

Study the effect of partial thyroidectomy on reproductive activity on female rabbit and protective role of Dehydroepiandrosterone hormone

Batool A.H*¹ Abdul Emmer O.I*¹ Ayed H.H*²

¹ Biology department/ Collage of Education for pure sciences/ University of Karbala /Iraq

² physiology department/ Veterinary Meedicine/ University of Karbala/Iraq

Abstract

This study designed to investigate the role of (DHEA) hormone oral administration on serum level of DHEA-Sulfat, FSH, E2, and LH and ovary tissue after partial Thyroidectomy.

The experiment includes twenty-five adult female rabbit weighting 1500-2000 gm. were divided into five groups (5/group) as follows. (G1) Thyroidectomy only, (G2) Thyroidectomy and administration orally 2mg/kg DHEA hormone (G3) control group (G4) only administration orally 2mg/kg DHEA hormone (G5) Shame group. Fasting blood samples were collected after 4 week for to estimated of Dehydroepiandrosteron-sulfate (DHEA-S) and Follicle-stimulation hormone (FSH) and Estrogen hormone (E2) and luteinizing hormone (LH) and each group were sacrificed for histological study of Thyroid gland .the result showed significant increase of serum DHEA-S,FSH,E2,LH in DHEA groups as compared with control group and histological section revealed significant change in ovary.

INTRODUCTION

Reproductive process is a vital process for survival, requiring a balance at the molecular, hormonal and cellular level, from the ovarian follicle maturation of the ovary to implantation of the embryo in the uterus and at all stages, endocrine involvement very important including levels of thyroid hormones. (1) Thyroid hormones affect sex hormones (reproductive hormones) in general, such as Estrogen and Progesterone, in order to maintain the normal function of the ovaries and reach the egg to maturity, untreated or Undiagnosed thyroid diseases can be a direct cause of infertility as well as fertility. This is why thyroid function is normally necessary for fertility and to maintain a healthy pregnancy in the early days of pregnancy (2). Thyroid diseases are the most common endocrine disease in females at reproductive age.(3) Many studies suggest that hypothyroidism or hypothyroidism is a sign of weakness of the adrenal gland and is therefore a sign of hypothyroidism, particularly DHEA. This is common in people with thyroid disorders (4) **Dehydroepiandrosterone** hormone, or **DHEA hormone**, produced essential in the adrenal cortex (especially in zone reticular is), the gonads, and the brain(5), where it functions as a metabolic intermediate in the biosynthesis of the androgen and estrogen steroids. This hormone is precursor to the process of bio-synthesis of androgens, estrogen sex steroids (6) . To investigate the harmful effect of hypothyroidism induced by partial thyroidectomy on some reproductive hormone levels and evaluates effect of DHEA hormone upon it.

MATERIALS AND METHODS

Table (1) represent the Chemical Material according to Origen and company.

Company	Origin	Material
BDH	England	Xylene
Merck	Germany	Paraffin Wax
BDH	England	Hemotoxylene & Eosin
Holden Medical	Netherlands	Ketamine
Rembon	Ireland	Xylazine
Merck	Germany	Formalin 10%
Cal biotech	America	DHEA-S hormone Kit
Elabscience	china	Estrogen Kit
Cal biotech	America	LH hormone Kit
Calbiotech	America	FSH hormone Kit
BDH	England	Ethanol
BDH	England	Chloroform
BDH	England	Canada balsam
AMS	America	DHEA hormone tablet

1- Animals and experimental design:

Twenty –five adult female rabbit with initial mean body weight of 1.5-2 kg and aged 8 months were used. The study was conducted at the animal house of pharmacology collage during summer ,the animal were randomly designed to 5 group (G1,G2,G3,G4,G5)

Group one (G1) five female rabbit were partial thyroidectomy only

Group two (G2) five female rabbit were partial thyroidectomy and oral administration 2 mg/kg of dhea hormone.

Group three (G3) five female rabbit Water and regular food were given as a positive control group.

Group four (G4) five female rabbit were Intake only orally with 2 mg / kg body weight DHEA hormone

Group five (G5) five female rabbit is shame group.(Only a surgical incision of the skin was promised as a negative control group).

