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Review Article

Physiological And Histological Effects Of Dexamethasone:Literature Review Article

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ABSTRACT

Dexamethasone, a corticosteroid, exhibits similarities to a naturally produced hormone synthesised by the adrenal glands. It is commonly used as a replacement for this substance in situations where the body's synthesis is inadequate. The substance possesses the capacity to mitigate inflammation, encompassing symptoms such as swelling, heat, redness, and pain. It is frequently used in the management of particular forms of arthritis, dermatological conditions, haematological disorders, renal, ocular, thyroid, and gastrointestinal disorders, including colitis. Moreover, it is employed in the treatment of patients with severe allergies and asthma. Dexamethasone is also used for the therapeutic management of certain types of cancer. This scholarly essay presents a thorough examination of the notable physiological and histological changes caused by the administration of the dexamethasone drug. Numerous modifications generated by this medicinal substance have been reported by multiple researchers.

INTRODUCTION

1-Dexamethasone

Dexamethasone (Dex), alternatively referred to as Decadron, is a synthetic corticosteroid hormone characterised by an extended period of effective activity. Doctors frequently prescribe it for the treatment of inflammatory diseases due to its strong anti-inflammatory effects [1]. The aforementioned problems encompass arthritis, oedema, insufficiency of adrenal hormones, erythema of the skin, diminished responsiveness to adrenal hormones, asthma, and renal illnesses [2]. Dextran, a molecule with the therapy of asthma, rheumatoid arthritis, and several autoimmune illnesses, dextran, a molecule having the chemical formula C22H29FO5 with a molecular weight of

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392.5, is utilised [3]. A commonly seen form of dex is dexamethasone sodium phosphate, which is a solution with a biological half-life ranging from 36 to 72 hours. [4,5,6]. Dexamethasone has the capacity to pass through the placenta while being active and shows a comparable level of effectiveness [7]. The transfer of Dex from the mother to the foetus occurs quickly [8]. Studies on reproductive toxicity in rats, mice, hamsters, and rabbits have shown that dexamethasone causes various deformities in the embryo and foetus, such as skeletal defects, an enlarged cleft palate, decreased thymus, adrenal weight, abnormalities in the spleen, liver, kidney, and lungs, as well as growth suppression [9]. We observed pregnant mice from the seventh to the ninth day of gestation. Researchers have observed that the man-made glucocorticoid dexamethasone causes abnormalities in the placenta and hinders embryonic development [10]. Endogenous hormones exhibit low or no binding affinity to corticosteroid-binding globulin, whereas the body more readily absorbs dexamethasone due to its stronger affinity [11].

Pharmacokinetics.

The mechanism behind the action of glucocorticoids is complex.

The initial stage of glucocorticosteroid (GC) cellular action involves the attachment of the hormone to particular cytoplasmic receptors [15, 16]. This is the stage where the hormone attaches to chromatin and initiates the unique biological reaction. The complex nature of glucocorticosteroid GCs leads to their migration towards the nucleus. Targeted protein synthesis initiates this process in most tissues [4]. The glucocorticoid receptor (GR) belongs to the protein family of steroid hormone receptors [17]. Glomerular cytokines (GCs) are a class of lipophilic steroid hormones that are commonly associated with carrier proteins in the bloodstream. These proteins include corticosteroid-binding globulin (in the case of endogenous steroids) and albumin (for both endogenous and synthetic steroids) [18]. The binding of GR to cortisol exhibits a strong affinity, facilitating the dissociation of molecular chaperones, such as heat shock proteins, from the receptor within the cellular environment [19]. The activities of cortisol manifest in three distinct manners. The initial step involves the migration of the cortisol-glucocorticoid receptor complex towards the nucleus, where it forms a homodimeric complex with DNA sequences known as glucocorticoid-responsive elements (GRE). The complex formed as a result of this process binds either corepressor or coactivator proteins, which alter the chromatin structure. This alteration either facilitates or hinders the assembly of the crucial transcription machinery and the beginning of transcription by RNA polymerase II [19]. Furthermore, the regulation of additional genes that are responsive to glucocorticoids involves the intricate connections between the cortisol-glucocorticoid receptor complex and many transcription factors, including nuclear factor kB (NFkB) [18, 20]. The glucocorticoid signalling pathway, also known as the nongenomic pathways, involves the use of membrane-associated receptors and second messengers as the third mechanism of actin [21, 22]. The inhibition of inflammation by the glucocorticoid receptor is achieved through three distinct methods, including direct effects, indirect genomic effects, and nongenomic processes. The variety in glucocorticoid signalling is attributed to variations in the structure and expression of the gene [23]. The genomic structure has three transcription initiation sites, each of which generates an alternate first exon that is connected to a shared exon 2. However, the first exon does not undergo translation. Dexamethasone has the ability to upregulate all three GR transcripts to a similar extent in acute lymphoblastic leukaemia T cells but decreases these transcripts to varying

