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O-085 In-depth analysis of embryo development: Differences among monosomic, trisomic and chromosomally chaotic embryos compared to euploid embryos

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Abstract

Study question

Is there any visible variation in the development of aneuploid embryos depending on the type of chromosome abnormality?

Summary answer

There were significant visible differences in the development of euploid, monosomic, trisomic and, especially, chaotic embryos.

What is known already

Aneuploidy rates are remarkably high in in vitro fertilized human embryos, with up to 50% of embryos diagnosed as aneuploid based on preimplantation genetic testing for aneuploidies (PGT-A). However, very little is known about the impact of specific aneuploidies during the early human embryo development. A recent publication showed that embryos with single chromosomal gain or loss reached the blastocyst stage later or earlier depending on the chromosome affected (Shahbazi et al., 2020). In our study, we wanted to detect observable differences in embryo behavior between embryos with different chromosomal abnormalities during the entire in vitro development.

Study design, size, duration

This was a retrospective study including 2,500 blastocysts with PGT-A results. Embryos were cultured in EmbryoScope systems until the fifth/sixth day of development (up to the time of trophectoderm biopsy). Automatic-annotations for division times and quality gradings were supervised routinely by senior embryologists using Guided Annotations Tool. Out of the total, 1,000 were euploid embryos used for reference and 1,500 were aneuploid embryos with one or more defects, including monosomic, trisomic and chromosomally chaotic embryos.

Participants/materials, setting, methods

Chromosome analysis was performed using next-generation sequence technology. Then, an in-depth analysis of time-lapse videos and supervised-automatic annotations was performed. We calculated the proportion of embryos, in each aneuploid category, that reached one specific event later than the expected value for euploid embryos plus one standard deviation. Later, we calculated the "relative risk" of an embryo of reaching the milestone late. We did the same for the time between milestones and for pairs of milestones.

Main results and the role of chance

Every aneuploid category was more likely to reach each specific embryo developmental event later than euploid embryos and the time gaps between developmental milestones were also statistically longer in aneuploid embryos ($p < 0.0001$). The following results were the most interesting relative risks (RR) when we compared the proportion of embryos (in each aneuploid category) to the proportion of euploid embryos (RR for euploid = 1). For reaching the division time to two cells (t2): 1.31 in monosomic embryos, 1.50 in trisomic embryos and 2.43 in chaotic embryos. For the division time to four cells (t4): 1.42 in monosomic embryos, 1.54 in trisomic embryos and 3.07 in chaotic embryos. For the division time to eight cells (t8) and the time of starting blastulation: 1.45 in monosomic embryos, 1.22 in trisomic embryos and 2.74 in chaotic embryos. Combined milestones were stronger indicators than each milestone by itself, the RR were: 1.63 in monosomic embryos, 1.81 in trisomic embryos and 3.35 in chaotic embryos for t2 and t4; 1.50 in monosomic embryos, 1.80 in trisomic embryos and 2.84 in chaotic embryos for t2 and t8; 1.46 in monosomic embryos, 1.90 in trisomic embryos and 3.43 in chaotic embryos for t4 and t8.

Limitations, reasons for caution

At this stage, we did not go down to specific chromosome abnormality as there were very few cases in each fully detailed category. Also, not all the embryos reached every developmental milestone.

Wider implications of the findings

Aneuploid embryos were significantly different from euploid embryos in the first five days of development. A large proportion of aneuploid embryos could be rejected because their developmental milestones falling outside the normal range. This could form part of an automated system for determining euploidy/aneuploidy from observation of embryos in vitro.

Trial registration number

1902-VLC-018-MM