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## **THE EFFECT OF DEXAMETHASONE AND PREDNISOLONE ON CALCIUM AND SODIUM CONCENTRATIONS IN MALE RABBITS**

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### **ABSTRACT**

*This article was conducted to investigate the side effects of dexamethasone and prednisolone drugs in a dose (0.2 mg/kg) on calcium and Sodium in the *Lepus cuniculus domesticus* rabbits. Thirty domestic male rabbits, aged 7-9 months and their weights (1250 - 1500 g). The animals were randomly distributed into 6 groups and each group contains 5 rabbits. The first group (Control) was the control group where the diet was given with normal drinking water. The second group (A) was given Dexamethasone (0.2 mg/kg) with the diet and regular drinking water. The third group (B) was given Prednisolone (0.2 mg/kg) with the diet and regular drinking water. The fourth group (C) given the drug Prednisolone (0.2 mg / kg) and vitamin C with a concentration of (30 mg/kg) with the diet and regular drinking water. The fifth group (D) given the Dexamethasone (0.2 mg/kg) and vitamin C with a concentration of (30 mg/kg) with the diet and regular drinking water. The sixth group (E) given dexamethasone and prednisolone together with a concentration of (0.2 mg/kg) and vitamin C with a concentration of (30 mg /kg) with the diet and regular drinking water. The results showed a significant increase in calcium and sodium concentration compared with control group. The study showed that chronic use and high doses of these drugs cause obvious damage to the kidneys and impede the process of glomerular filtration and this leads to the loss of balance between the elements in the body.*

**Keywords:** Prednisolone, Dexamethasone, Calcium, Sodium.

## **I. INTRODUCTION**

Natural Glucocorticoids are produced from the adrenal glands and function on many physiological functions in the body that are essential for sustaining life [1]. Glucocorticoids and their biologically active synthetic derivatives differ in their physiological function within the body and synthetic corticosteroids are used as an alternative therapy when the production of natural hormones by the adrenal gland decreases [2]. Complications of steroid therapy depend on the duration of the treatment and the size of the dose and The long-term use of steroid drugs causes many side effects, including diabetes, insulin resistance, hypertension, osteoporosis, hypothyroidism, lack of reproductive glands, retinopathy, gastritis and colitis [3]. Prednisolone is an active drug and can metabolize in a variety of tissues, including liver, lung, kidney, and skin [4-5]. Prednisolone is also used to treat a wide range of acute and chronic disorders of the body, including arthritis, asthma, allergies, hepatitis, adrenal glands, and some diseases blood, cardiac, neurological, and many inflammatory conditions [6]. Dexamethasone is a biologically active steroid drug [7]. Dexamethasone is used in many conditions such as rheumatoid arthritis, severe allergies, skin diseases, asthma, chronic obstructive pulmonary disease, adrenal insufficiency, It is taken through the vein, muscle or by mouth [8]. The kidneys are one of the most important organs to maintain the current internal stability of the body by regulating the balance of body fluids in terms of volume and concentration of different substances, where it works to create a state of balance between the incoming and outgoing electrolytes [9]. The ability of the kidney is concentrated in maintaining the total osmotic pressure of the body fluids and also the ability to modify and regulate the release of water and electrolytes such as sodium and calcium [10]. Controlling the concentration of urine by reducing or increasing the secretion and reabsorption of substances with large osmotic effect, especially sodium ions [11]. Patients with asthma and taking steroid drugs for a long time also suffer from osteoporosis and decreased levels of calcium in the blood because of inhibition of absorption of calcium in the intestine [12]. This study confirmed that steroid drugs inhibit osteoblasts and stimulate Osteoclasts, which, in turn, act on bone mineral resorption, as well as the release of calcium, which is depleted of the bone by the kidneys, thus reducing its level in the bones and inhibition of absorption in the intestine, leading to osteoporosis [13]. This study aimed to know the role of dexamethasone and prednisolone on calcium and sodium in the blood of male rabbits .

