

Comparison Between Hysteroscopic Proximal Tubal Occlusion Versus Laparoscopic Salpingectomy on Pregnancy Rates Following Intracytoplasmic Sperm Injection in Infertile Cases of Hydrosalpinx: Controlled Clinical Trial

Original
Article

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ABSTRACT

Introduction: Tubal Factor of infertility resulting from various forms of subperitoneal damage remains a widespread cause of female infertility, accounting for more than 35% of all cases of female infertility. Probably the most severe form of tubal pathology is hydrosalpinx.

Objective: To assess and compare pregnancy outcomes in hydrosalpinx patients treated by hysteroscopic tubal occlusion and laparoscopic salpingectomy before IVF.

Material and Methods: A controlled, clinical trial between January 2020 to December 2020 was conducted, including a total of 78 women, of whom 39 were assigned to hysteroscopic proximal occlusion, and 39 were assigned to laparoscopic salpingectomy.

Results: 27/39 (69.2%) of patients who were operated upon by laparoscopic salpingectomy (LS) showed positive qualitative blood HCG test, while only 16/39 (41%) of those who were operated upon by hysteroscopic tubal occlusion (HPTO) showed positive qualitative blood HCG test, the difference in percentages of positive primary outcome between patients operated upon by LS and HPTO are statistically significant ($X^2=6.271$, $P<0.05$, $RR=1.688$, $CI(1.097-2.596)$). So we rejected the Null hypothesis of our research question that suggested that HPTO is of no difference in the pregnancy outcomes compared with Laparoscopic Salpingectomy (LS). Besides, we found that 24/39 (61.25%) of patients who underwent LS showed positive fetal heart sounds at eight weeks, versus 15/39 (38.5%) of those who underwent HPTO. The difference in Fetal heart sounds in 8 weeks between patients underwent LS and HPTO is statistically significant ($X^2=4.154$, $P<0.05$, $RR=1.6$, $CI(1.002-2.56)$).

Conclusion: Laparoscopic salpingectomy (LS) is superior to Hysteroscopic tubal occlusion (HTPO) in terms of fetal heart sounds at eight weeks and higher pregnancy rate following IVF/ICSI upon adjusting the age and infertility status as confounders.

Key Words: Hysteroscopic tubal occlusion, IVF/ICSI, laparoscopic salpingectomy.

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INTRODUCTION

Infertility affects around a 13% of all women and 10% of all males. The most prevalent cause of female infertility is tubal factor infertility, which is one of the several forms of tubo-peritoneal damage. More than 35 per cent of all instances of female infertility are caused by it^[1,2].

After 12 months of frequent and unprotected sexual intercourse, infertility is defined as the inability to achieve a clinical pregnancy. It is believed that between 8% and 12% of reproductive-aged couples in the globe are affected. Males are reported to be primarily responsible for 20–30% of infertility cases, although they also contribute

to 50% of all cases. Secondary infertility is the most prevalent kind of female infertility, which is caused by infections in the reproductive system^[3-5]. Female infertility represents approximately 65% of the overall causes for infertile couples. The major causes of female infertility are anovulation, fallopian tube disease, pelvic adhesions, endometriosis, and unexplained infertility^[6,7].

Women with hydrosalpinges have lower implantation and pregnancy rates due to a combination of mechanical and chemical factors thought to disrupt the endometrial environment. Evidence suggests that the presence of hydrosalpinx reduces the rate of pregnancy with assisted reproductive technology^[8,9].

The aim of this research is to assess and compare pregnancy outcomes in hydrosalpinx patients treated by hysteroscopic tubal occlusion and laparoscopic salpingectomy before IVF.

SUBJECTS AND METHODS

The study was carried out in the Kasr Al Ainy Hospital, Cairo University, and patients were recruited from the outpatient clinic.

Clinical trial registration: NCT04335864.

The study

Started from March 2020 to –November 2020.

All patients were subjected to the following steps before including them in the study:

Full medical history, general examination, local examination, per vaginal and bimanual examination for any tenderness, discharge, anomalies, detection of the size of the uterus, cervical mobility and any cervical or adnexal masses or tenderness and Speculum examination for inspection of the cervix and visualization of the discharge.

Hysterosalpingography (HSG)

Recent hysterosalpingography was done within the last six months showing unilateral or bilateral fallopian tube dilatation with or without decreased contrast in the peritoneal cavity.

