Abstract title:
Prediction of successful ICSI cycles by Oxidation-reduction potential (ORP) and sperm DNA fragmentation (SDF) analysis. A Prospective study.

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Study question:
Does the clinical utilization of SDF and ORP tests helps in accurate prediction of fertilization in ICSI cycles?

Summary answer:
SDF and ORP testing could be used as a valuable diagnostic tool in IVF clinics to predict fertilization but not blastulation in ICSI cycles.

What is known already:
Seminal oxidative stress (OS) and sperm DNA fragmentation (SDF) are two advanced sperm function tests that are increasingly used in the evaluation of infertile men. OS has recently been identified as a major mediator in the various causes of male infertility. It is well established in the literature that a high percentage of SDF due to various factors including OS has adverse effects on ART outcomes.

Study design, size, duration:
This prospective pilot study evaluated a total of 50 patients undergoing ICSI treatment for male factor infertility (n=50). The study was carried out from June 2017 to December 2018 and was approved by Biomedical Ethics Committee of the University of the Western Cape, Cape Town, South Africa. All participants signed written informed consent form.

Participants/materials, setting, methods:
The fluorometric TUNEL assay (Promega Corporation, Madison, USA) and the MiOXSYS system (Aytu Bioscience, Englewood, CO) were used to measure SDF and the oxidation-reduction potential (ORP), respectively. The data generated was then correlated with the fertilization and blastulation rates. Statistical analysis including ROC curve analysis was performed. The study included patients using autologous fresh gametes only and excluded all day 3 embryo transfers and advanced maternal age.

Main results and the role of chance:
ROC curve analysis to predict fertilization and blastulation rates used published cut off values of 36% TUNEL-positive cells for SDF and 1.36 mV/10\(^5\) sperm/ml, respectively for ORP. For SDF (P<0.0001 for fertilization and P=0.0087 for blastulation), the ROC curve analysis resulted in a sensitivity of 67.6% and 89.7%, specificity 84.6% and 50.0%, positive predictive value 92.6% and 89.7% and negative predictive value 47.8% and 50.0% for fertilization and blastulation, respectively. [APA1] The areas under the curve (AUC) were 0.830 and 0.699 for fertilization and blastulation rate, respectively. For ORP (P<0.001), the analysis showed a sensitivity of 100.0%, a specificity of 62.9%, a positive predictive value of 55.6% and a negative predictive value of 95.0% with an AUC of 0.834 for fertilization. However, no significance was seen for blastulation (P=0.8146).

Limitations, reasons for caution:
The results observed in this study should be confirmed using a larger number of samples.

Wider implications of the findings:
The study demonstrated strong predictive capabilities of SDF and seminal ORP measurement in the
clinical setting. This information is useful in providing the clinician with a valuable diagnostic tool for prediction of fertilization in ICSI cycles.

**Trial registration number:**
Not Applicable.

**Keywords:**
Oxidation-reduction potential
Sperm DNA Fragmentation
ICSI
Male Infertility
ART