THE EFFECT OF HCG, 17 B-ESTRADIOL AND HYDROCORTISONE ON BLOOD CHOLESTEROL, HDL,LDL TG ,TOTAL PROTEIN, GLUCOSE ,PH AND BODY WEIGHT IN FEMALE RABBITS.

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ABSTRACT

The aim of this study is to investigate the effect of human chorionic gonadotophic (HCG), 17β-estradiol and hydrocortisone on some blood parameters and body weight in female rabbits.

Twenty local rabbits were subdivided randomly and equally into four groups . The1st group used as control . The 2nd group was injected daily (30 IU /kg B.W) HCG intramuscularly . The 3rd group was injected subcutaneously daily with 0.1 mg /kg B.W s/c 17 β -estradiol and the 4th group was injected daily 0.1 mg /kg B.W intramuscularly hydrocortisone. After five weeks blood serum was tested for total Cholesterol, HDL(height density lipo-protein), LDL (low density lipo-protein), TG (triglycerides), total protein and pH. Body weight was taken dialy from first day .

The results showed that the administration of HCG raised high significantly LDL(p<0.01) while total Cholesterol , TG, glucose failed to reach the significant level, .However HCG significantly lowered HDL (p<0.01) Total protein and body weight were decreased with no change in blood pH compared with the control group. The treatment with 17 β -estradiol decreased the level of cholesterol , , TG and lowered significantly HDL(p<0.05 and increased significantly LDL (p<0.05) . Glucose and total protein were increased with no significant effect on body weight and pH compared with the control group. While hydrocortisone increased ,HDL ,TG ,LDL and glucose and decreased cholesterol and total protein level moreover body weight and pH did n't effected.

INTRODUCTION

Hormones are chemical compounds which have biological activities and play an important role in metabolic process (1). It had been shown that 17β -estradiol decreased cholesterol and lower Triglycerides (TG) (2). (3) showed that after oral administration of higher dose of estrogen total cholesterol decreased significantly. Another study showed that 17β - estradiol lowered glucose because of raising insulin level(4). However anther study found that 17β - Estradiol inhibited the insulin and increased glucose(5). (6) Investigated that contraceptive which contain estradiol decreased HDL and LDL. While on other Investigation found that estradiol increased HDL and TG

significantly decreased (7) . (8) found that 17β -estradiol increased HDL and cholesterol level and decreased LDL and total protein . About the effect of estradiol on body weight a study pointed that estradiol increased the body weight (9).

(10) found that HCG enhanced HDL-cholesterol transport. Another study found that HCG increased blood glucose (18.78%) (11). (12) found HCG increased cholesterol but estradiol decreased it level and gave evidence that estradiol and hydrocortisone have similar effect on serum glucose, HDL, LDL and all of them increased serum glucose ,LDL, HDL and total protein , but show different effect on triglycerides.

A study found that pregnant gilts treated with hydrocortisone caused an increased in total blood serum cholesterol, triglycerides and total protein(13).

Thus the main purpose of the study is to investigate the different effects of HCG, estradiol and hydrocortisone on some blood parameters as comparative study between them to ovoid the risk of blood parameters alteration.

MATERIAL AND METHODS

Twenty female rabbits from local markets weighted 500-700 gram were divided equally and randomly into four groups , 1^{st} group used as control 2^{nd} group were injected daily HCG (30 iu /kg B.W) i/m. (MC-Chypre company), the 3^{rd} group were injected daily with 0.1 mg /kg B.W s/c β -17estradiol (Syva .lab company) and the 4^{th} group were injected daily 0.1 mg /kg B.W i/m hydrocortisone(Alvertran Werfft AG-Viena company)

Animal weighed daily till the end of treatment, after five weeks animals were anaesthetized by inhalation of Diethyl ether and rapidly dissected and blood sample were collected from the abdominal vein(vena cava) in glass centrifuge tubes then centrifuged for 15 min at 1000 g ,Sera were separated and tested for total Cholesterol, HDL,LDL,TG total protein and glucose concentration were determined automatically using auto analyzer,(Randox kits) SLIM 260 - Ascreen Master produced by SEAC, while the pH of blood serum measured by pH strips.

