HISTOLOGICAL TOXIC EFFECT OF NANDROLONE DECANOATE ON THE KIDNEY OF MALE RABBITS: *Part one*

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ABSTRACT

Over the past several decades it has been known that there are an increase in the prevalence of anabolic steroid use by athletes. The pathophysiology and prognosis of anabolic-androgenic steroid use remains unclear. The aim of this study is to investigate the histological toxic effects of nandrolone decanoate on the kidney of male rabbits. 21 rabbits were divided into three groups; each consists of 7 animals. The control group was injected with normal saline. Group (I) received 2mg/kg body weight, and group (II) received 6mg/kg body weight. Animals received the dose weekly for 2 months duration. There was an increase in the weights of kidney of group (II) compared to other groups. The histological pattern of the kidney of group(I) was nearly normal, while kidney of group (II) showed more severe pathological damage which includes enlargement and hypercellularity including the mesangial cells of the renal glomerular tuft with narrowing of Bowman's capsule. Vacuolar degeneration of the lining epithelium of the proximal convoluted tubules and some tubules showed sloughing and necrosis of the epithelial cells. These results showed that nandrolone decanoate had histological toxic effects on the kidney of rabbits.

INTRODUCTION

Any drug administered to the body will cause burden on the kidney. Over the past several decades it has been known that there are an increase in the prevalence of anabolic steroid use by athletes. As the use of anabolic steroid is illicit, much of our knowledge of their side effects is derived from case reports, retrospective studies, or comparisons with studies in other similar patient groups.[1] To investigate whether the steroid-induced chemical abnormalities seen in athletes are accompanied by histological changes, we select the renal system for this study. The drug used in this study is called nandrolone decanoate which is an anabolic-androgenic steroid. Although nandrolone decanoate can cause acute renal failure as a side effect but it is widely used in patients with end stage renal failure as adjuvant therapy to the parenteral nutrition.[2] The pathophysiology and prognosis of anabolic-androgenic steroid use remains unclear. Many workers attempted to quantify the side effects of testosterone administration in humans.[3] As is unethical to administer high doses of anabolic-androgenic steroid in humans, in the current study we have used animals to determine the pathology resulting from anabolic-androgenic steroid use. The main objective of this research is to identify the histological toxic effect of nandrolone decanoate at different doses on the kidney.

MATERIALS AND METHODS

Twenty one rabbits were divided into three groups, each group consists of 7 animals. The control group received only normal saline. Group (I) administered 2mg/kg body weight, and group (II) received 6mg/kg body weight. Animals received the dose by deep intramuscular injection weekly for 2 months duration. Animals were killed by ether inhalation, quickly dissected and the kidney weights were recorded for all animals. Small slices of kidney were taken about 3-4 mm thickness and fixed in 10% formalin solution, then the tissue dehydrated in graded alcohol and cleared by xylol and embedded in paraffin. Two blocks from each portion was done and thin section of 5 micron were made using Reicheart Rotary Microtome. Sections were mounted on slide and stained with hematoxylin and eosin stain.[4]

Statistical analysis:

The kidney weights were recorded and values were considered statistically significant when $P \leq 0.05$. Statistics were done using Duncan's test.[5]

OBSERVATIONS AND RESULTS

All animals including the control group showed good appetite. Aggressive behavior and movements were noticed in group (II). The weights of kidneys of all groups were recorded

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in grams, the mean weight of kidneys of the control group was (10.50g±0.35g), for group(I) it was (11.14g±0.43g), for group (Π) it was (13.30g±0.90g). There was significant increase in the mean kidney weights in group (Π) at P≤0.05 compared to control group and group (I).(**Table-1, Fig-1**)

Table 1. Mean ±SD of the weights of the kidneys of rabbits groups.

Groups	weights of the kidney (g) (mean ±SD)
Control	10.50± 0.35(b)
I	11.14± 0.43(b)
Π	13.30± 0.90(a)

Different letters vertically means significant difference at P≤0.05.