degrees in a B-cell ine [24, 25]. This suggests that there may be functional differences among exons 1A, 1B, and 1C. These arguments emphasise the significance of comprehending the regulation of glucocorticoid receptor expression in both healthy and diseased states [19].

Literature review

The impact of dexamethasone on physiological alterations and enhanced productivity in broiler chickens

The primary aim of this study was to assess the impact of dexamethasone on physiological alterations and productive outcomes in broiler chickens. The grill chickens were allocated into seven distinct groups and administered dexamethasone at varying doses, namely 0 mg kg1 (control group), 1, 2, 3, 4, 5, and 6 mg kg1. Regarding their dietary habits, On days 1, 7, 14, and 21 of the experimental period, various parameters were examined in broilers, including the percentage of heterophils, lymphocytes, heteropil/lymphocyte ratio, haemoglobin concentration, packed cell volume, total white blood cell count, body temperature, respiratory rate, and productive performances (feed intake, average daily gain, feed conversion rate, and body weight). The study showed that many things about the broiler chickens got better, like their heterophil-to-hemolymphocyte ratio, total white blood cell count, body temperature, respiratory rate, packed cell volume, and feed intake (P 0.05). On the contrary, there was a decrease observed in lymphocytes, haemoglobin levels, the average daily increase, and the body weight of broilers [26].

This study investigates the impact of dexamethasone medication on the haematological and histological parameters of mice that have been subjected to experimental bacterial infection.

the study included four distinct groups of balb/c mice, each consisting of ¹ animals. Participants in Groups 1, 2, and 3 received daily injections of dexamethasone for a duration of three days. Additionally, they were subjected to experimental infection with Pasteurella multocida, a strain of Escherichia coli that contained the recombinant plasmid ABA392. Furthermore

The bacterium Staphylococcus aureus, in that order, In contrast, group four functions as the control group. At 24, 48, and 72 hours after infection, there was a significant rise in the overall number of white blood cells. Additionally, the differential leukocyte count showed a significant increase in neutrophils and a decrease in lymphocytes and monocytes in all animals treated with dexamethasone. This increase was particularly prominent in groups 1 and 2 after infection in all animals. At the 72-hour mark following infection, the histological analysis demonstrates the presence of hemorrhagic characteristics in the lungs of mice treated with dexamethasone and infected with Pasteurella multocida. However, this feature is not observed in mice treated with dexamethasone or infected with S. aurus. These findings suggest that the recombinant plasmid AB392 may contain a sequence that encodes a virulent factor of Pasteurella multocida [7].

This study investigates the impact of zinc and dexamethasone on several haematological and biochemical tests in male rabbits.

This study aimed to examine the impact of oral administration of zinc at a dosage of 15 mg/kg bw per day and injection of dexamethasone at a dosage of 4 mg/kg bw for a duration of 30 days on haematological biochemical tests and histological alterations in the liver and spleen of male rabbits. A total of thirty bunnies were utilised, which were subsequently separated into three randomised groups, with each group consisting of ten male rabbits. The control group was provided with a standard diet consisting of food and water. The zinc group, on the other hand, received a daily oral

