Pre- and Post-Operative changes in Urinary Estrogen Metabolites in Women with Endometriosis

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Introduction: Endometriosis is an estrogen dependent gynecological disease characterized by the presence of endometrial tissue outside of the endometrial cavity. This disease affects 12% of reproductive aged women and 45% of women with this disease report infertility. Growth and progression of endometriotic lesions occurs through estrogen dependent pathways that have been characterized, and these endometriotic lesions possess the necessary enzymes to aromatize various steroids into estrogens. To date, little is known about the estrogenic metabolism in patients with endometriosis. Therefore, there is a critical need to measure both parent and estrogen metabolite levels in women with endometriosis compared to women without disease. We hypothesize that premenopausal women with endometriosis have a hyperestrogenic urinary profile compared to women without the disease.

Materials/Patients/Methods: Using a repetitive sampling model, we collected single urinary samples on the day of surgery (DOS) and then 1-2 weeks post-surgical intervention (PSI). To date, 32 patients have been included (19 histologically confirmed endometriosis and 13 controls). Surgical intervention occurred at St. John’s Hospital or Memorial Medical Center, Springfield, IL. All study patients were being treated with hormonal contraception to induce ovarian suppression while on study. Urine (20-50 ml) was collected at the specified time points in a sterile container and then transferred to the lab where it was centrifuged to remove cell debris, placed in 1.5 ml aliquots and then stored at -20°C until analyzed. Liquid chromatography/tandem mass spectrometry (LC-MS/MS) was used to quantify estrogens in 1 ml of urine in PBS. The following estrogens were detected: parent estrogens, estrone and estradiol (17Beta-estradiol); estrogen metabolites, 2'-hydroxyestrone, 2'-methoxyestrone, 2'-hydroxyestradiol, 2'-methoxyestradiol, 2'-hydroxyestrone-3'-methyl ether, 4'-hydroxyestrone, 4'-methoxyestrone, 4'-methoxyestradiol, 16a-hydroxyestrone, 17-epiestriol, 16-ketoestradiol and 16-epiestriol. Urine was enzymatically hydrolyzed with glucuronidase/sulfatase buffer, extracted, derivatized and then detected with stable isotope-labeled internal standards. Estrogens were quantified against calibration curves, normalized to urinary creatinine and marked quality control samples and standards were used in each assay.

Results: We found that patients with endometriosis had elevated levels of 17Beta-estradiol at both DOS and PSI time points compared to control subjects. Postoperative urinary levels of 17Beta-estradiol were reduced compared to DOS, suggestive that surgical removal of lesions may impact estradiol production. In the 2-OH pathway, we found reduced levels of 2'-methoxyestrone at PSI, yet no change in the other 2-OH metabolites. We did not find any difference in 4-hydroxyestrone between groups (the other 4-OH metabolites were not detected). For the 16-OH pathway, we found that 16-keto-17Beta-estradiol was elevated at PSI in patients with endometriosis. No change was noted in the other 16-OH metabolites.

Conclusions: Overall, these data imply that women with endometriosis have aberrant estrogen metabolism possibly from increased levels of the parent estrogen 17Beta-estradiol, which may in part originate from lesion aromatization. Surgical removal of lesions may temporarily and partially reduce estrogen levels derived from the lesions, which may aid in controlling adjacent lesion growth and progression of the disease as a partial explanation for postoperative disease control. In addition, they may aid in the future to assess the extent of disease prior to surgery.

Keywords : Endometriosis, Estrogen, Estrogen Metabolites
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