Data were represented as means \pm S .D , and percentage differences; the statistical analysis by Student- t -test (14).

RESULTS

The administration of HCG to female rabbits for 5 weeks raised the level of blood serum Cholesterol (49.25%), TG(120.75%)(table1) and glucose(18.78%),table(2),and high significant increased in LDL (92.5%)(p<0.01) table(1), and significant decreased in the level of HDL(-35.48%) (p<0.01) table (1), and non significant decreased in total protein (-18.90%) in serum. Body weight were decreased (-14.88) but blood pH was not effected .Table (3) .

The study show that 17 β -estradiol decreased the level of cholesterol (-47.53%), TG(-43.34) (table1) and caused significant decreased in HDL(-33.33%)(p < 0.05) and increased the level of LDL(22.24%) (p < 0.05) table(1). glucose(17.58%) and total protein (20.13%)(table2) with no significant effects on body weight and pH. Table (3).

Hydrocortisone Caused increased in the level of LDL (58.35%) ,TG(12.35) (table1) and glucose (26.34%)(table2) and decreased the cholesterol (-14.98%)(table1) and Total protein(-12.3%) with no effect on blood pH and body weight. Table(3).

Table (1) :The effects of HCG, $17~\beta\text{-estradiol},$ and hydrocortisone on cholesterol ,LDL HDL and TG. n=5

	Control	HCG		17 β- estradiol		Hydrocortisone	
Mg/dl	Mean SD	Mean <u>+</u> SD	Diff %	Mean <u>+</u> SD	Diff %	Mean <u>+</u> SD	Diff %
Cholesterol	93.4 <u>+</u> 17.08	98 <u>+</u> 3.742	49.25	49 <u>+</u> 8.524	- 47.53	79.33 <u>+</u> 33.068	- 14.98
LDL	20 <u>+</u> 15.03	38.5 <u>+</u> 19.014	** 92.5	27.8 <u>+</u> 5.803	*22.24	31.67 <u>+</u> 17.793	58.35
HDL	31 <u>+</u> 6.18	20 <u>+</u> 8.246	**- 35.48	20.676 <u>+</u> 7.586	*- 33.33	24 <u>+</u> 12.96	- 22.58
Triglyceride	$100 \\ \pm 20.12$	120.75 <u>+</u> 19.149	20.75	56.667 <u>+</u> 44.78	- 43.34	121.33 <u>+</u> 17.931	12.3

%Difference = Percentage difference of control

SD= standard deviation

** P< 0.01

	Control	HCG		17 β- estradiol		Hydrocortisone	
	Mean <u>+</u> SD	Mean <u>+</u> SD	Diff %	Mean <u>+</u> SD	Diff %	Mean <u>+</u> SD	Diff %
Total protein Mg/dl	7.3 ± 1.04	5.925 <u>+</u> 1.082	- 18.90	5.83 <u>+</u> 1.065	20.13	6.4 <u>+</u> 1.104	-12.3
Glucose Gm/dl	$83.9 \\ \pm 8.52$	99.668 <u>+</u> 0.471	18.78	100.33 <u>+</u> 7.586	17.58	106.66 <u>+</u> 9.977	26.34
pН	$7.3 \\ \pm 0.081$	7.2 <u>+</u> 0.08	-1.36	7.267 <u>+</u> 0.124	-0.45	7.3 <u>+</u> 14.29	0.00

Table (2): The effects HCG, of 17β -estradiol and hydrocortisone on total protein, glucose and pH. n=5

%Difference = Percentage difference of control

SD= standard deviation *P < 0.05

** P < 0.03

Table(3): The effects of HCG, 17 β-estradiol, and hydrocortisone on body weight. n=5

	control	HCG		17 β -estradiol ්		Hydrocortisone	
	Mean <u>+</u> SD	Mean <u>+</u> SD	Diff %	Mean <u>+</u> SD	Diff %	Mean <u>+</u> SD	Diff
Body weight	663.333 181.637	559.091 <u>+</u> 165.58	-14.88	646.341 <u>+</u> 171.92	-3.64.	526.136 205.462	22.45
gm	<u>+</u>					<u>+</u>	