dose of zinc at a dosage of 15 mg/kg.BW for a duration of 1, 2, 3, and 4 weeks. Dexamethasone with zinc group: Administer dexamethasone at a dosage of 4mg per kilogramme. Bw. The experiment involved administering I.M. dialy for 1 and 2 weeks, and then 15 mg/kg of zinc during the 3rd and 4th weeks. Administered orally. In order to assess packed cell volume (PCV), white blood cells (WBCs), and red blood cells (RBCs) with differential leukocyte counts, blood samples were collected directly from the heart at two- and four-week intervals. Separate the blood sample into plasma and analyse the glucose and cholesterol levels in milligrammes per deciliter (mg/dl). Rabbits were euthanized, and their organ tissue was extracted from the body for histological examination of the liver and spleen. The findings indicated a reduction in red blood cell (RBC) count, pcv, following administration of zinc at a dosage of 15 mg/Kg.Oral administration of dexamethasone at a dosage of 4 mg/kgBw resulted in an elevation in white blood cell count, particularly neutrophil cells, in the zinc group. Additionally, biochemical testing revealed an increase in glucose and cholesterol levels following treatment with dexamethasone at a dosage of 4 mg/kg. I observed an elevation in the levels of red blood cells (RBCs), platelets (PCV), white blood cells (WBCs), and differential leukocyte count. Additionally, there was a reduction in glucose and cholesterol parameters. Histological examination revealed alterations in the liver following treatment with dexamethasone at a dosage of 4mg per kilogramme. The spleen tissue exhibited necrosis and pigmentation, accompanied by haemorrhage, following the administration of dexamethasone at a dosage of 4mg per kilogramme in the dexamethasone + zinc group. The findings also indicated that zinc, when administered at a standard dosage, had a temporary positive impact on the immune system due to its influence on other minerals like copper, leading to anaemia. On the other hand, dexamethasone, a medication used for its anti-inflammatory properties, only had a short-term effect [27].

The study investigates the kinetics of glucose metabolism modifications mediated by dexamethasone in a healthy adult population. The kinetics of glucose tolerance impairment induced by dexamethasone were assessed in six healthy human participants by three 75-g oral glucose tolerance tests. During the preceding 2 days, they were administered dexamethasone at a dosage of 4 ± 0.5 mg/day. In a separate instance, the participants received a single dose of dexamethasone (0.5 mg) 150 minutes before consuming the glucose load. In the third instance, the participants received a placebo. There was a substantial rise in postload plasma glucose levels following both a 2-day dexamethasone treatment and a single dose of dexamethasone, as compared to the control group ($P < 0.05$). Dexamethasone did not have any impact on the metabolic clearance rate of glucose, which resulted in a drop of 20–23%. However, it did not influence total glucose turnover ([6,6-2H]glucose), total (indirect calorimetry), exogenous glucose oxidation (13CO2 production), or the suppression of endogenous glucose generation. Plasma insulin levels exhibited an elevation following a 2-day administration of dexamethasone but did not show any significant rise following a single dosage of dexamethasone. In a further series of tests, the impact of a solitary administration of dexamethasone on insulin sensitivity was evaluated in a cohort of six individuals without any health conditions while subjecting them to a 2-hour euglycemic hyperinsulinemic clamp. The use of dexamethasone did not have a substantial impact on insulin sensitivity. According to the findings, the injection of dexamethasone in an acute manner has been found to negatively affect oral glucose tolerance while not significantly reducing insulin sensitivity [28].

An investigation on the impact of dexamethasone on hepatic function in male rats subjected to paraguat.

A research investigation was undertaken to assess the efficacy of dexamethasone (Dx) in the management of liver function tests in male albino rats with experimental paraquat (PQ)-induced oxidative stress. The trial involved three groups of rats: the control group, the PQ group (administered orally at a dosage of 50 mg/kg), and the PQ group with Dx (administered orally at a dosage of 50 mg/kg and/orally at a dosage of 4 mg/kg, respectively) for a period of 15 days. Results revealed that treatment with PQ caused a mortality rate in a ratio of 30%,significantly increased ($p \leq 0.05$) of glucose, cholesterol, bilirubin concentrations and alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase and amylase activities but the concentrations of both triglycerides and serum proteins were reduced compared with control whereas the treatment of PQ- treated rats with Dx decreased mortality rate (30%) and corrected the activity of serum transaminases, alkaline phosphatase enzymes whereas Dx treatment induced an elevation in amylase activityin addition to the elevation of concentrations of total cholesterol, total protein and albumin in comparison with values of PQ- treated rats, Dx did not affect the concentration of glucose. Ultimately, the administration of Dx in rats effectively remedied the majority of liver function tests affected by PQ-induced toxicity [29].

The use of dexamethasone during pregnancy induces hypertension and kidney damage in rats.

