Editorial

Sperm DNA fragmentation test results reflect the overall quality of the whole semen specimen

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Dr. Drevet in his commentary (1) responding to the practice recommendations for Sperm DNA Fragmentation (SDF) testing based on clinical scenarios by Agarwal *et al.* (2) elegantly discussed the biological effect of DNA fragmentation and its implications to the paternal contribution of the male gamete. The author goes further by elaborating on the likely result of the interactions between sperm with damaged DNA and oocytes with different DNA repair capability.

We concur with the author that the integrity of sperm DNA is crucial for normal fertilization, embryo development, and successful implantation. Evidence indicates that the main pathways leading to SDF occur during sperm transport through the seminiferous tubules and epididymis transit (3). In fact, chromatin compaction is still ongoing during epididymal transit, making it vulnerable to excessive reactive oxygen species (ROS) generated in the epithelial cells of epididymis under physicochemical stressors (4,5). As endonucleases may cleave DNA of mature live sperm (6), sperm DNA damage may ensue through distinct pathways, including hydroxyl radical, nitric oxide, and activation of sperm caspases and endonucleases, thus explaining the high rates of SDF in live ejaculated sperm.

In the context of varicocele, ROS are released not only in endothelial cells of the dilated pampiniform plexus and testicular cells but also in the principal cells of the epididymis (7,8). Apart from varicocele, the epididymis can be the origin of SDF in infectious and inflammatory states, including spinal cord injury (9), post-vasectomy reversal (10), and clinical or subclinical epididymitis (11). In these conditions, SDF may result from excessive ROS production by spermatozoa themselves in response to a more prolonged epididymal transit and infiltrate polymorphonuclear leukocytes.

Lastly, Dr. Drevet highlights an important take-home message: that despite providing only a global assessment of DNA fragmentation level (without specific information about the severity of DNA fragmentation—single or double strand breaks—and the sites of breaks—intron or exon), the test result is enough for counseling about ART success and genetic risks that may exist following fertilization with such DNA-damaged spermatozoa. Dr. Drevet's observations suggest that SDF reflects the overall quality of the whole specimen that goes beyond the fragmented sperm detected by the test result. While most studies exploring the predictive ability of SDF testing for pregnancy have measured SDF in the neat semen [reviewed by Esteves *et al.* (12)], the predictive ability of sperm DNA fragmentation in the post-processing specimens (for use in ART) warrants further investigation.

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Footnote

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References

1. Drevet JR. Sperm DNA integrity testing: a valuable addition to the tool box of infertility clinicians. Transl Androl Urol 2017;6:S590-1.
2. Agarwal A, Majzoub A, Esteves SC, et al. Clinical utility of sperm DNA fragmentation testing: practice recommendations based on clinical scenarios. Transl Androl Urol 2016;5:935-50.
3. Muratori M, Tamburrino L, Marchiani S, et al. Investigation on the origin of sperm DNA fragmentation: role of apoptosis, immaturity and oxidative stress. Mol Med 2015;21:109-22.
4. Hamada A, Esteves SC, Agarwal A. Insight into oxidative stress in varicocele-associated male infertility: part 2. Nat Rev Urol 2013;10:26-37.
5. Rubes J, Selevan SG, Sram RJ, et al. GSTM1 genotype influences the susceptibility of men to sperm DNA damage associated with exposure to air pollution. Mutat Res 2007;625:20-8.
6. Sotolongo B, Huang TT, Isenberger E, et al. An endogenous nuclease in hamster, mouse, and human spermatozoa cleaves DNA into loop-sized fragments. J Androl 2005;26:272-80.
7. Agarwal A, Hamada A, Esteves SC. Insight into oxidative stress in varicocele-associated male infertility: part 1. Nat Rev Urol 2012;9:678-90.
8. Cho CL, Esteves SC, Agarwal A. Novel insights into the pathophysiology of varicocele and its association with reactive oxygen species and sperm DNA fragmentation. Asian J Androl 2016;18:186-93.
9. Brackett NL, Ibrahim E, Grotas JA, et al. Higher sperm DNA damage in semen from men with spinal cord injuries compared with controls. J Androl 2008;29:93-9; discussion 100-1.
10. Smit M, Wissenburg OG, Romijn JC, et al. Increased sperm DNA fragmentation in patients with vasectomy reversal has no prognostic value for pregnancy rate. J Urol 2010;183:662-5.
11. Ollero M, Gil-Guzman E, Lopez MC, et al. Characterization of subsets of human spermatozoa at different stages of maturation: implications in the diagnosis and treatment of male infertility. Hum Reprod 2001;16:1912-21.
12. Esteves SC, Sharma RK, Gosálvez J, et al. A translational medicine appraisal of specialized andrology testing in unexplained male infertility. Int Urol Nephrol 2014;46:1037-52.

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