## II. MATERIALS AND METHODS

### A. *Experimental Animals and Design*

The experiment included 30 male *Lepuscuniculuadomestica* rabbits obtained from the Veterinary Hospital of the Ministry of Agriculture - Samarra Agriculture Division, aged 7-9 months and their weights ranged 1250 - 1500 g Distributed were randomly assigned to 6 groups, 5 rabbits per group, control group: I returned control group and standard diet with drinking water, group A: Dexamethasone (0.2 mg/B.W) with standard diet and drinking water, group B: Prednisolone (0.2 mg/B.W) with standard diet and drinking water, group C: Prednisolone (0.2 mg/B.W) with vitamin C (30 mg/B.W) with standard diet and drinking water, group D: Dexamethasone (0.2 mg/B.W) with vitamin C (30 mg/B.W) with standard diet and drinking water, group E: Dexamethasone (0.2 mg/B.W) and prednisolone (0.2 mg/B.W) with vitamin C (30 mg/B.W) with standard diet and drinking water. The experiment lasted for 21 days and for all groups. Doses were taken supposition according design experience.

### B. *Drugs used in the study*

- Dexamethasone: This drug was used in the form of pills and was manufactured by Samarra company for the manufacture of medicines and medical supplies - Samarra / Iraq, available in local pharmacies, the concentration of this drug 0.5 mg . The pills were well milled and dissolved with distilled water mediated by Gavage tube on a daily basis.
- Prednisolone : This drug was used in the form of pills and was manufactured by Samarra company for the manufacture of medicines and medical supplies - Samarra / Iraq, available in the local pharmacies and the concentration of this drug 5 mg . The pills were well milled and dissolved with distilled water mediated by Gavage tube on a daily basis .
- Vitamin C: This vitamin was used in the form of pills 500 mg available in local pharmacies, and manufactured by company : Basic Nutrition UAE. The pills was well milled and dissolved with distilled water and then orally injected by Gavage tube daily .

### C. *Blood sampling*

After 21 days of experimentation, the animals were kept for 20 hours and then anesthetized with chloroform. The blood samples then obtained directly from the heart in the Cardiac puncture. 8-10 ml of blood, were obtained and placed in Test tubes free of anticoagulants left for about a quarter of an hour at room temperature (25°C) and placed In the centrifuge

at 3000 / rpm for 15 minutes and then serum were moved to separate tube and kept in new clean plastic tubes and kept at (-20 °C) until required hormones tests were carried out.

#### D. Study Parameters

- Calcium was estimated using ELISA Kit (Biomerieux) according to manufacturer instructions [14].
- Sodium was estimated using ELISA Kit (Spainreact) according to manufacturer instructions [14].

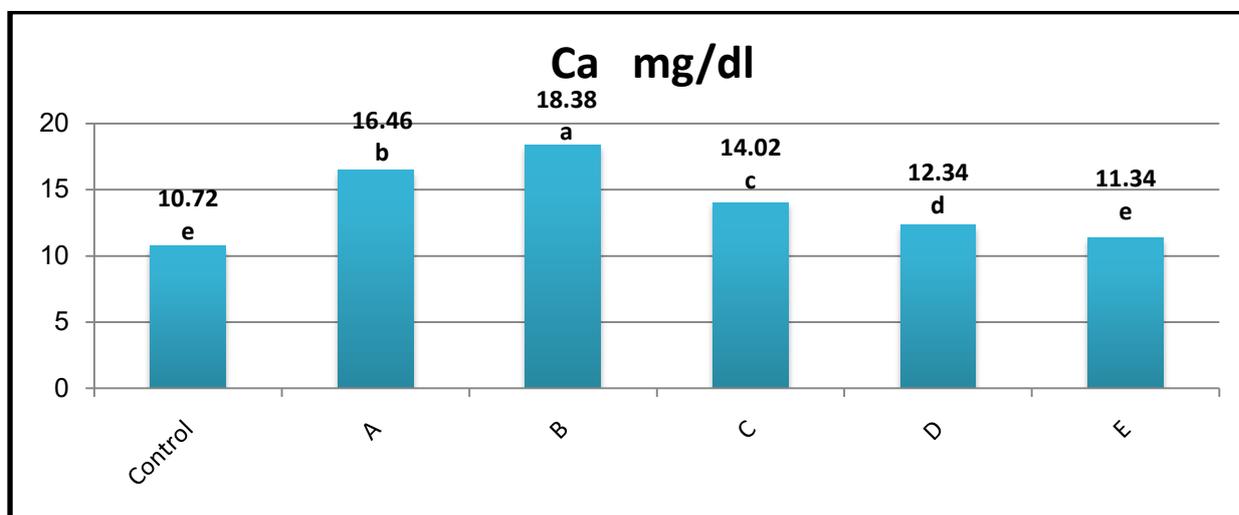
#### E. Statistical analysis

The results were statistically analyzed using the Minitab program . In order to extract the differences between the experimental groups with emphasis on these differences by extracting the standard error (Stander Error) Statistical analyzes were conducted according to Duncan were identified the probability level ( $P \leq 0.05$ ).

