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Endometrium metabolomic profiling reveals potential biomarkers for diagnosis of endometriosis at minimal-mild stages.

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Abstract

BACKGROUND:

The sensitivity and specificity of non-invasive diagnostic methods for endometriosis, especially at early stages, are not optimal. The clinical diagnostic indicator cancer antigen 125 (CA125) performs poorly in the diagnosis of minimal endometriosis, with a sensitivity of 24%. Therefore, it is urgent to explore novel diagnostic biomarkers. We evaluated the metabolomic profile variation of the eutopic endometrium between minimal-mild endometriosis patients and healthy women by ultra-high-performance liquid chromatography coupled with electrospray ionization high-resolution mass spectrometry (UHPLC-ESI-HRMS).

METHODS:

Our study comprised 29 patients with laparoscopically confirmed endometriosis at stages I-II and 37 infertile women who underwent diagnostic laparoscopy combined with hysteroscopy from January 2014 to January 2015. Eutopic endometrium samples were collected by pipelle endometrial biopsy. The metabolites were quantified by UHPLC-ESI-HRMS. The best combination of biomarkers was then selected by performing step-wise logistic regression analysis with backward elimination.

RESULTS:

Twelve metabolites were identified as endometriosis-associated biomarkers. The eutopic endometrium metabolomic profile of the endometriosis patients was characterized by a significant increase in the concentration of hypoxanthine, L-arginine, L-tyrosine, leucine, lysine, inosine, omega-3 arachidonic acid, guanosine, xanthosine, lysophosphatidylethanolamine and asparagine. In contrast, the concentration of uric acid was decreased. Metabolites were filtered by step-wise logistic regression with backward elimination, and a model containing uric acid, hypoxanthine, and lysophosphatidylethanolamine was constructed. Receiver-operating characteristic (ROC) analysis confirmed the prognostic value of these parameters for the diagnosis of minimal/mild endometriosis with a sensitivity of 66.7% and a specificity of 90.0%.

CONCLUSIONS:

Metabolomics analysis of the eutopic endometrium in endometriosis was effectively characterized by UHPLC-ESI-HRMS-based metabolomics. Our study supports the importance of purine and amino acid metabolites in the pathophysiology of endometriosis and provides potential biomarkers for semi-invasive diagnosis of early-stage endometriosis.