EFFECTS OF FLUOXETINE (SSRI) ON THE UROGENITAL SYSTEM OF ALBINO RATS

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Sexual disorders are the common side effects of SSRI group of antidepressants, although, recently SSRIs have emerged as an effective new treatment modality for premature ejaculation in a dose of 40 mg/day. Some evidences suggest that SSRIs can cause untoward sexual experiences such as changes in sexual desire, sexual performance and sexual satisfaction. Reliable estimates of the incidence and severity of untoward experiences are difficult to obtain, however, in part because patients and physicians may be reluctant to discuss them. Accordingly, estimates of the incidence of untoward sexual experience and performance, cited in product labeling, are likely to underestimate their actual incidence. In patients enrolled in U.S. major depressive disorder, OCD and bulimia nervosa placebo-controlled clinical trials, decreased libido was the only sexual side effect. There are no adequate and well controlled studies examining sexual dysfunction with Fluoxetine treatment. There have been spontaneous reports in women taking Fluoxetine of orgasmic dysfunction, including anorgasmia. Because Fluoxetine is prototype of SSRIs and most commonly used in different doses for different psychiatric disorders such as for depression and phobias in low doses i.e. 10 and 20 mg/day but in high doses up to 80 mg/day for OCD and bulimia nervosa. For almost all the psychiatric illnesses the SSRIs are used for long duration. Therefore, the

objective of the present study was to deduce the comparative safety of Fluoxetine in acute and subacute therapy and to study the histological changes in various cells of urogenital system of albino rats after intraperitoneal injection of Fluoxetine in different doses. 72 albino rats were taken for the study which was conducted in 3 phases of 2, 4 and 12 weeks duration. Each phase consisted of 24 rats. These 24 rats were further subdivided into 4 groups of 6 rats each (3 males and 3 females). Group 1 (Control) received intraperitoneal injection of vehicle (normal saline). Group 2, Group 3 and Group 4 received 10 mg, 20 mg and 40 mg/kg of body weight/day intraperitoneal injection of Fluoxetine respectively.

After administration of drugs, the tissues were collected from kidney, ureter, and urinary bladder for the urinary system. Testis, epididymis, seminal vesicle and prostate were dissected for the male genital system and uterus and ovary for female genital system. The tissues were fixed in formalin, processed and tissue blocks were made in paraffin wax. 4-5 μ thick sections were cut and stained with haematoxylin and eosin. The sections were examined under low and high power (magnification) and selected slides were photographed. Microscopic changes in the form of degeneration, hyperplasia and hypertrophy were noted in response to injuries caused by Fluoxetine (SSRI). The compensatory hyperplasia was considered as an initiating and promotional

event to protect the Germinal Epithelium of the testis. The decrease in the thickness of the epithelium at the end of 12 weeks in the experimental rats of Group 3 (20 mg/kg/day) and at the end of 2 weeks in Group 4 (40 mg/kg/day) indicated the degeneration of the epithelium. The number of Sertoli cells decreased constantly in all groups of experimental rats of all phases. The number of Spermatogonia A (pale and dark type) and Spermatogonia B also decreased as the duration and dose of Fluoxetine increased except in Group 3 (20 mg/kg/day) at the end of 4 weeks in which an increase number was noted probably due to compensatory hyperplasia. The number of primary spermatocytes decreased constantly as the duration and dose of Fluoxetine increased. In the epididymis there was hypertrophy of epithelial cells with intracytoplasmic vacoulation as the duration and dose of Fluoxetine increased. Proliferation of villi was observed in the seminal vesicle with narrowing of lumen and decrease of seminal fluid as the duration and dose of the drug increased. Proliferation of the lining epithelium was observed in the acini along with degenerative changes in the form of denuded cells in the lumen of prostatic acini with decreased cell height as the duration and dose of the drug increased.

In the uterus there was focal thickening of the mucosa of the endometrium. The mucosal tubular glands penetrated more into the stroma with increased branching. The myometrium became thickened and dispersed at

places where it came in contact with the tubular glands. These observations were found as the duration and dose of Fluoxetine increased. In the ovary the mean number of atretic follicles increased as the duration and dose of Fluoxetine increased.

In the Urinary System dilatation of proximal convoluted tubules and collecting tubules were seen in all the experimental groups in comparison to controls. There were no significant changes in the diameter of distal convoluted tubules (DCT) in all the experimental groups in comparison to the control group of rats. Similarly, no significant changes were observed in the histology of the ureter in the experimental groups. In the urinary bladder a decrease in the epithelial thickness was observed as the duration and dose of Fluoxetine increased.

Sexual disorders and decreased germ count reported in patients on antidepressant Fluoxetine (SSRI) might be due to histological changes in the reproductive system and accessory reproductive organs via its indirect central and peripheral effects through the increased concentration of free Serotonin (5–HT). The present histological study results confirmed the previous reports about the Fluoxetine induced infertility and sexual disorders. We have also noted some histological changes in the urinary system in the form of dialatation of PCT and CT. In present scenario every person of any age group and sex may

suffer or pass from a period of anxiety and depression and therefore needs a prescription for use of these drugs. There is an essential need to know their safe dose and duration. A further research is essential to know whether these changes in the male and female genital system are reversible or irreversible. Clinicians must take precautions in prescribing the dose and duration of Fluoxetine to their patients. There is a need of further study to know the cause of changes noted in urinary system by Fluoxetine.