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Original Research Article

Effects of Finasteride on Prostate Gland Weight, Spermatogenesis and Fertility in Mice

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Abstract

Finasteride is a drug used in treatment men with benign prostatic hyperplasia (BPH), blocks the action of an enzyme called 5 alpha-reductase enzyme; an enzyme that converts testosterone to dihydrotestosterone (DHT). DHT plays an important role to cause benign prostatic hyperplasia (BPH), so this action will increase testosterone levels in the body, which decreases prostate size, therefore the finasteride used for BPH treatment. To evaluate effects of different doses of finasteride on prostate weight, spermatogenesis and fertility in mice. Eighty mature fertile male mice between 8-12 weeks age were used divided into four groups every group consist of 20 males. First group (control group G1) received distil water only (low dose group G2) treated with finasteride (0.006) mg/daily dose, (recommended dose group G3) treated with finasteride (0.03) mg/daily dose and last (double dose group; G4) treated with finasteride (0.06) mg/daily dose orally administrated mice for 90 days for all treated groups. After 90 days of treatment, the mating was achieved. Recording new borns in four groups, after then sacrifice male mice in four groups and remove testis and prostate whereas prostate weight detected for male to observe the differences, and testis for histological study, the specimens independently read. Evaluate histology of testis to observe the process of spermatogenesis in the testis of each group. Results: It showed that there are effects of finasteride on morphology and histology of testis as well as spermatogenesis of all groups. The effects of finasteride on fertility by reduce rate of newborns and also effects on psychological behaviors included reduces aggressive in male mice and finally the effects on body weight where as it caused a slight body weight gain. The results concluded after treatment with finasteride during 90 days there was alteration of prostate weight and shrinking in size without effect on spermatogenesis, as well as, histological change occurs in testis, that effect on male fertility, also there is change on psychological behaviors of male mice.

Keywords: Finasteride, spermatogenesis and Prostatic hyperplasia

INTRODUCTION

Infertility is a disease characterized by the failure to establish a clinical pregnancy after 12 months of regular and unprotected sexual intercourse (Vander and Wyns, 2018). For healthy young couples, the chance of getting pregnancy within the first year of fertility is 85 %. Although advances in the diagnosis and treatment of infertility, the pregnancy rate remains stable (Esteves et al., 2011).

Finasteride blocks the action of an enzyme called 5-alpha-reductase. It will increase testosterone levels in the body, which decreases prostate size and increases hair growth on the scalp. Randomized organized trials of

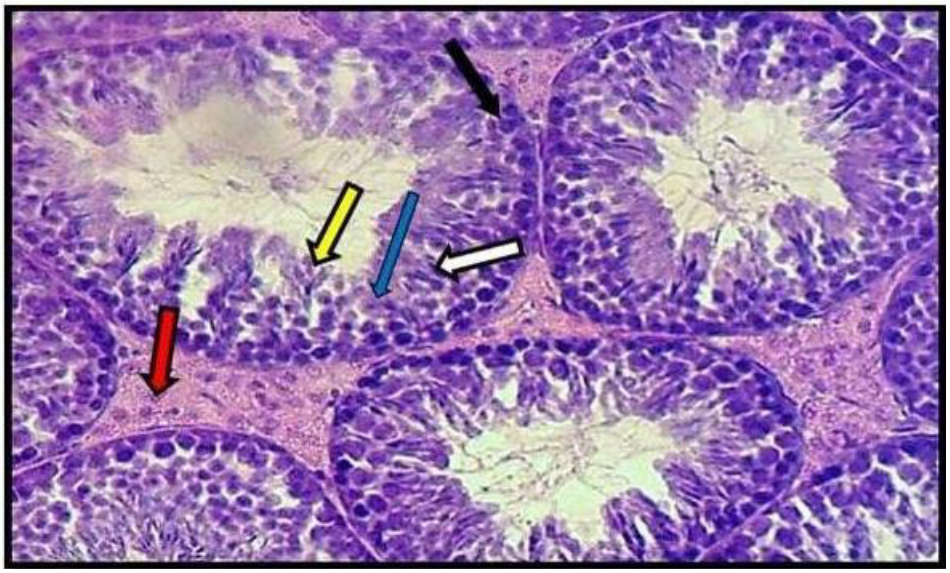


Figure 1. Cross section through normal mice testis showing: Sertoli cell (blue arrow), Interstitial cells (leydig cell), spermatogonia (black arrow), spermatocyte (white arrow), and spermatid (yellow arrow) stained by (H&E, 40X)

finasteride for treatment of these two conditions have established increased rates of sexual dysfunction including low libido and erectile dysfunction (Traish et al., 2011).

