Article

Effects on Embryo Transfer in Patients with Hydrosalpinx Pretreated with Different Treatments: A Network Meta-Analysis

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Abstract: Hydrosalpinx can affect the success of embryo transfer (ET). We made a network meta-analysis (NMA) to compare the effects of five hydrosalpinx pretreatments of ET, including salpingectomy, hydrosalpinx aspiration, interventional ultrasound sclerotherapy, proximal tubal occlusion and salpingostomy. This study was based on data-set available from the published studies. The relevant studies were retrieved from Cochrane Library, PubMed and Embase from the inception to January 2017. Data was extracted from cohort studies and the combination of direct and indirect evidence was conducted to assess odds ratio (OR) and surface under the cumulative ranking curves (SUCRA) values of the effects of five hydrosalpinx pretreatments of ET. Thirteen eligible cohort studies were included in this NMA. The results of this NMA demonstrated that compared with the control group (without any treatment), salpingectomy and hydrosalpinx aspiration had comparatively higher ongoing pregnancy rate and implantation rate, interventional ultrasound sclerotherapy had comparatively higher implantation rate. In addition, the cluster analysis revealed that salpingectomy and interventional ultrasound sclerotherapy had better effects on ET. Taken together, this NMA suggested that salpingectomy and interventional ultrasound sclerotherapy had better effects on embryo transfer in patients with hydrosalpinx.

Keywords: hydrosalpinx; embryo transfer; effects; cohort study; Bayesian network model

1. Introduction

Hydrosalpinx, as a chronic condition of ampullary dilation of the fallopian tube, which fills with water or fluid, occurs frequently in tubal diseases that are a common cause of female infertility [1,2]. Most commonly it is caused by primary ovarian malignancy with fallopian tube involvement or primary fallopian tube carcinoma [3]. About 40% of female infertility is tubal infertility, and it is the most common indication for in vitro fertilization and embryo transfer (IVF-ET). Approximately 10–30% of women with tubal infertility seeking IVF treatment have hydrosalpinx [4]. Hydrosalpinx adversely affects endometrial receptivity and oocyte quality as it affects impaired endometrial and ovarian blood flows [5]. The association of hydrosalpinx with decreased pregnancy and implantation rates in IVF cycles has been confirmed by overwhelming scientific evidence [6,7]. Since the detrimental effect of hydrosalpinges on the outcome of IVF-ET has been well proved, some prophylactic treatments before IVF-ET have been proposed, such as salpingectomy, hydrosalpinx aspiration, interventional ultrasound sclerotherapy, proximal tubal occlusion and salpingostomy, etc. However, there is still a controversy for the best pretreatment of hydrosalpinx before IVF-ET.

In 2016, a study investigated the impact of salpingectomy in the patients with IVF treatment on the ovarian response, and found that salpingectomy in infertile patients with hydrosalpinx or ectopic pregnancy does not have any negative effect on their subsequent fertility treatment [8]. However, Tarek et al. found that prophylactic salpingectomy in women with hydrosalpinx had reproductive risks and it could affect pregnancy rates [9]. Furthermore, Chu et al. answered the question: What is the chance of natural conception when salpingostomy is used to treat hydrosalpinx? They made a systematic review and suggested that salpingostomy is an alternative treatment strategy to tubal clipping or salpingectomy in patients presenting to fertility services with hydrosalpinx [10]. A random-effect NMA compared the effectiveness of surgical treatments for hydrosalpinx before IVF-ET, and found that proximal tubal occlusion, salpingectomy and hydrosalpinx aspiration for the treatment of patients with IVF-ET scored consistently better than those who received no treatment. Proximal tubal occlusion appeared to be the most effective intervention, followed by salpingectomy [11]. Zhou et al. investigated whether hydrosalpinx aspiration during oocyte retrieval could improve the clinical outcome of in vitro
fertilization-embryo transfer (IVF-ET), and then found that the aspiration of hydrosalpinx occurring during controlled ovarian hyperstimulation can significantly improve the clinical outcomes of IVF-ET, but is not beneficial for the hydrosalpinx occurring before controlled ovarian hyperstimulation [12]. A research has compared three treatments prior to IVF-ET in patients with hydrosalpinx, including ultrasound sclerotherapy, hydrosalpinx aspiration, bilateral salpingectomy. The results revealed that there is no significant difference between ultrasound sclerotherapy group and bilateral salpingectomy group in terms of the rates of embryo implantation, biochemical pregnancy, clinical pregnancy, multiple pregnancy and early abortion, whereas the rates of embryo implantation, biochemical pregnancy, and clinical pregnancy in hydrosalpinx aspiration group are significantly lower than those in the other two groups, and in hydrosalpinx aspiration group, the rate of early abortion is relative higher than that in the other two groups [4].

