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Abstract title:

Mitochondrial (mt) DNA copy number may affect blastulation timing

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Study question:

Is the mtDNA content affecting embryo development ability?

Summary answer:

Embryos carrying higher mtDNA copy number seem to need more time to achieve blastocyst stage, but it's not related with the expansion capacity after warming.

What is known already:

Descriptive studies looking at the mtDNA load in blastocysts have shown that those blastocyst with higher quantities have more chances to be aneuploid, to have lower embryo quality as well as worst implantation potential. Few studies speaks about timings during embryo development, since cellular differentiation during blastulation have high energy demands, and mitochondria may supply the required ATP, we aimed to evaluate the relationship between mtDNA copy number and the time of blastulation and recovery after warming.

Study design, size, duration:

Retrospective study comprising a total of 229 embryos from a total of 134 patients undergoing PGT-A between 2017 and 2018. Embryos were divided in two study groups depending of the values of mtDNA relative quantities. Group A: 102 embryos carrying values above the median and Group B: 127 with values below or equal to the median value.

Participants/materials, setting, methods:

Embryos were cultured under embryoscope and biopsied on day 5 or 6. The calculation the mtDNA score was done by NGS. The number of reads mapping to the mitochondrial genome was divided by the number of reads mapping to the nuclear genome T-student was used for statistical comparisons

Main results and the role of chance:

The relative mtDNA content in the analyzed blastocysts ranged from 4 to 135. When comparing the two groups, we observed that blastocysts with higher mtDNA values, group A, needed more time to commence blastulation (101.64 h) and to expand (108.54 h) that the group B, 97.78 h and 104.16 h respectively ($p < 0.0001$). Patient with embryos belonging to group B were 38.7 ± 3.7 years old compared to patients of the group B 37.8 ± 3.9 ($p > 0.05$). Significant lower quality embryos were found in the group A (51%) compared with Group B (32%). Thirty three embryos were warmed and left in culture up to 3.6 h before transfer. In these cases the mtDNA content did not affect to the ability of embryos to re-expand.

Limitations, reasons for caution:

Higher mtDNA quantity negatively affected blastulation and expansion timing, however worse embryo quality was observed as well. Body mass index or stimulation parameters can be also contribution factors of the results. In order to confirm these results, other variables and bigger sample size need to be considered.

Wider implications of the findings:

Higher mtDNA may be indicative of cellular stress and mitochondrial dysfunction, under this situation embryos not only may encounter more

Trial registration number:

Not applicable

Keywords:

Embryo development

blastocyst

mitochondrial DNA copy number