### III.RESULTS

#### a) Concentration of Calcium

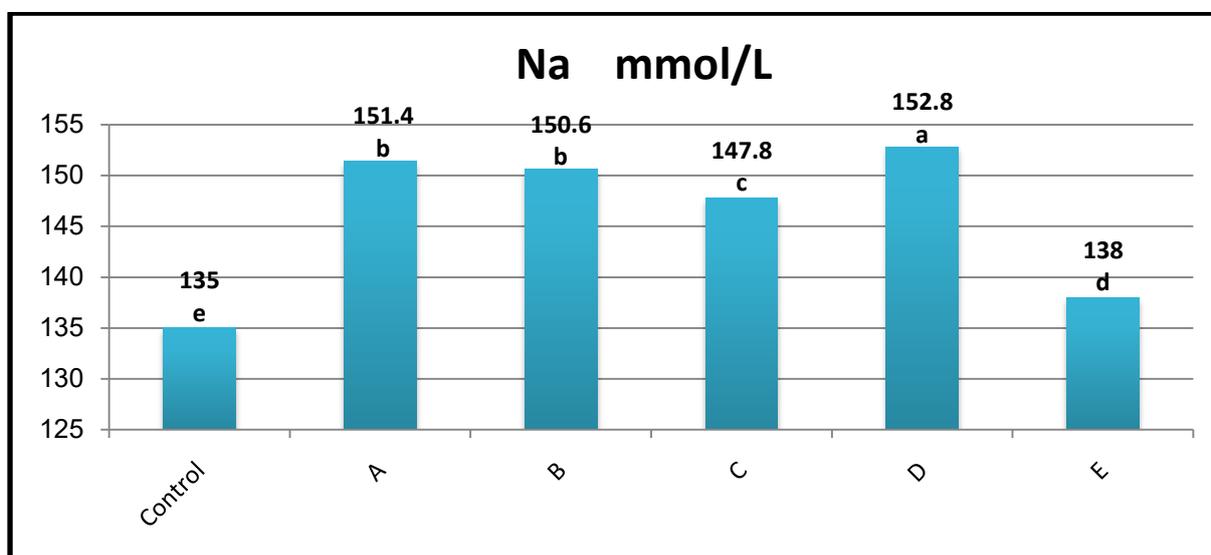
The results of current study, as shown in “Fig. 1”, showed a significant increase( $P \leq 0.05$ ) in all groups A, B, C, D, ( $16.46 \pm 0.5$ ) ( $18.38 \pm 0.1$ ) ( $14.02 \pm 2.2$ ) ( $12.34 \pm 2.5$ ) mg/dl respectively compared with control group ( $10.72 \pm 0.5$ ) mg/dl and not significant difference in group E, ( $11.34 \pm 0.1$ ) compared with control group ( $10.72 \pm 0.5$ ) mg/dl.



**Fig. 1.**The calcium concentrations in the studied doses compared with control group.

## b) Concentration of Sodium

The results of current study, as shown in “Fig. 1”, showed a significant increase ( $P \leq 0.05$ ) in all groups A, B, C, D, E, ( $151.40 \pm 1.1$ ) ( $150.6 \pm 1.1$ ) ( $147.80 \pm 0.8$ ) ( $152.80 \pm 0.8$ ) ( $138 \pm 1.5$ ) mmol/L respectively compared with control group ( $135 \pm 0.7$ ) mmol/L .