Although there are a lot of studies discussing the clinical outcomes of treatments in patients with hydrosalpinx, there is no comprehensive comparison for the pretreatment of hydrosalpinx in patients undergoing IVF-ET. Thus, in the current study, we used multiple-treatments meta-analysis, also known as mixed-treatment comparisons meta-analysis or network meta-analysis, which allows the integration of data from direct and indirect comparisons, to compare the effects of five treatments prior to IVF-ET in patients with hydrosalpinx. Simultaneously, we aimed to provide a clinically useful summary of the results from the multiple-treatments meta-analysis that can be used to guide treatment decisions.

2. Materials and Methods

2.1. Literature Search

An electronic search of English databases such as Cochrane Library, PubMed and Embase for articles published from the inception to January 2017 was performed, from which we searched the targeted references manually with the principle of combination of key words and free words. The search terms included hydrosalpinx, IVF-ET, salpingectomy, proximal tubal occlusion, cohort study, etc.

2.2. Inclusion and Exclusion Criteria

The inclusion criteria were: (1) cohort studies; (2) interventions: control (without any treatment), salpingectomy, hydrosalpinx aspiration, interventional ultrasound sclerotherapy, proximal tubal occlusion and salpingostomy; (3) study subjects were women aged 20–40 years with hydrosalpinx and undergoing embryo transfer; (4) outcome indicators including ongoing pregnancy rate, clinical pregnancy rate, implantation rate, ectopic pregnancy rate or abortion rate. The exclusion criteria were: patients with presence of any other known cause of infertility or abortion, patients contraindicated for hormone therapy, patients with acute cervicitis, studies with insufficient data integrity, non-cohort studies, duplicate publications or studies, case reports, systematic reviews, summaries, and non-English studies.

2.3. Data Extraction and Quality Assessment

Search for suitable literature, extraction of data and assessment of study quality was performed independently by two investigators, and disagreements were resolved by seeking advice from professional persons. More than two reviewers independently assessed the methodological quality of the included studies based on the Newcastle-Ottawa Scale(NOS) [13], and the standards of NOS were as follows: (1) cohort selection: representativeness of the exposed cohort (NOS1), the non-exposed cohort drawn from the same community or a different source (NOS2), secure record or structured interview (NOS3), demonstration that outcome of interest was not present at start of study (NOS4); (2) cohort comparability: study controls for selecting the most important factor (NOS5), study controls for any additional factor (NOS6); (3) cohort outcome: independent and blind assessment (NOS7); was follow-up long enough for outcomes to occur (NOS8); all subjects were accounted for complete follow-up or subjects lost to follow up unlikely to introduce bias (NOS9). The total scores of NOS were 9 points, and more than 5 points can be included in the meta-analysis.

2.4. Statistical Analysis

Firstly, we adopted traditional pairwise meta-analysis to perform a direct comparison of various kinds of treatment arms. Heterogeneity among the studies was tested by Chi-square test and I-square test [14]. Secondly, R 3.2.1 was used for drawing network diagrams. In the diagram, each node represented each intervention, the node size represented the sample size, and the line thickness between nodes represented the study numbers. Thirdly, we did a comparison of different interventions using Bayesian network meta-analysis. The basis of each analysis was non-informative priors to gain effect sizes and precision. After four chains and a 20,000-simulation burn-in stage, convergence, and lack of auto-correlation were examined and confirmed. Finally, direct probability statements were come from an additional 50,000-simulation stage [15]. We used the node-splitting method to estimate the consistency between direct and indirect evidence, then chose the consistency model or inconsistency model based on the result, the consistency model was applied if \( P > 0.05 \) [16]. To get a better interpretation of ORs, the probability of every intervention was calculated to identify the most effective methods based on a Bayesian approach employing probability values summarized as the surface under the
cumulative ranking curve (SUCRA). The larger the SUCRA value is, the better the rank of the intervention is [17,18]. Cluster analyses were performed to group the treatments according to their similarity with regard to both outcomes [17]. R (V.3.2.1) package gmeta (V.0.6) as well as the Markov Chain Monte Carlo engine Open BUGS (V.3.4.0) were used for doing all computations.

