

Urinary Stone Formation and Testosterone Supplementation: Insights from a Cross-sectional Study in Athletes

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Abstract

Introduction: The use of exogenous testosterone has become increasingly prevalent in sports fields, raising concerns about its potential risks and benefits.

Methods & Materials: This study aimed to investigate the effects of testosterone supplementation on stone formation in the urinary tract and urine composition. A total of 1080 athletes participated in a two-year cross-sectional study, with 495 individuals receiving testosterone supplementation and 585 individuals serving as non-users. Blood and urine samples were collected, and CT scans were performed to assess stone presence.

Results: The results revealed a significant increase in crystalluria among testosterone users compared to non-users (38.2% vs. 2.7%, $p=0.004$). Imaging findings also showed a higher incidence of abnormal results in testosterone users (25.2% vs. 4.3%, $p=0.0017$), with kidney calcification, pelvic and calyceal stones, ureteral stones, and bladder stones observed.

Conclusion: However, further metabolic studies are required to establish a definitive cause-and-effect relationship between testosterone use and stone formation. This study sheds light on the potential risks associated with exogenous testosterone use and highlights the need for evidence-based recommendations in sports and athletic performance.

Key words: Athletes; Crystalluria; Testosterone; Urolithiasis

Introduction

In recent decades, various sports fields worldwide have undergone significant changes, accompanied by a growing trend in the use of supplements and chemical drugs. The prescription of testosterone has witnessed a substantial increase, primarily driven by revisions in professional recommendations. Concerns have been raised regarding a potential link between testosterone therapy and a higher risk of conditions such as cardiovascular disease, thromboembolic events, obstructive sleep apnea, benign prostatic hyperplasia, and prostate cancer. On the other hand, there is also a suggestion that testosterone therapy could serve as a beneficial treatment option for managing prediabetes. As a result, extensive ongoing discussions are taking place regarding the appropriate candidates for testosterone therapy among individuals with hypogonadism.

Indeed, the utilization of androgenic steroids has emerged as a worldwide epidemic, with a cumulative global lifetime prevalence of 6.4 percent in men and 1.6 percent in women [1]. However, the

administration of testosterone can result in numerous side effects, such as metabolic alterations, hormonal imbalances in the pituitary gland, thrombotic events, and elevated blood concentrations, among others [2-4].

One of the prevalent and significant practices is the utilization of steroids, particularly by athletes and bodybuilders [5].

Despite extensive research conducted on the impact of testosterone on the urinary system, several aspects remain unclear. In certain studies, a correlation has been observed between testosterone levels and the development of urinary stones, while in others, this association has been contradicted. [6-9].

In certain studies, conducted on animal models, it has been observed that higher serum testosterone levels were found in cases where urinary tract stones were present. However, the cause-and-effect relationship

of this association has not been definitively established. Furthermore, in some other studies, this relationship has been contradicted [10].

In light of the growing prevalence of exogenous testosterone use among athletes, it has become imperative to investigate its effects on stone formation within the urinary tract and its potential impact on urine composition. The findings from previous studies have provided insights into the subject, indicating a correlation between elevated serum testosterone levels and the presence of urinary tract stones in animal models. However, the exact cause-and-effect relationship behind this association remains uncertain.

To address these knowledge gaps, our study aims to delve deeper into the effects of exogenous testosterone use on stone formation within the urinary tract. By analyzing urine samples and conducting comprehensive examinations, we seek to uncover any alterations in urine compounds that may be influenced by exogenous testosterone administration. This research is crucial in shedding light on the potential risks and implications associated with the increasing trend of exogenous testosterone use among athletes.

Through meticulous data collection, rigorous analysis, and adherence to ethical guidelines, our study endeavors to contribute to the existing body of knowledge surrounding the effects of exogenous testosterone on the urinary system. By gaining a better understanding of these effects, we can inform medical professionals, athletes, and policymakers about the potential consequences and provide evidence-based recommendations regarding the use of exogenous testosterone in sports and athletic performance.

Methods & Materials:

In this cross-sectional study, we investigated a total of 1374 professional and non-professional bodybuilding athletes. At the outset, the participants were provided with comprehensive explanations regarding the study's objectives, and written consent was obtained from each individual. Subsequently, blood samples were collected to measure testosterone levels, electrolytes, and complete blood cell counts. Urine samples were examined for the presence of crystalluria, evidence of urinary stones, and other metabolic disorders. Additionally, a CT scan of the abdomen and pelvis, without contrast but with reconstruction of Coronal sections, was performed to detect the presence of stones in the kidney, ureters, bladder, and ureter.

Patients with pre-existing metabolic issues, abnormal testosterone levels during the initial measurement, indications of stones or metabolic disorders in urinalysis, and those with other factors predisposing them to stone formation were excluded from the study. Ultimately, a total of 1126 patients were included, and 1080 patients successfully completed the study.

