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The Effect of Betamethasone Injection on Sexual Hormones Concentration in Female Mice

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Abstract: Betamethasone stimulates production of necessary enzymes for reducing inflammatory responses. This drug is a long-acting steroid which produces quick anti inflammatory effects with long time effect. Effects of betamethasone on sexual hormes of female mice were studied in this study. Mice were divided in 5 groups (control, Placebo and 3 treatments groups) with 10 members in each group. Samples were kept in similar condition be synchronized in estrus cycle. Betamethasone was prepared in 0.1, 0.5 and 1 mg kg^{-1} doses and injected in peritoneum for 20 days. Control group was not injected while Placebo received normal saline. After 10 injections blood samples were prepared and the amounts of LH, FSH, strogen and progestron hormones were evaluated by RIA method. Obtained results showed that strogen, progesterone and LH were reduced by all treatment significantly whereas FSH was increased in 0.5 and 1 mg kg^{-1} groups. According to results, betamethasone affects sexual hormones dose dependently and then can affect female sexual potential.

Key words: Betamethasone, LH, FSH, strogen, progestron, mice

INTRODUCTION

Reproduction process includes a combination of physiological events which occur in their appropriate time. Endocrine system controls the timing of these processes via producing hormones (Rabin *et al*., 1990). By environmental stresses, reproduction process will be affected severely and animals will be in extinction danger. Physiological pressures like drug injection, heat stress, pregnancy period (especially in late gestation) and lactation period play important roles in reduction of reproduction capacity of female animal. Measurement criteria of reproduction quotient includes the number of insemnation rate per pregnancy, pregnancy amount per first insemnation, the number of open days and calving interval.

Betamethasone is one of anti inflammatory drugs. This drug changes DNA translation which changes cell metabolism and reduces inflamatory response. This drug is used for reducing short time pains of non-infectious inflammations. It has high anti inflammatory effect and researchers have proposed to study preference of bethametasone to dexametasone (Jobe and Soll, 2004). Betamethasone a corticostroide which is given for lung maturity in pregnancies which are in miscarry danger. It is used in 24-34 weeks of pregnancy and causes reduction in probability of respiratory distress syndrome and mortality percentage of intracranial hemorrhage and increase in viability of the premature infant. Bethamethasone affects pneumocytes type 2 of embryo's lung and helps alveolar surfactant and lung compliance (Gamsu *et al*., 1989). Glucocorticoides can improve the response of weak responsers indirectly by increasing serum level of growth hormone and IGF-1 and following increase in IGF-1 concentration in follicle liquid (Casanueva *et al*., 1990). Those have direct effects on ovarian steroidogenesis both in body and in laboratory (Ben-Rafael *et al*., 1988; Hsueh and Erickson, 1978; Michael *et al*., 1993). Also, one of probable mechanisms which pituitary-adrenal axis may affect reproduction performance is direct effect of glycocorticoides on target tissue (Rabin *et al*., 1990).

According to the earlier mentioned, this study carried out to investigate the effects of betamethasone injection on reproduction hormones of female mice.

MATERIALS AND METHODS

Little laboratory female mice were prepared in 25-35 g weight range and divided in 5 groups with 10 members in each group. Samples were kept in similar condition. Samples were kept in separate cages for 2 weeks with free access to natural light, food and water and 25-35°C temperature. This condition was continued also in injection period. Betamethasone was injected in peritoneum according to body weight:

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- The 1st treatment group: 0.1 mg kg^{-1} of body weight
- The 2nd treatment group: 0.5 mg kg^{-1} of body weight
- The 3rd treatment group: 1 mg kg^{-1} of body weight
- Placebo: Normal saline 9%
- Control: No injection
- All injection was done for 20 days every other day between 8 to 12 o'clock

To evaluate the effect of drug, all samples must be synchronized in estrus cycle. First, 0.5 microgram of cloprostenol drug was injected in peritoneum. After 3 days, 3 microgram of progesterone was injected under skin and 1 day later drug injection was started.

RESULTS AND DISCUSSION

FSH amount (mlu dL^{-1}) showed significant increase ($p<0.05$) in 0.5 and 1 mg kg^{-1} treatments. LH amount was decreased in all experimental groups significantly (Fig. 1). Estrogen hormone was reduced in all experimental groups significantly ($p<0.05$). Also, progesterone amount of all 3 treatments was decreased significantly ($p<0.05$) in proportion to control group (Fig. 2).