Transvaginal ultrasonography (mid-cycle) was performed. The uterus was scanned in the sagittal plane for detection of any endometrial abnormality, visible hydrosalpinx.

The patients were included in the study according to the following inclusion and exclusion criteria.

Inclusion criteria

Age of participants was between 18 and 40 years, Primary or secondary fertility, Diagnosis of unilateral or bilateral hydrosalpinx; diagnosed by HSG and Transvaginal U/S

Exclusion criteria

Patients with uterine factor infertility, male factor infertility, Medical or surgical conditions contraindicating pregnancy, Cases diagnosed with pre-existing ovarian pathology and Cases harbouring septic foci.

Randomization and allocation

Participants were assigned 1:1 hysteroscopic tubal occlusion (HPTO) and laparoscopic salpingectomy (LS) using simple randomization allocation. Two groups were generated: Group 1: 39 patients were operated upon by laparoscopic salpingectomy, Group 2: 39 patients were operated upon by hysteroscopic tubal occlusion.

IVF/ICSI

Patients started their IVF/ICSI treatment after four weeks after the treatment of their hydrosalpinges. IVF/ICSI was performed according to the protocol of Cairo University. Pituitary down-regulation could be achieved by the administration of GnRH agonists or GnRH antagonists. Doses of administration were noted. As well as the number of retrieved oocytes. Fertilization method and quality of transferred embryos.

Outcome measurement

The primary outcome was the Qualitative beta HCG test. The secondary outcome was ongoing pregnancy which was defined as the fetal heartbeat on ultrasound beyond 8-week gestation.

Sample size calculations

To calculate the sample size required, we used the standard power calculation for non-inferiority trials. According to literature⁵, we assumed that the pregnancy rate for the intervention group (HPTO) was 0.49, and the pregnancy rate of the control group (LS) was 0.51 with a non-inferiority margin 10%. The calculated sample size resulted in 39 patients in each group ($\alpha:0.025$ and $\beta:0.80$).

Ethical considerations

The study was approved by the Ethics Committee of the Faculty of Medicine, Cairo University, The researcher complied with International Guidelines for Research Ethics, An informed written consent was obtained from all patients enrolled in the study after explanation of the purpose and benefits of research and Autonomy and confidentiality were assured and maintained.

RESULTS

Patients recruited to the study according to the inclusion and exclusion criteria were 78 patients. Their age ranged between 25 to 40 years old; besides, all patients were either unilateral or bilateral hydrosalpinges identified on hysterosalpingography and vaginal ultrasonography, fifty-seven patients 72.2% of them had primary infertility status and 21 patients (26.6%) had secondary infertility status, (Table 1).

Table 1: Distribution of Age group, Infertility Status

| | | Frequency (n) | Percentage |
|--------------------|-----------|---------------|------------|
| Age Groups | 25-29 | 22 | 27.8% |
| | 30-34 | 29 | 36.7% |
| | 35-40 | 27 | 34.6% |
| Infertility Status | Primary | 57 | 72.2% |
| | Secondary | 21 | 26.6% |

Regarding the mean of age in the pregnancy outcomes groups ; the difference between patients who had positive and negative pregnancy test and positive and negative fetal heart sound at eight weeks' test was not statistically significant ($P>0.05$) (Table 2).

Table 2: Comparing Mean of Age in the Pregnancy Outcomes groups

| | Pregnancy test | | | Fetal heartbeat | | |
|----------------------|-----------------|------------------|----------------|-----------------|------------------|----------------|
| | Positive | Negative | <i>p-value</i> | Positive | Negative | <i>p-value</i> |
| N | 43 | 35 | | 39 | 39 | |
| Age Mean (\pm SD) | 32(\pm 3.99) | 33.2(\pm 4.6) | *0.203 | 32.1(\pm 4) | 32.9(\pm 4.6) | *0.403 |

The Correlation between Type of Infertility and the Pregnancy Outcomes It was found that there was no significant correlation between type of infertility and both pregnancy outcomes ($P>0.05$) (Table 3).

