INPLASY PROTOCOL

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Corresponding author:
Yushi Meng

469815401@qq.com

Author Affiliation:
Kunming Medical University.

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None declared.

Effect of compound oral contraceptive pretreatment on outcomes of controlled ovarian hyperstimulation and embryo transfer in patients with premature ovarian insufficiency: A systematic review and meta-analysis

Wang, YX[1]; Hou, ZJ[2]; Bie, J[3]; Chen, JS[4]; Yang, XL[5]; Su, Y[6]; Song, JM[7]; Liu, Y[8]; Meng, YS[9].

Review question / Objective: **Patients with premature ovarian insufficiency (POI), who experience infertility, primarily undergo in vitro fertilization and embryo transfer (IVF-ET); however, it is difficult to obtain high-quality embryos from patients with POI owing to high follicle-stimulating hormone (FSH) levels.Pretreatment with compound oral contraceptives (COC) can reduce FSH levels and improve IVF-ET outcomes of patients with POI.This systematic review and meta-analysis aimed to analyse the effect of COC pretreatment on the outcomes of controlled ovarian hyperstimulation (COH) and IVF-ET in patients with POI.**

Eligibility criteria: **1. Study participants had IVF/intracytoplasmic sperm injection (ICSI) or POI. POI criteria (meeting one of the following three criteria): (1) amenorrhea or sparse menstruation for at least 4 months, twice FSH > 25 IU/L (with an interval of more than 4 weeks) or FSH > 40 IU/L; (2) anti-Müllerian hormone (AMH) < 0.5-1.0 μg/L, or the number of basal sinus follicles (AFC) < 5-7; (3) basic FSH level of 10-15 IU/L. 2. COC was used to intervene before COH. 3. Randomized controlled trials (RCTs) with a blank or placebo control group.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 09 May 2022 and was last updated on 09 May 2022 (registration number INPLASY202250052).

INTRODUCTION

Review question / Objective: **Patients with premature ovarian insufficiency (POI), who experience infertility, primarily undergo in vitro fertilization and embryo transfer (IVF-ET); however, it is difficult to obtain high-quality embryos from patients with POI owing to high follicle-stimulating hormone (FSH) levels.Pretreatment with compound oral contraceptives (COC) can reduce FSH levels and improve IVF-ET outcomes of**

patients with POI.This systematic review and meta-analysis aimed to analyse the effect of COC pretreatment on the outcomes of controlled ovarian hyperstimulation (COH) and IVF-ET in patients with POI.

Condition being studied: The increase in the proportion of young premature ovarian insufficiency (POI) worsens infertility problems.IVF-ET has become the primary treatment for patients with POI.Controlled ovarian hyperstimulation (COH) is the premise of IVF-ET. However, the high follicle-stimulating hormone level of patients with POI leads to unsatisfactory COH outcomes.Current research remains controversial on whether COH outcomes will benefit from compound oral contraceptive (COC) pretreatment,and the appropriate population for COC pretreatment has also not been clarified.We searched all literature on COC pretreatment before COH in this study to analyse the effect of COC pretreatment on IVF-ET outcomes in patients with POI versus in patients with ovarian normal reserve.

METHODS

Participant or population: Patients with premature ovarian insufficiency (POI) and Patients with ovarian normal reserve (NOR).

Intervention: Pretreatment with compound oral contraceptives before controlled ovarian hyperstimulation.

Comparator: Control group with no COC pretreatment.

Study designs to be included: RCT and retrospective study.

Eligibility criteria: 1. Study participants had IVF/intracytoplasmic sperm injection (ICSI) or POI. POI criteria (meeting one of the following three criteria): (1) amenorrhea or sparse menstruation for at least 4 months, twice FSH > 25 IU/L (with an interval of more than 4 weeks) or FSH > 40 IU/L; (2) anti-Müllerian hormone (AMH) < 0.5-1.0 μg/L, or the number of basal sinus follicles (AFC) < 5-7; (3) basic FSH level of 10-15 IU/L. 2. COC was used to intervene before COH. 3. Randomized controlled trials (RCTs) with a blank or placebo control group.

Information sources: PubMed, EMBASE, Web of Science, Ovid, Cochrane Central Register of Controlled Trials (CENTRAL), China National Knowledge Infrastructure (CNKI), China Wanfang Medical Online, and China Biology Medicine disc (CBMdisc).

Main outcome(s): The study outcomes included four or more of the following: total Gn dose, number of days of COH, number of oocytes obtained, number of mature oocytes, number of embryos, number of high-quality embryos, clinical pregnancy rate, and live birth rate.

Quality assessment / Risk of bias analysis: The Cochrane risk bias assessment tool was used to assess the bias risk of the included RCTs, including selection, performance, detection, attrition, reporting, and other biases. The evaluations were categorized as having a low, unclear, or high risk of bias.

Strategy of data synthesis: Data analysis was performed using Stata software 15.0. The statistical effect of binary data is expressed as relative risk (RRs) and 95% confidence intervals (CIs), and continuous data are expressed as standardized mean difference (SMD) or mean difference (MD) and 95% CI. Heterogeneity between studies was evaluated using the Q-test and I2 test. According to the Cochrane Intervention Systematic Evaluation Manual, heterogeneity between studies was only caused by sampling error when I2 = 0% and moderate heterogeneity when I2 = 0–40%; I2 > 40%, indicating a high degree of heterogeneity. A random-effects model was used when I2 > 50%; otherwise, a fixed-effect model was employed and a subgroup analysis was performed (grouped by ovarian reserve, NOR group, and POI group). When the heterogeneity of the analysis results was high, a sensitivity analysis was performed by excluding the

included studies one by one, a subgroup analysis, or a regression analysis when a high degree of heterogeneity existed. Publication bias was not assessed because fewer than 10 studies were included.

Subgroup analysis: **Subgroup analysis was conducted to determine whether ovarian reserve variation was a potential source of heterogeneity.**

Sensitivity analysis: **Publication bias will be assessed by a Galbraith radial plot.**

Country(ies) involved: **China.**

Keywords: **premature ovarian insufficiency, compound oral contraceptive, IVF-ET, high-quality embryo, live birth rate.**

Contributions of each author:
Author 1 - Yixuan Wang.
Author 2 - Zhijin Hou.
Author 3 - Jia Bie.
Author 4 - Jingsi Chen.
Author 5 - Xiaoling Yang.
Author 6 - Ya Su.
Author 7 - Jiamei Song.
Author 8 - Yang Liu.
Author 9 - Yushi Meng.