**Fig. 2.** The sodium concentrations in the studied doses compared with control group.

## IV. DISCUSSION

The direct effect of steroid drugs on the inhibition of absorption of calcium in the intestine increase the subtract of calcium through the kidney, which leads to lower levels in the blood and this decrease in turn raises the levels of parathyroid hormone to compensate for the deficiency and increase levels of calcium in the blood through stimulation Osteoclasts work to release bone and thus release calcium and increase blood levels [15-16]. This may be attributed to the non-affected some groups treated with steroid drugs in addition to the role of increasing the secretion of calcitonin hormone regulates the levels of calcium in the body. Vitamin C reduce the side effects caused by steroids and play a role in helping to maintain bone mass and also bone formation [17]. This studies suggest that patients use steroids in low doses or high doses for a period of time may cause them osteoporosis and increase the risk of fracture because it prevents the absorption of calcium in the intestine, resulting in the secretion of Parathyroid hormone to compensate for the lack of calcium and also, calcium blood levels will increase as a result of stimulating osteoclasts cells to resorption of bone minerals, as well as increasing kidney stones, leading to osteoporosis [18].It may be attributed to the work of steroidal drugs to increase the water subtraction and increase the rate

of glomerular filtration in spite of an increase in the retention of sodium and increase absorption sodium in the intestine and may also be formed stones in the kidney as a result of increased urinary calcium and uric acid and this increases the concentration of sodium in the blood for not subtract out of the kidneys [19]. It is also due to the fact that steroid drugs have a direct effect on Osteoblasts by inhibiting their action and stimulating Osteoclasts by increasing the production of Parathyroid hormone and this increases the level of calcium in the blood and thus increase the Subtract renal addition to the inhibition of absorption in the intestine Which is gradually decreasing its level and therefore lead to osteoporosis, where dietary supplements of vitamin D and calcium should be taken to compensate for the shortage due to steroid drugs [20]. And the increase in the levels of serum minerals is the result of the effect of steroidal drugs on the balance of minerals in the bones, which works to reduce the activity of bone marrow cells and increase the regulation of osteoclastogenesis and osteolysis, which stimulates the resorption of the matrix and the release of metal in the blood [21]. Steroidal drugs work to retain salt without water retention and this is an important factor for increasing sodium concentration in the blood [22]. Steroidal drugs may affect the functions of some organs such as kidneys and liver and directly affect the glomerular filtration process by holding the sodium through the renal tubules and increasing the secretion of potassium in the blood, therefore, the sodium is transfer to the blood, where its concentration is increasing [23]. Due to the role of vitamin C in the high concentration of sodium through the work of this vitamin being an antioxidant, which plays a synergistic role with steroid drugs and thus increases the absorption of these drugs and transfer into the cells and effectively work on other systems of the body, kidney and liver [24]. And chronic use of steroids may lead to osteoporosis due to the depletion of bone minerals and their transfer to blood, including sodium, and thus subtract from the kidneys, causing sodium deficiency. Consequently, osteoporosis [25]. The differences we observe in totals may be due to the amount of active substance in drugs absorbed by the body from intestinal and its pharmacological movement.

## V. CONCLUSIONS

The study showed that the chronic use of these drugs and high doses cause clear damage to some organs of the body, including kidneys, leading to disruption of functions and as well the effective role of vitamin C in reducing the side effects caused by steroid drugs and improve the performance of kidney function and it also lead to disease Osteoporosis.

## REFERENCES

- [1] Becker, D.E. Basic and clinical pharmacology of glucocorticosteroids. *Anesthesia progress*, 2013, **60,1**: 25-32.
- [2] Catteral, W.A., Goodman, M.K.,Gildmans. The pharmacological basis of therapeutics 11 th edition. Chapter 14. 2006.
- [3] Al-muswie, R.T. Effect of long term Administration of hydrocortisone on some organs in females rats. *Journal of Univesity of Thi-Qar*, 2017, **12,4**: 34-44.
- [4] Borresen, S.W.Klose, M., Baslund, B., Rasmussen, A.K., Hilsted, L., Friis-Hansen, L., and Feldt-Rasmussen, U.. Adrenal insufficiency is seen in more than one-third of patients during ongoing low-dose prednisolone treatment for rheumatoid arthritis. *European journal of endocrinology*, 2017, **177,4**: 287-295.
- [5] Borlak, J., Van Bommel, F., Berg, T. N-acetylcysteine and prednisolone treatment improved serum biochemistries in suspected flupirtine cases of severe idiosyncratic liver injury. *Liver International*, 2018, **38,2**: 365-376.
- [6] Francisco, G.E., Honigberg, I.L., Stewart, J.T., Kotzan, J.A., Brown, W.J., Schary, W.L., andShah, V.P. In vitro and in vivo bioequivalence of commerical prednisone tablets. *Biopharmaceutics & drug disposition*, 1984, **5,4**: 335-344.
- [7] Valenzuela, O.A., Jellyman, J.K., Allen, V.L., Holdstock, N.B., and Fowden, A.L. Effects of maternal dexamethasone treatment on pancreatic  $\beta$  cell function in the pregnant mare and post natal foal. *Equine veterinary journal*, 2017, **49,1**: 99-106.
- [8] Bonfiglio, V.,Reibaldi, M., Fallico, M., Russo, A., Pizzo, A., Fichera, S., and Longo, A. Widening use of dexamethasone implant for the treatment of macular edema. *Drug design, development and therapy*, 2017, **11**: 2359-2372.
- [9] Slagman, M.C.,Sinkeler, S.J., Hemmeler, M.H., Waanders, F., Vogt, L., Kluin-Nelemans, H.C., and Laverman, G.D. Erythropoietin is reduced by combination of diuretic therapy and RAAS blockade in proteinuric renal patients with preserved renal function. *Nephrology Dialysis Transplantation*, 2010, **25,10**: 3256-3260.
- [10] Harrison, S., Jameson, J., Loscalzo, J. Harrison's Nephrology and> Acid-Base Disorders. *Me Graw Hill*, 2010, 322.

