Original article

The Prospected Health hazards of Wide uptake of Dexamethasone on Wister rat *Rattus norvegicus* (Wister, 1906)

Asma, A. Ahmed*, Ragda, E. Merghany and Anwer, A. Hamad

Department of Biology and Biological Technology, Faculty of Science and Technology, Al Neelain University,Khartoum

ARTICLE INFO

Article history:
Received 2016 December 25th
Reviewed 2017 January 15th
Accepted 2017 April 10th

Keywords
Dexamethasone
Hazards
Anatomy
Histopathology
Lung
Wistar rat
Rattus norvegicus

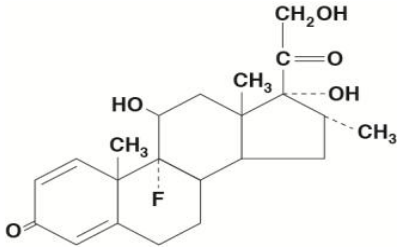
Abstract

The study was designed to assess the hazard of using synthetic glucocorticosteroid Dexamethasone without medical supervision. The study was done in Wister albino rat; Rattus norvegicus (Wister, 1906) of body weight range 91.0 - 137.0 g. The lab-retained rats were randomly divided to three groups according to dexamethasone daily oral ingestion. Groups 1 and 2 were given oral dose of 0.75mg/Kg. body weight and 1.5 mg/kg. body weight, respectively. The third group ingested distilled water. The experiment was terminated after 6 weeks. Rats then were scarified and dissected for anatomical and tissue collection for histological investigation. Rats treated with the above doses of dexamethasone experienced the following: changes in rats' behavior (aggressiveness), high heart palpitations, short breathing and wheezing. Morphological changes were expressed as skin bruises and hair falling and loss in body mass as well as pronounced damages in the anatomy and histology of the lungs.

***Corresponding author**; asmabdelrahmanahmed780@gmail.com

Introduction

Dexamethasone is a synthetic glucocorticosteroid, which has minimal mineralocorticoid activity. It is a potent anti-inflammatory drug with 25-50 times the potency of hydrocortisone and is up to sixteen times as potent as prednisolone. (Kara *et. al.,* 2007). It carries generic name dexamethasone and brand names: Decadron®, Dexasone®, Diodex®,Hexadrol®, and Maxidex®) (International Myeloma Foundation, 2006). The molecular formula is C22H29FO5 and the molecular weight is 392.47. It is designated chemically as 9-fluoro-11β,17, 21-trihydroxy-16α-methylpreg na-1,4-diene,3,20-dione and the structural formula is



Dexamethasone is a member of the glucocorticoid hormones. They are steroids but, unlike the "anabolic" steroids, these are "catabolic" steroids designed to break down stored resources of fats, sugars and proteins. So they may use as a fuel at the time of stress. Glucocorticoid hormones are produced naturally by the adrenal glands (International Myeloma Foundation, 2006).

Naturally occurring glucocorticoids, hydrocortisone, which also

have salt-retaining properties, are used as replacement therapy in adrenocortical deficiency states. Their synthetic analogs are primarily used for their potent anti-inflammatory effects in disorders of many organ systems. Glucocorticoids cause profound and varied metabolic effects. In addition, they modify the body's immune responses to diverse stimuli. Dexamethasone effects include activation of glucocorticoid receptors in the medulla, inhibition of central production of prostaglandins, and/or inhibition of the release of endogenous opioids (Lingaiah, et al. 2012).

Dexamethasone, which was given different vernacular names; was recently excessively used by young ladies as cosmetic means to gain body weight. This drug is distributed by local and non-medical or pharmacological dealers. The present study was carried out to evaluate the expected hazards of such unprecedented practice. This uncontrolled Dexamethasone uptake hazards were assessed on the experimental albino Wister rats *R. norvegicus*

Materials and Methods

Experimental Materials

Dexamethasone tablets were provided by an Official Private Drug Preparation Factory as SAMFASONE TABLETS of 1.5 mg. dose. Albino Wister rats, *Rattus norvegicus* (Wister, 1906), were brought from the Faculty of Veterinary Medicine/ University of Khartoum.

Experimental Design

The rats of body weight range 91.0 - 137.0 g. and body length range 13.0 - 15.2cm and retained in animal cages of dimensions 39 cm x 32 cm X 22 cm. The rats were retained for period of 7 days before the start of the experiment to urge them to cope with the lab condition. The rats were fed on diet prepared for experimental animals contain essential elements as follows: 16% protein, 3.0% fat, 60% carbohydrate, and 21% water and o.4% vitamins and minerals. Rats were fed for 6 weeks at twice intervals per day. Rats were divided to three groups, after adapted to the lab condition, as follows:

Group 1: were given the low-dose of dexamethasone (0.75 mg\ kg. body weight\day).

