Preimplantation Genetic Diagnosis International Society (PGDIS), Bangkok, Thailand 2018

Oral Presentation

80 mosaic embryo transfers in a single clinic with in-house PGT-A: What we have learned

Jack Tyndall[a]*, Andrea Victor[a,b], Darren Griffin[b], Alan Brake[a], Christo Zouves[a,c], Frank Barnes[a,c], and Manuel Viotti[a,c].

[a] Zouves Fertility Center, Foster City, California, USA

[b] School of Biosciences, University of Kent, Canterbury, United Kingdom

[c] Zouves Foundation for Reproductive Medicine, Foster City, California, USA

* presenting author.

Correspondence: manuel@zouvesfoundation.org

Keywords: mosaic, transfer, implantation, birth

Introduction

IVF clinics are routinely transferring embryos diagnosed through PGT-A as mosaic anueploid with greater frequency to patients who lack available euploid embryos. Nevertheless, there is a lack of evidence-based guidelines that establish which characteristics and genetic abnormalities affect a mosaic embryo's clinical predictive outcome.

Materials & methods

80 mosaic embryos were transferred at a single IVF program from August of 2015 through February of 2018. All embryos were tested in-house by high resolution NGS on trophectoderm biopsies obtained from blastocysts at 5-7 days of development. Karyotype profiles were analyzed for characteristics predictive of improved clinical outcomes. This study followed PGDIS guidelines defining mosaic embryos as containing whole or segmental chromosomal gains or losses between 20% and 80%.

Results

Of the 80 transferred mosaic embryos, 41 (51.3%) established a chemical pregnancy, 25 (31.3%) developed an embryonic sac (implantation), and 20 (25.0%) developed a fetal heartbeat (FHB). Of these 20, 11 resulted in a live birth and at the time of analysis 9 were ongoing pregnancies, meaning that no post-FHB miscarriages had occurred. Embryos derived from oocytes younger than 35 years old had a significantly higher implantation rate than embryos from oocytes 35 years or older (50.0% to 21.2%, n=28 and 52 respectively) as well as comparable implantation rates to euploid embryos from across all age groups (younger than 35 years, n=141: 51.1%; greater than 35 years, n=341: 48.4%). There was a noticeable difference in implantation rate between embryos with either a single chromosomal mosaic loss or gain (33.3%, n=45) and mosaic embryos with multiple chromosomal losses or gains (23.1%, n=26). Mosaic embryos displaying only a single segmental chromosomal abnormality had a higher chance of implanting and developing a FHB (n=26, 38.5%, 34.6%) than mosaic embryos with multiple segmental abnormalities or whole chromosome gains or losses (n=52, 26.9%, 21.2%) and also had a far lower chance of losing a pregnancy after an initial positive beta (23.1% to 46.2%, n=13 and 26 respectively). When the embryos were broken down by severity of mosaicism, we found that 20% to 50% (n=36) severity mosaic embryos were significantly more likely to implant and develop a FHB than the more severe mosaic 50%-80% embryos (n=12). Additionally, mosaic embryos were divided up by number of estimated abnormal cell lines present in the trophectoderm biopsy. The implantation rate for embryos estimated with only one aneuploid cell population was significantly higher than those with two (n=12, 33.3% vs n=12, 8.3%). Lastly, embryos diagnosed with mosaic trisomies did not have a significant difference in implantation or FHB development (n=30, 33.3%, 30.0%) from those with monosomies (n=28, 32.1%, 25.9%).

Conclusions

Embryos classified as mosaic are capable of producing healthy babies and should be considered for transfer when a euploid embryo is not available. When there are multiple mosaic embryos to select from for any given patient, our data suggests embryos diagnosed with a single segmental abnormality should be preferred, followed by those with less severe mosaicism as measured by number of affected chromosomes and severity of aneuploidy in the mosaic mix.