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STUDY AND MELANOCYTE ADRENOCORTICOTROPIC EFFECTS ON SUGAR METABOLISM AND IMMUNE RESPONSE IN RABBITS, *ORYCTOLAGUS CUNICULUS*

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ABSTRACT

The functioning of the pineal gland, the transducer body of environmental information to the neuroendocrine system was subjected to a circadian rhythm.

Melatonin is the main neuro-hormone expressing this operation. It is synthesized in the pinealocytes after conversion of serotonin via N-acetyl-transferase enzyme, the same subject to a photoperiodic modulation (activation of dark inhibition by light). Some scientists have suggested that melatonin is involved in diabetic disease and which expresses have a diabetogenic effect. To this study the effect of this hormone on glucose metabolism has long been subject to controversy agreeing in effect and hyperinsulinemic hypoglycaemic effect. In order to illustrate the level of interaction of melatonin with neuro-immune- corticotrophin axis and its impact on carbohydrate metabolism, we studied the impact homeostatic (glucose) through the solicitation of two control systems (gland pineal and corticotrophin axis). We and found that melatonin could have an indirect influence on insulin control (glucose metabolism) to the levels of the growth hormone axis (somatostatin) and adrenocorticotropic (corticotrophin). In addition, we have suggested that melatonin might limit the hyperglycaemic action of corticosteroids by direct action at peripheral level.

KEYWORDS: Pineal Gland, Melatonin, Neuro-Immuno-Corticotrop

INTRODUCTION

In an environment that is constantly changing, the cells and tissues of higher beings retain their dynamic balance throughout the life of the organism. Far from being fixed, these structures are replenished by the chemicals produced by the metabolism (metabolites hormones, neuro-hormones).

There must therefore be of neuro-immune neural mechanisms, neuroendocrine, endocrine, which control the physiological constants (internal temperature, physicochemical composition in Fluid media organization) of the internal environment and ensure its homeostatic balance. These adaptive reactions of the body under physiological aggressive situations following an unpredictable factor change of the environment within the physiology of stress. The axis is part of the autonomic nervous system, overarching systems controlling changes in homeostasis and probably participating with other neuroendocrine axes to restore a balance relating to environmental perturbations. HPA axis or hypothalamic-pituitary-adrenal axis follows the organization of major neuroendocrine systems.

The adrenal cortex, in the species mouse, secret corticosterone, and major metabolic stimulant is responsible for most of the physiological effects of the activation of hypothalamic-pituitary-adrenal system (Conn and Fajans, 1956). It is

placed under the control of a pituitary hormone, ACTH or corticotrophin, itself under the control of the hypothalamus and specifically to a population of neurons synthesizing CRF or CRH located in the parvicellular part of paraventricular nucleus of hypothalamus. The corticotrope axis operates cyclically. The main circadian rhythm and is characterized by a maximum secretory activity that proceeds the period of behavioral activity. This rhythm is synchronized by the circadian rhythm and the annual rate (Follenius *et al*., 1992).

In recent years, the designs of the pathophysiology of stress were gradually and profoundly changed by many discoveries focusing on the role immune regulator asked the corticotrope axis by stress or by administration of corticosteroids or ACTH (R.H. (Gisler and Schenkel-Hullinger,1971).The physiology of stress is conceptually simple: A relative imbalance in response to environmental perturbations instantly triggers adaptive secretions resulting mainly by the secretion of corticosteroids following a discharge of ACTH (Akana and Dallman,1992) . Meanwhile, the adrenal medulla releases adrenaline and noradrenaline sympathetic endings (Assenmacher *et al*., 1992). These two hormones, referred to as catecholamines allow metabolic adjustments (supply of carbohydrates to the brain and muscles from glycogen stored in the liver) and physiological necessary action. Glucocorticoids amplify and prolong the action of catecholamines: they allow in particular the mobilization of energy from non-carbohydrate reserves (lipids, proteins) of the body, through the mechanisms of gluconeogenesis. Furthermore, glucocorticoids exert their regulatory effects on the immune system. In this context, many recent studies have demonstrated the existence of interrelations between the immune and neuroendocrine systems (Krug and Krug, 1972). Not only may the immune system under certain conditions, secrete interleukins (interleukine-1 IL1, interleukin-2, gamma interferon) which have the effect of modulating the function (Fryer and Leung, 1982). But it has specific receptors many hormones and neuropeptides (Krug and Krug, 1972). In addition both neuroendocrine and immune systems are ontogenetic, anatomically and functionally interconnected (Deschaux and Rouabhia, 1981).

