Effect of bilateral orchidectomy on thyroid gland structure of adult albino rats and the role of Nandrolone Decanoate administration

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Abstract: Introduction: Thyroid gland is one of the non-classical target organs for androgen. The role of androgen in thyroid gland structure is not yet fully understood**. Aim of the study:** This work aimed to detect the effect of bilateral orchidectomy on thyroid gland structure of adult albino rats and the role of Nandrolone Decanoate (ND) administration. **Materials & methods:** Eighteen adult albino rats were equally divided into three groups; control (I), orchidectomized (II) and ND treated orchidectomized (III) groups. Rats in groups I and orchidectomized ones (II) were sacrificed after one month. Rats of group III were treated with 1 mg nandrolone decanoate /100 g body weight as a single intramuscular injection once a week for another successive 2 months. Animals' thyroids were dissected out and processed for light and electron microscope examination. Thyroid epithelial thickness as well as serum T3&T4 were estimated and statistically analyzed. **Results:** Thyroid gland of the orchidectomized rats showed some dilated thyroid follicles lined by flattened cells. Their cavities were distended with vacuolated colloid. Other follicles were lined by cuboidal cells with deeply stained nuclei and pale foamy cytoplasm. The follicular cells had heterochromatic nuclei, few apical electron dense secretory granules, dilated and fragmented cisternae of rough endoplasmic reticulum. Parafollicular cells had electron dense heterochromatic nuclei and apparently no secretory granules. Desquamated cells were observed in some follicular cavities. Mast cells were seen in the interstitium. With ND treatment, most of the follicles restore their normal architecture. They were lined by cuboidal follicular cells with euchromatic nuclei and moderately dilated cisternae of rough endoplasmic reticulum. Few follicles were lined by flattened cells. Some parafollicular cells had euchromatic nuclei, electron dense granules and mitochondria. Others still had electron dense nuclei and few electron dense granules. Estimated and analyzed follicular epithelial thickness as well as serum T3 and T4 confirmed the results. **Conclusion:** Orchidectomy induced variable structural alterations in the follicular and parafollicuar cells of thyroid gland. This deleterious effect may be mediated by disruption of cellular organelles that subsequently affects their function. Most of these changes were improved by ND treatment. So, it is considered a good therapy for hypogonadal persons.

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1.Introduction

Androgens; male steroids are secreted mainly from the testes in addition to adrenal glands. Testosterone is the most important circulating androgen in men. It is continuously produced and released into the circulation from cholesterol through a series of enzymatic transformations in the Leydig cells. Testosterone (TT) regulates many physiological processes as erythropoiesis, prostate physiology, secondary sexual characters as well as protein metabolism of muscle and bone. Reduction in its serum concentration usually present in most aging men. This reduction has been referred as male menopause, climacteric, hypogonadism, andropause or androgen deficiency in aging men (ADAM) **[1-4]**.

Hypogonadism is usually defined as failure of the testes to produce adequate amounts of gonadal hormones; testosterone and dehydroepiandrosterone **[5]**. It can be classified as primary or secondary type. Primary one usually results from disorders of the testes. Many diseases may lead to primary hypogonadism in addition to aging. It is usually associated with some genetic syndromes as Klinefelter's syndrome or congenital disorders as anorchism and cryptorchidism. It may be also associated with a history of testicular trauma, certain surgical procedures in the groin, mumps and autoimmune orchitis. It is occasionally seen with certain medication as radiation therapy, chemotherapy or with drugs that inhibit androgen synthesis as ketoconazole. Secondary hypogonadism results from disorders of the hypothalamus and the pituitary **[6-8]**.

In adult men, the normal range of serum TT level is approximately 300-1000 ng/dL. Men with serum TT level less than 200ng/dL are definitely suffering from hypogonadism. Those with serum TT level ranges from 200 and 300 ng/dL are probably hypogonadal. Hypogonadal persons may be in need of treatment according to their clinical presentation **[3,6]**.

Thyroid is a metabolically important gland essential for regulation of growth, development and basal metabolic rate. In several studies, significant disturbance of gonadal function was observed secondary to various thyroid gland disorders; hyper and hypothyroidism. In contrary, hypogonadal men usually suffer from various symptoms related to thyroid dysfunction as osteoporosis and decreased muscle mass and strength. So, the role of androgen on thyroid gland is still a matter of debate **[6,9,10]**.

Nandrolone Decanoate (ND) is a synthetic anabolic derivative of androgen used in the treatment of certain diseases as osteoporosis, muscle wasting and growth disturbances. ND is also utilized as testosterone-replacement therapy for cancer prostate and benign prostate hyperplasia (BPH). ND is one of the most widely used anabolic steroids. Structurally, it simulates testosterone however, it is considered as a weak androgenic steroid as it is transformed into dihydronandrolone (DHN). This metabolite is weaker than the parent ND and is far less likely to cause unwanted androgenic side **[11-13]**.

So, this work was done to study the possible effect of bilateral orchidectomy on thyroid gland structure of adult albino rats and the role of Nandrolone Decanoate (ND) administration.

2.Materials and Methods

Eighteen healthy adult male albino rats (4-6months) weighing 180-200 g were used in this study. They were housed in stainless-steel cages and were maintained in room temperature at 23ºC. They were allowed water ad libitum and were fed a standard diet. They were equally divided into three groups: a control (I), an orchidectomized (II) and Nandrolone treated orchidectomized (III) one. The control group is further subdivided into two equal subgroups; rats without any surgical procedure; non-operated (Ia) and sham operated rats (Ib). Rats of the group II and III were anesthetized with 50 mg sodium pentobarbital per kg body weight intraperitoneally. Under sterile condition, the scrotum was opened and spermatic cord was ligated to remove the testes bilaterally. Then, the scrotum was sutured. In sham operated (Ib), the same procedure was performed without orchidectomy **[4,5]**.

