

transcriptome derived from blastocysts (Yan et al 2013) that enable the study of their putative and functional protein interactions. The identification and characterization of these biomolecular interactions will provide new insights into cellular mechanism during embryo implantation.

Study design, size, duration: Here we show an integrative approach to study and characterize the biomolecular interactions between expressed genes in EECs and TCs respectively. This analysis was carried out using network methods on the human interactome (Rolland et al. 2014) in combination with 1.216 proteins from EECs mass spectrometry proteomic data during secretory phase (Hood et al 2015) and 14.230 transcripts from TCs (RNAseq, Yan et al 2013).

Participants/materials, setting, methods: Combined network approaches were used to characterize the resulting subnetwork of the human interactome based on subsets of genes expressed in TCs and EECs. Different biocomputational tools were used for data integration and network building (Bioconductor) and also for network representation and data curation (Cytoscape). The resulting cluster of genes from EECs physically interacting to TCs genes were used for functional enrichment analysis (GProfiler) and for detecting cellular mechanisms overrepresented during the early embryo-maternal interaction.

Main results and the role of chance: A Protein-Protein Interaction (PPI) network was built based on the direct interactions between EECs and TCs genes. The resulting subnetwork –which contains a total of 91 and 33 genes of TCs and EECs respectively– represents the core interactions between both cell types based on putative direct PPIs. Subsequent functional analysis of resulting clusters extracted from the curated network revealed an overrepresentation of biological processes such as; cytoskeleton organization (13 genes), Fructose metabolism (3 genes) and Intermediate filament organization (3 genes). We also found proteins of different cellular components related to extracellular regions such as exosomes that involved (17 genes), cytoskeleton intermediate filament (7 genes) and the supramolecular complex fibers (12 genes).

The network analysis showed two EECs proteins KRT13 and KRT15 that are part of the cytoskeleton and were connected with a high number of genes of TCs, 28 and 45 respectively. Other genes related to cytoskeleton organization were found moderately interconnected in the subnetwork such as GFAP (9 connections), KRT6A (7), EMD (7), PPL(6), KRT5 and DES (1).

Limitations, reasons for caution: The present study is based on published data and represents an approach to interrogate features of the interactome between expressed EECs proteins and TCs genes. The absence of a functionally validated protein representation of TCs could lead to decrease accuracy of assumptions compared with validated *in vivo* PPIs

Wider implications of the findings: EECs proteins that potentially interact with TCs have been revealed and put light over specific biological process during implantation. Our findings suggest a representative role of cytoskeleton and intermediate filament organization as well as exosome in the extracellular region, where could have a direct contact with the implanting blastocyst.

Trial registration number: N/A.

O-293 Does application of auto-cross linker hyaluronic acid in women following D&C for miscarriage with at least one D&C in history improve reproductive outcome?

A. Hooker^{1,2}, R. Leeuw de², H. Brolmann², J. Huirne²

¹Zaans Medical Center ZMC, Department of Obstetrics and Gynaecology, ZAANDAM, The Netherlands

²VU University Medical Center, Department of Obstetrics and Gynaecology, Amsterdam, The Netherlands

Study question: Does intrauterine application of auto-crosslinked hyaluronic acid (ACP) gel following dilatation and curettage (D&C) for miscarriage, in women with at least one previous D&C in history improve reproductive performance?

Summary answer: Application of ACP gel following D&C for miscarriage in women with at least one previous D&C seems to have a favourable effect on reproductive performance.

What is known already: IUAs are reported in 19% of women after miscarriage; women with more than one D&C had statistical significant more IUAs

compared to women with one D&C, OR 2.05. IUAs is associated with menstrual disturbances, cyclic pain and infertility. In the Prevention of Adhesion Post Abortion (PAPA-study), intrauterine application of ACP gel following D&C for miscarriage in women with at least one previous D&C significantly reduced the incidence and severity of IUAs. Although, the process of adhesion formation is not completely eliminated. It remains unclear if application of ACP gel improves fertility and reproductive performance.

Study design, size, duration: The present prospective, non-interventional long-term follow-up study was conducted in the Netherlands. 149 women with a (incomplete) miscarriage of less than 14 weeks with at least one D&C in history were preoperatively randomised to D&C plus ACP gel (intervention group) or D&C alone (control group) in the PAPA-study. The participants received questionnaires three, six and twelve months after the D&C-procedure. The aim of the current study was to evaluate reproductive performance after the D&C-procedure

Participants/materials, setting, methods: All women who participated in the PAPA-study were eligible to participate. Questionnaires were sent to 149 women, 77 women assigned to the intervention group and 72 to the control group, three, six and twelve months after the D&C-procedure. The questionnaires consisted of questions concerning demographics, complication, treatment received, menstrual pattern, contraceptive use, conception and reproductive performance. In women willingly to conceive, conception, miscarriage and ongoing pregnancy rates were assessed.

