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Zoology

EFFECT OF THIOUREA ON UTERUS OF FEMALE MICE

ANEES IQBUAL SHAIKH

Assistant Professor, Department of Zoology, MG Science Institute, Ahmedabad

KEYWORDS : .

The female reproductive system consists of a pair of ovaries attached to the dorsal wall of the abdomen behind the kidneys of the mesentery called mesovarium. Closely associated with each ovary but not in contact with it lies the funnel shaped end of the oviduct called fimbriated funnel. Each funnel leads into a narrow thin walled slightly convoluted faliopian tube which is lined internally by ciliated epithelium. Posteriorly each fallopian tube is continued into a thick walled, muscular, richly vascular and highly distensible uterus. The uteri open separately into a single median tube known as the vagina. The lower end of the vagina also meeta the urethra from the urinary bladder so that there is a single wide but short urinogenital canal or vestibule which is dorsal to the pubic symphysis. The vestibule opens to the exterior of the vulva.

Uterus

The uterus, a thick walled hollow, pear shaped organ with anterior flattening, lies about the center of the pelvis. The uterus is freely mobile and is capable of growth during pregancy. The uterus is made up of three major connective tissue layers (1) a thin outer perimetrium (2) a massive myometrium of smooth muscle and connective tissue, and (3) an inner most endometrium. From the physiological point, only two layers are recognised, the endometrium and the myometrium. The endometrium varies in thickness form 1-6 mm depending on the stage of the menstrual cycle as estrous cycle. It also varies with changes in the ovarian hormones and pregancy. Progesterone causes the stromal cells to enlarge, become pale and filled with lipid and glycogen. The normal endometrium responds to the fluctuating levels of ovarian steroids, this reflecting the stages of the ovarian cycles. The mymotrium is arranged in intricate layers of interlacing bundles of smooth muscle cells which respond to oxytocin.

It is very clear from the review of literature that thyroid hormone within a narrow range is required for proper functioning of somatic and gonadal tissues; otherwise hypothyroidic or hyperthyroidic condition develops which requires proper attention. Inclidenceof both hyperthyroidism, especially during pregnancy and hypothyroidism are comparatively higher in females than males. Detailed changes in the reproductive funciton of females during hypothyroidism is not clearly understood. Hence the present investigation was undertaken. We preferred the use of antithyroid agent (thiourea) over surgery because of the presence of cells producing thyrocalcitonin required for calcium homeostasis, and risk due to high regenerating capacity of thyroid cells. Mice were selected for experimental studies due to short estrous cycle and prolific breeding capability.

Materials and methods

ANIMALS:

Healthy, adult female albino mice (Mus musculus) of Swiss strain, weighing about 30-40 grams were used in the present experiments. The animals were housed in an air conditioned animal house at 26±20C and maintaiend on 12 hours of day light. The control as well as experimental animals were given standard chow and water ad-libitum. Animals of different groups of treatments were caged separately with a maximum number of 6 to 8 animals per cage.

PREPARATION OF THIOUREA:

Thiourea (A.R.) (NH2.CS.NH2) (mol wt 76.12) was obtained from S.D. Fine Chemicals Pvt. Ltd., Boisar-401501.

Required concentraiton of thiourea was dissolved in normal saline (0.9% sodium chloride in glass distilled water) prior to treatment.

DOSAGE, DURATION AND MODE OF TREATMENT:

Group-I : Control:

Animal of this group received intrapritoneal injecitons of 0.2 ml normal saline daily for 15 days.

Group-II : Low Does :

Animal of this group were injected with thiourea at a does of 0.2 mg/0.2 ml saline/mouse.day intraperitoneally for 15 days (10 mg/kg body weight).

Group-III : High Does :

Animal of this group were injected with thiourea 0.4 mg/0.2 ml saline/mouse/day intraperitoneally for 15 days (20 mg/kg body weight).

