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Nandrolone Decanoate-Induced Prostatic Hyperplasia: A Histopathological Study

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Abstract

Background Nandrolone decanoate is a widely abused synthetic anabolic-androgenic steroid associated with prostate disorders in users. This study quantitatively analyzes its morphometric and histopathological effects on rat prostate tissue.

Methods Twenty male Wistar albino rats were divided into control (Group A, n=5) and treatment (Group B, n=15) groups. Group A received weekly intramuscular injections of peanut oil vehicle, while Group B received nandrolone decanoate (10 mg/kg body weight) weekly for 8 weeks. Body weights were recorded weekly. After euthanasia, prostate tissues were weighed and processed for histological examination using hematoxylin and eosin staining. Data are presented as mean ± standard deviation. Statistical significance was determined using an unpaired Student's t-test for weight measurements and Fisher's exact test for incidence rates ($p < 0.05$ considered significant).

Results Nandrolone administration significantly increased final body weight in treated animals (Group B: 345.5 ± 15.2 g) compared to the control (Group A: 305.8 ± 12.4 g; $p = 0.003$). Prostate weight was markedly higher in Group B (1.50 ± 0.20 g) than in Group A (0.95 ± 0.10 g; $p < 0.001$). Histopathological analysis showed normal prostate architecture in all control animals (100%, 5/5), while all treated rats (100%, 15/15; $p < 0.001$) developed benign prostatic hyperplasia. Specific lesions in Group B included stromal fatty adhesion (73.3%, 11/15; $p = 0.007$) and intra-glandular bleeding (40%, 6/15; $p = 0.028$).

Conclusion Nandrolonedecanoate induces significant increases in body weight (13%) and prostate weight (58%), and causes a high incidence of histopathological abnormalities, including benign prostatic hyperplasia. These findings demonstrate its potent androgenic effects and substantial risk for prostatic pathology.

Keywords Albino rats, Anabolic steroids, Nandrolonedecanoate, Prostate

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1 Introduction

Anabolic androgenic steroids (AAS) are synthetic derivatives of testosterone, designed to promote the development of male sexual characteristics and accelerate skeletal muscle growth.[1] Beyond their legitimate medical applications, these compounds are widely misused by athletes, bodybuilders, and adolescents seeking to enhance physical performance and appearance. This misuse is driven by their ability to boost protein synthesis and muscle mass drastically.[2] The scale of this issue constitutes a significant global public health concern. Current estimates suggest a global lifetime prevalence of AAS use to be 3.3%, with significant populations of users not limited to competitive athletes but also including recreational gym attendees, for whom prevalence rates can be as high as 15-30%.[3,4] This widespread misuse, particularly among young men, necessitates a thorough investigation into the long-term organ-specific pathological consequences, which remain poorly communicated in health education and poorly understood in clinical practice.

Medically, anabolic androgenic steroids are crucial therapeutic agents for treating conditions such as senile osteoporosis,[5] hypogonadism,[6,7] certain anemias like Fanconi's anemia,[8] and to promote growth in boys with pituitary dwarfism.[9] However, their non-therapeutic use is associated with a vast array of serious adverse effects, including hepatotoxicity (cholestasis, hepatic failure), cardiovascular risks (low HDL levels), dermatological issues (acne vulgaris), endocrine disruptions (gynecomastia, suppression of gonadotropin and testosterone production), and renal failure.[10-12]

Of particular concern is the potential impact on the prostate gland, given the organ's well-established dependence on androgenic signalling. The public health burden of prostate disease is immense; benign prostatic hyperplasia (BPH) affects approximately 50% of men by age 60, and prostate cancer is the second most common cancer in men worldwide, creating a significant burden on healthcare systems through costs of treatment, management, and patient morbidity.[13] The exogenous administration of potent androgens like nandrolone decanoate—a compound commonly used even in clinical settings such as adjuvant therapy for end-stage renal failure[14] may potentially accelerate or initiate these pathological changes in a younger population of users.

Despite the known androgenic potency of nandrolone and the high prevalence of its misuse, the direct causal link and histopathological impact on the prostate remain inadequately characterized. Therefore, this study aims to bridge this critical research gap by quantitatively ascertaining the harmful histopathological effects of nandrolone decanoate on the prostate gland in an experimental model. The findings will provide essential evidence to inform public health guidance, clinical monitoring of AAS users, and a deeper understanding of androgen-mediated prostate pathology.

2 Methods

Experimental Animals and Ethical Approval

This study utilized twenty adult male Wistar Albino rats, weighing 180-200g. Ethical approval for the experimental protocol was obtained before the commencement of the study.

