EFFECT OF ESTRADIOL DIPROPIONATE ON UTERINE AND VAGINAL GLYCOGEN CONTENT OF PARKES (P) MICE

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Summary : Administration of estradiol dipropionate (20 μg/day; for 7 days) to ovariectomized (7 days) mice produced about three fold increase (180%) in uterine glycogen content while approximately four fold decrease (76%) in vaginal glycogen as compared to their control values. Differences in glycogen content after 7 and 14 days of ovariectomy were statistically insignificant in both the organs. Although estradiol dipropionate had a great effect on the glycogen content of uterus and vagina but this effect remained more or less unchanged after causing alteration in duration (7 and 14 days) of estradiol dipropionate treatment in relation to different time intervals (7 and 14 days) after ovariectomy. So there was no time dependent response in uterine and vaginal glycogen content after 7 days onwards either in relation to ovatiectomy or estradiol dipropionate treatment.

The opposite trend (increase in uterus and decrease in vagina) of glycogen content in response to estradiol dipropionate may be possibly due to a greater accumulation (than utilization) in uterus while greater consumption (than accumulation) in vagina.

Key words : estradiol diproprionate ovariectomy glycogen uterus mice vagina

INTRODUCTION

Various workers (8,4) have reported a decrease in uterine glycogen level after ovariectomy and an increase on estradiol administration to ovariectomized rats. A 200% increase was found in the glycogen content of rabbit uterus after 5 days of estrogen treatment (6). Estradiol (50 μg) administration to an ovariectomized rat raised uterine glycogen level by 170% in 48 hr (7). Ovariectomized rats treated with estradiol showed an elevation in uterine glycogen concentration within 2 hr and a steady state after 12 hr upto 24 hr; and onwards a decline was observed (1). An increase in uterine glycogen level while a decrease in vaginal glycogen were reported in response to estradiol treatment to ovariectomized albino rats (2).

Changes in carbohydrate metabolism have long been considered important under the control of hormones elaborated from several endocrine entities. In animal cells, glycogen is the main carbohydrate which is largely responsible for energy production to

meet the demand of various cellular activities. It is well known that estrogen plays a significant role in maintaining the normal histophysiological status of female genital system in mammals. Thus keeping in a view the importance of glycogen on one hand and estrogen on other hand, the present experimental protocol was designed to evaluate the effect of estradiol on glycogen metabolism at a dose which was enough to produce a normal histological response in uterine and vaginal tissues of P-mice.

MATERIAL AND METHODS

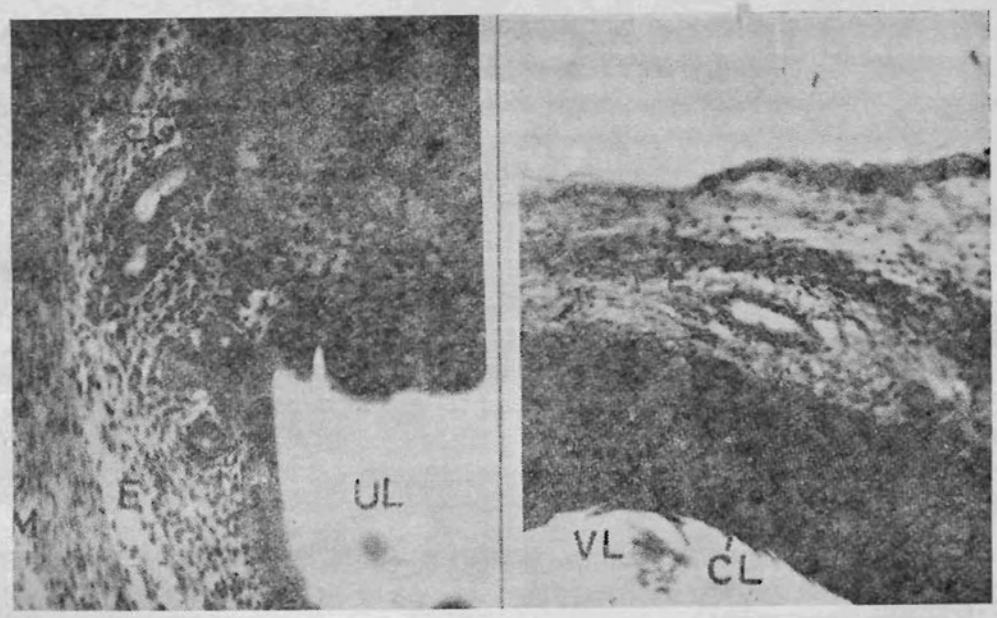
All mice employed in the study were 70-100 days old mice of the Parkes (P) strain bred in the animal house of the Department of Zoology, Banaras Hindu University. The parental stock came from the Central Drug Research Institute (CDRI), Lucknow. Mice were kept at normal room temperature under the natural photo-period. They were maintained on standard laboratory mice feed (Hindustan Lever Ltd., Bombay) and had unrestricted access to drinking water. Bilateral ovariectomy was performed in virgin females and they were grouped as follows :

