

Research Article

Comparing Betamethasone and Dexamethasone Effects on Concentration of Male Reproductive Hormones in Mice

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Abstract: Most of chemical drugs have side effects on various parts of body. It is necessary to identify these effects to better use of drugs. Betamethasone and Dexamethasone are two of the most usual drugs in human and animal medication. The effect of these drugs on concentration of male reproductive hormones of mice was the goal of this study. Eighteen matured male mice were divided into eight groups including control, placebo and six treatment groups. Placebo group was received physiological serum only and treatments were Betamethasone (0.1, 0.5 and 1 mg/kg) and Dexamethasone (0.1, 0.5 and 1 mg/kg) which were injected in peritoneum every other day and for twenty days. After 20 days, blood samples were taken and FSH, LH and testosterone levels were measured using Eliza test method. Obtained data were analyzed using one way analysis of variance and mean comparison was done using Duncan's multiple ranges test and SPSS program. Results showed that 0.5 mg/kg of Betamethasone and all levels of dexamethasone caused significant increase in FSH concentration. For LH hormone, 1 mg/kg of Betamethasone and 0.1 mg/kg of Dexamethasone caused significant decrease whereas 1 mg/kg of Dexamethasone increased it significantly. Testosterone was increased significantly by 1 mg/kg of Dexamethasone. So, mentioned drugs are effective on hormone action of reproductive system dose dependently and probable effect of them must be considered in time of using.

Keywords: Betamethasone, Dexamethasone, FSH, LH, mice, testosterone

INTRODUCTION

Dexamethasone is a synthetic glucocorticoid with 50 times more tendency than cortisol to conjugate with glucocorticoid receptor. This drug is used for preventing inflammations (Czock *et al.*, 2005; Schacke *et al.*, 2002). Glucocorticoids enforce a negative feedback on inflammatory responses via reducing production, secretion and action of inflammatory mediators like interleukin 1 β and are used mainly as anti inflammation matters (Kapcala *et al.*, 1995). Direct effect of glucocorticoids on target tissue is producing sexual steroids (Rabin *et al.*, 1990). In a study for determining various effects of Dexamethasone on inflammation of lipopolysaccharide and controlling sexual hormones in matured mice reported that Dexamethasone suppressed corticosterone level of serum but didn't affect LH and testosterone level of serum and it controlled also the expression of interleukin 1 β and response of inflammatory system (Hedger *et al.*, 2001). Dexamethasone causes reduction in basic level of testosterone hormone in blood and reduces its periodic secretion from 1 to 4 days after injection (Berger and Clegg, 1985). Betamethasone is a corticosteroide which is proposed for lung maturity of embryos in danger of Preterm birth. It is proposed in 24 to 34 weeks of

pregnancy and has effect like reduction in appearance of respiratory distress syndrome; death caused by brain bleeding and increases in probability of live babies. Betamethasone affects pneumocytes type 2 of embryos lung and helps lung maturity via increase in Alveoli surfactants and lung compliance (Gamsu *et al.*, 1989). Studies show that side effects of Betamethasone are highly less than Dexamethasone (Jobe and Soll, 2004; Lee *et al.*, 2006). In a study, Betamethasone medication was studied. Results showed that it caused reduction in red blood cells and hemoglobin and increase in white blood cells especially neutrophil which became normal after one week (Vaisbuch *et al.*, 2002). Some researchers have recommended lately doing studies about preference of Betamethasone to Dexamethasone (Jobe and Soll, 2004). So this study was conducted to compare effects of Betamethasone and Dexamethasone on concentration of sexual hormones in male mice.

