Effect of salpingectomy on ovarian response to hyperstimulation during in vitro fertilization: a meta-analysis

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Objective: To compare ovarian response to hyperstimulation during IVF between patients who did and did not undergo salpingectomy.
Design: Meta-analysis.
Setting: University-affiliated teaching hospital.
Patient(s): Patients undergoing IVF who did and did not undergo salpingectomy.
Intervention(s): None.
Main Outcome Measure(s): The total dose of gonadotropin, duration of hyperstimulation, E level on the day of hCG injection, number of oocytes retrieved, and basal FSH level were evaluated because these reflect ovarian response.
Result(s): Twenty-five studies were identified through searches conducted on PubMed, Cochrane Libraries, Ovid, Web of Science, Science Direct, China National Knowledge Infrastructure, and Wanfang Database through October 2015. The 25 studies included 1,935 patients who underwent salpingectomy and 2,893 who did not. Fixed-effects and random-effects models were used to calculate the overall combined risk estimates. The results of the meta-analysis suggest that salpingectomy impairs ovarian response to hyperstimulation. The total dose of gonadotropin was significantly increased after combined salpingectomy (inverse variance [IV] 0.10 [95% confidence interval (CI) 0.03, 0.16]; $I^2 = 30\%$) and bilateral salpingectomy (IV [95% CI] 0.23 [0.09, 0.37]; $I^2 = 36\%$). The number of oocytes retrieved decreased significantly after unilateral salpingectomy (IV [95% CI] −0.17 [−0.27, −0.06]; $I^2 = 31\%$) and bilateral salpingectomy (IV [95% CI] −0.20 [−0.32, −0.08]; $I^2 = 48\%$). In addition, a statistically significant reduction was found between the number of oocytes retrieved from the ipsilateral and contralateral ovary (IV [95% CI] 0.25 [−0.40, −0.10]; $I^2 = 48\%$). Finally, bilateral salpingectomy may lead to an increase in the FSH level (IV [95% CI] 0.39 [0.20, 0.59]; $I^2 = 0\%$). Heterogeneity moderators were identified by performing subgroup and sensitivity analyses. No evidence of publication bias was observed.
Conclusion(s): This meta-analysis indicated that salpingectomy may impair ovarian response to hyperstimulation during IVF. Further high-quality research is needed to confirm our findings and to develop therapeutic methods that are alternatives to salpingectomy for maternal well-being. (Fertil Steril® 2016;106:322–9. ©2016 The Authors. Published by Elsevier Inc. on behalf of the American Society for Reproductive Medicine. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).)
Key Words: In vitro fertilization, meta-analysis, ovarian response, salpingectomy

Discuss: You can discuss this article with its authors and with other ASRM members at http://fertstertforum.com/fanm-salpingectomy-hyperstimulation-ivf/

Assisted reproductive technology (ART) has developed rapidly since the first baby as a result of IVF, Louise Brown, was born in 1978, when IVF was still an experimental technique. More than 200,000 babies are born worldwide each year via ART (1, 2); to date, a total of approximately 5 million have been born (3). Currently, ovarian hyperstimulation, which aims at retrieving sufficient oocytes for fertilization, is one of the most important steps in the routine procedure of ART. Many situations arise in the clinic that may lead to an unsatisfactory ovarian response after ovulatory hyperstimulation. One potential difficulty is a history of salpingectomy.

Salpingectomy is a treatment option in cases of hydrosalpinx and ruptured ectopic pregnancy. Because of the close relationship between the mesosalpinx and ovarian blood supply, salpingectomy may compromise ovarian response (4). Numerous studies have compared ovarian response to IVF procedures between patients who

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underwent salpingectomy and a control group of infertile females who did not undergo salpingectomy; however, the results are inconsistent. Some studies reported that salpingectomy causes a reduction in ovarian response (5–15), whereas others reported no change (16–29). A meta-analysis of the current literature had not been reported previously. Given the inconsistency of the existing studies, we conducted a meta-analysis to provide a comprehensive comparison of the ovarian response to hyperstimulation during IVF between patients who underwent salpingectomy and those who did not.

