Clinical Benefits of Culturing Monopronucleated Zygotes Derived from Intracytoplasmic Sperm Injection Cycles

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Objective: To evaluate the developmental competence and aneuploidy status of blastocysts derived from monopronucleated (1PN) zygotes following intracytoplasmic injection (ICSI) and preimplantation genetic testing for aneuploidy (PGT-A).

Design: Prospective, cohort study using chi-square tests to assess differences ($p<0.05$) in blastocyst formation, biopsy/cryopreservation rate and euploidy status between 1PN and two pronuclei (2PN) zygotes.

Materials and Methods: Fertilization was assessed ~16-18hrs post-ICSI for the presence of 2PN. All zygotes were cultured in LG medium + additives and subdivided by PN status. Blastocyst formation was assessed on days 5, 6 and 7 of development, and blastocysts of suitable quality were biopsied and/or cryopreserved. The trophectoderm samples were analyzed at Ovation Genetics for aneuploidy using NGS.

Results: We obtained 75 1PN zygotes from 54 fresh ICSI cycles, representing 26.60% of the total fresh ICSI cycles. Twenty-six (34.67%) developed to the blastocyst stage, with 14 (18.67%) being biopsied/cryopreserved. From the same fresh ICSI cycles we also obtained 626 2PN zygotes of which 456 (72.84%) developed to the blastocyst stage, and 372 (59.43%) were biopsied and/or cryopreserved. Both the 1PN blastocyst rate and the 1PN biopsy/cryopreservation rate were found to be significantly lower than that of 2PN-derived embryos. Interestingly 85.71% of the biopsied 1PN blastocysts reported a euploid result, compared to 53.03% for 2PN blastocysts. The latter euploidy rates were determined to be higher ($P<0.05$) for 1PN- than 2PN-blastocysts.

Conclusions: Previously, 1PN zygotes were routinely considered abnormal and thus discarded. Our data confirms that 1PN zygotes can develop into euploid blastocysts. This coincides with previous work showing the potential of 1PN zygotes to develop into genetically normal blastocysts capable of producing healthy live births. A standard protocol for the selection of normal 1PN embryos derived from ICSI cycles has however not yet been established. Our data suggests that in fresh ICSI cycles blastocyst stage growth followed by biopsy and PGT-A testing can select for euploid 1PN embryos. However, while PGT-A using NGS technology is designed to detect numerical abnormalities of whole chromosomes, it does not have the ability to screen for uniparental disomy or haploidy. Therefore, to consider female 1PN-derived embryos for transfer additional genetic testing is suggested to discern if the embryo is diploid with a bi-parental genome. These tests and additional data recovery are ongoing as we seek to discover the clinical value of 1PN, ICSI-derived zygotes, especially in cycles where few blastocysts are produced or biopsied.

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