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

Mohammad Reza Samieinasab[(1)], Mohammad Reza Shahraki[(2)], Fatemah Samieinasab[(3)], Somayeh Najafi[(4)]

Short Communication

Abstract

BACKGROUND: Anabolic-androgenic steroids have been associated with several side effects range. 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

Date of submission: 22 Jan 2014, ***Date of acceptance:*** 25 Apr 2015

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.[1-4] The AAS are a family of lipophilic hormones derived from cholesterol that includes the natural male hormone, testosterone, together with numerous synthetic testosterone derivatives.[5] AAS are used in medical clinics as well as with the purpose to improve physical performance of individuals submitted to physical training.[6] Although AAS have valid medicinal uses, nontherapeutic abuse also occurs.[7,8] Recent increases in androgen prescriptions are evident.[9,10] Some of the common orally administered AAS include nandrolone decanoate (ND), oxymetholone, oxandrolone, and stanozolol.[11] ND is frequently used to treat many diseases such as human immunodeficiency virus-associated muscle wasting,[12] prostate cancer and benign prostate hyperplasia, and well-known androgen-dependent diseases.[13] However, despite such therapeutic beneficial potentials, chronic, and unregulated use of ND result in undesirable outcomes, including hepatic toxicity,[14] alteration of thyroid function,[15] cardiovascular toxicities.[16] Many studies concluded that androgen therapy is associated with high incidence of adverse effect in lipid profiles,[17] while others have shown that ND has no marked effect on the lipid profile.[18] In the study by Ghorbanihaghjo et al.,[19] treatment with ND was affected in total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL), and liver enzymes in rats.[17]

1- Assistant Professor, Isfahan Cardiovascular Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran
2- Associate Professor, Department of Physiology, School of Medicine, Zahedan University of Medical Sciences, Zahedan, Iran
3- Ayatollah Golpayegani Hospital, Qom University of Medical Sciences, Qom, Iran
4- MSc Student, Cardiac Rehabilitation Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran
Correspondence to: Fatemah Samieinasab, Email: dr.94samieinasab@gmail.com

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).[20-22] 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.[23] 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.[24] 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 these factors 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]

Hough[37] 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-clinical 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.

Acknowledgments

This study was extracted from a thesis by Fatemah Sameinasab. The authors gratefully acknowledge the authorities at the Zahedan University of Medical Sciences for financial support of this study.

Conflict of Interests

Authors have no conflict of interests.

References

1. Yesalis CE, Kennedy NJ, Kopstein AN, Bahrke MS. Anabolic-androgenic steroid use in the United States. JAMA 1993; 270(10): 1217-21.
2. Bahrke MS, Yesalis CE. Abuse of anabolic androgenic steroids and related substances in sport and exercise. Curr Opin Pharmacol 2004; 4(6): 614-20.
3. Johnston LD, O'Malley PM, Bachman JG, Schulenberg JE. Monitoring the Future: National Results on Adolescent Drug Use: Overview of Key Findings, 2007. Bethesda, MD: National Institute on Drug Abuse, Department of Health and Human Services, National Institutes of Health; 2008.
4. Sjoqvist F, Garle M, Rane A. Use of doping agents, particularly anabolic steroids, in sports and society. Lancet 2008; 371(9627): 1872-82.

