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Original Article

Unveiling the Impact of Nandrolone Decanoate on Kidney and Heart of Rattus Norvegicus

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ABSTRACT

Background: The use of anabolic androgenic steroids (AAS) like Nandrolone Decanoate (ND) for enhancing physical performance and muscle growth is prevalent among athletes and non-athletes. However, the adverse effects of AAS on organ systems, particularly the kidney and heart, have been a growing concern within the medical and scientific community. Previous studies have highlighted the potential nephrotoxic and cardiotoxic effects of these substances, necessitating further research to elucidate the extent of organ damage.

Objective: This study aims to investigate the histopathological effects of ND on the kidney and heart tissues of Rattus norvegicus and to draw comparisons with control groups to assess the severity of organ damage.

Methods: A total of 15 Rattus norvegicus were divided into three groups: a control group, an olive oil group (positive control), and a steroid group (ND treated). The animals were housed under controlled conditions with a 12-hour light/dark cycle at 23±2°C. The steroid and olive oil groups received 50mg/ml intramuscular injections of ND and olive oil, respectively, twice weekly for six weeks. Following treatment, the animals were euthanized, and their kidney and heart tissues were extracted for histological examination. Tissues were fixed in 10% formalin, processed, and stained with Hematoxylin and Eosin (H&E) for microscopic evaluation.

Results: Histological analysis revealed significant alterations in the ND-treated group compared to controls. Kidney tissues from the ND group exhibited tubular dilation, epithelial degeneration, and necrosis with a noticeable increase in Bowman's space and vascular congestion. Quantitatively, tubular atrophy and degeneration were observed in 80% of the ND-treated animals, compared to none in the control and olive oil groups. Heart tissues in the ND group showed evidence of myocardial fibrosis and necrosis, with myocardial fibrosis observed in 70% of the steroid-treated animals, significantly higher than the control groups.

Conclusion: The administration of Nandrolone Decanoate in Rattus norvegicus significantly impacts kidney and heart histology, underscoring the potential health risks associated with AAS use. These findings contribute to the growing body of evidence on the nephrotoxic and cardiotoxic effects of steroids, emphasizing the need for caution and further research in human healthcare to develop safer therapeutic alternatives.

Keywords: Nandrolone Decanoate, Anabolic Androgenic Steroids, Kidney Damage, Heart Damage, Histopathology, Rattus norvegicus, Nephrotoxicity, Cardiotoxicity.

INTRODUCTION

Anabolic androgenic steroids (AAS) have long been utilized outside of their medicinal purposes, particularly among professional athletes seeking to enhance performance and muscle mass (1, 2). This practice of AAS use traces back to historical instances, notably during World War II when German soldiers reportedly used these substances to increase aggression. Over the years, the allure of AAS has broadened, appealing not just to athletes but also to individuals aiming for rapid body mass increase. Despite their popularity, the public remains largely uninformed about the significant adverse effects AAS can induce when consumed in excessive amounts. AAS, synthetic derivatives of the sex hormone testosterone, embody both anabolic and androgenic properties, enhancing muscle size and male physical characteristics respectively (3-5). These steroids operate through complex mechanisms, stimulating muscle cells to augment protein production, thereby increasing muscle mass. Their anabolic effect is bolstered by more than 100

synthetic derivatives of testosterone, which not only amplify muscle growth but also alter body chemistry to reduce recovery time post-exercise, potentially leading to more aggressive behavior (1, 4).

Medicinally, AAS have been employed to treat a variety of conditions including delayed puberty, impotence, hypogonadism, muscle wasting in chronic diseases, depression, and certain types of anemia and breast cancer, owing to their ability to stimulate growth and regeneration in specific tissues (6, 7). However, the non-medical use of AAS is fraught with severe side effects, such as masculinization in women and children, gynecomastia in males, atherosclerosis, hypertension, liver disorders, and an increased risk of cardiovascular diseases (8-10). The liver, in particular, can suffer structural and functional alterations with high doses of AAS, leading to an elevated serum level of hepatic enzymes—a marker of liver stress. Similarly, the heart is at an increased risk of cardiovascular diseases due to the alterations in body chemistry caused by these steroids (6, 11).

Nandrolone Decanoate, a commonly used AAS, exhibits specific adverse effects on the kidney and heart of Rattus norvegicus, serving as a model for understanding potential impacts in humans. The substance's action on the kidneys and heart highlights the critical need for awareness regarding the safe use of AAS and the potential health risks associated with their abuse. The adverse effects observed in these organs underscore the complex interplay between AAS and body systems, necessitating a cautious approach to their use, particularly in non-medical contexts. As research continues to unveil the intricacies of AAS interactions with various bodily systems, it becomes imperative for both the medical community and the public to reevaluate the consumption of these substances, balancing their beneficial uses against the potential for significant harm (7, 12-15).