- [11] Passmore, R. Physiology of the kidney and body fluids. *Quarterly Journal of Experimental Physiology and Cognate Medical Sciences*, 1963, **48,4**: 439-440.
- [12] Sutter, S.A., Stein, E.M. The skeletal effects of inhaled glucocorticoids. *Current osteoporosis reports*, 2016, **14,3**: 106-113.
- [13] Piemontese, M., Onal, M., Xiong, J., Wang, Y., Almeida, M., Thostenson, J.D., O'Brien, C.A. Suppression of autophagy in osteocytes does not modify the adverse effects of glucocorticoids on cortical bone. *Bone*, 2015, **75**: 18-26.
- [14] Tietz, N.W. "Fundamentals of Clinical Chemistry," Saunders, 4th ed, Philadelphia, 2006 :984-987.
- [15] Mazziotti, G., Formenti, A.M., Adler, R.A., Bilezikian, J.P., Grossman, A., Sbardella, E., and Giustina, A. Glucocorticoid-induced osteoporosis: pathophysiological role of GH/IGF-I and PTH/VITAMIN D axes, treatment options and guidelines. *Endocrine*, 2016, **54,3**: 603-611.
- [16] Pavlov, S.B., Babenko, N.M., Kumetchko, M.V., and Litvinova, O.B. Violations of cell-molecular mechanisms of bone remodeling under influence of glucocorticoids. *Regulatory Mechanisms in Biosystems*, 2018, **1,9**. 1-10.
- [17] Carr, A.C., and McCall, C. The role of vitamin C in the treatment of pain: new insights. *Journal of translational medicine*, 2017, **15,1**: 77-80.
- [18] Sambrook, P.N. How to prevent steroid induced osteoporosis. *Annals of the Rheumatic Diseases*, 2005, **64,2**: 176-178.
- [19] Lorraine, I.M.K., John, A.C. Physiologic and pharmacologic effects of corticosteroids. *Holland-Frei Cancer Medicine*, 2013, 34-67.
- [20] Compston, J. Glucocorticoid-induced osteoporosis: an update. *Endocrine*, 2018, **61**: 7-16.
- [21] Cherian, K.E., Kapoor, N., Paul, T.V. Glucocorticoid-induced osteoporosis. *Indian journal of endocrinology and metabolism*, 2017, **21,5**: 652-660.
- [22] Tien, K.J., Wang, S.Y., Yang, C.Y., and Chou, C.W. Hyponatremia-associated coma caused by glucocorticoid replacement for adrenal crisis in an unrecognized central

diabetes insipidus patient. *The Kaohsiung journal of medical sciences*, 2013, **29,9**: 519-520.

[23] Al-khayat, T.H., Al-gazally, M.E., Aemma, M.A.A. Serum Electrolytes and Minerals Status in Asthmatic Patients on Corticosteroids. *Medical Journal of Babylon*, 2010, 7.3-4: 359-369.

[24] Annex, I. "Summary of product characteristics," *Section*,2014, **4** : 2-8.

[25] Polak, P., Husa, P., Kubesova, H.M. Severe osteoporosis-the story of chronic medication-related hyponatremia. *Vnitřní lékařství*, 2016, **62,2**:152-156.