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Effect of Nandrolone Decanoate on Serum FSH, LH and Testosterone Concentration in Male Albino Mice

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ABSTRACT [ENGLISH/ANGLAIS]

Various drug addiction are increasing among various populations throughout the world. Anabolic androgenic steroids (AAS) rank among the drugs most widely abused with the goal of improving athletic ability, appearance or muscle mass. Despite widespread abuse of AAS, the endocrine effects of supraphysiologic doses of these compounds remain unclear. This study was conducted to investigate the effect of nandrolone decanoate, the most commonly abused AAS, on serum levels of gonadotropins (FSH and LH) and male sex hormone (testosterone) in male albino mice. Blood samples were collected from normal control and nandrolone decanoate treated (2.5mg/week administered intramuscularly for 13 weeks) male albino mice, and serum levels of FSH, LH and testosterone were measured by enzyme immuno assay (EIA) technique. The results show a highly significant decrease ($p < 0.01$) in the serum levels of FSH, LH and testosterone in nandrolone decanoate treated male albino mice compared to that of the normal control group. This study concludes that nandrolone decanoate abuse suppresses the reproductive axis which may lead to sexual suppression and infertility.

Keywords: Anabolic-androgenic steroids, FSH, LH, Mice, Nandrolone decanoate, Serum, Testosterone

RÉSUMÉ [FRANÇAIS/FRENCH]

Toxicomanie Divers sont en hausse chez les différentes populations à travers le monde. Les stéroïdes anabolisants androgènes (SAA) se classent parmi les médicaments les plus largement abusé dans le but d'améliorer la capacité sportive de masse, l'apparence ou le muscle. Malgré de nombreux abus de l'AAS, les effets endocriniens de doses supraphysiologiques de ces composés restent flous. Cette étude a été menée pour étudier l'effet de la nandrolone décanoate, la plus couramment consommée AAS, sur les niveaux sériques de gonadotrophines (FSH et LH) et l'hormone de sexe mâle (testostérone) chez des souris mâles albinos. Des échantillons de sang ont été collectées à partir des contrôles normaux et décanoate de nandrolone traités (2.5mg/week administré par voie intramusculaire pendant 13 semaines) chez les souris mâles albinos, et les taux sériques de FSH, LH et de testostérone ont été mesurés par l'enzyme immuno essai (EIE) technique. Les résultats montrent une diminution très significative ($p < 0,01$) des taux sériques de FSH, LH et de testostérone dans la nandrolone décanoate traiter des souris mâles albinos par rapport à celle du groupe contrôle normal. Cette étude conclut que la nandrolone décanoate supprime l'abus de l'axe de reproduction qui peut conduire à la suppression sexuelle et l'infertilité.

Mots-clés: Stéroïdes anabolisants-androgéniques, FSH, LH, Souris, la nandrolone décanoate, sérum, la testostérone

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INTRODUCTION

Anabolic-androgenic steroids (AAS), the synthetic derivatives of testosterone, are the commonly abused drugs used by some athletes to improve their physical fitness and appearance, of which nandrolone decanoate is one of the most common [1]. AAS are pharmacologically important in the treatment of reproductive system dysfunction, anaemia and breast cancer [2]. However, studies confirm AAS abuse by non-competitive athletes as well as non-athletic sub-groups to gain euphoria [3-6]. Reports indicate that AAS are taken by the abusing athletes at supraphysiological doses which are usually 10

to 100 fold the recommended therapeutic dose [7]. AAS have been abused, traditionally, in drug-use cycles of 6-14 weeks followed by a drug-free period to prevent building up tolerance to AAS [8].

AAS abuse impacts upon several hormone systems like the hypothalamic-pituitary-adrenal (HPA), hypothalamic-pituitary-thyroid (HPT) and hypothalamic-pituitary-gonadal (HPG) axes [9-12]. The administration of high doses of exogenous androgens in men has been reported to result in decreased levels of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) through negative impact on the hypothalamic-pituitary-gonadal

(HPG) axis with reduced endogenous testosterone production leading to decreased spermatogenesis, reduced semen density, testicular atrophy and abnormal sperm morphology attributing to infertility [13-24]. Normal spermatogenesis requires a 50-fold higher androgen concentration in the testis as compared to the peripheral serum [25]. However, reports indicate that azoospermia is not achieved in normal men despite using a moderately large testosterone dosage (300mg/week) though it failed to trigger spermatogenesis [17].