The various groups of animals, preatment, number of animals, duraiton of treatment and day of autopay are summarized in the following table

Groups	Treatment	Duration of treatment (days)	Autopsy day
I Control	0.2 ml saline/mouse/day	15	16th day
II Low Dose	0.2 mg thiourea/0.5 ml/mouse day	15	16th day
III High does	0.4 mg thiourea/0.5 ml/mouse day	15	16th day

At the end of treatment, the animals were weighed and sacrificed by cervical dislocation. Required organs were isolated, blotted free of blood and weighed.

ESTROUS CYCLE OF FEMALE MICE:

The estrous cycle or reproductive cycle in female mice is completed in 4-5 days. The vaginal epithelium undergoes changes controlled by the changing hormonal milieu and these changes are correlated to changes in the uterine wall.

The eatrous cycle occurs in 4 stages during which characterestic changes occur in the vaginal smear. The estrous cycle is therefore atudied by making stained preparations of the vaginal smear.

Procedure:

A medicinal dropper containing 1-2 drops of normal saline was gently inserted into the vagina of amouse. After aspirating once or twice, the vaginal fluid collected in the dropper was smeared on a clean microscopic glass slide and allowed to semi-dry. Vaginal smears, stained with Ehrlich's Haematoxylene for 4-5 minutes were observed under the microscope.

Results:

Estrous cycle:

Estrous cycle in control mice was of 4-5 days. Treatment of mice with low ans high dose of thiourea drastically changed the estrus cycle. In treated animal cyclicity was normal upto 11-12 day of treatments; thereafter it was abruptly stopped and animals remained continuosly in one stage (Table-3).

Table : Showing phosphorylase activity and protein content in the uterus of control, low-does and high does thiourea treated mice.

Parameters	Controls	Low does Treated	High does Treated
phosphorylase acitivity (μg phosphorus released/100 mg fresh tissue weight/15 minutes)	1.42 0.11	0.74 0.04*	0.39 0.04*
Protein (mg/100 mg fresh tissue weight	27.92 0.51	19.56 0.49*	11.72 1.01*

value are mean $\pm$S.E. n = 8
* : significant at P < 0.001

Uterus:

Phosphorylase:

Phosphorylase activity in the uterus of control and thiourea treated mice were presented in Table. A significant (P(0.00)) reduction in activity was recorded with both low and high dose of thiourea treatment for 15 days.

Protein:

Data shown in Table clearly indicate significantly (P(0.00)) reduced protein content in the uterus of thiourea treated mice. Reduction in protein content was more pronounced in high does treated mice than that of low does ones.

Glycogen:

Thiourea (low and high does) treated to mice for 15 days caused increase in glycogen content of uterus. Data was found statistically significant (P(0.001)) over control value.

Cholesterol:

Cholesterol content in the uterus of control mice was 0.61 mg/100 mg fresh tissue weight. Thiourea treatment (both low and high does) for 15 days caused significantly (P(0.001) increased cholesterol content.

DISCUSSION

The results revealed that the body weight did not alter significantly in all the treated groups of mice as compared to that of control. Non-significant increase in body weight might be due to the subcutaneous depositions of fat and/or other metabolic alterations. Absolute and relative organ weights did not significantly change in all treated groups of animals as compared to control.

Results shown in Table-3 revealed anovulatory and irregular cycles in thiourea treated mice. The estrous cycle is shorter (4 or 5 days vs. 21 days) in rat/mice (Buthcer et al., 1974; Smith et al., 1975) since the corpora lutea of estrous cycle are only partially activated steroidogenically (Buthcer et al., 1974; Smith et al., 1975). Stages of eatrous cycle and their inter-conversions are mainly governed by the female sex hormones, estrogen and progesterone. mainly synthesized in the ovary. The serum level of these hormones are controlled by the secretion of pituitary gonadotrophins and hypothalamic releasing hormones (Lerner, 1969). Furthermore through feedback mechanism, the level of gonadotrophins are controlled by the estrogens and progesterone. Progesterone is known to maintain the luteal phase in cyclic rats (Nalbandov, 1970).

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