The interaction between the corticotrope axis and the immune system in the context of an adaptation to pathogenic assaults triggers the same type of reactions. In this respect, it has been reported that the immune defense is a homeostatic response that contributes to maintaining the integrity and proper functioning of cells and tissues (Maestroni and Pierpaoli, 1981).

In addition, stress is known to have influence pineal function (Lynch, and M.H. Deng, 1986). The relationship between the pineal gland and the immune system has been made by (Fernandes *et al*., 1979). On circadian variation in immune responsiveness (suggesting that the pineal gland may have a possible role in this variation) (Jankovic *et al*., 1970). Who showed that adult rat's pinealectomy cause immunosuppressant (Maestroni and Pierpaoli, 1981). Found an altered lymphoid tissue in following the depression of the immune response in rats were therefore induced inhibition of melatonin secretion by exposure to a photoperiod of 24L (Becker *et al*.,1988). Working on pinealectomized rats have shown that the absence of the pineal gland secretion causes histological alterations in root tissue.

OBJECTIVES OF THE STUDY

The objective of this study is to the internal environment and ensures its homeostatic balance. These adaptive reactions of the body under physiological aggressive situations following an unpredictable factor change of the environment within the physiology of stress. The axis is part of the autonomic nervous system, overarching systems controlling changes in homeostasis and probably participating with other neuroendocrine axes to restore a balance relating to environmental perturbations

METHODS

Chemicals and Reagents

The Dexamethasone was obtained from renaudin France laboratory is a type of steroid medication. It has anti-inflammatory and immunosuppressant effects. It is 25 times more potent than cortisol in its glucocorticoid effect, while having minimal mineralocorticoid effect.

The Adrenocorticotrophic hormone (ACTH), also known as corticotrophin, is a polypeptide tropic hormone produced and secreted by the anterior pituitary gland. It is an important component of the hypothalamic-pituitary-adrenal axis and is often produced in response to biological stress (along with its precursor corticotrophin releasing hormone from the hypothalamus). Its principal effects are increased production and release of corticosteroids.

Animals

The present study was conducted on 30 male rabbits (4-5 months old, body weights from 1600-2000 g). Handling of the animals occurred in compliance with the Guidelines for the Care and Use of Animals for Scientific Purposes. The animals were caged in a well-ventilated animal room with a 24 h dark/light cycle and a controlled temperature18 to 24C°; all animals had free access to a standard diet and drinking water adlibitum.

The animals were placed in large metal cages adapted 61cm in length, 51cm in width and 51cm height are arranged on two superimposed rows. These cages are equipped with feeders and waterier with movable tray for easy cleaning.

The temperature of the animal is maintained properly by an electric heater. Photoperiod is programmed with an adjustable clock.

The animals are docile and easy to handle; they are divided into six experimental groups due to 05 animals per cage.

Experimental Design

The animals were placed in large metal cages adapted 61cm in length, 51cm in width and 51cm height are arranged on two superimposed rows. These cages are equipped with feeders and waterier with movable tray for easy cleaning.

The temperature of the animal is maintained properly by an electric heater. Photoperiod is programmed with an adjustable clock.

30 rabbits were randomly divided into five groups, which consisted of five rabbits per group. Different groups of rabbits were administered freshly prepared (l'ACTH synthétique and Dexamethasone) orally via gavage at specific concentrations between

The animals were treated via intramuscular gavage once daily for ten days as follows. For group one, the control group, Group two was intramuscular administered 100 mg/ml/day + Light (L24) of ACTH. Group three was administered 10 mg/Kg/day + Dark (D24) of dexamethasone. Group four was administered 100 mg/Kg/day + Light (L24) of ACTH. Group five was administered 10 mg/Kg/day+ Dark (D24) of dexamethasone. Body weights were recorded, and clinical observations were made daily. Twelve hours after the last dose was received, the animals were fasted and blood samples

(2.5 ml) were obtained from the ear vein.

The sera were separated for measurement of protein, glucose, Lymphoid Organs Rate of weight change, Variation of lymphocyte count, protein and glucose. Immediately following the blood sample collection, the animals were then sacrificed and their testes were rapidly excised and weighed with an electronic analytical balance.

Statistical Analysis

All statistical analyses used were tested using t-test and analysis of variance (ANOVAs) and were conducted with the SPSS 10.0 (SPSS Inc., Illinois, and USA) compu program. Values of ($P < 0.05$) were considered significant.