3. Results
3.1. Baseline Characteristics of Included Studies

At first, 869 potential articles were retrieved from the electronic databases. Among of these articles, 42 studies were duplicates and thus removed. After screening the title and abstract, 198 irrelevant studies were excluded specifically for being letters or reviews (n= 35), non-human studies (n = 75), non-English studies (n = 88). Next, 319 studies were excluded after more detailed full text assessment: studies those were not cohort study accounted for 136, unrelated to ET or hydrosalpinx were 265 and 214, respectively. One additional study was removed after further assessment due to lack of integrity in data presentation. Finally, thirteen cohort studies, published between 1997 and 2016, were selected for analysis in the current NMA study [4,19–30] (Supplementary Figure 1). A total of 1,659 patients undergoing ET with hydrosalpinx were included in this study. Among them, the number of patients treated by salpingectomy was relatively large (Figure 1). Among all the included studies, subjects of seven studies were Caucasians, four studies were Asians, two were Africans, and 2 were three-arm trails, 11 were two-arm trails. Baseline characteristics of the included studies were summarized in Supplementary Table 1. The NOS risk of bias assessment for all included studies was shown in Supplementary Figure 2.

![Network evidence diagrams for different hydrosalpinx treatments in patients undergoing ET.](image)

**Figure 1.** Network evidence diagrams for different hydrosalpinx treatments in patients undergoing ET. a, NMA study of the number of patients in terms of ongoing pregnancy rate. b, NMA study of the number of patients in terms of clinical pregnancy rate (per transfer cycle). c, NMA study of the number of patients in terms of clinical pregnancy rate (per embryo transferred). d, NMA study of the number of patients in terms of clinical pregnancy rate (per included patients). e, NMA study of the number of patients in terms of implantation rate. f, NMA study of the number of patients in terms of ectopic pregnancy rate (per included patients). g, NMA study of the number of patients in terms of ectopic pregnancy rate (per embryo transferred). h, NMA study of the number of patients in terms of abortion rate. IUP = intrauterine pregnancy.
3.2. Pairwise Meta-Analysis of Five Pretreatments of ET in Patients with Hydrosalpinx

Compared with the control group, salpingectomy brought higher ongoing pregnancy rate and clinical pregnancy rate in patients with hydrosalpinx undergoing ET (OR = 12.46, 95%CI = 1.51-103.05; OR = 7.43, 95%CI = 1.49-36.93, respectively), hydrosalpinx aspiration group had higher ongoing pregnancy rate, clinical pregnancy rate and implantation rate (OR = 10.67, 95%CI = 1.22-93.13; OR = 2.60, 95%CI = 1.23-5.50; OR = 2.09 95%CI = 1.25-3.49, respectively), and interventional ultrasound sclerotherapy had comparatively higher clinical pregnancy rate (OR = 15.57, 95%CI = 1.90-130.54). Compared with salpingectomy group, hydrosalpinx aspiration group had relatively lower clinical pregnancy rate (OR = 0.39, 95%CI = 0.22-0.69) and implantation rate (OR = 0.53, 95%CI = 0.37-0.74), and its’ abortion rate (OR = 2.95, 95%CI = 1.10-7.90) was relatively high (Table 1).