After one month, the blood samples from the rats' tails of group I and II were collected for determination of T3, T4 and then were sacrificed. Rats of group III were treated with 1 mg Nandrolone Decanoate /100 g body weight as a single intramuscular injection in the hind limb once a week for another successive 2 months **[14]**. Then, blood samples from the rats' of this group were collected for determination of T3 and T4 and then they were sacrificed. Nandrolone Decanoate was manufactured by Chemical Industrial Development Co; CID.

At the time of scarification of each group, rats were anesthetized with 50 mg sodium pentobarbital per kg body weight intraperitoneally and then intracardiac perfusion was done by 2.5% glutaraldhyde buffered with 0.1 M phosphate buffer at pH 7.4 for partial fixation of the thyroid gland. Then it was processed for light and electron microscopic examinations. Specimens for light microscope examination were fixed in 10% neutral formol saline for 24 hours and were processed to prepare 5 µm thick paraffin sections for Haematoxylin & Eosin **[15]**.

Specimens for electron microscope examination were immediately fixed in the same perfusion fixative (2.5 % glutaraldehyde) for 2 hrs and postfixed in 1% osmium tetroxide buffered with 0.1 M phosphate buffer at pH 7.4 for 1 hr. Then, they were dehydrated in ascending grades of ethyl alcohol and embedded in epoxy resin to prepare semithin sections and ultrathin sections using a Leica ultracut (UCT) (Glienicker, Berlin, Germany). Semithin sections (1 µm thick) were stained with 1% toluidine blue for light microscope examination **[15]**. Ultrathin sections were stained with uranyl acetate and lead citrate **[16]**.They were examined with a JEOL JEM 1010 transmission electron microscope (Japan) in the Electron Microscope Research Laboratory (EMRL) of the Histology and Cell Biology Department, Faculty of Medicine, Zagazig University (Egypt).

Morphometric study:

The epithelial height of the thyroid follicles was measured using a Leica Qwin 500 (England) image analyzer computer system in the Histology and Cell Biology Department, Faculty of Medicine, Cairo University. The procedure was performed using H&E stained sections at a total magnification of X400 by measuring 10 non-overlapping fields from each specimen.

Statistical analysis:

Data for all groups were expressed as mean ± standard deviation (X±SD). The data obtained from the image analyzer were subjected to SPSS program version 15. Statistical significant difference was determined by one way analysis of variance (ANOVA). The probability values (P) $< 0.05 < 0.001$ and > 0.05 were considered significant, highly significant and non-significant respectively.

3.Results

I-Histological results:

Light microscope examination of sections in the thyroid gland of the control adult rats (Ia and Ib) showed that the thyroid parenchyma was formed of multiple variable sized follicles with interfollicular cells in between. Follicular cavities contained homogenous acidophilic colloid **(Fig. 1)**. The follicles were lined by simple cuboidal epithelium with two

types of cells; follicular and parafollicular cells. Follicular cells, the most abundant cells had central round nuclei **(Fig. 2)**. Parafollicular cells were scarce with pale stained cytoplasm. They were resting on the basement membrane and their apices didn't reach the follicular lumen. These follicles were separated by delicate vascular connective tissue stroma **(Fig. 3)**.

Electron microscope examination of the ultrathin sections of the same group showed that the follicular cells had basal euchromatic nuclei with thin peripheral rim of heterochromatin. Their cytoplasm contained well developed parallel cisternae of rough endoplasmic reticulum, mitochondria and large moderate electron dense cytoplasmic colloid droplets. Small electron dense secretory granules were observed in their apical cytoplasm. Apical lateral surface of follicular cells showed tight junctions **(Fig. 4)**. Parafollicular cells contained euchromatic nuclei, numerous small secretory granules with variable electron densities and mitochondria **(Fig. 5)**.

Light microscope examination of sections in the thyroid gland of the orchidectomized (II) adult rats showed some dilated thyroid follicles. These follicles were lined by flattened cells with flattened nuclei. Their cavities were distended with vacuolated colloid **(Fig.6)**. Other follicles were lined by cuboidal follicular cells with deeply stained nuclei and pale stained foamy cytoplasm (**Fig.7**). Parafollicular cells had corrugated nuclei and vacuolated cytoplasm **(Fig. 8)**. Mast cells were seen in the interstitium close to blood vessels **(Fig. 9)**.

Electron microscope examination of the ultrathin sections of the same group showed that many thyroid follicles lost their architectures. Their follicular cells exhibited various ultrastructural pictures. Some of them contained moderately dilated cisternae of rough endoplasmic reticulum, Golgi complex and few apical electron dense secretory granules **(Fig. 10)**. Others had euchromatic nuclei with peripheral rim of heterochromatin and markedly dilated cisternae of rough endoplasmic reticulum. Most of the follicular cells had corrugated heterochromatic nuclei and some of them were surrounded by fragmented dilated rough endoplasmic reticulum. Desquamated follicular cells were noticed within some follicular lumen **(Figs. 11&12)**. Parafollicular cells had electron dense heterochromatic nuclei and apparently no secretory granules **(Fig. 13)**. Mast cells with numerous cytoplasmic electron dense secretory granules were observed in the interstitial connective tissue between the affected follicles **(Fig. 14)**.