Group 2: were given the high-dose of dexamethasone (1.5mg\Kg. body weight\day).

Group 3: controls were ingested distilled water.

The doses of dexamethasone were calculated according to the rat's body weight. The dose was administered orally. The controlled group was given distilled water instead. The experiment continued for six weeks. The rats' conditions were checked daily and notes were taken for any changes concerning the morphology, behavior, or any abnormalities.

Rats were sacrificed by the end of the 6 weeks; dissected and general anatomy was examined. Tissue samples from the lungs were collected randomly from each experimental group. Tissues were prepared for histological examination using standard paraffin wax impeding method and hematoxylin eosin staining.

Results

General Observations

Administration of excess dexamethasone was illustrated by some aggressive behaviour displayed by treated rats especially those under high dose (1.5 g/kg. body weight.). All treated rats exhibited short breathing, wheezing and difficulty of respiratory inhalation. They also exhibited an increase in heart palpitation. In addition, all the treated rats show low appetite.

Morphological changes were observed in some of treated rats. The changes were confined to skin and eyes. These included skin dryness and bruises that lead to falling of skin hair (plate 1). The eyes became constricted and dry. In all the treated rats, loss in body weight and thinning of muscles was evident.

Plate (1). Bruises and falling of skin hair (↑) due to excess use of dexamethasone

The Dexamethasone impact on survival rate

The rat mortality was assessed after treatment with dexamethasone for 6 weeks. The frequency of mortality was calculated from the survival rate i.e. as percentage number of survival rats from the total number of experimental rats. Rate of mortality calculated as 1- survival rate. Results were recorded in Table (1).

Table (1) Frequency of mortality (%) of experimental rats treated with dexamethasone for 6 weeks.

The duration (weeks)	The number of survived rats/ total	Frequency of mortality (%)
1st	18/18	0
2nd	18/18	0
3rd	14/18	22.2
4th	13/18	27.8
5th	10/18	44.5
6th	10/18	44.5

The dexamethasone impact on the general anatomy of treated rats

The anatomical changes were confined to the lungs, liver, the thyroid and adrenal glands. The rats of treated with 0.75 g/kg body weight showed collapse and shrinkages of the lung as shown in plate (2).

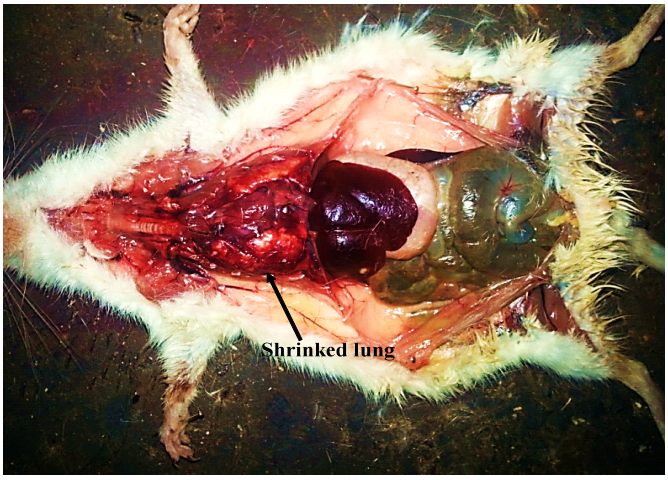


Plate (2). Collapse and shrinkages in the lung of rat treated with 0.75 g/kg body weight for 6 weeks

Rats treated with 1.5 g/kg body weight showed further changes in the external structures of the lung presented by bleeding and polycystic lungs as shown in plate (3).

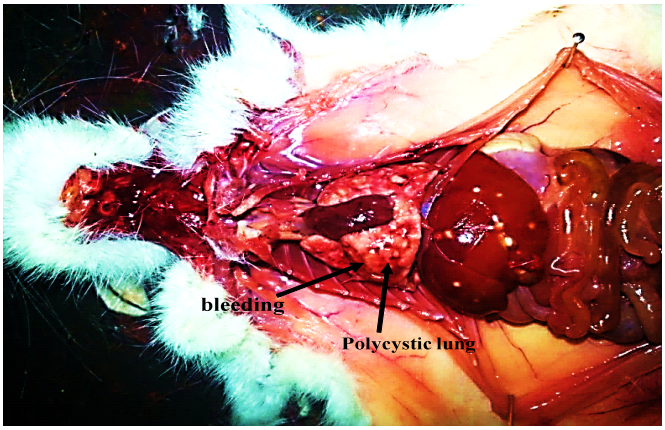


Plate (3) Changes in the external structures of the lung presented by polycysts on lung of a rat treated with 1.5 g/kg body weight after 6 weeks.

