9th Yazd International Congress and Student Award on Reproductive Medicine with 4th Congress of Reproductive Genetics

Key Lectures

K-28
PGT-A in ART anno 2021: An update

Jaroudi S, Fatemi HM.
ART Fertility Clinics and Genomics, Abu Dhabi, United Arab Emirates.
Email: Souraya.Jaroudi@artfertilityclinics.com

Preimplantation genetic testing for aneuploidy (PGT-A) is increasingly employed in assisted reproductive technology (ART). By sifting out embryos with abnormal chromosome numbers (aneuploid), PGT-A should theoretically improve pregnancy success. However, earlier versions of PGT-A were ineffective, and in some cases, detrimental, due to biopsy-induced trauma and because the technology at the time could analyse only a fraction of all chromosomes. More recently, the emergence of technologies enabling all chromosomes to be analysed and a switch to less traumatic blastocyst-stage biopsy have seen widespread uptake of PGT-A. Assessing the full impact of blastocyst biopsy PGT-A requires consideration of multiple factors, including embryonic mosaicism, the sensitivity of the technological platform used, embryo loss during long-term in vitro culture, embryo cryopreservation, and inter-clinic variability in expertise. PGT-A has been shown to increase the success of in vitro fertilization (IVF), by reducing the risk of miscarriage, shortening the time to pregnancy, and allowing more confident single embryo transfers without compromising outcomes. While it is widely accepted that chromosome aneuploidy, a common feature of human embryos, is a major cause of IVF failure, miscarriage and congenital defects, controversy remains around the routine implementation of PGT-A in clinical practice. The possibility of bypassing biopsy with non-invasive PGT-A (niPGT-A) is becoming highly attractive. niPGT-A via the analysis of cell-free DNA (cfDNA) present in the spent culture media is currently an area of active development. Furthermore, next-generation sequencing increased the resolution and sensitivity of PGT-A allowing the identification of chromosomal mosaicism and the detection of segmental copy number variations (CNVs), both areas of disagreement due to their uncertain clinical significance. The concordance rates between PGT-A results from the original trophectoderms samples and re-biopsies have been shown to be reduced for mosaic or segmental CNVs compared to euploid and whole chromosomal aneuploidy results. Nonetheless, segmental errors are believed to be responsible for 6% of clinical miscarriages and can result in genetic conditions, such as Cri-du-chat, accounting for approximately 0.05% of births. Variable mosaicism rates based on single TE biopsies (2-13%) are influenced by the next-generation sequencing assay adopted, the stimulation protocols and the IVF laboratory culture conditions. As biopsies are not necessarily representative of the whole embryos, the true prevalence and clinical implications of blastocyst mosaicism are still under question. CNVs are increasingly recognised as natural events in the preimplantation embryo. Furthermore, observations of developmental competence in a subset of mosaic blastocysts reaching healthy live births lead to the suggestion of corrective mechanisms. However, there is no direct evidence to support this theory at present. The effects of low-moderate level mosaicism on ongoing pregnancy rates remain unclear, with studies examining the transfer of such embryos reporting conflicting data. Elucidating the uncertainties around mosaicism and segmental CNVs within well designed studies would lead towards improved PGT-A and patient management in ART.