RESULTS

Weighing lymphoid organs after sacrificing the animals reveals the same weight changes both the spleen Table I. There was a significant difference in animals (rabbit) control was noticed [(D24 = (0.60 ± 0.292 g) and L24 = (0.34 ± 0.152 g)]. In animals (rabbit) treated with dexamethasone (Dexamethasone + D24, L24 + Dexamethasone): There was a significant decrease in spleen weight in animals brought to the darkness continues and treated with dexamethasone (D24 + Dexamethasone) compared to controls [D24 Dxm + = (0.28 ± 0.084 g) VS D24 = (0.60 ± 0.292 g)]. There was a significant decrease in spleen weight in animals exposed to continuous light and treated with dexamethasone (L24 + Dexamethasone) compared to controls [L24 + Dxm = (0.22 ± 0.11 g) VS L24 = (0.34 ± 0.152 g)] . In animals (rabbit) treated with ACTH (ACTH + D24, L24 + ACTH): Treatment with ACTH caused the same trends as well to light that darkness [ACTH D24 + = (0.3 ± 0.071 g) VS D24 = (0.60 ± 0.292 g)].

There was a significant decrease in spleen weight in animals exposed to continuous light and treated with ACTH (L24 + ACTH) compared with controls [L24 + ACTH = (0.38 ± 0.13 g) VS L24 = (0.34 ± 0.152 g)]. The effect of ACTH is greater than that of dexamethasone.

In control group (D24 and L24): There was a significant increase in the rate in animals exposed or made darkness (D24) compared with controls exposed to continuous light (L24) [D24 = (36.0 ± 1.581) VS L24 = (34.4 ± 2.074) In animals (rabbit) treated with dexamethasone (Dexamethasone + D24, L24 + Dexamethasone) Table II. There was a significant increase in lymphocyte levels in animals exposed to continuous light and treated with dexamethasone (L24 + Dexamethasone) compared to controls L24 [L24 + Dxm = (49.2 ± 2.864) VS L24 = (34.4 ± 2.074)].

There was a significant decrease in the animal cell rate ratio revealed continuous darkness and treated with dexamethasone (D24 + Dexamethasone) compared to controls D24 [D24 + Dxm = (31.6 ± 1.581) VS D24 = (36.0 ± 1.581)]. ACTH therapy in animals exposed to continuous light (L24 + ACTH) made a significant increase from the witnesses L24 [L24 + ACTH = (45.6 ± 2.966) VS L24 = (34.4 ± 2.074)] There was a significant increase in animals treated with ACTH and placed in the dark (D24 + ACTH) compared to controls (D24). [ACTH D24 + = (34 ± 2.408) VS D24 = (36.6 ± 2.408)]. The effect of ACTH is less marked than that of dexamethasone.

In control animals (D24 and L24) There was a significant decrease in protein levels in animals exposed to continuous light (L24) compared with controls placed in the dark (D24) [L24 = (6.71 ± 0.835 g/dl) VS D24 = (8.174 ± 1.913 g/dl)] Tables III. In animals (rabbit) treated with dexamethasone (Dexamethasone + D24, L24 + Dexamethasone):

We reported a significant decrease in animals placed in the dark (D24 + Dexamethasone) compared with controls placed in the dark (D24) [D24 + Dexamethasone = (3.994 ± 1.037 g/dl) VS D24 = (8.174 ± 1.913 g/dl)].

No significant decrease in protein levels in animals exposed to continuous light and treated with dexamethasone (L24 + Dexamethasone) compared to controls L24 [L24 + Dexamethasone = (6.806 ± 0.868 g/dl) NS L24 = (6.71 ± 0.835 g/dl)] Tables IV. ACTH treatment provided the following results: No significant decrease [L24 + ACTH = (6.734 ± 1.127 g/dl) NS L24 = (6.71 ± 0.83 g/dl 5)]. Significant reduction [ACTH D24 + = (3.474 ± 0.942 g/dl) VS D24 = (8.174 ± 1.913)].

In control group (D24 and L24) In animals put to the D24 dark, we reported a smaller increase A highly significant difference in blood glucose levels than the previous compared with controls exposed to continuous light L24 [L24 = (1.118 ± 0.019) VS D24 = (0.91 ± 0.058)]. In animals (rabbit) treated with dexamethasone (D24 + Dxm, L24 + Dxm)

We have reported a significant increase in blood glucose exposed to continuous light and treated with dexamethasone (L24 + Dxm) compared to controls exposed to continuous light L24 [L24 = (1.1 ± 0.101 g/l) VS D24 = (0.91 ± 0.058 g/l)].

In animals brought to the darkness D24 + ACTH the smaller increase compared to the D24 controls [ACTH D24 + = (1.112 ± 0.113 g/l) MVS D24 = (0.91 ± 0.058 g/l)].

