Repeat ovarian stimulation cycles in oocyte donors: Results from a cohort study

A. Zavala-Garcia, MD[1], B. Lozano-Moreno, Biol.[1], JM. Moreno-Garcia, Biol.[2], R. Lopez-Sanchez, Biol.[2], JJ. Lopez-Galvez, MD, PhD[3]

1. Master Program Reproductive Medicine and Genetics, Miguel Hernandez University, Unidad de Reproducción, Hospital HLA Clínica Vistahermosa, Alicante, Spain
2. Clinical Embriology Laboratory, Unidad de Reproducción, Hospital HLA Clínica Vistahermoa, Alicante, Spain
3. Unit of Assisted Reproduction, Unidad de Reproducción, Hospital HLA Clínica Vistahermoa, Alicante, Spain

Background and Study Question

The number of patients requiring oocyte donation is thought to be greater than the number of eligible donors; which is a trend that will most likely keep growing within the following years. Recruiting the same donor multiple times is a way to overcome this demand, which is why the need to further investigate effects of repeated stimulation cycles of oocyte donation. Optimizing donor recruitment and understanding how their characteristics influence outcomes in recipients is essential. Even though a handful of studies have explored factors associated to pregnancy from oocyte donor cycles with contradictory results, they've studied few cycles in small populations.

Study Question: Are there diminishing changes in total FSH dose, follicular count, retrieved meiosis metaphase II (M2) oocytes and pregnancy rates in up to 4 repeated donor cycles?

Table 1. Oocyte donor demographic data according to age group per cycle. A total of 188 cycles from 47 patients.

Characteristics	Total Population** (N=188 cycles)	P-Value
Female Age, *years*	24.09 ± 3.70	0.280*
BMI, *kg/cm²*	21.42 ± 2.42	0.180*
Normal Weight,+	21.07 ± 2.07	0.128*
Overweight,#	24.46 ± 1.34	0.005$
Obesity,+	-	-
Menstrual Characteristics		
Menstruation, *Days*	4.85 ± 1.56	2.014
Cycle Length, *Days*	30.02 ± 3.81	4.441
Regular Menstruation, +	140 (74.46)	-
Past Pregnancy, +	134 (71.27)	-
Smoking Habit, %	122 (64.89)	-

BMI: Body Mass Index, Kg: Kilogram, Cm: Centimeter
*P-Value analyzed by Kolmogorov-Smirnov test (P<0.05)
$P-Value analyzed by Shapiro test (P<0.05)
**Mean ± σ
+ n(%)=176 (93.61)
# n(%)=12 (06.38)

Methodology

We performed a retrospective cohort study from January 2012 to October 2019. The study population consisted of women who underwent at least 4 stimulation protocols for oocyte donation, for a total of 47 women and 188 ovarian stimulation cycles. We performed mean, standard deviation, and for inferential analysis: Shapiro test, and Student's T. For categorical variables Chi Squared.

The sample size for this study was based on the number of patients recruited at the Unit of Reproduction *UR Cli nica Vistahermosa*, in Alicante, Spain; a private, tertiary reference center. Inclision criteria: (1) women 18-35 years, (2) no primary or secondary infertility, (3) seeking to become an egg donor, (4) not pregnant, (5) conventional stimulation protocol, (6) at least four stimulation cycles.

Results and Conclusions

Demographic data and stimulation protocols are presented in tables 1 and 2. Repeat COS stimulation cycles for OD does not affect total retrieved number follicles, oocytes, M2 oocytes in up to 4 cycles. Pregnancy rates are similar through four cycles. This is suggestive of a lack of impairment in ovarian response from multiple cycles of oocyte donation.

However, we found a statistically significant difference in the total number of days in stimulation of Cycle 3 and 4 when compared to baseline.

Table 2. Patient controlled ovarian stimulation protocols and oocyte retrieval according to cycle number from cohort.

Variables	Cycle 1 (n=47)	C. 1V2 P-Value	Cycle 2 (n=47)	C. 1V3 P-Value	Cycle 3 (n=47)	C. 1V4 P-Value	Cycle 4 (n=47)
Donor age, *years*	22.89 ± 3.59	0.224	23.81 ± 3.66	0.064	24.28 ± 3.57	0.001**	25.36 ± 3.64
Total COS Dose							
FSH, *UI*	1890.60 ± 561.61	0.053	2168.62 ± 795.08	0.003**	2211.70 ± 268.49	2.54	2500.85 ± 499.22
T. Stimulation, *Days*	9.60 ± 1.19	0.008**	10.30 ± 1.32	0.058	10.04 ± 1.06	0.001**	10.43 ± 1.19
T. Antagonist, *Days*	4.32 ± 1.16	0.139	4.64 ± 0.90	0.624	4.43 ± 0.93	0.053	4.77 ± 1.05
Oocyte Retrieval							
Total Follicles	16.72 ± 5.84	0.985	16.74 ± 5.30	0.624	17.28 ± 6.34	0.361	18.06 ± 8.14
Total Oocytes	15.30 ± 6.55	0.385	16.47 ± 6.47	0.660	16.72 ± 7.34	0.524	16.21 ± 7.32
Total M2	11.70 ± 5.02	0.180	13.21 ± 5.81	0.188	13.71 ± 5.71	0.390	12.74 ± 6.60
Pregnancy Rate, n/%	28 (59.57)	0.5337+	24 (51.06)	0.5337+	24 (51.06)	0.6774+	25 (53.19)

COS: Controlled Ovarian Stimulation, FSH: Follicle-Stimulating Hormone, M2: Metaphase II Oocyte, C.: Cycle
*P-Value analyzed by Student's T test
+P-Value analyzed by χ^2 test
**Statistically significant value (P-Value <0.05) when compared with baseline (i.e. Cycle 1)