The testes have an unusually thick dense connective tissue capsule, and the tunica albuginea, covers each testis. The tunica albuginea is composed of a layer of collagen fibers, within which embedded fibroblasts, myocytes, are mast cells, nerve fibers, and nerve endings. The outer part of tunica albuginea, the tunica vaginalis, consists of a flattened layer of mesothelial cells overlying a well-developed basement membrane. It forms a sac with two components; a visceral portion and a parietal layers separated by a thin layer of serous fluid (Mills, 2007). The effect of finasteride on spermatogenesis and its use by male partners during pregnancy is a topic that has garnered interest recently. This newer treatment indication has resulted in far more men who are of reproductive age using the drug and has caused some to consider finasteride's effect on both fertility and pregnancy (Eric and Robert, 2010). This study aims to know the effects of fenasitride therapy on reproductive system morphologically and histologically.

MATERIAL AND METHODS

Eighty Healthy mature fertile males mice, and ninety mature females fertile mice were used, age of 8-12 weeks old and 25-30 gm. Body weight was obtained from the animal house of High institute of infertility diagnosis and Assisted Reproductive Technologies (ART) after prepare in all the instrument and material specialized for this work. The experimental animals (male mice) were divided to four groups. Group one (G1) control group: (given just orally distal water). Group two (G2) low dose group: Animals were given orally 0.006 mg finasteride daily for 90 days. Group three (G3) recommended: the animals were given orally 0.03 mg finasteride daily for 90 days. Group four (G4) high dose group: the animals were given orally 0.06 mg finasteride daily for 90 days.

After 90 days of treatment with finasteride the five males from each group enter intercourse by adding male to three mature female in one cage, and observed vagina plug and recording newborns in every group and remained mice were sacrificed by cervical dislocation and then, they fixed on the dissecting table and incised, opened the abdomen transversely and finally the testis was dislocated and rinsed in normal saline (Junquira and Carneiro, 2005). For each male mice, the histological evaluated of testis by fixed in formalin 10 % then stored in 70% ethanol alcohol for routine histological techniques, paraffin sections with 5 microns thickness were prepared and stained with Harries hematoxylin-eosin stain, the specimens independently read (McConnell et al., 1998a). Prostate were extracted then washing with normal saline and removed from other tissue like bladder tissue surrounding of prostate gland then weight prostate for each male mice in four groups. The dose of drug per male mice equal 0.03 mg, whereas one tablet of finasteride 5 mg / 60 kg B.W (normal dose) in human. As 5 mg tablet of finasteride divided by 0.03 mg (dose per mice) = 166.6 As One tablet enough for 166 male mice (McConnell et al., 1998b).

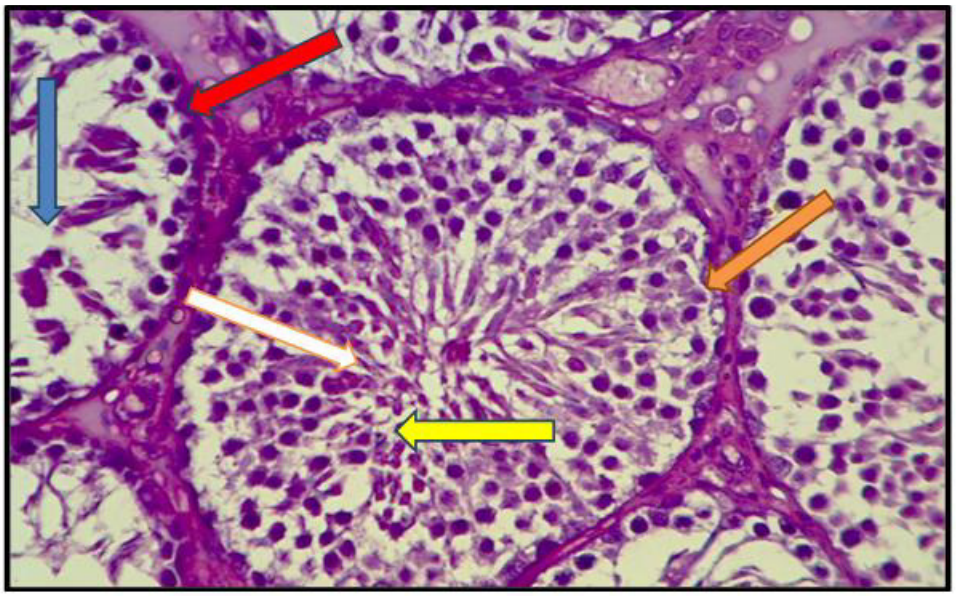


Figure 2. Section from treated mice testis showing: Separation of spermatogonia from basement membrane (green arrow), cell death (blue arrow), narrow lumen (white arrow), decrease of spermatid (yellow arrow), decrease spermatogenesis, defects of architecture of the tissue, decrease in interstitial area and vacuoles (red arrow) and decrease in leydig cell. (H&E, 40X)

