CONCLUSIONS: pET of R patients using good quality embryos in consideration with embryonic developmental speed can improve reproductive prognosis.

IMPACT STATEMENT: pET considering embryonic developmental speed may be effective not only when good quality embryos are transferred, but also when euploid embryos, which are often advanced in expansion grade when thawed, are transferred. Further prospective studies are required.

P-485 11:25 AM Wednesday, October 18, 2023

EXPOSOME PROFILING REVEALS WIDESPREAD ENVIRONMENTAL POLLUTANT EXPOSURE IN SEMINAL PLASMA AND PREVIOUSLY UNKNOWN ASSOCIATIONS WITH MALE FERTILITY. Haotian Wu, Ph.D,[1] Vrinda Kalia, PhD,[2] Katherine E. Manz, PhD,[3] Lawrence Chillrud, B.A.,[4] Nathalie Hoffmann Dishon, MA,[5] Gabriela L. Jackson, BA,[2] Raoul Orvieto, M.D.,[6] Christian K. Dye, PhD,[2] Adva Aizer, PhD,[5] Hagai Levine, MD,[7] Marianthi-Anna Kioumourtzoglou, ScD,[2] Kurt Pennell, PhD,[8] Ronit Machtinger, MD, PhD,[6] Andrea A. Baccarelli, PhD[2] [1]Columbia University Mailman School of Public Health, NY; [2]Columbia University Mailman School of Public Health; [3]Brown University; [4]Northwestern University; [5]Chaim Sheba Medical Center; [6]Sheba Medical Center, Ramat Gan, Israel; [7]Hebrew University-Hadassah; [8]Brown University, RI.

OBJECTIVE: There is evidence that indicators of male fertility are in decline globally, but the underlying causes have yet to be fully elucidated. While the environment is likely a major contributor, our current knowledge of environmental determinants of male fertility does not explain this phenomenon. This study aimed to examine and profile organic pollutants in seminal plasma, including both known priority environmental chemicals and previously uncharacterized chemicals, and to discover previously uncharacterized male reproductive environmental toxicants.

MATERIALS AND METHODS: Semen samples were collected from male partners from 100 couples undergoing assisted reproductive treatment at the Sheba Medical Center (Israel) after 2-7 day abstinence. Semen parameters were assessed for sperm concentration, percent motility, and total motile sperm. Using a QuEChERS (quick, easy, cheap, efficient, rugged, and safe) extraction method, targeted and non-targeted organic pollutant exposures were measured from seminal plasma using gas chromatography. We used linear regression for individual exposure modeling, principal component pursuit (PCP) to remove noise and identify latent patterns in exposure data, and Bayesian Kernel Machine Regression (BKMR) to model multiple pollutants simultaneously. In individual exposure models, we corrected for multiple testing via false discovery rate (FDR).

RESULTS: We detected 118 of 119 organic pollutants in our targeted panel in $\geq$1 sample and 814 non-targeted spectral peaks in all samples, showing widespread detection of organic pollutants in seminal plasma. We used PCP, a machine learning pattern recognition approach, on our targeted panel and derived a low-rank matrix in which one component (explaining 17.4% of the variance in the data) was both driven by etriadizole, a common pesticide, and associated with total motile sperm ($p<0.001$) and concentration ($p=0.03$). This was confirmed by the exposome-wide association modeling approach using individual chemicals, where we found that etriadizole was negatively associated with total motile sperm (FDR $q=0.01$) and concentration ($q=0.07$). Using PCP on 814 non-targeted spectral peaks identified a component that was associated with total motile sperm ($p=0.001$). BKMR identified one principal driver of this association, which was analytically confirmed to be N-Nitrosodiethylamine (level-1 confidence) and consistent with linear models ($p=0.01$).

CONCLUSIONS: Among the many detectable chemicals in seminal plasma, we identified etridiazole and N-nitrosodiethylamine as previously uncharacterized potential reproductive toxicants. We show that our approach, combining novel machine learning methods and modern statistical models, is consistent with results obtained from traditional statistical approaches, but is far more efficient in identifying associations using realistic sample sizes.

IMPACT STATEMENT: Our study not only identified potential contaminants of concern for male reproductive health, it can address methodological needs as a proof of concept for our new analytical pipeline that may be adopted in other reproductive studies with high-dimensional predictors.

