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Article

Biochemical Changes of Dexamethasone on Liver and Kidney Functions in Laboratory Mice *Mus musculus* L.

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ABSTRACT

Background: The present study sought to verify the effect of dexamethasone on the biochemical changes in different organs, such as liver and kidney organs of both sexes, male and female mice. Materials & Method: Muc muscular males and female mice (n=48) were used. To determine the effects of dexamethasone on the biochemical changes of liver and kidney organs, mice received a low dose (2mg/kg) and a high dose (4 mg/kg) of dexamethasone continuously for one month. Result: The results showed a significant increase ($P<0.05$) in Liver enzymes (ALP, AST, ALT). The urea and creatinine levels also increased in the treated mice and both sexes with the pesticide compared with the control group.

Keywords: mice, histological, liver, kidney, dexamethasone, toxicity

INTRODUCTION

Glucocorticoids (GCs) are widely used in clinical practice due to their anti-inflammatory, immunomodulatory, anti-allergic and anti-shock effects. GCs of patients with severe DILI have been recommended in cases where serum TBIL levels are exacerbated in patients under regular treatment, regardless of whether or not the serum ALT level decreases [1]. In addition, GCs may be administered empirically to patients with marked signs of hypersensitivity or autoimmunity and patients who have not significantly improved or even worsened biochemical indicators after withdrawal of the offending drug(s). Gradual therapy with tapering of the steroid dose is used most often in clinical practice. Prednisone 15 to 20 mg/kg/day for 3 days has been reported to successfully treat patients with severe DILI without apparent side effects. Abrupt withdrawal of corticosteroids is not recommended because it can sometimes lead to the reversal of liver injury [1]. Analysis based on the US DILI Network database showed that GCs were used in up to 82.0% of DILI patients who died or underwent liver transplantation and 36.6% of DILI patients who survived [2]. Although the debate over the scientific evidence for the effectiveness of GCs has raged unabated for many years, some studies have confirmed their effective role in DILI. Hou FQ and colleagues retrospectively investigated 70 DILI patients with hepatocyte injury whose TBIL is ≥10 × ULN. The results showed that patients treated with GCs had a higher accuracy rate for DILI without any side effects. Moreover, the recovery time was longer in patients who did not receive GCs than those who did [3]. A retrospective, single-center study by Hu PF et al. Included 203 patients with severe DILI, showed that 53 patients had a higher cure rate and a shorter recovery time after treatment for GCs. They conclude that short use of corticosteroids is strongly recommended for severe DILI patients with hyperbilirubinemia [4]. Sundaram S and Herroero-Herrero JI, respectively, have reported

successful treatment of DILI with GCs [5,6]. On the contrary, several investigations have refuted the effects of white blood cells in DILI. Karkhanis J and colleagues evaluated the effect of doping in ALF retrospectively. They collected clinical data for 131 patients with drug-induced ALF, 16 of whom received treatment for GCs. The results revealed that CSCs did not improve the overall survival rate in drug-induced ALF [7]. Wan YM et al. Enrollment of 90 patients with severe DILI to verify the efficacy and safety of prednisone. The results revealed that prednisone therapy is safe but not beneficial and even harmful at a daily dose of >40 mg to treat severe DILI [8]. Pang L and colleagues retrospectively studied the features and outcomes of patients hospitalized with DILI. They found that recovery time and recovery rate for 32 acute DILI patients treated with GCs did not improve significantly compared with the non-GCS group. However, it is encouraging that the accuracy rate for patients with fulminant hepatic failure was higher than that of the non-steroidal treatment group (57.1 vs. 25.0%) (Bang et al., 2018). These results suggest that GCs may have a potential therapeutic effect on DILI, but improper dose and timing may be counterproductive. Thus, GCs should be fully evaluated before application and used with extreme caution in DILI.

