RESEARCH ARTICLE

Physiological Effects of Sertraline on Lipid Profile and Some Biochemical Parameters of Laboratory Mice

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ABSTRACT

Objective: This study is aimed to reveal the anticipated effects of sertraline on some physio-biochemical parameters.

Materials and Methods: A total of 42 adult male mice of 30–35 grams weight were adopted. Mice were randomly allocated into three groups; control, sertraline high, and sertraline low. The experiment extended for 3 months. The control group mice were dosed with distilled water. The sertraline low group was dosed with 8 mg sertraline hydrochloride, and the sertraline high group was dosed with 12 mg sertraline hydrochloride. All groups were dosed orally and daily for three months.

Results: The results revealed that sertraline causes hyperlipidemia (LDL, VLDL, CHO, and TGs), elevation in hepatic enzymes (AST, ALTS, and ALP), urea, sodium, and creatine of both treated groups and the effects were more severe in sertraline high group comparing them with the control at ($p \leq 0.05$).

Conclusions: Sertraline does affect lipid milieu besides renal and hepatic functions.

Keywords: Hepatic enzymes, Hyperlipidemia, Mice, Sertraline, Zoloft.

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INTRODUCTION

Zoloft is the commercial brand under which sertraline is sold. If one must classify sertraline, it falls in a cabinet of medicaments referred to as selective serotonin reuptake inhibitors or, as usual syncopated (SSRIs).[1] These medicines are widely used in the field of neurological and psychological medical treatment to treat or alleviate insomnia, anxiety,[2] phobias, depression [3], disappointments, and others.[4] Serotonin receptors are bodily spread and not exclusively situated in the nervous system.[5] The primary task of serotonin in the nervous system is to promote sleep besides mood and related topics while it functions another task in the body's other organ.[6] In the field of studies about anti-depressant medicines, plenty of these studies took on their shoulders the neurological aspects of these medicines. Some other studies have reported that anti-depressant medicine have very hazardous side effects on different body functions or organs like abdominal pain and nausea,[7] epistaxis and sexual malfunctions,[8] growth problems.[9] Thus, we targeted the other proposed anticipated effects of sertraline on some mice's physio-biochemical indicators and not the neurological ones.

MATERIALS AND METHODS

Experimental Animals

Forty-two adult male mice of 30–35 gram weights 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 seven mice in each cage. The room temperature was set at 24 ± 1°C, 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 experimental conditions were complied with and applied according to the Institutional and National Guide for the Care and Use of Laboratory Animals (1996) which the International Committee of Medical Journal Editors recommended–"Uniform Requirements for Manuscripts Submitted to Biomedical Journals" (2006). Animals were fed a standard mice diet recommended by the subcommittee on laboratory animal nutrition (1995) along the experiment

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Table 1: Sertraline effect on lipid profile of mice.

GROUPS	*TGs (mg/dL)*	*CHO (mg/dL)*	*HDL (mg/dL)*	*LDL (mg/dL)*	*VLDL (mg/dL)*
Control	c 156 ± 15.6	c 95.67 ± 6.02	a 55 ± 5.4	c 9 ± 2.8	c 31.17 ± 3.1
SERT (L)	b 220.33 ± 17.8	b 173.33 ± 11.05	b 39 ± 8.1	b 90 ± 9.8	b 44 ± 3.6
SERT (H)	a 288.3 ± 26.3	a 245.83 ± 32.9	c 27.83 ± 7.3	a 160.33 ± 32.6	a 57.83 ± 4.9
LSD	64.33	72.5	11.16	70.33	12.83

The numbers represent the mean ± standard deviation. Different letters refer to a significant differences among groups at ($p \leq 0.05$).

Table 2: Sertraline effect on blood electrolytes of mice.

GROUPS	*Urea (mg/dL)*	*Creatine (mg/dL)*	*Sodium (mmol/L)*
Control	c 39.67 ± 4.54	b 0.41 ± 0.07	b 161.17 ± 17
SERT (L)	b 50.83 ± 7.46	a 0.63 ± 0.1	a 181.67 ± 7.03
SERT (H)	a 67.67 ± 8.54	a 0.63 ± 0.19	a 189.83 ± 7.73
LSD	11.16	0.216	20.50

The numbers represent the mean ± standard deviation. Different letters refer to a significant differences among groups at ($p < 0.05$).

Table 3: Sertraline effect on Liver enzymes and serum proteins of mice.