Light microscope examination of the sections in thyroid gland of the orchidectomized rats treated with ND (III) showed that most of the follicles almost restore their normal architecture. They were lined by low cuboidal epithelial cells with pale stained nuclei. Others were still lined by flattened cells with flattened nuclei. The follicles contained homogenous colloid with variable amount **(Figs. 15&16)**. Some parafollicular cells had pale stained nuclei and cytoplasm. Others still have deeply stained cytoplasm **(Fig. 17)**.

Electron microscope examination of the ultrathin sections of the same group revealed that many follicular cells had euchromatic nuclei with peripheral rim of heterochromatin. Their cytoplasm contained moderately dilated cisternae of rough endoplasmic reticulum, Golgi saccules and apical electron dense granules **(Fig. 18)**. Some parafollicular cells had euchromatic nuclei and their cytoplasm contained electron dense granules and mitochondria. Others had electron dense nuclei and few electron dense granules **(Fig. 19)**.

II-Morphometrical and statistical results:

Statistical analysis of the epithelial thickness of thyroid follicles showed decrease in its thickness in Orchidectomized group as compared with the control one. However, this thickness was increased in Nandrolone Decanoate treated orchidectomized group as compared with the orchidectomized one approaching control level **(Table1)**.

Statistical analysis of serum level of T3 and T4 of orchidectomized group revealed a decrease in both T3 and T4 in orchidectomized group as compared with control one. However, the both hormones were increased in Nandrolone Decanoate treated orchidectomized group as compared with the orchidectomized one approaching control level **(Tables 2&3)**.

Table (1): Comparison between epithelial thicknesses (μm) in the different studied group

	X±SD	F	*P*
Control (I)	**9.2±1.5**	**10.01**	**<0.001****
Orchidectomy (II)	**5.8±1.3**		
ND treated (III)	**7.9±1.7**		

Table (2): Comparison between T3 level (ng/ml) in the different studied group

	X±SD	F	*P*
Control(I)	**2.4±0.04**	**1285.71**	**<0.001****
Orchidectomy (II)	**1.8±0.02**		
ND treated (III)	**2.1±0.01**		

Table (3): Comparison between T4 level (ng/ml) in the different studied group

	X±SD	F	*P*
Control (I)	**137.2 ± 3.26**	**671.38**	**<0.001****
Orchidectomy (II)	**101±1.25**		
ND treated (III)	**125.7±1.76**		

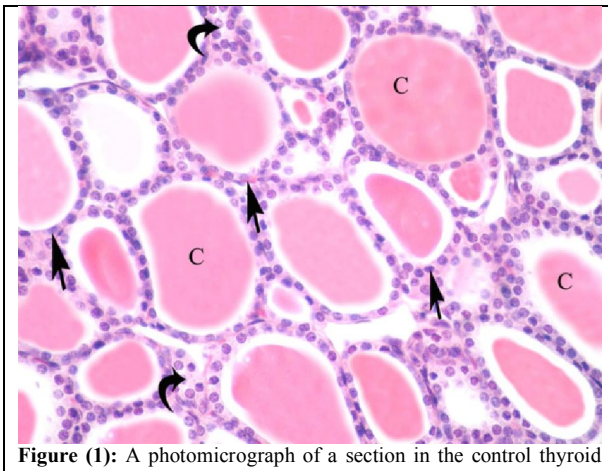

Figure (1): A photomicrograph of a section in the control thyroid gland showing multiple variable sized thyroid follicles (arrows) with interfollicular cells (curved arrows) in between. Follicular cavities contain homogenous acidophilic colloid (C). (H&E X 400)

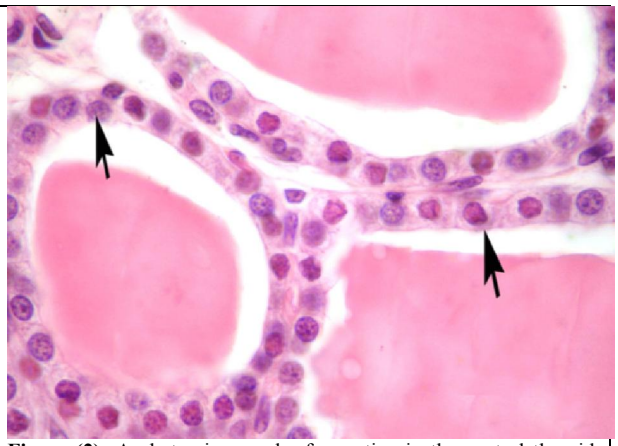

Figure (2): A photomicrograph of a section in the control thyroid gland showing the follicular cells (arrows) with central round nuclei. (H&E X 1000).

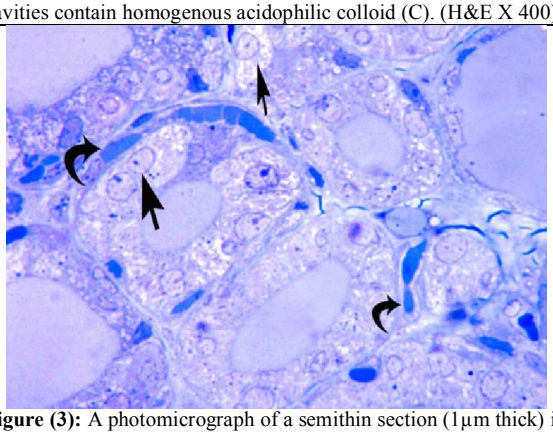

Figure (3): A photomicrograph of a semithin section (1µm thick) in the control thyroid gland showing the parafollicular cells (arrows). They are scarce with pale stained cytoplasm. They are resting on the basement membrane and their apices didn't reach the follicular lumen. The follicles are separated by delicate vascular connective tissue stroma (curved arrows). (Toluidine blue: X 1000).

