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RESEARCH ARTICLE

INFLUENCE OF EXOGENOUS ESTRADIOL ON THE LIPIDS PROFILE, AST, ALT AND ALP OF INTACT AND CASTRATED MALE RABBITS

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ABSTRACT

This study was conducted to investigate the changes on lipids profiles, AST, ALT and ALP enzymes of (intact and castrated) males rabbits due to exposure to estradiol benzoate via intramuscular injection route each alternative day for 30 days period. The result of this study shown that the injection of estradiol benzoate at doses of 40, 80 and 120 µgm/ rabbit intramuscularly were not induced any significant ($P>0.05$) changes on lipids profile of intact and castrated male rabbits while HDL was significantly ($P<0.05$) increased at a dose 40 µg in intact male rabbits. AST and ALP were significantly ($P<0.05$) decreased in castrated male rabbits but not changed ($P>0.05$) in intact male rabbits, while ALT was not changed ($P>0.05$) in castrated and intact male rabbits expect at a dose of 120 µgm was shown significant ($P<0.05$) increase in intact male rabbits.

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INTRODUCTION

Oestrogen is the major hormone for reproductive functioning as well as the sexual differentiation and behaviour (Balthazart *et al.*, 2009). Although estrogen was historically believed to be a female hormone, but there is growing evidence of a biological role of this steroid in the male reproduction (Todiodi, 2010). An animal body naturally produces three main form of oestrogen; these are estradiol-17beta (E2), estrone and estriol (Deborah Moskowitz, 2006). Estradiol-17beta is the most physiologically active type of oestrogen. The steroidal compounds were used for anabolic purposes in food animals as exogenous oestrogens have been used to increase the secretory characteristics of growth hormone in several animal species (Mistral *et al.*, 2007; Colak *et al.*, 2011). There was differences between the natural and synthetic steroids in their effects on body due to difference in affinity for binding to globulin, biological activity in plasma, metabolism, and half-life (Anna-Maria, and Niels, 1999). Lipids profiles and enzymes are parameters used in the routines tests done for assess the health of animals. And the exposure to exogenous oestrogen may have effect on these parameters. There was a study on mice male and female fed with estrogen found that, HDL, AST and ALT were significant increase in male but

LDL, Cholesterol, and Triglycerides were not shown any changes (Islam, 2013). Estrogens, particularly when unopposed by progesterone, can increase triglyceride levels through reduced triglyceride-clearing enzymes and increased endogenous triglyceride synthesis (Mantel-Teeuwisse *et al.*, 2001). Oestrogen (E2) directly enhances insulin sensitivity and suppresses lipogenesis in peripheral tissues (Yonezawa *et al.*, 2012). While (Liao *et al.*, 2011) stated that administration of estradiol reduced the levels of total cholesterol, and low-density lipoprotein (LDL) cholesterol. On the other hand (Smith, and Sizto, 1983) have noted increased ALT and AST with lowered ALP activities during three months treatment of oral contraceptives. Therefore, this study intends to investigate the changes on lipids profiles, AST, ALT and ALP enzymes of (intact and castrated) males rabbits due to exposure to estradiol benzoate via intramuscular injection each alternative day for 30 days period.

MATERIALS AND METHODS

Description of Experimental Site

This research was conducted at the Nyala City in South Dar Fur State Sudan.

Experimental Animals and Management: Seventy two adult male rabbits weighing 2.1 ± 0.1 kg at the beginning of the experiments were being used. They housed under individual

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cage 50 x 50 cm they had free access to standard rabbit food and tap water. The necessary ethical approval for the animal experimentation was taken from the Nyala University's Animal Welfare Committee.

Treatments

The animals were divided in two groups of rabbits (Thirty six per group). One group were subjected to bilateral orchietomy and used as castrated group, the other group of rabbits was used as intact group. Each group was further divided randomly to four sub-group (six for each sub-group). Each three sub-groups of intact and castrated animals were treated once each alternative day with the intramuscular injections of estradiol benzoate (Estradiol® Animal health care Australia) at doses of (40, 80 and 120 µg/ rabbit), respectively for thirty days, whereas the fourth sub-group of each receive placebo and act as control group.

The results were expressed in form of mean ± standard deviation. Difference between the mean in lipids profiles and enzymes in the study of different groups were assessed by independent T- test. Results were considered statistically significant when the P- value was less than 0.05.

RESULTS

The effects of Estradiol benzoate on lipids profiles of intact male rabbits were presented in Table (1). There was significant ($P < 0.05$) increase in HDL in the 40 µg estradiol treated group. On the other hand there was in significant ($P > 0.05$) decrease in triglycerides and LDL. However, there is no significant difference ($P > 0.05$) between 40 µg, 80 µg and 120 µg estradiol treated and control sub-groups in cholesterol and HDL. The lipids profile data of castrated male were shown on table (2). There were no significant ($P > 0.05$) differences in means of

Table 1. The effects of estradiol benzoate on Lipids profile of intact males rabbits

Parameters	Control	40µg estradiol	80µg estradiol	120µg estradiol
Triglycerides mg/dL	58.25± 2.58	23.25± 1.71	10.75± 1.71	13.00±1.41
Cholesterol mg/dL	28.25± 6.08	29.25± 7.23	19.25± 4.79	29.00± 1.81
HDL mg/dL	09.89± 2.79	16.73± 5.69*	12.08±3.05	12.78± 5.39
LDL mg/dL	13.25± 3.30	07.50± 1.73	03.25± 1.50	03.45± 0.64

