

Effect of Dexamethasone on Drug Adrenal Gland of Male Albino Mice

Rihab Galib Mohammed Al- Zuhairy
Dentistry Collage, Babylon University

Abstract

This paper regards in the study of the effect of different doses of dexamethasone drug on adrenal gland, through measuring its layers thickness and this was done by treating (45) adult Swiss balb/c male mice with the doses: 0.2 , 0.4 , 0.8 and 1.6 mg/kg (B.W) s.c. for 2, 4 weeks for each dose.

Results showing significant differences at the doses: 0.8 and 1.6 mg/ kg on adrenals cortex , some of layers affected by 0.4 mg/ kg but no significance by 0.2 mg/ kg, while cortical glomerulosa & medulla part never be affected as a long time in compare with control group.

/ 1.6 0.8 0.4 0.2 : / (45)

/ 0.8 1.6

/ 0.2 / 0.4

(Medulla) (Glomerulosa)

I- Introduction

I-I Adrenal Gland

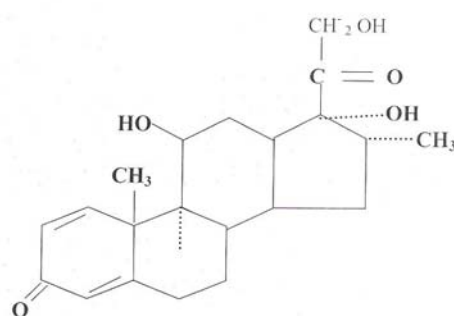
The body has two adrenal gland each of which weighs about 4 gms, lie at the superior poles of two kidneys. The inner part (medulla) secretes hormones such as epinephrine and norepinephrine that affected blood pressure, heart rate, sweating and other activities also regulated by the sympathetic nervous system.

The outer oart (cortex) which has 3 distinct layers (zone glomerulosa: which secrtes aldosterone , zona fasciculate and zona reticularis : they are secrete both glucocorticoids and androgens). (Guyton , 1997).

II-I- Dexamethasone

Is a potent synthetic analogue hydro-cortisone it is used in human medicine for the treatment of a wide range of disease . This wide range of therapeutic use reflects the broad spectrum of pharmacological actions of the corticosteroid hormones, which effects on several important biochemical path ways and cellular transport mechanisms (Toutian *et al.*, 1983).

The half life of dexamethasone in human serum about 90-100 minutes (Weisenberger, 1972).



The structure of dexametasone

The glucocorticoids have functions just as important to the long continued life of the animal. At least 95% of the animal. At least 95% of the glucocorticoids activity results from the secretion of cortisol, some of glucocorticoids function are:

The stimulation of gluconeogenesis (formation of carbohydrate from proteins and some other substances) by liver. Cortisol also causes a moderate decrease in the rate of glucose utilization by the cells everywhere in the body. Other function is the increasing liver protein and plasma protein and mobilization of fatty acids. Also it prevents the development of inflammation by stabilization of the lysosomal membranes. (White, 1984; Zilva *et al.* 1988; Sakamoto and Mokuda, 1997).

II- Materials and Methods

I-II - Materials

(45) adult male Swiss balb/c mice with about (12) weeks in age and (25-30 gms) in weight were used in this research, bred under standard conditions (14 hrs of light and 22-28 °C). Aqueous solution of dexamethasone /iic cipros company. This drug packed in glass ampule of a capacity 2 ml.

Animals injected with: 0.2, 0.4, 0.8 and 1.6 mg/kg BW s.c. for 2 and 4 weeks for each dose, these treatment groups were compared with control group which treated with normal saline 0.9%.

All animals were sacrificed, Adrenal glands were weighted then kept in Bouins solution for histological preparation.

II-II Methods

Slides were prepared according to (Presnell, 1997). Microscopic measurements of the thickness of adrenal gland is done by using the ocular micrometer after its calibration with stage micrometer for different magnifications. Results were analyzed statistically by using (CRD) test and the significance was tested by finding LSD (Scheffer, 1969).

III- Results

Results showing non-significance differences by the treatment with the dose 0.2 mg/kg of dexamethasone related to the thickness of adrenal affected with this treatment (Table1).

While there were high significant increment $P > 0.05$ showed by relative weights of adrenal glands which increases at the dose 0.4 mg/kg for (4 weeks) however it decreases as the dose increases mean at 1.6 mg/kg for both 2 and 4 weeks in compare with control group (Table1).

