rate while minimizing the multiple birth rate and results in similar cumulative live birth rates, when compared to fresh DBT. Outcome implications should be discussed with patients and individualized. Given the added risk of multiple pregnancies in this age group, eSBT is preferential in women 40-43 years of age.

O-219 Wednesday, October 19, 2016 11:45 AM

METHOTREXATE TREATMENT OF ECTOPIC PREGNANCY DOES NOT IMPACT OVARIAN RESERVE OR CLINICAL OUTCOME, REGARDLESS OF THE DURATION OF TIME SINCE EXPOSURE. L. Sekhon,[a,b] J. Rodriguez-Purata,[a] J. A. Lee,[a] M. C. Whitehouse,[a] A. B. Copperman.[a,b] [a]Reproductive Medicine Associates of New York, New York, NY; [b]Obstetrics, Gynecology & Reproductive Science, Icahn School of Medicine at Mount Sinai, New York, NY.

OBJECTIVE: Methotrexate (MTX) is a minimally invasive treatment for ectopic pregnancy. As it targets rapidly dividing cells, there is concern it may affect proliferating germinal cells in the ovary, ovarian reserve. Most centers recommend patients wait 2-3 months before attempting subsequent fertility treatment, It is not known whether recent MTX exposure increases the incidence of meiotic error within oocytes, contributing to embryonic aneuploidy. We sought to investigate the effect of MTX treatment and the interval of time from its administration to subsequent fertility treatment on ovarian reserve and IVF outcome.

DESIGN: Retrospective cohort study, case control study

MATERIALS AND METHODS: All patients who received MTX in a prior cycle and underwent subsequent IVF ± ET from 2003-2016 were included. The interval of time from administration to the start of their subsequent cycle was calculated. Paired t-test compared ovarian reserve markers (day 3 FSH) and cycle parameters pre- and post-MTX. Linear and binary logistic regression were performed to identify if interval since MTX modified implantation and early pregnancy loss.

RESULTS: A total of 491 patients received MTX and underwent subsequent COH (n=339) with fresh ET (n=279) or frozen-thawed (FET) (n=198). The interval from MTX to subsequent cycle start, cycle characteristics and clinical outcome of COH and ET cycles are shown (Table). After controlling for the increase in patient age, FSH, egg yield and fertilization, total gonadotropin dose required and blastocyst count were similar among pre- and post-MTX COH cycles. Intercycle variation in these parameters was not correlated with the MTX time interval. PGS was performed in 51 subsequent COH cycles with a 49.2% aneuploidy rate. Controlling for oocyte age and MTX dose, aneuploidy was not correlated with MTX interval. Odds of failed implantation (OR 1.0 [95% CI 1.0-1.001], p=0.3) and pregnancy loss (OR 1.0 [95% CI 0.9-1.0], p=0.8) were not influenced by MTX interval.

CONCLUSIONS: In agreement with the existing literature, these results suggest ovarian reserve and IVF outcomes are not compromised by MTX treatment of ectopic pregnancy. The interval of time from MTX did not impact cycle outcome or the incidence of aneuploidy. To date, this is the only study to assess embryonic aneuploidy following MTX exposure. Though the results are reassuring regarding MTX safety, large-scale, multicenter studies are required to confirm these findings.

O-220 Wednesday, October 19, 2016 12:00 PM

IMPACT OF THE OXYTOCIN RECEPTOR ANTAGONIST (ATOSIBAN) ADMINISTERED SHORTLY BEFORE EMBRYO TRANSFER ON PREGNANCY OUTCOME AFTER INTRACYTOPLASMIC SPERM INJECTION (ICSI). S. A. Hebisha,[a] B. A. Aboelazm,[a] H. M. Adel,[a] A. I. Ahmed.[b] [a]Gynecology, Alexandria University - Faculty of Medicine, Alexandria, Egypt; [b]Obstetric and Gynecology, MFM Division, Department of Medical Genetics, Wayne State University, Detroit, MI.

OBJECTIVE: To evaluate the impact of the oxytocin receptor antagonist (Atosiban) administered shortly before embryo transfer on implantation and pregnancy rates in patients undergoing intracytoplasmic sperm injection (ICSI) using long agonist protocol.

DESIGN: Randomised controlled trial.

