

# Chronic Administration of High Doses of Nandrolone Decanoate on the Pituitary-Gonadal Axis in Male Rats

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**Background:** Anabolic-androgenic steroids (AAS) are abused by athletes.

**Objectives:** The present study was designed to evaluate chronic administration of high doses of nandrolone decanoate (ND) on the pituitary-gonadal axis and hematological parameters in normal male rats.

**Materials and Methods:** Thirty Wistar-Albino male rats were divided assigned to control (C), placebo (P) and test (T) groups (n = 10). Group T received 15 mg/kg intramuscular (IM) ND for eight weeks. Group P received the same volume of peanut oil, but group C did not receive any agent during the trial period. At the end, animals were anesthetized, killed and blood samples collected from cervical vessels. Serum follicle stimulating hormone (FSH) and luteinizing hormone (LH) levels were determined by sensitive rat gonadotropins kit, using ELISA methods. Serum testosterone and hematological parameters were measured by ordinary laboratory methods. Obtained data was analyzed using SPSS 17 by ANOVA and Tukey statistical tests. Results were expressed as Mean ± SD. Statistical difference considered significantly by P < 0.05.

**Results:** Serum testosterone, LH, FSH, weight gain, food and water intake in group T were significantly decreased compared to other groups (P < 0.05). In addition erythrocyte, leucocytes, hemoglobin and hematocrit in group T were significantly increased compared to those of other groups (P < 0.05).

**Conclusions:** Chronic administration of high doses of ND can alter serum FSH, LH and testosterone and hematological parameters in male rats.

**Keywords:** Nandrolone Decanoate; Testosterone; Rats

## 1. Background

Nandrolone decanoate (ND) is an anabolic-androgenic steroid (AAS) used by athletes to improve their athletic ability and muscle mass (1). Anabolic-androgen steroids had various benefits for patients with anemia (2). Administration of ND for six months could increase hemoglobin and hematocrit in anemic men (3). Chronic AAS administration may alter the melanocortin system activity and appetite and food intake in rats (4). Studies showed that chronic administration of ND induces deep changes to mental health in rats (5) and causes DNA damage in leukocytes, liver, bone marrow, brain and testicle cells in mice (6). Sex steroid hormones can have a direct performance on the pituitary, follicle stimulating hormone (FSH) and luteinizing hormone (LH) secretion (7). Androgenized female rats showed alteration in the morphometric thickness of the luminal epithelium, myometrium and perimetrium associated with infertility when treated with steroids in the pre-gestational period (8).

## 2. Objectives

Since ND is abused by athletes and youth, the aim of the present study was to evaluate the effect of high doses of ND administration on serum FSH, LH, weight gain, food and water intake and hematological parameters in male rats.

## 3. Materials and Methods

**Animals:** This experiment was performed on 30 Wistar-Albino male rats, weighing 200-230 grams kept in Zahedan University of Medical Sciences animal house and distinctly housed in cages. The present study received institutional ethical approval from the animal research committee of Zahedan University of Medical Sciences (issued 89-2362). After a week, animals were weighed by EK-b10 Japan digital balance (first weight) and divided into three groups randomly as follows; control (C), placebo (P) and test (T) groups (n = 10):

Group T received 15 mg/kg IM, ND for eight weeks (4) daily, but group P received the same volume of Peanut

oil during the trial period. Group C did not receive any agents in experimental period.

### 3.1. Drug Preparation

ND Iran Hormone (L.P.D.I.C) was purchased from a city drugstore and sustained in the appropriate temperature.

### 3.2. Collection of Blood Samples

At the end of trial period, animals were weighted (final weight) and deeply anesthetized by diethyl ether (Merck Germany), killed and blood samples were collected from cervical vessels. At first, blood samples were collected in CBC tube (coated with EDTA) for hematological parameters measurements. Residual blood samples were collected in ordinary vials and centrifuged at 3000 rpm for 10 minutes to separate serum. Serum was removed (BH-1200 type Iran) and stored at -70°C for further analyses.

### 3.3. Measurements

Serum FSH and LH were measured by sensitive rat kit

(Cusabio Biotech Co. LTD, China), using ELISA method. Serum testosterone was measured by standard laboratory (Mino bine human kit USA) methods. Hematological parameters measured by usual laboratory methods.

### 3.4. Statistical Tests

Obtained data was analyzed using SPSS 17 (IBM, New York, USA) by ANOVA and Tukey tests. Results were expressed as mean  $\pm$  SD. Statistical difference considered significant at  $P < 0.05$ .

## 4. Results

Serum Testosterone, LH and FSH levels in group T were significantly decreased compared to those of C and P groups (Table 1,  $P < 0.05$ ). Moreover, weight gain, food and water intake in group T were significantly decreased compared to those of C and P groups (Table 2,  $P < 0.05$ ). In addition, erythrocytes, leucocytes, hemoglobin, hematocrit and platelet levels in group T were significantly increased compared to those of C and P groups (Table 2,  $P < 0.05$ ).

