

Original research article

Histological assessment of ovaries and uterus of rats subjected to nandrolone decanoate treatment

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Abstract

This study aimed to analyze the effects of nandrolone decanoate on the ovaries and uterus of adult females rats. This drug was administered intraperitoneally, at one, two and three doses of 3 mg nandrolone decanoate/kg of body weight, respectively, in the first, second and third week of treatment. The females of the control group received a physiological solution. The rats treated with nandrolone decanoate showed estral acyclicity and there was destruction of follicular units and an absence of corpus luteum in the ovaries. In the uterus, the drug promoted morphological alterations, characterized by vacuolated epithelium and endometrial stroma fibrosis. Ovary, uterus and pituitary weights were not affected by the steroid treatment. Nandrolone decanoate affects the sexual cycle and promotes histological alterations in the ovaries and uterus of adult female rats.

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1. Introduction

Androgenic anabolic steroids (AAS) are synthetic analogues of testosterone, recommended for the treatment of many medical pathologies that include renal insufficiency, endometriosis and hereditary angioedema [1]. However, AAS have been abusively and indiscriminately used by many men and women, athletes and nonathletes, to increase muscular mass, strength and dexterity [2].

The beneficial potential of anabolic steroids comes with undesirable side effects, such as increase in serum triglycerides and cholesterol levels, hepatic toxicity and increase in hepatic and hematological cancer [3,4]. These agents also promote adverse effects on spermatogenesis [5] and ovarian cyclical activity [1,6]. The abusive use of anabolic steroids by women is associated with facial hair growth, voice deepening, clitoris enlargement and irregular menstrual cycles [7].

Among many AAS, nandrolone decanoate, commercially known as Deca-Durabolin (Brazil), is considered the most

popular steroid on the market [8]. Studies using AAS have examined physiological and behavioral responses in males [9] and females [6,10]. Use frequency of such agents by women is less established than it is in men [11] and little information exists on AAS effects on female reproduction, from a morphologic point of view. The objective of this study was to analyze the effects promoted by nandrolone decanoate on the histology of ovaries and uterus of adult female rats.

2. Materials and methods

Adult female rats from the Wistar lineage were obtained from the Paulista State University (UNESP-Botucatu, SP, Brazil) and kept at the Faculty of Sciences and Letters (UNESP-Assis, SP, Brazil) under adequate conditions of temperature (22–24 °C) and luminosity (12-h light/dark cycle). The females received water and commercial ration *ad libitum*. The experimental protocol followed the ethical principles in animal research adopted by the Brazilian College of Animal Experimentation.

Nandrolone decanoate, commercially known as Deca-Durabolin (Organon, Brazil), produced in 1-mL ampules packaging, contained 50 mg of the androgenic substance.

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The females were weighed and distributed at random into two experimental groups. The treated group ($n=5$) received the drug intraperitoneally in doses of 3 mg/kg of body weight, administered in one, two and three doses, respectively, in the first, second and third week of treatment, at the same time of day (1:00 p.m.). Choosing the dose and administration plan of the drug was based on Brazilian athletes' usage of the AAS at fitness centers. The females in the control group ($n=5$) received a physiological solution of 0.9% saline, with the same procedure adopted for the treated group.

Weekly records of the animals' body weights were obtained and daily monitoring was carried out of the estral cycle by means of vaginal cytology.

The rats were weighed and killed by inhalation of ethyl ether 72 h after the last injection. The ovaries, uterus, pituitary and liver were removed and weighed. The reproductive organs were fixed in Bouin's solution and 5- μ m-thick sections, embedded in Paraplast (Labware-Oxford, St. Louis, MO, USA), were stained by hematoxylin and eosin for a histological study.

Body weight data and ovaries, uterus, pituitary and liver weights were statistically analyzed by means of nonparametric Kruskal–Wallis variance analysis complemented by Tukey test. The results are expressed as median values and discussed at 5% significance.

3. Results

Body and hepatic weights of rats treated with anabolic steroid were significantly higher ($p<.05$) than those found in control rats, but there was no significant effect ($p>.05$) of the treatment on the weight of the reproductive organs and pituitary (Table 1).