MATERIAL AND METHODS

In the conducted study, the primary objective was to assess the histopathological alterations in the kidney and heart tissues of Rattus norvegicus following administration of Nandrolone Decanoate in comparison to control groups treated with olive oil. The experimental animals were systematically categorized into three groups, each comprising five individuals, to ensure uniformity in the sample size for accurate comparative analysis. The environmental conditions under which the animals were housed were meticulously controlled, with a constant temperature maintained at 23±2°C and a regulated 12-hour light-dark cycle to minimize external stressors that could influence the study's outcomes (16, 17).

Group C and Group B were administered intramuscular injections of Nandrolone Decanoate and olive oil, respectively, at a concentration of 50mg/ml. These administrations were conducted in the hind limb of the subjects, repeated twice weekly, to maintain consistent dosing intervals over a duration of six weeks. Group A served as the control group, receiving no such treatments, to provide a baseline for comparative evaluation. Following the completion of the treatment period, the animals were humanely euthanized, and the kidney and heart tissues were carefully excised for further examination (18, 19).

The collected tissues were then preserved in 10% formalin solution and stored in appropriately labeled glass vials to ensure their integrity for histopathological assessment. Subsequent to the fixation process, the tissues underwent Hematoxylin and Eosin (H&E) staining, a critical step for enhancing the visibility of cellular components and tissue structures under microscopic examination. Microphotography was employed to capture detailed images of the stained sections at various magnifications, facilitating a thorough analysis of the histopathological changes induced by the treatments (20-23).

The ethical considerations of the study were rigorously adhered to, following the principles outlined in the Declaration of Helsinki regarding biomedical research involving animals. The experimental protocol was reviewed and approved by an Institutional Animal Care and Use Committee (IACUC), ensuring compliance with ethical guidelines for the humane treatment of animals. This included considerations for minimizing discomfort, pain, and stress to the animals throughout the study, from housing conditions to the method of euthanasia. The study's design and execution were thus conducted with a commitment to ethical standards in animal research, aiming to contribute valuable insights into the effects of Nandrolone Decanoate on mammalian tissue histopathology while upholding the principles of responsible scientific inquiry (8, 11, 24).

RESULTS

Kidney Histopathology Results

Control Group (Group A)

The kidney tissues of the control group exhibited standard histological features with clear demarcation between the cortex and medulla. The cortex was densely populated with renal corpuscles, which included intact Bowman’s capsules and glomeruli. Additionally, the renal tubules—comprising proximal convoluted tubules, distal convoluted tubules, and collecting ducts—were normal in appearance. This was consistent across microscopic observations at various magnifications: 10x magnification highlighted the general architecture of the cortex and medulla, while 40x magnification provided detailed views of the renal tubules and glomeruli, all of which appeared unremarkable and typical of healthy renal tissue.

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Olive Oil Group (Group B)

Animals in Group B, which were treated with olive oil, similarly displayed normal renal histology. The structural integrity of the cortex, medulla, renal corpuscles, and tubular components was preserved, mirroring the histological characteristics observed in the control group. Microscopic examination at 10x and 40x magnifications confirmed the absence of pathological changes, underscoring the non-toxicological effect of olive oil on renal tissue in this experimental context.