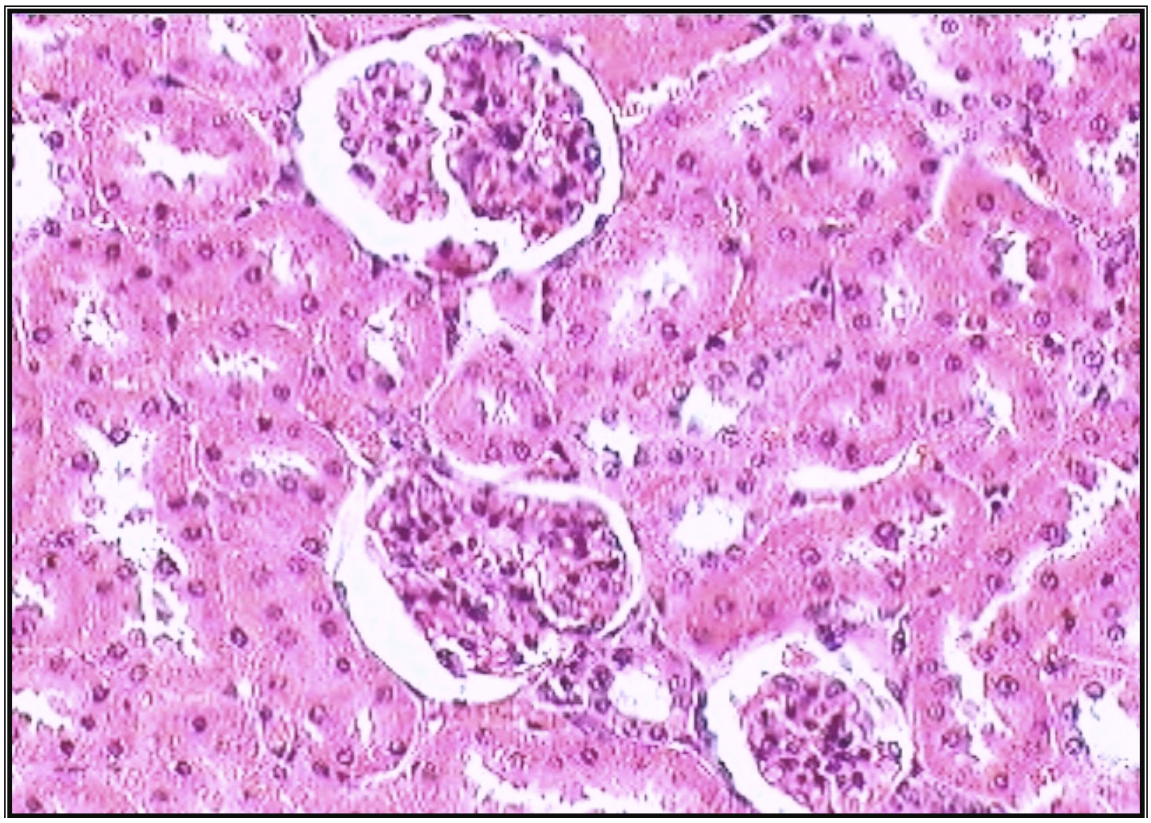

Fig 1. Photomicrograph of kidney of control group showing the renal corpuscles and convoluted tubules (H&E X 400).

The histological pattern of the kidney of group (I) was nearly normal except that there was an engorgement of some interstitial blood vessels **(Fig-2)**. Histological cross-sections of the kidney of all animals of group (Π) showed more severe pathological damage which includes enlargement and increase cellularity of the renal glomerular tuft including the mesangial cells which led to narrowing of Bowman's capsule. Vacuolar degeneration of the lining epithelium of the proximal convoluted tubules and some of them showed sloughing and necrosis of the epithelial cells. The distal convoluted tubules and the collecting ducts were preserved and not affected. Engorgement of some interstitial blood vessels can also be seen, and in some vessels hyaline casts were found obliterating their lumen (**Fig-3)**.

