Journal of Education for Pure Science
Vol.15, No.2 (2025)
DOI: https://doi.org/10.32792/jeps.v15i2.450
Website: jceps.utq.edu.iq Email: jceps@eps.utq.edu.iq

Effect study of paroxetine and escitalopram on gametogenesis of rats Rattus norvegicus

Zaman S. Madlool [1*] Zainab A.Hussain[1]

[1]Department of Biology, Faculty of Education for Pure Science, University of Thi-Qar, Thi-Qar, 64001,Iraq

[*]zamansubhi@utq.edu.iq

Received 7 / 6 /2024, Accepted 18 / 9 /2024, Published 1 / 6 /2025

This work is licensed under a Creative Commons Attribution 4.0 International License.

Abstract:

Background: The current study designed to investigate the influence of paroxetine and escitalopram on gametogenesis of rats; Method: The current study was conducted in the animal house of Biology department- College of Education for Pure Sciences-Thi Qar University, for the period from 25April to25 May, 2024. The experiment included three groups (5 females and 5 males), control group: Inject with normal saline, second group: Inject with paroxetine (10 mg/kg), whereas third group: Injected by escitalopram (20mg/kg); Results: The results showed histological changes in the testicle and ovary. Results indicted a non-significant down in the numbers of (Spermatogonia, Primary spermatocytes and Spermatids)in the injected groups. The results indicates a significant low in the numbers of primordial follicles, non-significant differences in the second group and a significant differences in the third group for primary follicles, non-significant differences in the second group and significant differences in the third group for secondary follicles; Conclusion: We concluded the negative histological effect of these drugs on testicular and ovarian tissue was reflected in the gametogenesis, which led to a decrease in this process.

Keywords: Depression, Testis, Ovary, Serotonin.

1-Introduction

Depression is significantly increasing among societies [1].One of the types of antidepressants used to treat depression in the short and long term are selective serotonin reuptake inhibitors (SSRIs), and they are also the first-

line medications to treat depression [2]. SSRIs increase the condensation of serotonin in the synaptic cleft by discouragement its reuptake [3]. Paroxetine and escitalopram are SSRIs used to treat anxiety and depression [4].Treatment with these medication causes several neurochemical and hormonal changes which are answerable for negativity effects on the reproductive system [5]. SSRIs cause negativity sexual action like decreased libido and erectile dysfunction [6].

Infertility is a trouble of the female or male reproductive system, realize by the inability to obtain a pregnancy after one year or more of regular ungrounded sexual intercourse [7].Medication play a possible part in the source of male infertility . SSRIs medication may influence the signs of infertility[8]. The main aim of the current study was designed to investigate the influence of paroxetine and escitalopram on gametogenesis of rats.

2-Related work

[9] showed, there was a decrease in the concentration of the hormone Testosterone with an increase in the concentration of the hormone FSH. As for the levels of LH and MDA, there was no significant change in them when male laboratory rats were treated with a group of antidepressants.

[10] showed that treating male laboratory rats with the drug fluvoxamine induced programmed cell death of the testicular tissue, causing damage to it, and a reduction in sperm motility and locomotion.

The study [11] indicated a decrease in the numbers of corpus callosum, corpus luteum, and prenatal vesicles when female rats were treated with the antidepressant fluoxetine.

3- .Material and method

3.1.Study sample

In this study, thirty healthy that aged 12-14 week old rats they were equally divided into 3 groups in both sexes, the control group: Inject with normal saline (2ml), second group: inject with paroxetine (10mg/kg), Escitalopram was injected in third group :Injection of (20mg/ kg).The animals were injected daily for four weeks. Ethical approval was obtained according to the numbered book 7/54/1322.

3 .2 Work method

The rats were dissected to prepare the testicular and ovary tissueaccording to methods of [12].

3.3 Statistical analysis

The data were analyzed by using ANOVA to determine mean and standard error, $p \leq 0.05$ was considered as significant in this study .

4- The results

3.1 Effect of paroxetine and escitalopram on spermatogenesis in male rats

The results showed non-significant decrease in the numbers of (Spermatogonia , Primary spermatocytes and Spermatids) in all treated groups compared with the control group at the probability level (P≤0.05) as showed in Table 1 and Figures 1,2,3,4 and5.

