ORIGINAL ARTICLE: ASSISTED REPRODUCTION

Meta-analysis: does salpingectomy have a deleterious impact on ovarian response in in vitro fertilization cycles?

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Objective: To investigate the impact of salpingectomy in patients with IVF treatment on ovarian response.
Design: Meta-analysis.
Setting: Not applicable.
Patient(s): Patients under treatment for infertility, during the cycles before and after treatment by salpingectomy for hydrosalpinx or ectopic pregnancy.
Intervention(s): PubMed, MEDLINE, EMBASE databases, and CENTRAL in Cochrane Library up to July 2015. Either a fixed- or a random-effects model was used to calculate the overall combined risk estimates. The subgroup analysis was planned a priori before data were collected and analyzed.
Main Outcome Measure(s): The amount of gonadotropin administered, the peak E_2 level, the number of oocytes retrieved, and the number of pregnancies.
Result(s): After the final screening, 12 of the studies were retrospective and six were prospective. In this meta-analysis, 1,482 patients were enrolled, including a total of 657 patients with salpingectomy and 825 without salpingectomy. The comparisons before and after salpingectomy of the peak E_2 level (SMD = −0.182; 95% confidence interval [CI], −0.166, 0.101; I^2, 85.45%), the total gonadotropin dose used for stimulation (SMD = 0.127; 95% CI, −0.054, 0.308; I^2, 84.49%), and number of oocytes retrieved (SMD = −0.060; 95% CI, −0.189, 0.070; I^2, 63.93%) did not reveal any significant differences. The number of pregnancies before and after salpingectomy did not differ significantly (odds ratio [OR] = 1.180; 95% CI, 0.854, 1.630; I^2, 34.01%).
Conclusion(s): Salpingectomy in infertile patients does not have any negative effect on their subsequent fertility treatment, but further studies should be performed before this result can be considered definitive. (Fertil Steril® 2016;■:■–■. ©2016 by American Society for Reproductive Medicine.)
Key Words: Salpingectomy, ovarian response, in vitro fertilization

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Hydrosalpinx has a detrimental effect on IVF-ET outcome (1). In a comprehensive meta-analysis, evaluating a total of 5,569 cycles in patients without and 1,144 with hydrosalpinx, Zeyneloglu et al. demonstrated significant reductions in pregnancy rates and increased miscarriage rates in patients with hydrosalpinx undergoing IVF-ET compared with those without hydrosalpinx (2). Salpingectomy to remove hydrosalpinx has been shown to improve pregnancy rates (3). However, the ovarian response in IVF cycles subsequent to salpingectomy due to hydrosalpinx remains unclear. Some studies reported a significant decrease in the ipsilateral ovarian response after salpingectomy due to hydrosalpinx (1, 4). On the other hand, there are reassuring data to suggest that ovarian compromise does not occur after salpingectomy (5).

In cases of ectopic pregnancy, salpingectomy is a common operation (6). It may also be performed as

Received March 1, 2016; revised May 23, 2016; accepted May 31, 2016.
S.-H.Y. has nothing to disclose. J.Y.L. has nothing to disclose. S.-N.K. has nothing to disclose. H.W.C. has nothing to disclose. S.Y.P. has nothing to disclose. C.L. has nothing to disclose.
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Fertility and Sterility® Vol. ■, No. ■, ■ 2016 0015-0282/$36.00

http://dx.doi.org/10.1016/j.fertnstert.2016.05.030

prophylaxis against the occurrence of ectopic pregnancy when the fallopian tubes are damaged (7). However, before embarking on such an irreversible treatment in patients with high risk of ectopic pregnancy without hydrosalpinx, the short-term and long-term implications of salpingectomy must be considered. Most women who undergo salpingectomy due to ectopic pregnancy aspire to keep reproductive capability. However, infertility treatment will be inevitable, especially when both salpinges are removed. In this context, it seems important to determine whether salpingectomy harms ovarian function. Nevertheless, the ovarian response in IVF cycles subsequent to salpingectomy due to ectopic pregnancy remains unclear. Lass et al. reported that the ipsilateral ovary could be adversely affected after salpingectomy (8). However, Tal et al. reported that unilateral salpingectomy did not affect ipsilateral ovarian response (9).

