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Asian Pacific Journal of Reproduction

journal homepage: www.apjr.net



Original research

http://dx.doi.org/10.1016/j.apjr.2015.12.006

Cytoarchitectural variations in selected rat tissues following the administration of estradiol valerate in aged female rats

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ARTICLE INFO

Article history:
Received 30 Dec 2014
Received in revised form 16 Oct 2015
Accepted 2 Nov 2015
Available online 17 Dec 2015

Keywords:
Estradiol velerate
Ovary
Uterus
Vagina
Liver
Endometrial epithelial cell

ABSTRACT

Objective: To study the histomorphological changes with reference to estradiol valerate administration in aged female albino rats.

Methods: The observations showed in young, aged and aged administered with estradiol valerate (Progynova tablets) at the dose of 2 mg/day through oral gavages for one week. The histomorphological changes were observed in ovary, uterus, vagina and liver.

Results: Estradiol velerate administration improves the ovarian stroma and germinal epithelium. The vascular hyaline degeneration reduces. Vascular protective effects of estrogen are well established. The administration may be associated with endometrial hyperplasia and neoplasia. The stroma was comparatively less edematous with less active endometrial glands. The uteri exhibited endometrial epithelial cell pseudo stratification and hypertrophy. The vaginal histoarchitecture showed increased epithelial proliferation of the vaginal wall and improving thickening. Estradiol velerate does not showed any effect on liver architecture.

Conclusions: The administration of estradiol valerate showed its vascular protective effects. It does not showed any effect on liver architecture.

1. Introduction

Estrogens are important in the growth, differentiation and function of female reproductive tissues. Estrogen is recognized as a prime hormone in regulation of female reproductive physiology [1]. Menopause, a normal state of ovarian hormone deficiency, dramatically affects older women, often producing disabling consequences. The incidence of metabolic syndrome also called insulin resistance syndrome, increases substantially during menopause [2] and advancing age. The free levels of sex hormones were decreased during aging, which may indicate an important role of sex hormones in metabolic homeostasis. Estrogen replacement is frequently the treatment of choice for maintaining reproductive function and bone mineral density in post-menopausal women and amenorrheic adolescents [3]. While estrogen's effect on the reproductive system and bone are well established, less is known about how it affects other tissues. The present study aimed to study

the structural changes in reproductive tissues and liver for toxicity evaluation following the administration of estradiol valerate to aged female rats.

2. Materials and methods

In the present study healthy female albino rats were used. The rats were purchased from Sri Raghavendra Enterprises, Bangalore, India and divided in to three groups, each group containing 6 rats. First group are young rats (4 months), second group are aged rats (20 months) and third group are aged rats administered with estradiol valerate (Progynova tablets, Bayer Zydus Pharma Pvt. Ltd) (2 mg/day) [4] orally for one week with gastric gavages method. Animals were housed in a clean polypropylene cage under hygienic conditions in well ventilated clean air conditioned room, with photoperiod of 12 h light and 12 h dark cycle at (25 ± 2) °C, with a relative humidity of $(50 \pm 5)\%$. The rats were fed with standard laboratory feed supplied by Hindustan Lever Ltd, Mumbai and water ad libitum. The usage of animals was approved by the institutional animal ethical committee, in its resolution no: 13/2012-2013(i)/a/CPCSEA/IAEC/SVU/CC -AL dt.01-07-2012. Twenty four hour after the last dose, the animals were autopsied and tissues like ovary, uterus, vagina

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Peer review under responsibility of Hainan Medical College.

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and liver were fixed immediately after isolation in Bouin's fluid for 24 h. The tissues were dehydrated in various grades of alcohol, cleaned in xylene and after embedding in paraffin, blocks were prepared. Paraffin sections of 5 μ m thickness were cut with rotary microtome and processed for staining. Sections were stained with hematoxylin and the water staining was made with eosin. 10 sections were taken for each tissue. The light microscope with digital camera was used for photography.

3. Results

The histological changes were observed in young, aged and estradiol valerate administered to aged female rat tissues like ovary, uterus, vagina and liver.

3.1. Histological observations in ovary

The young rat ovarian histoarchitecture showed the normal ovoid shape with normal structure of follicles in different stages of development and densely cellular stroma. The developing follicles were well placed and embedded in ovarian stroma together with graafian follicles, corpus lutea and atretic follicles (Figure 1A and D).

The histology of aged rat ovary showed an obvious reduction in the number of follicles and corpora lutea. The cortex reduces its dimensions, the follicular apparatus is progressively diminished and the primary follicles completely disappear. Vascular hyaline degeneration is present both in the cortical and medullary stroma (Figure 1B and E).

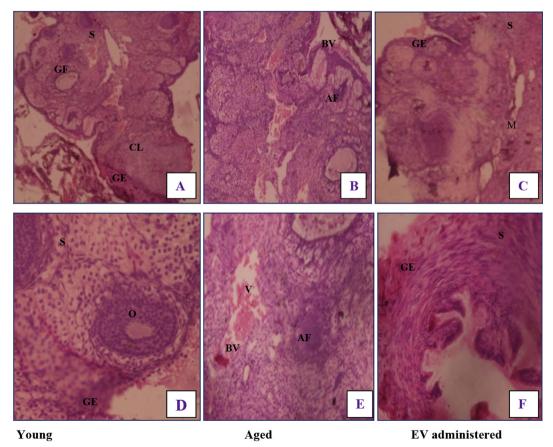
In histology of EV administered aged ovary improved ovarian stroma and germinal epithelium were observed. The vascular hyaline degeneration reduces (Figure 1C and F).

3.2. Histological observations in uterus

The histology of young uterus, exhibited a well differentiated serosa, muscularis and endometrial layers. Many well developed glands were also present and the stroma was densely cellular. The endometrium made up of a single layer of columnar epithelium. In myometrium the lamina propria connected with the compactly arranged smooth muscle layer, surrounded by the serosa and deep to it a rich network of blood vessels (Figure 2A andD).

In aged uterus the uterine lumen was slit-like and lined with small atrophic cuboidal cells. The stroma appeared dense and compact having few, small, inactive uterine glands. The luminal epithelium was low cuboidal and appeared in irregular, the uterine stroma was thickened. The myometrium and endometrial layers were reduced in thickness (Figure 2B and E).

In EV administration the uterine lumen was enlarged. The luminal epithelial cell height was reduced. The stroma was comparatively less edematous with less active endometrial glands (Figure 2C and F).



AF: Atretic follicle; M: Medulla; BV: Congested blood vessel; GF: Graffin follicles; C: Cortex; O:Ovum; CL: Corpus Luteum; S: Stroma; GE: Germinal Epithelium

V: Vascular hyaline degeneration

Figure 1. Histological observations of ovary (Hematoxylin and eosin; A,B,C in Mag. ×100; D, E &F are in Mag. ×400).

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