ISSN 0975-2366
DOI: https://doi.org/10.31838/ijpr/2020.SP1.122

Review Article

Study of some Physiological and Biochemical parameters in female offspring born from dams treated with Dexamethasone during lactation period

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Received: 09.04.20, Revised: 10.05.20, Accepted: 08.06.20

ABSTRACT
The present study amid to investigate the effect of dexamethasone on some hematological and biochemical parameters on offspring from dams rats treated during lactation ,therefore we used twelfth male rats mated with twenty four adult female .The rats divided into three equal groups ,group one control the female rats treated normal saline , group two the dams treated during lactation S.C dexamethasone 150 mg/kg.BW for ten days ,group three the dams treated during lactation S.C dexamethasone 150 mg/kg.BW for thirty days . After that the offspring scarified and measured the hematological and biochemical .The results showed that RBC. Hb, PCV, MCH, MCV and MCHV did not reach a significant while WBC and lymphocyte appeared decreased ,granulocyte increased .The AST ,ALT and ALP showed increased significantly ,TC and TG appeared increased while LDL showed decreased significantly .

Keywords: Dexamethasone, Rats, lactation

INTRODUCTION

onset of lactation are accompanied by the activation of neurobiological systems that are directly related to reproductive functions (6). During this period of time, the ultimate goal of a mother's behavior is to ensure the survival of herself and her pups. For this purpose, many other behaviors are inhibited, and the female is largely focused on her offspring. For a rat, maternal behaviors include nest building, lactation, pup licking and grooming, and pup retrieval and defense (6). In addition, lactating female rats exhibit high levels of aggression during the first 2 week after delivery, which is called maternal aggression, to protect their pups from a male intruder to the nesting area (5).

The maintenance of lactation depends on the persistence of the connection of the mother with her offspring. Both prolactin and oxytocin are secreted from the pituitary gland under the regulatory control of the hypothalamus, are involved in lactation, and act as important components of the neurobiological pathways underlying the initiation and maintenance of maternal behavior (7). Suckling stimulates a rapid increase in plasma prolactin and oxytocin; however, these hormones are also secreted in response to several other stimuli, including increased plasma osmotic pressure, blood volume expansion, sexual intercourse, and a wide range of physical and psychological stressors. It has

Dexamethasone (DEX) (also known by the brand names Decadron, Dexasone, Diodex, Hexadrol, and Maxidex) is an exogenous steroid that provides negative feedback to the pituitary to suppress the secretion of ACTH, Specifically, dexamethasone binds to glucocorticoid receptors in the basal medial hypothalamus, which lies outside the blood brain barrier, resulting in regulatory modulation (1). DEX is one of the medications used in the treatment of multiple myeloma, it is a synthetic adrenocortical steroid. Adrenocortical steroids, also known as glucocorticosteroids or corticosteroids, are produced naturally by the adrenal glands in the body (2).

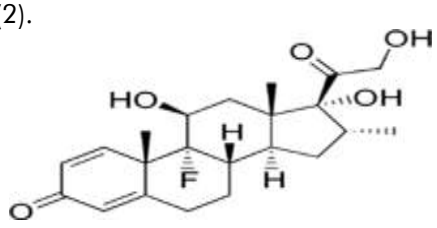

Fig.1: Chemical structures of (DEX) (3).

Maternal behavior is probably the most important pro-social behavior of the mammalian mother, ensuring the well-being and development of her offspring, and interestingly, the maternal behavior in the lactating rat is high in the early phase of lactation but decreases with progression of motherhood (4, 5). The end of pregnancy and the

polyethylen tubes at (– 20c) until used for biochemical analysis (9).

Hematological study

The hematological tests were done in the privet laboratory by using Hematology auto analyzer (Huma Counts 5) made in Germany company serial no.160247 the instrument can measures and calculates 22 different parameters .The Hematology auto analyzer containing four solution(HC5 – BASOLYSE containing cyanide free lyse reagent ,HC-LYSECF containing cyanide free lyse reagent ,HC5 – EOLYSE containing cyanide free lyse reagent and HC- Cleaner cleaning solution used to clean fluidics system) and the instrument have a printer mechanic inside with thermal paper . The hematological parameter estimated by this instrument were, (RBC, WBC. DWBC, Hb, and PCV).

Biochemical test:

The biochemical tests were done in the privet laboratory by using chemistry auto analyzer made in Germany by human star company serial no.20628 the machine has 54 wells which numbered from 1 to 54 , The serum samples deposited in each specific wells . The reagent was put in a special container beside the wells The serum biochemical parameters estimated by this instrument were lipid profile (triglyceride , total cholesterol ,HDL-c ,LDL-c, AST, ALT, ALP)

RESULTS

The effect of Dexamethasone on offspring on:-

Hematological parameters

According to the results seen in Table (1), there is no a significant differences were showed in RBC count , Hb concentration and PCV percentage in group two ,offspring which results from female treated dexamethasone during lactation in 10 and 30 days compared with control group .The same table appeared also MCV , MCH and MCHC no a significant differences in value in group two and three compared with control group .

been demonstrated that glucocorticoids may reduce prolactin and oxytocin secretion (8).