5. Pope HG, Brower KJ. Anabolic-androgenic steroid-related disorders. In: Sadock BJ, Kaplan HI, Sadock VA, Editors. Kaplan and Sadock's Synopsis of Psychiatry. Philadelphia, PA: Lippincott Williams & Wilkins; 2010.
6. Sullivan ML, Martinez CM, Gennis P, Gallagher EJ. The cardiac toxicity of anabolic steroids. Prog Cardiovasc Dis 1998; 41(1): 1-15.
7. Dotson JL, Brown RT. The history of the development of anabolic-androgenic steroids. Pediatr Clin North Am 2007; 54(4): 761-9, xi.
8. Fitch KD. Androgenic-anabolic steroids and the Olympic Games. Asian J Androl 2008; 10(3): 384-90.
9. Basaria S, Wahlstrom JT, Dobs AS. Clinical review 138: Anabolic-androgenic steroid therapy in the treatment of chronic diseases. J Clin Endocrinol Metab 2001; 86(11): 5108-17.
10. Ottenbacher KJ, Ottenbacher ME, Ottenbacher AJ, Acha AA, Ostir GV. Androgen treatment and muscle strength in elderly men: A meta-analysis. J Am Geriatr Soc 2006; 54(11): 1666-73.
11. Buttner A, Thieme D. Side effects of anabolic androgenic steroids: pathological findings and structure-activity relationships. Handb Exp Pharmacol 2010; (195): 459-84.
12. Saha B, Rajadhyaksha GC, Ray SK. Beneficial effects of nandrolone decanoate in wasting associated with HIV. J Indian Med Assoc 2009; 107(5): 295-9.
13. Kuhn CM. Anabolic steroids. Recent Prog Horm Res 2002; 57: 411-34.
14. Yu-Yahiro JA, Michael RH, Nasrallah DV, Schofield B. Morphologic and histologic abnormalities in female and male rats treated with anabolic steroids. Am J Sports Med 1989; 17(5): 686-9.
15. Fortunato RS, Marassi MP, Chaves EA, Nascimento JH, Rosenthal D, Carvalho DP. Chronic administration of anabolic androgenic steroid alters murine thyroid function. Med Sci Sports Exerc 2006; 38(2): 256-61.
16. Franquni JV, do Nascimento AM, de Lima EM, Brasil GA, Heringer OA, Cassaro KO, et al. Nandrolone decanoate determines cardiac remodelling and injury by an imbalance in cardiac inflammatory cytokines and ACE activity, blunting of the Bezold-Jarisch reflex, resulting in the development of hypertension. Steroids 2013; 78(3): 379-85.
17. Navarro JF. In the erythropoietin era, can we forget alternative or adjunctive therapies for renal anaemia management? The androgen example. Nephrol Dial Transplant 2003; 18(11): 2222-6.
18. Johansen KL, Mulligan K, Schambelan M. Anabolic effects of nandrolone decanoate in patients receiving dialysis: a randomized controlled trial. JAMA 1999; 281(14): 1275-81.
19. Ghorbanihaghjo A, Argani H, Rohbaninoubar M, Rashtchizadeh N. Effect of Nandrolone Decanoate on serum lipoprotein (a) and its isoforms in hemodialysis patients. Lipids Health Dis 2004; 3: 16.
20. Kindlundh AM, Lindblom J, Bergstrom L, Nyberg F. The anabolic-androgenic steroid nandrolone induces alterations in the density of serotonergic 5HT1B and 5HT2 receptors in the male rat brain. Neuroscience 2003; 119(1): 113-20.
21. Magnusson K, Hallberg M, Hogberg AM, Nyberg F. Administration of the anabolic androgenic steroid nandrolone decanoate affects substance P endopeptidase-like activity in the rat brain. Peptides 2006; 27(1): 114-21.
22. Penna C, Abbadessa G, Mancardi D, Tullio F, Piccione F, Spaccamiglio A, et al. Synergistic effects against post-ischemic cardiac dysfunction by sub-chronic nandrolone pretreatment and postconditioning: role of beta2-adrenoceptor. J Physiol Pharmacol 2008; 59(4): 645-59.
23. Quanhong L, Caili F, Yukui R, Guanghui H, Tongyi C. Effects of protein-bound polysaccharide isolated from pumpkin on insulin in diabetic rats. Plant Foods Hum Nutr 2005; 60(1): 13-6.
24. Andreato LV, Del Conti Esteves JV, Almeida FN, da Silva Ribeito TA, Barrena HC, Barnabé Peres S. Use of the anabolic steroid nandrolone decanoate associated to strength training in Wistar rats. Biological Sciences 2013; 35(2): 283-91.
25. Hartgens F, Kuipers H. Effects of androgenic-anabolic steroids in athletes. Sports Med 2004; 34(8): 513-54.
26. Urhausen A, Torsten A, Wilfried K. Reversibility of the effects on blood cells, lipids, liver function and hormones in former anabolic-androgenic steroid abusers. J Steroid Biochem Mol Biol 2003; 84(2-3): 369-75.
27. Ansell JE, Tiarks C, Fairchild VK. Coagulation abnormalities associated with the use of anabolic steroids. Am Heart J 1993; 125(2 Pt 1): 367-71.
28. Hartgens F, Rietjens G, Keizer HA, Kuipers H, Wolffenbuttel BH. Effects of androgenic-anabolic steroids on apolipoproteins and lipoprotein (a). Br J Sports Med 2004; 38(3): 253-9.
29. Garevik N, Skogastierna C, Rane A, Ekstrom L. Single dose testosterone increases total cholesterol levels and induces the expression of HMG CoA reductase. Subst Abuse Treat Prev Policy 2012; 7: 12.
30. Katsanos CS, Grandjean PW, Moffatt RJ. Effects of low and moderate exercise intensity on postprandial lipemia and postheparin plasma lipoprotein lipase activity in physically active men. J Appl Physiol (1985) 2004; 96(1): 181-8.
31. Gold J, Batterham MJ, Rekers H, Harms MK, Geurts TB, Helmyr PM, et al. Effects of nandrolone decanoate compared with placebo or testosterone on HIV-associated wasting. HIV Med 2006; 7(3):

146-55.
32. Sattler FR, Schroeder ET, Dube MP, Jaque SV, Martinez C, Blanche PJ, et al. Metabolic effects of nandrolone decanoate and resistance training in men with HIV. Am J Physiol Endocrinol Metab 2002; 283(6): E1214-E1222.
33. Nunez M. Hepatotoxicity of antiretrovirals: incidence, mechanisms and management. J Hepatol 2006; 44(1 Suppl): S132-S139.
34. Boada LD, Zumbado M, Torres S, Lopez A, Diaz-Chico BN, Cabrera JJ, et al. Evaluation of acute and chronic hepatotoxic effects exerted by anabolic-androgenic steroid stanozolol in adult male rats. Arch Toxicol 1999; 73(8-9): 465-72.
35. Labrie F, Luu-The V, Calvo E, Martel C, Cloutier J, Gauthier S, et al. Tetrahydrogestrinone induces a genomic signature typical of a potent anabolic steroid. J Endocrinol 2005; 184(2): 427-33.
36. Fontana K, Aldrovani M, de Paoli F, Oliveira HC, de Campos Vidal B, da Cruz-Hofling MA. Hepatocyte nuclear phenotype: the cross-talk between anabolic androgenic steroids and exercise in transgenic mice. Histol Histopathol 2008; 23(11): 1367-77.
37. Hough DO. Anabolic steroids and ergogenic aids. Am Fam Physician 1990; 41(4): 1157-64.
38. Vieira RP, Franca RF, Damaceno-Rodrigues NR, Dolhnikoff M, Caldini EG, Carvalho CR, et al. Dose-dependent hepatic response to subchronic administration of nandrolone decanoate. Med Sci Sports Exerc 2008; 40(5): 842-7.

How to cite this article: Samieinasab MR, Shahraki MR, Samieinasab F, Najafi S. **Influence of nandrolone decanoate administration on serum lipids and liver enzymes in rats.** ARYA Atheroscler 2015; 11(4): 256-60.