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Effects of Boldenone consumption and resistance exercise on hepatocyte morphologic damages in male wistar rats

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ABSTRACT

The purpose of present study was to investigate, the effects of anabolic steroid Boldenone (BOL) with eight weeks of resistance training on Structural changes in rat liver. 28 Male adult wistar rats, 12 weeks old and 228/53±7/94 g initial body weight were randomly assigned to four groups: group1: Control+Placebo(C), group2: training+Placebo(T), group3: training+BOL 2mg/kg (BOL2), and group 4: training+BOL, 5mg/kg (BOL5). The resistance training protocol consisted three exercise sessions weekly by 5 reps/3 sets of climbing a ladder (The initial weight attached was 50% of their body weight and increased with 10% per week throughout the training period) for lasted 8 weeks. At the end of the experiment, for light microscopic study Slides were prepared. Sections stained of rat's livers showed no any cell degeneration and cytoplasmic lipid vacuoles in all groups but few samples were seen. Indeed, congested blood sinusoids and cell infiltration, were seen in both BOL-treated groups but with higher in BOL-treated with higher dosage (BOL5). Hepatotoxic effects were severe in group treatment received 5 mg/kg body weight and directly depended on the doses. The present results showed that BOL has a marked adverse effect on the liver tissue, even with low– dose and resistance training. As a result, athletes should not use to enhance muscle mass and strength.

Keywords: Anabolic androgenic steroids, Boldenone, resistance training, liver damage.

INTRODUCTION

Anabolic androgenic steroids (AAS) are synthetic derivatives of the male testosterone hormone that have been modified to improve their anabolic rather than androgenic activity[1]. The anabolic effects of AAS promote protein synthesis, muscle growth and erythropoiesis [2]. Hence, AAS are used to enhance strength and durability of canine, equine and human athletes [3]. 17b-Boldenone (17b-Bol), also called 1-dehydrotestosterone,androsta-1, 4-diene-17b-ol-3-one, is asteroid with androgenic activity that differs from17b-testosterone (17b-T) by only one double bond at the 1-position. Important steroids closely related to17b-Bol and 17b-T are the 17b-boldenone epimer, i.e.17a-boldenone, androsta-1, 4-diene-3, 17-dione (ADD)and androst-4-ene-3, 17-dione (AED). These two diketo substances, ADD and AED, are precursors of17b-Bol and 17b-T, respectively, in humans and different animal species[4]. BOL increases muscle size owing to promotion of positive nitrogen balance by stimulating protein production and reducing protein destruction, as well as causing retention of body water, nitrogen, sodium, and potassium and calcium ions [5]. Like other androgenic steroids, BOL is classified by the International Agency for Research on Cancer (IARC) in class 2A (growth promoters – steroids), as a probable human carcinogen (e.g. prostate and liver tumors), with a carcinogenicity index higher than that of other androgens, such as nandrolone, stanozolol and testosterone and is thus a banned substance [4]. Despite these restrictions, AAS are easily obtained. The abuse of AAS can lead to serious and irreversible organ damage [6]. Among the most common adverse effects of AAS that have been described are reduced fertility [7], hypertension [8], atherosclerosis [9], blood clotting [10],

hepatic neoplasms and carcinoma [11], tendon damage [12], psychiatric and behavioral disorders [13]. Our liver is the largest blood reservoir in our bodies, through which all our blood will eventually pass. This is useful for another function of the liver, which is to remove toxins from the blood. In the case of circulating drugs, the liver combats them by breaking them down and limiting how long they remain effective for – this is why drugs have different dosage allowances because if a drug is absorbed quickly, it needs to be taken more regularly to keep the concentrations in the blood at the correct levels. Similarly, a slowly absorbed drug will require longer intervals between administrations. This rule is apparent for all types of drugs, including recreational drugs. Drugs are not the only products in our bodies that the liver works to remove. Lipids absorbed in the intestine are transported to the liver by the portal circulation where they are taken up by the hepatocytes. These fatty acids can be 1) oxidized to ketone bodies 2) used for the synthesis of cholesterol 3) used for synthesis of triglycerides. There have been relatively few studies which have investigated the detrimental effects of BOL administration on male function. These have explored their role as growth promoters on testis; bulbourethral glands and prostates of vealcalves[14],on reproductive function of stallions and on reproductive performance of male rats [15]. Hence, this study was performed to determine the effects of high-dose administration of BOL on liver weight, and Histopathological features of the liver of mature male wistar rats.