Table 3: Correlation between Type of Infertility and the Pregnancy Outcomes

| | Pregnancy test | | | Fetal heartbeat | | |
|-------------|----------------|----------|----------------|-----------------|----------|----------------|
| | Positive | Negative | <i>p-value</i> | Positive | Negative | <i>p-value</i> |
| Infertility | Primary | 32 | 25 | 29 | 28 | |
| | Secondary | 11 | 10 | 10 | 11 | 0.799* |
| | | 56.1% | 43.9% | 50.9% | 49.1% | |
| | | 52.4% | 47.6% | 47.6% | 52.4% | |

Pregnancy outcomes Incidence after IVF/ICSI

The patients were divided into two groups of 39 patients in each group. Group (1) were operated upon by laparoscopic salpingectomy (LS), and group (2) were operated upon by hysteroscopic tubal occlusion (HTPO). After the intervention, the following pregnancy outcomes were assessed and resulted in:

I- Sample group (1)

Out of 39 patients that had LS, 27 patients had positive qualitative serum b HCG test, and 12 patients had negative qualitative serum b HCG test following IVF/ICSI as shown in (Table 4).

Table 4: Pregnancy outcomes in sample group (1) /LS

| Sample group (1) LS | Pregnancy test | Fetal heart sound at eight weeks | | Total |
|---------------------|----------------|----------------------------------|----------|-------|
| | | Positive | Negative | |
| | Positive | 24 | 3 | 27 |
| | Negative | 0 | 12 | 12 |
| | Total | 24 | 15 | 39 |

II- Sample group (2)

III- In comparison with patients in group (2) that had HPTO, out of 39 patients, 16 patients (41%) had positive qualitative serum b HCG test and 23 patients 59% had negative qualitative serum b HCG test following IVF/ICSI as shown in (Table 5). Later, 15 patients out of 16 positive serum b HCG showed fetal heartbeat on ultrasound beyond eight weeks gestation, and 24 patients (61.5%) showed no fetal heartbeat on ultrasound beyond eight weeks gestation, totally as shown in (Table 5).

Table 5: Pregnancy outcomes in sample group (2) /HPTO

| Sample group (2) HPT | Pregnancy test | Fetal heart sound at eight weeks | | Total |
|----------------------|-------------------|----------------------------------|----------|-------|
| | | Positive | Negative | |
| | Positive | 15 | 1 | 16 |
| | Negative | 0 | 23 | 23 |
| | Total | 15 | 24 | 39 |
| Timing interval | Type of procedure | | | Total |
| | LS | HPT | | |
| | <10 weeks | 21 | 24 | 45 |
| | 10-16 weeks | 12 | 11 | 23 |
| | >16 weeks | 6 | 4 | 10 |
| | Total | 39 | 39 | 78 |

Timing interval of starting IVF after the procedure Regarding the time spent between the performance of Laparoscopic salpingectomy and ICSI, 21/39 females underwent ICSI after less than ten weeks, 12/39 have underwent ICSI after 10-16 weeks, and 6/39 have underwent ICSI after more than 16 weeks (Table 5).

Regarding the time spent between the performance of hysteroscopic tubal occlusion (HTPO) and ICSI, 24/39 females have underwent ICSI after less than ten weeks, 11/39 have underwent ICSI after 10-16 weeks, and 4/39 have underwent ICSI after more than 16 weeks (Table 5).

The number of attempts of IVF performed to achieve pregnancy

In the Laparoscopic salpingectomy group, 16/27 females achieved pregnancy after the first attempt, 7/27 females achieved pregnancy after the second attempt, and 4/27 females achieved pregnancy after the third attempt. (Table 6).

The number of ICSI attempts performed to achieve pregnancy in the Hysteroscopic tubal occlusion (HTPO) group, 9/16 females achieved pregnancy after the first attempt, 5/16 females achieved pregnancy after the second attempt, and 2/16 females achieved pregnancy after the third attempt.

Table 6: The number of attempts of IVF performed to achieve pregnancy

| | | Type of procedure | | Total |
|--------------------|----------------|-------------------|-----|-------|
| | | LS | HPT | |
| Number of attempts | First attempt | 16 | 9 | 25 |
| | Second attempt | 7 | 5 | 12 |
| | Third attempt | 4 | 2 | 6 |
| | Total | 27 | 16 | 43 |

Correlation between pregnancy test and the Type of intervention

Showed that 69.2% of patients who operated upon by LS showed positive qualitative blood HCG test, while only 41% of those who operated upon by HPTO showed positive qualitative blood HCG test, the difference in percentages of positive primary outcome between patients operated upon by LS and HPTO are statistically significant ($X^2=6.271$, $P<0.05$, $RR=1.688$, $CI(1.097-2.596)$).