TABLE I : Grouping of bilaterally ovariectomized mice for further treatment of estradiol dipropionate.

Group	*Subgroup*	*Duration after ovariectomy* (days)	*Duration of estradiol dipropionate treatment* (days)
A	A_1	7	—
	A_2	14	—
B	B_1	7	7
	B_2	7	14
	B_3	14	7
	B_4	14	14

Estradiol dipropionate (in ampoules) was purchased from Ciba-Geigy Ltd., Bombay as ovocyclin* tradename which is a pure follicular hormone. Each ampoule contains one *ml*; (=5 *mg*) and the desired concentration of injection was prepared with the help of a neutral oil (olive oil) . The dose of estradiol dipropionate (20 μg/day; for 7 days) was standardized and it was found to be enough to produce the normal histological response in uterine (Fig. 1-A) and vaginal (Fig. 1-B) tissues of 7 days ovariectomized mice. Thus the estradiol dipropionate at a dose of 20 μg per female per day was injected subcutaneously and three mice from each subgroup were sacrificed by decapitation at 24 hr

*Registered Trade Mark



A B

Fig. 1-A : Transverse section of a mouse uterus. After 7 days of bilateral ovariectomy, mouse was administered estradiol dipropionate (20 μg/day) continuously for 7 days. Abbreviation : UL ; uterine lumen. E; Endometrium. EG; Endometrial glands. M; Myometrium.

1-B : Transverse section of a mouse vagina. After 7 days of bilateral ovariectomy, mouse was treated with estradiol dipropionate (20 μg/day) continuously for 7 days. Abbreviation : VL; Vaginal lumen. CL; Cornified layer. EL; Epithelial layer. FL; Fibrous layer.

TABLE II : Uterine and vaginal glycogen content of P-mice in response to different duration after ova ovariectomy and estradiol dipropionate treatment in relation to different time intervals after ovariectomy.

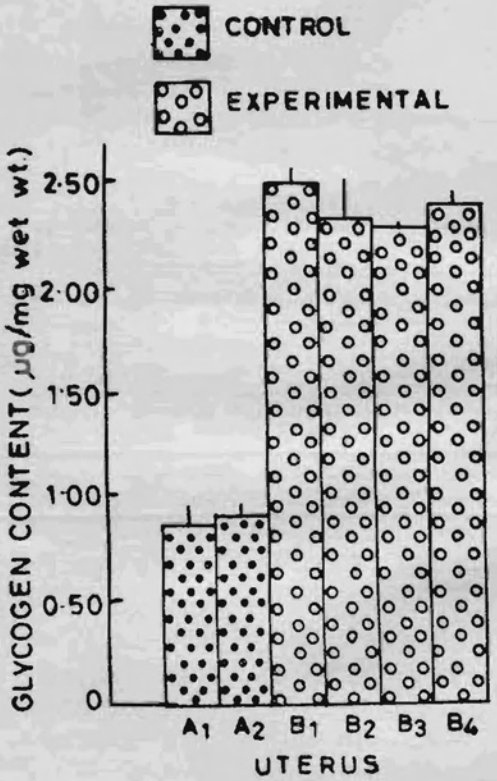
Group	*Subgroup*	*Uterine Glycogen Content* (μg/*mg* wet wt.)	*Vaginal Glycogen* (μg/*mg*. wet wt.)
A (Control)	A_1	0.869±0.061	2.480±0.072
	A_2	0.878±0.051	2.368±0.115
B	B_1	2.437±0.063 (P<0.001)	0.584±0.008 (P<0.001)
	B_2	2.263±0.170 (P<0.005)	0.706±0.045 (P<0.001)
	B_3	2.229±0.026 (P<0.001)	0.664±0.040 (P<0.001)
	B_4	2.326±0.052 (P<0.001)	0.547±0.093 (P<0.001)

