Commentary

Recognizing sperm DNA fragmentation testing in clinical evaluation of male fertility

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The paper by Agarwal *et al.* (1) presents guidelines prepared by an expert group indicating the testing of sperm DNA fragmentation (SDF) as a useful diagnostic tool in male fertility evaluation. Evidence based approach is used to indicate that SDF testing would be of immense clinical value and could be used as a reference by practicing urologists and reproductive specialists. The present work reviews the clinically available tests for SDF and the common clinical manifestations encountered in Urology clinics. Convincing evidences have been put forth by the authors advocating clinical utility of SDF in dealing with the cases of male infertility.

Clinical determination of infertility in men is very crucial but is dependent on the procedures used in semen analysis. DNA, being the most important package carried in the sperm, its integrity emerges as a very important parameter for the evaluation of infertility. The evaluation of DNA integrity in the spermatozoon is not a new concept. As early as in 1980, Evenson suggested DNA integrity as very important independent marker of fertility in both animals and men (2). Study of DNA damage (fragmentation) has been emerging as a valuable tool for the evaluation of male fertility. In recent years, large volume of literature has accumulated on sperm DNA fragmentation which has advocated the incorporation of sperm DNA fragmentation testing in clinical practice. The Practice Committee of the American Society for Reproductive Medicine (ASRM), in spite of acknowledging the relationship between sperm DNA damage and either semen parameters and/or outcome of assisted conception, recommends that: 'there is insufficient evidence to recommend the routine use of sperm DNA integrity tests in the evaluation and treatment of the infertile couple' (3). There are four sperm DNA tests which are most often used; the Single-cell gel electrophoresis (Comet) assay, Sperm Chromatin Structure Assay (SCSA), the terminal transferase dUTP nick end labeling (TUNEL) assay, and the Sperm Chromatin Dispersion (SCD or Halo) test. All of them measure different aspects of DNA damage and have different sensitivities. However, since none of them were perceived as providing an indication of specific DNA sequences could have triggered ASRM not to recommend routine use of sperm DNA integrity tests in the evaluation and treatment of infertile couple. It is quite surprising that although strong data supporting sperm DNA testing is available, there is still reluctance in accepting and incorporating these tests in routine clinical evaluation. The ASRM could have taken a more balanced overview and could have taken cognizance from around 100 papers published in reputed journals over the past three decades (4).

The present work of Agarwal *et al.* addresses the controversy and presents guideline for fertility clinicians advocating the clinical utility of sperm DNA fragmentation testing. The first part the review illustrates the clinically available tests for SDF testing. The second part deals with the commonly encountered clinical scenarios followed by an evidence-based analysis of the clinical utility of SDF which has been generally acknowledged as a valuable tool for evaluating male fertility. SDF testing is indicated in patients

with clinical varicocele and borderline to normal semen parameters. Saleh and coworkers (5) described high levels of sperm DNA damage in infertile patients with varicocele. The higher DNA fragmentation index (DFI) values have been shown to be related to high levels of reactive oxygen species (ROS) and decreased antioxidant defense in seminal plasma with varicocele. After varicocelectomy sperm parameters significantly improved and SDF was significantly decreased. The evidence put forth by the authors suggests that SDF testing would help clinicians to select candidates for varicocelectomy especially in low grade varicocele and borderline to normal semen parameter results. The significance of male factors on fertilization and embryo development is also very clearly demonstrated by establishment of link between DNA fragmentation and recurrent spontaneous abortions or failure of artificial reproductive techniques. Low DFI values, both spontaneous and with assisted reproductive techniques, have been associated with higher pregnancy rates. The authors have, therefore, concluded that oocyte quality may be a very important determinant for the negative effect of SDF. Thus, it is recommended that DNA fragmentation testing is carried out in patients with failure of artificial reproductive techniques. A recent meta-analysis study has also supported this view (6). A number of lifestyle factors have been implicated with oxidative stress induced SDF. Infertile men with exposure to environmental contaminants or having other lifestyle risk factors such as smoking and obesity have been suggested to undergo SDF test so that further response to interventional treatments could be monitored. It seems very appropriate though it needs further in-depth investigation. The authors have also advocated that the patients with unexplained infertility should also be subjected to SDF testing in addition to conventional semen analysis.

It seems very logical to conclude that SDF testing could be used as a very useful diagnostic tool in evaluating the status of male fertility. In spite of some controversies the evidences put forth by the authors regarding the role of SDF testing and indications are too compelling to be taken lightly. It is, therefore, only too logical to recognize the guideline along with the routine proposed by the authors and to include SDF testing in the evaluation of male factor fertility along with semen analysis.

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Footnote

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References

1. 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.
2. Evenson DP, Darzynkiewicz Z, Melamed MR. Comparison of human and mouse sperm chromatin structure by flow cytometry. Chromosoma 1980;78:225-38.
3. Practice Committee of the American Society for Reproductive Medicine. The clinical utility of sperm DNA integrity testing: a guideline. Fertil Steril 2013;99:673-7.
4. Lewis SE, John Aitken R, Conner SJ, et al. The impact of sperm DNA damage in assisted conception and beyond: recent advances in diagnosis and treatment. Reprod Biomed Online 2013;27:325-37.
5. Saleh RA, Agarwal A, Sharma RK, et al. Evaluation of nuclear DNA damage in spermatozoa from infertile men with varicocele. Fertil Steril 2003;80:1431-6.
6. Cissen M, Wely MV, Scholten I, et al. Measuring Sperm DNA Fragmentation and Clinical Outcomes of Medically Assisted Reproduction: A Systematic Review and Meta-Analysis. PLoS One 2016;11:e0165125.