MATERIALS AND METHODS

The study was conducted in Khorasgan branch of Islamic Azad University. 80 male mice from Balb/c race and in weight range of 30 ± 5 g were prepared and kept for two weeks in similar condition with free access to food, water, normal light and appropriate

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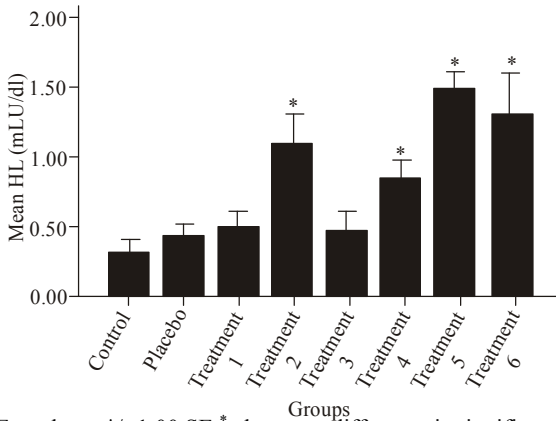
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temperature and moisture. These favorite conditions were continued for whole period of study. Samples were divided in eight groups with ten members including control, placebo and six treatment groups. Betamethasone and Dexamethasone drugs were used each in three doses: 0.1, 0.5 and 1 mg/kg which were injected in peritoneum. Placebo group was only received normal saline 9% and control group was not injected.

Injections were done for twenty days every other day and one day after last injection, blood samples were prepared using guillotine method. Eliza method and gamma counter machine were used to measure FSH, LH and testosterone hormones. The study was done in completely randomized design with... replications and obtained data were analyzed using SPSS program and Duncan's multiple ranges test ($p \leq 0.05$) was used to compare means.

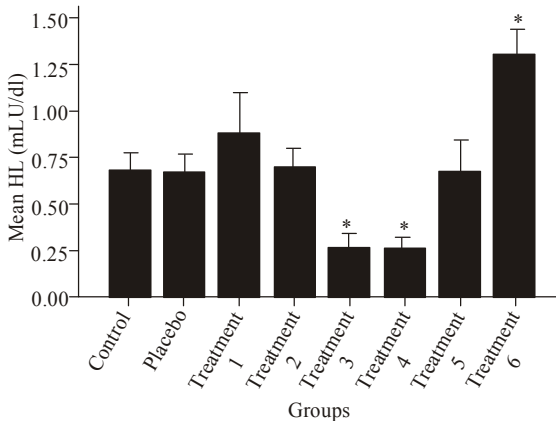
RESULTS

Mean comparison of FSH level in serum showed significant increase ($p \leq 0.05$) in 0.5 mg/kg of



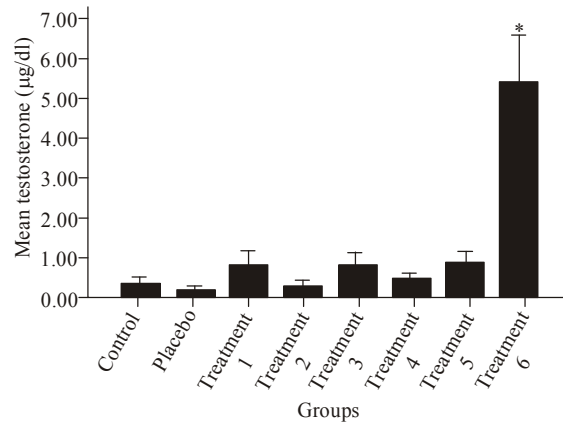
Error bars: \pm 1.00 SE. *: the mean difference is significant at the 0.05 level: ($p \leq 0.05$)

Fig. 1: FSH amount of studied groups



Error bars: \pm 1.00 SE. *: the mean difference is significant at the 0.05 level: ($p \leq 0.05$)

Fig. 2: LH amount of studied groups



Error bars: \pm 1.00 SE. *: the mean difference is significant at the 0.05 level: ($p \leq 0.05$)

Fig. 3: Testosterone amount of studied groups

Betamethasone and all doses of Dexamethasone (Fig. 1).

Doses 1 mg/kg of Betamethasone and 0.1 mg/kg of Dexamethasone caused significant reduction ($p \leq 0.05$) in LH level and 1 mg/kg of Dexamethasone increased it significantly ($p \leq 0.05$). Other doses didn't affect the LH amount (Fig. 2).

The amount of testosterone hormone was increased significantly ($p \leq 0.05$) by 1 mg/kg of Dexamethasone whereas other treatment didn't change it (Fig. 3).