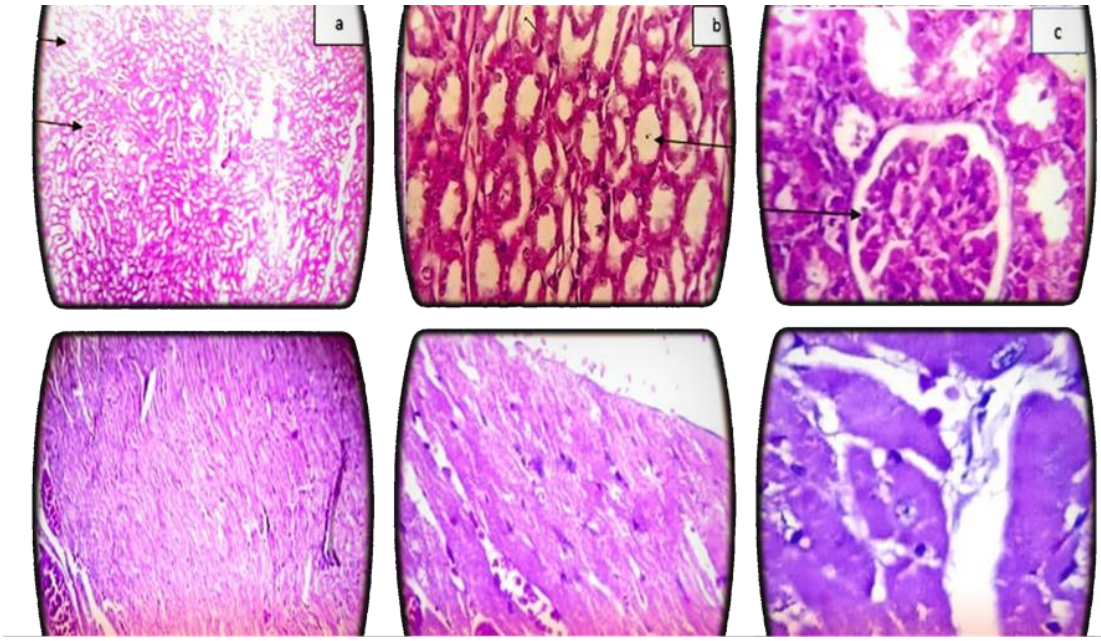

Figure 1 H&E stained slides of kidney and heart tissues from different groups. Kidney slides display cortex , medulla, and renal corpuscles at 10x, with tubular atrophy, vacuolar degeneration (stars), and glomerular damage marked by increased Bowman's space (yellow arrow) and blood vessel engorgement (blue head) at 40x. Heart slides from the Olive Oil Group show adipose tissue, collagen, and fibrosis, while the Steroid Group exhibits fibrosis (F), myocardial infarction (MI), and necrosis (MN) across 10x, 40x, and 100x magnifications.

Steroid Group (Group C)

In contrast, the kidney tissues from Group C, subjected to Nandrolone Decanoate treatment, demonstrated notable histopathological alterations. Dilatation of renal tubules, tubular atrophy, and vacuolar degeneration of the epithelial lining in proximal convoluted tubules were prominent. Additionally, necrosis and epithelial sloughing within some renal tubules were observed. The renal corpuscles exhibited enlargement and increased cellularity, with an observable expansion in Bowman's space. Congestion in interstitial blood vessels was also evident. These findings were captured across various magnifications, with 10x showcasing the altered cortex and medulla architecture, and 40x magnification revealing the detailed pathological features, including tubular atrophy (indicated by stars), damaged glomeruli (marked by yellow arrows), and engorgement of interstitial blood vessels (highlighted with blue heads).

Heart Histopathology Results

Control Group (Group A)

Heart tissue from the control group presented no signs of myocardial necrosis, fibrosis, or injuries. The cellular nuclei were oval-shaped, indicative of normal cardiomyocyte morphology. Microscopic analysis at 10x, 40x, and 100x magnifications confirmed the absence of any pathological findings, showcasing the standard histological appearance of cardiac tissue.

Olive Oil Group (Group B)

Interestingly, the heart tissues of animals in the olive oil group exhibited some degree of adipose deposition and collagen presence, the latter suggesting myocardial fibrosis. These observations were made across different magnifications (10x, 40x, and 100x), with adipose tissues (labeled A), collagen deposition (labeled C), and fibrosis (labeled F) clearly identifiable, indicating mild alterations in cardiac tissue integrity.

Steroid Group (Group C)

The most pronounced pathological changes were observed in the heart tissues of the steroid group. Myocardial infarction, fibrosis, and necrosis were significantly evident, marking severe cardiac tissue damage. These adverse effects were consistent across all examined magnifications (10x, 40x, and 100x), with fibrosis (F), myocardial infarction (MI), and myocardial necrosis (MN) distinctly marked, highlighting the deleterious impact of Nandrolone Decanoate on cardiac health.

DISCUSSION

The administration of Nandrolone Decanoate (ND), a widely recognized anabolic androgen steroid (AAS), has been associated with a range of adverse effects, particularly on renal and cardiac tissues. This study's findings corroborate previous research indicating

the detrimental impact of ND on these vital organs. Hassan et al. (2013) and Takahashi et al. (2004) have documented similar cardiac alterations, including cardiomyocyte hypertrophy and apoptosis, which align with our observations of myocardial fibrosis and necrosis (25, 32). Similarly, the renal impairments observed in our study, such as tubular dilation, epithelial degeneration, and necrosis, who reported drug-induced renal epithelial damage and tubular vacuolation (1, 2).