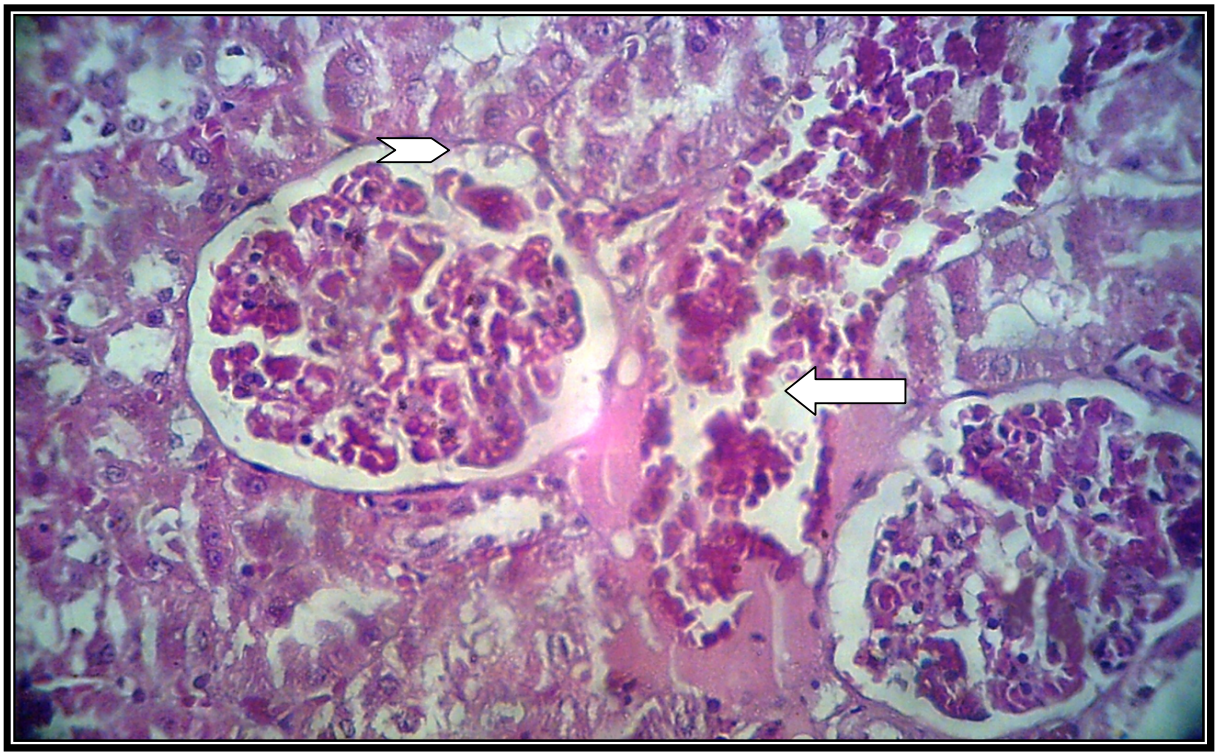

Fig 2. Photomicrograph of kidney of group I, Interstitial blood vessels congested with blood (arrow), epithelial cells of proximal convoluted tubules were normal(arrow head) (H&E X 400).