Mean with superscript stars within the row was significantly different ($P < 0.05$)

Table 2. The effects of Estradiol benzoate on Lipids profile of castrated males rabbits

	Control	40µg estradiol	80µg estradiol	120 µg estradiol
Triglycerides mg/dL	58.25± 2.58	14.25± 1.26	13.50± 1.73	15.00± 8.68
Cholesterol mg/dL	28.25± 6.08	34.25± 4.79	25.00± 4.08	24.25± 3.30
HDL mg/dL	09.89± 2.79	17.35± 4.12	11.83±4.60	14.75± 2.47
LDL mg/dL	13.25± 3.30	12.00± 1.41	04.50± 1.29	09.50± 1.00

Table 3. The effects of estradiol benzoate on AST, ALT and ALP Enzymes of intact males rabbits

	Control	40 µ estradiol	80µg estradiol	120 µg estradiol
AST	72.75± 2.31	51.75± 4.43	55.25± 1.25	82.25±4.80
ALT	65.75± 1.10	56.50± 3.51	120.00± 3.16	118.00± 6.77 *
ALP	77.00± 5.88	27.75± 7.23	36.25±6.65	41.50± 1.88

Mean with superscript stars within the row was significantly different ($P < 0.05$).

Table 4. The effects of Estradiol benzoate on AST, ALT and ALP Enzymes of castrated males rabbits

	control	40 µg estradiol	80µg estradiol	120 µg estradiol
AST IU/mL	72.75± 2.31	28.00± 2.94*	24.75± 3.50*	40.25±7.04
ALT IU/mL	65.75± 1.10	77.50± 2.04	47.00± 1.87	80.25± 1.06
ALP IU/mL	77.00± 5.88	17.50± 3.11*	14.50± 1.29*	13.00± 0.82*

Mean with superscript stars within the row was significantly different ($P < 0.05$).

Blood collection

After the of treatment period, a five ml of blood samples were collected from the heart into plan plastic containers using disposable syringe, and the serum samples were being harvested into *Eppendorf* tubes, deep-frozen for later analysis of lipids profiles, AST, ALT and ALP enzymes.

Serum Analysis

Automate chemistry analyzer (MINDARY) and reagent Biosystem® Spain made were used for analysis of lipids profiles AST, ALT and ALP enzymes in serum.

Statistical analysis

The statistical analyses were done using the SPSS statistical program, version 20 for Windows (IBM SPSS Statistics 20 IL, USA).

lipids profiles between 40 µg, 80 µg and 120 µg estradiol treated and control groups, despite the presence of increase on HDL and decrease on triglycerides of 40 µg, 80 µg and 120 µg estradiol treated groups, and LDL in 80 µg estradiol treated group. The response of AST, ALT and ALP enzymes of intact male rabbits to different estradiol benzoate doses were presented in Table (3). There was significant ($P < 0.05$) increase in ALT in the 120 µg estradiol treated sub-group, in significant ($P > 0.05$) increase in ALT in the 80 µg estradiol treated sub-group, in significant ($p > 0.05$) decrease in ALP between 40 µg, 80 µg, 120 µg and 0 µg estradiol treated sub-groups. However, there were no significant ($p > 0.05$) changes in AST between 40 µg, 80 µg, 120 µg and 0 µg estradiol treated sub-groups. The AST, ALT and ALP enzymes data of castrated male rabbits were present on table (4). There was significant ($P > 0.05$) decrease on AST of 40 µg and 80 µg estradiol treated sub-groups, and significant ($P > 0.05$) decrease on ALP on 40 µg, 80 µg and 120 µg estradiol treated sub-groups. On the other

hand there were no significant changes between 40 µg, 80 µg and 120 µg estradiol treated and control sub-groups in ALT, and 120 µg estradiol treated and control sub-groups in AST.

DISCUSSION

The differences between the action of natural and synthetic steroid hormones must be put in consideration as (Anna-Maria, and Niels, 1999) were mentioned. However, these effects are dependent on the type of oestrogen used, doses and administration route (Daniel *et al.*, 2009). The effect of estrogen on lipids profiles (Cholesterol, HDL, LDL, and triglycerides) in this study were agree with that obtained by (Islam, 2013). And the result of HDL in sub-group 40 µg of intact male rabbits it could be agree with the study of (Herrington *et al.*, 2000) who reported that estrogen produced significant increases in HDL. Increase of enzyme ALT in the 120 µg estradiol treated sub-group of intact rabbits was agree with study of (Islam, 2013), and the decrease in ALP of 40 µg, 80 µg and 120 µg estradiol treated sub-groups of castrated rabbits were agree with the similar studies in the effect of estrogen in oral contraceptives (Smith, and Sizto, 1983; Stock *et al.*, 1985). While the result of AST and ALT were disagree with that found by (Islam, 2013).

Conclusion

This study concludes that the injection of estradiol benzoate at doses of 40, 80 and 120 µgm/ rabbit intramuscularly were not induced changes on lipids profile of intact and castrated male rabbits while HDL was significantly increased at a dose 40 µg in intact male rabbits. AST and ALP were significantly decreased in castrated but not changed in intact male rabbits, while ALT was not changed in castrated and intact male rabbits expect at a dose of 120 µgm was shown significant increase in intact male rabbits.

Conflict of interest

The authors declare that they have no conflict of interest.

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