Considering the results, LH amount was reduced in all treatment groups. LH is regulated by negative feedback and by controlling secreting sexual hormones via pituitary-gonadal system. Therefore, increase in estrogen and progesterone reduces LH secretion from anterior pituitary which is resulted in LH reduction (Ben-Rafael *et al*., 1988). GnRH hormone from hypothalamus stimulates secreting LH from pituitary and LH causes stability of corpus luteum and therefore increases in progesterone secretion. But in this study, betamethasone caused instability of corpus luteum by controlling LH secretion and therefore reduced progesterone secretion (Hsueh and Erickson, 1978).

FSH was increased in 2 experimental groups significantly. Considering that GnRH hormone from hypothalamus simulates FSH secretion from front pituitary and this hormone in ovary increases follicle growth and then increases estrogen in ovary, a negative feedback is produced and reduces FSH secretion from front pituitary (Michael *et al*., 1993). Betamethasone reduced ovarian estrogen in this study and prohibited negative feedback for FSH, therefore FSH was increased in experimental groups. Progesterone controls production of follicle stimulating hormone highly and it seems that opioid peptides of brain are mediator of this negative effect.

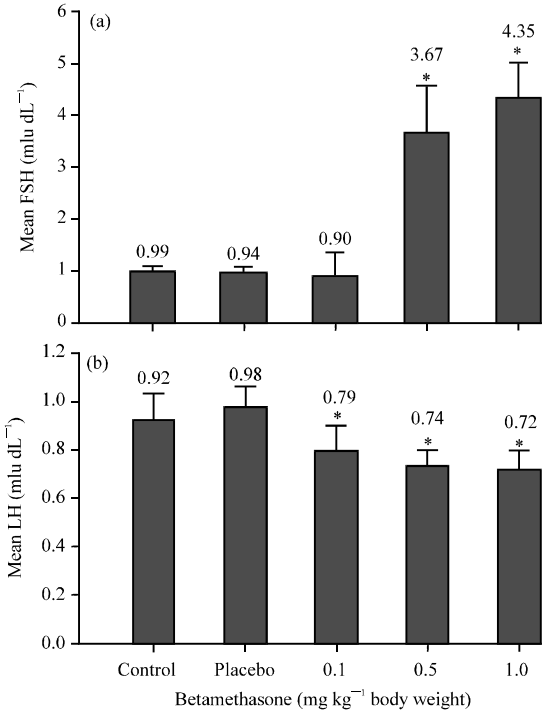

Fig. 1: LH and FSH amounts in studied groups: Error bars: 95% CI; *The mean difference is significant at the 0.05

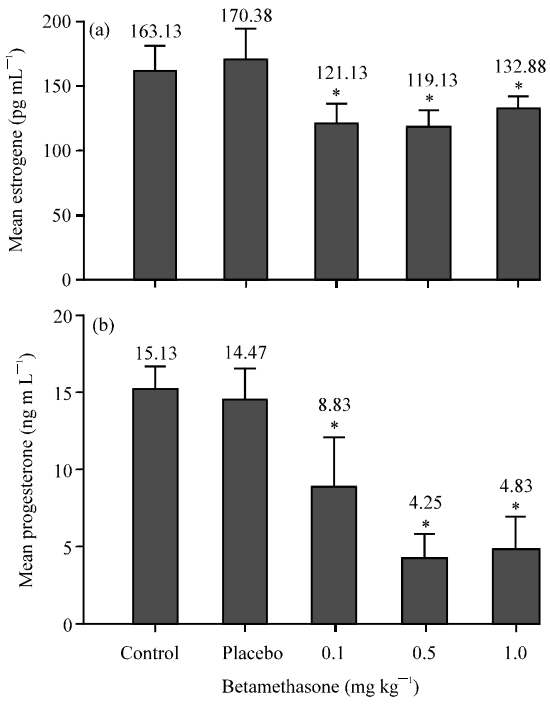

Fig. 2: Estrogen and progesterone amounts in studied groups: Error bars: 95% CI; *The mean difference is significant at the 0.05

Obtained results showed that amount of estrogen hormone in granulosa cells of follicle are responsible of estrogen production of ovary. At first, same small antral follicles start to grow and make estradiol. Some of these follicles will undergo atresia (Rabin *et al*., 1990). From remaining follicles, dominant follicle is selected and the highest amount of estradiol is being secreted in this stage. On the other hand, inhibine hormone in dominant follicle controls FSH secretion specifically.

CONCLUSION

Considering the results, betamethasone reduces estrogen secretion which causes instability of corpus luteum in ovary and reduces progesterone production. Also, this drug reduces estrogen production by follicles and therefore FSH negative feedback is not occurred and increases FSH production. On the whole, betamethasone can affect sexual potential of female sex dose dependently.

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