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Title:

IS PATERNAL AGE ASSOCIATED WITH EMBRYO ANEUPLOIDY?

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Background:

Although the impact of advanced maternal age on embryo aneuploidy has been investigated extensively, minimal research has focused on the association between advanced paternal age (APA) and embryo aneuploidy. Previous studies of chromosomal abnormalities in human sperm have shown an increased incidence of aneuploidy involving chromosomes 21 and 22, as well as the sex chromosomes,[1] but no study to date has evaluated if a positive association exists between APA and the rate/type of embryonic aneuploidy.

Objective:

This study sought to investigate whether there is a correlation between increasing paternal age and rate of embryo aneuploidy, as well as incidence of trisomy 21, 22, and sex chromosome aneuploidies.

Materials and Methods:

In this retrospective cohort study, patients who underwent ovum donation (OD) cycles with intracytoplasmic sperm injection (ICSI) and preimplantation genetic screening (PGS) from 2012-2017 were included. Oocyte and partner age, fertilization rate, blastulation rate, biopsy rate, aneuploidy rate, and specific whole chromosome copy number variants were recorded. Affected chromosomes were categorized by size (large chromosomes: 1-12, X vs. small chromosomes 13-22, Y) and centromere position to determine if there was a difference in the chromosomal patterns of aneuploidy. Age was treated as a continuous variable. Data was analyzed using linear and logistic regression models.

Results:

The study included 126 oocyte recipient cycles. A total of 884 embryos were biopsied, revealing an overall aneuploidy rate of 22.5%. Mean donor oocyte age was 27.0 ± 3.0 (21-34 years). Mean male partner age at time of IVF was 45.3 ± 7.4 (30-68 years).

In this young fertile donor population, oocyte age did not modify the proportion of biopsied embryos found to be aneuploid (β=0.04, p=0.65). Controlling for donor oocyte age, there was no significant association between male partner age and IVF laboratory outcomes (Table 1). Controlling for donor oocyte age, paternal age did not significantly impact the aneuploidy rate (β=0.12, p=0.20), even when aneuploidy was categorized by the affected chromosomes' size and centromere position (small: OR 1.02 [95% CI 0.97-1.07], p=0.43; large: OR 1.04 [95% CI 0.99-1.09], p=0.16). Paternal age did not impact the odds of sex chromosome aneuploidy (OR 0.98 [95% CI 0.89-1.08], p=0.74) or incidence of trisomy 21 (β=-0.004, p=0.73) and trisomy 22 (β=-0.01, p=0.054).

Conclusions:

Oocyte age continues to be the primary driver of IVF outcome and aneuploidy rates. In a well-controlled study, we demonstrated that despite a trend towards decreased fertilization, blastulation, and biopsy rates, advancing paternal age does not have a statistically significant impact on IVF outcomes or aneuploidy rates. Future studies would benefit from focusing on both genomic and non-genomic drivers of embryonic competence.

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None

References:

[1]R. Ramasamy, K. Chiba, P. Butler, D.J. Lamb. Male biological clock: a critical analysis of advanced paternal age. Fertil Steril 2015: 103(6):1402-1406.

Table 1:

The relationship between paternal age and IVF laboratory outcomes (controlling for donor oocyte age)

	Parameter estimate	P value
Fertilization rate	-0.29	0.07
Blastulation rate	-0.46	0.05
Biopsy rate	-0.41	0.09