

# 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\*

P.K. MEHROTRA

*Division of Endocrinology,  
Central Drug Research Institute, Lucknow-226001*

**Summary :** Effect of two different dose ratios of estrogen (E) and progesterone (P) (1:1000; 1:10,000) on the morphological and biochemical response of the uterus, cervix and the vagina of ovariectomized estrogen pretreated rats was studied. It was observed that the dose ratio of E & P at 1:1000 did not produce any remarkable ponderal and histological changes from that seen under the influence of estrogen alone. Whereas, in the dose ratio of E & P at 1:10,000 progesterone appeared to inhibit the effect of estrogen. The biochemical response of the uterus, cervix and vagina, however, varied from each other in both the dose ratios.

**Key words :** Estrogen & Progesterone ratio

Female genital tract

## INTRODUCTION

The dose ratio of estrogen (E) and progesterone (P) plays a vital role in maintaining normal reproductive status of the female genital system. To obtain the optimal dose ratio, these hormones have been studied in different dose ratios and at different time intervals in a number of species (9,12,14). The interaction of the two hormones mainly depends upon their dose ratio, the administration time and the parameter/tissue used for the assessment of such activity; for *e.g.* while the progesterone pretreatment abolished the estrogen response on the uterine epithelium (14), it had no effect on the vaginal cornification when given prior to or in combination with estrogen (5,6). Cecil and Bitman (2) reported that the pretreatment of progesterone reduced the estrogen-induced rise in uterine glycogen; conjoint treatment of E&P had, however, no effect. On the other hand, Bo *et al.* (1) showed that the progesterone, in a conjoint treatment, lowered the estrogen-induced rise of uterine glycogen. These contradictory findings prompted the present investigator to study the effects of the two different dose ratios of E&P on the female genital tract of albino rats.

## MATERIALS AND METHODS

Female rats (120-180 g) of the Institute colony maintained under uniform husbandry conditions (temp.  $75 \pm 2^\circ\text{C}$ ) were bilaterally ovariectomized. After 10 days the animals were divided into 4 groups of 10 rats each. Animals of Gr. I served as control and were injected with sterile

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olive oil (0.1 ml/day for 7 days). Rats of groups II, III and IV received estradiol dipropionate (0.5 µg/day for 7 days). Progesterone was injected to the rats of Gr. III (0.5 mg/rat) and Gr. IV (5.0 mg/rat) commencing from 4th day of estrogen treatment daily for four days. Thus estrogen and progesterone administered to groups III and IV were in the ratio of 1:1000 and 1:10000 respectively; both the hormones were injected by subcutaneous route. The rats were autopsied 24 hr after the last injection. The uterus, cervix and the vagina were dissected out, weighed on a torsion balance (0.1 mg) and processed for biochemical analyses (4). Few pieces of each organ were fixed in Bouin's fluid for histological studies.

## RESULTS

Table I indicates that the estrogen as well as both the dose ratios of E&P increased the wet weight of the uterus, cervix and the vagina of ovariectomized rats, but there was no significant difference from that of the estrogen control in any organ except cervix. Estrogen alone and both the dose ratios of E&P also lowered the total solids of the uterus and vagina ( $P < 0.01$ ) but not of the cervix ( $P > 0.05$ ). Protein contents, in contrast, were increased by estrogen in every organ ( $P < 0.01$ ): E&P at 1:1000 produced the same effect but only in the cervix and vagina ( $P < 0.01$ ). The effect produced by E&P at 1:10,000 was just the reverse to that induced by E&P at 1:1000.

TABLE I: Effect of estrogen and progesterone on the weight and biochemical changes in uterus, cervix and vagina of albino rat.