Table 1: influence of paroxetine and escitalopram on spermatogenesis in male rats

groups	Spermatogonia	Primary spermatocytes	Spermatids
First group (control) (n=5)	41.78 ± 1.5 a	44.08 ± 1.6 a	51.01 ± 2.5 a
Second group (n=5)	35.7± 1.9 a	40.7± 1.5 b	45.7± 1.9 a
Third group (n=5)	29.8 ±1.8 a	39.8 ±1.3 c	44.8 ±2.8 a
L.S.D	13.4	10.4	9.4

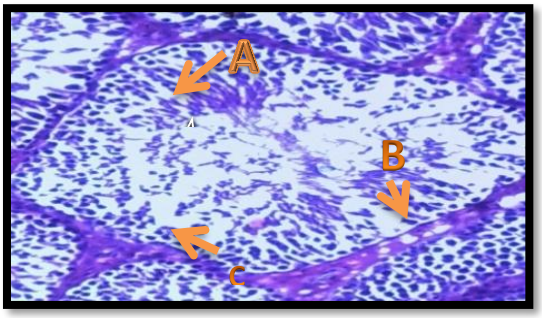

Fig 1 C.S of testis of control group indicates normal spermatogenesis A—spermatogonia ,B- connective tissue ,C-leydig cells(400XH&E)

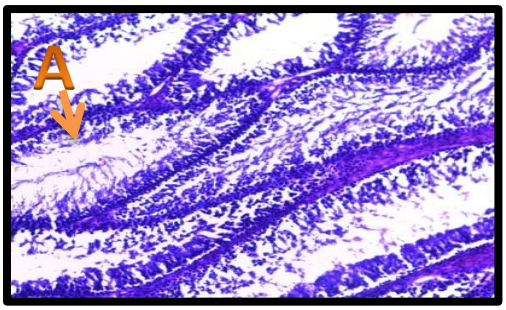

Fig 2C.S of testis of control group indicates normal spermatogenesis A--seminiferous tubules (100XH&E)

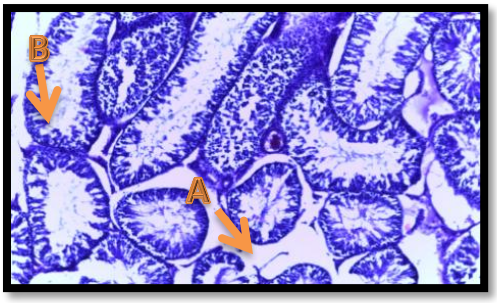

Fig 3 C.S of testis of second group indicates
decrease in spermatogenesis shows A- dissociation of connective tissue, B-decrease of number of spermatogonium (400XH&E)

3.2 Effect of paroxetine and escitalopram on oogenesis in female rats

The results indicates a significant low in the numbers of primordial follicles, non-significant differences in the second group and a significant differences in the third group for primary follicles, non-significant differences in the second group and significant differences in the third group for secondary follicles as shown in Table 2and Fig6,7,8.

Table 2: Effect paroxetine and escitalopram on oogenesis in female rats

groups	Primordial follicles	Primary follicles	Secondary follicles
First group (control)(n=5)	12.00 ± 0.50a	9.5 ± 0.23a	5.22 ± 0.60 a
Second group(n=5)	7.93 ± 0.48b	8.83± 0.90 a	5.80 ± 0.28 a
Third group(n=5)	7.17 ± 0.78c	5.67 ± 0.48 b	3.99 ± 0.59 b
L.S.D	1.8	1.9	1.5

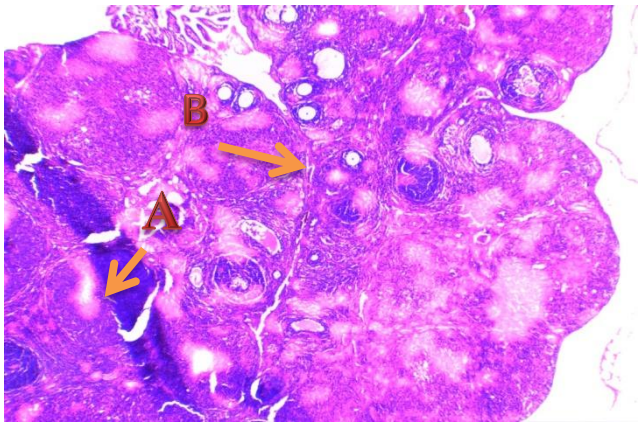

Fig 4 C.S of ovary of control group indicates a normal oogenesis A-Primary oocyte B-secondary oocyte (400XH&E)

