Functional state of endometrium during the «window of implantation» can be assessed with mRNA expression level of PAEP, DPP4, MSX1 and HLA-DOB genes.

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Introduction

Human implantation is a complex and multifactorial process. The success of implantation depends on the quality of the embryos and the readiness of the endometrium for embryo nidation. We carried out multivariate analysis of expression data of endometrial tissue at different stages of menstrual cycle to identify a complex of potentially informative genes. Further we tested the markers for determining the receptive status of the endometrium using the real-time quantitative polymerase chain reaction (qRT-PCR).

Aim of the study

To determine the most informative markers for assessing the functional state of endometrium during the "window of implantation" and creating a model for assessment of the readiness of endometrium for embryo implantation.

Results

Differences in the level of mRNA expression of all the studied genes in the receptive endometrium were found in comparison to the pre-receptive one, which allowed us to classify two functional states of the endometrium. The results of histological examination responded to the stage of maturation of the endometrium in 78.7% of cases. Receptive endometrial status can be determined based on the integral evaluation of mRNA expression level of PAEP, DPP4, MSX1 and HLA-DOB genes.

Materials & Methods

47 women with tubal infertility and a successful IVF pregnancy participated in the study. Pipelle endometrial sample was performed during the supposed «window of implantation» in natural cycle with subsequent histological study, and transcriptional profile of genes GPX3, PAEP, DPP4, TAGLN, HABP2, IMPA2, AQP3, HLA-DOB, MSX1, POSTN determined by reverse transcription and real-time quantitative polymerase chain reaction (qRT-PCR). Bioinformatical analysis of open access data of normal endometrium expression performed in order to search for key genes and their expression changes in the processes of endometrial regeneration. The first stage of bioinformatic analysis is the search for data suitable for studying the selected object. In this case, it was interesting for us to study the expression of genes in the normal endometrium in different phases of the menstrual cycle. For this purpose, a search was made in the database of expressions ArrayExpress [<https://www.ebi.ac.uk/arrayexpress/>]. For the first stage of further work, a data set was selected E-GEOD-6364 (<http://www.ebi.ac.uk/arrayexpress/experiments/E-GEOD-6364/>). In this data set, samples of normal endometrium are available for analysis in three stages: proliferative (n=5), early secretory (n=3), and medium secretory (n=8). First of all, we loaded the data to R [<https://cran.r-project.org/>], the data were normalized using the method of quantile normalization implemented in the limma package, then samples of normal endometrium were selected, and analyzed using principal component analysis.

Conclusion

The model for determining a personalized "window of implantation" is offered for practical application in ART.

Fig.1. Change in the level of mRNA expression in the receptive endometrium as compared to the pre-receptive endometrium.