EFFECT OF ESTROGEN ADMINISTRATION ON THE SEMINAL VESICLE OF ADULT ALBINO RAT A MORPHOLOGICAL AND HISTOLOGICAL STUDY

THESIS

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Abstract

Key Words

- Seminal Vesicle.
- Estrogen.
- Rat.

In the present work, 60 adult male albino rats were used and divided into three groups. One control group and two experimental groups were exposed to different estrogen treatments, a weekly low (L) dose (140 µg/kg body weight) a daily therapeutic (T) dose (1 mg/kg body weight).

All the experimental groups showed weight loss compared to the control group which showed a weight gain. The histological examination revealed the presence of epithelial and stromal hyperplasia as an outstanding effect in all the experimental groups in a dose dependant manner. Other common changes included inflammatory infiltration. Only the therapeutic dose groups showed signs of dysplasia in the form of pleomorphism. Ultrastructural examination of different experimental groups revealed variable degrees of degenerative changes.

CONTENTS

INTRODUCTION

AND AIM OF THE WORK

Androgens have important role on differentiation, development and maintenance of epithelial cells in seminal vesicle as well as in the prostate (**Mata, 1995).**

The stroma in rat seminal vesicle depends on both androgen and estrogen in its maintenance and proliferation, and this hormonal dependancey is similar to that of canine and human prostates **(Partin and Rodriguez, 2002).**

The rat seminal vesicle is a better model to investigate the stromal-epithelial interactions via sex hormones and peptides of growth factor families which are transported or mediated by microvasculatures than the prostate in rat models **(Ono et al., 2004).**

The aim of the present work was to study the different effects of estrogen on seminal vesicle tissue using morphological and histological techniques, trying to clarify the role of estrogen in the normal growth of the seminal vesicle.

Male reproductive system of the rat

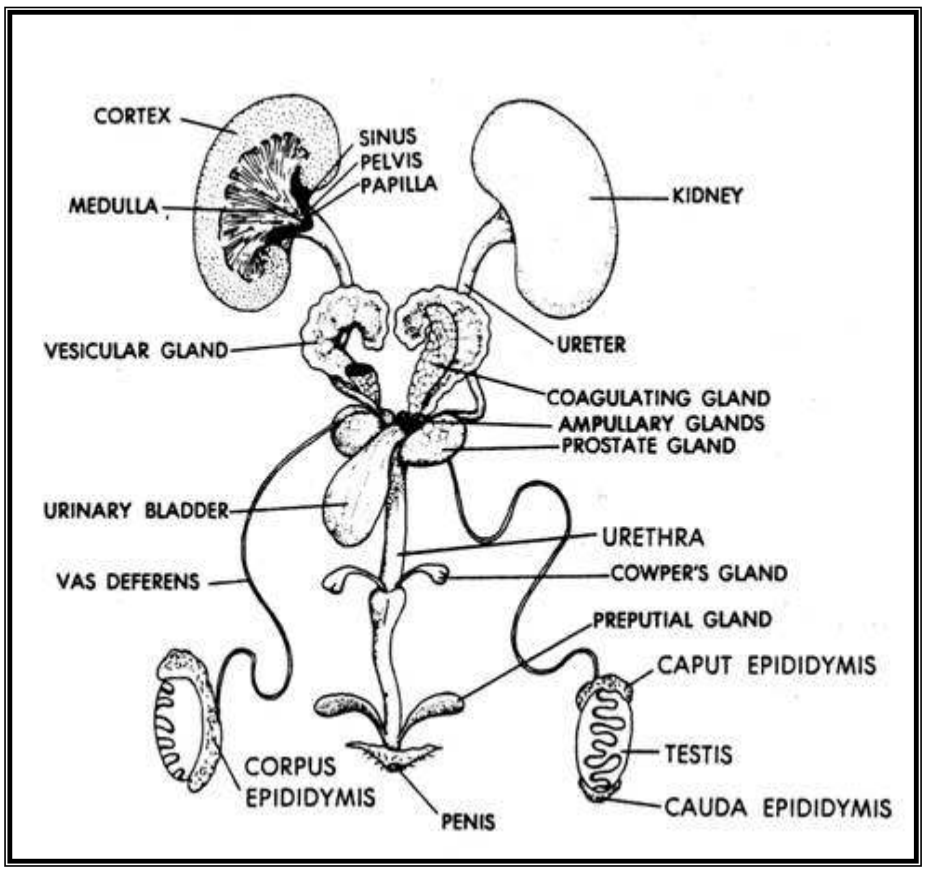
Anatomical considerations:

The rat is one of the most widely used research animals in reproductive physiology. The rat also is useful in assessment of toxicologic insults to the reproductive tract. The testes of the male lie in two separate thin-walled scrotal sacs located between the anus and the prepuce**.**The rat has five pairs of accessory sex glands located within the pelvis and surrounding the bladder: the glands of the ductus deferens; two pairs of prostate glands, oriented dorsal and ventral to the ductus deferens; one pair of large scythe-shaped seminal vesicle; and one pair of coagulating glands in close association to the vesicular glands. The paired bulbourethral glands are in association with the bulboglandular muscle **(Coffey, 1992).**

The seminal vesicles and coagulating glands are important for fertility in rats. Both organs secrete fluids that are necessary for appropriate formation of a vaginal plug. The role of the vaginal plug is not well understood beyond the observation that pregnancy is rare in the absence of its formation, but it is suspected to act as a reservoir for the gradual release of sperm or to prevent the outflow of sperm

from the vagina **(Sofikitis et al., 1992).**

Figure (1): Male urogenital system, ventral view.



Development of the urogenital System

The excretory system of the rat begins as a nephrogenic ridge that runs from the 9th to the 12th somites. The pronephric tubules and the anterior portion of the pronephric duct degenerate, but the more caudal portion of the pronephric duct persists and is referred to as the Wolffian duct. In the rat, the Wolffian duct appears at the end of day 10 **(Driscoll et al., 1986).**

The mammalian gonad first develops through an indifferent or bisexual state, with the default sex being the female. During the indifferent gonadal stage, both the Wolffian and Mullerian ducts are present. The Wolffian (mesonephric) duct is in close association with the gonad and empties into the urogenital sinus, **(Driscoll et al., 1986).**

In the male, the genital tract develops primarily from two embryonic anlagen: the Wolffian ducts and the urogenital sinus. The formation of the male phenotype involves the secretion of the hormones testosterone, secreted from the fetal testicular Leydig cells that stimulate the mesonephric (Wolffian) duct and urogenital sinus to differentiate, and anti-Mullerian duct hormone (Mullerian-inhibiting substance) that destroys the Mullerian duct over

days 18 to 22 in the rat**.**The Wolffian duct, whose epithelium is mesodermal in origin, gives rise to the epididymis, ductus deferens, seminal vesicle, and ejaculatory duct. The urogenital sinus, whose epithelium is derived from endoderm, gives rise to the prostate, bulbourethral glands, urethra, and periurethral glands. The mesonephric tubules give rise to the efferent ducts **(Timms et al., 2002).**

Male Reproductive Secretions

Male reproductive fluids may be used for studies of fertility, sperm morphology and sperm function and can be easily collected from epididymis, prostate and seminal vesicles during terminal surgery or at necropsy **(Creasy and Foster, 1991).**

Ryan et al. (1988) reported that the vas deferens of the rat can also be removed, cannulated and flushed to provide sperm samples to simply and accurately measure exocrine testicular function.

Excision of the cauda epididymis and collection of sperm from the distal portion of this anatomic structure are also often used to analyze sperm motility and velocity **(Timms et al., 2002).**

Samples may be aspirated with a capillary tube from a small incision in the excised epididymis.Alternatively, the epididymis can be placed in appropriate media, excised and sperm allowed to diffuse into the media **(Klinefelter et al., 1991).**

Sperm can be collected from various portions of the female reproductive tract following breeding **(Vreeburg et al., 1974).**

However, total numbers of sperm ejaculated cannot easily be quantified by this technique and samples cannot be used for artificial insemination because the ejaculate coagulates **(Timms et al., 2002).**

Rats was also reportedly ejaculate spontaneously and the specimen can be collected if the rats are prevented from orally grooming the genital area. Finally, the ductus deferens can be surgically anastomosed to the urinary bladder for continuous collection of sperm from urine **(Vreeburg et al., 1974).**

Seminal vesicle of the rat

Introduction:

The seminal vesicles are male accessory sexual glands found in many species of more than 4000 mammalian species alive on the earth. They lie inferior and lateral to the ampullae of the ductus deference against the fundus of the bladder **(Amir et al., 2008).**

After puberty, the gland secretes a fluid called seminal vesicle secretion (SVS), which accumulates in its lumen. SVS contains both protein and non-protein components. When ejaculated, SVS squirts into the urthera, contributing the major part of the liquid portion of seminal plasma, which is the complex biological fluid formed from mixing of various fluids in the male reproductive tract. It has been found that extirpation of the seminal vesicle from mice and rats greatly reduces fertility, demonstrating the importance of SVS to sperm modification under natural circumstances **(Peitz and Olds-Clarke, 1986)**.