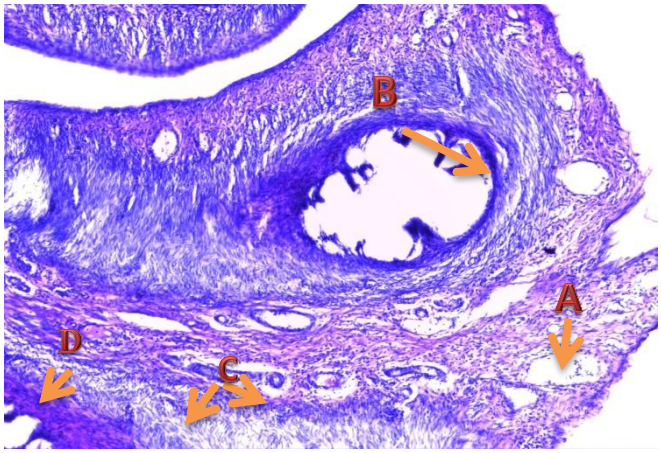

Fig 5 C.S of ovary of second group indicates decrease in oogenesis A-odema B- follicle cavitation C-erosion D- inflammatory cell infiltrations**.**

(400XH&E)

5. Discussion

In the current study, the process of spermatogenesis depends on (testicular-pituitary- hypothalamus axis [13]. The liberation of FSH and LH the release via GnRH hormones from hypothalamus, FSH hormone interpose in process of formation of sperms by the binding to expert receptors, and LH catalyze the liberation of the testosterone via influencing on leydig cells via attachment to its receptors located in leydig cells[14,10, 15], so the fade in the number of (Spermatogonia , Primary spermatocytes and Spermatids) is either due to a low condensation of testosterone [16],or because of the influence on LH and FSH hormones [9] has shown a low in the condensation of LH and FSH hormones when taking these medications.

[17]suggests that that the effect of antidepressants on sperm is due to the effect of ATP production by inhibiting of oxidative phosphorylation in sperm mitochondria , or by Interference with lipids of phosphate in the mitochondrial membrane and interfering with the sulfhydrl group in the membrane of sperm . [18] suggest that free radicals cause low in number of sperms and increased its deformities because they inhibit DNA synthesis and alteration of the structure of the sperms. [19]suggested that DNA damage leads to abnormalities in the head of the sperm.

The reason for the decrease in the number of follicles may be due to one side. As for a hormonal imbalance due to the lack of the hormones FSH and LH, [20] stated that the deficiency of these hormones leads to an impediment to the process of forming ovarian follicles and thus decreases their number, while the other side is a tissue defect in the ovaries and this was confirmed by the study The current one, as it showed a clear defect in the ovary.

6-Conclusion

Today, with the continuous increase in depression among societies, the consumption of antidepressants has become very common, and the most common types of antidepressants used to treat depression are selective serotonin reuptake inhibitors.

The negative histological effect of these drugs on testicular and ovarian tissue was reflected in the gametogenesis, which led to a decrease in this process.

Conflict of interest

The authors declare conflicts of interest.

Funding

Self-financing.

Acknowledgment

The authors would like to thank Dr. Zainab Hudhi for her assistance with this study.

References

[1] K. Harold ,S. Benjamin,"Comprehensive textbook of psychiatry," Vols. *1-2*. Williams & Wilkins Co, 1989, doi**:** 1989-97794-000**.**

[2] B. Alxenader, K. S. khalsa, C. M. Cameron., & J., Schiffman, "Current diagnosis and treatment of anxiety disorders,". *Pharmacy and Therapeutics*, *38*(1), 30,2013, doi: 23599668; PMCID: PMC3628173**.**

[3] M. B. Porter,, J. R. Brumsted, & Sites, C. K," Effect of prolactin on follicle-stimulating hormone receptor binding and progesterone production in cultured porcine granulosa cells,",*Fertility and sterility*, *73*(1), 99-105,2000, doi.: 10.1016/S0015-0282(99)00463-X .

[4] S. J. Davies, B. H. Mulsant, A. J. Flint,, B. S. Meyers, Rothschild, A. J., Whyte, E. M., ... & STOP-PD study group," SSRI-antipsychotic combination in psychotic depression: sertraline pharmacokinetics in the presence of olanzapine, a brief report from the STOP-PD study,", *Human Psychopharmacology: Clinical and Experimental*, *31*(3), 252-255,2016 ,**doi: 10.1002/hup.2532**.

[5] S. M. Attia, &, S. A Bakheet.," Citalopram at the recommended human doses after long-term treatment is genotoxic for male germ cell,", *Food and chemical toxicology*, *53*, 281-285,2013, **doi: 10.1016/j.fct.2012.11.051 .**

[6] A. B. Csoka, &, S. Shipko, "Persistent sexual side effects after SSRI discontinuation", *Psychotherapy and psychosomatics*, *75*(3), 187,2006, doi: 10.1159/000091777.