Treatment with dexamethasone has made the same changes to ACTH compared to controls group D24 and L24 [L24 + Dexamethasone = (1.45 ± 0.228 g/l) VS L24 = (1.118 ± 0.019 g/l)]; [D24+ Dexamethasone = (1.1 ± 0.101 g/l) MVS L24 = (0.91 ± 0.058 g/l)].

Table 1: The Effect of Dexamethasone and ACTH of Change in Spleen Weight (g) of Rabbits after 10 Days of Treatment

Treatment Group	Light (L24)	Dark (D24)
Control± **SD**	0.34 ± 0.152	0.60± 0.292
Dexamethasone (10 mg/kg/day) **±SD**	0.22 ± 0.11	0.28 ± 0.084
ACTH (100 mg/kg/day) **±SD**	0.38 ± 0.13	0.3 ± 0.071

Means within the same column carrying different letters are significantly different (P<0.05)

*mean of six determinations

Table 2: The Effect of Dexamethasone and ACTH of Change in Lymphocytes Ratio Varying of Rabbits after 10 Days of Treatment

Treatment Group	Light (L24)	Dark (D24)
Control	34.4± 2.074	36.0± 1.581
Dexamethasone (10 mg/kg/day)	49.2 ± 2.864	31.6 ± 1.581
ACTH (100 mg/kg/day)	45.6 ± 2.966	34 ± 2.408

Means within the same column carrying different letters are significantly different (P<0.05)

*mean of six determinations

Table 3: The effect of Dexamethasone and ACTH of Change in Protein Levels or δ Globulin (g / dl) OF Rabbits after 10 Days of Treatment

Treatment Group	Light (L24)	Dark (D24)
Control	6.71 ± 0.835	8.174 ± 1.913
Dexamethasone (10 mg/kg/day)	6.806 ± 0.868	3.994 ± 1.037
ACTH (100 mg/kg/day)	6.734± 1.127	3.474± 0.942

Means within the same column carrying different letters are significantly different (P<0.05)

*mean of six determinations

Table 4: The effect of Dexamethasone and ACTH of Change in Variation of the Blood Glucose (g / l) OF Rabbits after 10 Days of Treatment

Treatment Group	Light (L24)	Dark (D24)
Control	1.118 ± 0.019	0.91 ± 0.058
Dexamethasone (10 mg/kg/day)	1.45 ± 0.228	1.1 ± 0.101
ACTH (100 mg/kg/day)	1.84 ± 0.449	1.112 ± 0.113

Means within the same column carrying different letters are significantly different (P<0.05)

*mean of six determinations

DISCUSSIONS

The assessments of our results, namely the effect of melatonin on carbohydrate metabolism, do not find meaning only when the trends of variations of the parameters chosen in our study are correlated. Our results can be reformulated as follows:

Corticosteroid treatment affects changes in the immune response (photoperiod L24).

The ACTH treatment has significantly increased the spleen weight. These spleen weight changes following the loading of the corticotrope axis were obvious for us given the immunomodulatory role of the corticotrope axis has long been discussed by many researchers.

Have highlighted the inter rate thymus endocrine glands by studying the effects of various endocrine ablations, the action of hormones on their hormones spleen and thymus (Fryer and Leung, 1982). or those of the or ratectomie thymectomy or thymus extracts on these endocrine glands (Deschaux and Rouabhia, 1981).If adrenalectomy causes thymic and spleen, hypophysectomy results in the involution of spleen and thymus. The effects of thymectomy cause significant hormonal imbalance in the pituitary-adrenal axis (ACTH and corticosterone Drop) and pituitary-gonadal (decrease of LH and testosterone). Indeed, the administration of thymosin, lymphocyte maturation factor prepared by the thymus, spleen, kidney and liver and also important in tissue growth, directly stimulates the hypothalamic-pituitary-adrenal (Deschaux and Rouabhia, 1981).Thymectomy causes immune deficiency followed by hormonal imbalance manifested by a decrease of ACTH or corticosterone (Deschaux and Rouabhia, 1981).GH levels of LH and FSH are most affected (decrease of 50 to 80%). Conversely, the bias of the corticotrophin axis by an intense and long-term stress causes thymic involution and spleen. Note that, in our case, in addition to the action of corticosteroids, several factors could be involved in the growth of lymphoid organs and lymphocyte proliferation. Any approach would be oppressive or mapping. Effect of treatment with D24 photoperiod (solicitation of the pineal gland) comparing the level of the control groups (D24, L24) showed an increase of the cellular response (cell rate) and humoral (protein levels or globulins). In this respect, some authors have reported that inhibition of melatonin by ß-adrenergic agonists, injected during the night, followed by a reduction of the primary and secondary humoral response in response to the introduction of T antigens dependants (Maestroni and Pierpaoli, 1981). Melatonin significantly rises in normal mice, the production of primary antibodies after injection of sheep erythrocytes (Maestroni and Pierpaoli, 1981).