%Difference = Percentage difference of control SD= standard deviation *P < 0.05 ** P < 0.01

DISCUSSION

Hormones of the resent study (HCG, 17β - estradiol, and hydrocortisone) was demonstrate changes in some blood parameters. The results in table (1) show that HCG increased cholesterol(49.25%), TG(2075%) and LDL (92.5%) and cause significant decreased in HDL (-35.48%). (10) pointed that HDL was enhanced by HCG. (15) pointed that HCG have effects on fatty acids synthesis and may be lead to form new triglycerides.(11) reported that treatment with

HCG increased blood glucose and profoundly inhibited the development of diabetes this insure our result (18.78%). Table(3) showed that HCG decreased body weight (-14.88). A study found that women whom used HCG lost (20lb) of their weight within one month(**16**).

Table (1) showed that administration of **17** β - estradiol caused decreased in percentage differences of cholesterol (-47-53%), TG (-43.43%) and a significant increased in HDL (-33.33%), and LDL (22.24%) (p<0.05). A study found that estradiol increased HDL and TG(**17**). Another study found that estradiol activated the transformation of cholesterol to other hormones and this cause decreased in it in blood serum(**18**). As well as another investigated that 17 β -estradiol lowered the level of cholesterol and TG(**19**). While another researchers found that estradiol decreased cholesterol. and increased LDL and HDL, with no change in TG(**20**). And (**6**) investigated that contraceptives which contain estradiol caused decreased in HDL. Another study concluded that HDL increased at 3rd month and TG decreased(**21**). In another study found that estradiol reduced total cholesterol but increased significantly LDL (22.24%) (p<0.05). (**7**)showed that estradiol increased HDL and higher significant in serum total cholesterol and TG.

Estradiol caused increased in percentage differences in total protein (20.13%) and glucose (17.58%)(Table (2).An investigations found that 17β - estradiol lower the level of glucose because of raising insulin (4) While another study pointed that estradiol inhibit the insulin and increased glucose level (5). Estrogen have effect on carbohydrate metabolism and it might be therefore be expected that their use would result in corresponding increased glucose and the incidence of diabetes(23).While the resent study show that glucose decreased with no effect on HDL,LDL and TG after estrogen therapy(24).

Hydrocortisone decreased serum total cholesterol (-14.94%) and increased in TG (12.3%) .(25) concluded that the treatment with hydrocortisone increased the level of cholesterol and TG. Hydrocortisone increased serum glucose(26.32%).A study pointed that the decrease in corticosteroids lead to lowering blood glucose level (26). LDL was increased after administration of hydrocortisone (58.35%).(27) found that hydrocortisone increased plasma level of LDL due to reducing hepatic LDL receptors. The results in Table (2) showed 17B-estradiol , HCG and Hydrocortisone had no significant effects on blood pH. Hydrocortisone and HCG decreased total protein while 17B-estradiol caused no significant increased table(1).

The resent study concluded that 17 β -estradiol and hydrocortisone have the similar effect on serum cholesterol , HDL and LDL .and 17 β - estradiol, hydrocortisone and HCG have the same effect on glucose and all of them have no significant effect on total protein and body weight and the pH , and this may be due to their chemical structure and mode of actions.

تأثير الهرمون المشيميHCG و الاستراديول-17 بيتا و الهيدروكورتزون في بعض في الدم ووزن الجسم في إناث الأرانب

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الخلاصة

استهدفت هذه الدراسة تأثير الاستراديول - 17 بيتا و الهرمون المشيمي HCG و الهيدروكورتيزون على بعض مقاييس الدم ووزن الجسم في إناث الأرانب .

استخدم (20) أرنبا محلياً وضعت في أقفاص وقسمت إلى أربع مجاميع تجريبية ، اعتبرت المجموعة الأولى مجموعة سيطرة وحقنت المجموعة الثانية بالعضلة بـ 30 وحدة دولية (I.U)/كلغم من هرمون المشيمي HCG أما المجموعة الثالثة فحقنت تحت الجلد (0.1 ملغم/كغم من هرمون الاستراديول بيتا 17 والمجموعة الرابعة فحقنت 0.1 ملغم: كغم من هرمون الهيدروكورتيزون في العضلة جمعت العينات في نهاية الأسبوع الخامس.

