

Effect of Norethisteron Heptanoat Treatment on the Mammary Glands of Albino Rat (Wistar Strain): Histological Aspect

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Abstract

Mammary glands contains a rich network of connective tissue, stroma and varying amounts of adipocytes. Two types of connective tissues an interlobular connective tissue and Intralobular connective tissue. Norethisterone was the first highly active oral progestational agent to be synthesized and to achieve wide spread use along with its acetate and enanthate esters. Noristerat or norethisterone or norethindrone or heptanoate is a depot progestogen for hormonal contraception. NOR-HN administration of the mammary gland results in atrophy of the epithelial cells & ducts.

KEYWORDS- Interlobular, Intralobular, Noristerate, NOR-HN, atrophy.

INTRODUCTION:-

NORETHISTERONE HEPTANOATE

Norethisterone was the first highly active oral progestational agent to be synthesized and to achieve wide spread use along with its acetate and enanthate esters.

Noristerat or norethisterone or norethindrone or heptanoate is a depot progestogen for hormonal contraception., Engren, (1974) have defined norethisterone as an androgen with a typical progestational effect at sufficiently higher doses. Progestogen causes the glandular elements of the mammary glands to grow and develop into secretory epithelium with the ultimate effect of acting in concern with other hormones particularly PRL, to facilitate milk production . Present study is aim to observe the effect of Nor-Hn a synthetic progesterone on mammary gland histology and related hormonal changes.

MATERIAL AND METHODS

ANIMALS:

Young, healthy, sexually mature female albino rats of Wistar strain (120-150 gms body weight) with normal reproductive history were procured from Haffkine Biofarmaceuticals. The animals were kept under uncontrolled room ambient temperature and photoperiod . Food pellets marketed by Lipton India Limited and water provided **ad libitum**. The rats were acclimatized for a month to the laboratory conditions prior to the commencement of any experiment .

The animals were divided into control and experimental groups, female Rats belonging closely to a certain weight group were selected , the reason for which all the groups of Rats at the commencement of the treatment did not weigh the same. The treatment lasted for 24 weeks duration i.e 24 injection of i.m.injectable Norethisterone heptanoat of 100% purity which is available in the market with same trade name.

On the completion of the treatment period, the animals were weighed and sacrificed

under light ether anaesthesia. The **mammary gland** was quickly excised cleared off the adhering fat blotted and weighed after which processed for the various light microscopic studies.

MAMMARY GLAND :



Fig.1(X-40)



Fig. 2(X-120)

Fig.1&2 Micrograph of control Mammary gland.

Note excretory duct (Exd), adipocytes (Ad), and intralobular connective tissue.

Mammary gland is a compound alveolar gland that develops from the lower layer of the epidermis . It consists of a number of lobes separated by broad bands of dense connective tissue . The lobes are divided into lobules by connective tissue septa, from which strands extends into secreting units. The intralobular connective tissue is fine areolar. The alveoli of each lobules open into small intralobular ducts , which unite to form interlobular ducts and these in turn lead to the main excretory ducts (figs.1) .

Stroma : Mammary glands contains a rich network of connective tissue, stroma and varying amounts of adipocytes. Two types of connective tissues are present , 1) interlobular connective tissue composed of variously dense fibrous connective tissue containing ducts , lobules and clusters of fat cells. 2) Intralobular connective tissue which are embedded the ductules and alveoli of each lobules . It has an abundant ground substance and a few reticular fibers but there are no fat cells within lobules (figs. 2) .

Adipose tissue covers the surface of the mammary glands and is also present between lobes of glandular tissue (figs. 2).

NOR-HN TREATED MAMMARY GLAND:

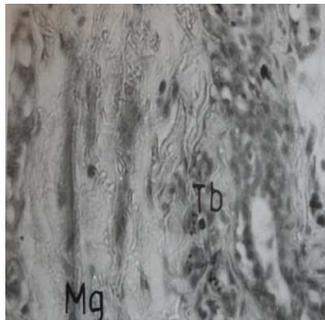


Fig. 3 (X-40)

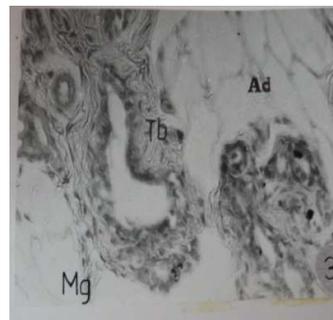


Fig. 4 (X-120)

Fig. 3&4 Norethisterone heptanoate treated rat mammary gland.

The micrograph showing inactive tubuloalveolar (Tb), atrophied duct (Dt)

and adipocytes (Ad).

Norethisterone treated mammary gland appears totally inactive and hardly resembles the control gland. The secreting tissue is represented by scattered ducts, around the terminal portion of which one may see a few collapsed or very small follicles and a few solid cords of intralobular epithelial tissue is lying in a thin investment of loose connective tissue, is surrounded by a dense mass of collagenous fibers. The connective tissue occupies by farther greater proportion of the section (fig.3,4) . The ducts are seen to be lined with one to two layers of cuboidal cells and distended adipocytes are wide spread.

DISCUSSION

NORETHISTERONE HEPTANOATE (NOR-HN) TREATMENT :

Norethisterone was the first highly active progestational agent to be synthesized and achieved wide spread use along with its acetate and enanthate esters. Norethisterone acetate or heptanoate a synthetic steroid is an oral substance used clinically and has a more potent progestational effect than the natural hormone progesterone by injection. Norethisterone are a typical in comparision with progesterone (Richard Edgren, 1974).

MAMMARY GLANDS :

The major developmental role of progesterone on the normal breast has been postulated to be the formation of lobular alveolar structures during pregnancy (Topper & Freeman 1980). This is supported by the observation that mammary glands in mice develop ductal structure upon exposure to estrogen and progesterone (Lydon et al. 1995). The influence of progesterone is likely to be proliferative in this process. Progesterone also exert a differentiating effect on the breast through its role in lactation (Dinny Graham, 1997).

But in the present experimental investigation, NOR-HN administration of the mammary gland results in atrophy of the epithelial cells & ducts.

However, progesterone either decreases or has no effect on the proliferation of normal breast epithetium in nude mice (McManus et al. (1984) and Laidlaw et al. (1995)). Gompel et al. (1986) reported that the progesterone decreased cell proliferation. Our histological observation with progestogenic agents supports the above results.

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