

Studies of Norethisterone Heptanoate Treated Vagina of Albino Rat (Wistar strain) : Histological aspects

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Abstract

Norethisterone was the first highly active oral and injectable 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. Norethisterone as an androgen with a typical progestational effect at sufficiently higher doses. The objective was to study the subcellular structural response to norethisterone to establish a structural, functional properties concerning its contraceptive efficacy. Norethisterone brings about morphological changes in the vaginal epithelium cells.

KEYWORDS : Norethisterone, enanthate ester, hormone, contraceptive, Vagina, Epithelium

Introduction:

The pharmacokinetics of synthetic progestins can vary depending on the route of administration and whether the progestin is given alone or in combination with an estrogen. Animal studies are of little relevance to humans because of differences in absorption and metabolic clearance among various species. Progesterone plays role in the regulation of reproductive cycles, but the mechanism(s) involved are poorly understood (Fotherby, et.al 1977).

The objective was to study the subcellular structural response to norethisterone to establish a structural, functional properties concerning its contraceptive efficacy.

Progestogens were found to have a range of actions which were dose dependent (Larsson-Cohn et al. 1970a). The contraceptive effectiveness of a number of these progestogens had been described (Larsson-Cohn et al.1970b and Moghissi and Marks,1971).

An intramuscular injection of 200mg of a synthetic progestogen (Norethisterone oenanthate, Norigest) compound produced antifertility effect . Its efficacy appeared to be similar to that of DMPA (Geraldine et al. 1975) .

NORETHISTERONE HEPTANOATE

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.

Drug Chemistry:

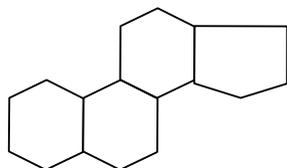
NORETHISTERONE (HEPTANOATE)

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.

Chemistry

Norethisterone (norethindrone) C₂₀ H₂₆ O₂

17 α -Ethinyl-19-nortestosterone, 17 β -hydroxy-19-nor-17 α -pregn-4-en-20-yn-3-one, 17 α -ethinyl-17 β -hydroxy-19-nor-androst-4-en-3-one.



Molecular weight = 298.4

Solubility

In alcohol 1 in 150

In water 1 in 10,000

Norethisterone is a white or creamy white odourless, crystalline powder with a slightly bitter taste.

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 **vagina** was quickly excised cleared off the adhering fat blotted and weighed after which processed for the various light microscopic studies.

OBSERVATIONS AND DISCUSSION

CONTROL RAT VAGINA :

The vagina is a fibromuscular tube which forms the opening of the female reproductive tract. The wall of vagina consists of three layers, a mucosa membrane, a muscularis layer and outer adventia .

The mucus membrane, in turn consists of stratified squamous epithelium and an underlying connective tissue (fig.1&2). Connective tissue papillae project into the under surface of the epithelium, giving epithelial connective tissue junction an uneven appearance. Epithelial cells contains darkly stained , centrally located nuclei (figs.1 &2).

Muscularis is also known as lamina propria . It is made up of more dense connective tissue near the epithelium but becomes more loosely knit towards the muscularis. (figs.1&2).

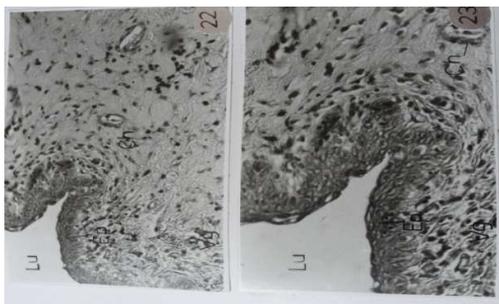


Fig. 1(X-40) Fig. 2 (X-75)

Fig.1 &2- Micrograph of untreated rat vagina

Showing part of vaginal lumen(Lu),
epithelium (Ep), and venous channel (Ch).

NOR- HN TREATED VAGINA :

Treatment with norethisterone brings about morphological changes in the vaginal epithelium cells. Epithelium cells are in a proliferative phase more towards the basal region , rested on loosely arranged lamina propria . Secretory cells are not observed but certain mucus like substance is accumulated in the lumen (figs 3&4).

Undulated epithelial linings are commonly found. Connective tissue is loosely arranged along the dilated lamina propria (figs.3&4).The stroma is relatively loose and edema is absent .

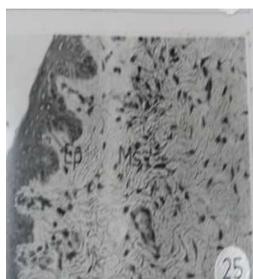


Fig. 3 (X-40)

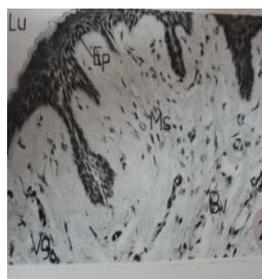


Fig. 4 (X-75)

Vaginal section after norethisterone treatment showing poliferated epithelial cells (Ep) and dilated lamina propria (Ms) and loose stroma (STR).

The vagina is a fibromuscular tube that connects the uterus with the exterior of the body and serves as a copulatory receptacle and birth canal. In the present study vaginal epithelium after the norethisterone treated vagina, there was accumulated of mucus. Maqueo et al. (1964) studied human vagina and revealed that the vaginal epithelium responded more promptly after treatment with progestogenic compound knowing the fact that the vaginal cells are more sensitive to hormonal stimuli than endometrium, a more consistent and intense response to progestational stimuli was found in the vaginal cytology.

REFERENCE

1. Clarke and Sutherland (1990). Progestin regulation of cellular proliferation. **Endocrine Reviews (1990) Vol. II.**
2. Fotherby K (1985). Oral contraceptive. **Contraception (1985); 31: 367 - 394.**
3. Fotherby et al (1977) .Effect of norethisterone oenanthate on serum gonadotrophin level. **Contraception (1977).**
4. Maqueo et al. (1964). Endometrial histology and vaginal cytology during oral contraception with sequential estrogen and progestin. **Am. J. Obstet. and Gynecol. (1964); 90: No. 3.**
5. El- Mahgoub S. and Karim, M. (1972). The long term use of injectable norethisterone enanthate as a contraceptive. **Contraception, (1972), 5(1): 21.**
6. Richard Engren (1974). Progestogens as contraceptive **J. Of Reprod. Med. (1974); 13 : No.2.**
7. Geraldine et al. (1974). Plasma levels of Norethisterone in women receiving norethisterone oenanthate intramuscularly., **Contraception (1975) vol. 12(1), 45-51.**
8. Larsson and Cohn U.Johansson, ED.B. Wide, L and Gemezell (1970 b) : **Acta Endocrinologica ; 63:38.**
9. Moghissi K.S. and Mark C. (1971). Effects of microdose norgestrel on endogenous gonadotropic and steroid hormones, cervical mucus properties, Vaginal cytology and endometrium. **Fertil. Steril. (1971) ; 22 : 424.**
10. Turner- Text Book Of Endocrinology. (1976)