



PHYSIOLOGICAL AND HISTOLOGICAL STUDY OF THE EFFECT OF FINASTERIDE DRUG (PROSTACARE - 5MG) ON THE FERTILITY OF ALBINO MALE RATS

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Abstract

Their study was led to explore the impact of finasteride (Prostacare) on testicular capacity in *Rattus norvegicus*. Forty five matured male rats with body weight of (200-300g) and (8) to (10) weeks of age were divided into (3) groups (15 rats/group). The first group was given orally with distilled water as a control and the others (second and third) were given orally with two concentrations of finasteride (5mg /kg.b.w and 10mg /kg.b.w) daily for a period of (eight weeks). After the finish of the experiment ,rats was scarified for the purpose of histological study and measurement of organ weights in the laboratory. The results showed a significant ($p<0.05$) decrease in the body, testis, epididymis and prostate gland weights in compared with the control. Also the results of histological examination of testis and epididymis showed a significant ($p<0.05$) reduce in the seminiferous tubules diameters and reduction in number of the leydig's cells, while there was a significant ($p<0.05$) rise in the interstitial space between tubules compared to the control group. The results was showed necrosis in the seminiferous tubules of the testis.

Key words : Finasteride , testis , BPH, necrosis, sexual dysfunction.

Introduction

Finasteride is an inhibitor of human 5α -reductase resulting in the decrease of DHT formation (Sheikh *et al.*, 2015). Finasteride is using for treatment of the male pattern hair loss (MPHL) and benign prostatic hypertrophy (BPH) have demonstrated increased rates of sexual dysfunction including low libido and erectile dysfunction (Michael, 2015).

Any changes in the Testosterone / Dihydrotestosterone ratio in male progeny born from females fertilized by finasteride-treated male rats can result in impairment of testicular physiology and data demonstrate that finasteride cause sperm DNA damage (Kolasa-Wolosiuk *et al.*, 2016). Finasteride was introduced to treat patients with benign prostatic hyperplasia (BPH), and it has shown its effects in reduction of prostate volume and decrease of prostate-specific antigen (Kun, 2004). Finasteride alters sperm morphology in a way that indicates necrosis (Collodel *et al.*, 2007).

Materials and Methods

Preparation of Finasteride (Prostacare) solution

Finasteride (Prostacare - 5mg/kg.b.wt./day), which dose for Human. Matured male albino rats were used for this experimental study. The treated groups with prostacare with two doses (5 mg/kg.b.wt. and 10 mg/kg.b.wt.) were administered orally to male albino rats using separate sterilized oral dosing needle for a period of eight weeks were therapeutic doses calculated for the weight of the rats. The control group received the same volume (distilled water) alone.

Experimental animals

Forty five mature, healthy, fertile and adults albino male rats (*Rattus norvegicus*) aged (8-10) weeks were obtained from the animal house of College of Veterinary, Al-Qadisiyah University, Iraq. The weight range was 200-300 gm. The animals were housed in plastic caged. The caged were embedded with wooden shelves, under natural (12hr) light and (12hr) dark. The animals were caged at lab temperature of 23 – 25°C and the animals

were feed *ad libitum*. The animals were reproduced to obtained a propitiate numbers of animals. They were divided into three groups (15 animals D group).

Laboratory analysis

Animals weight has been recorded before and after the dosage by using electrical balance. Animals were Sacrifice by cervical dislocation, Immediately after Sacrificed the abdominal cavity was opened in overturned (T) shape and then the male reproductive organs were extirpated (testes, epididymis and prostate gland). The adipose tissues were removed. These reproductive organs were placed on a filter paper to be weighted with an electrical balance.

Histological study

Testes, epididymis and prostate gland were kept in Bouin's solution for 24 hr then they are washed by 70% ethyl alcohol for several times until the yellow colour was removed. Testes were kept in ethyl alcohol 70% of until use. Dehydration, clearing, infiltration, embedding, sectioning, staining and mounting were respectively done to prepare the slides for histological examination according to Bancroft and Stevens (1982).

Statistical analysis

The results were expressed as (Mean \pm Standard Error). T-test was used for the comparison between control and other groups in the measured parameters. One-way analysis of variance (ANOVA) followed by least significant difference (LSD) analyses at 0.05% probability of levels. All statistical analysis was performed using Excel program and Magastat program The test of significance was placed at $p < 0.05$.

Results

The results also showed a significant decrease ($p < 0.05$) in body weight after treatment with

concentrations of 5mg /kg.b.wt. and 10mg/kg.b.wt. of the drug compared to control group. There was a significant ($p < 0.05$) decrease in the rate of testes weights , epididymis weights and prostate gland weights of animals treated with Prostaglandin at two the concentration in compared to control group.