Main results and the role of chance: Of the 149 women eligible to participate, six women were lost to follow-up after three months and nine women after six and twelve months. The overall response rate for the questionnaires was 96% at three months and 94% at six and twelve months. The response rate in the intervention group was 94.8% after three, six and twelve months and respectively 97.2%, 93.1% and 93.1% after three, six and twelve months in the control group, there were no difference between the groups. In both groups 62 women attempted to conceive. After twelve months 44 women (71%) conceived in the intervention group compared to 40 women (64.5%) in the control group (Fisher exact test, $p = 0.56$). One pregnancy was terminated on social indication in the control group on social grounds and in the intervention group a woman had a extra uterine pregnancy, requiring surgical management. The cumulative miscarriage rate in the intervention group was 14.5% compared to 22.5% in the control group (Fisher exact test, $p = 0.79$). The cumulative ongoing pregnancy rates were respectively 71.0% and 64.5% (Fisher exact test, $p = 0.79$).

Limitations, reasons for caution: The sample size was of the current follow-up study is small and was not powered for reproductive outcomes. The results are based on the answers provided by the participants, making it not possible to draw solid conclusions. It remains unclear whether known and unknown factors could have influenced the results.

Wider implications of the findings: Application of ACP gel following D&C for miscarriage reduces the incidence and severity of IUAs in women with at least one D&C in history. Prevention of IUAs is essential because of the association between IUAs and complications while application of ACP gel seems to improve reproductive performance.

Trial registration number: NTR3120 (Dutch Clinical Trial Registry).

SELECTED ORAL COMMUNICATIONS

SESSION 75: FROM LABORATORY TO CLINIC

Wednesday 5 July 2017

Room C

14:00–15:15

O-294 Personalised scheduling of embryo transfer at the moment of highest endometrial receptivity according to ER Map® test significantly improves clinical outcomes

J. Sarasa¹, J. Aizpurua², I. Jurado¹, B. Rodriguez-Estrada¹, M.C. Garcia-Poyo¹, A.B. Climent³, P. Martinez-Ortiz³, M. Enciso¹

¹iGLS, Genetics, Alicante, Spain

²IVF Spain, Reproductive Medicine, Alicante, Spain

³IVF Spain, Statistics, Alicante, Spain

Study question: Does identifying the window of implantation using the molecular tool ER Map[®] improve ART outcomes on patients with previous IVF failed cycles?

Summary answer: The use of ER Map[®] test for endometrial receptivity evaluation and personalised scheduling of embryo transfer during the moment of highest receptivity improves ART outcomes.

What is known already: The endometrium reaches a receptive status for embryonic implantation around day 19-21 of the menstrual cycle. During this period, known as the window of implantation (WOI), the endometrium shows a specific gene expression profile suitable for endometrial function evaluation. ER Map[®] is a molecular diagnostic tool able to accurately predict endometrial receptivity status by analysing this gene expression profile on an endometrial biopsy by high-throughput RT-qPCR. In this study the experience of the application of ER Map[®] for WOI identification and personalised scheduling of embryo transfer is studied for the first time.

Study design, size, duration: This is a retrospective study comparing pregnancy rates of patients with and without displaced WOI when embryo transfer was scheduled on the moment of highest endometrial receptivity (WOI time-frame) as recommended by ER Map[®] (group A), or according to standard endometrial evaluation and deviating more than 12 h from ER Map[®] recommendation (group B). ER Map[®] clinical results comparison was performed on 204 couples undergoing egg donation treatment between March and November 2016.

Participants/materials, setting, methods: Women with 2 or more previously failed IVF cycles were included in the study. Endometrial biopsy samples were obtained in an HRT cycle at P₄+5.5. Samples were classified by ER Map[®] into 'Receptive', 'Pre-receptive' or 'Post-receptive'. In cases where a WOI displacement was detected, a second biopsy to confirm the displacement and to schedule embryo transfer on the moment of highest endometrial receptivity was performed. Once the WOI was confirmed, embryo transfer was recommended accordingly.

Main results and the role of chance: Preliminary results indicate that a total of 57 out of 204 patients (27.95%) with previous failed cycles were found to have a displaced WOI. Within this group of patients, a significantly higher pregnancy rate was achieved when embryo transfer was scheduled according to ER Map[®] prediction compared to transfers that followed traditional endometrial evaluation methods and deviated more than 12 h from ER Map[®] recommendation (75.51% vs 33.33%, X² Test with Yates' correction $p < 0.01$). More than double pregnancy rates were achieved when these patients' WOI displacement is identified and managed adequately.

No difference in pregnancy rates was observed in patients whose WOI was not displaced (i.e. patients whose endometria were classified as 'Receptive' at P₄+5.5) when embryo transfer schedule was guided by either ER Map[®] or traditional evaluation methods (73.20% vs 70.00%). No positive nor negative effect of the application of ER Map[®] was observed on these patients. The effectiveness of ER Map[®] strategy depends on patient endometrial receptivity diagnosis.

Limitations, reasons for caution: The retrospective and non-randomised design of the study may be a reason for caution. A wider spectrum of infertility conditions and patient characteristics is desirable to define more precisely the group of patients that could potentially benefit from the assessment of endometrial receptivity and personalised embryo transfer using ER Map[®].