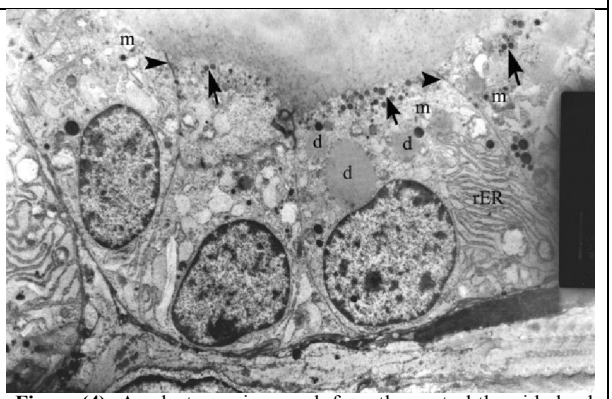

Figure (4): An electron micrograph from the control thyroid gland showing that the follicular cells have basal euchromatic nuclei with thin peripheral rim of heterochromatin. Their cytoplasm contains well developed parallel cisternae of rough endoplasmic reticulum (rER), mitochondria (m) and large moderate electron dense cytoplasmic colloid droplets (d). Small electron dense secretory granules (arrows) are observed in their apical cytoplasm. Apical lateral surfaces of follicular cells show tight junctions (arrow heads). (Mic. Mag. X4000).

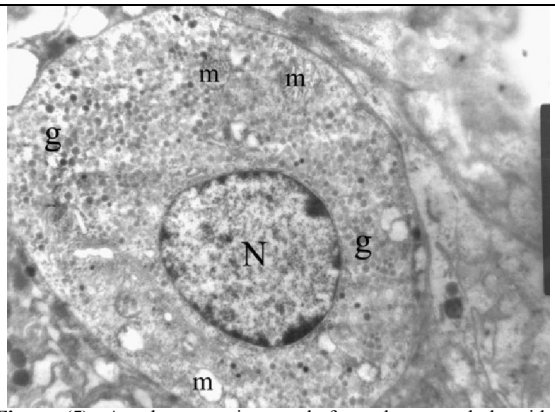

Figure (5): An electron micrograph from the control thyroid gland showing that parafollicular cell contains euchromatic nucleus (N), numerous small secretory granules (g) with variable electron densities and mitochondria (m). (Mic. Mag.X5000).

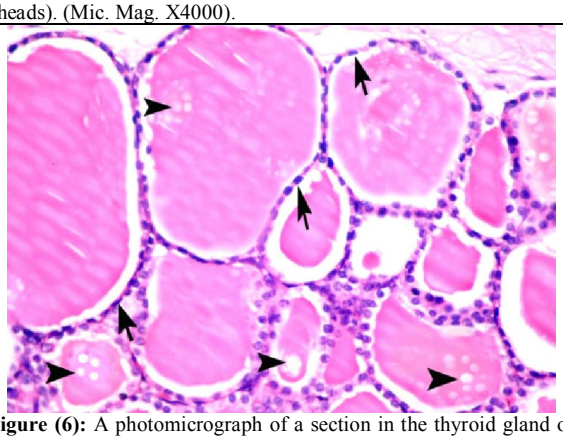

Figure (6): A photomicrograph of a section in the thyroid gland of the orchidectomized adult rats showing some dilated thyroid follicles. These follicles are lined by flattened cells (arrows) with flattened nuclei. Their cavities are distended with vacuolated colloid (arrow heads). (H&E X400).

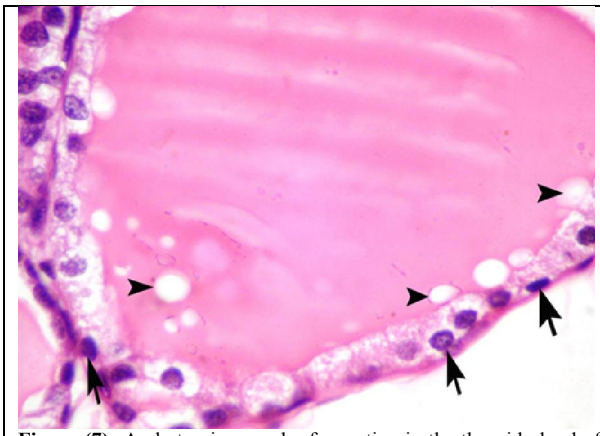

Figure (7): A photomicrograph of a section in the thyroid gland of the orchidectomized adult rats showing a thyroid follicle that lined by follicular cuboidal cells (arrows) with deeply stained nuclei and pale stained foamy cytoplasm. Vacuoles (arrow heads) are also noticed in the colloid. (H&E X1000).