Also the results of seminiferous tubule showed there was a significant ($p < 0.05$) decrease in the diameter of the seminiferous tubule in the treated groups (5mg / kg.b.wt. and 10mg/kg.b.wt.) compared to control group. The results showed there was a significant ($p < 0.05$) decrease in the diameter of the epididymis tubule in the treated groups in compared to control group. Significant ($p < 0.05$) decrease in the diameter of the prostate glands in the treated groups (5mg /kg.b.wt. and 10mg/kg.b.wt.) compared to control group. The histological examination also proved that the treated rats groups (5mg /kg.b.wt. and 10mg/kg.b.wt.) showed a significant ($p < 0.05$) increase in the interstitial space compared to the control groups, also the results was showed necrosis in some seminiferous tubules of the testis of albino male rats that treated with two doses of finasteride.

Histological of testes, epididymis and prostate gland

The results in fig. 1 showed normal testis sections of control group, also show decrease in the diameter of seminiferous tubules and increase the interstitial space. In fig. 2 the histological examination of epididymis show decrease in the diameter of tubules. The fig. 3 showed decrease in the diameter of the prostate gland.

Discussion

The decrease of the body mass may be recognized to many factors such as the deficiency in the Testosterone levels (Rolf *et al.*, 2002). Testosterone is playing a major role in the growth of male reproductive tissues for example the testes and prostate as well as helping

Table 1 : Effect of different concentrations Finasteride (5mg/Kgb.wt. and 10mg/kg b.wt.) on the rate of body weight, testes weight, epididymis weight and prostate gland weight.

Treatments Groups	Body weight (gm.) (Mean \pm SEM)	Testes weight (gm.) (Mean \pm SEM)	Epididymis weight (gm.)(Mean \pm SEM)	Prostate gland weight (gm.)(Mean \pm SEM)
Control	250.43 \pm 9.93	1.4057 \pm 0.0433	0.7214 \pm 0.0099	0.2243 \pm 0.0084
Prostaglandin (5 mg/kg.b.wt)	211.86 \pm 2.97a	1.1986 \pm 0.0192a	0.5686 \pm 0.0202a	0.1471 \pm 0.0092a
Prostaglandin (10mg/kg.b.wt)	194.29 \pm 2.04ab	1.0557 \pm 0.0157ab	0.4614 \pm 0.0147ab	0.1029 \pm 0.0042ab
L.S.D. 0.05	3.33	0.020	0.016	0.006

Date represented (Mean \pm SEM)

a = representing a significant ($P < 0.05$) differences in comparison to control. **b** = representing a significant ($P < 0.05$) differences in comparison to between two treatments (5,10 mg/kg.b.wt.).

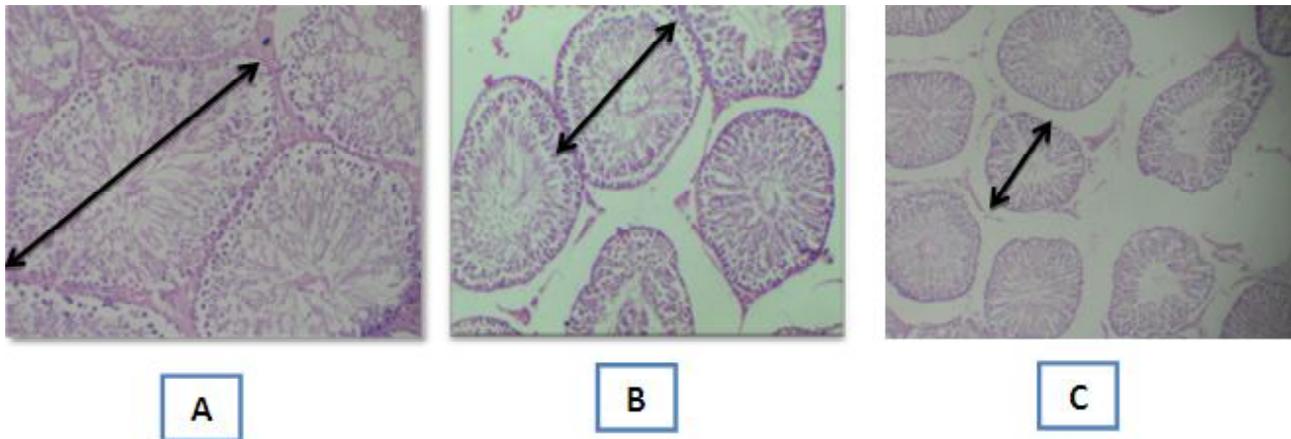


Fig. 1 : The histological examination of testis show decrease in the diameter of seminiferous tubules and increase the interstitial space. A : Control, B: treated with prostacare (5mg /kg.b.wt.), C: treated with prostacare (10mg /kg.b.wt.).

