American Society for Reproductive Medicine 2019 Scientific Congress & Expo
October 12 to 16, 2019 ● Philadelphia, PA, USA

Title:

SPERM DNA FRAGMENTATION INDICES ARE NOT CORRELATED WITH BLASTULATION OR EUPLOIDY RATES IN PATIENTS UNDERGOING IVF WITH PGT-A

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Objective:

It has been postulated that the sperm DNA integrity correlates with embryo development and implantation potential, also that men who suffer from high sperm DNA fragmentation experience a higher probability of sperm aneuploidy and meiotic anomalies. Theoretically, embryos from men whose ejaculates display elevated DNA fragmentation could be at a greater risk of aneuploidy following fertilization. Still, published data regarding the impact of sperm with high DNA fragmentation is highly heterogeneous and limited by small sample size, use of dated genetic testing platforms, and/ or analysis of patients with recurrent pregnancy losses. The objective of this study is to examine the correlation between indices measuring sperm DNA damage and embryo quality and euploidy rate in a diverse population of infertile couples undergoing IVF/ICSI with preimplantation genetic testing for aneuploidy (PGT-A)

Design:

Retrospective cohort analysis

Materials and Methods:

All patients undergoing ICSI/PGT-A from 2012-2019 were included in the analysis. Cases in which Sperm DNA fragmentation Index (DFI) were analyzed were included. DFI was calculated using sperm chromatin dispersion, TUNEL, acridine Orange or Sperm chromatin structure assays. Patients were segregated into 2 groups: Normal DFI rate (≤30%) and Elevated DFI rate (≥30%)(2) Surgical extracted or frozen/thawed semen samples were excluded of the analysis. Demographic characteristics of populations, clinical embryology parameters, and embryonic euploidy rates were compared between cohorts. T-test, Xi2, and multivariate regression with a GEE model were used for data analysis

Results:

1108 blastocysts derived from 259 IVF/PGT-A cases were included in the study. The groups consisted of 126 cases (n= 543 embryos) with elevated DFI and 133 cases (n= 565 embryos) with normal DFI. Significant differences were found in mean male age (39.8 ±6, 37.8±5, p=0.004), female age (36.2±4, 34.8±4, p=0.007) and cases with normal morphological sperm analysis (37%, 56.3%, p=0.002) between cohorts. No differences were found in fertilization rate, zygotes achieving cleavage stage, and blastulation rates between study groups. Embryo euploidy rates were comparable (50.2% (n=273/543), 46.7 %(n=264/565), p=0.24)

After adjusting for female and male patient's age, BMI, AMH, normal semen analysis and number of biopsied embryos, there were no association with elevated DFI and lower odds of embryo euploidy (OR 1.39, CI95% 0.97-2.0, p=0.07)

Conclusion:

Although multiple studies have reported poor outcomes in patients with elevated DFI, the exact mechanism of action is unclear. Our study analysis showed no correlation between high sperm DNA fragmentation and fertilization, blastulation, or embryo euploidy rates. Our study adds to the expanding body of evidence that shows no significant relationships between elevated DNA fragmentation, embryo development, or chromosomal composition. Future studies assessing the oocyte DNA-repair mechanism following fertilization should be performed to better understand the immediate impact of sperm chromatin damage during ART intervention.