MATERIALS AND METHODS

Animals

28 mature male wistar rats, 12 week age, were housed in metal cages. Fed pelleted commercial feed and water was supplied without restriction. Rats in all groups received humane care in compliance with the animal care guidelines of the National Institute of Health, and the local ethical committee approved this study.

Experimental design

Rats were divided into 4 groups (7rats each). Group A rats served as Control+ Placebo group(C)
Group B: training+Placebo (T), Group C: training+BOL2$_{mg/kg}$ (BOL-2), Group D: training+BOL, 5mg$_{/kg}$(BOL-5). All groups were injected intramuscularly twice weekly for 2 months. The doses of BOL were calculated according to Paget and Barnes (1964).The resistance training protocol consisted three exercise sessions weekly by 5 reps/3 sets of climbing a ladder (The initial weight attached was 50% of their body weight and increased with 10% per week throughout the training period) for lasted 8 weeks.

Evaluated parameters

Histopathological studies

For light microscopy, the left and right lateral lobes were first trimmed into slices of 2–3-mm thickness before immersion in 10% neutral buffered formalin. The left and right medial lobes were fixed in formalin as whole lobes. After overnight fixation, representative sections were trimmed, embedded in paraffin, and stained with hematoxylin-eosin (H&E); a subset was also stained with the periodic acid-Schiff (PAS) method.

Statistical analysis

Statistical Analysis First normal data distribution and homogeneity of groups in order to test the Kolmogorov – Smirnovand Leuven was determined. For comparing means in pre-post test, paired T student test was used. All statistical calculations were performed using SPSS version 16.All data were presented as means with their standard errors, with the significance set at P<0/05.

RESULTS

Histopathology

Histopathological findings of liver were evaluated under light microscopy. Incidence and severity of lesions in BOL-treated groups are summarized in(Table 2).

Table2. Cellular damages observed in the liver sections of different groups

Groups	N	Cellular damages															
		Blood congested				**Inflammation**				**Degeneration**				lipid vacuoles			
		-	+	++	+++	-	+	++	+++	-	+	++	+++	-	+	++	+++
Control+ Placebo	**7**	**6**	**1**	**0**	**0**	**0**	**5**	**2**	**0**	**7**	**0**	**0**	**0**	**7**	**0**	**0**	0
Training+Placebo	**7**	**3**	**4**	**0**	**0**	**0**	**3**	**1**	**3**	**6**	**1**	**0**	**0**	**7**	**0**	**0**	0
Training +BOL2 $_{mg/kg}$	**7**	**1**	**6**	**0**	**0**	**3**	**4**	**0**	**0**	**7**	**0**	**0**	**0**	**7**	**0**	**0**	0
Training+BOL5 $_{mg/kg}$	**7**	**2**	**5**	**0**	**0**	**3**	**4**	**0**	**0**	**7**	**0**	**0**	**0**	**7**	**0**	**0**	0

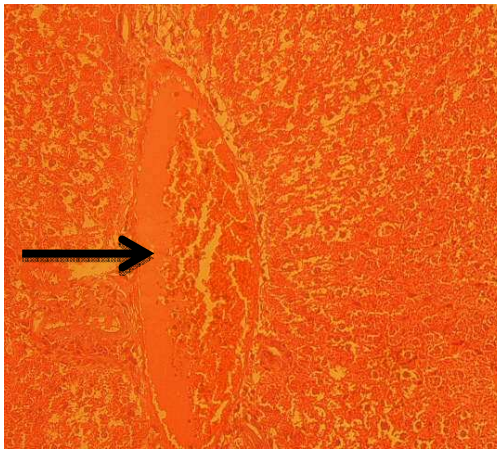

Fig 1. Photomicrograph of rat liver. Congested liver central vein. H&E. (X 100)