Dexamethasone is one of the most widely used dexamethasone Synthetic glucocorticoids with many properties such as anti-inflammatory, immunosuppressive and others [9]. It is associated with a wide range of diseases associated with metabolism [10,11]. Several studies have reported the effects of dexamethasone on various functions and systems of the body Like the effects of dexamethasone on rat body weight [12], above Rat Embryonic Development [13], Dexamethasone Effects on bone diseases [13], on the blood Electrolytes of mice [14], effect on muscle and bone System [15]. It affects the liver by causing steatosis [16], above Retinal neurons, optic nerve [11], and others. Prolonged use of dexamethasone has been associated with increasing its harmful effects, so we focus in our study on the Suggested effects of dexamethasone on blood lipids, electrolytes, red cell parameters, leukocyte parameters and liver enzymes of mice for a month.

MATERIAL AND METHODS

Experimental animals

Twenty-four adult male albino laboratory mice Mus musculus L. of Pulb/C strain of 20-22 mg weights were adopted. The animals were housed in standard open cages made of Plastic with stainless steel roofs. Temperature The room was set at 24 ± 1 °C, and the lighting was appropriate at -12 hours dark/light cycle mode. Long live animals Two weeks acclimatization before the experiment [17].

Experimental protocol

Animals are assigned into groups on a random pattern as below:

Control group

It houses 8 male mice. They were dosed intraperitoneally with 2 ml of 0.9% sodium chloride normal saline solution daily for 1 month.

Low dose group

Male mice of this group were dosed intraperitoneally with a 2 mL solution containing dexamethasone at 2 mg/kg daily for 1 month

High dose group

consisting of 8 male rats. Rats of the second treatment group were administered intraperitoneally with a 2 ml solution containing dexamethasone at 4 mg/kg daily for one month. The dose of dexamethasone was selected according to Dexamethasone, which was given for 1 month according to dexamethasone purchased from a local veterinary office supplier (a trademark of Merck, Germany).

Biochemical tests

Blood was drawn directly from the heart puncture from experimental animals after being anesthetized with chloroform. The serum is in special tubes for preservation after using the device Centrifuge until biochemical tests are performed.

Measured: ALT and AST enzyme activity measurement. Enzyme activity using the color method only using Reitmann and Frankel method [18].

ALT and AST enzyme activity measurements

The enzyme activity was measured using the colorimetric method only Using Reitmann and Frankel method [18] French. Biolabo supplied by Kit.

ALP enzyme assay

The enzyme activity was measured according to ALP enzyme assay Using the Kind and King method of [19] Biomerieux supplied from the company chromatic kit.

Urea measurement:

The serum urea level is measured using Kit Wills and Savory [20] supplied by French Biolabo.

Creatinine measurement

The Tietz method was used in measuring the creatinine level and using several French. Biolabo test fitted from the company [21].

RESULTS

Effect of Dexamethasone on male laboratory mice's liver functions. The statistical analysis results shown in Table 1 showed no significant differences in AST and ALP enzymes for the liver of male laboratory rats at the two doses. In contrast, the ALT enzyme was significantly decreased at the low dose only and with a probability percentage (P<0.05) compared to the control group.

Treatments	ALT IU/liter	AST IU/liter	ALP IU/liter
control group	128.875 [a] 21.389±	228.125 [a] 31.581±	10.277 [a] 2.268±
Low dose	102.250 [b] 12.00 7±	232.375 [a] 16.008±	10.801 [a] 1.2 21±
high dose	120.000 [a] 21.7 03±	215.250 [a] 2.00 3±	15.723 [a] 1.1 92±

Table 1. Effect of dexamethasone on liver function of male laboratory mice (average ± standard error n=8) a, b The difference of letters indicates a significant presence at the probability level (P<0.05)

Effect of Dexamethasone on liver functions of female laboratory mice. The results of Table 2 showed a significant increase at the probability level (P<0.05)) in AST and ALP enzymes for the liver of female experimental rats at both doses compared to the control group, in addition to a significant decrease in ALT enzyme in the low dose only, compared to the control group.

