A critical review of routine utilization of PGS in IVF

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Oocyte donor-recipient cycles (ODRCs) involve best-prognosis patients in all of in vitro fertilization (IVF), and produce highest pregnancy and live birth rates among IVF procedures. Yet even in ODRCs, a third of embryos are still aneuploid. Preimplantation genetic screening (PGS) involves a subset of preimplantation genetic diagnosis (PGD) procedures in which an embryo is biopsied to obtain genetic information prior to its transfer. In PGS the purpose is to establish whether an embryo is suitable for transfer (euploid) or should be discarded. The hypothesis underlying PGS assumes that aneuploidy is a principal cause of IVF failure, and that elimination of aneuploid embryos will improve IVF outcomes because of improved implantation and reduced miscarriage rates. Improved IVF outcomes after PGS should, therefore, also be observable in oocyte donor-recipient cycles. ODRCs, in which oocyte/embryo factors have been optimized but many embryos still appear to be aneuploid, represent a population with few confounding factors. ODRCs, therefore, represent a good patient population to investigate potential effects of PGS on IVF cycles, and should clearly demonstrate possible effects of PGS on pregnancy and live birth rates as well as declining miscarriage rates.

Recently we were given access to IVF outcomes in the national data base of the Society for Assisted Reproductive Technology (SART) with the goal of assessing the role of third parties in assisted reproduction. 33,756 patients initiated a first ODRC, among which 468 (1.39%) underwent PGS for assessment of aneuploidy alone. Live birth rates were significantly lower for PGS than non-PGS cycles (51.1 vs. 55.7%, P=0.04). Adjusted for patient and donor ages, oocytes retrieved, embryos transferred, race and reporting year, the odds of live birth in cycles with PGS were reduced by 28% (OR 0. 75 95% CI 0. 62 to 0.91; P = 0.003) in comparison to non-PGS cycles. Our analysis of nine years of national PGS data in ODRCs found that expectations of improved IVF outcomes have not been realized. Even in the last two years studied, with increasing utilization of the newer PGS 2.0, the procedure, still, failed to improve outcomes over non-PGS cycles. PGS was associated with increased utilization of eSET. However, even in association with eSET, PGS did not increase live birth rates nor decrease miscarriages. Our findings, therefore, lead us to question the use of PGS in ODRCs and, by extension, in all of IVF, which in a large majority represents less favorable prognosis patients.

Translational relevance: This presentation underscores the importance of understanding the basic biology of the human embryo. The failure of PGS to improve live birth rates in this best prognosis setting allows us to infer that the information derived from PGS does not provide utility to improve outcomes. The only explanations for such an observation are that the methods of genetic analysis of the biopsy material is flawed or that the basic biology of the embryo is too complex to allow a genetic diagnosis based on a 3 to 6 cell sample.