NEGATIVE EFFECTS OF SPERM NUCLEAR DNA DAMAGE ON THE FERTILITY POTENTIAL OF COUPLES WITH IDIOPATHIC AND MALE-FACTOR INFERTILITY

Ramadan A Saleh, Ashok Agarwal, Cleveland Clinic Foundation, Essam A Nada, South Valley University, Mohamed H El-Tonsy, al-Minya University, Donald P Evenson, Kjersten Larson, South Dakota State University

Objective: Rapidly accumulating data, in recent years, indicate that increased sperm DNA damage is detrimental to the fertility potential of men. The objectives of this study were to examine: i) levels of sperm DNA damage in infertile men with idiopathic and male-factor infertility, and ii) the effects of sperm DNA damage on the outcome of assisted reproductive techniques (ART).

Design: Prospective study

Materials/Methods: The study included 92 infertile couples with a normal female partner. Sixteen fertile sperm donors served as a control. All men had a genital exam by a male infertility specialist (AJT). Standard semen analysis (SA) was performed as per the World Health Organization guidelines (WHO, 1999). Sperm DNA damage was assessed by sperm chromatin structure assay (SCSA) and results expressed as DNA fragmentation index (DFI). Nineteen out of the 92 couples underwent intrauterine insemination (IUI), 10 in-vitro fertilization (IVF) and 4 intracytoplasmic sperm injection (ICSI).

Results: Couples were classified as idiopathic (normal standard SA and genital exam; n = 23) and male-factor infertility (abnormal standard SA with/without abnormal genital exam; n = 69). Levels (median, 25% & 75% percentiles) of DFI in the idiopathic (23 (15, 32)) and male-factor infertility (28 (18, 41)) groups were significantly higher than the fertile donors (15 (11, 21)) (P = 0.02 & 0.0001; respectively). The difference in DFI between the two patient groups was not statistically significant (P = 0.27). A clinical pregnancy (at least one ultrasound-confirmed intrauterine gestational sac at 4-6 weeks following ART) was achieved in 9 couples (5/19 with IUI, 3/10 with IVF and 1/4 with ICSI). The DFI was significantly higher in infertile men who failed to initiate a pregnancy with ART (38 (28, 43)) compared with those who succeeded (21 (13, 25); P = 0.001) and with the fertile donors (P = 0.0001). No pregnancy was achieved when DFI was greater than 28%. The DFI was negatively correlated with fertilization (r = -0.70; P = 0.03), embryo quality (r = -0.70; P = 0.03) and pregnancy (r = -0.45; P = <0.0001).

Conclusions: Our results indicate a significant increase in levels of sperm DNA damage in infertile men with idiopathic and male-factor infertility. In addition, the percentage of spermatozoa with DNA damage is significantly higher in infertile men who fail to initiate a pregnancy with ART compared to those who succeed. Failure of ART attempts may be, at least in part, due to the use of DNA-damaged spermatozoa. Large-scale, randomized trials are needed to verify the predictive potential of the DNA damage test in ART programs.

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