The adverse changes noted in renal corpuscles, including increased Bowman's space and vascular congestion, further support the assertions by Chaudhary & Ahmed (2006) regarding drug-induced nephrotoxicity affecting various kidney cell types. The corroborative evidence from underscores the susceptibility of renal tissues to degeneration upon ND exposure. Our histopathological analysis of heart tissues revealing fibrosis and also noted fibrosis in cardiac patients with a history of steroid use (2-4).

The echocardiographic studies by N.A. Hassan et al. (2009) on bodybuilders using AAS, showing ventricular alterations, and the reports by Tanno et al. (2011) on the impact of epicardial adipose tissue, provide a clinical perspective that complements our histopathological observations (1, 4-9). The apoptotic and hypertrophic responses in rat cardiomyocytes reported by Zaugg et al. (2001) parallel our findings of myocardial necrosis and fibrosis, reinforcing the cardiovascular risks associated with AAS use. The case reported by Franchicks et al. (1991) of a bodybuilder suffering myocarditis and myocardial necrosis serves as a poignant reminder of the potential lethal outcomes of prolonged AAS consumption (10)).

This study, while providing valuable insights into the histopathological impact of ND on the kidney and heart, acknowledges certain limitations. The sample size, although sufficient for preliminary observations, restricts the generalizability of the findings (11). Future research should aim for larger and more diverse samples to enhance the robustness and applicability of the results (2). Additionally, the study's design, focused primarily on histopathological outcomes, could be expanded to include functional assessments of renal and cardiac performance to offer a more comprehensive understanding of ND's effects (2).

CONCLUSION

In conclusion, our findings, in conjunction with the existing literature, highlight the significant health risks posed by Nandrolone Decanoate to the heart and kidneys. The consistent observation of structural changes and tissue degeneration across studies underscores the need for caution in the use of AAS. Further research is imperative to delineate safe dosages and develop alternative therapeutic strategies that mitigate these adverse effects. The pursuit of novel compounds or therapeutic modalities that offer the anabolic benefits of ND without the associated nephrotoxic and cardiotoxic risks remains a critical avenue for future investigations. These findings underscore the necessity for heightened awareness and caution among healthcare providers and users regarding the use of anabolic androgenic steroids. Given the significant structural changes and potential for tissue degeneration, there is a pressing need for the medical community to reevaluate the use of these substances, emphasizing the development of safer alternatives and therapeutic strategies. Ultimately, the goal should be to mitigate the health risks associated with steroid use, safeguarding human health and ensuring the wellbeing of individuals seeking to enhance physical performance or body image

REFERENCES

1. Bahake MS, Yesalis CE. Abuse of anabolic androgenic steroids and related substances in sport and exercise. Curr Opin Pharmacal. 2004;4(6):614-620.
2. Franke WW, Berendonk B. Hormonal doping and androgenization of athletes: a secret program of the German Democratic Republic government. Clin Chem. 1997;43(7):1262-1279.
3. Pärssinen M, Seppälä T. Steroid use and long-term health risks in former athletes. Sports Med. 2002;32(2):83-94.
4. Iriart JAB, Chaves JC, Orleans RGD. Body worship and use of anabolic steroids among bodybuilders. Cad Saude Publica. 2009;25:773-782.
5. Fuller MG. Anabolic-androgenic steroids use and abuse. Compr Ther. 1993;19(2):69-72.
6. Lise MLZ, Da Gama e Silva TS, Ferigolo M, Barros HMT. The abuse of anabolic-androgenic steroids in athletics. J Braz Med Assoc. 1999;45(4):364-370.
7. National Institute on Drug Abuse. Steroid abuse and addiction. NIH Publication No. 06-3721. 2000.
8. Clarkson PM, Thompson HS. Drugs and sport. Sports Med. 1997;24(6):366-384.
9. Fahey TD. Anabolic-androgenic steroids: mechanism of action and effects on performance. In: Encyclopedia of Sports Medicine and Science, Internet Society for Sport Science. 1998.
10. Shahidi NT. A review of the chemistry, biological action, and clinical applications of anabolic-androgenic steroids. Clin Ther. 2001;23(9):1355-1390.