The objective of the current investigation was to ascertain whether prenatal administration of dexamethasone induced a gradual elevation in blood pressure and kidney damage in rats. We administered either a vehicle or two intraperitoneal injections of dexamethasone (0.2 mg/kg body weight) per day to pregnant rats on gestational days 11 and 12, 13 and 14, 15 and 16, 17 and 18, or 19 and 20. Rats that were given dexamethasone on days 15 and 16 of pregnancy showed a 20% decrease in the number of glomeruli compared to the control group at 6 to 9 months of age (22 527³509 versus 28 050±561, $P<0.05$). This reduction in glomeruli was similar to the percentage decrease observed at 3 weeks of age. The rats, aged six to nine months, that were administered prenatal dexamethasone on days 17 and 18 of gestation exhibited a significant decrease of 17% in glomeruli (23,380³587) as compared to the control group of rats ($P<0.05$). Prenatal administration of dexamethasone to male rats on days 15 and 16, 17 and 18, and 13 and 14 of gestation resulted in increased blood pressures at 6 months of age. However, the latter group did not see a decrease in glomerular number. The administration of dexamethasone to adult rats on days 15 and 16 of gestation, administering dexamethasone to adult rats resulted in a higher number of glomeruli exhibiting glomerulosclerosis compared to the control rats. The findings of this study demonstrate that administering prenatal dexamethasone at various gestational stages in rats leads to a decrease in glomerular number, glomerulosclerosis, and hypertension. We noted the presence of hypertension in both animals with a decrease in glomeruli and those without, suggesting that a decrease in glomerular number is not the exclusive factor contributing to the onset of hypertension [30].

The efficacy of injecting a single dose of dexamethasone intravenously before surgery in minimising the occurrence of postoperative sore throats following endotracheal intubation.

Research Objective: The aim of this study is to assess the efficacy of two distinct dosages of prophylactic dexamethasone administered intravenously in mitigating the incidence of

postoperative sore throat subsequent to general endotracheal anaesthesia. The study comprised a total of 105 individuals who underwent various elective surgical procedures and were planned to receive general anaesthesia with endotracheal intubations. We randomly assigned the participants to three pre-operative groups.

The participants were administered intravenous substances or drugs. Group I consisted of 35 cases who received 2 ml of normal saline; group II consisted of 35 cases who received 4 mg of dexamethasone; and group III consisted of 35 cases who received 8 mg of dexamethasone. The occurrence and intensity of sore throat were evaluated using a visual analogue scale (VAS), with scores ranging from 0 to 10; 0 indicates no discomfort, and 10 indicates the most intense pain. Findings: There was no statistically significant difference observed in the duration of operation or intubation-induced trauma among the three groups. The study found that the occurrence of sore throats at 1 hour and 24- hours after surgery was 48.6%, 28.6%, and 42.9% in groups I, II, and III, respectively. However, these rates did not reach statistical significance [31].

The impact of administering varying doses of Dexamethasone on the reproductive system.

The present study aimed to explore the impact of dexamethasone on levels of LH, FSH, and testosterone. For this experimental study, a total of 40 adult male Wistar rats were divided into four groups, each consisting of ten members. The control group rats were administered saline solution, whereas the experimental group rats were intraperitoneally injected with dexamethasone at doses of 0.4, 0.7, and 1 mg/kg each day for a duration of 10 days. On the subsequent day of the final injection, the rats underwent anaesthesia, and plasma samples were collected from their cardiac tissue. The levels of FSH, LH, and testosterone were subsequently evaluated, and the obtained data were subjected to analysis using SPSS software and the Dunnett test. The Pars kit was utilised to conduct hormonal tests for LH, FSH, and testosterone, and subsequently, the groups were compared. The study demonstrated no significant alteration in the targeted hormones up to a dose of 0.7 mg/kg. However, larger doses, specifically a dose of 1 mg/kg, resulted in significant changes in the concentration of LH, FSH, and testosterone in the experimental group compared to the control group ($P<0.05$). The study findings revealed that regular administration of dexamethasone resulted in various alterations in LH, FSH, and testosterone levels, leading to detrimental effects on the reproductive system of male rats [32].

This study investigates the impact of dexamethasone on lung development and exterior morphological characteristics in the early embryonic stages of Swiss albino mouse embryos of the Mus masculus species.