The suggested possible mechanisms for ovarian compromise were related to the disruption of common blood supply during surgery, with a consequently negative impact on steroid production and follicular development (1).

The aim of this meta-analysis was to investigate the impact of salpingectomy on ovarian response in patients undergoing IVF treatment, which was assessed as the peak E_2 level, the amount of gonadotropin administered, the number of oocytes retrieved, and the number of pregnancies.

MATERIALS AND METHODS

Search Strategy

Three of the authors of the present study (S.-H.Y., C.M.L., and J.Y.L.) designed the protocol and data extraction forms in accordance with the Preferred Reporting Items for Systematic Review and Meta-analyses guidelines (10, 11). Review and original articles were searched using MEDLINE, PubMed, and EMBASE databases and the Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Library up to July 2015. A combination of the following search terms was used: salpingectomy, ovarian reserve, ovarian response, ovarian function, infertility, and in vitro fertilization. These searches were performed by an accredited clinical librarian. All relevant reports were retrieved, and their reference lists were reviewed manually to identify further studies. A manual search of PubMed for related articles was also performed. No attempt was made to identify unpublished studies unless they had been released as online publications ahead of print. No reports from scientific meetings were included.

Selection Criteria

Criteria for article inclusion were established before the literature search. Inclusion was limited to studies that compared ovarian response and fertility treatment indicators in patients under treatment for infertility, during the cycles before and after treatment by salpingectomy for hydrosalpinx or ectopic pregnancy. There were no additional inclusion or exclusion criteria pertaining to the patient population. Eligible studies were included regardless of the type of fertility treatment and the method of salpingectomy procedure. Case reports and review articles were excluded. Study selection was performed independently by three of the reviewers (S.-H.Y., C.M.L., and J.Y.L.). Any disagreement was resolved unanimously by consultation and discussion with the fourth author (S.-N.K.).

Data Extraction

Two authors scored the studies and collected the information independently. The following data were recorded for each eligible study: demographics (name of the first author, publication year, country, and study period), methodologies (study design, number of patients included, treatment indication, and method of randomization if applicable), and outcomes (peak E_2 levels, amount of gonadotropin administered, number of oocytes retrieved, and pregnancy incidence) measured as a mean difference (MD) or an odds ratio (OR). When discrepancies occurred between the scores of the two investigators, a consensus was reached after discussion or involvement of the third investigator.

Quality Assessment

The quality and risk of bias of the included studies were assessed using the Newcastle-Ottawa scale (NOS) for the assessment of cohort studies and case-control studies, based on the recommendation of the Cochrane Collaboration (12). The NOS criteria include the following three categories: [1] selection, 0–4; [2] comparability, 0–2; and [3] exposure (case-control studies) or outcome (cohort studies), 0–3. Although there is no distinct cutoff to discriminate good studies, a limit of five stars has been suggested to identify studies at low risk of bias (13).

Statistical Analysis

Heterogeneity across studies was examined using I^2, which measures the percentage of total variation across studies (14). Substantial heterogeneity was defined as an I^2 value greater than 50% (15). In the absence of significant heterogeneity, a fixed-effects model was used, and in its presence, a random-effects model was used to estimate the MD and the combined OR for randomized and observational studies. Then a subgroup analysis was conducted for the type of study design (paired or unpaired) and indication of salpingectomy (hydrosalpinx or ectopic pregnancy). The subgroup analysis was planned a priori before data were collected and analyzed.

To evaluate the relationship between follow-up period after salpingectomy and MD of these variables, meta-regression was performed. To evaluate the influence of single studies on the overall estimate, sensitivity analysis was performed. Publication bias was evaluated using the Begg and Mazumdar rank correlation test (16), Egger's test (17), fail-safe N test (18), and Duval and Tweedie's trim-and-fill test (19). A funnel plot was constructed to assess publication bias (20, 21).

Comprehensive Meta-Analysis version 2.0 (Biostat) was used for all statistical tests. $P<.05$ was considered statistically significant for this meta-analysis. Data are presented