Multi-Center Evaluation of Oxidation-Reduction Potential (ORP) Assay in the Infertile Male


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OBJECTIVE

The objective of this study was to evaluate if the oxidation-reduction potential (ORP) levels found using the MiOXSYS System could reliably differentiate semen samples that meet the normal reference range of WHO criteria from those that do not. This study was carried out at 9 different institutions across the world. The study was approved by the Ethics committee of each participating institution (Cleveland Clinic, Cleveland, USA; Hamad Medical Center, Doha, Qatar; Dokkyo University, Osaka, Japan; The Doctor’s Laboratory, London, UK; VKF American Hospital, Istanbul, Turkey; Sohag University, Sohag, Egypt; Bezmi Alem Vakif University, Istanbul, Turkey; Tulane Medical Center, New Orleans, USA; and Assam University, Silchar, India. All subjects consented prior to participation. Participants (n=2010) were grouped into those that had all normal semen parameters (volume, concentration, morphology, total and progressive motility) according to WHO 2010 guidelines and those who failed to meet one or more criteria.

RESULTS

The MiOXSYS System (Aytu Bioscience, Inc.) measures the reduction potential (ORP) levels found using the MiOXSYS System could reliably differentiate semen samples that meet the normal reference range of WHO criteria from those that do not. The MiOXSYS System could reliably differentiate semen samples that meet the normal reference range of WHO criteria from those that do not. The MiOXSYS System could reliably differentiate semen samples that meet the normal reference range of WHO criteria from those that do not.

RESULTS (cont.)

Table 3: A backwards stepwise model was applied to further verify the logistic regression model and the rank of measures remained intact.

CONCLUSIONS

1. ORP levels can serve as adjunct to routine semen analysis in men undergoing infertility evaluation.
2. A reference value of 1.34 mV/10^6 sperm/mL for ORP provided the greatest predictability when distinguishing abnormal from normal semen quality among the 1644 patients undergoing infertility evaluation.
3. Abnormal ORP levels will be especially useful in pinpointing the altered functional status of the sperm in patients with idiopathic male infertility and thereby directing those men toward accurate therapeutic management.
4. Additional cases of normal semen quality will further strengthen the information obtained in this study.

Material and Methods

Following institution approval, semen samples were obtained from a total of 2010 patients. Participants were divided into two groups according to the WHO 5th edition guidelines (World Health Organization, 2010). Participants that met all six parameters were categorized as “normal semen parameters” (n=138) and those that failed to meet one or more of the six parameters were categorized as “abnormal semen parameters” (n=1506). The abnormal semen group had a semen volume <1.1mL, and/or sperm concentration <<15 x10^6 sperm/mL, and/or total sperm count <39 x10^6 sperm, and/or total motility <40%, and/or normal morphology <4%. The exclusion criteria for both groups included azoospermia, presence of STD or chronic disease, use of prescription, OTC medications or antioxidants. A total of 366 samples were missing one or more of the semen analysis measures and therefore were excluded during the statistical analysis.

RESULTS (cont.)

Table 2: Distribution of ORP in patients, showing the established cutoff value.

Figure 1. (a) MiOXSYS Analyzer (b) MiOXSYS Sensor.

Figure 2. A receiver operating characteristic (ROC) curve was used to identify the ORP (mV/10^6 sperm/mL) criterion i.e. cutoff, sensitivity, and specificity, positive predictive value, negative predictive value, and area under curve (AUC) that best predicted the normal and abnormal semen parameters.

Figure 3. Distribution of ORP in patients, showing the established cutoff value.

Table 1: Background information on the study population with a comparison of semen parameters between the normal (0) and abnormal (1) groups

1. Of the 1644 samples, 138 were found to have normal semen parameters and 1506 were found to have abnormal semen parameters (Table 1). The mean ORP value (mV/10^6 sperm/mL) in the semen of the abnormal group was 5.07 mV/10^6 sperm/mL whereas that of the normal group was 0.88 mV/10^6 sperm/mL (p = 0.000). ROC curve analysis of the six semen parameters and ORP (mV/10^6 sperm/mL) test results predicting normal versus abnormal semen quality values was performed to calculate test sensitivity, specificity, and positive and negative predictive values (Figure 2). At a cutoff value of 1.34 mV/10^6 sperm/mL ORP was able to differentiate between normal and abnormal semen quality with 98.1% sensitivity, 40.6% specificity, 94.7% positive predictive value, and 66.6% negative predictive value.

2. The distribution of subjects in the normal and abnormal groups above or below the established cutoff value of 1.34 mV/10^6 sperm/mL is depicted in Figure 3. The median ORP (mV/10^6 sperm/mL) level was below the established cutoff value of 1.34 mV/10^6 sperm/mL in the normal group, whereas it was above this cutoff in the group of abnormal group (p = 0.004). Only 1 of the 51 (less than 2%) participants in the control group fell below this cutoff.

3. A logistic regression model was performed on all measures (six semen analysis parameters and ORP measure) in order to determine the predictability of identifying abnormal / normal semen quality within the sample (Table 2). Measures were categorized according to overall contribution and significance. ORP ranked the highest (beta 2.88, p = 0.01) in terms of predicting abnormal / normal semen quality, followed by progressive motility (beta 2.29, p = 0.00), and total motility (beta .94, p = 0.005).

4. Additional cases of normal semen quality will further strengthen the information obtained in this study.

CONCLUSIONS

1. ORP levels can serve as adjunct to routine semen analysis in men undergoing infertility evaluation.
2. A reference value of 1.34 mV/10^6 sperm/mL for ORP provided the greatest predictability when distinguishing abnormal from normal semen quality among the 1644 patients undergoing infertility evaluation.
3. Abnormal ORP levels will be especially useful in pinpointing the altered functional status of the sperm in patients with idiopathic male infertility and thereby directing those men toward accurate therapeutic management.
4. Additional cases of normal semen quality will further strengthen the information obtained in this study.

CONCLUSIONS (cont.)

The results obtained from the study population indicated that the ORP levels found using the MiOXSYS System could reliably differentiate semen samples that meet the normal reference range of WHO criteria from those that do not. The MiOXSYS System could reliably differentiate semen samples that meet the normal reference range of WHO criteria from those that do not. The MiOXSYS System could reliably differentiate semen samples that meet the normal reference range of WHO criteria from those that do not. The MiOXSYS System could reliably differentiate semen samples that meet the normal reference range of WHO criteria from those that do not.

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