ASSESSMENT OF SPERM DNA INTEGRITY AND CHROMATIN MATURITY IN PATIENTS WITH TESTICULAR AND SYSTEMIC MALIGNECIES

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ABSTRACT

Objective: Sperm chromatin structure is of vital importance for successful embryo growth. The fertility potential of a semen sample is considered impaired if >27-30% of sperm have measurable DNA fragmentation, especially for in vivo and IUI fertilization. Men diagnosed with cancer resort to sperm cryopreservation for fertility preservation. It is imperative to evaluate the sperm chromatin in these cryopreserved specimens prior to their use in assisted reproductive techniques in order to predict the probabilities of success and to ensure the transmission of intact genetic material. The objective of our study was to assess sperm DNA fragmentation and chromatin maturity in cancer patients and fertile donors.

Methods: Spermatogenic, blinded, controlled study. Sperm DNA Integrity is essential for the accurate transmission of genetic information and for successful embryo growth. Disturbances in the organization of the genomic material into sperm nuclei has been negatively correlated with the fertility potential of the spermatozoa. The fertility potential of a semen sample is considered impaired if >27-30% of sperm have measurable DNA fragmentation, especially for in vivo and IUI fertilization (5). The sperm chromatin structure assay (SCSA) is a standardized method for assessment of percent of sperm with fragmented sperm DNA (DNA Fragmentation Index, %DFI) and the presence of sperm with immature nuclear maturation (High DNA Stainability Index, %HDS). The objective of our study was to assess sperm DNA fragmentation and chromatin maturity in cancer patients and fertile donors.

Design: prospective, blinded, controlled study.

Materials and Methods: Semen samples were collected and cryopreserved from 17 testicular and 27 testicular and systemic malignancy patients or those with systemic malignancy. Samples from 20 fertile donors were included as controls. The cryopreservation protocol was designed for the preservation of sperm DNA and chromatin integrity. Sperm samples were subjected to cryopreservation using the cryopreservation protocol and were subsequently thawed in a 37°C water bath for 4 minutes and assessed for post-thaw parameters.

Post-Thaw Assessment

Semen samples were assessed for concentration and viability after cancer therapy. Patients diagnosed with cancer were considered poor candidates for sperm cryopreservation because they may present with disease-induced suboptimal semen quality and cryosurvival. However, patients who cryopreserved semen may still be able to achieve a healthy live birth using one of the assisted reproductive techniques. It is not yet clear whether patients with local testicular malignancy or those with systemic malignancy are more prone to have sperm with compromised genetic material. It is also imperative to evaluate the sperm chromatin in cryopreserved specimens from cancer patients prior to their use in assisted reproductive techniques in order to predict the probabilities of success and to ensure the transmission of intact genetic material.

Results: Percentages of sperm DNA fragmentation and chromatin maturity in testicular and systemic malignancy patients and fertile donors were compared. Sperm DNA integrity was assessed using the sperm chromatin structure assay (SCSA). The presence of significant cryosurvival rates, DNA integrity and chromatin maturity in cancer patients allows for future fecundity as an option for fertility preservation regarding the transmission of intact genetic material if sperm banking is performed prior to chemo/radiotherapy.

Conclusions: Cancer patients show suboptimal sperm quality and cryopreservation tolerance even before receiving chemo or radiotherapy. While testicular and systemic malignancy patients had 2.0 and 2.3X higher %DFI scores and 1.4 and 1.3X higher %HDS scores than fertile donors, the cancer patients still had average %DFI and %HDS scores that fall into a moderate level of DFI scores and comparable in patients with testicular and systemic malignancies. The presence of significant Cryosurvival rates, DNA integrity and chromatin maturity in cancer patients allows for future fecundity as an option for fertility preservation. Cancer patients show suboptimal sperm quality and cryopreservation tolerance even before receiving chemo or radiotherapy.

MATERIALS AND METHODS

Semen samples were collected from 17 patients with testicular malignancy (can/carcinoma/in situ) and 27 patients with systemic malignancy (leukemia/lymphoma) prior to the initiation of chemotherapy or radiotherapy. Healthy proven fertile donors (n=20) were included as controls. All sperm assessments were made according to the WHO guidelines (4th edition, 1999).

RESULTS

- Patients with testicular malignancies had significantly lower sperm concentration and fertility (p<0.05). On the other hand, sperm concentration was comparable in patients with systemic malignancies and fertile donors.
- Sperm motility was significantly lower in patients with testicular and systemic malignancies compared to fertile donors (p<0.05 and p<0.01, respectively).
- %DFI values were significantly higher in patients with testicular and systemic malignancies compared to fertile donors (p<0.05 and p<0.01, respectively).
- %HDS values were comparable between all 3 study groups.

CONCLUSIONS

- Cancer patients show suboptimal sperm quality and cryopreservation tolerance even before receiving chemo or radiotherapy.
- Although testicular and systemic malignancy patients had 2.0 and 2.3X higher %DFI than fertile donors, these scores fall into a moderate level of DFI scores that is considered compatible with achieving pregnancy.
- Testicular and systemic malignancy patients have normal sperm chromatin maturation despite having 1.4 and 1.3X higher %HDS scores than fertile donors.
- The presence of significant cryosurvival rates, DNA integrity and chromatin maturity in cancer patients allows for future fertility in an assisted reproduction setting. Furthermore, it provides assurance regarding the transmission of intact genetic material if sperm banking is performed prior to chemoradiotherapy.
- All cancer patients should be offered the opportunity to cryopreserve their semen specimens regardless of the quality as an option for fertility preservation.