### Table 1. Estimated OR and 95%CI from pairwise meta-analysis of eight endpoints.

| Included studies | Comparisons               | Efficacy events | Pairwise meta-analysis |
|------------------|---------------------------|-----------------|------------------------|
|                  |                          | Ongoing pregnancy rate (per transfer cycle) |                     |
|                  |                           | Treatment1      | Treatment2             | OR (95% CI)      |
| 2 studies        | E VS. B                   | 26/123          | 45/107                 | 0.42 (0.19-0.93) |
| 1 study          | C VS. B                   | 19/76           | 29/75                  | 0.53 (0.26-1.06) |
| 1 study          | B VS. A                   | 23/47           | 1/14                   | **12.46 (1.51-103.05)** |
| 1 study          | E VS. A                   | 17/45           | 1/14                   | 7.89 (0.95-65.85) |
| 1 study          | C VS. A                   | 8/26            | 1/25                   | **10.67 (1.22-93.13)** |
|                  |                           | Clinical pregnancy rate |                     |
|                  |                           | C VS. B         | 22/76                  | 32/75             | 0.55 (0.28-1.07) |
|                  |                           | D VS. B         | 23/60                  | 17/43             | 0.95 (0.43-2.12) |
|                  |                           | D VS. A         | 15/35                  | 1/22              | **15.75 (1.90-130.54)** |
|                  |                           | B VS. A         | 38/107                 | 21/77             | 1.47 (0.78-7.28) |
|                  |                           | C VS. A         | 8/26                   | 2/25              | 5.11 (0.96-27.09) |
|                  |                           | per embryo transferred |                     |
|                  |                           | C VS. B         | 30/109                 | 53/108            | **0.39 (0.22-0.69)** |
|                  |                           | D VS. B         | 111/265                | 53/108            | 0.75 (0.48-1.17) |
|                  |                           | D VS. C         | 111/265                | 30/109            | **1.90 (1.17-3.09)** |
|                  |                           | B VS. A         | 26/47                  | 2/14              | 7.43 (1.49-36.93) |
|                  |                           | E VS. A         | 20/45                  | 2/14              | 4.80 (0.96-23.97) |
|                  |                           | E VS. B         | 27/60                  | 42/75             | 0.65 (0.33-1.29) |
|                  |                           | per included patient |                   |
|                  |                           | E VS. B         | 13/42                  | 25/43             | 0.55 (0.28-1.07) |
|                  |                           | F VS. B         | 102/178                | 146/269           | 1.13 (0.77-1.66) |
|                  |                           | C VS. A         | 27/86                  | 13/87             | **2.60 (1.23-5.50)** |
|                  |                           | B VS. A         | 40/116                 | 22/88             | 1.58 (0.85-2.92) |
|                  |                           | Implantation rate (per embryo transferred) |                     |
|                  |                           | C VS. B         | 65/439                 | 108/435           | **0.53 (0.37-0.74)** |
|                  |                           | D VS. B         | 152/591                | 72/245            | 0.83 (0.60-1.16) |
|                  |                           | E VS. A         | 30/172                 | 56/185            | **0.47 (0.25-0.87)** |
|                  |                           | D VS. C         | 152/591                | 40/244            | **1.77 (1.20-2.60)** |
|                  |                           | C VS. A         | 55/443                 | 24/379            | **2.09 (1.25-3.49)** |
|                  |                           | B VS. A         | 58/257                 | 29/165            | 1.33 (0.80-2.21) |
|                  |                           | E VS. A         | 2/45                   | 1/14              | 0.60 (0.05-7.22) |
|                  |                           | per included patient |                   |
|                  |                           | E VS. B         | 1/42                   | 1/43              | 1.02 (0.06-16.93) |
|                  |                           | F VS. B         | 12/178                 | 28/269            | 0.62 (0.31-1.26) |
|                  |                           | C VS. A         | 2/86                   | 2/87              | 1.02 (0.14-7.43) |
|                  |                           | B VS. A         | 2/116                  | 2/88              | 0.75 (0.10-5.46) |
|                  |                           | per embryo transferred |                   |
|                  |                           | E VS. B         | 2/123                  | 2/107             | 0.89 (0.12-6.47) |
|                  |                           | D VS. B         | 2/56                   | 1/41              | 1.48 (0.13-16.91) |
|                  |                           | C VS. A         | 2/360                  | 3/160             | 0.95 (0.43-2.12) |
|                  |                           | B VS. A         | 1/47                   | 1/14              | 0.28 (0.02-4.83) |
|                  |                           | E VS. A         | 1/45                   | 1/14              | 0.30 (0.02-5.06) |
|                  |                           | Abortion rate (n/IUP) |               |
|                  |                           | C VS. B         | 12/52                  | 8/85              | **2.95 (1.10-7.90)** |
|                  |                           | D VS. B         | 16/111                 | 5/53              | 1.62 (0.56-4.68) |
|                  |                           | D VS. C         | 16/111                 | 9/30              | 0.39 (0.15-1.01) |
|                  |                           | E VS. B         | 4/87                   | 4/90              | 1.03 (0.22-4.45) |
|                  |                           | F VS. B         | 7/178                  | 20/269            | 0.51 (0.21-1.23) |
|                  |                           | C VS. A         | 6/31                   | 4/13              | 0.58 (0.12-2.66) |
|                  |                           | B VS. A         | 9/83                   | 6/33              | 0.63 (0.20-2.02) |
|                  |                           | E VS. A         | 2/45                   | 1/14              | 0.60 (0.05-7.22) |