وأظهرت نتائج الدراسة الحالية أن هذاك تأثيرات في صفات الدم موضوع الدراسة (الكولسترول – LDL - HDL – HDL - HDL – HDL - HDL = HDL – HDL - HDL = HL البروتين الكلي – الجلسريدات الثلاثية – الجلوكوز – PH الدم – وزن الجسم) على حيوانات التجارب (الأرانب) واستخلص من الدراسة أن الهرمون المشيمي HCG ، فع مستويات الكولسترول % 49.25 و JDL = 49.25 و JDL = 0.25 (JDL = 0

REFERENCES

- (1) Kennth, S. (1998). Anatomy and Physiology, the unity of form and function's *Physiology and anatomy: 625-627*.
- (2) Hemerlaar, M;Kenemans, P; Bie, L; Van, D.; Weijer, Ph; Van, de; Mooren, MJ.(2006). Intranasal continuous combined 17β-eastradiol/northisterone therapy improve the lipid profile in healthy postmenopausal women .*Firtl.Apr*;85(4):979-88.
- (3) Huang, X.;Blackman, MR.; Hereman, K. ; Pabst, KM.; Harman, SM.; Caballero, B.(2004). effects of growth hormone and /or sex steroid administration on whole body protein turnover in healthy aged women and men. *Diabetologia Jul*; 47(7):1175-87.

- (4) Verma, S.; Srivvastava, RK.; Sood, S.and Sharma, S.(2005).Effect of estrogen on hypoglycemia- induce neurogilial impairment in overectomized rats. Methods Find Exp Clin Pharmacol ;Aug;27 (6);405 -9.
- (5) Nagira, k.; Sasoaka, T.; wada, T.; Fukui, K.; Ikubo, M.; Hori, S.; Tsuneki, H.; Satio, S.and kobavashi, M.(2006). Altered sub cellular distribution of estrogen receptor alpha is amplicated in estradiol –induced regulation of insulin signiling in 3T3-11 adipocytes.*EOcrinology*. *Feb*; 147(2):1020 8.
- (6) Skouby, SO. Enderaikat, J. ; Dusterberg, B. ; Schmidt, W.; Gerlinger, C.; Wessel, J. ; Goldestin, H. and Jesperson, J.(2005).A 1-year randomized study to evaluate the effects of adose reduction in oral contraception on lipid and carbohydrate metabolism :2 micr-ogram ethynill estradaiol combined with 100 microg levanorestrel. *contraception Feb;7(2);111-7*.
- (7) Yahaya, IA. and Afonja, OA,(2005) . Serum lipids in women on oral contraceptive in Zaria-Nigeria.*Postgrad Med J.Jun:12*(2)85-8.
- (8) Stevenson, JC.; Rioux, JE.; Koar, L.and Gelfand, M .(2005). 1-2 mg 17β estradiol combined with sequential dehydrogestrone have similar effects on the serum lipid profile of postmenpasual women: *Climacteric. Dec:* 8(4);352-9.
- (9) Salvatori, R.; Alba, M.; Fintini, D. (2005). Influence of estrogen administration On growth receptors growth hormone (GH) in GH-Deficient mice .*Exp Biol Med nov*;20(11)40-45.
- (10)Towns, R.; Azhar S.; Peegel, H.and Menon, KM. (2005).LH/HCG-stimulated androgen production and selective HDL-cholesterol transport are inhibitd by a dominant-negative CREB structure in primary culture of rat-theca-interstitial cell.*Endocrine.Aug*:27(3);269-77.
- (11) Khan, NA. ;Khan, A.; Saveloul, HF.and Benner, R. (2001).Inhibition of diabetes NOD mice by human pregnancy factor.*Hum.Immuonol:Dec;62(12):1315-23*.
- (12) Berg, AL.; Nelsson-Ehle, P.and Arnadottir, M. (1994). Direct effects of cortisone on plasma lipoprotein metabolism in man-studied in vitro and in vivo.*Metabolism .Jan:44(1):90-107*.
 - (13) Beentijes, JA. ;Vantol, A.; Sluitre, WJ.; and Dullaa,r M.(2000).Decreased plama cholesterolestrification and choleateryl ester transfer in hypopituittary patient on glucocorticoid replacement therapy.*Scand JClin Lab Inverst.May;60(3):189-98*.
- (14) Hine, J. and Wethrill, GB.(1975). Aprogramed test in statistic T .ex-2 godness of fit Chapman and Hill.london.
- (15) Richardson, Mc.; Cameron, IT.; Simons, CD.; Das, Mc.; Hodage, TE.; Zhang, Gabd Byren, CD.(2005).Insulin and chorionic gonadotropin cause a shift in the balance of regulating element –binding protein (SREBP)Isoforms toword the SREBP -1e isoform in culture of human granulosacells: *J Clin Endocrinol Metab*. *Jun :90(6): 3738-46*.
- (16) Michaela, R.(2004).abstracts from the first international work ship on HCG and obesity. *IFCOR p:5*.
- (17) Towns, R.; Azhar, S.; Peegel, H. and Menon, KM. (2005).LH/HCG-stimulated androgen production and selective HDL-cholesterol transport are inhibitd by a