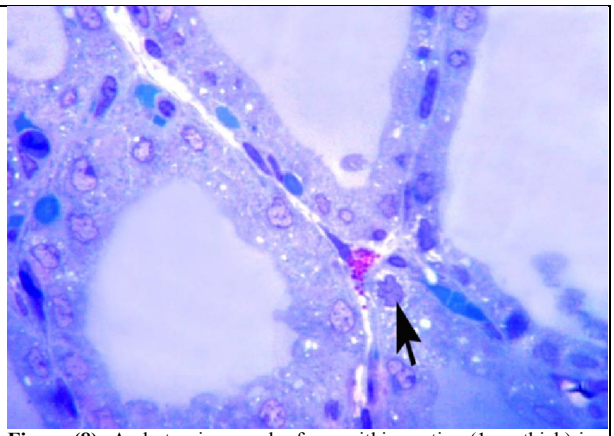

Figure (8): A photomicrograph of a semithin section (1µm thick) in the thyroid gland of the orchidectomized adult rats showing parafollicular cell (arrow) with corrugated nucleus and vacuolated cytoplasm. (Toluidine blue: X1000).

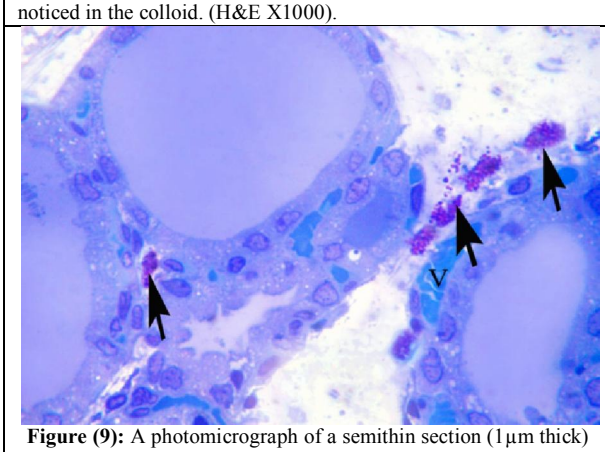

Figure (9): A photomicrograph of a semithin section (1µm thick) in the thyroid gland of the orchidectomized adult rats showing mast cells (arrows) in the interstitium close to blood vessels (v) (Toluidine blue: X1000).

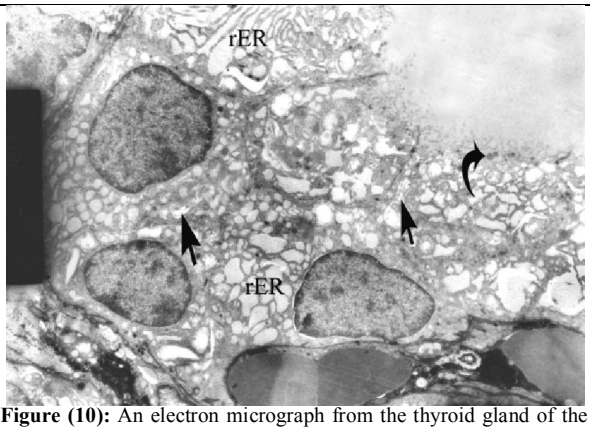

Figure (10): An electron micrograph from the thyroid gland of the orchidectomized rats showing that the follicular cells contain moderately dilated cisternae of rough endoplasmic reticulum (rER), Golgi complex (arrows) and few apical electron dense secretory granules (curved arrow). **(**Mic. Mag.X4000).

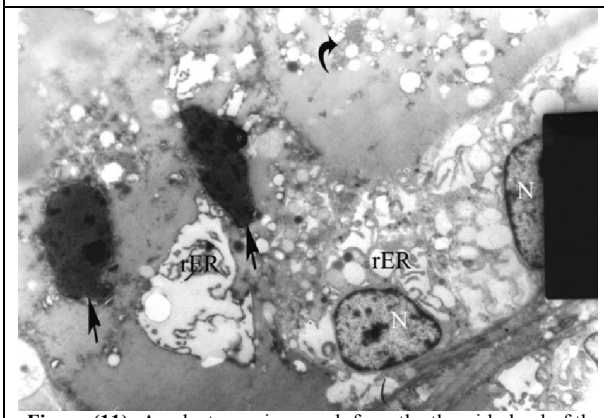

Figure (11): An electron micrograph from the thyroid gland of the orchidectomized rats showing that some follicular cells have euchromatic nuclei (N) with peripheral rim of heterochromatin and markedly dilated cisternae of rough endoplasmic reticulum (rER). Corrugated heterochromatic follicular cells nuclei (arrows) and desquamated follicular cells (curved arrow) within follicular lumen are also noticed. (Mic. Mag.X2500).

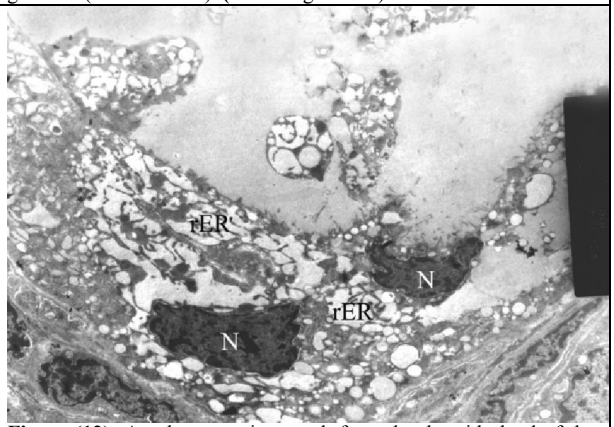

Figure (12): An electron micrograph from the thyroid gland of the orchidectomized rats showing corrugated heterochromatic nuclei (N) and fragmented dilated rough endoplasmic reticulum (rER) of follicular cells. (Mic. Mag.X4000).