The same author has shown that exposure of rats to continuous light (after three generations) generates deep histological alterations of lymphoid organs (Maestroni and Pierpaoli, 1981). The injection of exogenous melatonin restores

depressed immune function (Maestroni and Pierpaoli, 1981). Effect of melatonin on the variations of the immune response elicited by the administration of corticosteroids - The implementation of the second type of treatment that is photoperiodic regime D24 (note that the exposure of animals to continuous light we have considered controlling factor in determining the adaptive aspect of melatonin) had an effect tends more or less stable compared to the inhibition of melatonin, as well as for growth for lymphocyte proliferation. We can suggest that in addition to its direct inhibitory action on corticotropin axis, the pineal gland (or melatonin) seems lifted the effect exerted by corticosteroids at the periphery (spleen, thymus and lymphocytes). We can already release to the adaptive aspect of melatonin and its effect antistressant by its interaction with the corticotrope axis as suggested and therefore its immunomodulatory effect (Carrillo-Vico *et al*., 2005). We reported earlier that several hormones are interfering with the interaction between pineal gland corticotrope axis and immune system and that of these hormones, some of which are intimately involved in the regulation of glucose metabolism (or insulin) (growth hormone, a hormone thyroid hormone and adrenal cortex medulla, endorphins). Growth hormone, for example, shows an adjuvant growth factor for lymphocytes. It is active in synergy with thyroxin (Trout *et al*., 1988) . Its excess administration inhibits proliferation. On carbohydrate metabolism growth hormone increases the hepatic glucose output, the glucose turnover and uptake of glycogenic amino acids by the liver. On the peripheral tissues, its action is complex and diphasic insulin effects predominant for 30 to 120 minutes (increased glucose uptake, reduced lipolysis) later, insulin resistance, decreased glucose uptake, increased lipolysis. The islets of Langerhans, the exogenous growth hormone sometimes induces an increase in insulin response to glucose, according to exogenous melatonin increases the concentration of this hormone. Thyroxin, the immune system would have a permissive effect on the secretion and action of the thymic (Deschaux and Rouabhia, 1981).The administration of this hormone significantly increased metabolic rate. The thyroxin is inhibited under the effect of melatonin. Exogenous somatostatin exerts an inhibitory effect on both the proliferative response as the production of antibodies. Exogenous somatostatin inhibits secretion of growth hormone, glucagon and insulin (Davidson. 1987). Affects the pineal gland (melatonin) on carbohydrate metabolism. The assessment of our results, in this case the effect of melatonin on blood glucose, showed a decrease in blood glucose levels in almost all the groups (control, treated with dexamethasone and treated with ACTH) in the dark (pineal gland requested) compared to their equivalents (control, treated with dexamethasone and treated with ACTH) exposed to continuous light. In addition to the correlation of these results (blood sugar) with those obtained previously (organ weights and cell levels) are in the same sense (increase in treated with dexamethasone and ACTH in the absence secretion of melatonin compared to those treated in the dark). The role of melatonin in the maintenance of blood glucose has been discussed in several works. It has been shown that prolonged young affects the nocturnal secretion of melatonin (Röjdmark and Wetterberg, 1989). The blindness, which alters the circadian rhythm of melatonin, did significantly increase the glucose levels in rats (Benson and Daniel, 1990). In vitro studies led by (Gorray *et al*., 1979). Rat's show that incubation of pancreatic tissue with a global epiphysis extract leads to increased insulin secretion (Bailey *et al.,* 1974). The melatonin in vitro increased the rate of pancreatic glucose. Controversies noted by many authors agree, in fact, with the effect of hypoglycaemia and hyperinsulinemia (Csaba and Barath, 1971). The pinealectomy rats bulbectomisées increases the circulating level of glucose, glucagon and reduced that of insulin. This suggests that the pineal is necessary in maintaining normal levels of these two hormones (Gorray *et al*., 1979). Exogenous melatonin dose-dependent increases the level of glucose circulating in the ass in pigeons (John *et al*., 1971). And rats but has no effect on blood glucose levels in hamsters and in the male rat (Fed man, and Lebovitz, 1972). Show that melatonin increases the in vitro pancreatic glucose levels in hamsters. Our results confirm that the pineal gland, through its main melatonin secretion, can limit the hyperglycaemic action of glucocorticoids induced by

injection of synthetic ACTH or dexamethasone probably by inhibiting the peripheral level (pancreatic tissue or adipose tissue). We also suggest that melatonin has an effect on carbohydrate metabolism is probably exercised through control or modulation of somatostatin. Failure to control this hormone may directly affect glucose metabolism and hinder the secretion of Langerhans cells. This hormone (somatostatin) used in therapy seems to improve diabetes. Its use would be theoretically shown, since decrease glucagon levels, hyperglycaemic hormone, and the rate of growth hormone, diabetogenic hormone (Davidson, 1987).

