

Embryo culture media in human IVF

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Valorization

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In this Valorization paragraph the potential impact of the research described in this thesis is considered.

Relevance

During the last decade, the use of ART has increased significantly worldwide and thereby the number of children born after ART too. The etiology of the adverse perinatal outcome of ART children is still incompletely understood. The extreme differences in birth weight that have been observed in animal studies, such as the large offspring syndrome, have not been observed in humans. However, ART children may be predisposed for adult health risks. With the growing number of children conceived after ART, it is important that the safety of ART is investigated. We have shown that culture media have a significant effect on fetal development, birth weight and early postnatal weight. Moreover, the gene expression in human preimplantation embryos is affected by the type of culture medium used.

ART has turned into a multi-million dollar industry and in most countries it is mainly provided in the private health care sector. Delivery rates are an important factor for IVF clinics, as IVF patients use these for choosing their clinic of treatment. This could increase the pressure on IVF clinics to use the latest technology in hope to achieve the best results. New technologies might get introduced based on expected benefits, which might not have been proven by randomized controlled trials. In ART there are several examples of new technologies and methods which have been introduced in clinical practice without appropriate evidence-based practice showing that the procedure is safe and beneficial to the patient, that it is cost-effective, and that its benefits outweigh its potential harms. Examples are assisted hatching, blastocyst transfer, endometrial 'scratching', in vitro maturation, time-lapse monitoring of embryo development and vitrification. Furthermore, changes in culture media composition, stimulation regimens and laboratory protocols are often established worldwide without adequate validation.

Target groups

The results of this thesis are interesting for IVF professionals, culture medium manufacturers, health economists and health care providers/insurers, politicians and the European Society of Human Reproduction and Embryology (ESHRE). Furthermore, our research results are of interest to couples who are planning to undergo an IVF treatment. Are they aware that they might receive treatments that are not validated by RCTs and are they aware of the adverse outcome after

ART or of the possible long-term health effects? Couples undergoing an IVF treatment belong to a very vulnerable group, as they will do everything to get their own baby.

Activities/innovation

All papers have been published in a high-ranking scientific research journal. We have discussed our findings at national and international conferences to gain more attention for this topic. This has led to more research groups worldwide investigating the effect of culture medium and other ART related factors on human perinatal outcome. Currently, in our center we are involved in a study that investigates the effect of culture medium on the health of IVF children at the age of 9 years, with the focus on physiological (blood pressure and endothelial function), metabolic (lipid profile and glucose), and anthropometric (length, weight and skin fold thickness) examinations. Recently, in the Netherlands a new multicenter RCT started to compare pregnancy and perinatal outcome between the sequential culture medium Vitrolife G5 and Irvine's single step Continuous Single Culture medium. The ESHRE appointed a working group on culture media with members from the special interest groups Embryology, Safety and Quality in ART, and Genetics. This working group encourages constructive co-operation with IVF culture media manufacturers over transparency, composition and quality control parameters. Recently, Oxford University Press published a press release together with the RCT from this thesis and a review from the working group, which received worldwide attention.

The possibility that IVF culture media and other culture conditions are partly responsible for an adverse perinatal outcome in IVF children should not be ignored. However, the extend of the adverse outcome is still uncertain and large randomized studies are required to investigate the etiology of the adverse perinatal outcome. In addition, the full composition of embryo culture media should be made publically available by the companies that produce them. Companies should also report what studies have been performed to test these media and which endpoints have been analyzed.

Schedule and implementation

Before introducing changes to culture media composition, stimulation regimens and laboratory protocols into the clinical setting, IVF professionals need to consider their safety. New technologies should be evaluated for safety, effectiveness and cost-effectiveness. The use of the mouse embryo assay for preclinical testing should be discussed and the need for a more appropriate test should be recognized. Subsequently, human embryos should be made available

for research, and research should be performed on human eggs/sperm or embryos donated for research. Large clinical trials with follow-up of IVF pregnancies and children should become the standard.