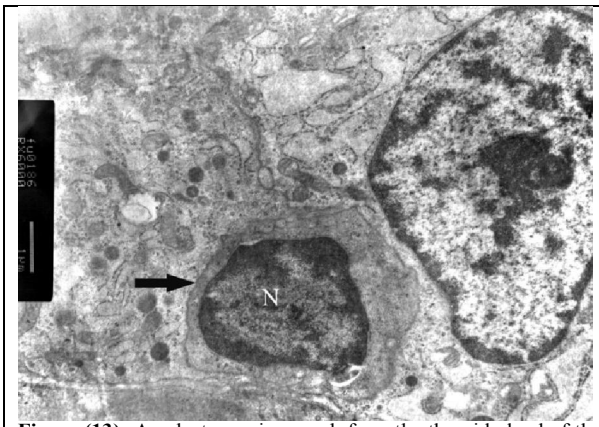

Figure (13): An electron micrograph from the thyroid gland of the orchidectomized rats showing a parafollicular cell (arrow) with electron dense heterochromatic nucleus (N) and apparently no secretory granules. (Mic. Mag.X5000).

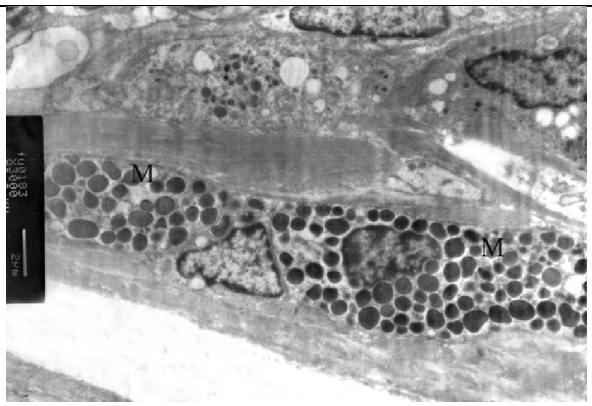

Figure (14): An electron micrograph from the thyroid gland of the orchidectomized rats showing mast cells (M) with numerous cytoplasmic electron dense secretory granules within the interstitial connective tissue. (Mic. Mag.X3000).

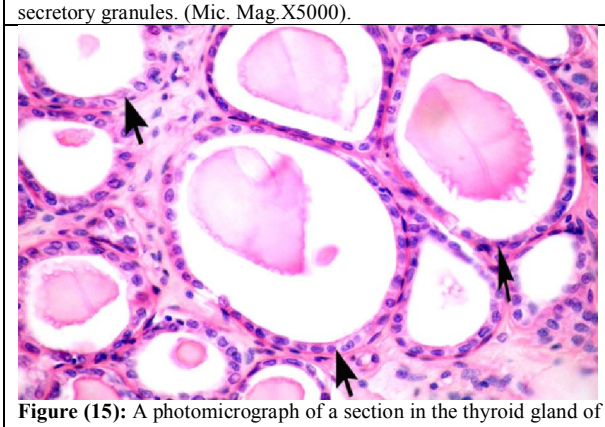

Figure (15): A photomicrograph of a section in the thyroid gland of the orchidectomized rats treated with ND showing that most of the thyroid follicles (arrows) almost restore their normal architecture. (H&E X 400).

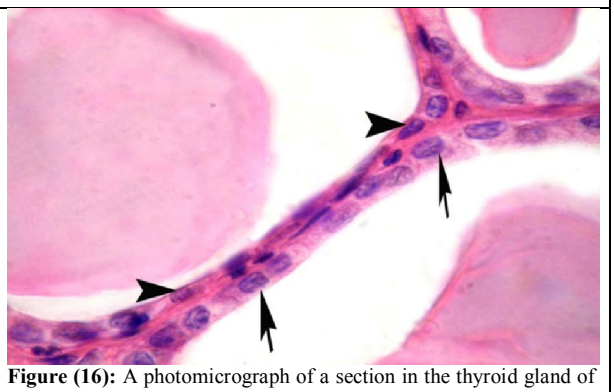

Figure (16): A photomicrograph of a section in the thyroid gland of the orchidectomized rats treated with ND showing that some follicles are lined by low cuboidal cells (arrows) with pale stained nuclei. Others are still lined by flattened cells (arrow heads) with flattened nuclei. The follicles contain homogenous colloid with variable amount. (H&E X1000).

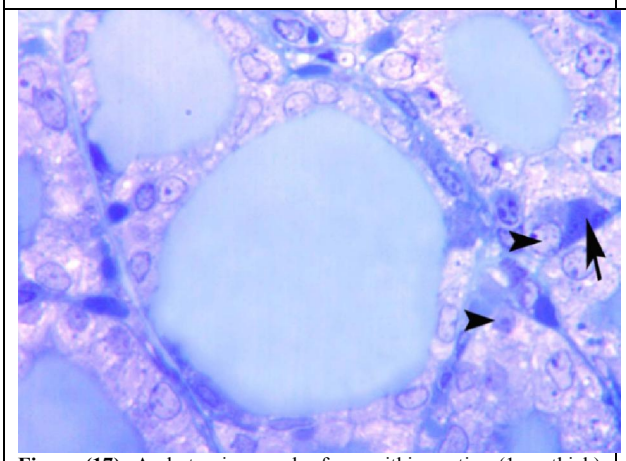

Figure (17): A photomicrograph of a semithin section (1µm thick) in the thyroid gland of the orchidectomized rats treated with ND showing some parafollicular cells (arrow heads) have pale stained nuclei and cytoplasm. Other one (arrow) still has deeply stained cytoplasm. (Toluidine blue: X1000).

