HIGH RATE OF THREE PRONUCLEAR (PN) ZYGOTES IS ASSOCIATED WITH DECREASED FERTILIZATION RATES OF THE RETRIEVED OOCYTE COHORT

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Background:

An increased proportion of triploid (3PN) zygotes (>25%) after intracytoplasmic sperm injection (ICSI) has been associated with decreased fertilization, clinical pregnancy and implantation rates after a fresh transfer[1].

Objective

Our objective was to evaluate if a rate of ≥15% 3PN zygotes after ICSI or insemination (INSEM) impacts fertilization, blastocyst (blast) formation and euploidy rates of the normally-fertilized oocyte cohort.

Materials and Methods

This is a retrospective cohort study from a large academic fertility center of all patients who underwent embryo banking or in vitro fertilization from 2020-2022 with INSEM, ICSI or both (SPLIT). Patients whose cycles were for donor egg, were cancelled, had 0 oocytes retrieved, and cycles with no fertilization (no 1PN, 2PN, and 3PN) were excluded. Patients were stratified by the proportion of 3PN zygotes (#3PN/#mature oocytes (MIIs)). Patients with <15% 3PNs (LOW) were compared to those with ≥15% 3PNs (HIGH). The primary outcomes were fertilization (#2PN/#MIIs), blast formation (#embryos biopsied/#2PN) and euploidy rates (#euploid embryos/#biopsied). Data were analyzed using Mann Whitney U, Chi Square, and linear regression tests (p<0.05 significant).

Results

5766 cycles were reviewed, 600 were excluded, and ultimately there were 4605/5166 (89.1%) cycles in the LOW group, and 561/5166 (10.9%) in the HIGH group. The LOW group had fewer INSEM cycles (LOW: 60.5%, HIGH 83.6%) and more SPLIT cycles (LOW: 1.0%, HIGH: 0.2%, overall p<0.001). LOW patients were younger (LOW: 37, HIGH: 39 years; p<0.001), had a higher anti-müllerian hormone (AMH) level (LOW: 2.0, HIGH: 1.8 ng/mL; p<0.001) and a lower cumulative gonadotropin dose (LOW: 3975, HIGH: 4050 IU; p<0.001). The LOW group yielded more oocytes (LOW: 13, HIGH: 9, p<0.001), MII oocytes (LOW: 10, HIGH: 7; p<0.001), and 2PN zygotes (LOW: 7, HIGH: 4; p<0.001). The LOW group also had a higher fertilization rate (LOW:78.3%, HIGH:66.7%, p<0.001). Overall blast formation was similar between the groups (LOW: 50, HIGH: 50%; p=0.13); however, the LOW group had a higher euploidy rate (LOW: 33.3, HIGH: 25.0%; p<0.001).

A sub-group analysis of the 1861 ICSI cycles (1770/1861 (95.1%) LOW, 91/1861 (4.9%) HIGH) demonstrated similar findings. Linear regression controlling for age and AMH in the total cohort demonstrated that a higher %3PN was associated with lower fertilization (B=-15.4, p<0.001), but not euploidy rates (B= -1.3, p=0.4). Linear regression of ICSI only cycles demonstrated a

higher %3PN was associated with both decreased fertilization (B=-18.5, p<0.001) and euploidy rates (B= -0.6, p<0.01).

Conclusions:
Patients with a higher proportion of 3PN zygotes had poorer ART outcomes, including fewer MII oocytes, 2PN zygotes, as well as decreased euploidy in ICSI cycles; suggesting that beyond polyspermy, a higher proportion of 3PN fertilization may indicate overall poorer oocyte quality of normally fertilized zygotes.

Support
None

References

1. Figueira RC, Setti AS, Braga DP, Iaconelli A Jr, Borges E Jr. Prognostic value of triploid zygotes on intracytoplasmic sperm injection outcomes. J Assist Reprod Genet. 2011 Sep;28(10):879-83. doi: 10.1007/s10815-011-9610-0. Epub 2011 Jul 30. PMID: 21805146; PMCID: PMC3220437.