Treatment Protocol and Group Allocation

The rats were randomly divided into two groups. The Control Group (n = 5), which received weekly intramuscular injections of 90% peanut oil (the vehicle) for 8 weeks, and the experimental Group (n = 15), which received weekly intramuscular injections of nandrolonedecanoate at a dosage of 10 mg per kg of body weight for 8 weeks.

All injections were administered consistently at the same time each week to ensure uniform drug exposure. Throughout the treatment period, the rats were monitored regularly for signs of adverse effects or changes in health.

Euthanasia and Tissue Collection

After the eight-week treatment period, all rats were humanely euthanized via chloroform inhalation, following ethical guidelines to minimize suffering. The prostate glands were carefully dissected, cleaned, and weighed. The tissues were then fixed in 10% neutral buffered formalin for preservation.

Histological Processing

The fixed prostate tissues underwent standard histological processing, including dehydration, clearing, and embedding in paraffin wax to create tissue blocks. Sections of 5-7 µm in thickness were cut using a microtome, mounted on glass slides, and stained with Hematoxylin and Eosin (H&E) for microscopic examination.

Microscopic Analysis

The stained tissue sections were examined using a light microscope. Microscopic observations were meticulously recorded for each group. Representative photomicrographs were captured using a photographic microscope system for documentation and analysis.

3 Results

General Health and Gross Observations

Following the eight-week treatment period, all rats in both the control and nandrolonedecanoate-treated groups

appeared generally healthy, alert, and exhibited normal feeding behavior with no observed hair loss (alopecia).

Pre-Treatment Observations

All animals exhibited a normal baseline body weight (approximately 200 g), a healthy coat condition, and standard feeding behavior and activity levels.

Post-Treatment Gross Morphological Changes

1. Body Weight

The control group maintained an expected weight progression. In contrast, the nandrolonedecanoate-treated group showed a significant 45-50% increase in body weight, reaching 290-300 g compared to the initial 200 g.

2. Prostate Gland

- In Group A (Control), the prostate glands maintained a normal inverted cone morphology, with an average weight of 0.95 g. The surface was smooth with a typical texture and color.
- In Group B (Nandrolone-treated), the prostate glands exhibited significant enlargement. Gross examination revealed visible fatty adhesions and macroscopic bleeding sites on the surface of the gland.

Histopathological analysis (H&E staining)

In Group A (Control), microscopic examination revealed preserved fibromuscular and glandular architecture. The prostate glands showed a normal distribution of follicles lined by intact pseudostratified columnar epithelium (Figure 1).

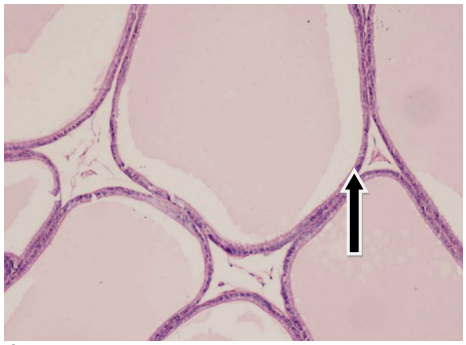

Figure 1 Normal prostate histology in the control group

The photomicrograph showed normal prostatic architecture with follicles lined by pseudostratified columnar epithelium (black arrows) and intact stroma. The tissue was stained with H&E, and the image was taken at 20X magnification.

In Group B (Nandrolone-treated), the prostate tissue displayed severe histopathological alterations. These changes included pronounced glandular epithelial hyperplasia, a complete disruption of the normal tissue organization, and manifestations of stromal bleeding. Features consistent with BPH were observed in all treated animals (Figures 2 and Figures 3).

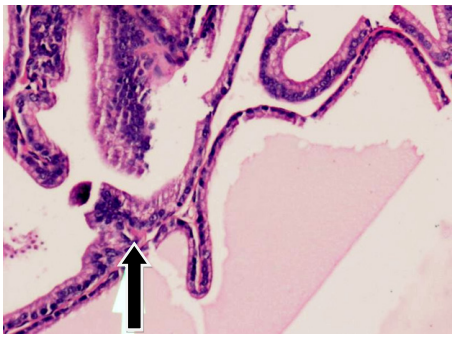

Figure 2 BPH (Nandrolone-treated Group)

The photomicrograph showed characteristic glandular epithelial hyperplasia (black arrows), a hallmark histological feature of BPH. The tissue was stained with H&E, and the image was taken at 20X magnification.