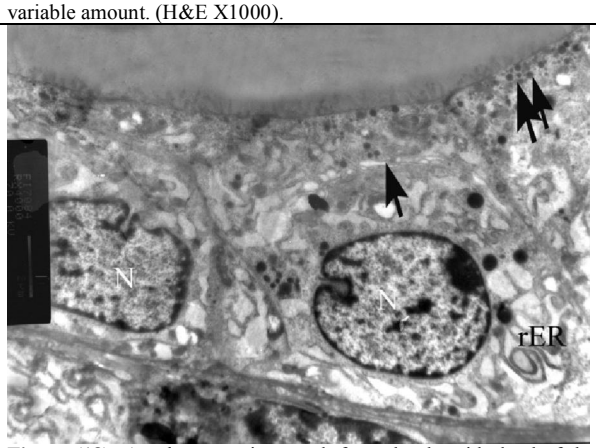

Figure (18): An electron micrograph from the thyroid gland of the orchidectomized rats treated with ND showing that the follicular cells have euchromatic nuclei (N) with peripheral rim of heterochromatin. Their cytoplasm contains moderately dilated cisternae of rough endoplasmic reticulum (rER), Golgi saccules (arrow) and apical electron dense granules (double arrows). (Mic. Mag.X4000).

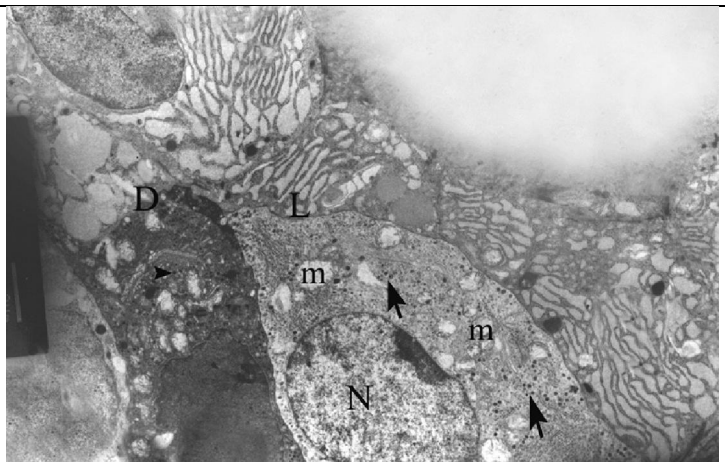

Figure (19): An electron micrograph from the thyroid gland of the orchidectomized rats treated with ND showing a parafollicular cell (L) contains euchromatic nucleus (N), small electron dense granules (arrows) and mitochondria (m). Other parafollicular cell (D) has electron dense nucleus and few electron dense granules (arrow head). (Mic. Mag.X5000).

4.Discussion

Endocrine system is the second key regulator of various body system functions after nervous system. Researchers assumed that the classic targets for androgen were male reproductive organs, bone, vascular system, gastrointestinal tract, immune system and skin. Thyroid gland is one of the non-classical target organs for sex steroids. In certain mammals, seasonal variations in plasma thyroxin concentrations were closely related to the seasonal variations in sex steroid concentrations. This pattern suggests that the thyroid axis could have a role in regulating gonadal activity and vice versa **[10,17,18]**.

In this work, statistical analysis of T3 and T4 showed significant decrease in orchidectomized group as compared with the control group. However, T3&T4 were increased in ND treated orchidectomized group as compared with the orchidectomized one approaching control level. It was claimed **[19]** that thyroid gland is one of the target organs of testosterone. Physiological amounts of testosterone stimulate thyrotropin secretion and induce growth of thyroid gland. It was reported **[20]** that gonadal steroids affect thyroid gland not only in a direct manner through androgen receptors on thyroid follicular cells but also indirectly through the hypothalamic–pituitary axis.

In this study, thyroid gland of the orchidectomized rats (II) revealed some dilated thyroid follicles. They were lined by flattened cells with flattened nuclei. These results were confirmed by the statistical analysis in which the follicular epithelial thickness decreased as compared with the control one. It was reported **[21]** that decreased activity of thyroid gland can be diagnosed by excessive aggregation of intrafollicular colloid as well as low follicular epithelium, which was extremely flattened in some areas of the gland. Some scientists attributed **[22]** the increase of follicles diameter to excess accumulation of colloid within follicular cavities. Others **[23,24]** documented that flat follicular cells were diagnosed as metabolically inactive or hypoactive cells and they are usually lined the follicles which distended by excess colloid.

Ultrastructural examination of the same group revealed many thyroid follicles lost their architectures. It was found **[25]** that the follicular organization is very important to the endocrine activity of thyroid gland. Any disturbances in follicular structure may affect synthesis of thyroid hormones.

Also, the orchidectomized thyroid gland examination showed that other follicles were lined by cuboidal follicular cells with pale stained foamy cytoplasm. Ultrastructurally, follicular cells contained moderately and markedly dilated cisternae of rough endoplasmic reticulum, Golgi complex and few apical electron dense secretory granules. Vacuolated or foamy cytoplasm has been attributed **[24,26]** to the presence of dilated cisternae of rough endoplasmic reticulum (rER). These markedly dilated cisternae of rER in combination with other cellular changes are an evidence of disruption to protein synthesis. The dilatation could be due to retention of aberrant protein within cisternae that might be a form of rER storage disease. This protein could not be processed, folded and transported to appropriate sites. Some scientists **[5]** demonstrated marked decrease in the number of major cytoplasmic organelles after orchidectomy due to decrease the stimulatory effect of TSH.

