ORIGINAL ARTICLE

# Impact of Testosterone to Induce Benign Prostatic Hyperplasia in Long Evans Rats

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**Abstract:**

*This experimental study was carried out in the Department of Anatomy, Sir Salimullah Medical College, Dhaka from January to December 2006. The objective of the study was to see the effects of testosterone on prostate and to measure the weight, length, transverse diameter and anteroposterior diameter of the organ, and also to estimate transvertical diameter of acini and percentage of stroma. Total 30 matured male Long Evans rats of age 8-10 weeks and weighing 200 to 300 gms were used in this study. They were divided into two equal groups. Group A was vehicle (olive oil) control group and Group B was testosterone treated group. The rats were sacrificed on the eleventh day. It was concluded that testosterone induces hyperplasia of the prostate resulting in increased weight, length, transverse diameter, anteroposterior diameter and higher values in trans-vertical diameter of acini and percentage of stroma.*

## 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. 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].

Growth of the prostate, normal and abnormal, is mediated by testosterone[4]. Benign prostatic hyperplasia (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 [5,6]. 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[7].

The incidence of BPH is age related, it is unusual before 40 years of age. The growth

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rate of BPH is slow, extending over years, but a small group of men have rapid enlargement of the gland caused by rapid growth of the glandular epithelium[8,7]. BPH is common in all countries of the world, and is a cause of urinary dysfunction. BPH usually goes unnoticed by the patient until it begins to obstruct the prostatic urethra[10]. The aim of the present study was to prepare an additional data for the urologists, surgeons and research workers.

**Materials and method:**

The study was carried out on 30 adult male rats (Long Evans strain) weighing between 200 and 300 gms and aged between 8 and 10 weeks. The hyperplastic effect of testosterone on prostate was evaluated using equal two groups of rats as follows: Group A (normal control) receiving vehicle only i.e 0.2 ml of olive oil subcutaneously daily for 10 days and Group B receiving testosterone subcutaneously 1.6 mg /kg body weight daily for 10 days. 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 Gieson's stain.

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:**

It was evident from the tables the mean (±SD) values of the prostate gland in Group A and in Group B. Values of the result were higher in testosterone treated rats (group B), than control group (group A), and the change between the groups was highly significant ($p<0.001$).

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

| Group | Mean ± SD | Range |
|---|---|---|
| A | 933.13 ±3.60 | 928 - 940 |
| B | 1184.67±28.00 | 150 - 1290 |
| A vs B | p <0.001 | |

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

| Group | Mean ± SD | Range |
|---|---|---|
| A | 1.13 ±0.01 | 1.10 - 1.15 |
| B | 1.23±0.03 | 1.18 - 1.28 |
| A vs B | p <0.001 | |

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

| Group | Mean ± SD | Range |
|---|---|---|
| A | 0.14 ±0.01 | 0.12 - 0.15 |
| B | 0.23 ±0.04 | 0.17 - 0.28 |
| A vs B | p <0.001 | |

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

| Group | Mean ± SD | Range |
|---|---|---|
| A | 0.07 ±0.01 | 0.06 - 0.08 |
| B | 0.12 ±0.02 | 0.09 - 0.15 |
| A vs B | p <0.001 | |

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

| Group | Mean ± SD | Range |
|---|---|---|
| A | 403.17 ± 49.66 | 370 - 492 |
| B | 527.67 ± 36.30 | 495 - 577 |
| A vs B | p <0.001 | |

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

| Group | Mean ± SD | Range |
|---|---|---|
| A | 14.83 ± 1.78 | 12.5 - 17.5 |
| B | 20.25 ± 0.69 | 19.0 - 21.0 |
| A vs B | p <0.001 | |

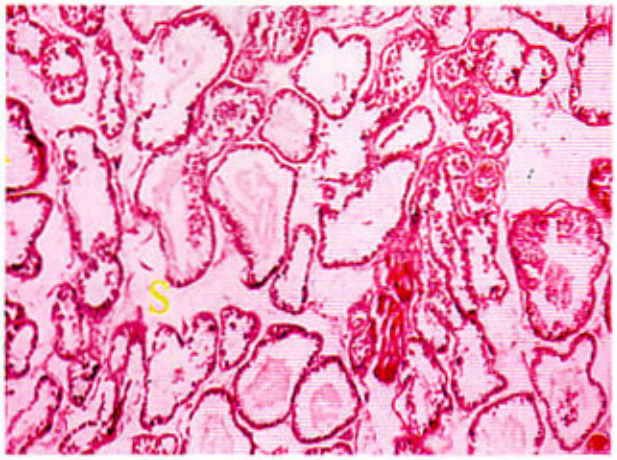


**Figure-1:** Photomicrograph showing normal prostatic tissues of vehicle control group (x 10).

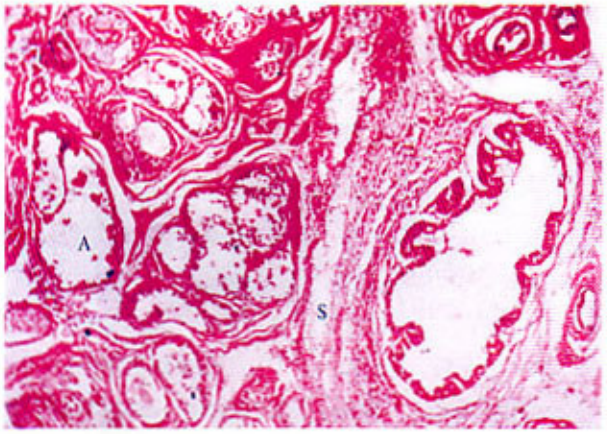


**Figure-2:** Photomicrograph showing hyperplasia of prostatic tissues of testosterone treated group (x 10).

**Discussion:**

In the present study, effects of testosterone on prostate were assessed through comparing general and histological variables. Weight of the prostate shows 20% higher values in testosterone treated rats than control rats. When compared statistically, difference was highly significant ($p<0.001$). Niu et al did the same work, which had slightly larger values (22%) than that of the present study[6].

Length of the prostate shows that the mean length of prostate in testosterone treated rats was higher than that of the vehicle control rats. Huttunen and Davies and Eaton observed that length of the prostate was high in all the rats treated with testosterone[2, 11]. Jong et al also observed similar effect on the length of the prostate[12].

In the present study, it was found that the mean of transverse diameter of the prostate in testosterone treated rats was significantly higher than that of vehicle control rats. The mean rise was two times more than the vehicle control rats. This result is an indication of testosterone induced prostatic hyperplasia. Davies and Eaton observed in their studies higher values in testosterone treated rats[2].

Mean change of anteroposterior diameter of prostate in testosterone treated rats was higher than the vehicle control rats and the mean change was almost two times more. Jong et al and Smith et al also observed a high mean value of anteroposterior diameter of prostate in testosterone treated rats[12, 13].

Diameter of the acini was increased by 20% in testosterone treated rats in comparison to vehicle control rats. The difference of mean values between the two groups was statistically significant ($p<0.001$). Smith et al found results in favour of this study; diameter of acini was increased in testosterone treated rats[13].

Percentage of stroma of prostate was increased in testosterone treated rats, which was two times more than vehicle control rats. Shapiro et al found in their study that the relative increase in proportion of stroma was related to the effects of testosterone on prostate[7].

The result of the present study would enrich the information pool on effect of testosterone

on prostate in producing benign hyperplasia. To establish a standard data for future research works, further studies are required using large number of samples and using different doses of testosterone.

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