Blastocyst biopsy and preimplantation genetic diagnosis for single gene diseases: a turnaround on the horizon?

In this issue of RBM Online, two independent studies, Feng et al. (2012) and Lathi et al. (2012), confirm the conclusions of an earlier cohort study on comparative genomic hybridization (CGH) after trophectoderm biopsy and vitrification (Schoolcraft et al., 2010). Feng and co-workers demonstrate that vitrification and warming of blastocysts has minimal effect on their viability, while Lathi and colleagues report that trophectoderm biopsy is feasible and successful in previously cryopreserved blastocysts. Feng et al. conclude that single blastocyst transfer should be the preferred option for patients with multiple embryos reaching the blastocyst stage in extended culture. The findings of these two studies and the earlier report by Schoolcraft and co-workers (2010) have important implications for the future direction of preimplantation genetic diagnosis (PGD) for single gene disorders as well as preimplantation genetic screening (PGS) for aneuploidy screening.

While the efficacy of PGS (using primarily non-array technologies) has been a topic of much discussion and controversy, PGD success rates have not been similarly scrutinized. The latest ESHRE PGD Consortium report published earlier this year (Harper et al., 2012) estimates that pregnancy rate after PGD is 29% per embryo transfer with an average of 1.9 embryos transferred in patients with an average maternal age of 33 years. Although a proper control group is lacking, this success rate appears to be modest at best considering that PGD patients are usually young and fertile and that the procedure allows for transfer of ‘normal’ embryos. A survey of data published by the Society for Assisted Reproductive Technologies (SART; 2010) for a roughly comparable group of ‘good prognosis’ patients (<35 years with male-factor infertility) reveals a live birth rate of 50% per embryo transfer, with an average of 2.0 embryos transferred. This would suggest that the pregnancy rates reported for PGD are lower than can be expected.

The perennial question is whether this reduction is attributable to pitfalls of the genetic testing technology, as outlined in the Consortium report (Harper et al., 2012) or the biopsy procedure itself, as has been argued in the case of PGS (Cohen and Grifo, 2007; Treff et al., 2011). The impressive success achieved with cryopreservation of blastocysts following trophectoderm biopsy and transfer of normal blastocysts after warming reported by Schoolcraft et al. (2010) and Lathi et al. (2012) support the latter proposition and further suggest that cleavage-stage embryos may sporadically be sensitive to invasive manipulation, particularly if the methodology is not optimized. It follows that both PGD and PGS should be moving toward the combined approach of biopsy at the blastocyst stage, comprehensive chromosome analysis, vitrification, and warming and transfer of a single normal embryo. Future ESHRE and SART reports will hopefully become more detailed to allow for meaningful analysis of data pertaining to this treatment approach.

References


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