The Dexamethasone Impact on lung Histology

The histological structure of the lung of untreated (control) rats exhibited no changes in the basic histological structure of the lung as seen (Plate 4).

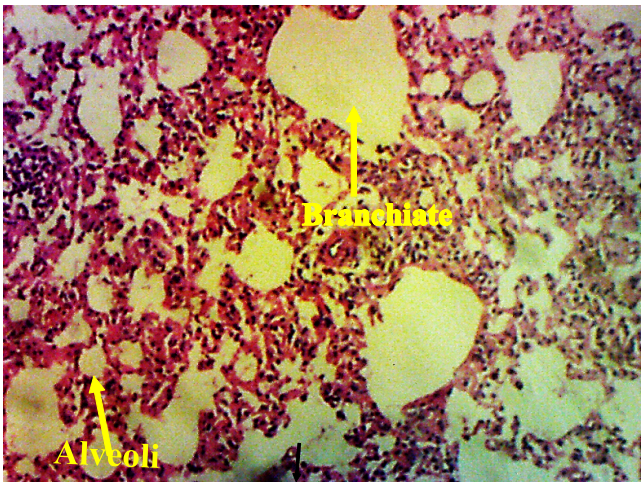


Plate (4). Histological structure of lung of rats (control) after 6 weeks. (H.E. X40).

The histological appearance of the lung of treated rats with

0.75g/kg B. W. dexamethasone showed hyperplasia and infiltration of interstitial cell to alveolar lumens and collapse alveoli as demonstrated in plates 5.1 and 5.2.

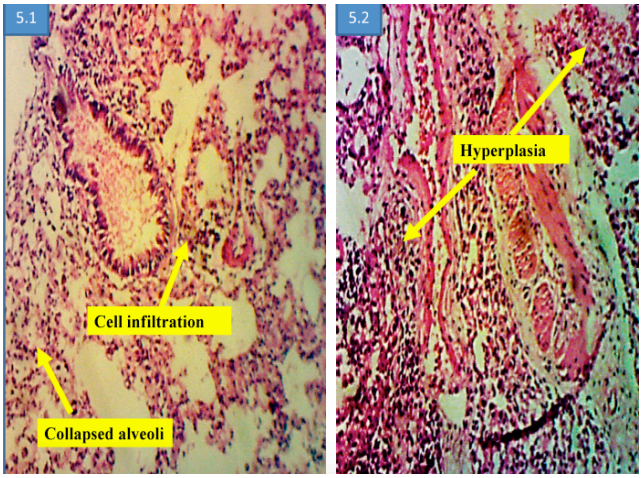
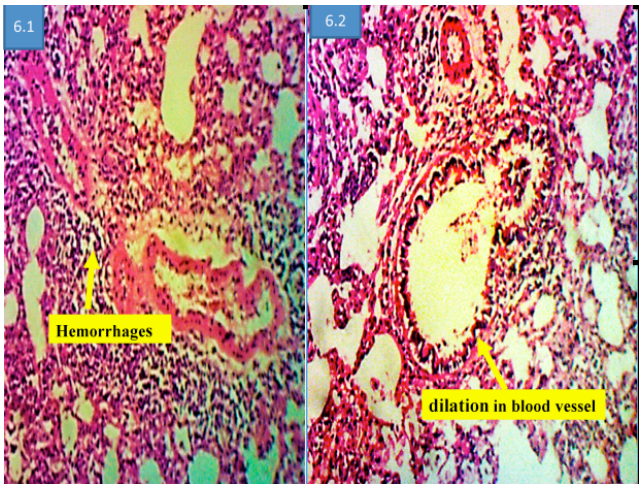


Plate (5.1 and 5.2) the histological structure of lung treated rats with 0.75g./kg B. W. dexamethasone for 6 weeks. (H.E. X40).

Besides, the changes caused by 0.75g./kg B. W treated by 1.5g. /kg B. dexamethasone dose show further damages exhibited with dilation in blood vessels, and frequent hemorrhages.



Plates (6.1 and 6.2). The histological structure of treated rats showing damages were exhibited with dilation in blood vein, and frequent hemorrhages. (H.E. X40).