Notes: OR = odds ratios; 95%CI = 95% confidence intervals; IUP = intrauterine pregnancy; A = control; B = salpingectomy; C = hydrosalpinx aspiration; D = interventional ultrasound sclerotherapy; E = proximal tubal occlusion; F = salpingostomy.
3.3. Inconsistency Test of Five Pretreatments of ET in Patients with Hydrosalpinx

The inconsistency tests of ongoing pregnancy rate, clinical pregnancy rate and abortion rate were performed by the node-splitting method. The results showed no inconsistencies among the studies concerning the results of the direct and indirect evidence of all outcomes (all \( P > 0.05 \)). Therefore, the consistency model was applied (Figure 2).

![Figure 2](image_url)

**Figure 2.** Node-splitting graphs for different hydrosalpinx treatments in patients undergoing ET. **a.** The inconsistency test of ongoing pregnancy rate. **b.** The inconsistency test of clinical pregnancy rate. **c.** The inconsistency test of abortion rate. \( A = \) control; \( B = \) salpingectomy; \( C = \) hydrosalpinx aspiration; \( D = \) interventional ultrasound sclerotherapy; \( E = \) proximal tubal occlusion; \( F = \) salpingostomy. IUP = intrauterine pregnancy.

3.4. The Main Results of Network Meta-Analysis

The results of this NMA demonstrated that compared with the control group, the salpingectomy and hydrosalpinx aspiration groups had higher ongoing pregnancy rate (OR = 25.89, 95%CI = 2.99-382.84; OR = 13.88, 95%CI = 1.46-215.61, respectively); hydrosalpinx aspiration and interventional ultrasound sclerotherapy created higher implantation rate (OR = 3.17, 95%CI = 1.35-9.16; OR = 2.12, 95%CI = 1.02-5.05; OR = 4.46, 95%CI = 1.57-20.47, respectively); but when it comes to clinical pregnancy rate, ectopic pregnancy rate and abortion rate, there was no difference between the five hydrosalpinx treatments in the effects on the result of ET (Figure 3; Table 2a,b).

![Figure 3](image_url)

**Figure 3.** Relative relationship forest plots for different hydrosalpinx treatments in patients undergoing ET. **a.** Ongoing pregnancy rate in after treatments of salpingectomy, hydrosalpinx aspiration and interventional ultrasound sclerotherapy. **b.** Implantation rate in after treatments of salpingectomy, hydrosalpinx aspiration and interventional ultrasound sclerotherapy; \( A = \) proximal tubal occlusion.
Table 2a. OR and 95% confidence intervals of six treatment modalities of four endpoint outcomes.