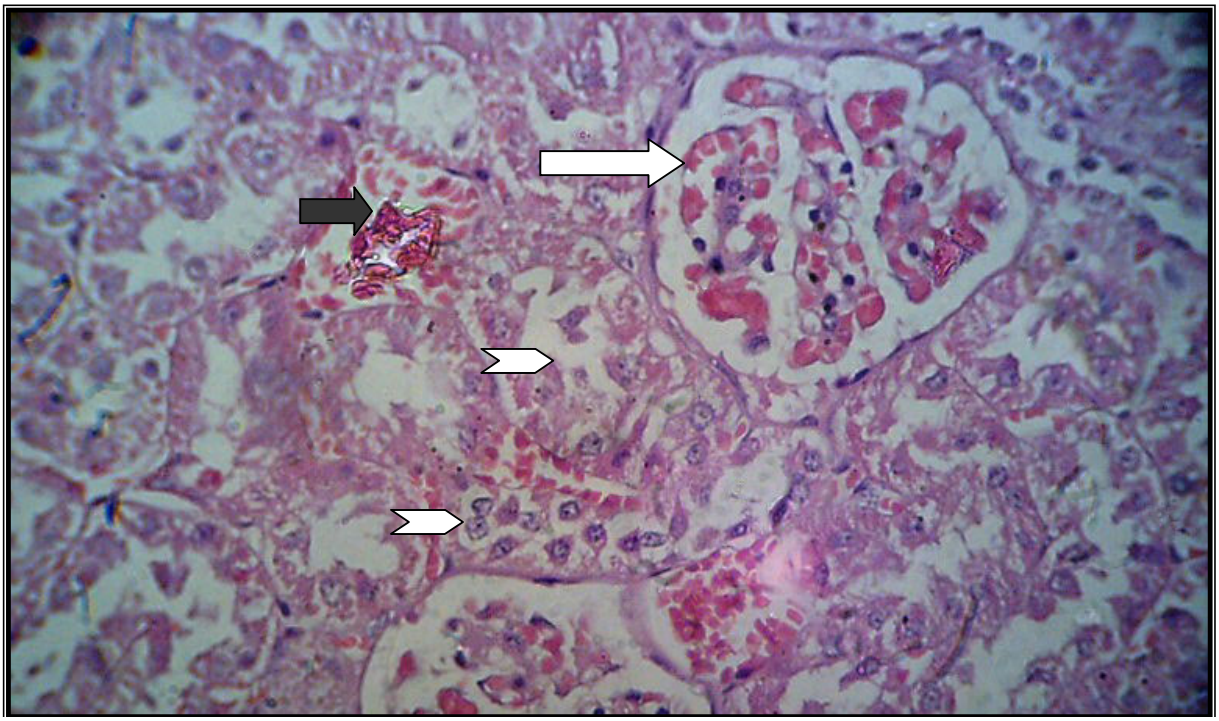

Fig 3. Photomicrograph of kidney of group II. There is enlargement and increased cellularity of the renal corpuscles (white arrow). Vacuolar degeneration of the lining epithelium of the proximal convoluted tubules and some of them showed sloughing and necrosis of the epithelial cells (arrow heads). Engorgement of some interstitial blood vessels (black arrows) (H&E X 400).

DISCUSSION

Drug-induced renal disease is common and responsible for a variety of pathological effects on the kidney. The kidney is structurally a complex organ, and any damage to the kidney are as complex as its structure. Toxic agents like drugs or other chemical agents can cause tubular and interstitial disorders.[6] There was an increase in the weights of the kidneys as the dose of the drug was increased. The mean weight of kidneys in (gram) for the control group was (10.50±0.35), and for group (I) it was (11.14±0.43). While the significant increase in the mean kidney weights was noticed in group(Π) which received the highest dose and it was (13.30±0.90). These results were coincide with the results of Hoseini *et al.,* they found that there was an increase in the size and weight of the kidney in mouse treated with nandrolone decanoate and this is due to tubular hypertrophy and increase in glomerular size and cellularity.[7] In the current study the renal histological sections of group (Π) showed vacuolar degeneration in the epithelium of the proximal convoluted tubules. In addition to congestion and dilatation of the interstitial blood vessels. Hyalinization of the wall of interstitial blood vessels and even formation of hyaline casts in their lumen. Also enlargement and hypercellularity of the renal glomeruli was evident. These findings were in agreement of Brownie *et al.*, they studied the effect of methylandrostenediol and androgens on the kidney. They found hyaline degeneration of the smaller arterioles, glomerular enlargement and hyalinization, tubular dilatation with cloudy swelling of the epithelial cells and hyaline casts in the tubular lumen.[8] Blantz *et al.* found that androgen when administered to ovariectomized rats led to tubular hypertrophy and increase in glomerular size.[9] Takahashi *et al.* stated the pathological changes in the rat kidney after administration of high doses of nandrolone decanoate. They found that the tubular epithelial cells were swollen, reduced in number and the distal tubules were partially hemorrhaged due to the toxic effect of the main metabolite of nandrolone decanoate on the tubules.[10] These findings indicate significant renal damage following androgenic-anabolic steroid administration. Some studies indicate the presence of androgen receptors in the kidney, while another study suggests they are only present within the urogenital tract.[11-13] Data from the current study suggest that androgenic-anabolic steroid affected the epithelial cells of urinary tubules via an androgen-dependent mechanism either directly or indirectly.

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