MATERIALS AND METHODS

Twelfth male rats and twenty four adults female rats were used in the present experiments ,their body weight arranged between (25± 5)g, the animals were housed in individual cages measuring (50x50 cm), in animal house of veterinary collage-university of Basra Iraq. All animals were exposed to the same environmental including climate feeding and adaptive on place for two weeks before treatment. the animals were divided randomly into three equal groups (four males plus eight female per group) then all female after divided to three group mated with males to design the experiments as follow

Group one control : -The dams rats were administered S.C normal saline through lactation days 1-30 .

Group two: - The dams rats were administered S.C dexamethasone 150μ g/kg.bw through lactation days 1-10

Group three; the dams rats were administered S.C dexamethasone 150μ g/kg.bw through lactation days 1-30 Respectively after that the female offspring were separated and sacrificed after puberty, after that we measure the following parameters:-

Collection of blood samples

All Blood samples were collected between (8- 10 hours am) in order to standardize the time of collection which may affected certain blood and biochemical parameters. Blood sample (5 ml) were collected from heart puncture. The(2ml) of blood collected from each animal were stored in plastic sample test tube containing ethylene diamine tetra acetic acid (EDTA) anticoagulant for hematological studies which done directly after collection , while another portion (3 ml) was deposited in to tube without anticoagulant and allowed to clot at room temperature . Then the blood samples were centrifuged at (3000 rpm) for 15 minutes and serum sample were stored in

Table 1: Effect of dexamethasone during lactation on Red blood cells parameters. (Mean ±SE), n=8

Groups	*Red blood cells parameters*					
	RBCs ($\times10^6$)	Hb g/dl	PCV %	MCV fL	MCH pg	MCHC g/dl
G 1 Control (normal saline)	5.47±0.47 a	11.10±1.01 a	35.57±2.93 a	62.66±1.15 a	20.16±0.48 a	35.40±0.75 a
G 2 Dexa. 150 mg/kg during Lactation for 10 D.	5.68 ±0.53 a	11.53±1.15 a	36.30±3.32 a	63.66±1.15 a	20.16±0.54 a	31.41±0.85 a
G 3 Dexa. 150 mg/kg during Lactation for 30 D.	6.26±0.50 a	12.02±1.07 a	38.16±3.11 a	61.25±1.08 a	19.95±0.51 a	31.80±0.79 a

The different letters refer to significant differences at ($p \leq 0.05$) .

Table 2: Effect of dexamethasone during lactation on WBC cells parameters. (Mean ±SE), n=8.

Groups	*white blood cells parameters*			
	WBCs($\times 10^3$)	Lym.%	Mon.%	Gran.%
G 1 Control (normal saline)	6.14±1.21 a	65.17±3.80 a	6.60±0.71 a	28.23±3.91 b
G 2 Dexa. 150 mg/kg during Lactation for 10 Days	6.80 ±1.38 a	63.44±4.31 a	6.64±0.81 a	31.91±4.43 b
G 3 Dexa. 150 mg/kg during Lactation for 30 Days	4.79 ± 1.29 b	55.20±4.03 c	6.46±0.76 a	37.37±4.14 a

The different letters refer to significant differences at ($p \leq 0.05$) .

serum AST, ALT and ALP concentration are presented in the table (3). A significant increase ($p \leq 0.05$) in AST concentration was observed in 10 and 30 days of lactation compared with control. The significant ($p \leq 0.05$) increase in ALT enzyme concentration was also observed in Dexamethasone treated group with advanced periods of lactation compared with control ,also the same table appeared a significantly ($p \leq 0.05$) increase with advanced periods of lactation in 10 and 30 days in ALP compared with control.

Table (2) show that the total WBC count and lymphocytes percentage decrease significantly ($p \leq 0.05$)in group three compared with group two and control, while the monocyte percentage didn't difference in all treated group compared with control. The same table showed that the granular cell percentage increased significantly ($p \leq 0.05$) in long period of lactation group three compared with group two and control

Liver function.

The effects of Dexamethasone 150 mg/kg.bw treatment for 10 and 30 days in lactation on the

Table 3: Effect of dexamethasone during lactation on liver enzyme. (Mean ±SE), n=8.