During the two-year study duration, patients engaged in regular exercise while maintaining adequate hydration. Efforts were made to minimize external factors that could contribute to stone formation. Among the participants, 495 individuals received a dosage of 100 mg of testosterone enanthate every two weeks, while the remaining 585 individuals did not receive any testosterone supplementation. It's important to note that the use of other oral supplements and multivitamins was identical between the two groups, and the researcher played no role in determining whether or not athletes used testosterone. The study was conducted in an observational manner.

After the two-year period, patients underwent re-examination. This involved the collection of blood samples to assess testosterone levels, electrolytes, and complete blood cell counts. Urine samples were analyzed for evidence of crystalluria, and a CT scan of the abdomen and pelvis, without contrast, was

performed to identify the presence of stones in the kidney, ureters, bladder, and ureter.

Results

To analyze the results obtained from the patient surveys in this study, participants were categorized into two groups: testosterone users and testosterone nonusers. Data collected were analyzed using SPSS version 27 software, with a significance level set at $P=0.05$.

The average age and weight of patients in both groups were comparable, showing minimal differences.

Regarding the examination of complete blood counts (CBC) in the patients, approximately 45.6% of testosterone users exhibited disorders, primarily characterized by elevated blood hematocrit levels, an anticipated side effect of exogenous testosterone use.

In the second examination, urine samples from patients revealed that 2.7% of non-testosterone users showed a disorder in U.A., defined as the presence of crystals in the urine. However, this rate increased to 38.2% among testosterone users, which was statistically significant ($P=0.004$).

Furthermore, the testosterone user group experienced a significant increase in testosterone levels, as expected due to frequent usage.

The noteworthy and thought-provoking aspect of this study lies in the examination of imaging results following testosterone administration. Abnormal imaging findings were observed in 4.3% of non-testosterone users, whereas 25.2% of testosterone users displayed abnormal results, demonstrating statistical significance ($P=0.0017$). Among the patients with abnormal imaging results after testosterone administration, 43% exhibited evidence of mild kidney calcification, 27% had stones in the pelvis and calyces, 22% had stones in the ureter, and 8% had bladder stones. Table 1 presents the results of the investigations conducted on the two groups of testosterone users and non-users.

Parameter	Without Testosterone	With Testosterone
Patients Number	585	495
Age Mean(years)	28.3	27.9
Weight Mean(kg)	74.54	76.03
Male/Female (percent)	93/7	98/2
Normal CBC in first study (percent)	100	100
Normal CBC in second study (percent)	98	45.6
Normal U.A in first study (percent)	100	100
Normal U.A in second study (percent)	97.3	61.8
Normal testosterone level in first study(percent)	100	100
Normal testosterone level in second study(percent)	98.6	54.8
Normal Imaging in first study(percent)	100	100
Normal Imaging in second study(percent)	95.7	74.8

Table1: Data of patients in brief

Discussion:

Currently, despite numerous studies conducted worldwide on the association between testosterone and the formation of urinary stones, this relationship remains ambiguous.

Several studies have demonstrated that urolithiasis or the formation of renal stones is three times more frequent in males and decreases with age in correlation with serum testosterone levels. These findings suggest a potential role played by male sex hormones in this process. Animal models have indicated that androgens exert a promoting action, while estrogens exhibit an inhibitory effect on kidney stone formation. These observations highlight the need for further investigation to determine the specific role of serum testosterone in the development of renal stones.(11).

However, another study revealed that urolithiasis was observed in intact male rats but not in female rats. Interestingly, when male rats were castrated and fed with ethylene glycol, the occurrence of renal stones decreased significantly from 71.4% to 14.3%. These compelling findings strongly suggest that serum testosterone levels play a crucial role in the formation of urolithiasis.(12).

Although in the analysis of the results of this study, the obtained data were expected and consistent with the results of other studies, but in the examination of imaging, the results were very thought-provoking. The high prevalence of stones in athletes who consume testosterone can be a proof of the positive effect of testosterone on the process of stone formation, although the increase in calcium levels seen in the consumption of testosterone can be a proof of this claim, but a definitive opinion on this matter requires metabolic studies. It is mostly based on an animal example.

This study was conducted on athletes whose normal metabolic process has slight differences from normal people in the society, which can be considered as a confounding factor in examining the role of testosterone in stone formation, for example, in these people, the basal metabolism are higher and the amount of uric acid production and excretion are also higher, which is considered as an effective factor in stone formation.

Conclusion:

This study demonstrated that testosterone users have a higher incidence of crystalluria and a greater prevalence of stone formation compared to non-users. However, to establish a conclusive standpoint, additional research and metabolic studies on animal models are necessary.

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Conflict of interest:

There is no conflict of interest in this study.

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