|                          | OR (95% CI)                      |
|--------------------------|----------------------------------|
| **Ongoing pregnancy rate** |                                   |
| (per transfer cycle)     |                                  |
| A                        | 2.59 (2.99, 3.82)                 |
| 0.04 (0.00, 0.33)         | B 0.54 (0.08, 4.07)               |
| 0.07 (0.00, 0.68)         | C 0.77 (0.06, 7.68)               |
| 0.10 (0.01, 1.06)         | D 1.30 (0.13, 16.00)              |
| **Clinical pregnancy rate** |                                   |
| (per transfer cycle)     |                                  |
| A                        | 3.87 (0.48, 46.02)                |
| 0.26 (0.02, 2.09)         | B 0.78 (0.06, 10.59)              |
| 0.33 (0.02, 3.41)         | C 2.26 (0.09, 60.51)              |
| 0.15 (0.01, 1.47)         | D 0.44 (0.02, 11.08)              |
| **Clinical pregnancy rate** |                                   |
| (per embryo transferred) |                                  |
| A                        | 8.99 (0.83, 106.86)               |
| 0.11 (0.01, 2.12)         | B 0.39 (0.05, 3.02)               |
| 0.28 (0.01, 6.13)         | C 1.90 (0.27, 14.03)              |
| 0.15 (0.01, 3.16)         | D 0.84 (0.07, 10.18)              |
| 0.17 (0.01, 1.87)         | E 1.20 (0.10, 14.83)              |
| **Clinical pregnancy rate** |                                   |
| (per included patient)   |                                  |
| A                        | 1.55 (0.37, 6.38)                 |
| 0.65 (0.16, 2.72)         | B 1.70 (0.29, 10.78)              |
| 0.38 (0.11, 1.13)         | C 0.19 (0.02, 1.90)               |
| 2.00 (0.27, 15.60)        | D 3.54 (0.48, 26.36)              |
| 0.58 (0.08, 3.99)         | E 0.28 (0.04, 2.07)               |

Notes: Odds ratios and 95% confidence intervals below the treatments should be read from row to column while above the treatments should be read from column to row. OR = odds ratio; 95%CI = 95% confidence intervals; A = control; B = salpingectomy; C = hydrosalpinx aspiration; D = interventional ultrasound sclerotherapy; E = proximal tubal occlusion; F = salpingostomy.

Table 2b. OR and 95% confidence intervals of six treatment modalities of four endpoint outcomes.

|                          | OR (95% CI)                      |
|--------------------------|----------------------------------|
| **Implantation rate**    |                                   |
| (per embryo transferred) |                                  |
| A                        | 3.17 (1.35, 9.16)                 |
| 0.32 (0.11, 0.74)        | B 0.67 (0.26, 1.64)               |
| 0.47 (0.20, 0.98)        | C 2.11 (0.70, 8.65)               |
| 0.22 (0.05, 0.64)        | D 0.35 (0.07, 1.62)               |
| 0.64 (0.15, 2.14)        | E 2.85 (0.62, 15.35)              |
| **Ectopic pregnancy rate** |                                   |
| (per included patient)   |                                  |
| A                        | 0.76 (0.07, 7.07)                 |
| 1.32 (0.12, 14.30)       | B 1.11 (0.05, 29.84)              |
| 1.12 (0.10, 14.37)       | C 1.00 (0.01, 92.48)              |
| 1.17 (0.01, 76.72)       | D 0.50 (0.02, 17.60)              |
| 2.27 (0.18, 26.52)       | E 0.99 (0.96, 58.14)              |
| **Ectopic pregnancy rate** |                                   |
| (per embryo transferred) |                                  |
| A                        | 0.36 (0.01, 24.45)                |
| 2.80 (0.04, 169.55)      | B 0.45 (0.00, 73.80)              |
| 6.11 (0.32, 403.25)      | C 5.17 (0.01, 6486.22)            |
| 1.51 (0.00, 341.80)      | D 0.47 (0.00, 54.35)              |
| 3.22 (0.04, 178.42)      | E 2.14 (0.02, 326.28)             |
| **Abortion rate**        |                                   |
| (m/IUP)                  |                                  |
| A                        | 0.38 (0.14, 1.54)                 |
| 2.61 (0.65, 7.35)        | B 2.38 (0.70, 6.76)               |
| 1.09 (0.28, 3.85)        | C 0.54 (0.13, 2.35)               |
| 2.08 (0.32, 10.39)       | D 0.95 (0.12, 9.24)               |
| 2.01 (0.25, 12.32)       | E 0.43 (0.04, 3.40)               |
| 5.48 (0.66, 33.15)       | F 2.30 (0.29, 21.93)              |

