Abstract Details

Session title: Embryology
Session type: Poster viewing
Presentation number: P-182

★ Abstract title:

Clinical validation of a non-invasive embryo selection algorithm combining time-lapse morphokinetics and the oxidative status of spent embryo culture media.

Biography

PhD Student at IVI RMA Global

R. Del Gallego Bonilla[1], L. Alegre[1], T. Cnaani[2], S. Shnizer[2], J. Remohí[1], M. Meseguer[1].
[1]IVI Valencia, IVF Laboratory, Valencia, Spain.
[2]Carmel Diagnostics, Thermochemiluminiscence, Kiryat Tiv'on, Israel.

Study question:

Determine if novel embryo selection technique based on spent´s embryo culture media oxidative profile combined with time-lapse morphokinetic analysis could predict implantation potential.

Summary answer:
Implanting transferred embryos showed a more extensive oxidative metabolism which, when combined with morphokinetic data, led to the development of a predictive algorithm.

What is known already:
Despite IVF's (*in vitro* fertilisation) widening application and technological progress, it remains associated with two main weaknesses that derive partly from our inability to adequately assess embryo quality: low implantation rates and high multiple pregnancy rates. Novel non-invasive strategies based on spent culture media analysis provide additional valuable data to current morphology and morphokinetic analysis performed by time-lapse technology. In particular, the assessment of the embryo's oxidative profile with the Thermochemiluminescence (TCL) Analyzer™ (Carmel Diagnostics, Israel) suggests a new approach in determining embryo's quality or viability and subsequent implantation potential.

Study design, size, duration:
A retrospective cohort study was performed with a total of 505 spent embryo culture media, including 205 single-embryo transfers (SET) with known implantation, from 390 IVF cycles. Embryos were cultured and monitored in independent-well slides in the time-lapse system incubator Embryoscope® (Vitrolife) and were subsequently transferred at blastocyst stage. Implantation potential and embryo quality at day 5 (Transferred+Vitrified vs. Discarded embryos) were considered, in terms of oxidation, to find a predictive profile of pregnancy success.

Participants/materials, setting, methods:
Oxidative status of 15 µl/embryo of Blastocyst medium (Cook) samples were assessed by the Thermochemiluminescence (TCL) Analyzer™, based on the heat-induced oxidation of biological fluids, leading to the production of light energy counted as photons emitted per second (**cps**). TCL parameters recorded were **cps** amplitude after 55 seconds (**H1**), 155 seconds (**H2**) and 255 (**H3**), in a 300-second period. Oxidative data was normalized with a smoothing algorithm (**sm**) and analyzed by the statistical test ANOVA.

Main results and the role of chance:
Regarding day 5 embryo quality, transferred and vitrified embryos showed significantly higher values (sig. <0.05) for the oxidative parameters **H1sm**, **H2sm** and **H3sm**. In addition, out of 205 transferred embryos, 54.1% succeeded at implantation showing again higher significant values (sig. <0.05) in the oxidative parameters. This therefore implies high quality embryos have a more extensive oxidative metabolism

exerting an oxidative load on their surrounding media. A combined assessment algorithm, including morphology, morphokinetics and the embryo's culture media oxidative status was subsequently developed as a predictive clinical tool of embryo selection, prior to transfer. Motato et al. (2016) morphokinetic model based on blastocyst expansion (**tEB**; optimal range ≤ 112.9 hours) and timing of transition from 5-blastomere embryo until 8-blastomere embryo (**t8–t5**; optimal range ≤ 5.67) was combined with TCL parameter **H2sm** (optimal range ≤ 92.96). A hierarchical classification was generated with six embryo categories (A - F) according to their implantation potential (76.5 - 29.2%).

Limitations, reasons for caution:
The present retrospective study and its developed selection algorithm require an additional prospective validation for its routine clinical use. Oxidative status database will increase while using TCL to pursue a more accurate **H2sm** optimal range.

Wider implications of the findings:
The fair correlation between TCL oxidative results, embryo quality and implantation potential proves its application as a clinical biomarker. Its combination with morphokinetic data aims for the improvement of our current selection criteria. A more accurate selection of the best embryo, especially in good-quality embryo cohorts, would determine IVF success.

Trial registration number:
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Keywords:
Thermochemiluminescence (TCL)
Oxidative profile
Implantation rate
Embryo selection algorithm