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SHORT COMMUNICATION

THE INFLUENCE OF NANDROLONE DECANOATE (DECA-DURABOLIN) ON THE PERIPHERAL CONVERSION OF ANDROSTENEDIONE TO OESTRONE

R. ANDRIESSE,* J. H. H. THIJSSEN and G. H. DONKER
Department of Clinical Endocrinology, University Hospital, State University of Utrecht, Utrecht, The Netherlands

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There is sufficient evidence that oestrogens play an important role in the development of human breast cancer. This has led to many efforts to inhibit the endogenous oestrogen production, especially in cases with metastases. Notwithstanding the removal of both ovaries, considerable amounts of oestrogens were detectable in the circulation of some women, explained by the peripheral conversion of androgens to oestrogens, mainly from androstenedione to oestrone.

Long before this mechanism was well-known, certain chemical compounds were clinically applied in the treatment of advanced or metastatic breast cancer, with often a remarkable regression of the tumor. Studies *in vitro* [1, 2] tested a great amount of steroids for being potential inhibitors of the aromatisation of androstenedione. The outcome of some of these studies suggested that a decrease of oestrogen synthesis could be achieved by aromatase inhibitors and that steroid induced regressions of some breast cancers resulted from inhibition of oestrogen production rather than a direct androgenic effect. Strong inhibition *in vitro* was found by among others testosterone [1], 7α-methyltestosterone [2, 3] and testolactone (Teslac) [4]. A substance, clinically used in the treatment of advanced cases of breast cancer, is nandrolone decanoate (Deca-durabolin), this drug can give a remarkable remission of some breast cancers [7]. We tried to demonstrate the influence of nandrolone decanoate on the peripheral conversion of androstenedione to oestrone.

In five healthy perimenopausal women, varying in age from 51 to 53 years, with an average weight, the conversion of androstenedione to oestrone was determined by the constant infusion technique, using [4-^{14}C]-androstenedione and [6,7-^{3}H]-oestrone, introduced by McDonald *et al.* [5] as described by Poortman *et al.* [6]. All subjects participated after informed consent. After determination of the basal situation, all subjects received an intramuscular injection with 50 mg nandrolone decanoate. The conversion of androstenedione → oestrone, was again determined by the same method, 16–21 days after the injection was given.

The results of the different conversion rates before and after injection of nandrolone decanoate are given in Table 1. In only one subject there was a distinctive decrease of the conversion after the injection; two other subjects showed no great differences in the conversion rate and two even an increase. A wide variation in the serum levels of oestrone and oestradiol was found in the subjects studied, due to the different hormonal status in which they were at the time of the experiment. In 3 out of the 5 subjects there was still a more or less regular menstrual cyclus, corresponding with high oestradiol levels. In Table 2 the mean values of the metabolic clearance rates (MCR) are summarized again. There are no differences between the values of the MCR's of androstenedione and oestrone before and after injection of nandrolone decanoate.

Table 1. Conversion of androstenedione to oestrone expressed in percentages, before and 16–21 days after injection with 50 mg nandrolone decanoate in 5 normal perimenopausal women

Subject	Before	After
S.	2.22	2.74
K.	3.70	2.71
v.d. L.	1.92	2.05
B.	2.70	2.59
d.C.	1.81	2.55
Mean	2.47	2.53

In our experiments we found no effect of treatment during 3 weeks with nandrolone decanoate (Deca-durabolin) on the conversion of androstenedione to oestrone. This conclusion does not exclude the possibility that treatment either of longer duration or with higher dosages could have an effect on the peripheral androgen–oestrogen conversion. However, results in breast cancer patients with nandrolone decanoate, as recently described by Chowdhury *et al.* [7], were obtained with 50 mg of the preparation every 2 weeks. It is therefore unlikely that the beneficial results in this study can be ascribed to a reduced conversion. A direct interaction of nandrolone decanoate with the oestrogen receptor is unlikely because the relative binding affinity of nandrolone decanoate compared to oestradiol is less than 0.001% as was found by Poortman (pers. comm.). Interaction with the specific androgen receptor protein present in a number of breast cancers may be of importance, although a relation of these receptors to endocrine therapy is still uncertain. Therefore the mechanism of action of nandrolone decanoate in advanced cases of breast cancers is still open for further investigations.

Table 2. Metabolic clearance rate (MCR) of androstenedione and oestrone in 5 normal perimenopausal women before and 2–3 weeks after injection with 50 mg nandrolone decanoate

	MCR of androstenedione L/24 h ± S.E.M	MCR of oestrone L/24 h ± S.E.M.
Before	2614 ± 402	2410 ± 366
After	2378 ± 210	2452 ± 221

* Reprints requests should be sent to R. Andriesse, Department of Clinical Endocrinology, Academisch Ziekenhuis, Catharijnesingel 101, Utrecht, The Netherlands.

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