MATERIALS AND METHODS

Literature Search

Unconstrained searches were conducted on PubMed, Cochrane Libraries, Ovid, Web of Science, ScienceDirect, China National Knowledge Infrastructure, and Wanfang Database with an end date of October 2015. The search terms included the following: "salpingectomy," "tubal disease," "hydrosalpinx," "ovarian response," "ovarian function," "in vitro fertilization/IVF," and "intracytoplasmic sperm injection/ICSI." References in seminal articles, review articles, and medical textbooks were reviewed. The grey literature and conference abstracts were not included in the search.

Outcome Measures

The main outcome of interest was the ovarian response to controlled ovarian hyperstimulation during IVF with and without salpingectomy. We compared the ovarian response not only between the salpingectomy and control groups but also between the ipsilateral ovary and contralateral ovary. Parameters including the total dose of gonadotropin (Gn) used, duration of hyperstimulation, estrogen (E) level on the day of hCG injection, number of oocytes retrieved, and basal level of FSH were used to reflect the ovarian response.

Selection Criteria

Identified studies were included in the meta-analysis if they [1] were published in English or Chinese; [2] had a prospective or retrospective design; [3] examined the ovarian response to controlled ovarian hyperstimulation during IVF; [4] used IVF and/or intracytoplasmic sperm injection as the exposure of interest; and [4] reported mean and standard deviations (SD). Studies were excluded if [1] they were review articles, federal government reports, or conference abstracts/presentations; [2] the same center and/or authors published articles that included patients in the same or overlapping period; or [3] the control group included patients with tubal surgery.

Data Extraction and Statistical Analysis

There was no contact with the authors of the selected studies for additional information. We performed a meta-analysis in accordance with MOOSE (meta-analysis of observational studies in epidemiology) guidelines (30). All analyses were based on previous published studies; therefore, no ethical approval or patient consent was required. A standardized data collection form was used for data extraction. We collected the mean and SD of parameters reflecting the ovarian response. In addition, we extracted characteristics of each study, including the first author's name, year of publication, study period, geographic region, type of study, details of the participants (number of cycles in the unilateral and bilateral salpingectomy subgroups, total number of cycles, and reason for salpingectomy, as well as the number of cycles and infertility reason for the control group), IVF protocol, outcomes, effects, and statistical method. Inverse variance (IV) weighting was used to measure the association between salpingectomy and ovarian response. The mean difference or standard mean difference and the corresponding 95% confidence interval (CI) were calculated using either fixed-effects or random-effects models in the presence of heterogeneity. In statistics, IV weighting is a method of aggregating two or more random variables to minimize the variance of the sum. Each random variable in the sum is weighted in inverse proportion to its variance. Inverse variance weighting is typically used to pool the odds ratio (OR) in a statistical meta-analysis to combine results from independent studies. Results are presented as IV and 95% CI. Statistical heterogeneity among the results of the included studies was identified and quantified formally with the I^2 statistic (31, 32). $I^2 \geq 50\%$ indicates substantial heterogeneity. Sensitivity analyses were conducted to explore possible explanations for heterogeneity and to examine the influence of various exclusion criteria on the overall risk estimate. We investigated the influence of a single study on the overall risk estimate by omitting one study each time. Subgroup analyses were performed by omitting studies within the same category according to the protocol type, geographic region, whether the study used a case–control or self-contrast method, and whether the study design was prospective or retrospective. Publication bias was assessed by visual inspection of the Begg's funnel plots (33). The software used for data extraction and analysis was Review Manager 5.3 (Copenhagen: Nordic Cochrane Centre, Cochrane Collaboration). $P<.05$ was considered statistically significant.

RESULTS

Literature Search

The literature search extracted 1,167 articles from the 7 databases. Most articles were excluded after the first screening on the basis of the title and abstract. Thirty-four articles were considered relevant to the topic and were read in full. Figure 1 shows the flow diagram of the selection process. Finally, 25 studies were included in the meta-analysis: 12 in English (5–7,10,15,16,19, 20, 23–25, 28) and 13 in Chinese (8, 9,11–14,17,18, 21, 22, 26, 27, 29).

Study Characteristics

Characteristics of the included studies, which were published between 1999 and 2015, are summarized in Supplemental Table 1 (available online). Nineteen studies were conducted in Asia, four were conducted in Europe, one was conducted in Africa, and one was conducted in the United States.