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THE ADMINISTRATION OF NANDROLONE DECANOATE MAY CAUSE MULTIPLE ORGAN FAILURE

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Abstract

Aim.In this study, it was aimed to investigate the effect of anabolic androgenic steroid nandrolone decanoate (ND) which commonly used for doping by sport players, on the relative weight of liver, spleen and gonads in male and female rats.

Methods.For this purpose, 60 rats (male =30, female =30) were used. Rats were divided into three groups as control group (0.5 mL 0.9% physiological saline, intraperiteonally (IP), peanut oil (PO) group (0.5 mL, IP) and ND group (10 mg/kg ND diluted in 0.5 mL peanut oil, IP). All injections were made daily for five days with a break for 2 days per week throughout the four weeks. The rats were euthanised at the end of the experiments and the relative weight of liver, spleen, testicle and ovaries were measured.

Results. It was determined that relative weight of liver in male rats and the relative weight of spleen in both male and female rats in ND groups were lower than those in control group ($p<0.05$). Moreover, it was found that the administration of ND increased the relative weight of testicles as compared to control group ($p<0.05$).

In conclusion, it is suggested that the decrement of relative weight of liver and spleen and the increment of relative weight of testicles may be an indicator for individual multiple organ failure and damage following long term administration of ND diluted in peanut oil.

Keywords: Nandrolone, liver, spleen, testis, ovaries.

Introduction

Hormones, described as androgens and synthesized from leydig cells of testes, are testosterone, androsterone and dehydroepiandrosterone (DHEA) (Stryer 1988, Yilmaz 1999).

The inhibiton and stimulation of synthesis and release of androgenes are provided by adenohypophysis origin hormones such as luteinizing hormone (LH) and follicle stimulating hormone (FSH) (Löffler and Petrides 1988). Testosterone and other androgens play a key role in the growth and development of the body by increasing protein synthesis, decreasing aminoacide and protein catabolism or preserving the nitrogen in fat-free body mass (Guyton and Hall 2001, Kuhn 2002, Kayaalp 2005, Gül 2008). Anabolic androgenic steroids (AAS) are synthetic drugs that have similar effects to testosterone (Kochakian and Yesalis 2000, Khun 2002). Recently, more than one hundred AAS drug has been developed. AAS drugs are sold by prescription in USA but in some countries, they are illegally sold. Oral administration of oxymetolone, oxandrolone, methandrostenolone, stanozolol and parenteral administration of nandrolone decanoate, nandrolone propionate, testosteone spionat, boldenon andesilenat are commonly abused AAS drugs (Evans 2004). Nandrolone (19-nortestosteron) is one of the most used AAS drug (Aksoy and Dağoğlu 1998, Verroken, 2001, Kuhn 2002, Maravelias et al ark 2005). Nandrolone is produced by elimination of C-19 methyl group from testosterone and its chemical name is 17β–hidroxy-19-norandrost-4-en-3-on (Furman 2007). Nandrolone decanoate (ND) is the conjugation of nandrolone and decanoic acid. This formation provides the high availability administration of ND such as both intramuscular and subcutan injection (Van der Vies 1993, FASS 2002, Furman 2007). Deca-Durabolin® , the injectable form of ND which is recently produced 25-200 mg /ml dose range under different brand names (i.e. Anaboline, Hybolin Deconoate, Elpihormo, Extraboline, Nandrolone Dec, Jebolan,Nurezan, Retabolil, Retabolin, Turinabol Depot etc.) in many countries, has been introduced into market in 1960s (Furman 2007).

AAS drugs cause ethical problems when they are used to increase performance by sport players in competitions, however uncontrolled usage of AAS may also induce serious side effects such as cardiovascular system failure, prostate gland diseases, lipid metobolism failure or insuline sensitivity (Bhasin et al 1996).

It has been reported that the application of ND have beneficial effects on bone tissue and the treatment of hip fracture in elderly patients, however it has different effects on proencephale, frontale, parietale and cortex parts of male rat brain (Kindlundh et al 2003,Tengstrand et al 2006).

The aim of the present study is determine the effect of nandrolone decanoate administration on relative organ weights in male and female rats.

Materials and methods

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In this study, 30-day-old, 60 Sprague Dawley rats which were obtained from Experimental Medicine Research and Application Center Selcuk University, were used. Rats were fed *ad libitum* with the same commercial rat diet. The ethics committee of Selcuk University, Faculty of Veterinary Medicine approved all procedures. Rats were randomly assigned to three groups of 10 male and 10 female rats each as follows; negative control (0.5 mL normal saline solution, IP), positive control (0.5 mL peanut oil, IP) and experimental (ND) (10 mg/kg within 0.5 mL peanut oil, IP) groups.) All injections were made daily for five days with a break for 2 days per week throughout the four weeks.

The mean body weight which was measured weekly from the beginning to end of the study, was used to re-calculate the dosage of ND. The relative organ weights (% g) were calculated by proportion of weights of liver, spleen, testis (left and right) and ovary to body weight of rats which were euthanised at the end of the experiments by cardiac puncture.

The statistical analysis was performed by SPSS 13,0 (SPSS 13,0 for Windows/ SPSS® Inc, Chicago, USA) and the results were expressed as mean ± SE. The results between groups were analyzed by ANOVA and Duncan's multiple range test. Independent *t* test was used to evaluate the results between male and female rats. In all cases, a probability of error less than 0.05 was selected as criterion for significance.

Results

The relative organ weight of liver, spleen, testes and ovary obtained end of the study is given at Table 1 and 2, respectively. It was observed that a decline of relative weight of liver and spleen was evident in ND group as compared to control group, however relative weight of left and right testes increased, whereas the relative weight of ovary did not change.