Each value in table is the mean of three individual determinations. ±SEM. Values of subgroup A_1 and A_2 were insignificant with each other. Similarly, values in subgroup B_1, B_2, B_3 and B_4 were also statistically insignificant in an intra-group (B) compasrion. Values in parenthesis indicate the P value after comparison of subgroup A_1 and B_1, A_1 and B_2, A_2 and B_3, A_2 and B_4; and all were significant.

after the last injection. Glycogen was estimated by Montgomery method (3) and content was calculated ($\mu g/mg$) of wet wt. of titssue) with the help of a linear standard curve of glycogen. Students 't' test was applied for statistical analysis of the obtained data.

RESULTS

Glycogen in uterus (Table II and Fig. 2) : Glycogen content after 7 and 14 days of ovariectomy were 0.869 and 0.878 $\mu g/mg$ wet wt. of tissue respectively. These values were insignificant ($P>0.20$) with each other. Likewise the glycogen content (2.437 $\mu g/mg$) of 7 days estradiol dipropionate treated mice (after 7 days of ovariectomy) showed statistically insignificant difference in comparison to the glycogen content



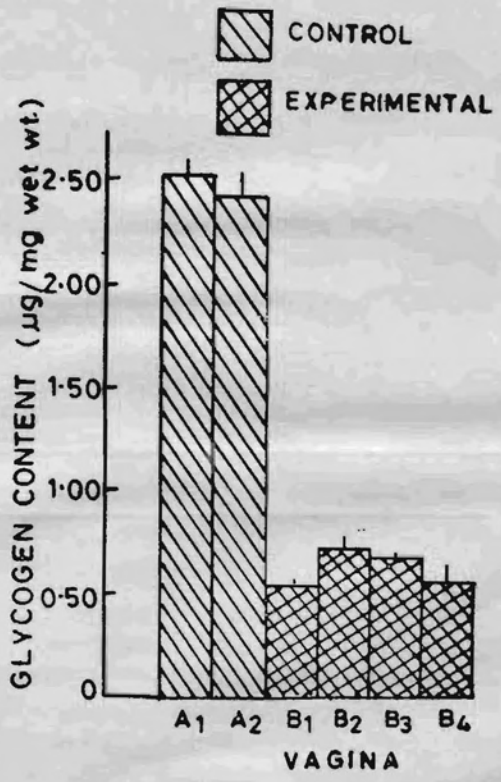


Fig. 2: : Glycogen content of uterus.

Fig. 3 : Glycogen content of vagina

Abbreviation : A_1=After 7 days of ovariectomy ; A_2=After 14 days of ovariectomy ; B_1=ovariectomy (after 7 days)+Est. diprop. (for 7 days); B_2= ovariectomy (After 7 days)+Est. diprop. (for 14 days); B_3=ovariectomy (After 14 days) +Est. diprop. (for 7 days); B_4= ovariectomy (after 14 days)+Est. diprop. (for 14 days). Est. diprop.=Estradiol dipropionate.

of subgroup B_2 (2.263; $P>0.20$), B_3 (2.229; $P>0.05$) and B_4 (2.326; $P>0.20$). However, the statistical comparison between the glycogen content of inter-subgroup A_1 and B_1 ($P<0.001$), A_1 and B_2 ($P<0.005$), A_2 and B_3 ($P<0.001$), A_2 and B_4 ($P<0.001$) presented significant differences.

Glycogen in vagina (Table II and Fig. 3) : Glycogen content after 7 days of ovariectomy was 2.480 *µg/mg* wet wt. of tissue and 2.368 *µg/mg* after 14 days of ovariectomy. And they were also insignificant ($P>0.20$) to each other. Similarly, the glycogen content (0.584 *µg/mg*) of 7 days estradiol dipropionate administered mice (after 7 days of ovariectomy) showed insignificant difference in comparison to subgroup B_2 (0.706; $P>0.05$), B_3 (0.664; $P>0.10$) and B_4 (0.547; $P>0.20$). While the glycogen content of A_1 and B_1 ($P<0.001$), A_1 and B_2 ($P<0.001$), A_2 and B_3 ($P<0.001$), A_2 and B_4 ($P<0.001$) were showing statistically significant difference with each other.

