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The extent of chromosomal mosaicism influence the clinical outcome of in vitro fertilization treatments

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Study question:

Can the extent of chromosomal mosaicism influence the development potential of mosaic embryos?

Summary answer:

Mosaic embryos with low aneuploidy percentage (<50%) have higher chances to result in healthy babies born compared to embryos with higher mosaicism levels (≥50%).

What is known already:

Embryonic mosaicism is a phenomenon characterized by the presence of two or more genetically distinct cell lineages, typically one with a chromosome abnormality and the other possessing a normal chromosome constitution. In a recent published study, we have demonstrated that mosaic embryos hold the potential to implant and result in the birth of healthy babies. As a consequence, the transfer of these embryos is now offered as an option for women who undergo in vitro fertilization (IVF) resulting in mosaic embryos but no euploid embryos. We hypothesize that the extent of mosaicism affect the IVF success rate.

Study design, size, duration:

The transfer of mosaic embryos at different aneuploidy percentage was offered to 73 women for whom IVF had resulted in no euploid embryos between May 2013-March 2016. The comparison of the clinical outcome obtained after transfer of mosaic embryos with low (<50%) and high (≥50%) aneuploidy percentage, was performed in order to assess a statistically significant difference in the development potential between the two groups.

Participants/materials, setting, methods:

To obtain reference curves for determination of mosaicism percentage we assessed 114 diploid/aneuploid mosaic reconstructed samples (10–90% mosaicism) using both next generation sequencing (NGS) and array-comparative genomic hybridization (array-CGH) techniques. All embryos were cultured to blastocyst stage; trophectoderm biopsy was

performed on Day-5 of development or Day6/7 for slow growing embryos. Comprehensive chromosome screening PGS was performed using either NGS or array-CGH methodologies.

Main results and the role of chance:

Transfers of mosaic embryos with a high percentage of chromosomally abnormal cells (≥50%) resulted in a live birth rate of 16.7% and involved a miscarriage rate of 10%. In contrast, mosaic embryos with a lower aneuploidy percentage (<50%) resulted in a live birth rate of 39.5%, with a miscarriage occurring in 7.0% of the transfers. All pregnancies that went to term were confirmed, through sampling of the chorionic villi and/or amniotic liquid, to have a normal karyotype. A comparison of the clinical outcomes between the groups, with low and high aneuploidy percentage, showed a significantly higher ongoing clinical pregnancy rate/embryo transfer (39.5% vs 16.7%; p=0.036), and baby born rate (41% vs 17%; P=0.027) in embryos with aneuploidy percentage <50% compared to embryos with a mosaicism level >50%. The biochemical pregnancy rate and miscarriage rate were not significantly different between the two groups.

Limitations, reasons for caution:

Additional clinical data must be obtained before this approach can be evaluated for routine integration into preimplantation genetic screening programs in women undergoing IVF. Transfer of mosaic embryos with purportedly “viable” aneuploidies should be considered with extreme caution.

Wider implications of the findings:

The results of this study further confirm that mosaic embryos can develop into healthy euploid newborns. We demonstrated that the extent of mosaicism affects the IVF success rate. Priority for transfer should be given to mosaic embryos with low mosaicism levels.

Trial registration number:

None

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None