dominant-negative CREB structure in primary culture of rat-theca-interstitial cell.*Endocrine.Aug*:27(3);269-77.

- (18) Pamela, C .Champ A. and Richard A. .(1994). Lippincott's illustrated review: *Biochemistry second edition*. *P*:209,225.
- (19) Osmanakaoglu, MA., Osmanagalu, S., osmanagaoglu, T., Okumus, B., and Bozcava, H.(2005). Effect of different preparation of hormone on lipid and glucose metabolism, coagulation factors, and bone mineral density in over weight and obese postmenopausal women *.Fertil Steril Aug 84(2) 384-93*.
- (20) Purnell, JQ.; Bland, LB.; Garzotto, M. ; Lemmon, D. ; Wersinger, EM. ; Ryan, CW.; Brunzell, JD. and Beer TM .(2006) . Effect of transdermal estrogen on level of lipids ,lipase activity and inflammatory markers in men with prostate canccccer.*J Lipid Res* .*Feb*; 47(2);349-55.
- (21) Balci, H.; Altunyurt, S.; Acar, B.; adiloglu, M.and Nvural, B.(2005).Effects of transdermal estrogen replacement therapy on plasma level of nitric oxide and plasma lipids on postmenopausal women *.Maturitas ,Apr.* 12(2);112-122.
- (22) AL –Azzawi, F.; Wahab, M; Sami, S.;Proudler, AJ.; Thompson, J. and Stevenson, J.(2004). Randomiaed trail of effects of estradiol in combination with either norethistone acetate or trimegestone on lipoproteins in poatmenopausa women: *Climactric*, *Sep* 13(20)119-129).
- (23) Godsland, IF.(2005).Oestrogen and insulin secreation;Diabetiology *Nov;48(11):2213-20.*
- (24) Herrmann, BL.; Janssen, OE. ; Broeker-Press, M.and Mann, K. (2005) .Effect of estrogen replacement therapy on bone and glucose metabolism in male with congenital aromatase deficiency .*Horm* .*Metab*:37(3)178-83.
- (25) Madej, A.; Romanowicz, K.; Einarsson, S.; Forsberg, M.; and Barciknwicki, B.(1997).Effect of glucocorticiod treatment on biochemical and hormonal blood parameters in early pregnant gilts.*Acta Vet Scand*:38(3);263-73.
- (26) John, A.. (1990). Medicine ; black well science . P:12:10.
- (27) AL-Rayyes, O.; Wallmark, A.andFloren, CH.(1997). Additive inhibitory effect of hydrocortisone and cyclosporine on low–density lipoprotein receptor activity in culture hepG2 cells.*Hepatology.Oct*;26(4):967-71.