Notes: Odds ratios and 95% confidence intervals below the treatments should be read from row to column while above the treatments should be read from column to row. OR = odds ratio; 95%CI = 95% confidence intervals; IUP = intrauterine pregnancy; A = control; B = salpingectomy; C = hydrosalpinx aspiration; D = interventional ultrasound sclerotherapy; E = proximal tubal occlusion; F = salpingostomy.
3.5. SUCRA Values of Five Pretreatments of ET in Patients with Hydrosalpinx

The SUCRA values of 5 pretreatments are summarized in Table 3. The SUCRA curves indicated that compared with ongoing pregnancy rate (per transfer cycle) and clinical pregnancy rate (per embryo transferred), salpingectomy had the highest SUCRA value (92.8% and 86.8%, respectively). As for clinical pregnancy rate (per transfer cycle) and implantation rate (per embryo transferred), interventional ultrasound sclerotherapy had the highest SUCRA value (85.0% and 91.8%, respectively). Compared with clinical pregnancy rate (per included patient) and ectopic pregnancy rate (per embryo transferred), hydrosalpinx aspiration had the highest SUCRA value (87.0% and 76.4%, respectively). Relative to ectopic pregnancy rate (per included patient) and abortion rate(n/IUP), salpingostomy had the highest SUCRA value (79.0% and 90.2%, respectively).

Table 3. SUCRA values of six treatment modalities under eight endpoint outcomes.

| SUCRA values (%) | Treatments | A | B | C | D | E | F |
|------------------|------------|---|---|---|---|---|---|
| Ongoing pregnancy rate (per transfer cycle) | 26 | 92.8 | 70.8 | NR | 61.3 | NR |
| Clinical pregnancy rate (per transfer cycle) | 31.8 | 70 | 62.8 | 85 | NR | NR |
| Clinical pregnancy rate (per embryo transferred) | 27 | 86.8 | 48 | 72.8 | 65.6 | NR |
| Clinical pregnancy rate (per included patient) | 45.2 | 67.6 | 87 | NR | 27.4 | 72.6 |
| Implantation rate (per embryo transferred) | 25 | 80.2 | 58 | 91.8 | 44.8 | NR |
| Ectopic pregnancy rate (per included patient) | 51.2 | 56.4 | 57.8 | NR | 56.4 | 79 |
| Ectopic pregnancy rate (per embryo transferred) | 42.4 | 63.8 | 76.4 | 52 | 65.2 | NR |
| Abortion rate(n/IUP) | 32.8 | 70.5 | 34.7 | 60.3 | 60.5 | 90.2 |

Notes:  SUCRA = surface under the cumulative ranking curves; NR = not report; IUP = intrauterine pregnancy; A = control; B = salpingectomy; C = hydrosalpinx aspiration; D = interventional ultrasound sclerotherapy; E = proximal tubal occlusion; F = salpingostomy.

3.6. Cluster Analysis of Five Pretreatments of ET in Patients with Hydrosalpinx

The cluster analysis revealed that salpingectomy and interventional ultrasound sclerotherapy had comparatively better effects on ET in the pretreatment of hydrosalpinx (Figure 4a–d).

Figure 4. Cluster analyses of different hydrosalpinx treatments in patients undergoing ET. a, A cluster analysis of patients with hydrosalpinx in terms of ongoing pregnancy rate. b, A cluster analysis of patients with hydrosalpinx in terms of
clinical pregnancy rate (per transfer cycle). c. A cluster analysis of patients with hydrosalpinx in terms of clinical pregnancy rate (per embryo transferred). d. A cluster analysis of patients with hydrosalpinx in terms of clinical pregnancy rate (per included patient). IUP = intrauterine pregnancy; A = control; B = salpingectomy; C = hydrosalpinx aspiration; D = interventional ultrasound sclerotherapy; E = proximal tubal occlusion; F = salpingostomy.