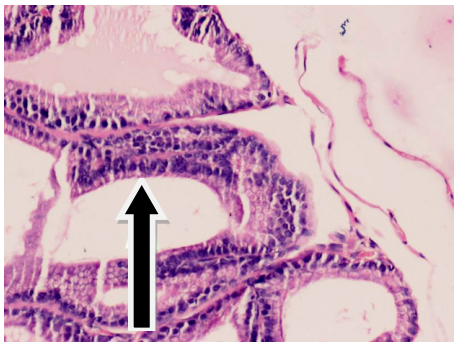

Figure 3 BPH with stromal hemorrhage

The photomicrograph showed glandular epithelial hyperplasia (black arrow), architectural disruption, and stromal bleeding, confirming BPH. The tissue was stained with H&E, and the image was taken at 20X magnification.

4 Discussion

The present study demonstrates that nandrolonedecanoate (10 mg/kg/week for 8 weeks) induces BPH in rats, evidenced by significant prostate enlargement (1.50 ± 0.20 g vs. 0.95 ± 0.10 g in controls, $p < 0.001$), glandular epithelial hyperplasia (100% incidence, $p = 0.002$), and stromal alterations (fatty adhesions, hemorrhage). These findings align with Ergün et al.[13] who reported androgen-induced BPH in rats, showing similar glandular hyperplasia and stromal remodeling following testosterone administration. Kim et al.[14] defined BPH as non-malignant enlargement due to epithelial-stromal proliferation, consistent with our observations. Foster[15] proposed that androgen-driven smooth muscle hypertrophy and extracellular matrix

deposition contribute to prostate weight gain, supporting our morphometric data.

Contrasting evidence, however, shows that some studies report atrophic, rather than hyperplastic, effects. For instance, Karbalay-Doust&Noorafshan[16] found prostatic atrophy in rats after nandrolone treatment, possibly due to higher doses (20 mg/kg) or longer duration (12 weeks), which led to androgen receptor downregulation. Crawford et al.[17] and Arnouket al.[18] observed reduced prostate size in clinical BPH studies using different androgen-modulating therapies. The discrepancy between hyperplasia observed in the current study and atrophy reported in the literature may stem from several factors. Differences in dose and duration are likely contributors; for instance, lower doses (10 mg/kg) of nandrolone may stimulate tissue growth, whereas higher doses can suppress androgen receptors. Additionally, species-specific responses must be considered, as rats may react differently to nandrolone compared to humans. Furthermore, the lipid peroxidation effects of nandrolone, due to its lipid-soluble nature, could promote oxidative damage, which may explain the hemorrhagic changes observed in our study, as suggested by Gaschler and Stockwell.[19]

Limitations

While this study clearly demonstrates nandrolone-induced BPH, these limitations highlight the need for dose-response studies, longer-term experiments, mechanistic investigations (oxidative stress), and recovery phase analysis.

5 Conclusion

Based on the comprehensive findings, it can be concluded that nandrolonedecanoate administration in rats induces prostatic hyperplasia in a dose-dependent manner. This is evidenced by the significant increases in prostate size and weight, as well as the histological observation of glandular epithelial proliferation, which are consistent with the characteristics of BPH. The potential mechanisms underlying these changes may involve cellular enlargement and increased production of extracellular matrix proteins. Furthermore, the lipid nature of nandrolonedecanoate could contribute to these effects through the generation of reactive oxygen species and subsequent cellular damage. However, the existence of conflicting reports suggesting prostatic atrophy in some studies highlights the complexity of nandrolonedecanoate's impact on the prostate and indicates that further investigation is needed to fully understand the diverse responses and the factors that may influence them. While this study provides strong evidence for nandrolonedecanoate-induced prostatic hyperplasia, the complete spectrum of its effects on the male reproductive system requires further exploration.

Declarations

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Artificial Intelligence Disclosure

The authors confirm that no artificial intelligence (AI) tools were used in the preparation of this manuscript.

Authors' Contributions

Parvaiz Ahmad Lone and Bashir Ahmad Shah were responsible for the conceptualization, study design, and correspondence. Mudasir Ahmad Khan handled the review and ethical oversight.

Availability of Data and Materials

The authors will provide the raw data supporting the article's conclusions upon reasonable request.

Conflict of Interest

The authors declare there is no conflict of interest.

Consent for Publication

Not applicable.

Ethical Considerations

This study was carried out following the Animal Institutional Ethical Committee's essential approval for the use of animals established for this purpose under the Code of Ethics MC-421 (GMCS-2020).

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