CONCLUSIONS

In our preliminary study is to support a multidiagram highlighting the interaction between pineal gland (melatonin) and nuero-immuno-corticotrope system and impact of these regulatory systems of homeostasis on carbohydrate metabolism, we found that:

Direct solicitation of the corticotrope axis by administration of synthetic ACTH, in the absence of melatonin secretion leads to an increase in the weight of lymphoid organs (spleen and thymus).

The increase in lymphocyte proliferative response and significant increase in blood sugar.

Dexamethasone, for against, despite its inhibitory effect on the corticotrope axis at pituitary level, generated the same positive effect on the immune system and blood sugar but this action is less compared to that of ACTH. This suggests that apart from the corticotrope axis, other glandulortropes and / or non glandulortropes axes appear to be involved in the increase in weight (spleen and thymus), the proliferative response and glucose.

Based on bibliographic data, we suggested that the growth hormone axis would have a wide scope in these changes.

The combination of the second type of treatment that is photoperiodic regime D24; that is, the solicitation of the pineal gland has a restorative effect limiting the action of the corticotrope axis and / or growth hormone.

We suggest that melatonin, in addition to his work glandulotrope (adrenal, thyroid) could exert direct effects on peripheral organs (thymus, pancreas, adipose tissue) limiting the hyperglycemic action of this or such hormone.

We can also assume that the insulin control (glycemic) by melatonin could be done by control or modulation of somatostatin, which recalls exerts a negative effect on insulin (Davidson, 1987). Glucagon and growth hormone increases the sugar in the blood.

The levels of probable actions of melatonin on carbohydrate metabolism:

The regulation of glucose metabolism is subject to direct or indirect action by melatonin considering the neuro-immune interaction adrenocorticotropic (adaptive appearance) and growth hormone, the action of their hormones on the immune system and glucose metabolism.

Melatonin acts by modulating the secretion of meadows somatostatin and corticotrophin releasing hormone (CRH).

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APPENDICES

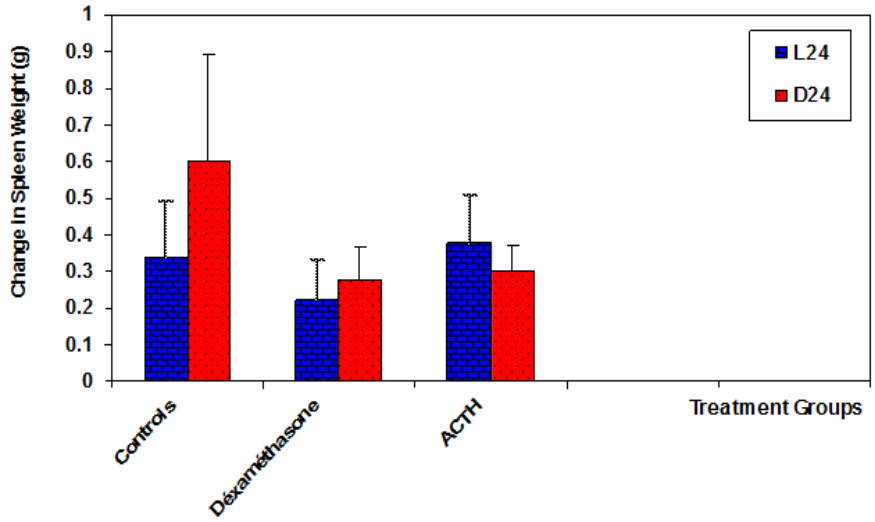

Figure 1: Change in Spleen Weigh t (g) of Rabbit treatment Intramuscular Administered 100 mg/ml/day + Light (L24) of ACTH. Group Three was administered 10 mg/Kg/day + Dark (D24) of Dexamethasone. Group Four was administered 100 mg/Kg/day + Light (L24) of ACTH. Group Five was Administered 10 mg/Kg/day+ Dark (D24) of Dexamethasone. After 10 days of Treatment. Values are given as Mean ± SD for Group of 5 Animals each Significant Difference: * Compared to Controls (*P≤0.05).