Table 1. The relative weight (% g) of liver and spleen following nandrolone decanoate administration in male and female rats (mean±SE).

Parameter (% g)	Control Female	Control Male	PO Female	PO Male	ND Female	ND Male
Liver	4,67±0,10^{a}	4,35±0,10^{b}	4,29±0,11^{b}	4,21±0,08^{bc}	4,28±0,06^{b}	3,96±0,06^{c}
Spleen	0,38±0,01^{a}	0,34±0,01^{b}	0,33±0,01^{b}	0,26±0,01^{c}	0,25±0,01^{c}	0,20±0,06^{d}

ND: Nandrolene decanoate, PO: Peanut oil. $^{a, b, c}$: Superscripts with different letters in the same row differs significantly ($p<0,05$).

Tablo 2. The relative weight of testes and ovary following nandrolone decanoate administration in male and female rats (mean±SE).

Parameter (% g)	Control	PO	ND
Left Testes	0,76±0,04^{b}	0,98±0,05^{ab}	1,16±0,05^{a}
Right Testes	0,76±0,03^{b}	0,95±0,07^{ab}	1,12±0,05^{a}
Ovary	0,03±0,01^{a}	0,03±0,01^{a}	0,03±0,01^{a}

ND: Nandrolene decanoate, PO: Peanut oil.$^{a, b}$: Superscripts with different letters in the same row differs significantly ($p<0,05$).

Discussion

It has been reported that liver disease and damage occur in patients using AAS drugs for the treatment, as well as in sport players using abused AAS drugs. (Gragera et al 1993, Bronson and Matherne 1997). The most common liver abormalities are subcellular changes in hepatocytes, cholestasis, peliosis hepatis, hepatocellular hyperplasia, carcinomas and general liver dysfunction (Hartgens and Kuipers 2004).

It has been indicated that the damage in liver following AAS administration is seriously harmful, when high dose of C-17 alkile androgens (i.e.Oxandrolone) is orally used. Therefore, sport players minimize the use of this kind of androgens because of the oral administration of AAS cause liver tissue damage due to hepatocellular metabolism of orally taken AAS to the gastro intestinal system and increasing resistance of hepatic inactivation to high dose AAS (Rahusen ve ark 2004).

There are limited reports related to morphological changes in liver following AAS administration, although there are numerous studies reporting the level of different liver enzymes. Vieira et al (2008) observed that the amount of collagen importantly increased in

parenchyma of rat liver, following above the pharmacological dose of ND along five weeks, while Gerez et al (2005) reported that liver weight of ND administered rats was higher as compared to control. Similarly, Karbalay-Doust and Noorafshan (2009) reported that liver weight of ND administered rats increased at the rate of 19-36%. However, Yu-Yahiro et al (1989) observed that the liver weight of ND administered rats was lower as compared to control groups at the sixth week of the ND application. In the present study, the decrement of relative liver weight of ND administered rats was consistent with the observation of Yu-Yahiro et al (1989) and it is suggested that this decrement may be due to the type of anabolic steroid, the form and duration of administration of the drug. Although there have been limited reports indicating the effect of AAS administration on spleen weight, Uhlén et al (2003) reported that ND administration did not alter the relative spleen weight and it is suggested that the reason of decreasing relative spleen weight may be due to the form and duration of administration of the drug.

In studies performed to investigate the effect of AAS on the histopathology of reproductive organs, it has been reported that during maintenance of spermatogenesis, the normal structure of spermatozoid changes and the motility and the density of spermatozoid decreases (Holma 1977, Knuth et al 1989). Takahashi et al (2004) observed that the administration of AAS caused serious morphologic disorders in testes, whereas Shah (2010) reported that the weight of testes and epididymis in rats decreased following ND administration Noorafshan et al (2005) reported a decline in testes volume and in seminiferous tubule length on 14th week of ND administration. However, the authors indicated that the decline in testes volume and weight following high dose of ND administration was not observed following low dose of ND administration, whereas the testes weight increased. Dong-Mok et al (2010) reported that oral administration of ND did not alter the testes weight in rats, similarly, Feinberg et al (1997) observed that pre and postpubertal injection of testosterone propionate did not affect testes weight. Minkin et al (1993) described that the administration of 10 and 50 mg ND increased body weight, diameter and weight of kidney at the end of 8th week of the experiment. In the current study, it was observed that ND administration increased the left and right testes weight and this finding was in accordance with Minkin et al (1993) and Noorafshan et al (2005), while this finding was inconsistent with some reports. Therefore, it is suggested that the discrepancies in the increasing testes weight obtained in this study as compared to other studies may be due to the application form and dose of ND (Noorafshan et al 2005) and the puberty age of the experimental animal.

In studies performed on female rats, it has been indicated that AAS applications cause disorders in oestrous cycle and delay the beginning of puberty by affecting FSH synthesis as same as LH synthesis in male rats (Gerez et al2005, Mobini Far et al2007). Moreover, it has been detected that vaginal oestrous in rats is suppressed in two weeks following ND administration (Blasberg et al1997). Although it has been detected that ND administration increases uterine weight and endometrial thickness (Obasanjo et al 1998), causes physiological and morhologic differentiations in rat uterus (Mobini Far et al. 2007), affects the ovarian weight (Camargo et al. 2009), Gerez et al (2005) reported that ND administration did not alter the ovary, uterus and hypophis weight. However, Bronson (1996) detected that AAS applications in female mice decreased the ovary weight. The absence of difference between relative weight of ovary as shown in the results of the present study was consistent with Gerez et al (2005) and it is suggested that the oestorus synchronization of rats is needed to obtain more reliable results.

Conclusion

New studies which include ND administration in long term and at different dose ranges are need to clearly detect the organ damage, besides, it is suggested that more reliable results may be obtained by supporting the findings with histopathological data.

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