[7] A. Jungwirth, A. Giwercman, H. Tournaye, Diemer, T., Kopa, Z., Dohle, G., ... & EAU Working Group on Male Infertility," European Association of Urology guidelines on Male Infertility", the 2012 update. *European urology*, *62*(2), 324-332,2012 doi:10.1016/j.eururo.2012.04.048**.**

[8] P. Brambilla, A. Cipriani, M. Hotopf, & Barbui, C," Side-effect profile of fluoxetine in comparison with other SSRIs, tricyclic and newer antidepressants: a meta-analysis of clinical trial data," *Pharmacopsychiatry*, *38*(02), 69-77, 2005,doi: 10.1055/s-2005-837806**.**

[9] V. S. Kumar, V. L. Sharma, Tiwari, P., Singh, D., Maikhuri, J. P., Gupta, G., & Singh, M. M," The spermicidal and antitrichomonas activities of SSRI antidepressants," Bioorganic & medicinal chemistry letters, 16(9), 2509-2512,2006,doi:10.1016/j.bmcl.2006.01.078

[10] Galal AA, Alam RT, Abd El-Aziz RM. Adverse effects of long-term administration of fluvoxamine on haematology, blood biochemistry and fertility in male albino rats: a possible effect of cessation. Andrologia. 2016 Nov;48(9):914-922. doi: 10.1111/and.12532. Epub 2016 Jan 15. PMID: 26771175.

[11] R.-Haro D, García-Alcocer G, Miledi R, García-Colunga J. Uptake of serotonin by adult rat corpus callosum is partially reduced by common antidepressants. J Neurosci Res. 2003 Oct 1;74(1):97-102. doi: 10.1002/jnr.10724. PMID: 13130511.

[12] J. D. Bancroft, & M. Gamble (Eds.), "Theory and practice of histological techniques," Elsevier health sciences,2008, doi: 10.4236/vp.2023.92003.

[13] S. R Babu, M. D. Sadhnani,M. Padmavathi, P., & Reddy, P. P," Evaluation of FSH, LH and testosterone levels in different subgroups of infertile males," *Indian Journal of Clinical Biochemistry*, *19*, 45-49,2004,doi:10.1007/BF02872388.

[14] M. Ahmed, D. Ali, A. H. Harrath, Hussain, T., Al-Daghri, N., Alokail, M. S., ... & Ghodesawar, M. A. G," Ultrastructural and hormonal changes in rat cauda epididymal spermatozoa induced by Boswellia papyrifera and Boswellia carterii," *Comptes Rendus. Biologies*, *337*(4), 250-257,2014, doi: 10.1016/j.crvi.2014.01.007**.**

[15] S. Ramaswamy, & G. F. Weinbauer,," Endocrine control of spermatogenesis: Role of FSH and LH/testosterone," *Spermatogenesis*, *4*(2), e996025,**2014,** doi:10.1080/21565562.2014.996025.

[16] Z. S. Madlool, S. A. Faris, &, A. M., Hussein ," Effect of sertraline and fluoxetine on the reproductive abilities of male rats Rattus norvegicus," *University of Thi-Qar Journal of Science*, *7*(1), 26-32,2019 doi: **10.32792/utq/utjsci/v7i1.244.**

[17] F. Erdemir, D. Atilgan, Firat, F., Markoc, F., Parlaktas, B. S., & Sogut, E," The effect of sertraline, paroxetine, fluoxetine and escitalopram on testicular tissue and oxidative stress parameters in rats," *International braz j urol*, *40*, 100-108,2014,doi:10.1590/S1677-5538.IBJU.2014.01.15**.**

[18] V. S. Kumar, V. L. Sharma, Tiwari, P., Singh, D., Maikhuri, J. P., Gupta, G., & Singh, M. M," The spermicidal and antitrichomonas activities of SSRI antidepressants," Bioorganic & medicinal chemistry letters, 16(9), 2509-2512,2006,doi:10.1016/j.bmcl.2006.01.078.

[19] D . Sanocka & M.Kurpisz,,"Reactive oxygen species and sperm cells ,"Reprod Biol Endocrinal 2(12) pp: 1-7**, 2006,**doi:10.1186/1477-7827-2-12**.**

[20] P. P. Trivedi, S. Kushwaha, D. N. Tripathi & Jena, G. B," Evaluation of male germ cell toxicity in rats: correlation between sperm head morphology and sperm comet assay,"*Mutation Research/Genetic Toxicology and Environmental* Mutagenesis, 703(2), 115-121 2010,doi:10.1016/j.mrgentox.2010.08.005.