Statistical Analysis

Statistical was done by SPSS V. 13 (statistical package for social sciences) to compare the results between groups (G2, G3, G4) and control group (G1) Data were expressed as mean ± standard error. The values were considered statistically significant when P-value ≤ 0.05 (SPSS, 2008). Statistical analysis was performed with SPSS V. 13 (statistical package for social sciences) to compare the results between with treatment finasteride groups (G2, G3, G4) as mentioned above

RESULTS

Histological Evaluation of Testis

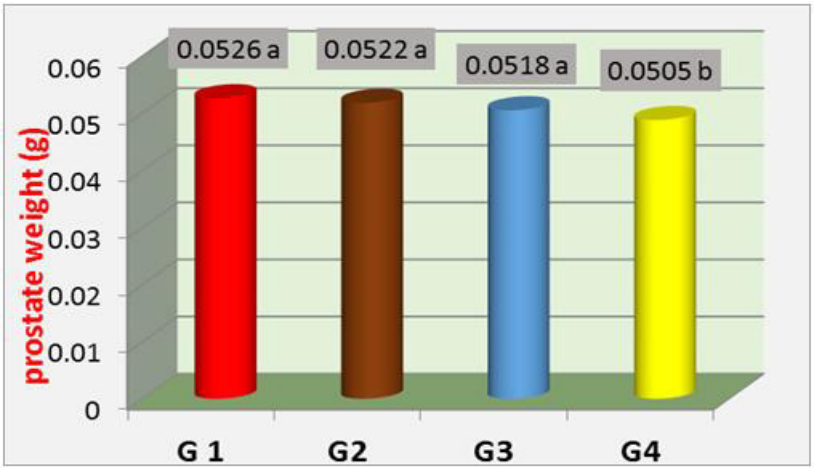
In control group, the H&E stain shows normal morphological and normal structure of seminiferous tubules, the normal arranged germ cells layer, spermatid observed lies close to the lumen and are spherical or polygonal cells, sertoli cells, relatively few in numbers and they are tall, columnar cells, their apical cell membranes are projected into the lumen of the seminiferous tubules, the nucleus is dark, clear, oval and located basally, the tubule basement membrane covered by fibrous tissue, and contains numerous connective tissue fibers and some cells with the characteristics of smooth muscle cells called myoid cells, between the seminiferous tubules, the interstitial cells (Leydig cells) were seen, as they are large polyhedral cells that have spherical nucleus (Figure 1). In treatment groups by different doses of finasteride (G2, G3, and G4) were used. After 90 days of administration, the section of testis stained by H&E stain in G2 and G3 shows no effects. In G4 the following effects are seen in the testis: Separation of spermatogonia from basement membrane, cell death, narrow lumen, decrease of spermatid, decrease spermatogenesis, defects of architecture of the tissue, decrease in interstitial area and vacuoles and decrease in leydig cell as shown in (Figure 2).

The Effect of Different Doses of Finasteride on Prostate Weight

The effects of finasteride on prostate weight showed in (figure 3). Non-significant differences ($P > 0.05$) of G2 (0.006 mg/mice/daily) when compared with control group. Non-significant differences ($P>0.05$) of G3 (0.03mg /mice/daily) as compared to control group G1. Significant reduction ($P<0.05$) in G4 (0.06mg /mice/daily) when compared to the control group G1.

The Effect of Different Doses of Finasteride on Body Weight

The effects finasteride on body weight shown Non-significant differences ($P>0.05$) in G2 when compared to the control group G1. Non-significant differences ($P>0.05$) with G3 when compared to the control group



(a) Means with similar superscripts within each column are non-significantly different (P>0.05). (b) Means with different superscripts within each column are significantly different (P<0.05).

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Figure 3a. Effect of finasteride on prostate weight on mice male.

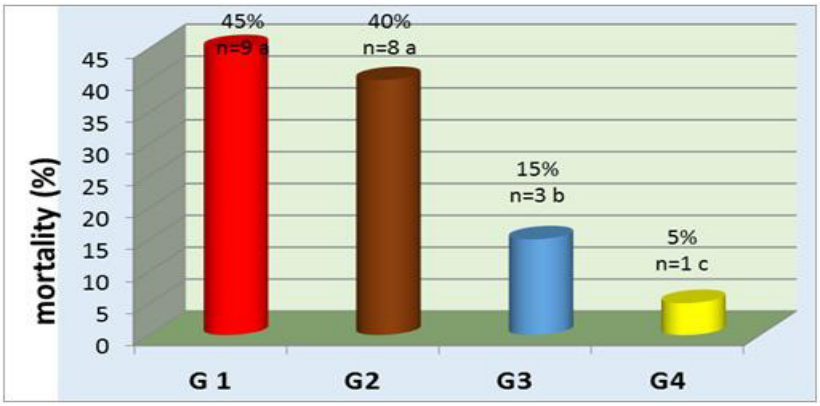

Figure 4. Illustrated total mortality in four groups during periods 90 days with treatment different doses of finasteride and control group
Ch2 = 17.44 P- Value = 0.004**

G1. Significant increase (P<0.05) in G4 when compared to the control group G1 as seen in figure (4). As well as the (table 1) reveals the inverse relationship between increased body weights of male mice and decreased of prostate weight.