The females of control group presented estral cyclicity during the experimental period, while the female rats of treated group showed persistent diestrus from the first week of treatment, indicating they had not ovulated. The vaginal smear of control females consisted of primarily cornified epithelial cells. In the treated group, the vaginal smear exhibited primarily leukocytes with some nucleated epithelial cells.

The ovaries of female rats of the control group (Fig. 1A) showed the peripheral region, or cortex, containing follicles at diverse maturation stages and a well-developed corpus luteum. The medular region was formed by loose connective tissue richly vascularized.

Table 1
Effects of treatment with nandrolone decanoate on body, ovaries, uterus, liver and pituitary weight

Group	Body weight (g)	Ovaries weight (g)	Uterus weight (g)	Liver weight (g)	Pituitary weight (g)
Control	245a ^a	0.978a	0.550a	8.880a	0.0056a
Treated	295b	0.906a	0.460a	11.880b	0.0440a

^a In the same column, identical letters do not differ statistically among themselves.

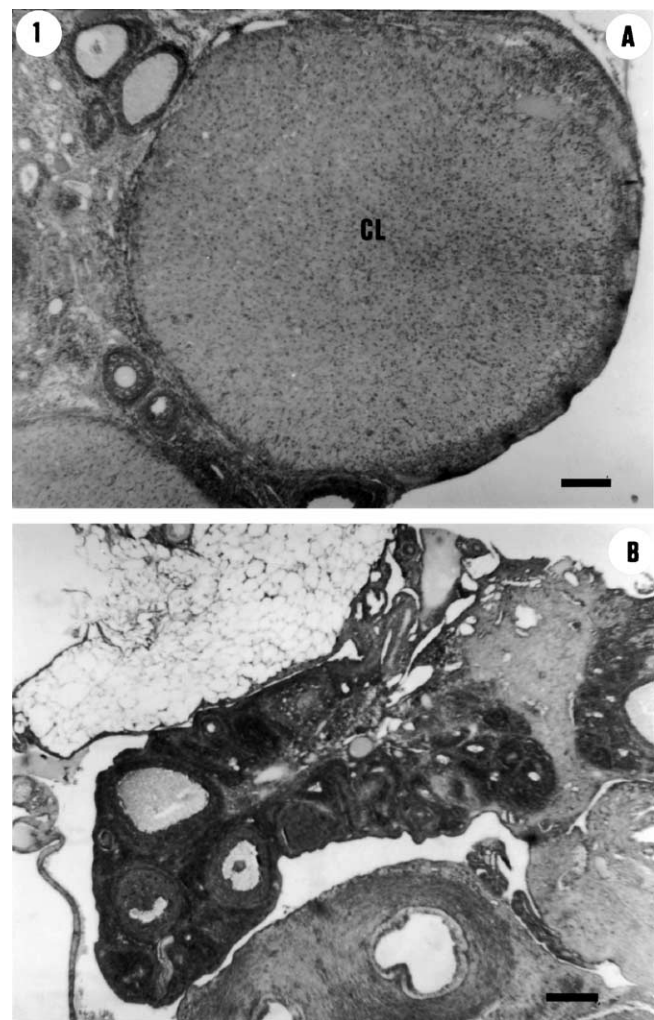


Fig. 1. Photomicrographs of rat ovary. Note the appearance of corpus luteum (CL) in the control group (A) and absence in the treated group (B) (hematoxylin and eosin; bar=170 μ m).

In the females treated with steroid (Fig. 1B), the ovaries showed absence of corpus luteum and destruction of the follicles units, characterized by intense follicular atresia and apparent reduction in the number and types of follicles.

In the animals of the control group (Fig. 2A), the epithelial cells of the uterine lumen lining were high, cylindrical, with their nuclei localized in the same level. The endometrial stroma was relatively thin, of loose aspect and with the presence of scattered lymphocytes in the tissue. Rare glandular and stromal cells showed mitotic activity. The glands presented nuclei supported in the base of cells. Some glands exhibited tortuosity and presence of few subnuclear vacuoles, and others presented tubular aspect. The uterus of female rats of control group showed morphologic characteristics that indicated the transition between the proliferative and secretory endometrium.

The females of the treated group presented uterine histology different from that verified in the control group. The characteristic morphology more evident in the uterus of females treated with steroid (Fig. 2B) was the presence of

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