ORIGINAL ARTICLE

Role of Finasteride on Testosterone Induced Prostatic Hyperplasia in Long Evans Rats

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Abstract:

Testosterone is the main male sex hormone responsible for growth of sexual character and accessory sex organs. Despite its effectiveness as a male sex hormone, it causes benign prostatic hyperplasia (BPH) resulting in urinary dysfunction. On the other hand, finasteride is a 4-azastroid which inhibit the hyperplastic effect of testosterone and benign prostatic hyperplasia. The objective of the study was to observe the effects of finasteride on testosterone induced prostatic hyperplasis in Long Evans rats. This experimental study was carried out in the Department of Anatomy, Sir Salimullah Medical College, Dhaka from January to December 2006. Total 45 matured male long Evans rats of age 8-10 weeks and weighing 200-300 gms were used in this study. They were divided into three equal groups. Group A was vehicle (olive oil) control group, Group B was testosterone treated group and Group C was testosterone and finasteride treated group. The rats were sacrificed on the eleventh day. It was concluded that finasteride is an effective drug successfully inhibiting the testosterone induced prostatic hyperplasia.

Introduction:

The prostate is an accessory gland of male reproductive system that surrounds the neck of male urinary bladder and the proximal portion of the urethra. The prostate consists of branched tubuloacinar glands embedded in a fibromuscular stroma. Clinically, prostate is an important pelvic organ for its affinity to diseases like benign prostatic hyperplasia (BPH). Testosterone is responsible for development of accessory sex organs and secondary sexual characteristics[1,2]. In the target tissue, testosterone is not the active form of the hormone; it is reduced to dihydrotestosterone (DHT) by an enzyme 5, α-reductase and is 10 times more potent than testosterone because it dissociates from the cellular testosterone receptor more slowly[3,4,5].

Growth of the prostate, normal and abnormal, is mediated by testosterone[6,7]. BPH is a non-malignant enlargement of prostate gland that commonly develops in the aging male. It is a hyperplastic process of the stroma and epithelial tissues of the prostate gland[8,9,10]. DHT binds to cytoplasmic receptor protein, forming a complex then migrates to the nucleus and binds to the nuclear testosterone receptor and induces the DNA-RNA transcription process which is mitogenic and leads to hyperplasia of the target organ[11,12,13].

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Finasteride is a 4-azastroid, belongs to a new class of specific inhibitors of 5-α reductase[14]. Results of the study confirm that finasteride inhibit the 5-α reductase and prevent formation of DHT[15] which is responsible for hypertrophied prostate gland. The aim of the present study was to prepare an additional data for the urologists, endocrinologist, general physician, surgeons and research workers regarding diseases of the prostate.

Materials and method:

Forty five adult male rats of Long Evans strain weighing between 200-300 gms of age 8-10 weeks were used. Pure olive oil, injection testosterone propionate and injection finasteride were also used. In experimental design, all the rats were divided into three groups and were sacrificed on the eleventh day of study by decerebration under ether anaesthesia.

Group A: This group served as the vehicle control group and comprised of 15 rats, each rat received an injection of 0.2 ml of olive oil (vehicle) daily for 10 days.

Group B: This group was the testosterone control group and comprised of 15 rats. Each rat received 0.32 mg testosterone propionate in 0.01 ml of suspension daily for 10 days and showed testosterone induced prostatic hyperplasia.

Group C: This group served as the finasteride treated rats and comprised of 15 rats. Each rat received 0.32 mg testosterone propionate in 0.01 ml of suspension and finasteride 0.01 mg at 0.02 ml of suspension daily for 10 days. This group showed the effectiveness of finasteride to inhibit testosterone induced prostatic hyperplasia.