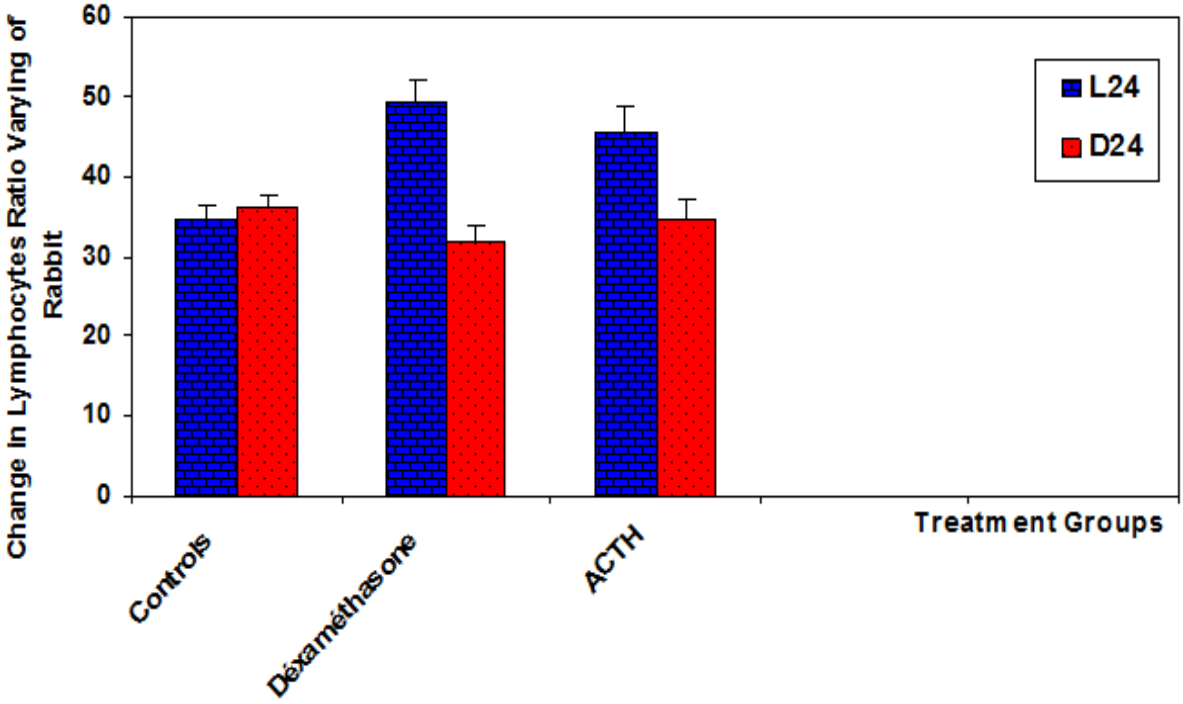

Figure 2: Change in Lymphocytes Ratio Varying of Rabbits Treatment Intramuscular Administered 100 mg/ml/day + Light (L24) of ACTH. Group Three was administered 10 mg/Kg/day + Dark (D24) of Dexamethasone. Group Four was administered 100 mg/Kg/day + Light (L24) of ACTH. Group Five was Administered 10 mg/Kg/Day+ Dark (D24) of Dexamethasone after 10 days of Treatment. Values are given as Mean ± SD for Group of 5 Animals Each Significant Difference: * Compared to Controls (*P≤0.05).

