American Society for Reproductive Medicine 2017 Scientific Congress & Expo
October 28 to November 1, 2017 • San Antonio, TX, USA

Title

SELECTIVE SEROTONIN REUPTAKE INHIBITORS, IVF AND PGT: HOW DOES EXPOSURE AFFECT OUTCOME?

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Objective:

Depending on exposure amount, selective serotonin reuptake inhibitors (SSRIs) can have a positive or negative influence on early embryo development (Khozhai et al., 1995; Il'kova et al., 2004). For example, exposure to fluoxetine has shown to benefit mouse embryonic blastocysts development, yet when exposed to extreme levels can inhibit formation (Kim et al., 2012). In a growing era of IVF-PGT, it is unknown how SSRI exposure influences cycle outcomes. This study sought to analyze if maternal SSRI exposure during IVF has any influence on blastocyst ploidy, implantation, and live birth rates.

Design

Retrospective cohort analysis

Materials and Methods

All patients who underwent a PGS cycle from January 2012 to February 2017 were included. Patients were segregated by SART age groups and SSRI exposure (Non-exposed versus Exposed). Ovum donation cycles, genetic translocations and cycles with incomplete EMR data were excluded. Student's t-test was used for continuous variables, X^2 test for categorical variables, and significance was confirmed a $p<0.05$. A sample size 356 blasts for each group was calculated to have an 80% power to detect a 10% difference rate in euploidy between cohorts, and also a sample size of 87 embryo transfers was calculated to have an 80% power to detect a 20% difference on implantation rates.

Results

Of the 12,342 embryos analyzed, 4.3% (n=519) were exposed to a SSRI while the remaining were not 95.7% (n=11,823). Overall euploid rate was 60%, aneuploidy rate 36.1%, and 3.9% inconclusive reports from the PGS laboratory. A significant difference was found in AMH levels (3.7 vs 2.7, $p<0.005$), and in euploidy rates for Group E (>43 years) (1.3 ±0.7 vs 0.5 ±0.5, $p=0.04$). No other differences were found in ploidy and inconclusive rates between groups. Of the 2132 SET cycles analyzed, 4.7% (n=97) of the cycles patients were exposed to a SSRI while the remaining were not 95.3% (n=2035). No differences were observed in the total number of live birth rate (28.5% vs 25.7%), ongoing pregnancy rate (21.3% vs 16.4%), implantation rate (71.3% vs 70.1%), clinical pregnancy (58.2% vs 59.7%), loss rate (21.3% vs 27.8%) and multiple pregnancy rate (0.6% vs 0%) between cohorts.

Conclusions

SSRIs are the most widely prescribed category of antidepressants in women of reproductive age. Treatment of anxiety and depression are complicated, and the health of the mother must be balanced against any potential embryo toxic, teratogenic, or development risks to their offspring. This study did not identify a difference in implantation or ongoing pregnancy rates in patients exposed to SSRIs. The rate of embryo euploidy was similar among patient cohorts. The observance of a significant decrease in euploid embryos in patients >43 was consistent with the knownd age-related decline of embryo quality. Long-term clinical trials would help to fully define the risk/benefit ratio of SSRI exposure during ART treatment.

Support

None.

Table 1

	NO SSRI Exposure (n=11823)	SSRI Exposure (n=519)	p-value
Age	36.1 (±3.9)	(±3.6)	NS
BMI	23.3(±4.1)	24.1(±4.5)	NS
AMH	3.7(±4.3)	2.72(±2.6)	<0.005
BAFC	10.1(±7.4)	9.0(±6.5)	NS
FSH	6.3(±3.1)	6.2(±3.7)	NS
Peak E2	2338(±2438)	2111(±1870)	NS
Number of blasts per cycle	5.7(±4.2)	5.3(±4.0)	NS

Table 2.

SART age group	SSRI exposure YES/NO	Euploid embryos means	Aneuploid enbryosmeans	Inconclusive report means
A	No (n=5141)	5.11(±3.5)	2.11 (±2.0)	0.3(±1.0)
	Yes (n=205)	4.9(±3.6)	1.6 (±1.6)	0.2(±0.5)
B	No (n=3180)	3.7(±2.5)	2.8(±2.0)	0.1(±0.4)
	Yes (n=160)	4.3(±2.7)	2.0(±2.2)	0.8(±0.2)
C	No (n=2659)	2.4(±1.8)	2.3(±2.0)	0.1(±0.4)
	Yes (n=91)	2.5(±2.2)	2.0(±1.7)	0.05(±0.2)
D	No (n=694)	1.5(±0.9)	2.2(±2.4)	0.09(±0.3)
	Yes (n=54)	2.0 (±0.7)	1.3(±1.3)	0.06(±0.2)
E	No (n=149)	1.3(±0.7)* p=0.04	1.8(±1.8)	0.08(±0.3)
	Yes (n=9)	0.5 (0.05)* p=0.04	1.7(±2.0)	0.1 (±0.3)

Outcome	NO SSRI exposure	SSRI exposure	p-value
Live birth rate	582(28.5%)	25(25.7%)	NS
Ongoing pregnancy rate	435(21.3%)	16(16.4%)	NS
Chemical pregnancy rate	1451(71.3%)	68(70.1%)	NS
Clinical pregnancy rate	1186(58.2%)	58(59.7%)	NS
Loss rate	434(21.3%)	27(27.8%)	NS
Multiple pregnancy rate	14 (0.6%)	0	NS

***P value <0.05**