INPLASY

Embryonic Causes of Implantation Failure: A Systematic Review and Procedures To Optimize Successful Embryo Transfer

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ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202410008

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 03 January 2024 and was last updated on 03 January 2024.

INTRODUCTION

Review question / Objective What is 1) the implantation rates of euploid versus untested embryo transfers; 2) the efficiency of transfer of good embryos in the maternal uterus as divided for age groups; 3) the transfer of good embryos into the maternal host uteri of gestational carriers as for age groups; 4) the transfer of donated gametes/embryos in the uteri of women utilizing gamete/embryo donation programs with the hope that identification of critical points in the implantation process will elucidate new areas for focused mechanistic studies that will lead to enhanced therapies.

Rationale The increasing age at which ART therapies are sought highlights the importance of better elucidating the potential role of the embryo in successful implantation. To better establish what are the diagnostic and treatment tools to choose in the two possible directions of embryonic and/or extra-embryonic deep effort before to consider both gametes donation and gestational carriers.

Condition being studied Infertility is a condition of the male or female reproductive system defined by the failure to achieve pregnancy after 12 months or more of regular unprotected sexual intercourse when the female partner is under 35 years of age and at 6 months when the female partner is 35 years of age or older One of the most important medical treatments to ameliorate infertility is in vitro fertilization and embryo transfer (IVF-ET) as part of the assisted reproduction (ART) programs: around the world that have resulted in the birth of over 12 million children . The most critical step in the IVF-ET programs and protocols is the embryo

transfer and implantation of the transferred embryo in the maternal endometrium. Of all embryos transferred, implantation occurs in only 25% to 30% of embryo conceived in vivo or in vitro. Several factors are involved . The quality of the embryo playing the most important role.

METHODS

Search strategy Database Search: A comprehensive search of the PubMed database was performed to identify relevant studies. The search strategy included the following keywords and combinations: "in vitro fertilization," "assisted reproductive techniques," "reproductive techniques, assisted," "IVF," "embryo implantation," "implantation failure," "embryo nidation," "endometrial receptivity," "endometrial decidualization," "blastocyst quality," "preimplantation genetic testing," "PTG-A," "preimplantation diagnosis," "aneuploidy," "donor cycles," "oocyte donation," and "gestational carrier." The search was limited to English-language articles. Registry Data: Data from the Society for Assisted Reproductive Technology (SART), the Centers for Disease Control and Prevention (CDC), the Australian and New Zealand registers, the Portuguese register, and the UK register were also included in this review.

Participant or population 1. Studies published in English. 2.Original research articles, including clinical trials, observational studies, and registry data.3. Studies investigating the role of embryonic factors in human embryo implantation.4. Studies reporting outcomes related to embryo quality, age, number of previous implantation failures, uterine factors, endometrial thickness, and other factors influencing successful implantation.

Intervention / Comparator 1 Efficiency of PGT-A screened embryo transfer versus untested embryo transfer ; 2 Comparison of euploid embryo transfer data within national registers of ART procedures between gestational and non gestational carriers.

Study designs to be included 2. Original research articles, including clinical trials, observational studies, and registry data.

Eligibility criteria 1. Studies published in English.2. Original research articles, including clinical trials, observational studies, and registry data.3. Studies investigating the role of embryonic factors in human embryo implantation.4. Studies reporting outcomes related to embryo quality, age, number of previous implantation failures, uterine factors, endometrial thickness, and other factors influencing successful implantation.

Information sources The systematic review and meta-analysis were conducted in electronic database of MEDLINE, Institute for Scientific Information (ISI) Web of Science and Scopus from January1st,1980 through December 1, 2023 by using a search strategy based on the Rayyan framework- AI powered tool for systematic literature review and following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Further, manual searches of reference lists from included studies supplemented the electronic database searches. Non-English reports, studies on animals, and studies published before 1980 were excluded. The study protocol was registered with Inplasy.

Main outcome(s) 1) implantation rates of euploid versus untested embryo transfers; 2) the efficiency of transfer of good embryos in the maternal uterus as divided for age groups; 3) the transfer of good embryos into the maternal host uteri of gestational carriers as for age groups; and, 4) the transfer of donated gametes/embryos in the uteri of women utilizing gamete/embryo donation programs.

Additional outcome(s) The margin of extra embryonic medical intervention to improve implantation success.

Data management Data Extraction Study Selection: Two independent reviewers screened titles and abstracts of retrieved articles to identify potentially eligible studies. Full-text articles were assessed for eligibility based on inclusion and exclusion criteria. Disagreements were resolved through consensus.Data Collection: Data were extracted from included studies using a standardized data extraction form. Information collected included study characteristics (authors, publication year, study design), patient demographics, intervention details, and relevant outcome measures.Data Synthesis and AnalysisMeta-Analysis: a meta-analysis was conducted to quantitatively synthesize the data. Pooled effect estimates and 95% confidence intervals were calculated using random-effects or fixed-effects models, as appropriate. Heterogeneity among studies was assessed using statistical tests (e.g., I^2 statistic).Assessment of Publication Bias: Publication bias was assessed using funnel plots and statistical tests (e.g., Egger's test) if a sufficient number of studies were included in the meta-analysis.Reporting Guidelines: The results of this systematic review

and meta-analysis were reported in accordance with PRISMA guidelines.

Quality assessment / Risk of bias analysis The risk of bias in individual studies was evaluated using appropriate tools (e.g., Cochrane Risk of Bias tool for randomized controlled trials, Newcastle-Ottawa Scale for observational studies).

Strategy of data synthesis Meta-analysis , Publication bias was assessed using funnel plots and statistical tests (e.g., Egger's test) if a sufficient number of studies were included in the meta-analysis.

Subgroup analysis Subgroup analyses were conducted to explore potential sources of heterogeneity, such as study design, patient characteristics, or methodological differencesNo further sub groups were analyzed.

Sensitivity analysis Sensitivity analyses were performed to assess the robustness of the results by excluding studies with a high risk of bias or by exploring the impact of specific study characteristics on the overall findings.

Language restriction English.

Country(ies) involved Italy.

Keywords "in vitro fertilization," "assisted reproductive techniques," "reproductive techniques, assisted," "IVF," "embryo implantation," "implantation failure," "embryo nidation," "endometrial receptivity," "endometrial decidualization".

Dissemination plans Publication in Peer-Reviewed Journals: Identify reputable journals in your field that publish systematic reviews and meta-analyses. Submit your paper to these journals. Prepare a well-written manuscript that includes the key findings, methodology, and implications of your study.

Contributions of each author

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