4. Discussion

The presence of hydrosalpinges in women has widely been considered as an adverse prognostic factor for IVF-ET outcome, reducing the implantation and pregnancy rates. Several previous studies have demonstrated that hydrosalpinx fluid may act directly on the ET [31–34]. What is the best choice for the pretreatments of hydrosalpinx prior to IVF-ET has always been a controversial issue. Hence, we conducted this network meta-analysis to compare the clinical outcomes of salpingectomy, hydrosalpinx aspiration, interventional ultrasound sclerotherapy, proximal tubal occlusion and salpingostomy in the treatment of hydrosalpinx before IVF-ET, and we found that salpingectomy and interventional ultrasound sclerotherapy had better effects on embryo transfer in patients with hydrosalpinx.

Firstly, pairwise meta-analysis were performed to directly compare five different pretreatments of hydrosalpinx before IVF-ET, and we found that compared with the control group, salpingectomy group had higher ongoing pregnancy rate and clinical pregnancy rate in patients with hydrosalpinx, and hydrosalpinx aspiration group had higher ongoing pregnancy rate, clinical pregnancy rate and implantation rate, and interventional ultrasound sclerotherapy had comparatively higher clinical pregnancy rate. Sharara and McClamrock suggested that cryopreservation of embryos and subsequent transfer after salpingectomy is the best management option for a subgroup of patients [35]. Aboulghar et al. reported that the aspiration of hydrosalpingeal fluid resulted in increased ovarian response and a significant increase in the number of embryos per transfer. The pregnancy rate was higher in the group of patients who had their hydrosalpinges aspirated, but this difference failed to reach a statistical significance [36]. Another study has proved that ultrasound sclerotherapy could improve IVF-ET outcomes of the women with hydrosalpinx by improving the blood flow of the uterine arcuate artery, and had no adverse effect on ovarian responsiveness and perinatal outcomes [37].

Secondly, the results of network meta-analysis further indicated that compared with the control group, salpingectomy group and hydrosalpinx aspiration group had relatively higher ongoing pregnancy rate and implantation rate; interventional ultrasound sclerotherapy group had higher implantation rate. Several studies had suggested that patients who underwent salpingectomy showed no impairment of ovulation stimulation variables in retrospective [33,38–41]. There was also a study finding that aspiration of hydrosalpinx at the time of oocyte retrieval could improve pregnancy rates and may be an acceptable alternative to salpingectomy and thought that aspiration of hydrosalpinx was a safe treatment for improving IVF outcomes [29]. A previous clinical study showed that interventional ultrasound sclerotherapy before IVF was a very effective and acceptable prophylactic intervention alternative to salpingectomy for patients with hydrosalpinx [24]. As evidenced by another study, compared with no intervention, hydrosalpinx aspiration contributed to increased clinical pregnancies rates but a similar miscarriage rate, which suggested that sclerotherapy prior to IVF could improve the fertility outcome and serve as an alternative to salpingectomy [42].

Thirdly, salpingectomy, interventional ultrasound sclerotherapy and salpingostomy were ranked comparatively higher with respect to SUCRA values, and the cluster analysis had further confirmed that salpingectomy and interventional ultrasound sclerotherapy had better effects on dealing with hydrosalpinx prior to IVF-ET. The results of SUCRA and cluster analysis were consistent with our study.

6. Conclusions

However, there are still some limitations in our study. Specifically, there was difference among the number of the included studies of the 5 interventions paired comparison, and then sample size among the included studies was different, which may impact our results. But, to make our study more reliable, we performed a cluster analysis of the eight outcome measures to draw a conclusion. Moreover, in this study, a comprehensive comparison of salpingectomy, hydrosalpinx aspiration, interventional ultrasound sclerotherapy, tubal occlusion and salpingostomy proximal in the treatment of hydrosalpinx before IVF-ET had been performed, so it has a certain clinical significance. On the basis of our results, we concluded that salpingectomy and interventional ultrasound sclerotherapy had better effects on embryo transfer in patients with hydrosalpinx. However, there is a need for further study as these interventions continue to evolve and are improved in the treatment of hydrosalpinx.

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