



CLINICAL BEHAVIOR AND HORMONAL ABNORMALITIES FOLLOWING DIFFERENT DOSES OF PROGESTERONE GIVING IN WHITE MICE FOR FOUR MONTHS DURATION

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ABSTRACT

This study aimed to identify clinical behavior and hormonal abnormalities in white mice. For this reason 4 groups of mice (20 each group 10 males and 10 females), were s/c injected daily with 0.15, 0.30, 0.45 mg / kg . b.wt, daily and for 4 months the 4th group injected with sunflower oil (0.075 ml) as a control group at the end of experiment (120 days), blood samples were taken from all groups of mice and record all clinical signs. The results showed different clinical signs and abnormal levels of progesterone, estradiol and testosterone in the 2nd and 3rd groups of mice received intermediate and toxic doses of progesterone.

KEYWORDS: clinical behavior and hormonal abnormalities following toxic doses of progesterone in white mice.

INTRODUCTION

Progesterone is a sex steroid hormone which conjugated with a estrogen to regulate the function of the accessory sex organs during an ovarian cycle^[1]. It is secreted mainly from the corpus luteum in the ovary and placenta^[2], also produced from cortex of the adrenal gland in both male and female^[3]. Small amounts of progesterone are also produced in the testes and glial cells of the brain in both sexes^[4]. Progesterone receptors are located in the uterus and mammary gland in female^[5] these receptors are also found in the testes and prostate in the male^[6]. Because of the importance of progesterone in the living body target organs this study aimed at to identify the clinical behavior and hormonal abnormalities of high doses of progesterone for long time treatment in body organs.

MATERIALS & METHODS

In this study 80 white mice were used (40 males and 40 females), 3 weeks ages, 15 gm weight, the animals were randomly divided into 4 groups (10 male and 10 female) each group, the male were separated from female in each group.

Medroxy progesterone as synthetic progesterone (Intervet, Holland) was diluted in sunflower oil^[7] and serial dilution was made. Three doses levels were prepared (0.15 mg,

0.30 mg, 0.45 mg kg. b.wt.) these 3 doses level were s/c injected daily injection was made for 120 days for each group of mice (1st, 2nd, 3rd group) the 4th group was injected s/c with 0.075 ml of sunflower oil as a control. At the end of treatment period, all the animal were sacrificed after withdrawing of blood and all clinical signs were recorded through the period of treatment and all the Hormonal assay done by^[8].

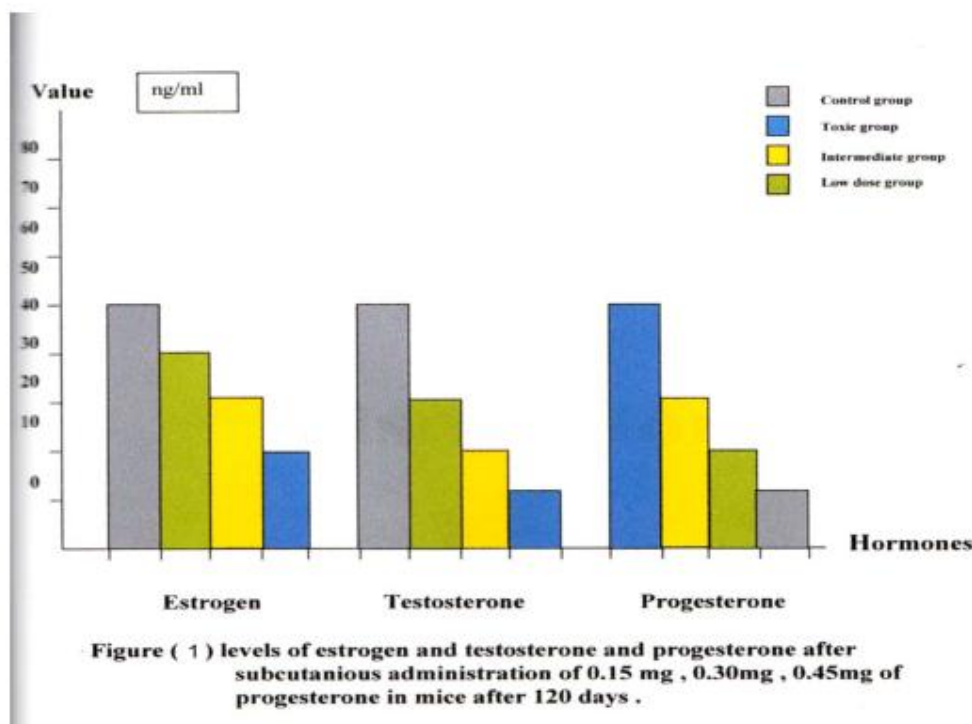
RESULTS

Behavioral changes

The behavioral changes of the females were varied among the three groups in the 1st group the animals appeared normal - In the 2nd and 3rd groups the animals appeared nervous and resist the injection in both males and female, both animals showed nervous signs, fought each other, sometimes showed traumatic injuries in their face and rotated around themselves, other signs in all males and females in the 2nd and 3rd groups were polydipsia, polyphagia and polyuria.