Also there were significant increasing $P > 0.05$ in whole adrenal diameter and when we examine the distinct layers we find significance effects (increment)

especially in the thickness of zona fasciculate and zona reticularis at the doses 0.4 and 0.8 mg/ kg for both 2 and 4 weeks , while they were decreased significantly at the dose 1.6 mg/kg for 2 and 4 weeks in compare to control group. Cotical glomerulosa and medulla portion never be affected by all doses.

Table(1): Effect of Different Doses of Dexamethasone Drug on Adrenal Gland

Dosage (mg/kg) Duration time (week) of treatment		Relative weight of Adrenal (%)	Diameter of Adrenal gland μ at magnification 4x	Thickness of cortex of Adrenal gland in μ at magnification 10x			Diameter of Medulla of Adrenal gland in μ at magnification 40x
				Thickness zona Glomerulosa μ at 40x	Thickness zona fasciculate μ at m. 40x	Thickness zona Reticularis μ at m. 40x	
Control		14.4 \pm 0.83	9700 \pm 970	5600 \pm 1627			465 \pm 152.5
				443 \pm 91.5	740 \pm 144	380 \pm 62.6	
0.2	2	14.08 \pm 1.09	9612 \pm 302.9	5830 \pm 466.9			425 \pm 16
				450 \pm 57	760 \pm 156	331 \pm 74	
	4	14.68 \pm 0.9	9800 \pm 3.7	5844 \pm 1725			418 \pm 13
				424 \pm 43	*903 \pm 366	352 \pm 31.6	
0.4	2	15.4 \pm 1.5	9876 \pm 559	5960			482 \pm 108
				470 \pm 87.6	*921 \pm 58.9	*584 \pm 150.5	
	4	*16.7 \pm 1.1	*11650 \pm 1529	*6250 \pm 1157.6			478 \pm 113
				465 \pm 75.7	*964 \pm 36	*502 \pm 137.7	
0.8	2	*16.5 \pm 0.7	*13050 \pm 1263	*6220 \pm 965.5			493 \pm 329.8
				456 \pm 219.7	*998 \pm 31	*644 \pm 52.4	
	4	*16.2 \pm 0.9	*14500 \pm 3000	*6840 \pm 2799.7			506 \pm 33
				447 \pm 335	*1018 \pm 52	*566 \pm 37.7	
1.6	2	*7.34 \pm 2.79	*8176 \pm 196.6	*2090 \pm 599.5			456 \pm 136
				460 \pm 37.5	*655 \pm 141.4	*238 \pm 46	
	4	*2.9 \pm 0.8	*6926 \pm 1016	*2110 \pm 579			468 \pm 151
				432 \pm 126	*622 \pm 101.5	*970 \pm 30	
LSD		1.76	223.3	149.99	368.8 \pm 68.2	137.2	141.33

* Significant difference at $P > 0.05$

Each number resemble the Mean of (5) animals

IV-Discussion

The statistical analysis of results showing the clear effect of dexamethasone drug on adrenal gland activity which can be estimated depended on the weight , diameter of gland also through the thickness of its layer.

From the table we observe significant increase $P>0.05$ in the weight, diameter and the thickness of zona fasciculata and zona reticularis but no glomerulosa at the doses: 0.4, 0.8 mg/kg bw for 2,4 weeks and this probably because of conditions that increase the output of mineral corticoids (aldosterone) cause hypertrophy of the zona glomerulosa while not affecting the pther two zones . On the other hand, those factors that cause increased secretion of cortisol and adrenal androgens caused hypertrophy of the zona fasciculate and reticularis while showing very little or no effect on the zona glomerulosa.

This is especial true of stimulation of the gland by adrenocortico trophic hormone (ACTH) (Guyton, 1997 ; Abdul-Jawad , 2002) found that injection male albino mice with 0.8 and 0.2 mg/ kg s.c for 4 weeks cause increment in gonads weights as compare with 0.2 mg/kg and control group, she contributed the reason probably that treatment with dexamethasone cause adenoma in the tissue which lead to increasing in gonads relative weights . Also the inhibitory role of dexamethasone on 17 α hydroxylase enzyme which important in androgens synthesis steps. (Lee *et. al.* 1999).