Groups	AST IU/L	ALT IU/L	ALP IU/L
G 1 Control (normal saline)	45.15±2.21 c	32.97± 6.25 c	51.28 ±4.46 c
G 2 Dexa. 150 μ g/kg during Lactation for 10 Days	139.52±2.21 b	45.71±3.81 b	325.52±12.91 b
G 3. Dexa. 150 mg/kg during Lactation for 30 Days	178.32±2.21 a	56.43±4.28 a	501.55±18.64 a

The different letters refer to significant differences at ($p \leq 0.05$

triglycerides concentration was recorded in Dexamethasone 150 mg/kg.bw in day 30 of lactation compared with control group. The serum concentration of LDL-c decreased significantly ($p \leq 0.05$) in both group two and three compared with control group.

Lipid profile

The results in table (4) show that the mean values of cholesterol concentration was significantly ($p \leq 0.05$) increase in day 20 of lactation compared with group two and control ,while a significant ($p \leq 0.05$) increase in serum

Table 4: Effect of dexamethasone during lactation on lipid profile. (Mean ±SE), n=8

Group	TC mg/dL	TG mg/dL	HDL mg/dL	LDL mg/dL
G 1: Control (normal saline)	53.81±6.13 b	38.71±9.6 b	26.34±1.9 a	21.15±8.57 a
G 2: Dexa. 150 mg/kg during Lactation for 10 Days	66.3±2.49 b	33.4±6.0 b	27.8±2.4 a	6.83±3.35 b
G 3: Dexa. 150 mg/kg during Lactation for 30 Days	74.03±3.07 a	64.51±15.4 a	26.42 ±3.3 a	5.53±3.07 b

The different letters refer to significant differences at ($p \leq 0.05$)

DISCUSSION

Effect of Dexamethasone on female rats during lactation on

Hematological parameters

The results in present study in table (1) showed the changes in value of RBC count, Hb concentration, PCV percentage, MCV, MCH and MCVH did not reach a significant when compared with control group. The result dis agreement with study done by (10) They suggested that the increase in red blood cell production was also evident through the generally increased absolute numbers of nucleated erythroid cell precursors per milligram of bone marrow, the highest increases were seen in the erythropoietin treated rats. Dexamethasone may stimulate erythropoiesis in our rats through a previous augmentation of erythropoietin production in the residual renal mass. The results of WBC count and differential WBC appeared decreased in WBC count and lymphocyte in group three only the results agreed with (11) He suggested that glucocorticoid cause neutrophilia primarily by inducing the increased release of neutrophils from the bone marrow reserve through the circulation. Associated changes in the differential leukocyte count include lymphopenia. Glucocorticoid-induced lymphopenia is attributed to lympholysis in blood and lymphoid tissue, and increased shift of lymphocytes from blood to their body compartments, or both. The leukocytopenia could be explained by differential white blood cell count pattern, the elevation of plasma glucocorticoid and increasing of circulating heterophil lymphocyte ratio, are the two most accepted indicators of the stress condition in birds. Besides heterophil/lymphocyte ratio of quails that receiving various dexamethasone concentrations was significantly different. However, dexamethasone Mechanism of corticosteroid-induced eosinopenia remains to be established unequivocally. Various mechanisms have been proposed, including decreased bone marrow release, intravascular lysis, and reversible sequestration in organs rich in the mononuclear phagocyte system, and increased migration in tissues.

Biochemical parameters:

Data in the present study revealed that serum liver enzymes (ALT, AST and ALP) increased in female offspring rats administered dexamethasone to dams compared with control (Table. 3). The results are agreement with the results of previous studies (12) they reported that elevated activity of ALT, ALP and AST refers to hepatotoxicity resulted from ROS, also the results agree with study done by (13), the results indicated a significant increases ($P \leq 0.05$) in the aspartate aminotransaminase (AST and alanine aminotransaminase (ALT) in all treated groups. These enzymatic changes may take place as a result of destruction of hepatocytes which are responsible for detoxication and their accompanying exodus the entrance enzymes to blood. The results dis agree with (14), the decreased levels of liver enzymes suggest that dexamethasone possess some hepato-protective properties and no interspecies difference in the liver response and mineral metabolism following dexamethasone treatment (15). Concerning lipid metabolism, the results of the present study revealed a significant increase ($P<0.05$) in serum total cholesterol, triglycerides, while decreased in LDL-c ($P<0.05$) in female offspring rats treated her dams with dexamethasone table (4). The results agreed with (16) they suggested that Dexamethasone induced hypercholesterolemia might be related to the interference of Dexamethasone with monocytes function in removing excess cholesterol as well as to the inhibition of cholesteryl esters hydrolysis and nitric oxide synthase (17). Related to TG, the high consumption of it will be an alternative source of energy in the states of stress (12) Regarding to the effect of Dexamethasone on TG, the elevation is due to the action of Dexamethasone in promoting TG- rich VLDL formation on one aspect and inhibiting lipoprotein lipase on the other aspect (18) .Also the results agreed with (16) they related to TC can be explained by induced oxidative stress and subsequent LDL oxidation, the LDL oxidized leading to incompatibility of LDL to their receptors on the cells.

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