Breakthrough for IVF?

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Elsevier today announced the publication of a recent study in *Reproductive BioMedicine Online* on 5-day old human blastocysts showing that those with an abnormal chromosomal composition can be identified by the rate at which they have developed to blastocysts, thereby classifying the risk of genetic abnormality without a biopsy. In a new study the same group has undertaken a retrospective study, using their predictive model to assess the likelihood of any embryo transferred resulting in a successful pregnancy, with very encouraging outcomes.

One of the greatest challenges in assisted reproduction is to find the one embryo, which can develop successfully. Now, combining time lapse imaging of IVF embryos cultured for 5 days to the blastocyst stage with trophoblast biopsy, it has proved possible to correlate the rate of blastocyst formation with chromosomal abnormalities. Such an approach should allow early and widely accessible non-invasive identification of the best embryo to place in the uterus.

"Recently the world of IVF has become very excited by the use of time-lapse imaging (TLI) of early human embryo development to follow the change of embryo morphology over time", explains Martin Johnson, Editor of *Reproductive BioMedicine Online*. "The data can then be compared with the outcome after the embryos are transferred. The hope is that this morphokinetic analysis will enable reproductive specialists to predict more successfully those embryos most likely to generate pregnancies. The advantage of using morphokinetic analysis to predict outcome is its minimal invasiveness."

The majority of embryos that fail to initiate a pregnancy do so because they have abnormal chromosomes. Unfortunately these embryos cannot be recognized by embryologists using conventional microscopy. Only biopsy of one or a few cells of the early embryo followed by preimplantation genetic screening (PGS) can establish whether the number of chromosomes is normal or not.

In their research Alison Campbell and colleagues of CARE Fertility, Nottingham, went one step further, describing the use of morphokinetic analysis to identify those embryos that have an abnormal chromosomal constitution. In that study, they cultured embryos under time lapse imaging to day 5, by which time they formed blastocysts. These were then biopsied by removing a few of the cells from the outer layer of the embryo, which will normally contribute only to the placenta. The biopsy was then analyzed for its chromosomal constitution. The authors then related the chromosomal make up of each embryo to its morphokinetic history. They found that a proportion of embryos with chromosomal abnormalities were delayed in initiating blastocyst formation and also reached the full blastocyst stage later than did normal embryos. The authors conclude that using this approach they could avoid exposing at least a subset of the embryos to invasive biopsy procedures.

"This non-invasive model for the classification of chromosomal abnormality may be used to avoid selecting embryos with high risk of aneuploidy while selecting those with reduced risk," said lead author Alison Campbell.

The same group has now applied this risk classification model retrospectively to examine the pregnancy outcomes in a series of unselected IVF patients without the use of PGS. A significant improvement in both implantation and live birth rates was observed when low risk embryos were transferred.

Scientist Markus Montag of the Department of Gynecological Endocrinology and Fertility Disorders, University Clinics of Heidelberg, said: "The idea of using time-lapse imaging and morphokinetic analysis is intriguing, because having available a completely non-invasive procedure to predict which embryo is euploid or aneuploid would allow the application of this technique for virtually every assisted reproduction cycle. The potential benefit of such an approach is obvious in view of published data on the incidence of aneuploidy even in oocytes from younger women."

More information: Modelling a risk classification of aneuploidy in human embryos using non-invasive morphokinetics, by Campbell, A., Fishel, S., Bowman, N., Duffy, S., Sedler, M., Hickman, C.F.L.; Reproductive BioMedicine Online; 26, 477- 485;DOI: 10.1016/j.rbmo.2013.02.006. The article appears in Reproductive BioMedicine Online, Volume 26, Issue 5 (May 2013), published by Elsevier. Available online on ScienceDirect.

Retrospective analysis of clinical pregnancy and live birth rate for IVF embryos classified for aneuploidy risk, without PGS, demonstrates the benefit of a time-lapse imaging derived model, by Campbell, A., Fishel, S., Bowman, N., Duffy, S., Sedler, M., Thornton, S.; This article is available as an Article in Press in Reproductive Biomedicine Online (May 17, 2013), published by Elsevier. Available online on ScienceDirect on May 17.

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