Influence of nandrolone decanoate administration on serum lipids and liver enzymes in rats

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Abstract

BACKGROUND: Anabolic-androgenic steroids have been associated with several side effects. This experimental study was conducted to evaluate the effects of nandrolone decanoate (ND, an anabolic steroid) on lipid profile and liver enzymes in rats in Iran.

METHODS: Forty adult male and female of Wistar strain rats were randomly assigned to four groups of 10 animals each: male control, female control, ND-male treated (15 mg/kg b.w./day), and ND-female treated (15 mg/kg b.w./day). Serum concentrations of total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol, aspartate aminotransferase (AST), and alanine aminotransferase (ALT) were measured in all studied groups.

RESULTS: Treating rats with ND (case group) resulted in a significant elevation of TC (69.4 ± 8.7), TG (101.6 ± 32.9) and ALT (72.2 ± 13.8) and significant reduction of LDL (6.4 ± 2.6) and AST (138.7 ± 19.4) as compared to control group in female rats. ND supplementation (case group) significantly increased TC (64.4 ± 6.2), AST (255.0 ± 32.0), and ALT (84.3 ± 3.8) in comparison with the control group in male rats.

CONCLUSION: Overall, our result indicated that the ND use can cause a negative effect on lipid profile and liver enzyme in rats.

Keywords: Aspartate Aminotransferase, Nandrolone Decanoate, Rat, Steroids

Introduction

During the past decades, the naturally occurring hormone testosterone and its synthetic derivatives [collectively termed anabolic androgenic steroids (AAS)] have been used by athletes, bodybuilders, and youths in order to increase muscle mass or enhance physical endurance. The AAS are a family of lipophilic hormones derived from cholesterol that includes the natural male hormone, testosterone, together with numerous synthetic testosterone derivatives. AAS are used in medical clinics as well as with the purpose to improve physical performance of individuals submitted to physical training. Although AAS have valid medicinal uses, nontherapeutic abuse also occurs. Recent increases in androgen prescriptions are evident. Some of the common orally administered AAS include nandrolone decanoate (ND), oxymetholone, oxandrolone, and stanozolol. ND is frequently used to treat many diseases such as human immunodeficiency virus-associated muscle wasting, prostate cancer and benign prostate hyperplasia, and well-known androgen-dependent diseases. However, despite such therapeutic beneficial potentials, chronic, and unregulated use of ND result in undesirable outcomes, including hepatic toxicity, alteration of thyroid function, cardiovascular toxicities. Many studies concluded that androgen therapy is associated with high incidence of adverse effect in lipid profiles, while others have shown that ND has no marked effect on the lipid profile. In the study by Ghorbanihaghi et al., treatment with ND was affected in total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL), and liver enzymes in rats.
In regard to the importance of knowing ND effects on liver and heart and inconsistent results of previous studies in this context, the present study aimed to assess the ND effects on lipid profile and liver enzymes in rats.

### Materials and Methods

This experimental study was performed in Zahedan University of Medical Sciences, Iran, at 2009. It was used forty adult male and female of Wistar strain weighing 180 ± 30 g. Rats purchased from the Pasteur Institute in Tehran, Iran.

The animals were housed in air-conditioned room maintained at 22 ± 2 °C, with a relative humidity of 50 ± 10% and a 12 hours light/dark cycle with free access to food (commercial rat chow: Pars Animal Feed Co., Tehran, Iran) and water.

This study was approved by the Ethics Committee of the Zahedan University of Medical Sciences under approval No. 1230 at 2009.

ND was prepared from Caspian Tamin Pharmaceutical Company (Guilan, Iran). The rats were randomly assigned to four groups of 10 animals each: male control, female control, ND-male treated (15 mg/kg b.w./day), and ND-female treated (15 mg/kg b.w./day). Duration of each treatment was 8 weeks.

Blood was withdrawn to estimate biochemical factors from the animals under ether anesthesia. The equipment was previously calibrated. Samples were maintained for 40 minutes at laboratory temperature and then centrifuged (1000 g for 15 minutes) to separate serum.

Lipid profile (mg/dl) [TC, TG, LDL-cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C)], and liver enzymes (U/L) [aspartate aminotransferase (AST) and alanine aminotransferase (ALT)] were assayed using routine enzymatic methods ( Pars Azmoon, Tehran, Iran) on an automated chemistry analyzer (Hitachi Model 902, Tokyo, Japan). All experiments were carried out in Zahedan University of Medical Sciences.

Statistical analyses were conducted using SPSS software for Windows (version 13, SPSS Inc., Chicago, IL, USA). The student t-test was used to compare mean values between groups. The results were expressed as mean ± standard deviation. A $P < 0.050$ was considered as statistically significant.

### Results

Effect of ND on serum concentrations of lipid profile parameters and liver enzymes in female and male groups are provided in table 1. Treating rats with ND resulted in a significant elevation of TC (69.4 ± 8.7), TG (101.6 ± 32.9), and ALT (72.2 ± 13.8), and significant reduction of LDL (6.4 ± 2.6) and AST (138.7 ± 19.43) as compared to control group in female rats. In contrast, the serum concentrations of HDL-C were statistically unchanged after the ND consumption in female group.