DISCUSSION

Considering the results, we can say that the effects of Dexamethasone and Betamethasone on reproductive hormones are dose dependent and 0.5 mg/kg of Betamethasone and 0.1, 0.5 and 1 mg/kg of Dexamethasone increased FSH concentrations but other treatments didn't affect it significantly. In an *in vitro* study on female rats treated by 60-600 ng/mL of Dexamethasone, it caused synthesis stimulation and secretion of FSH (Suter and Schwartz, 1985). Similar results were obtained in *in vivo* condition. These results showed that the reason of FSH increase is suppression of ovary action especially controlling inhibin secretion (Tohei and Kogo, 1999). Phillips and Clarke (1990) reported that Dexamethasone (2 mg/kg) didn't affect FSH of ewe which is not in agreement with this study. 1 mg/kg of Betamethasone and 0.1 mg/kg Dexamethasone reduced LH concentration and 1 mg/kg of Dexamethasone increased it. Hockett *et al.* (2000) showed that increase in glucocorticoid of plasma didn't affect LH concentration of cows and Phillips and Clarke (1990) reported also that Dexamethasone didn't have any effect on LH of ewe which is in agreement with this study. Espicer *et al.* (2001) showed in their studies which Dexamethasone didn't affect FSH and LH concentrations which is in opposition to previous *in vitro* studies on cow (Li and Wagner, 1983;

Padmanabhan *et al.*, 1983) and rat (Suter and Schwartz, 1985) and also in vivo studies on cow (Echternkamp, 1984), rat (Tohei and Kogo, 1999) and sheep (Daley *et al.*, 2000).

One of the mechanisms which is used by hypothalamus-hypophysis-Adrenal axis to affect sexual activity is direct effect of glucocorticoids on target tissue of sexual steroids (Rabin *et al.*, 1990). On the other hand inducing synthetic glucocorticoids can reduce hypothalamus's gonadotropin releasing hormone considerably (Fonda *et al.*, 1984; Dubey and Plant, 1985; Rosen *et al.*, 1988) and control FSH and LH releasing from hypophysis (Rosen *et al.*, 1988; Li and Wagner, 1983; Li, 1987; Brann *et al.*, 1990; Li, 1993). Glucocorticoids control steroid making of testicles via affecting hypothalamus and hypophysis (Bambino and Hsueh, 1981) and by direct control of p450scc and 3- β -hydroxysteroid dehydrogenase and p450s17 (Sapolsky, 1985; Hales and Payne, 1989; Monder *et al.*, 1994; Gao *et al.*, 1996) and specific receptor in leydig cells (Stalker *et al.*, 1989). Using 1 mg/kg of Dexamethasone increased testosterone concentration whereas other treatments didn't affect it. Previous studies have shown that glucocorticoids controlled testosterone secretion (Macky and Cidlowski, 1999). Bernier *et al.* (1999) reported that Dexamethasone and other glucocorticoid synthetic antagonists have control effect on testosterone production by leydig cells of testicle on media which is not in agreement with our results. Gao *et al.* (2003) showed in their study that increase in concentration of serum glucocorticoids due to stress caused controlling activity of testosterone making enzymes and reduction in leydig cells, then testosterone secreting would reduced. Hardy *et al.* (2005) reported also controlling act of glucocorticoids on testosterone production. in sixth treatment testosterone was increased by increase in LH amount which shows hypophysis stimulating effect on activity of testicles leydig cells, but in third and fourth treatments, in spite of LH reduction we don't see any significant effect on testosterone releasing. Considering the results, we can say that LH reduction has been compensated by feedbacks of testosterone secretion. The level of bloods testosterone is defined by steroid making activity of leydig cells. These cells make glucocorticoid receptors. Then testicle tissue is the first target of glucocorticoids action (Bahiru and Cheryl, 2003).

Results of this study show that FSH secretion is increased by Dexamethasone dose dependently while it is seen for LH in a specific dosage and this is really obvious for testosterone.

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