Wider implications of the findings: The application of ER Map[®] as a routine tool for the identification of cases of WOI displacement and personalised embryo transfer scheduling is an effective strategy for improving ART outcomes and achieving pregnancies on challenging repeated IVF failure cases.

Trial registration number: Not applicable.

O-295 Endometrial preparation: Impact of estrogen duration of administration before frozen-thawed blastocyst transfer on live birth rate

F. Kefelian¹, P. Santulli¹, M. Bourdon¹, L. Vienet-Legue¹, C. Maignien¹, V. Gayet¹, K. Pocate-Cheriet², L. Marcellin¹, J. Gonnot¹, C. Cervantes¹, V. Blanchet¹, C. Chapron¹

¹Université Paris Descartes- Faculté de Médecine- Assistance Publique—Hôpitaux de Paris AP- HP, Service de Gynécologie Obstétrique II and Reproductive Médecine Professor Chapron, Paris, France

²Université Paris Descartes- Faculté de Médecine- Assistance Publique—Hôpitaux de Paris AP- HP, Service d'Histologie-Embryologie-Biologie de la Reproduction, Paris, France

Study question: To investigate the impact of estrogen (E2) duration of administration before frozen-thawed blastocysts transfer on life birth rate.

Summary answer: Live birth rate significantly decreases as estrogen duration of administration increases before frozen-thawed blastocyst transfer.

What is known already: Different cycle regimens for endometrial preparation are used prior to frozen embryo transfer. Currently, one effective method is the hormonal replacement therapy with a sequential regimen with estrogen (E2) and progesterone, which aims to mimic the endocrine exposure of the endometrium in the normal cycle. There nonetheless remains a lack of knowledge concerning the optimal duration of exogenous E2 administration before transfer.

Study design, size, duration: This cohort study was conducted in a tertiary care university hospital between 01/01/2012 and 31/12/2015. Main inclusion criteria's were having a single frozen-thawed blastocyst transfer with an artificial endometrial preparation using exogenous estrogen (E2).

Participants/materials, setting, methods: A total of 1377 frozen-thawed blastocysts transfer were allocated to 4 groups according to the duration of E2 administration: ≤ 21 days (Group A, n = 330), 22-28 days (Group B, n = 665), 29-35 days (Group C, n = 289) and 36-48 days (Group D, n = 93). The main outcome measured was the live birth rate following frozen-thawed blastocysts transfer. Statistical analysis were conducted using univariate and multivariate logistic regression models.

Main results and the role of chance: Live birth rates significantly decrease with the increase of E2 duration before frozen-thawed blastocysts transfer (group A: n = 98 (29.70%), OR 1; Group B: n = 185 (27.82%), OR 0.91 CI95% 0.68-1.22; Group C: n = 63 (21.80%), OR 0.66 CI95% 0.46-0.95 and Group D: n = 16 (17.20%), OR 0.49 IC95% 0.27-0.89). In contrast, early pregnancy loss rate significantly increase with the increase of E2 duration before frozen-thawed blastocysts transfer (group A: n = 41 (28.47%), OR 1; Group B: n = 89 (31.79%), OR 1.17 CI95% 0.75-1.82; Group C: n = 35 (34.31%), OR 1.31 CI95% 0.76-2.27 and Group D: n = 17 (48.57%), OR 2.37 IC95% 1.12-5.05).

Obstetrical and neonatal outcomes were not significantly different among groups. After multivariate logistic regression, E2 duration of administration longer than 28 days before frozen-thawed blastocyst transfer was found to be an independent predictive factor of life birth rate (29-35 days versus ≤21 days: OR 0.68 95%CI 0.460-0.989; 36-48 days versus ≤21 days: OR 0.51 95%CI 0.269-0.953).

Limitations, reasons for caution: One limitation is linked to the observational design of this study: randomized clinical trials are needed to confirm these results.

Wider implications of the findings: In order to give patients the best chance to obtain a live birth after frozen-thawed blastocysts transfer, it seems important to limit estradiol duration of administration before ET. This study brings new insight to endometrial preparation using hormonal replacement therapy before frozen blastocysts transfer.

Trial registration number: NA.

O-296 Antioxidant Gene Expression of Peroxiredoxin (PRDX) decreases in granulose cells from oocytes of young women with low ovarian reserve

L. Ortega López¹, S. Cortés Gallego¹, L. Rancan², E.M. Vara Ameigeiras², P. Lopez Domínguez¹, J. Fernández Tresguerres³, P. Caballero Peregrín⁴, R. Núñez Calonge¹

¹Clinica Tambre, Embriology Lab, Madrid, Spain

²Universidad Complutense de Madrid, Department of Biochemistry and Molecular Biology, Madrid, Spain

³Universidad Complutense de Madrid, Department of physiology, Madrid, Spain

⁴Clinica Tambre, Clinician, Madrid, Spain

Study question: Is gene expression of antioxidant peroxiredoxin altered in cumulus (CCs) and granulose cells (GCs) from young women with reduced ovarian reserve compared with oocyte donors?