The exact adverse effects of AAS abuse are difficult to determine due to lack of clinical trials which mimic AAS abuse by athletes [26]. However, it has been reported that AAS compounds affect almost all body systems due to the presence of androgen receptors in all major body tissues [8].

Despite many researches on the effects of AAS compounds on different body systems, the endocrine effects of supraphysiologic doses of these compounds remain unclear. Therefore, the present study was conducted to investigate the effects of nandrolone decanoate on serum levels of gonadotropins (FSH and LH) and male sex hormone (testosterone).

MATERIALS AND METHODS

Animals

Forty adult male albino mice, weighing between 20-25 g (three to four months old), were randomly selected from the animal house of the Zoology Department of Gauhati University, Guwahati, Assam (India) after approval of the Ethical Committee of Animal Welfare of Gauhati University. Before starting the experimental procedure, all the animals were acclimatized in the animal room for four weeks and fed on standard animal diet. Adequate measures were taken to minimize pain or discomfort to the mice and the experiments were conducted in accordance with international standards on animal welfare and were also compliant with local and national regulations.

Animal Grouping and Treatment

The 40 animals were randomly divided into two different groups of 20 each: Group-I (Normal Control Group), receiving normal standard diet but did not receive any treatment; and Group-II (Experimental Group), receiving intramuscular injection of 0.1ml of 2.5 mg of nandrolone decanoate weekly during the experimental period of 13 weeks. In the present study, a dose of 2.5 mg Nandrolone is chosen only to ascertain the effect in this particular

lower dose (2.5 mg of Nandrolone is present in 0.1 ml of 25 mg Nandrolone decanoate solution) [27] as most work were conducted by injection of higher doses [17,28]. Doses were given mg/kg body weight.

Sample Collection and Estimation of Serum Levels of FSH, LH and Testosterone

On the day of sample collection the weight of the animals were recorded and a general examination with palpation of the abdomen and thorax was performed before actual collection of sample. 1 ml of blood samples were collected in sterilized vials from the caudal vein of the normal control group and the experimental group (nandrolone decanoate treated group) at different days interval as 10th, 20th, 30th, 45th, 60th, 75th and 90th days for the estimation of serum FSH, LH and testosterone concentrations by EIA (enzyme immuno assay) technique [29,30] using a UV-visual spectrophotometer

Statistical Analysis

The results obtained were statistically analyzed for t-test, percentage deviation, coefficient of variation (CV) and others following Croxton [31].

RESULTS

The obtained results are summarized in Table 1. The analysis revealed decreased levels of mean serum FSH, LH and testosterone in nandrolone decanoate treated group of male albino mice (with a dosage of 2.5 mg/ week during the experimental period of 13 weeks) as compared to normal control group.

In nandrolone decanoate treated group, the mean serum FSH values were observed to decline gradually from 14.2 ± 0.51 mIU/ml on 10th day to 8.7 ± 0.29 mIU/ml on 90th day of treatment. A gradual decline was also recorded in the serum LH and testosterone values from 18.3 ± 0.51 mIU/ml on 10th day to 10.4 ± 0.57 mIU/ml on 90th day, and 2.02 ± 0.09 ng/ml on 10th day to 1.09 ± 0.08 ng/ml on 90th day respectively (Table 1).

DISCUSSION

One of the most prominent effects of AAS abuse is the negative impact on the pituitary- gonadal axis [24,32]. AAS compounds stimulate hypogonadotropic hypogonadism coupled with decreased serum testosterone concentrations [14,16,33]. It was previously reported that there is a noticeable depression of serum FSH and LH in men abusing AAS resulting in impaired spermatogenesis including oligozoospermia to

azoospermia, abnormalities in sperm motility and morphology [9,22,24,33,34].