This study aims to investigate the impact of Dexamethasone on lung growth and external morphological aspects during early embryonic developmental stages. Additionally, it seeks to examine the levels of Alpha Fetoprotein.The study involved the random allocation of sixty pregnant mice into four groups, with each group consisting of 15 pregnant mice. All animals in each group were administered a specified dose of (Dex) at varied time intervals. The control group, on the other hand, received a solution of Normal Saline 0.9% via intravenous injection. At the conclusion of a specified gestational period, embryos were extracted from the mothers, and the mother's blood was collected to assess the levels of alpha-fetoprotein (AFP).The statistical analysis at a significance level of 0.05 indicates that different doses of Dexamethasone have a negative impact on the body weights of mice embryos. Additionally, the lengths of the embryos increase as the number and concentration of Dexamethasone increase. Furthermore, the overall

external morphological features of the embryos and their lung development are also affected by Dexamethasone. Specifically, Dexamethasone has a significant effect on lung development by influencing lung cell proliferation and activity, particularly in the long term and with repeated doses.Congenital abnormalities in embryos have been observed to result in various adverse outcomes, including embryonic death, placental damage, neural tube defects, trunk torsion, head haemorrhage, brain hypertrophy, liver hypertrophy, letter C shape embryos, swelling, convoluted tail, and short limbs.There has been a reported correlation between abnormal growth symptoms and changes in AFP levels [33].

The Impact of Dexamethasone and Oestrogen Administration on Leptin, Thyroid, Reproductive Hormone Concentration, and Lipid Profile of

This study aims to examine the impact of prolonged treatment with Dexamethasone (DEX.) and 17-estradiol (EST.) on body weight, hormone concentrations (specifically leptin, thyroid, and reproductive hormone), and the lipid profile of female rabbits' blood serum. A total of thirty rabbits from the nearby area were randomly and equitably divided into three distinct groups. The initial group served as a control group and received an injection of normal saline. Daily intramuscular injections of DEX at a dosage of 0.5 mg/kg B.W. were administered to the second group. The third group received a daily subcutaneous injection of 17 β-estradiol at a dosage of 0.3 mg/kg B.W. s/c. Each group in this trial underwent a 60-day treatment period, during which blood samples were obtained every 15 days. Leptin, LH, FSH, T3, T4, total cholesterol (TC), HDL (height density lipoprotein), LDL (low density lipoprotein), and TG (triglycerides) were measured in the serum. The body weight was measured at 15-day intervals, starting from the initial day. The study findings indicated a statistically significant decrease (P≈0.05) in body weight following the administration of both dexamethasone (DEX) and oestrogen (EST). Additionally, a substantial increase in leptin concentration was seen with the administration of dexamethasone (DEX). Treatment while significant decreased with Oestrogen (EST.) treatment, in the other hand LH and FSH concentration showed significant decreased in both treatment dexamethasone (DEX.) and Estrogen(EST.) thyroid hormone show significant decreased with dexamethasone (DEX.) treatment and significant increased T3 & T4 hormone with Oestrogen (EST.) treatment ascompare with control while the increase in the T4 it occurred only in the periods (45 and 60) days within treatment groups, lipid profile (TC,TG,LDL, HDL,VLDL) show significant increased with DEX. treatment while Significant decreased with EST. treatment [34].

Dexamethasone has been found to augment fertility and elevate pre-ovulatory serum prolactin levels in immature rats that have been primed with eCG or hCG.

To investigate the impact of dexamethasone (1 mg/kg) administered during the later phases of follicular development on litter size, oocyte release, and pituitary hormone levels, we employed a gonadotropin-primed, immature rat model. Females treated with dexamethasone exhibited an increased release of oocytes during ovulation and subsequently gave birth to larger litters, suggesting the viability of the oocytes. The survival rate until weaning age remained unaffected; however, pups born to females treated with DEX exhibited a reduced average weight at weaning. Serum levels of FSH and LH were measured at 12, 24, and 48 hours after electrocardiography (ECG) and did not demonstrate any differences between animals treated with dexamethasone and the control group. However, females treated with DEX exhibited a

protracted pattern of increased prolactin levels. Prolactin, typically increased during periods of proestrous hormone, might influence the growth of hair follicles. Dexamethasone improves fertility and fecundity by potentially influencing follicle formation through the action of prolactin or by directly impacting the ovary. The findings of this study have the potential to enhance our comprehension of the efficacy of DEX in the context of assisted reproductive therapy for women [35].

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