GROUPS	*AST (U/L)*	*ALT (U/L)*	*ALP (U/L)*
Control	b 75.67 ± 8.77	c 55 ± 8.80	b 162.17 ± 10.16
SERT (L)	a 378.50 ± 35.03	a 282.5 ± 21.88	a 193.5 ± 12.43
SERT (H)	a 355.17 ± 53.12	b 230 ± 53.68	a 191.83 ± 14.34
LSD	279.50	52.50	29.66

The numbers represent the mean ± standard deviation. Different letters refer to a significant differences among groups at ($p < 0.05$).

period, which continued for three months. Mice were given free access to food and water *ad libitum* during the period of the experiment.

Experimental Design

1. *Control Group:* Fourteen male mice were daily dosed orally with 1 mL of distilled water for three months.
2. *Sertraline Low (SERT L) treated group:* Fourteen male mice were dosed orally (8 mg/mouse) of sertraline daily for three months.
3. *Sertraline High (SERT H) treated group:* Fourteen male mice were dosed orally (12 mg/mouse) of sertraline daily for three months. Sertraline hydrochloride (Sigma-Aldrich) was dissolved in distilled water and dosed to the mice as 1-mL containing the certain dose in both treated groups. Oral LD50 of sertraline for mice = 548 mg/kg.[10] Oral dosing of all animal groups was done by the use of oral gavage.

Specimens' Collection

Blood samples were collected from the animals at the end of the three months of the experiment. The mice's blood sampling technique was applied according to the recommendations and methods of Diehl *et. al*.[11]

Biochemical Parameters

All the studied biochemical parameters were found out by the use of a special medical laboratory device PKL (POKLER ITALIA, biochemical auto-analyzer).

Statistical Analysis

One way ANOVA test was depended to get the least significant difference (LSD) and the means ± standard deviation.

RESULTS

Table 1 elucidates that sertraline treatment lead to significant elevations in low-density lipoproteins (LDL), triglycerides (TGs), very low-density lipoproteins (VLDL), and cholesterol (CHO) besides a significant declination in HDL and these increments and decrements were directly proportion with the increment of sertraline dose. The hepatic enzymes AST, ALT and ALP were elevated significantly in both treated groups without a significant differences between them while the creatine, urea and sodium were elevated significantly and the urea elevation was more significant in a direct proportion with sertraline dose increment (Tables 2 and 3). All the previous parameters were compared between the treated groups and with the control group at ($p < 0.05$).

DISCUSSION

Sertraline is one of the most abundant anti-depressants and it was obvious in our study to cause significant hyperlipidemia, elevations in hepatic enzymes, urea and creatine. This comes in accordance with the study of Kesim *et al* and al-Uboody *et al*.[12,13] The elevated lipids and hepatic enzymes can be explained by these mechanisms: Sertraline has been reported to cause oxidative stress in rats by (Battal *et al* 2014), (Azimzadeh *et al* 2017).[14-15] The oxidative stress in a

simple explanation leads to imbalance between the ability of body defenses to neutralize the annihilating effect of reactive oxygen, nitrogen and halogen species which in turn will cause devastation to the cellular membranes of all types including those pertaining to the lipids (Singh *et al* 2009; Leopold and Loscalzo 2009; Mashima *et al* 2001, Al-Uboody *et al* 2017).[16-19] The peroxidation of cellular lipid membranes of especially blood vessels will cause dysfunctions of intracellular oxidative and antioxidative mechanisms yielding damage to the vascular endothelia of them (Fang and Davies 2012; Ding *et al* 2013).[20,21] These damaged vascular endothelia will shed many cascades of growth and chemotactic factors which predispose to the precipitation of oxidized lipids especially LDL and accumulation of atherosclerotic factors such as platlets aggregation and monocytes which in turn will yield more precipitation of lipids and many inflammatory reactions might occur and foam cells are formed resulting in the atherosclerotic lesions and much more hyperlipidemia results accompanied by elevations in hepatic enzymes, urea and creatine due to the initial oxidative damage (Förstermann, 2008; Maiuri *et al* 2013; Wang *et al* 2014; Wang *et al* 2014 b; Zhou *et al* 2014).[22-26]

CONCLUSIONS

Based on our results in this study, we can say that sertraline does cause hyperlipidemia, elevations in hepatic enzymes and effects on renal functions. We recommend for further studies comprising Sertraline effects on different body organs and functions rather than the neurological sides.

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