MONOAMINE OXIDASE ACTIVITY IN THE PITUITARY OF MICE AFTER ESTROGEN, PROGESTERONE AND CENTCHROMAN TREATMENT

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Summary: Monoamine oxidase activity (MAO) was estimated in the pituitary of ovariectomized mice after a single administration of estradiol-dipropionate (0.01 *mg/kg;* im), progesterone (1 *mg/kg;* im) and centchroman (1.25 *mg/kg* ip). Estrogen and progesterone were found to decrease the enzymic level, as compared to control, while centchroman remarkably increased it. The significance of dissimilarity in the pituitary threshold for steroidal and nonsteroidal molecule is discussed.

Key words: estrogen progesterone centchroman MAO mouse pituitary

INTRODUCTION

Earlier studies have shown that 5-hydroxytryptamine (5-HT) neurons exert an inhibitory action on the secretions of luteinizing hormones releasing factor (LRF) (4, 5). 5-HT is also reported to inhibit FSH and stimulate prolactin release when injected into the 3rd ventricle of male rats (3). Estrogen is known to act by inhibiting of the feedback mechanism and the action is believed to be mediated through 5-HT neurons (2). Studies are on record to show that progesterone also produces a complex influence on 5-HT metabolism, thereby increasing its turnover in a dose-dependent manner (7).

Under normal conditions 5-HT synthesis is required to fulfil functional needs of the brain and it is believed that the excess amount of 5-HT is retained by the *intraneural pool* (identified as vesicular bindings), or metabolized by intraneuronal monoamine oxidase activity. Thus, the feedback control of release of 5-HT, available for functional activity, is likely to be converted by the vesicular bindings or monoamine oxidase activity.

Centchroman, a nonsteroidal antifertility drug developed by this Institute is reported to possess hypophyseal gonadotrophin modulating action in human (8). Accordingly, the present study was undertaken to assess the role of centchroman at the level of biogenic amines by estimating monoamine oxidase activity in mouse pituitary. For comparison, correlative studies with estrogen and progesterone were also taken.

MATERIALS AND METHODS

Adult female mice of the Institute colony 30-40 g, maintained under uniform husbandry conditions (temp : 75±2°F), were ovariectomized and after 10 days of rest period were

divided into four groups (10 animals each). Gr. I served as control and the animals received olive oil only, a vehicle for steroids. To the animals of groups II-IV, estradiol-dipropionate (0.01 *mg/kg*; im), progesterone (1 *mg/kg*; im) and centchroman (1.25 *mg/kg*; ip) respectively were administered once only and animals autopsied 48 hrs later. The pituitary was dissected out carefully, weighed on a torsion balance and processed for estimating monoamine oxidase activity as per the method of Krajl *et al.* (6).

RESULTS AND DISCUSSION

As indicated in Table I, monoamine oxidase activity of mouse pituitary was lowered following administration of estrogen and progesterone (Gr. II/Gr. III vs. Gr. I, $P<0.01$). On the contrary, the centchroman markedly elevated the enzyme level (Gr. IV vs. Gr. I, $P< 0.01$; Gr. IV vs. Gr. III/Gr. II, $P<0.001$).

TABLE I: Monoamine oxidase activity in the pituitary of mice after estrogen, progesterone and centchroman treatment.

Groups	*Treatments*	*MAO Units/0.1 ml of homogenate of pituitary/60 min*
I	Ovariectomized (control)	0.172 ± 0.006
II	Ovariectomized + Estrogen (0.01 *mg/kg*)	0.0693 ± 0.01
III	Ovariectomized + Progesterone (1 *mg/kg*)	0.061 ± 0.001
IV	Ovariectomized + Centchroman (1.25 *mg/kg*)	0.561 ± 0.01

The results of the present study showing a low level of MAO under the influence of estrogen and progesterone, supports the findings of Kalra *et al.* (1) who demonstrated that the inhibitory feedback mechanism of estrogen is mediated through 5-HT neurones, which in turn may lower the activity of MAO in pituitary.

Progesterone was also found to lower the MAO level in pituitary. Contrary reports are on record pertaining to the role of progesterone in modulating MAO activity. Meyerson and Lewander (9) observed no change in the 5-HT turnover, whereas Tonge and Greengrass (11) and Ladisich (7) reported a phenomenal lowering of MAO in rats treated with progesterone. Though the present study is not exactly similar with those stated *vide infra*, it indicates that progesterone could act in a manner similar to estrogen.

However, the same is not the case with centchroman which markedly raised the level of MAO in mouse pituitary. It is quite possible that centchroman acts through a positive feedback, thereby raising the enzymic activity. Indeed, centchroman is reported to raise the

LH level in human female, causing induction of ovulation (10) and modulate pituitary gonadotrophin and prolactin release in female rats (12).

Whatsoever the action of these substances may be, it is evident from the present study that the pituitary threshold for steroidal *vis-a-vis* nonsteroidal molecule is different.

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