Discussion and conclusions

The damage in the different organs recorded in the present study was similar to that reported by a number of previous studies. According to Fussell and Kellyb (1991), 2.5 mg/day / kg dexamethasone treatment resulted in reduced food intake and rapidly inhibited whole-body and lung growth in young growing rats. In addition, Ribeiro *et al.,* (1993) showed that in vitro and *in vivo* use of Dexamethasone affected a number of different cellular and physiological responses. However, Zhang *et al*., (2007) proved that when intravenous injection of dexamethasone was administered on lung the following therapeutic effects became evident: most lung tissue was restored and there was slight edema of the interstitium and alveolar space. The results of the present study are in agreement with the findings of Barreiro *et al*. (2010), who reported that dexamethasone treatment was accompanied with acute lung and liver inflammations induced by microcystin-LR.

Lingaiah *et al.,* (2012), reported that ingestion of dexamethasone resulted in many side effects including reduction in growth of children, acne and fragile thin and easy bruising skin. Khalida, and Shaya (2011) studied two groups of female rabbits, each consists of seven females which received a daily intramuscular injection of dexamethasone sodium phosphate (1.5 mg/kg b. w.) for 15 days. Their findings showed changes in rabbits' skin colour, which became pale yellow, coupled with weakness or breathlessness, inflammation of the heart in association with heart attack and certain inflammatory muscular disorders and inflammation of the eyes.

The results of the present study are in agreement with the findings of many previous studies that reported hazards and drastic damages in the vital biological systems by the wide use of dexamethasone. Yet, Barreiro *et al*. (2010) showed that dexamethasone treat acute lung and liver inflammation induced by microcystin-LR. Locally, dexamethasone used by a wide sector of young women as means of weight gaining. This depends on the fact that Dexamethasone increases triacylglyceride levels, caused an imbalance in lipid metabolism that leads to hyperlipidemia (Singh and Reddy, 2015). In addition, dexamethasone sodium phosphate injection was accompanied by Stomach upset, headache, dizziness, menstrual period changes,

trouble sleeping, increased appetite and weight gain (WebMD, LLC 2016).

Recommendations

*Dexamethasone uptake must be under supervision of pharmaceutical and medical authorities.

*Control the delivery in site out pharmacies specials in cosmetic shop and markets

*More awareness about the expected hazards caused by uptake of dexamethasone without medical supervision and consultant.

Acknowledgements

We express our gratefulness and profound gratitude to Al Neelain University, Faculty of Science and Technology, Department of Biology and Biological Technology for sustain the experimental lab condition and the support of department laboratories staff and instrumentations.

References

Barreiro, E .J, Valença, S. S, Saldiva, P. H.N, Faffe, D. S, and Zin, W. A, (2010). Can lassbio 596 and dexamethasone treat acute lung and liver inflammation induced by microcystin-LR? *J. Toxicon*. 5, 604 – 612.

Fussell, J. C., Kellyb, F. J. (1991). Effects of dexamethasone on lung protein turnover. *Biochemic. J.*, 8, 93-97.

International Myeloma Foundation (2006). Understanding Dexamethasone and Other Steroids. Published by International Myeloma Foundation, North Hollywood, USA: 8-12.

Kara. A. (2007). Dexamethasone; An all-purpose Agent, *Australian Anesthesia* 65-70.

Khalida, I., Shaya, I., (2011). The effects of dexamethasone on the histology and histochemistry of thyroid gland in female rabbits. *J. Med. Sci.,* 9: 209-217.

Lingaiah .H.B, Thamaraiselvan .R, Periyasamy .B.M, (2012). Dexamethasone induced alterations in lipid peroxidation, antioxidants; membrane bound atpase in Wister albino rats. *Int. J. Pharm. Sci.* 4(3), 497-499

Ribeiro, S, Tandon ,R, Grunhaus, L, and Greden, J. F.,(1993). Dexamethasone suppression of corticosteroid secretion: evaluation of the site of action by receptor measures and functional studies. *Am. J. Psychiatry*. 150, 1618–1629.

Singh, K. V. and Reddy, K. R. (2015). Management of Diabetes mellitus and its complications by Lodhra: A review Article. https://www.researchgate.net/publications/296547038

William. W. D, Fengqion L., Shan S. W., Cindy .X.M, Gupta .S, T Jin .T, Spaner .D, Krylov, S. N, Zhang .Y, Ling .W and Yang B. B, (2014). Inhibition of Dexamethasone - induced fatty Liver development by reducing mir-17-5p levels. *The American Society of Gene and Cell Therapy*, 1-12.

WebMD, LLC (2016). Dexamethasone sodium phosphate injection: Uses, Side Effects, Interactions, Pictures, Warnings and Dosing – WebMD.

Zhang, X. P, Zhang .L, Wang .Y, Cheng, Q. H, Wang, J. M, Cai. W, Shen, H. P and Cai .J. (2007). Study of the Protective Effects of Dexamethasone on Multiple organ injury in rats with severe acute pancreatitis . *J. Pancreas*. 8(4), 400-4001