Hormonal Assay

Biochemical analysis showed suppression of estrogen and testosterone and elevation of progesterone levels in all groups (Fig -1).



DISCUSSION

Behavioral modification

Most of the animals in the 2nd and 3rd group showed some behavioral changes, polydipsia, polyuria, polyphagia, these changes were accompanied subcutaneous edema and adipose tissue.

These results agreed with those found by other workers^[9] on rats and human, these changes related with synthetic progesterone induced polyphagia together with subcutaneous adipose tissue deposition, other workers reported that the prolonged treatment with progesterone induced diabetic like signs associated with increased level of sugar and reduced level of insulin in body^[10] and the combination of synthetic progesterone with some receptors of aldosterone in the renal tubules leading to many hundred times of sodium transport than in normal state causing water retention and appearance of subcutaneous edema^[11].

Hormonal Assay

The results showed suppression of testosterone that resulted from the effect of high level of progesterone which cause suppression of GNRH (2.11) which released from the hypothalamus and effect on pituitary gland to release the FSH which is responsible for the activity of sertoli cells and LH which enhance the secretion of testosterone from leydig cells so exogenous progesterone will cause suppression of FSH and LH together with inhibition of spermatogenesis and antagonize the estrogen and testosterone in the blood^[12,13].

CONCLUSION

Both intermediate and toxic doses of progesterone induced different clinical behavior and steroid hormonal abnormalities.

REFERENCES

- [1]. Titze, I.W (1987) Text book of clinical chemistry, 4th .ed, Saunders company, philaadelphia, USA.PP : 65 -66 .
- [2]. Guyton, C.A. (1991) Text book of Medical physiology, 8th .ed. Saunders Company, Philadelphia, USA. pp: 810-892.
- [3]. Tausk, M. (1971) Pharmacological endocrine system and related drug and antifertility agent in International Encyclopedia of pharmlology and therapeutic, New York, Ny pergamon press, pp: 120.
- [4]. Lorrain, A., Fitzpatrick, F. and Good, A. (1999) .Micronized progesterone, clinical in dication comparison with treatment Fertile – sterill, J.22: 450-454.
- [5]. Maclusky, N.J., Mcween, B.S. (1980) progestin receptor in the developing rat brain: distribution and propertles of cytoplasmic progestin binding sites .J. clin. Endocrin .106: 192-202.
- [6]. Curtis, H.S., Couse, J.F. and Koroch, K.S. (2000) Estrogen receptor transcription and transactivation, estrogen receptor knockout mice, what their phenotype reveal about mechanism of estrogen action Breast cancer Res. 2: 345 -352.
- [7]. Sulaiman, G.M. (2002) The effect of testosterone on the sugar content of the thymus gland in albino male mice. Bioch. J. 8: 69-70.

- [8]. Salman , Y.J. (2007) Serological cross reation among causative agents of women abortions, Toxoplasma, SMV, Rubella, hepatitis B and C, Tiekrit J . Pharm . sci. 3(20) 102 – 111.
- [9]. Simon, J.P., scools, M.A. and wounders, E.F. (1998) Effect of medroxy progesterone acetate on food intake, body composition and resting energy expenditure with advanced non – hormone sensitive cancer cancer J.82:553-560.
- [10]. Vonkep, P.A., Utian, W.H. and Vrmeulen, A. (1981) the controversial climacteric caster England, Mtp. Press, 1:8-11.
- [11]. Williams, C.L., Stancel, G.M. (1996) Estrogen and progestin 9th ed New York, NY pp: 1411-1440.
- [12]. Crews, J.K. and Khalil, R.A. (1999) antagonistic effect of estradiol, progesterone and testosterone on ca^{+2} entry mechanism of coronary vasoconstriction arteriosclerosis. *Thromb.Vasc.Boil.*19: 1034-1040
- [13]. Jordian, A. (1994) A toxicology of deptomedroxy progesterone acetate 49:89-210.