Finally, the results showed that laparoscopic salpingectomy (LS) is superior to Hysteroscopic tubal occlusion (HTPO) in terms of ongoing pregnancy rates following IVF/ICSI (Table 7).

Table 7: Correlation between Pregnancy test and Type of intervention prior IVF/ICSI

| Intervention | Pregnancy test | | | <i>p-value</i> |
|---------------|----------------------|----------|-------|----------------|
| | Positive | Negative | | |
| LS | No. | 27 | 12 | 39 |
| | % | 69.2% | 30.8% | 50% |
| HPT | No. | 16 | 23 | 39 |
| | % | 41% | 59% | 50% |
| Total | No. | 48 | 30 | 78 |
| | % | 61.5% | 38.5% | 100% |
| Relative risk | RR, CI (1.097-2.596) | | | 1.688* |

DISCUSSION

Tubal factors account for approximately 25% of cases of infertility, and the most severe manifestation of tubal disease is hydrosalpinx, accounting for 10-30% of tubal diseases.

In this RCT, we compared Hysteroscopic tubal occlusion versus salpingectomy regarding the pregnancy outcomes following Intracytoplasmic sperm injection in the infertile cases of hydrosalpinx. Seventy-eight women were assessed for tubal factor infertility and randomized for assignment for each surgical intervention group. We found that laparoscopic salpingectomy (LS) is superior to Hysteroscopic tubal occlusion (HTPO) in terms of fetal heart sounds at eight weeks following IVF/ICSI.

In comparison with other similar studies, it was found similarities in the general conclusion, which is the superiority of laparoscopic salpingectomy (LS) to Hysteroscopic tubal occlusion (HTPO) in terms of pregnancy outcomes following IVF/ICSI^[10].

In a related trial, forty-five infertile women had their hydrosalpinges surgically treated with salpingectomy or proximal tubal cauterization. Within three months after surgery, an *in vitro* fertilization-embryo transfer was conducted. Patients with hydrosalpinx who received proximal tubal cauterization before an IVF cycle had clinical pregnancy and implantation rates that were higher (73 % and 36 %, respectively). These pregnancy and implantation rates are similar to those seen in tubal factor infertility patients who underwent salpingectomy (46% and 24 %, respectively)^[11,12].

Proximal tubal occlusion has been widely utilized in clinics based on the benefits of this procedure as a simple operation, highly successful, rapid rehabilitation, minor injury, no requirement of general anaesthesia as well as no severe complications happening like intestinal canal obstruction and blood vessels damage which are commonly occurred in operative laparoscopy or laparotomy^[13,14].

And regarding the safety of these techniques, a study was conducted aimed to determine whether hysteroscopic tubal occlusion will produce the same efficacy as laparoscopic tubal occlusion of hydrosalpinx prior to IVF/ICSI in the Endoscopy Unit of the Women's Health Center, Faculty of Medicine, Assiut University, Assiut, Egypt. The study phase included 27 patients with uni- or bilateral functionless hydrosalpinges, who were randomly divided into two groups. Group A comprised 14 patients who were randomly allocated for laparoscopic occlusion. Group B included 13 patients scheduled for a hysteroscopic approach. Laparoscopic occlusion of the isthmus part of the fallopian tube was carried out using bipolar diathermy in 9 (64%) cases, or clips in 3 (21.4%) cases in Group A.

Rollerball electrode of the resectoscope was utilised for occlusion of the tubal ostium in Group B. In both groups, hysterosalpingography or sonohysterography was carried out one month later to confirm tubal occlusion. In Group A, the procedure was possible and successful in 10 cases (76.9%), while in Group B, hysteroscopic access and occlusion were achieved in 12 (85.7%) and 9 (64.2%) cases, respectively. Hysteroscopic tubal occlusion showed shorter operative time (9 ± 2.8 versus 24 ± 4.8 min, $p=0.0001$) and hospital stay (2 ± 1.8 versus 5 ± 1.1 h, $p=0.0001$). Second-look office hysteroscopy was performed in 8 cases in Group B and revealed no significant corneal lesions at the site of hysteroscopic occlusion^[15,16].

