine does effect rats' sperm count and sperm availability and morphology.

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