In vitro human preimplantation embryo development in an adapted culture system based on human uterine fluid composition and uterine pH.

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Ethical review	Approved WMO
Status	Completed
Health condition type	Other condition
Study type	Observational non invasive

Summary

ID

NL-OMON49697

Source
ToetsingOnline

Brief title
Embryo culture in four different culture media

Condition

- Other condition

Synonym
infertility, subfertility

Health condition

subfertiliteit

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,ZonMW

Intervention

Keyword: culture environment, embryo, uterus

Outcome measures

Primary outcome

The primary outcome is the blastocyst formation rate.

Secondary outcome

Secondary outcomes are embryo quality based on morphological assessment and

cell count, embryo metabolism, embryo gene expression, and embryo methylation

pattern.

Study description

Background summary

IVF has revolutionized reproductive medicine. Currently around 2 million IVF treatments are provided worldwide each year. However, live birth is achieved in only about one third of all treatments started. Therefore, there is a strong incentive to improve IVF efficacy, and one of the main targets is to optimize human embryo culture conditions as it is well known that better embryo culture results in better quality embryos and subsequently higher pregnancy rates after IVF.

One of the most important components of embryo culture is the embryo culture medium being used. There are several embryo culture media for human IVF that are commercially available nowadays. The choice of embryo culture medium affects the pregnancy rate after IVF, as well as child outcomes, such as the birth weight of children born. Even after 40 year of IVF, it remains unclear which medium is best for human embryo culture. One of the reasons is that research on the human in vivo environment of preimplantation embryos is very limited, due to the difficulty of such measurements.

Our group has now measured physiological conditions (temperature and pH) in the human uterus and analyzed uterine fluid samples on the presence and concentration of 37 components during the *implantation window*, i.e. the time during a menstrual cycle a preimplantation embryo would normally implant. Until now such measurements have never been performed in such detail. From these results we concluded that, by using currently available embryo culture media, the in vitro environment of pre-implantation embryos in IVF laboratories worldwide actually differs from the natural in vivo environment in the human uterus. Based on these measurement we constructed a new embryo culture medium that should mimic the in vivo conditions better than the culture media that are currently being used. We hypothesize that this will result in improved IVF efficacy.

We would like to test this by culturing donated left-over IVF embryos in a culture medium currently being used for human IVF (control group) and compare this with our new medium with a different pH and different composition based on the human in vivo uterine conditions. To be able to discriminate between the effect of the different pH and different medium composition we also constructed two *intermediate culture media*, one where we only changed the pH, and one where we only changed the composition compared to the control medium.

If successful, that is if we find similar or improved in vitro embryo development with our new embryo culture medium, we will proceed with a clinical pilot study, but this pilot study is beyond the scope of the current application.

Study objective

The primary objective of our proposal is to determine embryo development of donated human preimplantation embryos in four different culture media: (1) standard culture medium (control group), (2) culture medium with a uterine-like pH, (3) culture medium with a uterine-like composition, (4) culture medium with a uterine-like pH and composition.

Study design

Randomization of thawed human preimplantation embryos that were donated for research after IVF on day 3 or 4 of development to one of the following four groups: (1) standard culture medium (control group, pH 7.3±0.1), (2) culture medium with a uterine-like pH (pH 6.8±0.1), (3) culture medium with a uterine-like composition, (4) culture medium with a uterine-like pH and composition. There will be stratification for maternal age, embryo quality and IVF center of origin during randomization.

Study burden and risks

Only left-over donated preimplantation embryos will be used for this study. The couples that donated these embryos have already finished their IVF treatment and have given written consent for the use of their left-over cryopreserved embryos for research purposes when embryo storage for IVF purposes was terminated. No incidental findings are expected from the proposed research. No additional involvement is required for the couples and therefore there is no burden, risk or benefit associated with this study.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Inclusion criteria

Vital thawed human left-over preimplantation embryos, consisting of a minimum of 5 blastomeres that comprise >=50% of the whole embryo, that were donated for research.

Exclusion criteria

Of all human left-over day 3 or 4 embryos that were donated for research: embryos that did not survive the freeze-thawing procedure or embryos that consist of less than 5 blastomeres and/or are less than 50% vital.

Study design

Design

Study type:	Observational non invasive
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	12-02-2022
Enrollment:	700
Type:	Actual

Ethics review

Approved WMO

Date:	22-03-2020
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL72270.000.19