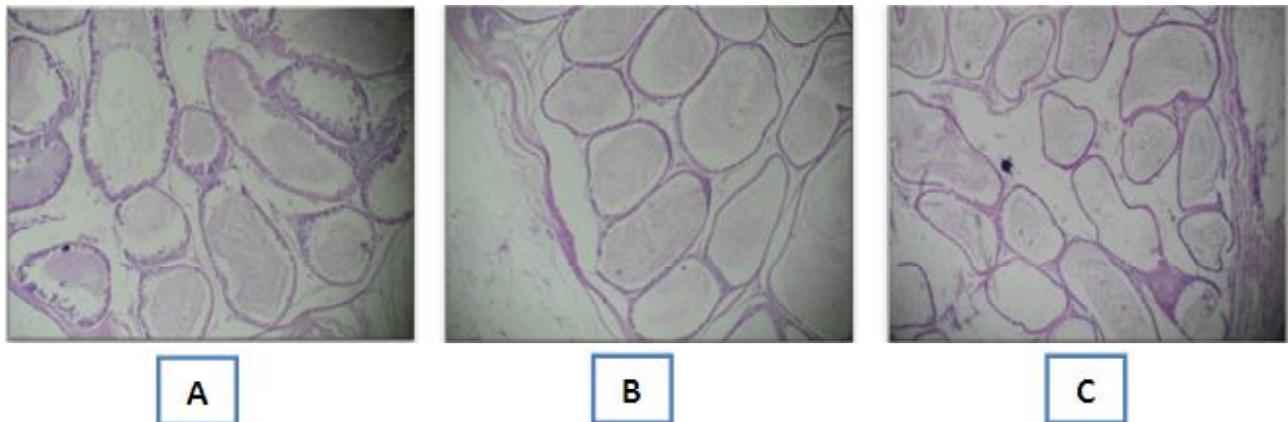


Fig. 2 : The histological examination of Epididymis show decrease in the diameter of tubules. A:Control , B: treated with prostacare (5mg /kg.b.wt.), C: treated with prostacare (10mg /kg.b.wt.).

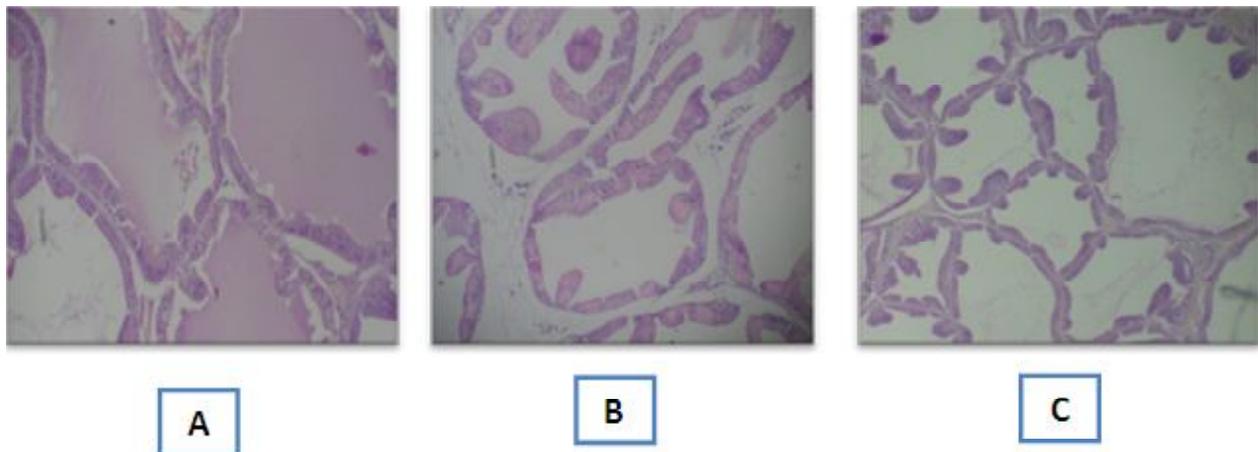


Fig. 3 : The histological examination of Prostate gland show decrease in the diameter. A:Control , B: treated with prostacare (5mg /kg.b.wt.), C: treated with prostacare (10mg /kg.b.wt.).

secondary sex characteristic such as improved muscle, bone mass and growing of body (Alwachi, 2008).

The impacts of the medication on testicles weight was in consistence with who saw that alpha blockers caused decrease in testicular weight (Mocktary, 2007).

This came about because of the huge lessening of spermatogenic cell number as confirm by the examination of stained testicles sections (Giuliano, 2006).

The decrease was recognized to the decline in the level of the T hormone. Some studies have exposed that

the creation and decrease of testicular testosterone leads to decrease of the diameter of epididymis tubule in rats (Nair *et al.*, 2002).