MATERIALS AND METHODS: one hundred and eighty two women, prepared for intracytoplasmic sperm injection for male or tubal factor infertility, using long agonist protocol were divided randomly into two groups; Group A (n=91) who received 7.5 mg Atosiban by slow IV injection and Group B (n=91) who received placebo as sodium chloride 0.9% solution also by IV injection 20 minutes before embryo transfer (blastocyst stage ET). Pregnancy and implantation rates were compared among the two study groups.

RESULTS: Pregnancy rate was significantly higher in group A (atosiban group) (58/91) compared to group B (44/91) ;(63.7% vs 48.4% respectively, p=0.037*). Also, implantation rate was significantly higher in group A (atosiban group) compared to group B ;(45.20%, vs 34.69% respectively, P=(0.045*). All of the intermediate cycle parameters were also comparable.

CONCLUSIONS: Atosiban in the given dose and regimen improved both implantation and ongoing pregnancy rates in patients undergoing ICSI using blastocyst stage embryo transfer.

References:

1. Mansour R, Tawab N, Kamal O, El-Faissal Y, Serour A, Aboulghar M, Serour G. Intrauterine injection of human chorionic gonadotropin before embryo transfer significantly improves the implantation and pregnancy rates in in vitro fertilization/intracytoplasmic sperm injection: a prospective randomized study. Fertil Steril. 2011; 96(6):1370-1374.e1.
2. Hong KH, Forman EJ, Werner MD, Upham KM, Gumeny CL, Winslow AD, Kim TJ, Scott RT Jr. Endometrial infusion of human chorionic gonadotropin at the time of blastocyst embryo transfer does not impact clinical outcomes: a randomized, double-blind, placebo-controlled trial. Fertil Steril. 2014; 102(6):1591-1595.e2.
3. Goto S, Kadowaki T, Hashimoto H, Kokeguchi S, Shiotani M. Stimulation of endometrium embryo transfer (SEET): injection of embryo culture supernatant into the uterine cavity before blastocyst transfer can improve implantation and pregnancy rates. Fertil Steril. 2007; 88(5):1339-43.
4. Parikh FR, Nadkarni SG, Naik NJ, Naik DJ, Uttamchandani SA. Cumulus coculture and cumulus-aided embryo transfer increases pregnancy rates in patients undergoing in vitro fertilization. Fertil Steril. 2006; 86(4):839-47.
5. Barad DH, Yu Y, Kushnir VA, Shohat-Tal A, Lazzaroni E, Lee HJ, Gleicher N. A randomized clinical trial of endometrial perfusion with granulocyte colony-stimulating factor in in vitro fertilization cycles: impact on endometrial thickness and clinical pregnancy rates. Fertil Steril. 2014; 101(3):710-5.

Post-methotrexate ovarian stimulation and embryo transfer: demographics & cycle characteristics

	Controlled ovarian stimulation (n=339)	Fresh ET (n=279)	FET (n=152)
Interval since MTX (days)	359.5 +/- 378.4 (range: 64-2251)	341.1 +/- 381.4 (range: 64-2251)	422.4 +/- 483.5 (range: 32-2585)
Cumulative MTX dose	108.1 +/- 40.3	107.4 +/- 40.3	104.2 +/- 35.4
Patient age	36.9 +/- 4.5	36.7 +/- 4.6	34.4 +/- 4.2
Day 3 FSH	6.4 +/- 3.9	6.4 +/- 4.1	6.9 +/- 3.5
Endometrial thickness at transfer (mm)	N/A	9.6 +/- 2.3	9.3 +/- 2.3
Cumulative gonadotropin dose	3808.4 +/- 1448.3	N/A	N/A
Oocytes retrieved	12.7 +/- 7.5 (n=4292)	N/A	N/A
Mean number of blastocysts	2.7 +/- 3.7 (n=927)	N/A	N/A
Aneuploidy rate	49.2% (n=91/185)	N/A	N/A
Implantation rate	N/A	45.8% (128/279)	31.7% (184/262)
Early pregnancy loss rate	N/A	25.4% (71/279)	18.4% (28/152)

Comparison between the two studied groups according to implantation and pregnancy rates

	Group A (n=91)	Group B (n=91)	test of significance	p value
ET				
Min-Max.	1.0 - 2.0	1.0 - 2.0		
Mean± SD	1.60 ± 0.49	1.62 ± 0.49		
Total no. of ET	146.0	147.0		
Implantation				
MIn-Max.	0.0 - 2.0	0.0 - 2.0	t=2.018*	0.045*
Mean± SD	0.74 ± 0.66	0.55 ± 0.58		
Total no. of implantation	67.0	50.0		
Implantation rate	45.20%	34.69%		
No. of pregnant cases	58	44	t=4.372*	0.037*
Pregnancy rate	63.7%	48.4%		