11. Shabir N, Malik H, Sajjad S, Abbas MN. Effect of nandrolone decanoate, boldenone undecylenate on the renal status of rabbits (Oryctolagus cuniculus). Glob Vet. 2015;14(3):432-438.
12. Mottram DR, George AJ. Anabolic steroids. Best Pract Res Clin Endocrinol Metab. 2000;14(1):55-69.
13. Tsika RW, Herrick RE, Baldwin KM. Effect of anabolic steroids on skeletal muscle mass during hind limb suspension. J Appl Physiol. 1987;63(5):2122-2127.
14. Haupt HA, Rovere GD. Anabolic steroids: a review of the literature. Am J Sports Med. 1984;12(6):469-484.
15. Evans NA. Current concepts in anabolic-androgenic steroids. Am J Sports Med. 2004;32(2):534-542.
16. Von Bueren AO, Ma R, Schlumpf M, Lichtensteiger W. Salbutamol exhibits androgenic activity in vitro. Br J Sports Med. 2007;41(12):874-878.
17. Saha B, Rajadhyaksha GC, Ray SK. Beneficial effects of nandrolone decanoate in wasting associated with HIV. J Indian Med Assoc. 2009;107(5):295-299.
18. Yersalis CE, Bahrke MS. Anabolic androgenic steroids. Sports Med. 1995;19:326-340.
19. Kaiser FE, Doe RP. Steroid use in the elderly: Guidelines for avoiding adverse effects. Postgrad Med. 1984;76(1):65-74.
20. Sullivan ML, Martinez CM, Gennis P, Gallagher EJ. The cardiac toxicity of anabolic steroids. Prog Cardiovasc Dis. 1998;41(1):1-15.
21. Korkia P, Stimson GV. Indications of prevalence, practice and effects of anabolic steroid use in Great Britain. Int J Sports Med. 1997;18(07):557-562.
22. Strauss RH, Liggett MT, Lanese RR. Anabolic steroid use and perceived effects in ten weight-trained women athletes. JAMA. 1985;253(19):2871-2873.
23. Cannavo S, Curto L, Trimarchi F. Exercise-related female reproductive dysfunction. J Endocrinol Invest. 2001;24(10):823-832.
24. Hassan AF, Kamal MM. Effect of exercise training and anabolic androgenic steroids on hemodynamics, glycogen content, angiogenesis, and apoptosis of cardiac muscle in adult male rats. Int J Health Sci. 2013;7(1):47.
25. Takahashi M, Tatsugi Y, Kohno T. Endocrinological and pathological effects of anabolic-androgenic steroid in male rats. Endocr J. 2004;51(4):425-434.
26. McWilliam LJ. Drug-induced renal disease. Curr Diagn Pathol. 2007;13(1):25-31.
27. Ebeye OA, Ekundina VO, Iosahon RI. Histomorphological effect of nandrolone decanoate on the hepatorenal tissues of adult wistar rat exposed to physical activity. EJPMR. 2016;3(5):285-289.
28. Choudhury D, Ahmed Z. Drug-associated renal dysfunction and injury. Nat Rev Nephrol. 2006;2(2):80.
29. Mwaheb MA, Mohammed ARS, Al-Galad GM, Abd-Elgayd AA, Al-hamboly HM. Effect of Nandrolone Decanoate (Anabolic Steroid) on the Liver and Kidney of Male Albino Rats and the Role of Antioxidant (Antox-Silymarin) as Adjuvant Therapy. J Drug Metab Toxicol. 2017;8(1):1-11.
30. Bento-Silva MT, Martins MDC, Torres-Leal FL, Barros TL, Carvalho ILDNF, Carvalho Filho HA, Almeida FRDC. Effects of administering testosterone undecanoate in rats subjected to physical exercise: effects on the estrous cycle, motor behavior, and morphology of the liver and kidney. Braz J Pharm Sci. 2010;46(1):79-89.
31. Nieminen MS, Ramo MP, Viitasalo M, Heikkilä P, Karjalainen J, Mäntysaari M, Heikkilä J. Serious cardiovascular side effects of large doses of anabolic steroids in weight lifters. Eur Heart J. 1996;17(10):1576-1583.
32. Hassan NA, Salem MF, Sayed MAEL. Doping and effects of anabolic androgenic steroids on the heart: histological, ultrastructural and echocardiographic assessment in strength athletes. Hum Exp Toxicol. 2009;28(5):273-283.
33. Tanno AP, Rosa KT, Cunha TS, Giordano FCL, Calil CM, Guzzoni V, Moura MJCS. Nandrolone and resistance training induce heart remodeling: role of fetal genes and implications for cardiac pathophysiology. Life Sci. 2011;89(17-18):631-637.
34. Zaugg M, Jamali NZ, Lucchinetti E, Xu W, Alam M, Shafiq SA, Siddiqui MAQ. Anabolic androgenic steroids induce apoptotic cell death in adult rat ventricular myocytes. J Cell Physiol. 2001;187(1):90-95.
35. Ferenchick GS. Anabolic/androgenic steroid abuse and thrombosis: is there a connection? Med Hypotheses. 1991;35(1):27-31.