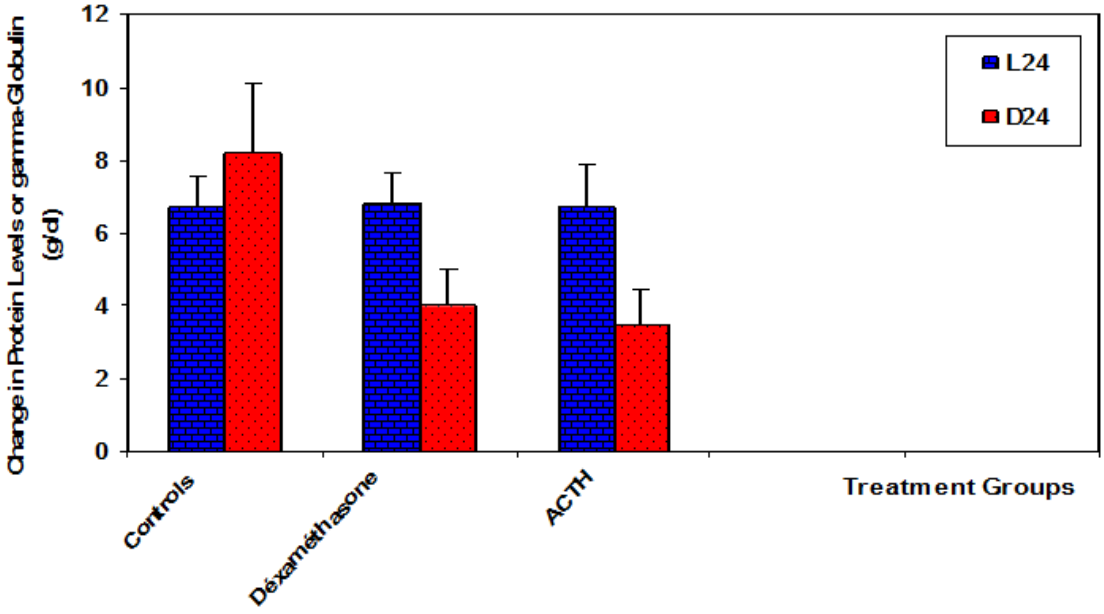

Figure 3: Change in Protein Levels or δ Globulin (g / dl) of Rabbits Treatment Intramuscular Administered 100 mg/ml/day + Light (L24) of ACTH. Group Three was administered 10 mg/Kg/day + Dark (D24) of Dexamethasone. Group Four was administered 100 mg/Kg/day + Light (L24) of ACTH. Group five was Administered 10 mg/Kg/day+ Dark (D24) of Dexamethasone. After 10 days of Treatment. Values are given as Mean ± SD for Group of 5 Animals each Significant Difference: * Compared to Controls (*P≤0.05).

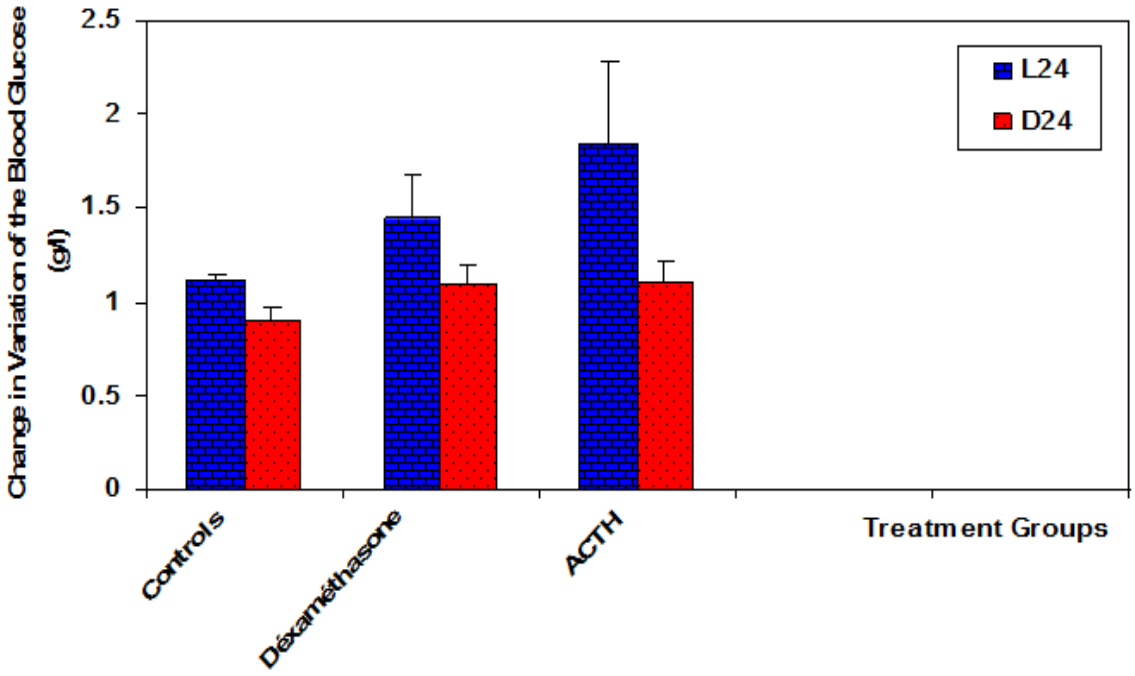

Figure 4: Change in Variation of the Blood Glucose (g / l) of Rabbits Treatment Intramuscular Administered 100 mg/ml/day + Light (L24) of ACTH. Group Three was administered 10 mg/Kg/day + Dark (D24) of Dexamethasone. Group Four was Administered 100 mg/Kg/day + Light (L24) of ACTH. Group Five was administered 10 mg/Kg/day+ Dark (D24) of Dexamethasone. After 10 days of Treatment. Values are given as Mean ± SD for Group of 5 Animals Each Significant Difference: * Compared to Controls (*P≤0.05).