Dehydroepiandrosterone (DHEA), produced in America by AMS, was administered by a stomach tube (2 mg / kg) for 4 weeks. The solution was obtained by dissolving one tablet of (50 mg) in 25 ML Distilled water .

Procedure of Partial Thyroidectomy surgical according to the (7).

Hormone : hormonal test according to the Enzyme-Linked Immunosorbent Assay by use ELISA Reader system

Histological section : histological preparations according to method which described in (8)

The statistical analysis of the study of hormonal criteria was carried out using the statistical program (9) to study the effect of aggregates in the studied criteria using the Chi-Square box. The differences between the mean were compared with the least significant difference (LSD).Result

Effect of DHEA hormone and Thyroidectomy on mean of DHEA-S ,FSH,E2,LH concentration is shown in table (2) this shows a significant increase (p<0.01) in DHEA-S and Estradiol E2 in (G2,G4) compare with positive control (G3) and shame group (G5) and significant decrease in (G1) compare to other group In the same table shows significant increase (p<0.01) in FSH and LH hormone in (G2,G4) group compare with other group .and decrease him in (G1) group.

RESULTS:

Table (2) effect of Thyroidectomy and Dhea hormone on concentration level of DHEA-S, FSH, E2, LH Mmol/dl in serum female rabbit

LH	E2	FSH	DHEA-S	Group
0.63 ±0.009 B	103.24 ± 0.96 C	0.65 ±0.02 BC	3.17 ±0.06 C	G1 Thyroidectomyonly
0.73 ±0.05 A	120.75 ±0.54 A	1.58 ± 0. 04 A	5.27 0.22,± B	G2 Thyroidectomy and dhea 2mg/kg
0.62 ±0.006 B	111.46 ±2.06 B	0.61 ± 0.02 C	3.51 ±0.09 C	G3 Positive control
0.73 ±0.007 A	125.71 ±3.01 A	0.72 ±0.03 B	7.50 ±0.23 A	G4 Dhea only 2mg/kg
0.63 0.006 B	113.40 1.11 B	0.63 0.02 BC	3.24 0.15 C	G5 Sheem group
0.0788	5.2465	0.0977	0.502	LSD

Mean + SE (n=5 rabbit/group)

Capital letters indicate a significant (p<0.01) difference groups

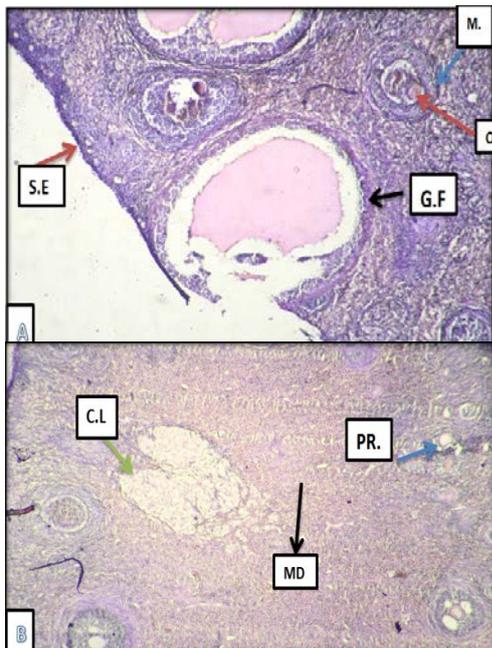


Figure (1) histological section in ovary of female rabbit in control group (positive and negative control) (A) showed the superficial epithelium SE and Graafian follicle (G.F), and mature follicle M (B) showed the corpus luteum C.L and medulla MD and primordial follicles (PR) (H&E 10X)

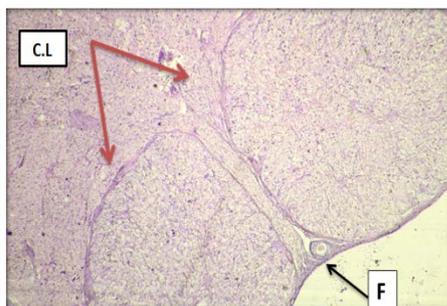


Figure (2) Histological change in ovary of female rabbit in thyroidectomy group; Showed decrease number of ovarian follicles (H&E stain, 40X).

