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Title:

OPTIMIZING EMBRYO DEVELOPMENT AND INCUBATOR UTILIZATION IN A PRECISION IVF LABORATORY SETTING?

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Objective:

With the rapid increase in cycles of in vitro fertilization (IVF) cycles over the past few years, optimizing incubator space utilization is a priority of the modern embryology laboratory. Incubators play a crucial role in providing stable and appropriate culture conditions for optimizing embryo development and clinical outcomes. IVF centers with large caseloads are most challenged by available space; and they must balance how to best to utilize incubators while achieving optimal individual culture conditions (with regard to environmental exposures, changes in gas content, and temperature fluctuations due to overuse) and cycle outcomes. The study aimed to determine whether differences in incubator capacity is associated with laboratory outcomes following extended blastocyst culture.

Materials and Methods:

The study included patients who underwent controlled ovarian stimulation (COH) for in vitro fertilization (IVF) from 2016 to 2018. Embryos were cultured up to day 7, and select blastocysts underwent pre-implantation genetic testing for aneuploidy (PGT-A). All patient samples (oocytes and embryos) were

cultured in Panasonic MCO-5M incubators in an embryology laboratory. Incubator set points were kept at 5.8% CO_2, 5.0% O_2, and 37.0ºC. Embryos were cultured in sequential media and plated by trained embryologists per standard laboratory operating procedure. Groups were separated by the number of shelves and patient cycles per incubator: (Group A: one shelf, with oocyte/embryo yield from up to 3 patient cycles; Group B: two shelves, with oocyte/embryo yield from up to 6 patient cycles.) Patients' oocyte/embryos were randomly assigned to incubators based on available embryology laboratory space. Patient age, body mass index (BMI), anti-Müllerian hormone (AMH), basal antral follicle count (BAFC), estradiol (E2) and progesterone (P4) at time of surge, cumulative gonadotropin (GND) dose, total number of oocytes and of metaphase II (MII) oocytes retrieved, number of fertilized oocytes, type of fertilization method (intracytoplasmic sperm injection (ICSI) vs. conventional insemination), number of blastocysts, day of trophectoderm (TE) biopsy, and number of euploid blastocysts were determined. The rate of MII development, fertilization, blastulation, and euploidy was also measured. Data were analyzed using a Student's T-test, Chi-squared and multivariate logistic regression.

Results:

Of the 3867 cycles analyzed, approximately 39% of cycles were in group A (n=1512) and 61% were in group B (n=2355). Patient age, BMI, AMH, BAFC, Surge E2, Surge P4, and cumulative GND did not differ between groups. The total number of oocytes, number of MII oocytes, fertilized oocytes, blastocysts, blastocysts biopsied, and euploid blastocysts were similar between incubator groups. The MII rate, fertilization rate, blastulation rate, and euploid rate did not significantly differ between groups A and B, before and after adjusting for confounders (Table 1).

Conclusions:

Embryonic development was not correlated by the amount of biological specimens contained in the associated incubator. No significant differences in fertilization rate, blastulation rate, or euploidy rate of

embryos cultured on a single shelf or double shelf incubator system were observed. Embryologists can be reassured that in laboratories with highly-trained staff, increased embryo storage per incubator unit is not detrimental to oocyte/embryo development and patient outcome. While environmental exposures, temperature fluctuations, and pH shifts within the IVF laboratory setting are of vital importance in the culture of embryos, high volume programs can be reassured that modern incubators are clinically efficient and can yield consistently good reproductive outcomes.

Table 1:

Baseline Demographics and Cycle Characteristics based on Location of Incubator

	Group A (n=1512)	Group B (n=2355)	P Value
Age (y)	37.6 ± 4.3	37.5 ± 4.6	0.56
BMI (kg/m^2)	24.3 ± 4.6	24.3 ± 4.7	0.91
AMH (ng/mL)	2.9 ± 4.0	2.7 ± 3.1	0.21
BAFC	11.3 ± 6.4	11.3 ± 6.8	0.99
Surge E2 (pg/mL)	2067 ± 1176	2039 ± 1141	0.47
Surge E2 (pg/mL)	0.84 ± 0.48	0.85 ± 0.54	0.68
Cumulative GND (IU)	3940 ± 1295	4012 ± 1324	0.10
Number of Oocytes Retrieved	13.1 ± 8.8	13.2 ± 9.0	0.98
Number of MIIs	10.2 ± 7.4	10.3 ± 7.4	0.85
MII Rate	79.0 ± 17.8%	79.2 ± 17.9%	0.85
Type of Insemination - Conventional - ICSI - Split	 111 (7.3%) 1395 (92.3%) 6 (0.4%)	 162 (6.9%) 2188 (92.9%) 5 (0.2%)	0.49
Number of Fertilized Oocytes	7.9 ± 6.0	7.8 ± 6.0	0.76
Fertilization Rate	76.8 ± 20.0%	76.2 ± 20.0%	0.41
Number of Blastocysts	6.0 ± 5.0	5.9 ± 5.0	0.51
Blastulation Rate	69.5 ± 27.1%	68.3 ± 27.8%	0.21
Number of Blastocysts Biopsied	4.4 ± 3.7	4.2 ± 3.6	0.24
Day of Blastocyst Biopsy - Day 5 - Day 6 - Day 7	 721 (67.6%) 303 (28.4%) 42 (3.9%)	 1004 (62.0%) 543 (33.5%) 73 (4.5%)	0.01
Number of Euploid Embryos	2.1 ± 2.4	2.1 ± 2.4	0.61
Euploidy Rate	43.9 ± 34.2%	43.4 ± 34.5%	0.71