The luminal epithelial cells showed a marked reduction in cytoplasm and their secretory activity became diminished after finasteride treatment for 10 days and the lumens of prostate glands that markedly reduced in size and administration of finasteride led to additive effects on the thickness of the prostate epithelium, for this reason the diameter of prostate gland which reduced (Ma *et al.*, 2004).

The effect of finasteride is proportionately similar in both peripheral and transition zones for both volumetric and morphometric changes (Marks *et al.*, 1999).

The reduction in the diameter of seminiferous tubules could be referred to the reduction in testosterone hormone level, since testosterone has an important role in the development and growth of male reproductive ducts and epithelial cells of epididymal tubules (Umezu *et al.*, 2004).

The reason of degeneration and necrosis changes in seminiferous tubules in rats group treated with finasteride may be due to the reduced number of Leydig's cells, which lead to the reduction in level of testosterone hormone which are responsible of active division of spermatogenic cells in spermatogenesis therefore, the reduction in level of T hormone leads to the damage of these cells and then damage in the seminiferous tubules (Guyton and Hall, 2000).

Increase in the spaces between seminiferous tubule resulting from low number in Leydig's cells and this lead to increase diffusion of fluid inside interstitial tissues (Luis *et al.*, 1986).

References

- Alwachi, S. N. (2008). *Endocrine Glands and Hormones*. 1st ed. Dar- Al Fiker publishing company, Jordan (In Arabic).
- Bancroft, J. D. and A. Steven (1982). *Theory and practice of histological techniques*. 2nd ed. Churchill Livingstone, Edinburgh, London pp : 662 .
- Collodel, G, G. Scapigliati and E. Moretti (2007). Spermatozoa and chronic treatment with finasteride: a TEM and FISH study. *Arch. Androl.* **53** : 229-233.
- Giuliano, A. F. (2006). Impact of medical treatments for benign prostatic hyperplasia on sexual function. *BJU. Int.*, **97(2)** : 34-38.
- Guyton, A. C. and J. E. Hall (2000). Reproductive and hormonal function of male (and the pineal gland). In: *Text book of medical physiology*. A.S. and saunders company. London, Toronto, Philadelphia. 9th ed. pp:916-928.
- Kolasa-Woźosiuk, A., K. Misiakiewicz-Has, I. Baranowska-Bosiacka, I. Gutowska, M. Tarnowski, M. Tkacz and B. Wiszniewska (2016). Connexin 43 expression in the testes during postnatal development of finasteride-treated male rat offspring. *Archives of Medical Science* **2** : 1-9.
- Kun, Y. C. (2004). Effects of Finasteride on Prostate Volume and Prostate-specific Antigen. *Original Article*, 571-574.
- Luis, C., J. Carneiro and A. John (1986). *Basic histology*. 5th ed. Lange medical publications. California PP:67-96.
- Michael S. Irwig (2013). Decreased Alcohol Consumption Among Former Male Users of Finasteride with Persistent Sexual Side Effects/ : A Preliminary Report, 1-4.
- Ma, Z., T. H. Nguyen and T. H. Huynh (2004). Reduction of rat prostate weight by combined quercetin – finasteride treatment is associated with cell cycle deregulation. *Journal of Endocrinology*, **1** : 493-507.
- Marks, L. S., A. W. Partin, F. J. Dorey, G. J. Gormley, J. I. Epstein, J. B. Garris and J. B. D. E. Kernion (1999). Long-term effects of finasteride on prostate tissue composition. **4295**(98).
- Mocktary, M., M. Shariati and J. Amiri (2007). Effect of Tamsulosin on serum testosterone and gonadotropins concentration in adult male rats. *Journal of Rafsanjan University of Medical Sciences*, **6(1)** : 1-6.
- Nair, N., R. S. Bedwal and R. S. Mathur (2002). Effect of adrenalectomy on rat epididymidis. *Asian . J. Androl.*, **4** : 273-279 .
- Rolf, C., S. Von Eckardstein, U. Koken and E. Nieschlag (2002). Testosterone substitution of hypogonadal men prevents the age dependent increase in body mass index, body fat leptin seen in healthy ageing men: results of a cross – sectional study. *Europ. J. Endocrinole* **146** : 505-511.
- Sheikh, S., A. Ahmad, S. M. Ali, M. U. Ahmad, M. Paithankar, D. Saptarshi and V. Hemant (2015). A New Topical Formulation of Minoxidil and Finasteride Improves Hair Growth in Men with Androgenetic Alopecia, **6(1)** : 6-11.
- Umezu, M., S. Kagabu, J. Y. Jiang, S. Nimura and E. Sato (2004). Developmental hormonal profile in raw rats with congenital hypothyroidism accompanying increased testicular size and infertility in adulthood. *J. Reprod. Dev.*, **50(6)** : 675-684.