ABSTRACT

In a study aimed to identify the toxopathic effect of long term estradiol benzoate treatment in male and female rats. eighty rats of both sexes 1.5 months age were taken and divided into 4 equal groups each group 10 males and 10 female. Animals in the first three groups received 0.002, 0.004, 0.008 mg of estradiol benzoate (EB) /rat/day/ S/C for 100 days (Therapeutic, intermediate and toxic dose respectively). Animals at 4th group received sunflower seed oil as a control group. During the treatment a behavioral changes were appeared in male animals, vigor, rough at 10-14 days of injections, especially in toxic group – most of affected organs were Kidneys, pancrease, spleen, adrenal as non target organs whereas, the target organs showed different pathological changes. Other organs liver, lungs, brain and gastrointestinal tracts seemed unaffected. The most organs affected were presented in toxic group of treatment.

KEYWORD: Kidneys, pancrease, spleen, adrenal.

INTRODUCTION

Estrogen are a family of structurally related hormones which play a role in many different tissues types affecting both male and female physiology.[1]

The highest amount of estrogen receptors are found in the target tissues with reproductive functions such as mammary gland, ovaries, uterus, vagina. In these tissues estradiole stimulate the cell proliferation and biosynthesis of progesterone receptor[2] In male organs the estrogen receptors detected in the epididymis and prostates, in addition the action of estrogens in other non target organs like brain, bone, kidney, heart and liver, whereas, the action of estrogen in target organs of female responsible for all the sexual maturation activities in the female reproductive organs[3] for this reason this study aimed to identify all toxopathic changes induced by long term treatment with estradiol benzoate in rats target organs.

MATERIALS AND METHODS

Eighty rats (40 males and 40 females), 1.5 months age, divided into 4 equal groups (10 males and 10 females), Animals at the first three groups received 0.002, 0.004,0.008 mg of estradiol benzoate / rat/day / S/C for 100 days as a Therapeutic, intermediate and toxic doses respectively. The 4th groups were received sunflower seed oil as a control, all the animals were housed and kept until the end of experiment, during the experiment we recorded all behavior changes and at the end of experiment all the rats were sacrificed and recorded all the lesions on the organs and pieces 1x1 cm of lesions were taken, cut at 5 microne thickness and stained with hematoxyline and eosin.[5]

RESULTS

Macroscopical findings
All the reproductive organs of females and males showed abnormal appearance comparable to the normal appearance of the control group. Both the uteri showed in size except pyometra and large uterus size in toxic group of estradiol benzoate treatment. Ovaries showed multiple cysts ranging 2-4 mm diameter. The male organs tests showed small in size and atrophied, comparable to control group. All these macroscopical changes were more predominant in the toxic group.

Microscopical findings
Mammary gland
Showed cystic dilation of the interlobular ducts, some of these ducts filled with secretion, these lesions were predominant in the toxic groups together with hyperplasia of epithelia lining the ducts. In male all these changes were seen i.e acinar proliferation, cystic dilation of interlobular ducts giving a gynaecomastial features in male rats. (Fig.1).
(Fig.1) Mammary gland of rat showed hyperplasia of ductal epithelia.
With mild inflammatory reaction (arrow) X 100 (H & E).

Uterus
Showed squamous metaplasia of the endometrial glands in low and intermediate doses of estradiol benzoate treatment together with hyperplasia and squamous metaplasia in toxic group, the hyperplasia giving anastomosing cord like growth may be considered a preneoplastic changes. The uterus in some rats of toxic group showed extensive suppurative exudates composed of dead and living neutrophils together with necrotic tissue debris infiltrating the endometrial and subendometrial regions (pyometra) (Fig.2).

(Fig.2) Uterus of rat showed cystic endometrial metaplasia (arrow) X 100 (H & E).

Ovaries
Showed multiple growing follicles with cystic dilation of some follicles filled with serous fluid, there is no graviain follicles and no corpora lutea seen in all the ovaries of treated groups with estradiol benzoate. (Fig.3)

(Fig.3) Ovary of rat showed increase number of follicles (arrow) with different stage of development X 100 (H & E).

Tests and epididymis
Showed inhibition of spermatogenesis, loss of germinal layer lining seminiferous tubules together with multinucleated spermatid giant cells in the lumen of seminiferous tubules indicating a degeneration process.

(Fig.4) Testis of rat showed loss of spermatogenesis. X100 (H&E).

Seminal vesicles and prostate
Showed lack of secretion and degeneration of epithelial lining together with fibroblasts proliferation in the stromal tissues, also cystic dilation of prostatic acini with hyperplasia of their epithelial lining, all these lesions were more predominant in the toxic group. (Fig.5).
is loss and inhibition of spermatogenesis in testes and epididymis indicating the antagonistic effect of estrogen against testosterone.\cite{13} together with testicular degeneration accompanied with occurrence of spermatid giant cells which seen in most of sections of testes in toxic group. The inhibitory effect of estrogen on testes and similar inhibitory effect occur in prostate and Seminal vesicles, so lack of secretions, shrinkage of acini, and fibroblasts proliferation in the stroma, all these changes resulted in atrophy of male sexual organs\cite{12, 13} both those workers considered these lesions as preneoplastic changes.

Mammary gland in both male and female were affected by hormonal stimulation, estrogen in these cases caused stimulatory and functional activity on mammary tissues accompanied by cystic dilation and hyperplasia of mammary acini.\cite{14, 15} whom considered that these hyperplasia increase the risk of cancer in mammary tissue a similar findings were reported.\cite{8}

REFERENCES

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