**Table 1.** Chronic Administration of High Doses of ND on FSH, LH and Testosterone in Male Rats <sup>a,b</sup>

Parameters	Groups			P Value
	C	P	T	
FSH, IU/L	28.11 $\pm$ 2.89	29.19 $\pm$ 4.73	22.17 $\pm$ 2.19 <sup>c</sup>	$P < 0.002$
LH, IU/L	8.21 $\pm$ 3.53	9.41 $\pm$ 1.92	4.82 $\pm$ 1.62 <sup>c</sup>	$P < 0.001$
Testosterone, $\mu$ g/dL	4.62 $\pm$ 2.39	5.11 $\pm$ 1.20	1.09 $\pm$ 0.58 <sup>c</sup>	$P < 0.02$

<sup>a</sup> Abbreviations: C, control; FSH, follicle stimulating hormone; LH, Luteinizing hormone; P, Plasebo; and T, Test.

<sup>b</sup> Based on ANOVA and Tukey test, FSH, LH and testosterone values in group T were significantly decreased compared to those of C and P groups.

<sup>c</sup>  $P < 0.05$ ;  $n = 10$ .

**Table 2.** Chronic Administration of High Doses of ND on Weight Gain, Food, Water Intake and Hematological Parameters in Male Rats <sup>a,b</sup>

Parameters	Groups			P Value
	C	P	T	
Weight, g	239.6 $\pm$ 13.5	237.9 $\pm$ 11.6	212.4 $\pm$ 11.6 <sup>c</sup>	$P < 0.001$
Food intake, g	15.1 $\pm$ 1.9	15.6 $\pm$ 1.1	14.1 $\pm$ 1.3 <sup>c</sup>	$p < 0.002$
Water intake, mL	43.4 $\pm$ 4.4	44.6 $\pm$ 2.3	40.6 $\pm$ 2.3 <sup>c</sup>	$P < 0.02$
Hemoglobin, gr/dL	14.5 $\pm$ 2.2	14.82 $\pm$ 51	16.41 $\pm$ 1.21 <sup>c</sup>	$P < 0.03$
Leucocytes, cell/ $\mu$ L	7200 $\pm$ 800	69200 $\pm$ 970	8600 $\pm$ 1100 <sup>c</sup>	$P < 0.01$
Erythrocyte, mL/ $\mu$ L	5.81 $\pm$ 1.2	5.22 $\pm$ 1.2	6.95 $\pm$ 1.3 <sup>c</sup>	$P < 0.01$
Hematocrit, %	43 $\pm$ 4	43 $\pm$ 3	48 $\pm$ 4 <sup>c</sup>	$P < 0.01$
Platelets, 1000cell/ $\mu$ L	230 $\pm$ 34	228 $\pm$ 30	320 $\pm$ 42 <sup>c</sup>	$P < 0.02$

<sup>a</sup> Abbreviations: C, Control; P, Plasebo; and T, Test.

<sup>b</sup> Based on ANOVA and Tukey tests, weight gain, food and water intake values in group T were significantly decreased compared to those of group C, but hematological parameters were increased compared to other groups.

<sup>c</sup>  $P < 0.05$ ;  $n = 10$ .

## 5. Discussion

Chronic administration of ND at high dose decreased plasma FSH, LH, testosterone, weight gain and food and water intake in male rats. In addition, erythrocytes; hemoglobin, hematocrit, Leukocyte and platelets values were increased in group T. High doses of AAS used for

athletic enhancement can lead to irreversible organ damage such as reduced fertility and gynecomastia in males (9). Moreover, AAS has a high affinity for the androgen receptor in central and peripheral tissues and causes impairments in hypothalamicpituitary-gonadal axis (9).

In addition, Kuhn CM reported that AAS affects androgen receptors and alters enzymatic aromatization of testosterone derivatives to increase its affinity to estrogen receptors (10). Our finding exposed that ND decreased serum LH and testosterone secretion in the group T. These results are the same as Alsio (11), which reported that AAS administration was probable to reduce hypothalamic-pituitary-gonadal axis activity by affecting physiological feedback mechanisms. Bijlsma et al. (7) in a pilot study found that ND administration in male patients with rheumatoid arthritis caused significant decreases in serum Testosterone and FSH levels. Our findings showed that FSH value in group T was significantly decreased compared to that of other groups and it was the same as literature study (10). Oda and El-Ashmawy (12) reported that chronic administration of ND caused decrease in testes and epididymis weights, but did not show any significant changes in weight gain in normal rabbits. Our results are different with that of Oda and El-Ashmawy (12). This difference is probably due to different used animals. Our findings were in accordance with the theory that sex steroids hormones can act directly on the hypothalamus-pituitary-testis axis and resulting in selective FSH and LH secretion (8). In addition, our outcome was in agreement with that of Shokri et al. (13), which revealed that exercise training increases the amount of apoptosis in the spermatogenic cell lineage by supraphysiological dose of ND in rats. Our study revealed that weight gain, food and water intake in group T were significantly decreased compared to those of other groups, which is in accordance with the literature (14). Bhasin et al. (14) found that erythrocytes, hemoglobin and hematocrit were improved dose dependently in healthy men aged 18 to 50 years who received AAS and changes in levels of hemoglobin and hematocrit were related to changes in testosterone concentrations compared to those of placebo group. In the present study, erythrocyte, hemoglobin, hematocrit, leukocyte and platelets values in group T were significantly increased compared to those of other groups and confirmed by another investigation (14). This is presumably because chronic ND administration in the present study increased metabolism, serum erythropoietin concentration and stimulated hematopoiesis in bone marrow.

In conclusion, chronic administration of high doses of ND administration could alter serum FSH, LH, testosterone, weight gain, food and water intake and hematological parameters in male rats.

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