All the animals were sacrificed on the eleventh day by decerebration under ether anaesthesia. The abdomen was opened by a midline incision extending from xiphoid process to the symphysis pubis. The transverse incision was made extending 2 cm laterally on each side from the midpoint of the first incision. The prostate was dissected out, and loose areolar tissue and fat associated with the organs were cleaned by careful dissection. The organs were then weighed on an electric balance and recorded in milligram. For measurement of length, transverse diameter and anteroposterior diameter a slide caliper with a vernier scale was used and the results were recorded in centimeter. The specimens were persevered in 10% formol saline solution for histological examination. Out of 15 prostates in each group histological studies were carried out on six randomly selected specimens. The tissues were dehydrated in ascending concentration of alcohol, cleared in xylene, infiltrated and embedded in paraffin. Sections of the tissues were of 6 μm thickness and were stained with haematoxylin and eosin (H & E); stromal elements and muscles were stained with van Giemson's stain (Figs.-1, 2 and 3).

Average diameter of the acini at low power field of microscope (x10) was measured. Three different fields were chosen from each slide and in each field three acini were chosen to measure their diameter. A trans-vertical diameter was calculated by taking the mean of the longest and the vertical diameter. From the three trans-vertical diameters, the average trans-vertical diameters for each slide were calculated. From the six mean trans-vertical diameters, the mean diameter for each group was calculated. All these diameters were measured with the help of an ocular

micrometer adjusted to a stage micrometer. The readings were converted to values by microscopic standardization and expressed in micrometer.

The proportion of structural stroma of prostate were determined by using a "Point Counting technique". A replica of Zeiss integrating eye piece was prepared with a transparent plastic sheet containing a graticule of 25 points and was placed into the eye piece. Visual field of the slide was divided into equal eight parts by drawing four lines on the cover slip. Thus, counting 25 points on each field, a total of 200 (25x8) point position were recorded for each slide. The total number of points hitting inter-acinar prostatic stroma was summed up and expressed as a percentage of the stroma.

Results:

The tables revealed the mean (±SD) values of the prostate gland in group A, group B and group C. Values of the results were higher in testosterone treated rats (group B) than control group, (group A). After treatment with finasteride (group C) values of the result were less than group B but not up to the control group A.

Table-I: Comparison of weight (mg) of prostate between groups of rats (n-15)

Group	Range	Mean ± SD
A	928 – 940	933.13 ± 3.60
B	1150 – 1260	1184.67 ± 28.00
C	975 – 990	983.00 ± 4.93
A vs B	p <0.001	
A vs C	p <0.001	

Table-II: Comparison of length (cm) of prostate between groups of rats (n-15)

Group	Range	Mean ± SD
A	1.10 – 1.15	1.13 ± 0.01
B	1.18 – 1.28	1.23 ± 0.03
C	1.15 – 1.17	1.16 ± 0.01
A vs B	p <0.001	
A vs C	p <0.001	

Table-III: Comparison of transverse diameter (cm) of prostate between groups of rats (n-15)

Group	Range	Mean ± SD
A	0.12 – 0.15	0.14 ± 0.01
B	0.17 – 0.28	0.23 ± 0.04
C	0.17 – 0.20	0.18 ± 0.01
A vs B	p <0.001	
A vs C	p <0.001	

Table-IV: Comparison of anteroposterior diameter (cm) of prostate between groups of rats (n-15)

Group	Range	Mean ± SD
A	0.06 – 0.08	0.07 ± 0.01
B	0.09 – 0.15	0.12 ± 0.02
C	0.08 – 0.10	0.09 ± 0.01
A vs B	p <0.001	
A vs C	p <0.001	

Table-V: Comparison of diameter (μm) of acini between groups of rats (n-6)

Group	Range	Mean ± SD
A	370 – 492	403.17 ± 49.66
B	495 – 577	527.67 ± 36.30
C	462 – 477	467.50 ± 5.05
A vs B	p <0.001	
A vs C	p <0.01	

Table-VI: Comparison of percentage of stroma between different groups of rats (n-6)

Group	Range	Mean ± SD
A	12.5 – 17.5	14.83 ± 1.78
B	19.0 – 21.0	20.25 ± 0.69
C	16.0 – 18.5	17.08 ± 0.86
A vs B	p <0.001	
A vs C	p <0.01	

Discussion:

The weight, length, transverse diameter and anteroposterior diameter of the prostates were higher in all testosterone treated rats, and in comparison to vehicle control rats the values were highly significant (p<0.001). Similar findings were observed by Bruchovsky et al, Smith et al, Davis and Eaton and Niu et al[1,2,6,13]. The increase in values were due to hyperplasia of the acini and stroma of the prostate in testosterone treated rats. Shapiro et al, Wilson et al and Elias and Hyde[7,10,14] also found similar results in their study. In finasteride treated rats, the weight, length, transverse diameter and anteroposterior diameter of the prostate were lower in comparison to testosterone treated rats and the difference was highly significant (p<0.001). Diameter of the acini and percentage of the stroma of the prostate in finasteride treated rats was lower than that of testosterone treated rats and the difference was significant (p<0.01). Shapiro et al, Simon et al and Huttunen et al[7,8,11] observed the similar finding in their study. Results indicate effectiveness of finasteride against hyperplastic effect of testosterone.

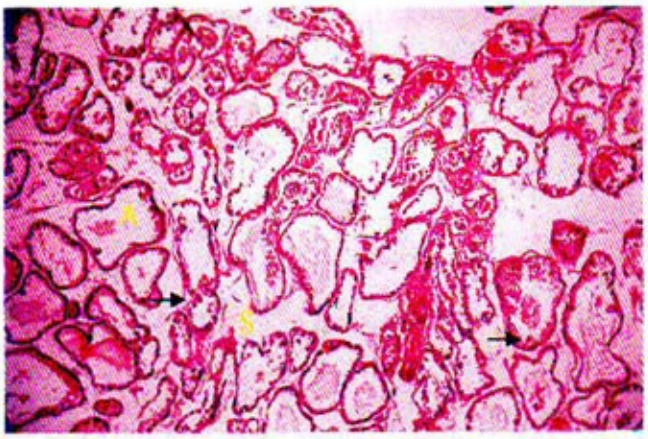

Figure-1: A low power (X10 objective) photomicrograph showing vehicle-treated prostatic tissue of rat; acini (A), stroma (S), epithelium (arrow). H & E stain.

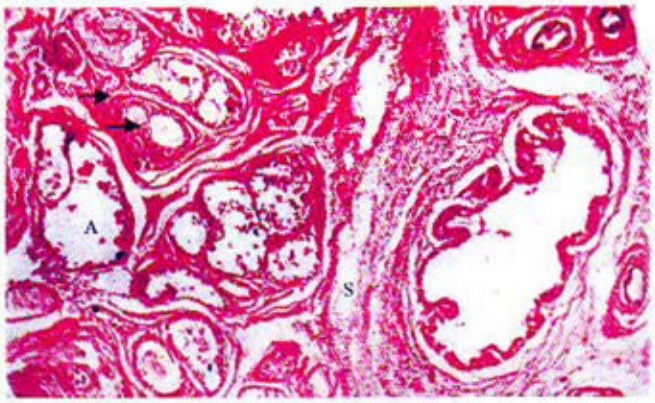

Figure-2: A low power (X10 objective) photomicrograph showing testosterone-treated hypertrophied prostatic tissue of rat; acini (A), stroma (S), epithelium (arrow). H & E stain.

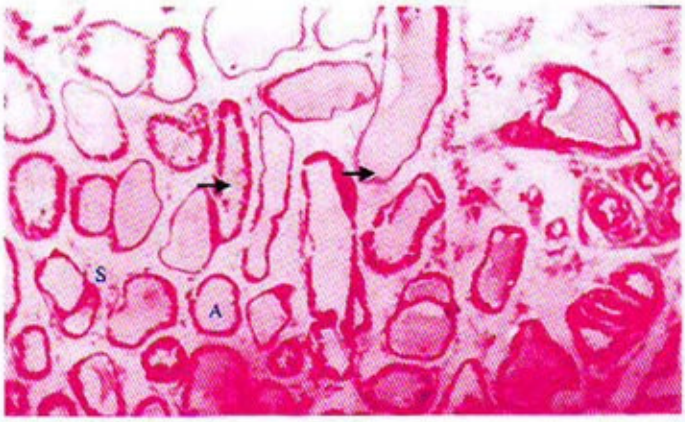

Figure-3: A low power (X10 objective) photomicrograph showing testosterone plus finasteride-treated atrophied prostatic tissue of rat; acini (A), stroma (S), epithelium (arrow), basement membrane (arrow). H & E stain.

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