6. Mansour R. Minimizing embryo expulsion after embryo transfer: a randomized controlled study. Hum Reprod. 2005; 20(1):170-4.
7. Abou-Setta AM, Peters LR, D'Angelo A, Sallam HN, Hart RJ, Al-Inany HG. Post-embryo transfer interventions for assisted reproduction technology cycles. Cochrane Database Syst Rev. 2014 Aug 27; 8:CD006567.pub3.
8. Bulletti C, de Ziegler D. Uterine contractility and embryo implantation. Curr Opin Obstet Gynecol. 2005; 17(3):265-76.
9. Pierzyński P, Zbucka-Kretowska M. Uterine contractile activity at embryo transfer–as a new pharmaco-therapeutic target in assisted reproduction. Ginekol Pol. 2014 Aug; 85(8):609-13.
10. Ng EH, Li RH, Chen L, Lan VT, Tuong HM, Quan S. A randomized double blind comparison of atosiban in patients undergoing IVF treatment. Hum Reprod. 2014; 29(12):2687-94.
11. Zhu L, Che HS, Xiao L, Li YP. Uterine peristalsis before embryo transfer affects the chance of clinical pregnancy in fresh and frozen-thawed embryo transfer cycles. Hum Reprod 2014b;29:1238-43.12.
12. Moraloglu O, Tonguc E, Var T, Zeyrek T, Batioglu S. Treatment with oxytocin antagonists before embryo transfer may increase implantation rates after IVF. Reprod Biomed Online. 2010; 21 (3):338-43.
13. Lan VT, Khang VN, Nhu GH, Tuong HM. Atosiban improves implantation and pregnancy rates in patients with repeated implantation failure. Reprod Biomed Online. 2012; 25(3):254-60.
14. Pierzynski P, Reinheimer TM, Kuczynski W. Oxytocin antagonists may improve infertility treatment. Fertil Steril. 2007; 88(1):213.e19-22.
15. Zhu L, Xiao L, Che HS, Li YP, Liao JT. Uterine peristalsis exerts control over fluid migration after mock embryo transfer. Hum Reprod. 2014; 29(2):279-85.

O-221 Wednesday, October 19, 2016 12:15 PM

MATERNAL ENDOMETRIAL SECRETIONS 24 HOURS PRIOR TO FROZEN EMBRYO TRANSFER IS PREDICTIVE OF IMPLANTATION OUTCOME.

J. C. Parks,[a] B. R. McCallie,[a] J. A. Reisz,[b] M. J. Wither,[b] W. B. Schoolcraft,[a] M. Katz-Jaffe.[a] [a]Colorado Center for Reproductive Medicine, Lone Tree, CO; [b]University of Colorado Denver, Aurora, CO.

OBJECTIVE: It is well known that successful implantation is dependent on the intricate dialogue between a competent embryo and a receptive endometrium. On the maternal side, specific biological changes in adhesion need to occur for attachment, while tight regulation of signaling pathways are crucial for the embryo. The objective of this study was to examine the uterine fluid in association with implantation outcome 24 hours prior to, and at the time of euploid embryo transfer.

DESIGN: Research study.

MATERIALS AND METHODS: Infertile patients (n=48) were recruited with IRB consent prior to a frozen embryo transfer (FET) with euploid blastocysts. Uterine secretions were collected by aspiration (~2-5ul), either 24h prior to, or at the time of FET. Uterine secretome analysis was performed blinded of implantation outcome using qPCR for miRNA analysis (n=12) and mass spectrometry (n=36) for metabolite (UHPLS-MS, Thermo) and protein analysis (LC-MS/MS, Thermo). MiRNA profiles were analyzed by REST© statistical software. MS data was converted with MassMatrix and processed with Maven (Princeton Univ). MS/MS data was examined using Mascot™ (v 2.2) and Scaffold (v 2.06). Validation of target genes was performed using qPCR on endometrial biopsies (n=14) and cryopreserved blastocysts (n=14) donated with patient consent.