Treatments	ALT IU/liter	AST IU/liter	ALP IU/liter
control group	119.875 [a] 13.584±	74.410 [a] 10.733±	14.022 [a] 1.974±
Low dose	154.000 [b] 10.326±	111.29 [b] 34.288±	13.597 [b] 4.225±
high dose	122.000 [a] 8.591±	172.52 [b] 14.086±	10.174 [b] 2.341±

Table 2. Effect of dexamethasone on liver function of female laboratory mice (average ± standard error n=8) a, b The difference of letters indicates a significant presence at the probability level (P<0.05)

Effect of Dexamethasone in kidney functions of male laboratory mice. Table 3 shows a significant increase in the probability ratio (P<0.05) in urea and serum creatinine for male laboratory mice injected with the high dose of the pesticide only compared to the control group.

Treatments	Urea mg/dL	Creatinine Mg/dL
control group	31.807 [a] 1.959±	0.587 [a] 0.043±
Low dose	33.698 [a] 2.543±	0.683 [a] 0.131±
high dose	42.178 [b] 4.583±	0.945 [b] 0.129±

Table 3. The effect of dexamethasone on the kidney functions of male laboratory mice (average ± standard error n=8)

Effect of Dexamethasone on kidney functions of female laboratory mice

The results of the current study shown in Table 4 showed a significant increase with a probability ratio (P<0.05) in the urea concentration of the serum of female laboratory mice injected with the high dose only compared to the control group. While there was no

significant difference in creatinine concentration in the low dose compared to the control group.

Treatments	Urea Mg/dL	Creatinine Mg/dL
control group	25.395 [a] 4.8 80±	0.4 89 [a] 0.171±
Low dose	30.500 [a] 6.500±	0.5 21 [a] 0.108±
high dose	27.273 [b] 7.389±	0.7 51 [a] 0.356±

Table 3. The effect of dexamethasone on the kidney functions of female laboratory mice (average ± standard error n=8) a, b The difference of letters indicates a significant presence at the probability level (P<0.05)

DISCUSSION

In this study, we looked at the effects of dexamethasone on the liver, kidney and some serum biochemical parameters of the rats. In rats fed a regular diet, high levels of dexamethasone resulted in high levels of amine-transmitting enzymes, urea and cholesterol. There was no evidence of sexual dimorphism in these observations. Drug-induced liver injury can be classified into three clinical patterns based on serum ALT and ALP ratios from the first available biochemical test: hepatocellular, cholestatic, or mixed injury (liver injured target cells) [22]. Dexamethasone, a corticosteroid, is similar to a natural hormone produced by adrenal glands. It often replaces this chemical when the body does not make enough of it. It relieves inflammation (swelling, heat, redness, and pain) and treats certain forms of arthritis: skin, blood, kidney, eye, thyroid, and intestinal disorders (e.g., colitis), severe allergies, and asthma. Dexamethasone is also used to treat certain types of cancer [1]. According to data from the US DILI Network, GCs were utilized in up to 82.0 percent of DILI patients who died or required liver transplantation and 36.6 percent of DILI patients who survived [2]. Although the controversy over the scientific evidence supporting GCs' effectiveness has raged unabated for years, certain research has shown their effectiveness in DILI. Hou FQ and colleagues looked back at 70 DILI patients with hepatocyte damage and a TBIL of 10 ULN. The findings revealed that patients given GCs had a greater DILI accuracy rate with no adverse side effects. Although the controversy over the scientific evidence supporting GCs' effectiveness has raged unabated for years, certain research has shown their effectiveness in DILI. Hou FQ and colleagues looked back at 70 DILI patients with hepatocyte damage and a TBIL of >10 x ULN. The findings revealed that patients given GCs had a greater DILI accuracy rate with no negative side effects [23]. Compared to the non-GCS group, recovery duration and rate for 32 acute DILI patients treated with GCs did not improve significantly. The fact that the accuracy rate for patients with fulminant hepatic failure was higher than the non-steroidal therapy group (57.1 vs. 25.0 percent) is encouraging [24]. These findings imply that GCs may have a therapeutic effect on DILI, but the wrong dose and timing could be harmful. As a result, GCs should be thoroughly reviewed before being used in DILI and utilized with extreme caution.

CONCLUSION

Low and high doses of dexamethasone used in male and female mice caused pathological alteration of tissue structure of kidney and liver organs. Moreover, short use of corticosteroids is strongly recommended for severe DILI patients with hyperbilirubinemia.

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