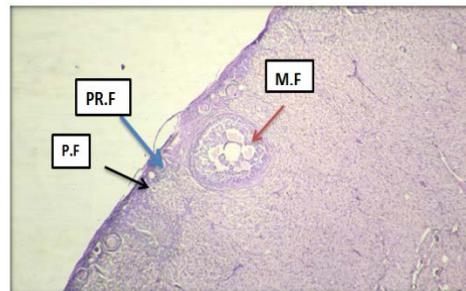


Figure (3) Histological change in ovary of female rabbit in thyroidectomy and treated with 2 mg/kg of DHEA hormone showed normal ovary tissue with primary PR.F and primordial P.F and mature M.f follicles (H&E stain,10X).

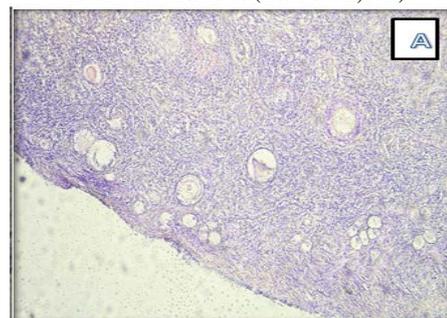


Figure (4) Histological change in ovary of female rabbit in treated with DHEA only group; Showed increase number of ovarian follicles (H&E 10X) in (A) and Mature ovarian follicle (H&E stain, 40X).in (B).

DISCUSSION

The result shows that, serum level of DHEA-S and Estrogen E2 and Follicles stimulating hormone FSH increased significantly after treated with DHEA hormone. The secretion of this steroid hormone stimulates by Adrenocorticotrophic hormone, ACTH, which is produced from the anterior pituitary gland under the control of the hypothalamus. This hormone directly affects other endocrine glands such as adrenal glands, ovaries and testes. (10). thyroid hormone level in serum regulates Level of DHEA Hormone. The precursors of Steroid hormones synthesized in the adrenal glands is cholesterol. The results showed a significant increase in the concentration of DHEA-S after treatment with 2 mg / kg of the hormone. and a significant decrease in the concentration of DHEA-S in the surgical group. The decrease in thyroid hormones, where thyroid hormones affect the levels of DHEA in the serum through its effect on the enzyme cytochrome P450, which is responsible for the completion of the conversion of cholesterol to the hormone pregnelone, which is an important step for the manufacture of all steroid hormones including DHEA, where the researchers (11) showed a significant decrease in Nash I This enzyme in the totals of rats removed, including thyroid Thyroidectomy and that the process of surgical removal has led to a decline in the process of fully Steroidogenesis in the adrenal gland.

Hypothyroidism may lead to failure of sex steroids by disrupting the functioning of hypothalamus-pituitary ovarian axis. Thus, a clinical picture in close relationship with menstrual irregularity, infertility, miscarriage and complications of unwanted pregnancy may occur(12)

(13) As it's known, cells such as oocytes, cumulus cells and granulosa cells contain thyroid hormone receptors. In hypothyroidism, both the local effect of thyroid hormones on these receptors and prevention of release of pulsatile GnRH from hypothalamus lead to failure of healthy ovulation and prevent formation of high quality oocytes (14) corpus luteum insufficiency due to disruption of LH release and hyperprolactinemia due to increased TRH release may also increase negative influences over normal menstrual cycle.(15) strong influence of thyroid hormones in the regulation of ovarian and endometrial function (16). It is therefore important that thyroid gland should function normally to maintain healthy reproduction.(17) The increase or decrease in the concentration of thyroid hormones leads to impaired reproductive functions.(18) One of the dangers of hypothyroidism is the damage to the female reproductive system, which is considered the most important cause of infertility in females because it leads to disruption of ovarian functions (19) One of the causes of infertility is the decrease in the number of ovarian follicles in females during childbearing age, which leads to the occurrence called premature ovarian failure (20).

Although, the last twenty years has given more attention to the benefits of DHEA for aging in both males and females, especially on skin and bones because the adrenal production of DHEA and its metabolite (DHEA_S) has been reported to decline linearly with age (21). In this study showed the increase number of ovarian follicles after treated with 2 mg/kg of DHEA .because the DHEA hormone may stimulate the ovarian follicular growth and differentiation (22).