Therefore, daily injection of estradiol dipropionate to ovariectomized (7 days) mice continuously for 7 days caused a significant increase (about 3 fold or 180%) in uterine glycogen content while a significant decrease (about 4 fold or 76%) in vaginal glycogen content as compared to their values of 7 days ovariectomized mice (control). There was no time dependent response in glycogen content after 7 days onwards either in relation to ovariectomy or estradiol dipropionate treatment at different duration after ovariectomy.

DISCUSSION

Estrogen-induced increase (about 3 fold) in uterine glycogen requires two assumptions for explanation. First, estradiol somehow brings the conversion of glycogen synthetase D to I. Thus synthetase I/D ratio is increased and concomitantly glycogenesis is stimulated (8). Second, the accumulation of glycogen proceeds at a greater pace than the utilization in uterine tissues (5). First assumption may be accepted in case of vagina for the effect of estradiol on glycogen synthesis at enzymatic level but there was four fold decrease in glycogen content as compared to its control value. Therefore for decreased vaginal glycogen content, the second assumption may be argumented but in reverse manner i.e. the consumption of glycogen occurs at a greater scope than storage.

Insignificant differences between the values of Group B with each other (subgroups : B_1, B_2, B_3 and B_4) in uterus may indirectly support the finding of other workers (1) that the concentration of uterine glycogen remained stable from 12 hr to 24 hr after estradiol administration. Tha case may be also similar to explain the maintenance of declined vaginal glycogen content in group B.

Declined uterine glycogen after ovariectomy is due to lack of sufficient estradiol. Here, the value of glycogen content is probably a manifestation of the combined effect of glycogen utilization and insulin action on carbohydrate metabolism. However, increased vaginal glycogen after ovariectomy may be due to increase in accumulation rate of glycogen than its consumption rate. Perhaps, after ovariectomy, the constancy in decreased uterine glycogen and increased vaginal glycogen of 7 and 14 days ovariectomized mice was maintained by action of other hormones (glucagon, insulin, epinephrine).

Therefore, according to physiological need, the estradiol is playing a vital role in regulation of uterine and vaginal glycogen content upto certain extent. Probably, differences in the degree of glycogen accumulation and consumption are affecting the glycogen level in uterus and vagina of P-mice.

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REFERENCES

1. Bitman, J., H.C. Cecil, M.L. Mench and T.R. Wrenn. Kinetics of *in vivo* glycogen synthesis in estrogen-stimulated rat uterus. *Endocrinology*, **76** : 63-69, 1965.
2. Mehrotra, P.K. Studies on the physiology and biochemistry of female genital tract of albino rats : response of uterus, cervix and vagina to two different dose ratios of estrogen and progesterone. *Ind. J. Physiol. Pharmac.*, **20** : 235-238, 1976.
3. Montgomery, R. Determination of glycogen. *Arch. Biochem. Biophys.*, **67** : 378-386, 1957.
4. Paul, P.K. and P.N. Duttagupta. Inhibition ofcestrogen-induced increase in hepatic and uterine glycogen by progesterone in the rat. *Acta Endocr.*, **72** : 762-770, 1973.
5. Segal, S.J., W. Scher and S.S. Koide. Chapter 7 : Estrogens, Nucleic acids, and Protein synthesis in uterine metabolism. pp. 139-201. In : Biology of the Uterus (Ralph M. Wynn ed. 1977). Plenum Press, New York.
6. Telfer, M.A. and F.L. Jr. Hisaw. Biochemical responses of rabbit endometrium and myometrium to oestradiol and progresterone. *Acta Endocr.*, **25** : 390-404, 1957.
7. Walaas, O. Effect of oestrogen on the glycogen content of rat uterus. *Acta Endocr.*, **10** : 175-190, 1952.
8. Williams, H.E. and H.T. Provine. Effect of estradiol on glycogen synthesis in rat uterus. *Endocrinology*, **78** : 786-790, 1966.