Abstract Details

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Abstract title:

Differential proteomic analysis of endometrial fluid suggests increased inflammation and extracellular matrix remodeling in non-implantative IVF cycles

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Study question:

Is there any difference in the protein composition of the endometrial fluid aspirate obtained the day of embryo transfer in cycles achieving and not achieving pregnancy?

Summary answer:
We found 212 differentially expressed proteins when comparing ‘implantative’ and ‘non-implantative’ cycles, that is, those resulting in implantation success and failure.

What is known already:
Endometrial fluid allows non-invasive characterization of the endometrium, and may contain important information on its receptivity when performing in vitro fertilization (IVF) cycles. Endometrial side of implantation has usually been studied with endometrial biopsy in a cycle prior to embryo transfer, focusing on "receptive/non-receptive" endometria, and with low-throughput proteomic techniques.

Study design, size, duration:
We have compared the protein expression patterns in endometrial fluid aspirated from 38 women undergoing IVF, corresponding to 18 implantative and 20 non-implantative cycles using a high-throughput differential proteomic approach. The study period was 12 months.

Participants/materials, setting, methods:
The population under study consisted of 38 women aged 18-40 years old, undergoing their first or second IVF/ intracytoplasmic sperm injection cycle, with normal uterus and endometrium, and 1-2 good quality embryos, and embryo transfer being performed on day 3. Endometrial fluid aspiration was performed immediately before the embryo transfer.

Filter-aided sample preparation was used for the in-solution tryptic digestion of the proteins present in the samples, followed by label-free mass spectrometry analysis

Main results and the role of chance:
From the 716 proteins detected in the differential proteomics analysis, 212 significantly differed in abundance between the groups under analysis ($p<0.05$). Bioinformatic analyses denoted the deregulation of important processes governing receptivity, such as extracellular matrix remodeling, proteolytic activity and inflammatory signaling, and antimicrobial activity within the set of differential proteins. The results suggest higher activity of cytokines, including TNF, OSM and IL6, as well as lower activity of progesterone in non-implantative cycles. In addition, a number of pregnancy-related differential proteins were pinpointed in the mechanistic association analysis.

Limitations, reasons for caution:

Our results were obtained from patients with normal uterus and endometrium and with good quality embryos, who had fresh day-3 embryo transfer, in stimulated cycles. Therefore, our observations may not be applicable to poor prognosis cases or non-stimulated cycles.

Wider implications of the findings:
This work provides insights into the molecular features of implantative IVF cycles using non-invasive methods. It reveals that endometrial fluid aspirate may reflect an increased inflammatory state in non-implantative endometrium. This knowledge opens a new avenue for improving embryo transfer strategies and increasing pregnancy rates.

Trial registration number:
Not applicable.

Keywords:
FASP
endometrial fluid
ivf
implantative/non-implantative IVF cycles
inflammation