In orchidectomized rats, some follicular cells nuclei appeared deeply stained. Ultrastructurally, most of the follicular cells had corrugated heterochromatic nuclei. It was claimed **[24,26]** that the dilated rER compress the nucleus leading to the appearance of nuclear indentation and irregularity. Additionally, disruption in protein production within the dilated

cisternae might prevent synthesis of apoptosis inhibitors as Bcl-2 and/or loss of essential proteins involved in cellular homeostasis leading to cellular degeneration. It was found **[27]** that hypothyroidism led to excessive production of reactive oxygen species; ROS resulting in oxidative stress and subsequently lipid peroxidation and cell death.

In the same group, thyroid follicular cavities were distended with vacuolated colloid. It was reported **[21,28]** that prominent aggregation of colloid in follicles' cavities means an inactive thyroid state. Inhibition of pinocytosis of the colloid causes more accumulation in the follicular lumen, thereby increasing the follicular diameter and diminishing the height of follicular epithelium**.** So, vacuolated colloid might be due to defect in pinocytosis of thyroglobulin follicular cell.

Some follicular lumina of orchidectomy group showed desquamated follicular cells. Certain researchers **[29]** reported that the degenerated follicular epithelial cells are susceptible to slough off. Furthermore **[30,31]** not only degenerative follicular cells were detected but also detached apical parts of the cytoplasm of other follicular cells. These changes could be attributed to cellular distension with accumulated colloid which resulted in cellular disruption.

In orchidectomized rats, parafollicular cells had corrugated nuclei and vacuolated cytoplasm. Ultrastructurally, these cells had electron dense heterochromatic nuclei and apparently no secretory granules. It was known **[32,33]** that calcitonin is responsible for lowering the serum calcium concentration by suppressing osteoclast activity. Synthesis of calcitonin and its release were decreased in conditions of androgen deficiency. Until now the relationship between androgen and calcitonin is not fully understood although androgen receptors were detected on parafollicular cells. Some authors **[34,35]** showed few parafollicular cells with few dark granules. Testosterone hormone not only alters the parafollicular cell structure but also reduced the synthesis and release of calcitonin. These changes were accompanied by marked reduction of trabecular bone density. So, osteoporosis is the main complaint during aging and in cases suffering from androgen deficiency.

In the same group, mast cells with numerous cytoplasmic electron dense secretory granules were seen in the interstitium close to blood vessels. It had been stated **[36,37]** that mast cells are significantly affected by sex steroids. Androgen hormone has an inhibitory effect on mast cells. Castration results in significant increase in mast cell numbers. It was reported **[24]** that mast cells participate in the process of thyroid hormone secretion. TSH stimulates the release of serotonin from mast cells and subsequently activates follicular cells to extend pseudopodia for engulfment of thyroglobulin from the follicular lumen.

In this study, examination of the thyroid gland of the ND treated orchidectomized rats (III) revealed that most of the follicles almost restore their normal architecture. They were lined by low cuboidal epithelial cells with pale stained nuclei. Others were still lined by flattened cells with flattened nuclei. The follicles contained homogenous colloid with variable amount. Ultrastructurally, the follicular cells had euchromatic nuclei with peripheral rim of heterochromatin. Their cytoplasm contained moderately dilated cisternae of rough endoplasmic reticulum, Golgi saccules and apical electron dense granules. It was established **[19]** that androgen modulates thyroid function not only by its direct influence on thyroid cell proliferation but also through indirect effect upon the hypothalamic pituitary axis. Androgen receptors in thyroid gland are usually under the regulation of sex steroids that might have an essential role not only in thyroid pathogenesis, but also in the normal development and growth of the thyroid. Some researchers added **[14,19]** that androgen increase TSH synthesis, secretion and also sensitize thyrocytes for TSH. Furthermore, TSH inhibits the synthesis of insulin growth factor (IGF)-binding protein so as to increase the availability of IGF to promote growth of thyroid epithelium. Therefore, the interplay between sex steroids, TSH and growth factors has an important role in regulating thyrocyte proliferation. Other authors mentioned **[5]** that the stimulating effect of TSH on follicular cell function is modulated by the action of various molecules as growth factors, neuropeptides and some peptides derived from parafollicular cells.

Some parafollicular cells had pale stained nuclei. Ultrastructurally, they had euchromatic nuclei and their cytoplasm contained electron dense granules and mitochondria. Others had electron dense nuclei and few electron dense granules. It was reported **[38]** that besides the presence of distorted parafollicular cells, active parafollicular cells were detected due to long-lasting effects of steroid hormones administration. Moreover, it was added **[39]** that parafollicular cell activity subjected to more complex regulatory factors as thyroid transcription factor 1 (TTF-1), which is typically expressed by follicular cells. This factor is calcium-modulated and involved in calcium homeostasis. So, the new evidence of interdependence between the two endocrine cell populations of the thyroid gland is established. Some scientists **[33,34]** detected androgen receptors in most surgically resected thyroid tumor as C cell hyperplasia. Through these receptors steroids have a regulatory effect on thyroid parafollicular cells function.

Conclusion:

From the results of this work, we concluded that orchidectomy induced variable structural alterations in follicular and parafollicuar cells of thyroid gland. This deleterious effect may be mediated by disruption of cellular organelles that subsequently affects their function. Most of these changes were improved by Nandrolone decanoate treatment. So, it is considered a good therapy for hypogonadal persons.

Recommendations:

So, susceptible persons for androgen deficiency; especially senile men must do periodic assay of thyroid hormones.

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