Commentary

The quest of finding the perfect spermatozoon

Cristian O'Flaherty

Departments of Surgery (Division of Urology) and Pharmacology and Therapeutics, McGill University and the Research Institute, McGill University Health Centre (MUHC), Montréal, Canada

Correspondence to: Dr. Cristian O'Flaherty, DVM, PhD. Departments of Surgery (Division of Urology) and Pharmacology and Therapeutics, McGill University and the Research Institute, McGill University Health Centre (MUHC), Montréal, Canada. Email: cristian.oflaherty@mcgill.ca.

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Infertility is a health problem that touches around 15% of couples worldwide and male infertility is the sole cause in half of these cases (1,2). Since the development of assisted reproductive techniques (ART) particularly intracytoplasmic sperm injection (ICSI), it has been a challenge to select the very best spermatozoon to inject into the mature oocyte. This quest has not been easy and up to now there is no diagnostic tool to assure the health of the selected sperm.

Due to the lack of high percentages of success rate for ART it is mandatory to develop new strategies to select and improve the quality of the sperm sample to be used either for *in vitro* fertilization (IVF) or ICSI. There is increasing number of studies that raise a red flag in terms of the safety of the sperm sample to be used in ART (3,4). In this review, Agarwal *et al.* (5) aim to deliver useful guidelines for sperm DNA fragmentation testing based on commonly encountered clinical scenarios and considering what the different test measure and their feasibility in terms of costs and practicality for the clinic.

Studies using animal models and human spermatozoa are providing increasing evidence that sperm DNA fragmentation is a major culprit for abnormal reproductive outcomes (6-9). What is important to address is that the sperm chromatin is a complex structure with all its components being susceptible to damage. Spermatozoa from cancer survivors have a variety of sperm chromatin damage from single and double DNA strand breaks to different levels of DNA compaction due to either low levels of protamination, loss of disulfides bridges between protamines or in some cases due to both. Particularly in the case of levels of DNA compaction, it has been reported that an overoxidation of thiol groups is associated with male infertility (10,11), thus caution must be taken at the time of analyzing this characteristic of the sperm chromatin and highlights the importance of an appropriate balance in the redox status of the sperm nuclear thiol groups. These findings indicate that sperm chromatin quality should be defined by analyzing separate components. Moreover, the way these men recovered their sperm chromatin integrity varied among individuals and with time (12,13).

It is now evident that the standard semen analysis does not help clinicians to decide, in some cases, what therapeutic path to follow to help infertile men. Thus, it is imperative to find new alternatives that will provide sufficient information to better understand male infertility. The inclusion of sperm chromatin structure assays as those indicated by Agarwal *et al.* (5) can be of help in the treatment of male infertility. However, there is still not enough evidence that these tests can predict the reproductive outcome. There are two important issues that need to be addressed in order to support or not the introduction of these techniques in clinical practice: (I) standardization of these assays using unified protocols and (II) development of randomized controlled studies with sufficient number of participants. However, standardization can be difficult to implement and efforts from large institutions and recognized research groups in the field must come together to accomplish these goals. It is also time for governments to get involved by funding these studies as the outcome of this research may help to design new diagnostic and treatment strategies to maximize subsidized reproduction assisted programs.

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