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Serum Levels of Androstenedione, Testosterone and Dehydroepiandrosterone Sulfate in Patients with Premature Ovarian Failure to Age-Matched Menstruating Controls

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Key Words

Premature ovarian failure

Androstenedione

Testosterone

Dehydroepiandrosterone sulfate

Abstract

Serum concentrations of androstenedione, testosterone and dehydroepiandrosterone sulfate (DHEAS) were measured in 29 patients with premature ovarian failure (POF) and an identical number of age-matched normal control subjects. The study was aimed at determining possible differences in androgen concentrations of ovarian and adrenal origin in POF patients and age-matched normal menstruating controls. Serum testosterone and DHEAS concentrations in the 2 populations were not significantly different. The serum androstenedione concentration in the POF patient group ($3,077.50 \pm 1,122.33$ pmol/l) was significantly lower than in age-matched normal control subjects ($4,167.70 \pm 1,381.09$ pmol/l, $p < 0.005$), possibly reflecting the loss of ovarian androstenedione secretion and/or a subtle defect in adrenal steroidogenic capacity.

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Introduction

Premature ovarian failure (POF) is most commonly due to autoimmune destruction of the ovaries leading to menopause before the age of 40 [1, 2]. In contrast to woman with natural menopause, patients with POF not only have deficiency of estrogens but also have the potential for loss of ovarian androgens because of atrophy of the ovarian cortex which occurs to a greater extent in POF patients than in women with naturally occurring menopause. The present study was performed to define the difference in the serum concentrations of androstenedione (AS), testosterone (TT), and dehydroepiandrosterone sulfate (DHEAS) in patients with POF and in age-matched normal menstruating controls.

Serum AS and TT are derived from both the adrenals and the ovaries with much of the circulating TT in women

being peripherally produced from androgen precursors such as AS [3-5]. DHEAS is primarily of adrenal origin [6].

Materials and Methods

Twenty-nine patients with POF participated in the study. POF was diagnosed on the basis of elevated gonadotropin levels in patients with complete cessation of menses occurring before the age of 40 years. All participants were enrolled in an assisted fertilization program at the

University of California, Irvine. The patients ranged in age from 26 to 40 years (mean $\pm$ SD, 34 $\pm$ 4 years). In view of the potential influence of age on serum androgen concentrations, serum AS, TT and DHEAS concentrations were also measured in age-matched normal control subjects (29 subjects precisely age-matched). Studies were performed using a protocol approved by the Human Subjects Research Committee, University of California, Irvine.

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Blood Sampling

Blood was removed from an antecubital or other forearm vein for measurement of TT, AS, and DHEAS. Sampling was performed at the time of the initial visit (09.00-09.30 h), and before the patients received any form of estrogen treatment. Blood sampling was performed in the early follicular phase of the menstrual cycles in the age-matched normal control subjects.

Immunoassays

Testosterone. Samples were extracted using ethyl acetate/hexane and then fractionated using celite chromatography. Fractionated samples were analyzed by radioimmunoassay (RIA) using 125T-TT and rabbit anti-TT antibody. Bound/free separation was achieved using the enhanced second antibody technique [7]. Sensitivity of the assay was < 0.04 nmol/l. Inter- and intraassay variations were < 12 and < 11 %, respectively.

Androstenedione. AS extracted and fractionated from serum as with TT was assayed by radioimmunoassay [8]. Tritiated AS was added to each sample prior to extraction to correct for recovery. Sensitivity of the assay was 105 pmol/l. Inter- and intraassay variations were < 12 and < 8%, respectively.

Dehydroepiandrosterone Sulfate. Serum samples were diluted 1:5,000 before assay. The RIA was performed using rabbit anti-DHEA monosuccinate and 125-DHEAS. The samples were incubated for 2.5 h at room temperature while bound/free separation was achieved using anti-rabbit γ -globulin (second antibody) [9]. Sensitivity of the assay was 130 pmol/l. Inter- and intraassay variations were < 9 and < 8%, respectively.

Statistical Analysis

Statistical analysis was performed using Student's t test for grouped observations and the Mann-Whitney U test. The level of significance was < 0.05.

Results

The serum TT, AS and DHEAS concentrations in the age-matched normal menstruating controls were 0.97 ± 0.19 nmol/l, $4,167.70 \pm 1,381.09$ pmol/l, and $4,513.46 \pm 2,247.51$ nmol/l, respectively. The serum TT and DHEAS concentrations were not significantly different in the POF patients and the normal menstruating controls. However the serum AS concentration in the control patients was significantly higher than in the POF patients ($p < 0.005$).

Discussion

Patients with POF not only have estrogen deficiency but also have the potential for loss of ovarian androgens because of atrophy of the ovarian cortex which occurs in POF patients to a greater extent than in women with naturally occurring menopause.

The results of this study showed that the serum TT and DHEAS concentrations in POF patients and in an age-matched normal control population were not significantly different. However, the serum AS concentrations in the menstruating controls were significantly lower than that

measured in the POF patients. The significantly lower serum androstenedione concentration in the POF patients compared to the normal menstruating control subjects suggests a loss of ovarian contribution to AS secretion and/or a subtle defect in adrenal steroidogenic capacity compared to normal age-matched controls. The long-term implications of this relative AS deficiency in patients with POF remain to be determined.

The serum TT concentration in the POF patients was 0.96 ± 0.38 nmol/l. The DHEAS and AS concentrations in POF patients were $3,399.70 \pm 2,070.01$ nmol/l and $3,077.50 \pm 1,122.33$ pmol/l, respectively.

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