

The State of Semen Analysis over Time

Contrary to public opinion on the causes of infertility, male factor accounts for over 50% of infertility during reproductive age of couples and even there are several reports on its increase during the recent years. Semen analysis as one of the main laboratory tests provides valuable information about male fertility status. In spite of huge development in diagnostic tests and laboratory innovation, this test has never lost its place and importance during the last decades and many researchers focused on its standardization and accuracy. Furthermore, World Health Organization (WHO) has emphasized its importance and published the book entitled "WHO Laboratory Manual for the Examination of Human Semen and Semen-Cervical Mucus Interaction" for standard methods in semen analysis. This book is upgraded periodically and its fifth edition was published in 2010. Although there is consensus on the importance and position of semen analysis in diagnosis of male infertility, numerous reports have challenged the practice due to its lack of compliance with spermogram results. In fact, in less than 10% of men with normal semen parameters, there is no ability to conceive naturally. On the other hand, equally the same number of men with abnormal semen parameters are quite fertile and have no problem to have a child through natural pregnancy. The low sensitivity and specificity of semen analysis results led to a new direction for studies and researches on cellular and molecular aspects of human and mammalian spermatozoa to find a more sensitive and specific biomarker of sperm quality during the last decades. The outcome of these attempts was the introduction of several sperm function tests including zona-free hamster oocyte penetration assay, sperm zona pellucida binding assay, acrosome reaction, sperm migration assay, computer aided sperm analysis (CASA), hyaluronon binding assay (HBA), sperm chromatin integrity and maturity (1).

In spite of the benefits and efficient performance of above assays in comparison with semen analysis, the low sensitivity and specificity of the first four assays and the need for salt-stored zona pellucida, hamster oocytes or human donated eggs led to their decreased use in sperm evaluation over time. Therefore, the older tests were gradually replaced by more accurate tests such as sperm nucleus and chromatin evaluation. Sperm DNA and chromatin evaluation has attracted more attention during the recent decade due to its high correlation with sperm quality, fertilizing ability, embryo quality and pregnancy outcome. Therefore, along with increased clinical research on the role of sperm chromatin, a broad range of researches were focused on innovating new methods and equipments for assessment of sperm chromatin quality. Currently, different types of cytchemical tests such as aniline blue, toluiden blue, chromomycine A3 and acridine orang stainings, sperm chromatin dispersion (SCD), sperm chromatin structure assay (SCSA), comet assay and TUNEL assay are available for sperm DNA and chromatin evaluation and each of them has its own advantages and disadvantages (2).

Although more sensitive and accurate tests are available for sperm nucleus evaluation, the main problem of these methods is their damage to the sperm during evaluation, so the evaluated normal sperm cannot be used in IVF procedures. Moreover, it is probable that the obtained results of diagnostic assays would not be consistent with the outcomes of treatment plan due to the extremely heterogeneous sperm population of semen. Consequently, this defect has led to a new generation of assays that select sperm based on surface charge (electrophoresis and zeta potential), apoptosis (magnetic cell sorting and glass wool), membrane maturity (hyaluronic acid binding) and ultramorphology (high magnification) without damaging the selected spermatozoa. In these cases, selection of sperm via hyaluronane binding or annexine V binding or electrical charge provides functional sperm with good quality which can be used for oocyte fertilization (3).

Although the initial results of these assays are satisfactory, the findings are preliminary and further clinical trials are needed to validate their safety and efficacy before their implementation in ART practice. In addition, these assays do not provide direct assessment of sperm chromatin. Consequently, future research should be focused on promotion and optimization of sperm chromatin assays without any damage to sperm quality for its subsequent use during *in vitro* fertilization. The review article of professor Evgeni and his colleagues entitled "Human Sperm DNA Fragmentation and its Correlation with Conventional Semen Parameters" discussed this subject in detail in current issue. We hope it will be welcomed and used by clinicians, scientists and other audiences of journal of reproduction and infertility.

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