Table 1. Show the effect of treatment of finasteride in four groups on body weight and prostate weight.

Animals	G1	G2	G3	G4
WEIGHT of PROSTAT(mg)	0.0526±0.0007 NS*	0.0522±0.0005 NS*	0.0518±0.0005 NS*	0.0505±0.0006 S**
BODY WEIGHT(mg)	32.02±0.734 NS*	32.8±1.078 NS*	33.2±1.067 NS*	35.6±0.748 S**

*(NS) Non-significant differences (P>0.05) between group G2 and group G3 compared to group G1. ** (S) Significant differences (P<0.05) between group G4 compared to group G1.

Table 2. The effect of different doses of finasteride on total number of newborn

Number female	G1	G2	G3	G4
15	6.45±0.4 A	5.4±0.326 B	4.14±0.594 B	3.57±0.39 B

Means ± S.E.M.
Number of female mice per group=15
A. Non-significant differences (P>0.05)
B. Significant decrease (P<0.05) between group treated with different doses of finasteride G2, G3 and G4 compared to control group G1.

The effect of different doses of finasteride on number newborns

Reveal the (Table 2) the results of number of total newborns in each group after 90 days treatment with different doses of finasteride (G2, G3, G4) and control group G1. Significant reduction (P<0.05) in the number total of newborns were assessed after 90 days of treatment with different doses (low, normal and double) G2,G3,and G4 respectively When compared to control group G1 therefore, there are clear drop newborns in groups with treatment of finasteride especially group double dose G4 compared with control group G1.

The effect of finasteride on behavior psychological in male mice

When observe the behavior of males in the four groups we noticed that there are more quiet and less aggressive between males treated with finasteride especially in G4 when compared with control group G1 also there was more mortality rates in males in control group G1 because of fighting between males while groups treated by finasteride G2, G3 and G4 are less mortality than G1 control group. This indicates an effect of finasteride on behavior of male mice.

The Figure (4) shows the mortality rates in male mice after 90 days of treated groups. Non-significant differences (P>0.05) in total mortality in G2 when compared to the control group. Significant differences (P<0.05) in total mortality in groups treated (G3, G4) when compared to G1.

DISCUSSION

Results of this study concluded that finasteride increases body weight of males after treatment during 90 days especially in normal dose group (G3) and double dose group (G4). This rise in weight is significant compared to the control group. Therefore, increased body weight occurred because of the rise in the level of testosterone by finasteride, which is blocked to convert DHT, whereas testosterone on somatic cells is responsible for appearance secondary male characteristics and building muscle and skeleton .

The study showed the effect of finasteride on decreased birth rates, especially in treatment of the double group (G4) compared to the control group (G1). This result agrees with Glina S et al., who mentioned that finasteride decreases the libido because of the effect finasteride has on testosterone metabolism (Glina, 2013). While 'Donnel O also certified that finasteride has an effect on fertility when they showed the use of finasteride promote a significant decrease of the serum level of DHT and decrease the volume of plasma seminal (Donnel, 1999).

The results of present studies indicate the effect of finasteride to reduce the weight of the prostate. This study, showed changes in weight of prostate, these changes might be mainly due to finasteride, reduction in secretion in the tubules gland of prostate this mean reduction in size of the cell of columnar epithelium versus normal weight in control group.

In this study, testis showed no significant histological, morphological changes that happened on testis after treatment with finasteride. This result agrees with Fuh (1999) who observed that chronic treatment with daily

dose of finasteride does not affect spermatogenesis or semen production in young men (Lewis, 1992). Lewis et al., concluded that no effect on spermatogenesis in 47 men eat 5 mg of finasteride. Moreover, Nancy declared a 1mg dose of finasteride for does not effect on spermatogenesis (Nancy, 1999).

CONCLUSION

From the results of the present study, it can be concluded that: No significant alteration in spermatogenesis after treatment with finasteride. Significant reduction in weight of prostates after treatment with finasteride. Alteration in histology and morphology in prostate, where there is decrease secretion of tubules gland of prostate as well as reduction on size cuboidal epithelium of tubules gland of prostate. There was reduction of fertility of males mice after treatment with finasteride, Alteration of psycho-logical behaviors of male mice after treatment.

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