ND administration significantly increased TC (64.4 ± 6.2), AST (255.0 ± 32.00), and ALT (84.3 ± 3.8) in comparison with the control group, while there was no statistically significant difference in other factors (TG, LDL-C, and HDL-C) in male rats.

### Discussion

Among the various anabolic steroids available, ND is presented as one of the most used. Evidence from the current study indicated a trend toward increase of the TC, TG, and ALT and decline of the HDL-C in female rats and enhancement of the TC, AST, and ALT in male rats after ND consumption.

### Table 1. Effects of nandrolone decanoate on serum concentrations of lipid profile parameters and liver enzymes in experimental groups

| Gender | Group (n = 40) | Total cholesterol (mg/dl) | Triglyceride (mg/dl) | Low-density lipoprotein (mg/dl) | High-density lipoprotein (mg/dl) | Aspartate aminotransferase (U/L) | Alanine aminotransferase (U/L) |
|--------|---------------|--------------------------|---------------------|-------------------------------|---------------------------------|-------------------------------|-------------------------------|
| Female (n = 20) | Control | 56.1 ± 7.9 | 77.1 ± 17.2 | 12.6 ± 6.6 | 43.6 ± 4.4 | 169.8 ± 37.70 | 59.8 ± 9.9 |
| | Case | 69.4 ± 8.7 | 101.6 ± 32.9 | 6.4 ± 2.6 | 42.6 ± 4.9 | 138.7 ± 19.43 | 72.2 ± 13.8 |
| | P | 0.020 | 0.050 | 0.020 | 0.640 | 0.030 | 0.020 |
| Male (n = 20) | Control | 54.1 ± 11.4 | 67.2 ± 15.4 | 9.2 ± 7.1 | 44.1 ± 4.2 | 169.7 ± 4.24 | 71.6 ± 8.9 |
| | Case | 64.4 ± 6.2 | 64.4 ± 16.1 | 7.9 ± 3.9 | 44.7 ± 4.8 | 255.0 ± 32.00 | 84.3 ± 3.8 |
| | P | 0.020 | 0.680 | 0.670 | 0.770 | 0.001 | 0.010 |

Student t-test was used to compare mean values between groups; P values are significant $P < 0.050$
Among the many toxic and hormonal effects of AAS that have been documented, attention has been turned recently to the increased levels of TC and LDL-C and decreased levels of HDL-C,25,26.

Although the results of the AAS effect on TC levels are conflict. Some studies have found that repeated supraphysiologic doses of AAS are associated with an increase in TC levels,27 whereas others have failed to find such an association.28 The reason for the discrepancy observed in the effect on TC after AAS administration may be the different study designs used, sampling time, type of AAS used, administration route, etc.29

In our study, ND was used and had an undesirable effect on TC levels.

Some studies comment that submaximal exercise induces an increase in hepatic lipoprotein lipase, which in turn leads to enhanced TG clearance and probably decreases plasma clearance of HDL constituents.30

In the Gold et al.,31 study in human immunodeficiency virus (HIV)-positive males, no significant differences were detected between the placebo and ND groups (150 mg) for changes in serum cholesterol (total, LDL, or HDL), and TG whereas in our study, significant differences were observed in female group and TC in male group.

Also finding of Hartgens et al.,28 and Sattler et al.32 study are inconsistent with our results. Hartgens et al.,28 found, ND (200 mg/week) did not influence serum TG, TC, HDL-C concentrations after four and 8 weeks of intervention. Sattler et al.32 illustrated no detrimental effects of ND on TG, or TC or LDL-C. HDL-C reduced transiently during ND treatment, but returned to near-baseline levels when assessed 12 weeks after the treatment was finished.

There is a broad variability among the results of the several human and animal studies on the hepatic injury, as well as on the criteria used to categorize the severity of hepatotoxicity.33 The determination of serum transaminase levels is generally considered to be of great value to detect toxic effects on the liver.34 However, the misinterpreted idea that the increase of only one hepatic enzyme could represent liver toxicity is frequently observed, when the ideal interpretation should be made using two or more hepatic enzymes.35 In our study, we found increased levels of two important enzymatic markers of the liver toxicity, demonstrating that ND treatment can lead to a state of hepatotoxicity.

There are much molecular evidences to suggest that AAS acts by activating genes related with the synthesis of liver enzymes.35 Gene alterations and/or epigenetic factors provoked by the use of AAS may be linked with hepatocellular dysfunction.36

Hough37 expressed, increase levels of AST, ALT, and lactate dehydrogenase are common in athletes who use steroids.

Vieira et al.,38 reported that ND administration leads to a dose-dependent increase in serum levels of the AST, ALT, and alkaline phosphatase in rats. These results suggest that subchronic treatment with ND, mainly administered at higher-than-therapeutic doses, are potentially deleterious to the liver, leading to incipient fibrosis.

The strong point of our study was sample size. 10 rats in each group decrease rate of error. The using of several doses of ND was better in this study.

With regard to the observed undesirable effects of ND, future human studies on people who take ND are greatly recommended to investigate side effects of ND and optimal dose of it.

Conclusion

Our result indicates that ND caused negative effects on lipid profile and liver enzymes in rats.

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Conflict of Interests

Authors have no conflict of interests.

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