INPLASY PROTOCOL

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None declared.

Therapeutic prospect on umbilical cord mesenchymal stem cells in animal model with primary ovarian insufficiency: A meta-analysis

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Review question / Objective: **Participants: experiment POI animal models; Interventions: human umbilical cord mesenchymal stem cells; Comparisons: POI animal models without hUCMSC therapy; Outcomes: estrous cycle situation, serum sex hormone level and ovarian follicle count; Studies: randomized controlled animal study; The aim of the review is to figure out whether hUCMSC can recover ovarian function in POI animal models.**
Condition being studied: **Primary ovarian insufficiency (POI) is a syndrome characterized by reduced or absent ovarian function (hypogonadism) and elevated levels of gonadotropins, specifically luteinising hormone (LH) and follicle-stimulating hormone (FSH). Etiologies of POI are various. Genetic disorders, autoimmune diseases, iatrogenic injuries like chemotherapy and radiotherapy, and infectious diseases all contribute to the development of POI. Main manifestation of POI includes decreased ovarian function and infertility. Patients may suffer from menopausal symptoms, such as increased cardiovascular disease, decreased bone mineral density, vulvovaginal atrophy, psychological distress and so on. Current treatment of POI is limited. HRT mainly ameliorates symptoms while ART can achieve fertility in some patients but faces many challenges in clinical practice because it's hard to get satisfied oocytes. Stem cell therapy is proved to be efficient in recovering organ functions and hUCMSC is one of the easiest cell to obtain. So we think hUCMSC is promising in treating POI.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 19 May 2023 and was last updated on 19 May 2023 (registration number INPLASY202350075).

INTRODUCTION

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can recover ovarian function in POI animal models.

Rationale: Primary ovarian insufficiency affects about 1% of women population. but current treatment is limited. HRT mainly ameliorates symptoms but can not reverse the aging of ovarian function. ART can achieve fertility in some patients but is hard and challenging in clinical practice. Stem cell therapy is a new method in regenrative medicine and is proved to be efficient in many other diseases. As POI is described as a decline of ovarian function, we conduct the meta-analysis to find out whether hUCMSC can recover ovarian function in POI animal models.

Condition being studied: Primary ovarian insufficiency (POI) is a syndrome characterized by reduced or absent ovarian function (hypogonadism) and elevated levels of gonadotropins, specifically luteinising hormone (LH) and follicle-stimulating hormone (FSH). Etiologies of POI are various. Genetic disorders, autoimmune diseases, iatrogenic injuries like chemotherapy and radiotherapy, and infectious diseases all contribute to the development of POI. Main manifestation of POI includes decreased ovarian function and infertility. Patients may suffer from menopausal symptoms, such as increased cardiovascular disease, decreased bone mineral density, vulvovaginal atrophy, psychological distress and so on. Current treatment of POI is limited. HRT mainly ameliorates symptoms while ART can achieve fertility in some patients but faces many challenges in clinical practice because it's hard to get satisfied oocytes. Stem cell therapy is proved to be efficient in recovering organ functions and hUCMSC is one of the easiest cell to obtain. So we think hUCMSC is promising in treating POI.

METHODS

Search strategy: We searched the Pubmed, Embase and Cochrane Library databases. Specific search strategy is "((Primary Ovarian Insufficiency) OR (Premature Ovarian Failure) OR (Gonadotropin-Resistant Ovary Syndrome) OR (Hypergonadotropic Ovarian Failure)) AND ((Stem cell) OR (Progenitor Cell))". To conclude, we used MeSH terms and their typical synonyms and combined them with 'OR'. Then, we combined the results of 'primary ovarian insufficiency' and 'stem cell' with 'AND'. All results from the date of database establishment to 1 April 2022 were included.

Participant or population: All types of established POI experiment animal models. In this review, BALB/c mice, CD1 (ICR) mice, C57BL/6 mice, albino Wistar rats and SD rats are included.

Intervention: Injection of hUCMSC via tail vein or ovary in situ injection in POI animal models.

Comparator: Established POI animal models without hUCMSC therapy.

Study designs to be included: Randomized controlled animal study.

Eligibility criteria: XReviews and meta-analysis, studies that are not associated with stem cell or POI, non-animal studies, case reports and animal studies without hUCMSC application.

Information sources: Data in Pubmed, Embase and Cochrane Library databases from the database establishment to 1 April 2022.

Main outcome(s): Estrous cycle; Serum E2, AMH, FSH and LH levels; Follicle number in ovary. We also conducted subgroup analysis based on calculate unit, injection location, stem cell concentration and transplantation time. Sensitivity analysis and funnel plot are also made to show if there is any publication bias.

Data management: We used RevMan 5.4 to record and analyse data from included studies.

Quality assessment / Risk of bias analysis: Study quality is qualifiedly assessed by using "SYRCLE animal experiment bias risk

assessment form." All included studies are of medium quality.

Strategy of data synthesis: Data were extracted by authors and qualifiedly assessed by using "SYRCLE animal experiment bias risk assessment form". We used risk ratios (RRs) with 95% confidence intervals (CI) for categorical data, and standardised mean difference (SMD) for numerical data to combine studies. All statistical data were analysed on RevMan 5.4.

Subgroup analysis: Subgroup analysis is conducted according to calculate unit, injection location, hUCMSC concentration, transplantation time and follicle type.

Sensitivity analysis: Sensitivity analysis is conducted by picking out studies one by one.

Language restriction: All studies published in English language are included.

Country(ies) involved: China, Iran and Saudi Arabia.

Keywords: primary ovarian insu ciency, human umbilical cord mesenchymal stem cells, animalmodel, meta-analysis, estrous cycle, hormone level, folliculogenesis.

Contributions of each author:

Author 1 - Xinrun Wang conducted study collection, indentification, data extraction, statistical disposal and drafted the manuscript.
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