Yhe results regards the dose 1.6 mg/ kg showing significant decrease $p>0.05$ for the same parameters and this probably because the dexamethasone drug being a synthetic 30 times as potent as cortisol which has direct negative feedback effects on:-

- 1- The hypothalamus to decrease formation of CRF.
- 2- The anterior pituitary gland to decreased ACTH, these help to regulate the plasma concentration of cortisol (Guyton , 1997).This results are compatible with (Ueberberg, 1964) who observed significant decrease in Body weight gain and in adrenal weights when he injected groups of rats with 50 mg/kg bw dexamethasone daily for 6 weeks , also the administration of 79 mg/kg bw/ day dexamethasone to female Wistar rats for 13 weeks cause increasing in adrenal glycogen level and reduction in adrenal corticoids. The postmortem examination found adrenal gland was markedly smaller with reduced weights when compared to controls, the adrenal cortex was narrowed due to loss of the regular structuring of the cells or cell columns , in addition to a reduction in lipids.

Also (Ueberberg, 1963) found that oral administration of 125 mg/kg bw/ day dexamethasone for 6 weeks in 5 mongrel dogs cause increasing in blood glucose values , the relative adrenal weight were decreased. In the adrenals, the zona fasciculate was narrowed.

From the table we found non- significant differences in medulla diameter and this can contributed to the nervous stimulation that activated the inner part of adrenal (medulla) which is innervated by presynaptic sympathetic nerve fibers and release catecholamines. The release of these "adrenergic or sympathetic " transmitters into the blood stream amplified the effects of the sympathetic branches of the outonomic nervous system at virtually all of the target organs of the sympathetic nervous system (D' Agata & Chrousos, 1987).

References

- D'Agata, R., and Chrousos , G. P. (1987). Recent Advances in Adrenal Regulation and Function. New York, Raven Press.
- Guyton, A. C. & Hall, j.e. (1997): Text book of medical physiology, W. B. Saunders Company. London. England. PP 1151-1167.

- Mokuda, O. and Sakamoto, Y. (1999): Periplcral insulin sensitivity decreased by elevated nou-estriified fatly acid level in dexamethason treated rats. *Diab. Nutr. Metab.*, 12:252-255.
- Persnell, J. K & Schreebman, M.P. (1997). *Humans Animal Tissue Techniques*. 5th edn . The Jobus Hopkins press Ltd. London.
- Sakamoto, J. and Hashimoto, K. (1986): Reproductive Toxicity of acrylaminde and related compounds in mice effects on fertility and sperm morphology., *Arch. Toxicol.* 59:201-205.
- Scheffer, W.C. (1969). *Statistics for biological sciences*. 2nd edn. Addison Westey Publishing company. California, London, Amesterdom.
- Shrivastava, A.,Lyon, A. and Mcintosh, N. (2000): The effect of dexamethasone on growth , mineral blance and bone mineralization in preterm infants with chronic lung disease . *Eur. J. Pediat.* 159:380-384.
- Toutain, P.L., Alvinerie , M. & Ruckebusch, Y. (1983). Pharmacokinetics of dexamethasone and its effect on adrenal gland function in the dog. *Am. J. Vet. Res.*, 44: 212-217.
- Uerberg, H (1963). Comparative experimental trials in dogs with pyridine -4- carboxylic acid (dexamethasone-21) ester (HE III) and dexamethasone. Unpublished report no. Ax-U-3d.d. 20-12-1963 from Dr. Ingelheim Vetmedica Gmbtt, Ingeltheim, Germany.
- Ueberberg, H. (1964). Comparative inrestigations in rats with substance HE III and dexamethasone .Unpublished report did. 23-3-1964 from Dr. Karl Thomas, GmbH, Biberach, Germany. Submitted to WHO by Boehringer Ingelheim Vetmedica GmbH, Ingelheim, Germany.
- Weisenberger, H. (1972). Species differences in the hydrolysis of the dexamethasone 21- is onicotinate by serum esterases *Klin. Wschr.* 50: 665.
- White, D.A. (1984): *Hormones & metabolic control:A medical students guide to control of various aspects of normal and abnormal metabolism* printed & bound in Great Britain by Butter & Tanner Ltd. London PP. 27-37.
- Zilva, J. F. ; Pannall, P. R. AND Mayne, P.D. (1988). : *Clinical chemistry in diagnosis and treatment* . Printed in Singapore by C.O.S.