27. The mid-secretory endometrial transcriptomic landscape in endometriosis: a

meta-analysis

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Abstract

Study question: Do women with endometriosis have a different endometrial gene expression

profile at the time of embryo implantation than women without endometriosis?

Summary answer: The endometrial gene expression profile of women with endometriosis

differs from that of women without endometriosis at the mid-secretory phase, although the

differences are small.

What is known already: About 50% of women with endometriosis suffer infertility. Several

molecular studies have suggested impaired endometrial receptivity in women with

endometriosis, while others have detected no dysregulation of endometrial receptivity.

Nevertheless, the previous endometrial transcriptome studies comparing women with and

without endometriosis have been performed in small sample size with limited statistical

power. We set out to systematically search and compile data of endometrial gene expression

signatures at the receptive phase in women with endometriosis versus control women. Based

on the obtained data, we conducted a meta-analysis of differentially expressed genes in order

to raise the power of the analysis for identifying the molecular profiles of receptive phase

endometria in endometriosis.

Study design size duration: A systematic literature search was conducted up to February

2022 following PRISMA criteria and included PubMed, Cochrane and Web of Science

databases. For the systematic search, the term 'endometriosis' was paired with the terms

'transcriptomics', 'transcriptome', 'gene expression', 'RNA-seq', 'sequencing' and 'array', by

using the Boolean operator 'AND' to connect them. Articles written in English were screened

and interrogated for data extraction.

Participants/materials setting methods: A meta-analysis was performed on the selected

studies to extract the differentially expressed genes described at the mid-secretory phase in

women with endometriosis versus women without endometriosis in natural cycles, using the

robust rank aggregation method. In total, transcriptome data of 125 women (78 patients and

47 controls) were meta-analysed, with a special focus on endometrial receptivity-specific

genes based on commercial endometrial receptivity tests.

Main results and the role of chance: In total, 8 studies were eligible for the quantitative

meta-analysis, gathering transcriptome data from the mid-secretory phase endometria of 125

women. A total of 7779 differentially expressed transcripts between the study groups were

retrieved (3496 up-regulated and 4283 down-regulated) and were meta-analysed. After

stringent multiple correction, there was no differential expression of any single molecule in

the endometrium of women with endometriosis versus controls, while enrichment analysis

detected that the pathways of chemotaxis and locomotion are dysregulated in endometriosis.

Further analysis of endometrial receptivity-specific genes highlighted dysregulation

of C4BPA, MAOA and PAEP and enrichment of immune and defence pathways in women

with endometriosis.

Limitations reasons for caution: Most of the studies included into the meta-analysis were

relatively small and had different study designs, which might have contributed to a bias.

Wider implications of the findings: The current meta-analysis supports the hypothesis that

endometrial receptivity is altered in women with endometriosis, although the changes are

small. The molecules and pathways identified could serve as future biomarkers and

therapeutical targets in detecting and treating endometriosis-associated infertility.

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