Editorial

The debate on sperm DNA fragmentation test goes on

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Dr. Malhotra, in his commentary (1), concisely summarized the practice recommendations by Agarwal et al. (2). While the author acknowledged the current evidence on sperm DNA fragmentation (SDF) test on one hand, he also highlighted the lack of support for routine use of SDF test in clinical practice by various guidelines on the other hand (3-6).

Semen analysis (SA) forms the pillar of evaluation of infertile male. The value of SA in prediction of natural pregnancy has been analyzed by various studies. One study demonstrated sperm morphology to have the best diagnostic potential with an area under the curve for receiver operator curve analysis of 78% by comparing conventional semen parameters of fertile and subfertile populations (7). However, the significant overlap of semen parameters between fertile and infertile men is a real concern (8). On the other hand, a more recent study supported the value of SDF as an independent attribute of semen quality in addition to conventional SA for male infertility evaluation (9). In addition to its predictive value on natural pregnancy, SDF test result correlates with outcomes of assisted reproductive technology (ART) (10). We believe that there is no single 'magic' test for diagnosing male infertility in the context of a complex human reproductive system. Correct interpretation of results from a panel of laboratory tests is often essential in the investigation of intricate systems involving multiple factors. The above debate promotes a clearer understanding on pros and cons of SA and SDF tests if viewed in a correct perspective. SA certainly has its role as an initial evaluation tool in assessing fertility potential of a male. However, it is also important to recognize the unique value of SDF tests in assessment of the paternal genome that may affect the health of the offspring. SDF would be a useful adjunct to SA but not necessarily superior to it. In fact, laboratory tests are not mutually exclusive to each other. Each test has its own limitation. A combination of selected tests offers additional complementary information that helps in coming up with a clinical diagnosis. After all, the usefulness of a laboratory test is more dependent on the appropriate application to a particular clinical scenario. The purpose of the practice recommendations by Agarwal et al. is not to disprove the value of other diagnostic tests. Rather, it is to maximize the predictive value of the SDF test in improving the evaluation of infertile male by identifying its most suitable place.

The lack of sufficient high grade evidence in support of routine application of SDF testing is a criticism often heard. Small and heterogeneous study populations, variations in methodology and inadequate experimental design are some of the reasons quoted (11). In fact, great efforts from researchers over the three decades has moved SDF testing from bench to clinical practice in the twenty first century. The test is currently available in a number of andrology laboratories worldwide. Although guidelines from various professional societies stressed the need for further evidence, the potential benefit of SDF testing in clinical practice is beginning to be recognized (3,5). Clearly, well-designed studies with adequate power and standard techniques will be invaluable, however, randomized studies in human

reproduction are often impractical. The involvement of couple in decision making, particularly when most of the couples have to pay for the infertility treatment, further complicate the issue and make randomization almost impossible. The quest for level 1 evidence before implementation of SDF testing may not be a realistic one. It also seems unfair when other practices in reproductive medicine, for example SA and ICSI, were widely employed clinically before high-level evidence and safety issues were resolved. Another important point to note is that SDF testing is non-invasive and its application does not pose major harm to patients, except the cost implication.

The body of evidence supporting the association between high SDF and natural pregnancy/ART outcomes is increasing. Certainly, different fertility specialists have their own viewpoints when analyzing the objective data. On one hand, the current practice of utilizing SA as the sole investigative tool for male infertility is not without its shortcomings. On the other hand, data on SDF testing may be considered as inadequate by guidelines from various professional societies. The clinical decision depends on the wisdom of each fertility specialist. Should we continue the current practice which is insufficient and withhold a potentially useful clinical test for infertile couples? Or should we embrace an emerging test with promising initial data and further refine the technique on its way of clinical application? We believe the practice recommendations by Agarwal *et al.* (2) provide clinicians with the basic knowledge of SDF testings which is essential for a wise decision. It also serves as a foundation for further debate on SDF testing since it is the best way to illustrate the principle and facilitate better understanding of the test.

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Footnote

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