It has been also demonstrated that protein and enzyme production is dependant on testosterone, which is formed mainly by the tests in males. Moreover, epithelial cell proliferation in the seminal vesicles seems to be testosterone

dependant in male mice **(Justulin et al., 2006).**

Development of the rat seminal vesicle:

Seminal vesicle morphogenesis begins on day 15 of fetal life with the dilation of the lower regions of the Wolffian duct, although rudiments are not seen until days 17 to 18 of gestation **(Hayward et al., 1996a).**

Just before birth, the seminal vesicle is essentially a hollow tube surrounded by mesenchyme, and a lumen is present at the very early stages of development of the seminal vesicles **(Sugimura et al., 1986).**

As the organ develops, the complexity of the epithelium increases as the epithelial buds grow laterally into the surrounding mesenchyme, elongate and bifurcate, and undergo secondary branching. Simultaneously, infolding of the epithelium into the ductal lumen increases, and at the end of development the seminal vesicle epithelia are characteristically described as “folded.” Hence, the complex topography of the seminal vesicles is due to lateral budding and branching as well as glandular infolding into the ductal lumen **(Risbridger and Taylor, 2006).**

The differentiation of seminal vesicle stroma to

smooth muscle also proceeds in an ordered process and is controlled by androgens. Castration reduces the smooth muscle layer and the expression of smooth muscle cell markers is lost in the reverse order of their expression during developmental maturation. The smooth muscle stroma is separated from the glandular epithelium by a lamina propria, including a periductal layer of fibroblasts **(Hayward et al., 1996b).**

As with the prostate, there is evidence that the seminal vesicles are responsive to estrogens as well as androgens and may be regarded as target tissues for both classes of steroid. This was most clearly demonstrated using another mouse model, the gonadotropins-deficient hpg mouse, which has postnatal deficiency in gonadotropins and testosterone but remains hormone sensitive **(Risbridger and Taylor, 2006).**

The seminal vesicles of adult hpg mice develop into rudimentary structures, and treatment with estrogen provided a means to distinguish between the direct actions of estrogens and indirect effects due to androgen suppression **(Risbridger and Taylor, 2006).**

With administration of estrogen, dual (proliferative and dedifferentiating) actions of estrogen on the seminal

vesicle epithelia and stroma were observed, including smooth muscle regression, fibroblast proliferation, inflammation, and basal epithelial cell proliferation and metaplasia **(Bianco et al., 2002).**

Structure of rat seminal vesicle:

Rat seminal vesicles are two tubular structures located between the urinary bladder and the rectum. Each vesicle is made up of a single convoluted duct that folds on itself and gives rise to well anastomosed ampullary and tubular diverticula; for this reason, seminal vesicles can be considered as branched tubulo-alveolar glands **(Mauro et al., 2009).**

Histologically, seminal vesicles are notable for their tortuous pathways, diverticula, pseudo-stratified columnar epithelium and cuboidal cells along the basal layer. In the lower part of the gland, the duct of the seminal vesicle joins the deferent duct and forms the ejaculatory conduct. Each vesicle is enveloped by a fibromuscular sheath. Three layers can be identified: the external adventitial one; the intermediate muscular one and finally the internal mucosa. The muscular layer is richly innervated by the orthosympathic nervous system and is composed of two

smooth muscle layers: the external longitudinal one and the internal circular one. The mucosa is structurally organized as a net; such organization significantly increases the surface area. The mucosa is composed of a columnar epithelium with a thin core of connective tissue, where numerous capillaries are present **(Mauro et al., 2009).**

Biochemistry of Estrogen

Sources of estrogen:

The major estrogens produced by females are estradiol 17β (E2), estrone (E1) and estriol (E3), E2 is the major secreted product in the ovary, it is then converted in the liver to E1 and E3 which have a lesser affinity to ER and are secreted in the bile. Estrogen is also secreted in breast milk in small amounts and catechol estrogen may serve as a neurotransmitter in the central nervous system (CNS). The plasma level in human females is as low as 50 pg/ml in the early follicular phase and reaches 350-850 pg/ml at the time of ovulation **(Chrouses et al., 2001).**

Of the circulating estrogen in young men, 75-90% comes from peripheral aromatization of testosterone to estrogen **(fig. 2)**, mainly in adipose tissue. 10-25% of estrogen is synthesized in the testes. The estrogen/androgen