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Words of Wisdom:

Re: Testicular Spermatozoa Have Statistically Significantly Lower DNA Damage Compared With Ejaculated Spermatozoa in Patients With Unsuccessful Oral Anti-oxidant Treatment

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Experts' summary

To compare levels of DNA damage in ejaculated and testicular spermatozoa collected on the same day of the intracytoplasmic sperm injection (ICSI) procedure, the authors conducted a prospective clinical study. They identified 12 men aged 33–64 yr at their institution. These men had persistently high DNA damage (>30%), as assessed by sperm DNA fragmentation analysis, and had previously undergone unsuccessful 3-mo oral antioxidant treatment. The antioxidant treatment included either a combination of vitamins, herbs, and supplements (coenzyme Q10, L-carnitine, zinc and selenium) or daily vitamins supplemented with 20 mg zinc and 200 µg selenium. Patients receiving concurrent antibiotic therapy or varicocele surgery were excluded from the study.

The ejaculated semen samples were stained with acridine orange, analyzed with flow cytometry, and reported as a DNA fragmentation index (DFI). The testicular tissue samples were analyzed with the TUNEL technique. Pre- and post-treatment DFIs were not significantly changed. The ejaculated spermatozoa showed three-fold higher DNA damage when compared with testicular samples (39.7% vs 13.3%), with the absolute differences in the level of DNA damage between two specimens ranging from –3.3% to –56.3%. Therefore, the authors suggest that retrieved testicular spermatozoa have a lower degree of DNA damage than ejaculated sperm in men who have persistently high DFI after previous unsuccessful oral antioxidant therapy. Prospective randomized controlled trials comparing pregnancy outcomes with ICSI are necessary to establish new standards of care.

Experts' comments

Because assisted reproductive technologies now are commonly used to circumvent virtually all types of male infertility, it is important to understand the differences among ejaculated, epididymal, and testicular sperm and their respective levels of DNA damage. High levels of sperm DNA damage can negatively affect reproduction. Sperm samples from infertile men have been shown to have significantly more DNA damage than samples from fertile counterparts [1]. Multiple reports have also implicated DNA damage with poor in vitro fertilization (IVF) results [2], although newer studies have not corroborated these findings.

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The causes of DNA damage are largely unknown, although evidence suggests that genetic defects may underlie some sperm DNA damage [3]. Spermatogenesis is controlled by selective apoptosis, and abnormal sperm are tagged for apoptosis in the same manner that all other cells are marked for programmed cell death. In addition, certain polymorphisms in the protamine gene have been implicated in male infertility and sperm DNA damage [4,5]. Evidence suggests that a malfunction in this process allows sperm with DNA damage to be transported in the ejaculate, a process referred to as *abortive apoptosis* [6].

If IVF or ICSI is to be performed using sperm with high DNA damage, consideration should be given to testicular sperm extraction only after less invasive treatments for known causes of DNA damage have failed, as testicular sperm extraction is an invasive and expensive procedure.

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