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Abstract title:

Marginal differences in preimplantation development between conventional IVF and ICSI in patients with non-male factor infertility: a sibling oocyte study.

Biography

Neelke De Munck studied Biomedical Science and Biotechnology at the University of Ghent, Belgium. She obtained her PhD, on the safety and efficiency of oocyte vitrification, at the Center for Reproductive Medicine in Brussels, Belgium, where she has also been working as a Clinical Embryologist for almost ten years. Since 2018, she is working as the Scientific Adviser and Clinical Embryologist at the IVI RMA Middle East fertility clinic in Abu Dhabi.

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Study question:

Are there differences in the morphokinetic behavior between conventional IVF and ICSI in cycles with pre-implantation genetic testing for aneuploidies?

Summary answer:
Preimplantation development is marginally, yet significantly different between embryos generated by conventional IVF and ICSI.

What is known already:
Conventional IVF results in a delayed (4 hours) pronuclear formation and first mitotic divisions when compared to ICSI on sibling oocytes. This difference disappears around the time of morula formation in donor oocyte cycles. On the other hand, it has also been shown in autologous oocytes that IVF blastocysts start to expand 3 to 4 hours earlier than ICSI-generated blastocysts. When standardizing for the time of pronuclear fading, the differences in early cleavage disappear between IVF and ICSI, while blastulation and blastocyst expansion occurs earlier for IVF embryos.

Study design, size, duration:
Prospective cohort study between November 2018 and April 2019, including 568 oocytes (30 patients) with non-male factor infertility for which half of the sibling oocytes were inseminated with conventional IVF (n=283) and the other half with ICSI (n=285). Embryos were cultured in an Embryoscope time-lapse incubator and trophectoderm biopsy was performed on good-quality blastocysts. The following timings were annotated: tPNf, t2-9, tSC, tM, tSB, tB, tEB, cc2(t3-t2), cc3(t5-t3), s2(t4-t3), s3(t8-t5) and Blast(tSB-t2).

Participants/materials, setting, methods:
Univariate ($p<0.20$) and multivariate ($p<0.05$) analysis was performed in order to find morphokinetic differences between conventional IVF and ICSI. A secondary analysis was performed which corrects for the difference in time of fertilization, by standardizing all time lapse parameters for the time of pronuclear fading. Subgroup analysis for all day 5+6 biopsied blastocysts was performed. Results are presented as average ± SD, Odds Ratio [95% CI].

Main results and the role of chance:

A total of 283 and 285 cumulus oocyte complexes were assigned to conventional IVF and ICSI of which 183 (64.7%) and 190 (66.7%) were normally fertilized, respectively. Conventional IVF generated 120 blastocysts that were biopsied, of which 59 (49.2%) were euploid, while 116 blastocysts were biopsied after ICSI of which 56 (48.3%) were euploid. Gender distribution (male/female) for blastocysts with informative outcome was 60/49 and 50/55, respectively.

When comparing the development of all normally fertilized zygotes between IVF and ICSI in the univariate model, a significant difference was found for tPNf ($p=0.005$), t2 ($p<0.001$), t3 ($p=0.001$), t4 ($p=0.003$), t5 ($p=0.001$), t6 ($p=0.096$), t7 ($p=0.177$) and Blast ($p=0.004$) of which only t2 remained significant in the multivariate model (OR: 1.282 [1.020-1.612], $p=0.033$); IVF: 29.3 ± 10.4 versus ICSI: 25.9 ± 5.1. After standardizing for tPNf, only corrected tSB ($p=0.009$) and Blast ($p=0.004$) showed significant differences between IVF and ICSI. However, only Blast appeared significant in the multivariate model: OR: 0.803 [0.648-0.994], $p=0.044$; IVF: 70.8 ± 8.2 versus ICSI: 72.5 ± 9.7. Taking into consideration the standardized kinetics of biopsied blastocysts, only a difference was observed for t2: OR: 1.519 [1.045-2.206], $p=0.028$; IVF: 3.4 ± 2.6 versus ICSI: 3.1 ± 3.3.

Limitations, reasons for caution:
Only couples with non-male factor infertility and a normal response to ovarian stimulation were included, and therefore, the results cannot be extrapolated to other patient populations.

Wider implications of the findings:
Following the recent debate on the over-use of ICSI, this study shows that conventional IVF results in the same number of blastocysts for biopsy with similar developmental kinetics, thereby reinforcing the use of conventional IVF in this patient population.

Keywords:
conventional IVF
Intracytoplasmic sperm injection
morphokinetic development
blastocyst