Commentary

Application of sperm DNA fragmentation test in clinical setting

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The concise guideline by the expert panel of andrologists/urologists has described the various tests used to determine sperm DNA fragmentation (SDF), their drawbacks and benefits. In addition, they have used a problem-based approach to illustrate the clinical utility of SDF (1).

In couples with subfertility, male factor accounts for 50% of the cases (2). Male fertility has traditionally been assessed by semen analysis, and although various techniques to assess/enhance sperm function evolved, currently not many are used in clinical practice. Most cases of male infertility are treated by assisted reproduction technology, mainly intracytoplasmic sperm injection (ICSI) using ejaculated sperm or surgically retrieved sperm from the epididymides or testes. In absence of any known cause for subfertility, which occurs in 15–30% (3), the treatment options are intrauterine insemination (IUI) or *in vitro* fertilization (IVF)/ICSI.

SDF test provides information on sperm DNA integrity, which is vital for fertilization and development of good quality embryo (4,5). We are aware that even in the presence of normal semen analysis there can be significant SDF. Hence the utility of this test is well justified for cases, which do not respond to standard treatment options (1), i.e., those with repeated IUI/IVF/ICSI treatment or those with recurrent pregnancy loss in first trimester.

This raises further questions as to:

(I) What causes SDF?

(II) Can it be measured effectively?

(III) If high SDF is identified what are further treatment options?

(IV) Are there any methods that can identify normal versus SDF affected sperm for ICSI?

(V) Are there treatments to reduce or revert SDF or any preventative methods?

These answers are very well highlighted in the guideline that also demonstrates the existing evidence for the clinical use of SDF test (1). However, practices differ globally and in the UK, the current National Institute for Health and Care Excellence (NICE) guidance on assessment and management of fertility does not recommend SDF test and nor does it recommend varicocele treatment for infertility (6).

Lifestyle factors including advanced male age, smoking, obesity, exposure to heavy metals and organochlorine pollutants increase oxidative stress, which in turn influence sperm DNA integrity (1). Not knowing the problem causes significant emotional and psychological distress to the couple. Using a standardized SDF method, if high fragmentation is observed, this can be discussed with the couple as a potential cause of subfertility. This information may help improve patient compliance on modification of such life style factors.

Furthermore, the methods used to test SDF are well illustrated in a tabulated manner in the guideline. It is important to have standardized tests that one can rely on and also have a defined cut-off that is between either more than 15% or 30%. A higher cut-off of SDF could be justified for considering alternative management plan.

An important question is: what can be done if the test shows high SDF? Apart from the use of antioxidants, there is suggestion of using testicular sperm instead of the epididymal ejaculate for ICSI. However, the counter argument is high risk of aneuploidy from testicular sperm and risk of miscarriage (6). The other factor under

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study is magnetic cell sorting of sperm with high SDF at ICSI (7). Recently, Pastuszek *et al.* (8) have studied the potential effect of sperm vacuoles on DNA fragmentation and whether it can help with sperm selection at ICSI (9). One can speculate the role of preimplantation genetic screening for selection of euploid embryos in presence of high SDF.

The guideline by Agarwal *et al.* (1) highlights the value of SDF and gives food for thought for translational research. More high quality, well-powered studies are required to assess SDF and methods that can be implemented to reduce SDF and improve outcomes. Caution needs to be exerted in considering this test routinely for all patients until further evidence is available.

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Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

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