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DOES STIMULATING OVULATION WITH LETROZOLE DURING FROZEN EMBRYO TRANSFER (FET) CYCLES IMPROVE PREGNANCY RATES IN OVULATORY WOMEN? Jessica Ka Wai Cheung, M.D.,[1] Katherine Koniares, M.D.,[2] Prachi N. Godiwala, M.D.,[3] Claudio A. Benadiva, H.C.L.D, M.D.,[4] Daniel R. Grow, M.D.,[5] Lawrence Engmann, M.D.[6] [1]University of Connecticut School of Medicine, Farmington, CT; [2]University of Connecticut Health Center, Center for Advanced Reproductive Services, Farmington, CT; [3]Center for Advanced Reproductive Services, University of Connecticut School of Medicine, Farmington, CT; [4]Univ. of Connecticut (REI Division); [5]University of Connecticut Health Center, Farmington, CT; [6]Center for Assisted Reproductive Services, University of Connecticut School of Medicine, Farmington, CT.

OBJECTIVE: Prior studies have shown higher pregnancy rates with FET following letrozole induced ovulation compared to those following natural ovulation. The aim of this study was to compare the pregnancy rates of natural (nat-FET) vs letrozole FET (let-FET) cycles in infertile women that were ovulatory.

MATERIALS AND METHODS: Retrospective cohort study performed in a university-affiliated fertility practice. All natural and letrozole FET cycles from 2015 to 2022 were included. Primary outcome was ongoing pregnancy rate (OPR). Secondary outcomes included rates of pregnancy (PR), biochemical loss, clinical pregnancy (CPR), clinical loss, and ectopic pregnancy. Continuous variables were compared using Student's t-test. Categorical variables were compared with Chi-square or Fisher's exact test. The outcomes were adjusted for BMI and age at embryo cryopreservation with multivariate logistic regression. A subgroup analysis including only PGT-A cycles was also performed.

RESULTS: A total of 2466 FET cycles were included, with 1907 natural (77%) and 559 (23%) letrozole cycles. Patients who underwent letrozole FET had a higher BMI (27.7 vs 26.3 kg/m2, $p < .01$) and were younger at embryo transfer (35.5 vs 35.9 years, $p = .047$) and embryo cryopreservation (35.0 vs 35.4 years, $p = .042$). The rates of PGT-A (37 vs 35%, $p = 0.25$) were similar between groups. OPRs were similar between groups as well as the PR, CPR, biochemical loss rate, clinical pregnancy loss rate, and ectopic pregnancy rate (table 1). The pregnancy rates remained similar between groups after adjusting for BMI and age at embryo cryopreservation using multivariate logistic regression. Among the 867 FET cycles that utilized PGT-A, OPRs were similar between groups despite a higher clinical loss rate in the letrozole group (table 1). The other pregnancy rates were similar between groups. The results were unchanged after adjusting for BMI and age at embryo cryopreservation.

All FET Cycles N = 2466	Letrozole FET N = 559 (23%)	Natural FET N = 1907 (77%)	*p*value
PR	77.8%	76.9%	.64
CPR	68.2%	66.6%	.51
OPR	60.1%	59.0%	.65
Biochemical loss rate	9.1%	9.6%	.81
Clinical loss rate	8.1%	7.6%	.73
Ectopic pregnancy rate	0.5%	0.8%	.78
FET Cycles with PGT-A N = 867	**Letrozole FET N = 659 (76%)**	**Natural FET N = 208 (24%)**	***p* value**
PR	80.3%	78.5%	.57
CPR	70.2%	69.0%	.75
OPR	61.5%	65.3%	.33
Biochemical loss rate	10.1%	9.0%	.62
Clinical loss rate	8.7%	3.8%	.005
Ectopic pregnancy rate	0%	0.5%	1.0

CONCLUSIONS: Among ovulatory women, the use of letrozole to stimulate ovulation was not associated with improved pregnancy rates.

IMPACT STATEMENT: This is the first study we are aware of that compared the pregnancy outcomes of natural FET to letrozole stimulated FET in women who are ovulatory. Our study suggests that letrozole might not improve pregnancy rates compared to natural FET cycles in ovulatory women.