Glutamate levels in embryo culture media determined by proton nuclear magnetic resonance (^{1}H NMR) metabolomics correlates with reproductive potential of embryos in women undergoing in vitro fertilization

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Objective: The sentinel issue surrounding multiple gestations following IVF is the inability to precisely estimate the reproductive potential of individual embryos with the currently used embryo grading systems based on embryo cleavage rate and morphology. Recently, metabolomic profiling of spent culture media using Raman and Near-infrared spectroscopy have been reported to predict reproductive potential of embryos. In this study we applied proton nuclear magnetic resonance (^{1}H NMR) spectroscopy to analyze metabolomic profile of embryo culture media and to identify components of the media that correlate with reproductive potential.

Design: Prospective study.

Materials and Methods: Spent media samples from embryos that failed to implant (n=17), and samples (n=17) from embryos that resulted in pregnancy and delivery were individually collected after embryo transfer on day 3, and evaluated using proton nuclear magnetic resonance (^{1}H NMR). The spectra obtained were quantified by integrating biomarker signals in the aliphatic region after baseline subtraction. Using a multivariate analysis, a model that calculates a viability index for each spectrum was developed. Sensitivity and specificity of predicting pregnancy (described as implantation and delivery) were calculated.

Results: Glutamate levels determined by ^{1}H NMR were higher in the culture media of embryos that resulted in a pregnancy. Viability indices calculated by ^{1}H NMR using the weighted coefficients of glutamate and alanine/lactate ratio quantities were higher for embryos that implanted and resulted in a delivery, compared to those that failed to implant ($P<.01$). Proton NMR spectroscopy predicted viability of individual embryos with a sensitivity of 88.2% and a specificity of 88.2%.

Conclusion: Metabolomic profile of spent embryo culture media using ^{1}H NMR correlates with the reproductive potential of embryos. The lower glutamate levels detected in culture media of embryos that failed to implant could potentially be due to the toxicity associated with increased embryonic glutamate uptake. Additional studies using complementary approaches are needed to further delineate molecular components associated with reproductive potential.