INPLASY PROTOCOL

Corresponding author:
Jing Xia

xiajingwhu@126.com

Author Affiliation:
Renmin Hospital of Wuhan University

Review Stage at time of this submission: Formal screening of search results against eligibility criteria.

Conflicts of interest: No.

The effect of autologous endometrial co-culture on pregnancy outcome in infertile patients: a meta-analysis

Xia, J[1]; Liu, BW[2]; Wu, GX[3]; Yang, J[4].

Review question / Objective: Dose autologous endometrial cell co-culture (AECC) improve the pregnancy outcome compared with conventional medium (CM) in infertile patients who undergo assisted reproductive technique (ART)?

Condition being studied: Infertility is defined as the inability of a couple to get pregnant after one year of normal intercourse without contraception. And the incidence of infertility is estimated to range from 10% to 13% of reproductive-aged couples worldwide, which has become a serious global public health problem. In recent years, scholars have used AECC for early embryo culture with the aim of exploring whether its application can improve pregnancy outcome in patients with IVF. However, the conclusions are still controversial. Therefore, a systematic review will be designed to appraise the effectiveness of AECC for pregnancy outcome of patients based on high-quality RCTs and Non-RCTs.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 04 August 2020 and was last updated on 04 August 2020 (registration number INPLASY202080009).

INTRODUCTION

Review question / Objective: Dose autologous endometrial cell co-culture (AECC) improve the pregnancy outcome compared with conventional medium (CM) in infertile patients who undergo assisted reproductive technique (ART)?

Condition being studied: Infertility is defined as the inability of a couple to get pregnant after one year of normal intercourse without contraception. And the incidence of infertility is estimated to range from 10% to 13% of reproductive-aged couples worldwide, which has become a serious global public health problem. In recent years, scholars have used AECC for

early embryo culture with the aim of exploring whether its application can improve pregnancy outcome in patients with IVF. However, the conclusions are still controversial. Therefore, a systematic review will be designed to appraise the effectiveness of AECC for pregnancy outcome of patients based on high-quality RCTs and Non-RCTs.

METHODS

Search strategy: We searched PubMed, Web of Science, EMBASE, Cochrane Library, Register and Meta-register for RCTs (http://www.controlled-trials.com), CNKI, WanFang, and VIP databases from inception until June 16th 2020 for all primary studies comparing the pregnancy outcome of AECC versus CM in early embryo culture in women who underwent ART. We combined manual retrieval of references and Google Scholar assisted retrieval, in order to avoid literature missing. Combination of Medical Subject Heading (i.e., MeSH) and text words were used. Search terms included: subfertility, polycystic ovary syndrome, poor ovarian response, high ovarian response, recurrent implantation failure, advanced maternal age, poor ovarian reserve, recurrent miscarriage, fertilization in vitro, intracytoplasmic sperm injections, assisted reproductive technologies, endometrium, co-culture techniques, autologous endometrial cell co-culture, AECC, etc.

Participant or population: All eligible female adults who underwent ART.

Intervention: Used autologous endometrial cell co-culture for early embryo culture.

Comparator: Used conventional medium for early embryo culture.

Study designs to be included: RCTs and Non-RCTs.

Eligibility criteria: (1) the target population was women underwent ART; (2) the literature type was conference abstract or article; (3) the study represented original clinical research, including RCTs and Non-

RCTs; (4) the early embryos of the intervention group and the control group were cultured by AECC and CM, respectively; (5) the outcome was the comparison of embryo quality or pregnancy outcome between the intervention group and the control group; (6) in Chinese or English language.

Information sources: PubMed, Web of Science, EMBASE, Cochrane Library, Register and Meta-register for RCTs (http://www.controlled-trials.com), China National Knowledge Infrastructure (CNKI), WanFang databases, and VIP databases.

Main outcome(s): Clinical pregnancy rate.

Additional outcome(s): Implantation rate; Live birth rate; Miscarriage rate; Ectopic pregnancy rate; Multiple pregnancy rate; Number of blastomeres per pre-embryo transferred; Embryo morphology and quality.

Data management: Studies were selected according to the inclusion and exclusion criteria by two researchers (Jing Xia and Bowen Liu) separately. Excluded studies that were obviously inconsistent by reading the title and abstract, then read the full text of the remaining studies. Any disagreements or doubts about whether or not the studies should be included, the two researchers would try to resolve it through discussion.

Quality assessment / Risk of bias analysis: The Cochrane Collaboration Risk of Bias tool was used to assess the risk of the included RCTs by two researchers. Specific evaluation items included the following domains: (1)random sequence generation; (2)allocation concealment; (3)blinding of participants and personnel; (4)blinding of outcome assessment; (5)incomplete outcome data; (6)selective reporting; (7)other bias.The Newcastle-Ottawa scale (NOS) score was adopted to evaluate the quality of Non-RCTs included. The full score was 9, and the higher the score, the better the quality of the studies. Judgment on each one was passed according to three items: selection of the study group,

selection of the study group, comparability between groups and ascertainment of exposed/not exposed cohorts.

Strategy of data synthesis: Stata 12.0 was used for data analysis and processing. For dichotomous data, all results were represented by RR and its 95% CI. And continuous data were represented by WMD and its 95% CI. P50%, showing significant heterogeneity, then the random-effects model was used. In order to evaluate the reliability of the combined results, we drew mainninf diagram for sensitivity analysis by Stata. And Begg and egger tests were used to evaluate the publication bias. The test level of our meta-analysis was set at α=0.05.

Subgroup analysis: Subgroup analysis will be based on the following conditions: 1) Number of previous ART failures; 2) Timing of embryo transfer; 3) Type of work; 4) Type of study.

Sensibility analysis: Sensitivity analysis will be performed to investigate the effect of a single study on the results by omitting one study at a time.

Country(ies) involved: China.

Keywords: Autologous endometrial cell co-culture; Co-culture Techniques; Endometrium; In vitro fertilization-embryo transfer; Embryo quality; Meta-Analysis.

Contributions of each author:
Author 1 - Jing Xia.
Author 2 - Bowen Liu.
Author 3 - Gengxiang Wu.
Author 4 - Jing Yang.