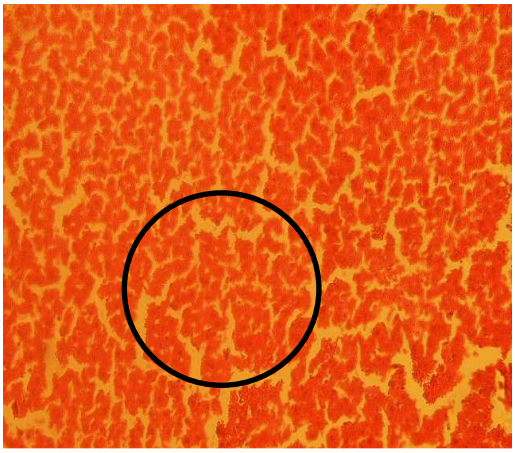

Fig 2. Photomicrograph of rat liver. Cell degeneration. H&E. (X 100)

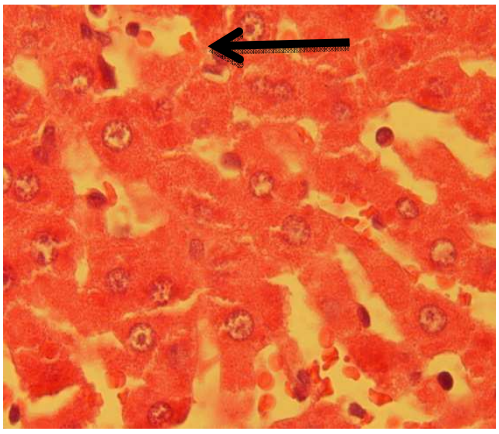

Fig 3. Photomicrograph of rat liver. Cell inflammation. H&E. (X 100)

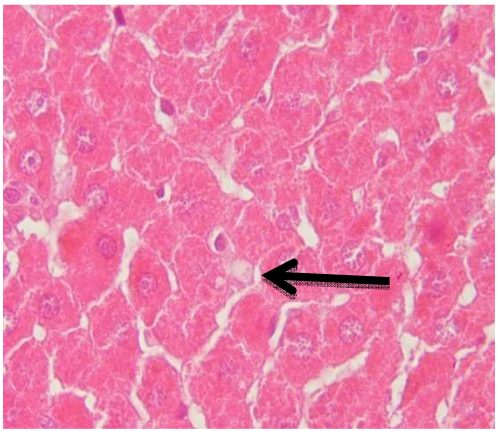

Fig4. Photomicrograph of rat liver. Cytoplasmic lipid droplets. H&E. (X 100)

DISCUSION AND CONCLUSION

Few papers have studied the effect of high dose BOL treatment on liver morphologic changes. The data from the present study indicate that sinusoid blood congestion observed in all groups but there were severe congestion in Boldenone treated with high dosage. In spite of mild damages, there were no any significant cellular degeneration and lipid vocuolations were seen between groups. Our results are in agreement with Ehab Tousson et al. [16] who reported that the anabolic steroid induced hepatotoxicity and with Boada et al. [17] who reported that the anabolic androgenic steroids have toxic effects in primary rat hepatic cultures. Flynn et al. [18] and Silvaet al. [19] reported that in spite of the growth promoting effects, anabolic steroids have shown adverse effects in cardiovascular, hepatic and endocrine systems. Injected Boldenone throughout portal vein reached to sinusoids and induces endothelial destruction. This causes red blood cell flow and increasing portal pressure and eventually induces build up collagen fibers in peripheral tissues and necrosis the cells. The more Boldenone injected, the more damage occurs. On the other hand, this event stimulates chemotaxic and lymphocytes immigration and finally inflammations. Indeed, Boldenone increases nitrogen retention, protein synthesis, appetite and stimulates the release of erythropoietin in the kidneys and reduces protein destruction. Moreover, it produces retention of body water, nitrogen, sodium, potassium and calcium ions. On the other side, Samah et al.[5] reported that anabolic androgenic steroids administration may cause some problems in the genital systems. They disturb the regular endogenous production of testosterone and gonadotropins that may persist for months after drug withdrawal. In conclusion, the Histopathological changes depend on dosage of Boldenone injection. So, athletes should be aware if they want to inject or consumption of such steroids to enhance their strength and hypertrophy.

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