Groups	Tissue weight (mg)	Total solids (g/100 g)	Protein (g/100 g)	Glycogen (mg/100 g)	Lactic acid (g/100 g)	Alkaline phosph. (mgP/100 g/hr.)
<i>UTERUS</i>						
I	114.5±7.28 (8)	36.35±0.57 (6)	14.37±0.13 (6)	45.8±6.9 (6)	1.03±0.09 (6)	505.0±34.0 (6)
II	296.4±14.65 (9)	23.87±0.54 (6)	18.22±0.19 (6)	69.7±3.4 (6)	1.55±0.11 (6)	595.0±19.7 (6)
III	267.5±14.00 (8)	24.85±0.85 (6)	14.77±0.26 (6)	63.0±1.5 (6)	1.22±0.05 (6)	428.0±27.6 (6)
IV	319.0±18.73 (9)	31.62±1.14 (6)	16.42±0.34 (6)	42.7±3.7 (6)	1.28±0.08 (6)	495.7±24.3 (6)
<i>CERVIX</i>						
I	20.70±1.41 (8)	49.38±1.95 (6)	10.80±0.24 (5)	46.7±2.3 (6)	0.88±0.10 (6)	551.3±11.71 (6)
II	65.28±3.51 (9)	45.00±2.50 (6)	12.13±0.32 (6)	69.5±3.6 (5)	1.58±0.07 (6)	910.8±14.5 (6)
III	57.50±3.00 (9)	51.83±1.38 (6)	17.58±0.46 (6)	53.5±1.7 (6)	2.46±0.12 (6)	521.7±32.0 (6)
IV	45.30±3.12 (9)	59.17±2.00 (6)	12.15±0.43 (6)	70.8±1.3 (6)	2.13±0.15 (6)	1072.0±23.3 (6)
<i>VAGINA</i>						
I	43.30±1.41 (8)	52.42±2.47 (6)	11.32±0.89 (6)	63.5±3.6 (6)	1.12±0.05 (6)	210.8±8.4 (6)
II	78.65±3.72 (9)	39.67±1.72 (6)	13.38±0.32 (6)	34.3±1.3 (6)	1.78±0.19 (6)	385.0±13.1 (6)
III	65.50±3.31 (9)	39.00±1.33 (6)	17.58±0.47 (6)	56.2±5.9 (6)	1.47±0.08 (6)	215.0±11.7 (6)
IV	71.40±4.12 (9)	39.25±1.68 (6)	12.15±0.43 (6)	62.2±7.5 (6)	1.39±0.09 (6)	322.5±16.7 (6)

No. in parenthesis indicate animals in case of tissue weights and tissue samples in case of biochemical constituents.

Estrogen also raised the glycogen level but only in the uterus and cervix: in vagina it was lowered. E&P (1:1000) elevated the glycogen level of the uterus ( $P < 0.01$ ) but not that of the cervix and vagina ( $P > 0.05$ ). E&P (1:10,000) did not change the uterine and vaginal glycogen ( $P > 0.05$ ) but markedly increased its concentration in cervix ( $P < 0.01$ ). The level of lactic acid was raised by estrogen and by both the dose ratios of E&P in all the three organs. The activity of alkaline phosphatase was also raised by estrogen in each tissue; E&P at 1:1000 did not change the enzymic activity in any organ ( $P > 0.05$ ) but E&P at 1:10,000 produced a rise in cervix and vagina; there was no change in the uterus.

Histological changes in the three organs following ovariectomy and after estrogen treatment were same as reported earlier (10). E&P at 1:1000 stimulated every organ. The cells of the uterine surface and glandular epithelia were columnar. The stroma was loose and edematous. The squamous epithelia of cervix and vagina were stratified and keratinized. The dose ratio of E&P at 1:10,000 transformed the columnar cells of the uterine surface epithelium into cuboidal. Glands were under developed and the stroma was compact. Cervical and vaginal epithelium were only few cell layers thick. Scant mucification was discernible in the vagina.

### DISCUSSION

The results of the present study indicate that both the dose ratios of E&P produced, in general, an increase in the wet weight of the uterus, cervix and the vagina as compared to ovariectomized control. Interestingly, the weight increase was not significantly different from that produced by estrogen alone. The results are, however, not in agreement with the findings of Garrison *et al.* (7) who noticed a reduction in the uterine weight with different dose ratios of E&P. This may be due to the fact that they (7) used only castrated rats while the rats in the present study were pre-treated with estrogen.

Histological manifestations are interesting in the sense that while the dose ratio of E&P at 1:1000 did not produce any remarkable alteration from that of the estrogen treated organs, the progesterone used in the dose ratio of 1:10,000 appeared to inhibit the estrogen-induced stimulatory changes in every organ. Restricted effects of progesterone over the estrogen-induced responses in the uterine surface and glandular epithelia and vaginal proliferation are reported in literature (3,5,11). Such effects indeed depended upon the time of administration and the dose ratio of the two hormones, the estrogen and progesterone.

The biochemical profile, on the contrary to ponderal and histological, presented the changes which varied not only between the two dose ratios but also between the three organs within the same dose ratio. For *e.g.* the glycogen level was raised (*vs.* ovariectomized control) by E & P at 1:1000 in the uterus but not in the cervix and vagina. Similarly, E & P at 1:10,000 produced a rise in glycogen concentration only in cervix and not in the other two tissues. Likewise, several examples may be cited with regard to other biochemical parameters. It is pertinent to mention

here that such type of dissimilarity in the response of the three organs has been reported earlier also (8,13).

The present study, therefore, reveals that the dose ratio of E&P is an important factor for assessing the interactions between the two steroids in the female genital tract. The dissimilarity observed in the biochemical response of the uterus, cervix and the vagina vis-a-vis the two dose ratios of E&P may be assigned to the differences in the rate of absorption and/or retention of the sex hormones in the target organs (15).

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