CONCLUSION

It revealed that Laparoscopic salpingectomy (LS) is superior to Hysteroscopic tubal occlusion (HTPO) in terms of our outcome fetal heart sounds at eight weeks and higher pregnancy rate following IVF/ICSI upon adjusting the age and infertility status as confounders. Infertile hydrosalpinx patients should undergo laparoscopic salpingectomy before starting IVF/ICSI cycles, as this improves the outcome (i.e. higher pregnancy rate and positive fetal heart sound at eight weeks gestation).

CONFLICT OF INTEREST

There are no conflicts of interest.

REFERENCE

1. Yen & Jaffe's Reproductive Endocrinology - 8th Edition. Accessed December 7, 2021. <https://www.elsevier.com/books/yen-and-jaffes-reproductive-endocrinology/9780323479127>
2. Hernandez-Nieto C, Sekhon L, Lee J, Gounko D, Copperman A, Sandler B. Infertile patients with inflammatory bowel disease have comparable in vitro fertilization clinical outcomes to the general infertile population. *Gynaecological Endocrinology*. 2020;36(6):554-557.
3. Vander Borgh M, Wyns C. Fertility and infertility: Definition and epidemiology. *Clin Biochem*. 2018;62:2-10.
4. Ahmed J, Rahim M, Sultana N, Begum R. Evidence-Based Diagnostic Approach to Tubal Factor Infertility. *BIRDEM Medical Journal*. 2014;4.
5. Hefny MEZ, Salah Eldin M, Ragab Abdelaziz B. Evaluation of Diagnostic Hysteroscopy as a Tool for Diagnosis of Tubal Factor of Infertility in Comparison to Diagnostic Laparoscopy. *Al-Azhar International Medical Journal*. 2020;1(9):230-235.
6. Camus E, Poncelet C, Goffinet F, *et al.* Pregnancy rates after in-vitro fertilization in cases of tubal infertility with and without hydrosalpinx: a meta-analysis of published comparative studies. *Hum Reprod*. 1999;14(5):1243-1249.
7. Jerome F. Strauss, Robert L. Barbieri, Yen and Jaffe's Reproductive Endocrinology (Eighth Edition), Elsevier, 2019, Chapter 22 - Female Infertility, Pages 556-581.e7,
8. Schlaff WD. A reconsideration of salpingectomy for hydrosalpinx before in vitro fertilization: why bother? *Fertil Steril*. 2019;111 (04):650-651.
9. Adedigba JA, Idowu BM, Hermans SP, Ibitoye BO, Fawole OA. The relationship between hysterosalpingography findings and female infertility in a Nigerian population. *Pol J Radiol*. 2020;85:e188-e195.
10. Sharma S, Roy Choudhury S, Bathwal S, *et al.* Pregnancy and Live Birth Rates Are Comparable in Young Infertile Women Presenting with Severe Endometriosis and Tubal Infertility. *Reprod Sci*. 2020;27(6):1340-1349.
11. Stadtmauer LA, Riehl RM, Toma SK, Talbert LM. Cauterization of hydrosalpinges before in vitro fertilization is an effective surgical treatment associated with improved pregnancy rates. *Am J Obstet Gynecol*. 2000;183(2):367-371.
12. Abbas AM, Hussein RS, Elsenity MA, *et al.* Higher clinical pregnancy rate with in-vitro fertilization versus intracytoplasmic sperm injection in the treatment of non-male factor infertility: Systematic review and meta-analysis. *J Gynecol Obstet Hum Reprod*. 2020;49(6):101706.
13. Bao HC, Wang MM, Wang XR, Wang WJ, Hao CF. Clinical application of operative hysteroscopy in treatment of complex hydrosalpinx prior to IVF. *Iran J Reprod Med*. 2015;13(5):311-316.
14. Darwish AM, El Saman AM. Is there a role for hysteroscopic tubal occlusion of functionless hydrosalpinges prior to IVF/ICSI in modern practice? *Acta Obstet Gynecol Scand*. 2007;86(12):1484-1489.
15. Elgarhy IM, Rammah AM, Bakry MMS. Comparison of ICSI Outcomes in Patients with Hydrosalpinx Pretreated with Either Laparoscopic Tubal Disconnection or Hysteroscopic Tubal Occlusion. *The Egyptian Journal of Hospital Medicine*. 2019;75(1):2054-2058.
16. Sabherwal G, Malik S, Sabherwal G, Malik S. Altered endometrial receptivity causes failure of IVF/ICSI in cases with tubal factor infertility. *Glob J Fertil Res*. 2018;3(1):001-005.