In the present investigation, with the experimental dosage (2.5 mg/week) of nandrolone decanoate, a highly significant decrease ($p < 0.01$) in the serum level of gonadotropins in general and testosterone was observed throughout the experimental period. However, no initial change (up to 20th day in the serum level of FSH, 30th day in serum LH level and 10th day in case of testosterone) was a significant observation in the present study. In case of FSH and testosterone, the decrease in serum level was found to be highly significant ($p < 0.01$) from 30th day

onwards and the decline was sustained up to the terminal part of the experimental period and on 90th day the mean values were found to be lowest with 37.86% (in case of FSH) and 47.85% (in case of testosterone) below the normal base line (Table 1). On the contrary, a delayed change was observed in case of LH where the decrease in serum level was found to be insignificant ($p > 0.05$) up to 30th day which gradually declined towards the end of the experimental period with highest amount of declination (42.86%) on 90th day from the normal base line (Table 1). This reduction in serum hormone level was observed to be positively correlated with the duration of treatment.

TABLE 1: This table shows the mean serum values of FSH, LH and Testosterone in normal control (Group-I) and experimental group (Group-II) of male albino mice

Parameters	Groups		DAYS OF TREATMENT						
			10 th	20 th	30 th	45 th	60 th	75 th	90 th
FSH (in mIU/ml)	Group-I (Normal Control Group)	Mean	14.4	14.4	14.6	14	14.2	14.4	14
		SEM ±	0.52	0.33	0.63	0.45	0.42	0.48	0.35
	Group-II (Nandrolone Decanoate treated Group)	Mean	14.2 ^{NS}	14.2 ^{NS}	12.6 ^{**}	12.2 ^{**}	8.8 ^{**}	9 ^{**}	8.7 ^{**}
		SEM ±	0.51	0.42	0.53	0.31	0.36	0.44	0.29
		% Deviation	-1.39	-1.39	-13.7	-12.86	-38.03	-37.5	-37.86
LH (in mIU/ml)	Group-I (Normal Control Group)	Mean	18.6	18.5	18	18	18.4	18.6	18.2
		SEM ±	0.45	0.42	0.35	0.35	0.39	0.45	0.42
	Group-II (Nandrolone Decanoate treated Group)	Mean	18.3 ^{NS}	18.4 ^{NS}	17.8 ^{NS}	16.2 ^{**}	16.3 [*]	12.6 ^{**}	10.4 ^{**}
		SEM ±	0.51	0.69	0.37	0.37	0.79	0.4	0.57
		% Deviation	-1.61	-0.54	-1.11	-10	-11.41	-32.26	-42.86
Testosterone (in ng/ml)	Group-I (Normal Control Group)	Mean	2.1	2.1	2.12	2.08	2.07	2.06	2.09
		SEM ±	0.07	0.07	0.07	0.07	0.07	0.07	0.08
	Group-II (Nandrolone Decanoate treated Group)	Mean	2.02 ^{NS}	1.92 [*]	1.49 ^{**}	1.11 ^{**}	1.26 ^{**}	1.14 ^{**}	1.09 ^{**}
		SEM ±	0.09	0.07	0.06	0.04	0.08	0.09	0.08
		% Deviation	-3.81	-8.57	-29.72	-46.63	-39.13	-44.66	-47.85

^{NS} - Not significant at $p > 0.05$; ^{*} - significant at $p < 0.05$; ^{**} - highly significant at $p < 0.01$

The findings of the present investigation are in conformity with the previous reports and agree well with the fact that increased level of exogenous androgens affects the hypothalamic-pituitary-gonadal axis by depletion of

endogenous androgen in the circulating fluid [9,14,16,33]. About 50% reduction in the serum levels of these hormones (testosterone, FSH and LH) in the present experimental set-up was found to be more or less

consistent suggesting negative feedback to the hypothalamus.

Thus, our findings clearly indicate that administration of nandrolone decanoate (2.5 mg/week) intramuscularly suppresses the reproductive axis and may result in male infertility. However, further investigation is needed to establish a causal link between nandrolone decanoate and male infertility.

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CONFLICT OF INTEREST

No conflict of interests was declared by authors

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