Does endometrial scratching improve clinical pregnancy rate in subfertile women undergoing intrauterine insemination or timed intercourse? A systematic review and meta-analysis

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Review question / Objective: Does endometrial scratching injury improve the clinical pregnancy rate in subfertile women undergoing intrauterine insemination or timed intercourse?

Condition being studied: Subfertility, commonly referred to as infertility, is a disease characterized by the failure to establish a clinical pregnancy after twelve months of regular, unprotected sexual intercourse. Intrauterine insemination (IUI) is a first line treatment for unexplained infertility and is widely performed in many countries. As we know, IUI is less invasive, less costly, and has better patient preference than does in vitro fertilization (IVF). Moreover, many studies have shown that women with UI will still conceive spontaneously with no specific treatment. Timed intercourse (TI) consists of observing the key signs that mark the fertile phase and having intercourse during that period to achieve pregnancy. Endometrial scratching injury (ESI), a technique suggested to improve the receptibility of the endometrium and therefore increase the probability of successful pregnancy. Although multiple RCTs have been completed in recent years, the effectiveness of this procedure outside of ART, in women or couples attempting to conceive via TI or IUI, remains unclear. Thus, the principal aim of the study was to systematically review and meta-analyze the pregnancy benefits and harms of ESI compared with sham procedure or no ESI for subfertile women or couples trying to conceive by IUI/TI.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 10 August 2020 and was last updated on 10 August 2020 (registration number INPLASY202080040).

INTRODUCTION

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METHODS

Search strategy: From inception to 1st July 2020, we searched PubMed, Embase, Cochrane Library, Web of science and Google Scholar database for published and unpublished randomized controlled trials (RCTs). We also searched the trials registers ClinicalTrials.gov (http://clinicaltrials.gov) and the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) (http://www.who.int/trialsearch/Default.aspx), using the keywords. Additionally, we hand-searched the references of relevant reviews, systematic reviews and included studies to locate other potentially eligible studies.

Participant or population: Subfertile women or couples trying to conceive by IUI or TI with and without endometrial scratching.

Intervention: Endometrial scratching injury performed before IUI or TI.

Comparator: A shame procedure or no intervention except for conventional IUI/TI procedure.

Study designs to be included: Only randomized controlled trials.

Eligibility criteria: 1. Subfertile women or couples trying to conceive by IUI or TI, with and without previous IUI failure history, 2. publications published in English, 3. the study represented original clinical research, 4. the literature type included both conference abstracts and full-text articles, 5. publications have the data on clinical pregnancy rates.

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Main outcome(s): Clinical pregnancy rate per randomized people.

Additional outcome(s): The secondary outcomes were: 1. miscarriage rates per clinical pregnancy, 2. biochemical pregnancy rate per randomized women, 3. ongoing pregnancy rate per randomized women, 4. multiple pregnancy rates per clinical pregnancy, defined as the presence of more than one gestational sac on transvaginal ultrasound, 5. ectopic pregnancy rate per clinical pregnancy, and 6. live birth rate (LBR) per randomized women.
Data management: Two review authors (BW-Liu and J-Chen) independently assessed whether the studies met the inclusion criteria, with disagreements resolved by consensus and discussion with a third author (YQ-Yang), if necessary. We screened the titles and abstracts of articles found in the search and discarded studies that were clearly ineligible. Then we retrieved the full text of all potentially eligible studies. We sought further information from the authors where papers contained insufficient information to make a decision about eligibility. For duplication or overlapping publications, the studies with larger number of cases and controls or been published latest were included.

Quality assessment / Risk of bias analysis: Cochrane Collaboration's 'Risk of Bias' assessment tool was used to evaluate the quality of RCTs. Seven domains related to risk of bias were evaluated: random sequence generation; allocation concealment (selection bias); blinding of participants and personnel (performance bias); blinding of outcome assessors (detection bias); incomplete outcomes (attrition bias); selective data reporting (reporting bias); other sources of bias (other bias). Authors' judgments were expressed as ‘low risk’, ‘high risk’ or ‘unclear risk’ or bias for each domain. Two independent reviewers (J Chen &BW-Liu) assessed trial quality, and any disagreements were resolved through consensus adjudication.

Strategy of data synthesis: Statistical analysis was performed using Review manager version 5.3 (Cochrane Collaboration, Software Update) and STATA software (Version 15.0, Stata Corp, College Station, Texas). For the dichotomous variables, risk ratio (RR) and their corresponding 95% confidence intervals (CIs) were used as summary statistics. Before the combined data were analyzed by meta-analysis, the heterogeneity assessment was performed by conducting a standard Cochrane's Q test with a significance level of α=0.10 and the I² statistical test. Meta-analysis was performed with a fixed effect model for studies without heterogeneity (P >0.1 and I² < 50%), and a random effect model for studies with statistical heterogeneity (P < 0.1 and I² > 50%) after data combination.

Subgroup analysis: Subgroup analyses were performed to evaluate the specific influence of clinical characteristics (type of article, different ESI timing, different ESI cycle, and type of methods to promote fertility) on the pooled RR for primary endpoints.

Sensibility analysis: Stata software was used to evaluate sensitivity with the ‘metaninf’ command.

Language: Only publications in English were searched and extracted.

Country(ies) involved: China.

Other relevant information: None.

Keywords: Endometrial scratching injury; infertility; artificial insemination; Intrauterine insemination; timed intercourse.

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