

INPLASY PROTOCOL

Cleavage and blastocyst embryo sequential transfer and IVF outcome

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Conflicts of interest:
None declared.

Review question / Objective: Sequential embryo transfer has been proposed to improve embryo implantation in women for in vitro fertilization (IVF), but the effect on the pregnancy outcomes remained ambiguous. This systematic review was conducted to investigate the efficacy of sequential embryo transfer on the IVF outcomes.

Condition being studied: Nowadays, transfer embryos in two embryonic development stages in the same cycle, that is, two-step transfer with cleavage and blastocyst embryo in the same treatment cycle, have already been applied in clinical practice. Sequential transfer not only has the advantage of high implantation rate of blastocyst, but also avoids the cancellation risk of transfer cycle with previously transferred cleavage embryos. However, there is no unified conclusion about the effect of sequential transplantation on in vitro fertilization and embryo transfer (IVF-ET) pregnancy outcomes.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 05 August 2021 and was last updated on 05 August 2021 (registration number INPLASY202180019).

INTRODUCTION

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sequential embryo transfer on the IVF outcomes.

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practice. Sequential transfer not only has the advantage of high implantation rate of blastocyst, but also avoids the cancellation risk of transfer cycle with previously transferred cleavage embryos. However, there is no unified conclusion about the effect of sequential transplantation on in vitro fertilization and embryo transfer (IVF-ET) pregnancy outcomes.

METHODS

Search strategy: This systematic review searched studies in PubMed, Cochrane Library, Web of Science, ScienceDirect and Wanfang databases by the combination of MeSH terms and free words published in recent two decades until January, 2021. The main search terms were ‘sequential embryo transfer’ or ‘consecutive embryo transfer’ or ‘sequential embryo transplantation’ or ‘sequencing embryo transfer’ or ‘interval double transfer’ or ‘two-step transfer’ and ‘IVF’ or ‘in vitro fertilization’.

Participant or population: In vitro fertilization and embryo transfer (IVF-ET) patients, frozenthawed embryo sequential transfer pregnancy outcomes were excluded.

Intervention: Sequential embryo transfer patients.

Comparator: Cleavage embryo transfer and blastocyst embryo transfer patients.

Study designs to be included: This systematic review included randomized controlled trials, cohort studies and case-control studies that compared IVF outcomes of sequential transfer of cleavage and blastocyst stage embryo with that of regular embryo transfer of Day 3 or Day 5.

Eligibility criteria: Studies published only as abstract or replicated published, as well as studies reported frozenthawed embryo sequential transfer pregnancy outcomes were excluded from this review.

Information sources: This systematic review searched studies in PubMed, Cochrane Library, Web of Science, ScienceDirect and Wanfang databases by the combination of MeSH terms and free words published in recent two decades until January, 2021.

Main outcome(s): Our results also measured the difference between the sequential transfer and cleavage embryo transfer group in chemical pregnancy rate, clinical pregnancy rate, embryo implantation rate, clinical miscarriage rate, multiple pregnancy rate, and live birth rate. Our results also measured the difference between the sequential transfer and blastocyst transfer group in clinical pregnancy rate, embryo implantation rate, clinical miscarriage rate, and multiple pregnancy rate.

Additional outcome(s): None.

Quality assessment / Risk of bias analysis: Publication bias was assessed using funnel plots. The analysis results for publication and related biases did not suggest evidence of bias.

Strategy of data synthesis: Relative Risk (RR) and its 95% confidence intervals (95% CI) will be calculated for the outcome new onset atrial fibrillation in each included trial based on intention to treat. Due to expected heterogeneity among the trials, Meta-analysis using the random-effects model will be conducted to pool RR.

Subgroup analysis: Two subgroup analyses will also be undertaken: repeated implantation failure (RIF) patients and not-RIF patients.

Sensitivity analysis: Generally I² test results exceeds 40%, which is considered to be high. Random effect model is used for analysis when I² exceeds 40%; otherwise, fixed-effect model will be adopted. Sensitivity analysis was performed by sequentially excluding individual studies. Sensitivity analysis was performed by sequentially excluding individual studies.

Language: English and Chinese.

Country(ies) involved: Mainland China.

Other relevant information: None.

Keywords: Sequential embryo transfer; Cleavage embryo transfer; Blastocyst embryo transfer; In vitro fertilization.

Contributions of each author:

Author 1 - Jianeng Zhang performed the systematic literature review and conducted the statistical analysis.

Author 2 - Chong Wang conceived and designed the study.

Author 3 - Huanhuan Zhang performed the systematic literature review.

Author 4 - Yan Zhou conducted the statistical analysis.