UTILIZATION OF TISSUE MEASUREMENTS OF STEROIDS TO ANALYZE THEIR SIGNIFICANCE IN THE DEVELOPMENT OF ENDOMETRIAL HYPERPLASIA IN PCOS PATIENTS

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Background: Polycystic ovarian syndrome (PCOS) is a common endocrinopathy affecting reproductive-age women, with a prevalence of 5-15% [1]. Common comorbidities include obesity, hyperinsulinemia, endometrial hyperplasia (EH), endometrial cancer (EC), and infertility [2]. While the role of estrogens in the development of EH/EC is well established, the effects of androgens on the endometrium remain unclear [3]. Recent findings suggest that women with PCOS and normal endometrial pathology have higher serum free testosterone (FT) and total testosterone (TT) compared to those with EH and EC. However, no studies have examined the endometrial tissue concentrations of hormones in PCOS women.

Objective: To evaluate the endometrial tissue and serum concentrations of testosterone (T) and estradiol (E2) in PCOS women with a normal endometrium and EH/EC, and to correlate these concentrations with various clinical parameters.

Materials and Methods: This was a preliminary, prospective cohort study conducted at a single REI clinic in a safety-net hospital. Reproductive-age women (18-40 years of age) diagnosed with PCOS using Rotterdam criteria were asked to participate. Blood was collected at the time of routine endometrial biopsy. Half the biopsy specimen was sent for histopathologic diagnosis, while the other half was used to measure tissue concentrations of T and E2 via mass spectrometry. Clinical parameters collected included ethnicity, body mass index (BMI), serum insulin and hemoglobin A1c (HbA1c), Ferriman-Gallwey score, endometrial thickness, and sex hormone binding globulin (SHBG). Characteristics between the 2 groups were compared using the Student's t-test or Mann-Whitney U test as appropriate. Correlation coefficients (r) were calculated via the Spearman correlation test. A p value <0.05 was statistically significant.

Results: Comparison of the benign pathology and EH/EC groups suggest lower serum TT and FT in the EH/EC group, while tissue TT levels remained unchanged (Table 1). Serum:tissue TT ratios were high in both groups as compared to low serum:tissue E2 ratios, suggesting conversion of T to E2 in the endometrium. In the benign pathology group, significant correlations were observed between serum TT, serum E2 ($r=0.39$, $p=0.021$), and SHBG ($r=0.38$, $p=0.027$). Additional correlations were seen between the serum:tissue TT ratio and both insulin ($r=0.39$, $p=0.02$) and HbA1c ($r=0.37$, $p=0.033$), with BMI nearing significance ($r=0.34$, $p=0.05$).

Table 1. Characteristics by Pathology

Characteristic	Normal/Benign (n=36)	Hyperplasia/EIN/Cancer (n=4)	P value
Age (years)	30.4 ± 5.6	28.7 ± 7.9	0.59
Ethnicity (%)			0.71
Hispanic	24 (66.7)	4 (100)	
Caucasian	1 (2.8)	0 (0)	
Not Hispanic/Latino	8 (22.2)	0 (0)	
Not documented	3 (8.3)	0 (0)	
BMI (kg/m^2)	35.5 ± 6.1	40.8 ± 5	0.11
FG Score	10.8 ± 7.9	13.5 ± 13.5	0.76
Endometrial Thickness (mm)	8.3 ± 2.5	11.1 ± 1.2	0.059
Tissue weight (g)	0.29 ± 0.22	0.59 ±0.35	0.058
Serum E2 (pg/mL)	65.4 ± 66.5	150 ± 180.3	0.23
Tissue E2 (pg/g)	565.9 ± 616.2	573.5 ± 675.3	0.98
Serum:Tissue E2 Ratio	0.68 ± 1.3	0.45 ± 0.65	0.85
Serum total T (ng/mL)	0.43 ± 0.19	0.29 ± 0.12	0.16
Serum free T (pg/mL)	8.26 ± 4.1	6.7 ± 2.8	0.49
Tissue T (ng/g)	0.15 ± 0.9	0.16 ± 0.16	0.77
Serum:Tissue TT Ratio	3.87 ± 2.9	3.81 ± 2.8	0.98
Serum insulin (uIU/mL)	57.3 ± 56.8	43.5 ± 38.9	0.6
HbA1c	5.9 ± 1.1	6.1 ± 1.2	1.0
SHBG (nmol/L)	27.8 ± 16.6	14.8 ± 2.9	**0.047**

Conclusions: Our findings indicate that serum TT concentrations are lower in the EH/EC group compared to the normal group, which aligns with previous studies. However, this decrease is not reflected in tissue TT concentrations. Due to the conversion of TT to E2 in the endometrium, serum TT concentrations may overestimate tissue TT concentrations by nearly fourfold. Correlation analysis suggests relationships between serum and tissue hormone concentrations and SHBG, insulin, HbA1c, and possibly BMI. Our data suggest that measuring steroids in endometrial tissue is helpful in evaluating their significance in the development of endometrial hyperplasia in PCOS patients. However, given our limited sample size, additional studies with a larger EH/EC cohort are warranted.

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