RESULTS: A notable uterine secretome profile of miRNA, metabolites and proteins was significantly associated with a negative, toxic environment both 24hrs prior to, and at the time of embryo transfer ($P<0.05$, >2 fold change). Specifically, 6 maternal miRNAs showed increased expression with negative implantation, including miR-17 ($P<0.05$). A known target gene of miR-17 through negative regulation is VEGFA, a signal protein essential for implantation and secreted by the receptive endometrium as well as the developing embryo. Validation of VEGFA expression was confirmed in endometrial cells and individual blastocysts. A total of 12 amino acids displayed decreased quantities in the uterine secretome associated with negative implantation ($P<0.05$, >2 fold change) including arginine, essential for blastocyst activation and trophectoderm motility. Additionally, the MUC protein family were observed at increased levels with implantation failure ($P<0.05$). MUCIN proteins are epithelial cell surface proteins that have considerable effect on endometrial function, creating a barrier to implantation.

CONCLUSIONS: Aberrant maternal uterine miRNA and molecular secretions allow for the characterization of implantation failure both 24 hours prior to, and at the time of FET. This compromised embryo-endometrial dialogue further impacts the transcription levels of key signaling molecules, resulting in significantly lower implantation success. Predicting the maternal molecular microenvironment ahead of embryo transfer may allow for fine tuning of procedures for IVF patients thereby improving implantation outcomes.

O-222 Wednesday, October 19, 2016 12:30 PM

SUCCESSIVE SINGLE EMBRYO TRANSFER CYCLES LEAD TO REDUCED RISK WITHOUT COMPROMISING SUCCESS RATES IN WOMEN UNDER 38.

K. Hunter Cohn,[a] H. Wu,[a] J. Schnorr,[b] F. Arredondo,[c] B. Miller,[d] M. P. Leondires,[e] J. Gutmann,[f] L. Weckstein,[g] J. Nulsen,[h] S. E. Katz,[i] P. C. Lin,[j] A. B. Copperman,[k] E. A. Widra,[l] P. Yurttas Beim.[a] [a]Celmatix Inc, New York, NY; [b]Coastal Fertility Specialists, Mount Pleasant, SC; [c]RMA of Texas, San Antonio, TX; [d]RMA of Michigan, Rochester Hills, MI; [e]RMA of CT, Norwalk, CT; [f]RMA of Philadelphia, Philadelphia, PA; [g]Reproductive Science Center of the San Francisco Bay Area, San Ramon, CA; [h]Center for Advanced Reproductive Services, Farmington, CT; [i]REACH, Charlotte, NC; [j]Seattle Reproductive Medicine, Seattle, WA; [k]Obstetrics and Gynecology, RMANY-Mount Sinai, New York, NY; [l]Shady Grove Fertility, Washington, DC.

OBJECTIVE: Patients are increasingly counseled to undergo single embryo transfer (SET) IVF to minimize multiple gestations. If the first transfer is unsuccessful, patients often pursue double embryo transfer (DET) on the successive attempt. Here, we sought to understand the risks and benefits of staying the course with SET after a failed cycle.

DESIGN: We performed a retrospective cohort study on IVF cycles from 12 different fertility treatment centers in the US from 2009-2015.

MATERIALS AND METHODS: We analyzed 8,588 autologous IVF cycles in women under 38 that involved an SET in cycle 1. 3,727 of these cycles failed and were followed by a successive IVF cycle with SET (n=1,815) or DET (n=1,912). Cycles with pre-implantation genetic screening (PGS) were excluded. Multivariate logistic regression models were used to evaluate the odds of ongoing pregnancy and multiples. Predictors were refined using least absolute shrinkage and selection operator (LASSO).

RESULTS: We observed that SET was performed in 36.9% of first cycles in women under 38. Of the patients whose cycles failed, we found that less than half persisted with SET. Our models showed, that on an individual patient basis, there was no significant difference in predicted likelihood of success with the first versus second SET cycle ($P=0.16$). Further, our models showed that first cycle outcome (e.g. miscarriage) had no significant impact on second cycle ongoing pregnancy rates. Evaluation of multiples rates found much higher risk for DET compared to SET (38.4 fold higher, $P<0.0001$).

CONCLUSIONS: We find that patients that have failed an SET cycle have no reduction in odds of ongoing pregnancy when performing a second SET attempt. We also found that those that choose to do a DET are at a significantly higher risk for multiples.

Supported by: Celmatix Inc.