REFERENCE

- 1- Nilay, K.; Akpak, Y.K.(2015). Thyroid disorders and fertility.Int J Res Med Sci. June, 3 (6) : 1299-1304
- 2- Poppe, K.; Velkeniers, B.; Glinoeer, D.(2008). The role of thyroid autoimmunity in fertility and pregnancy.Nat Clin Pract Endocrinol Metab. ;4:394-405.
- 3- Davis, L. B.; Lathi, R.B.; Dahan, M.H.(2007). The effect of infertility medication on thyroid function in hypothyroid women who conceive. Thyroid ;17:773-7.
- 4- Johnson, E.O; Calogero, A.E; Konstandi, M.; Kamilaris, T.C, La Vignera, S.,Chrousos, GP (2012).Effects of short- and long-duration
- 5- William, F.; Ganong, M.D.(2005). 'Review of Medical Physiology', 22nd Ed, McGraw Hill, , p. 362.
- 6- Thomas, S. (1996). *Concise Encyclopedia Biology*. Walter de Gruyter. p. 49.
- 7- Ben saad, M.M. and Maurel, D.L.(2004).Reciprocal interaction between seasonal testis and thyroid activity in zembra island.
- 8- Presnell, J.K. and Schreiberman, M.P. (1997).Humason's animal tissue techniques, 5thedn., John Hopkins Univ. Press, Balfimore, 546.
- 9- . SAS .2012 Statistical Analysis System ,Users Guide .Statistical Version 9.1 th ed SAS.Inst.Inc.Cary.N.C.USA.
- 10- Guyton, A C. and HALL, J. E.(2010).Textbook of medical physiology/11th Ed.
- 11- Benelli, C.(1982). Michel O, Michel R. Effect of thyroidectomy on pregnenolone and progesterone biosynthesis in rat adrenal cortex. J Steroid Biochem;16:749 54.2.
- 12- Gerhard, I; Becker ,T.; Eggert-Kruse, W.; Klinga, K.; Runnebaum, B.(1991). Thyroid and ovarian function infertile women. Hum Reprod 1991;6:338-45.
- 13- Poppe, K.; Glinoeer, D.(2003). Thyroid autoimmunity and hypothyroidism before and during pregnancy. HumReprod Update 2003;9:149-61.
- 14- Poppe, K. Glinoeer, D. ; Steirteghem, A.V.; Toumaye, H. ; Devroey, P. ; Schiettecatte, J. (2002). Thyroid dysfunction and autoimmunity in infertile women.Thyroid;12:997- 1001.
- 15- Negro, R.; Formoso, G.;Mangieri, T.; Pezzarossa, A.; Dazzi, D.; Hassan, H.(2006). Levothyroxine treatment in euthyroid pregnant women with autoimmune thyroid disease: effects on obstetrical complications.J Clin Endocrinol Metab ;91:2587-91.
- 16- Krassas, G.E; Poppe, K.; Glinoeer, D.(2010). Thyroid function and humanreproductive health. Endocr Rev; 31: 702-55.
- 17- Muderris, I.I.; Boztosun, A.; Oner, G.; Bayram, F.(2011). Effect of thyroid hormone replacement therapy on ovarian volume and androgen hormones in patients with untreated primary hypothyroidism. Ann Saudi Med; 31: 145-51.
- 18- Kang, J.H.; Kueck, A.S.; Stevens, R.; Curhan, G.; De Vivo, I.(2013). A large cohort study of hypothyroidism and hyperthyroidism in relation to gynecologic cancers. Obstet Gynecol Int: 743721.
- 19- Krassas, G.E.(2000). Thyroid disease and female reproduction. Fertil Steril 2000; 74: 1063-70.
- 20- Balla, A.(2003). Danilovich N, Yang Y, Sairam MR. Dynamics of ovarian development in the FORKO immature mouse: structural and functional implications for ovarian reserve. Biol Reprod; 69: 1281-93.
- 21- Parker, L.N. and Odell ,W.D.(1980). Control of adrenal androgen secretion Endocr Rev;4:392-410.
- 22- Hillier , S.G.; Whitelaw, P.F.; and Smyth, C.D. (1994). Follicular estrogen synthesis: the 2-cell two-gonadotropin model revisited . Mol Cell Endocrinol ;100:51-4.