Comparative study between laparoscopic tubal disconnection, ultrasound guided tubal aspiration and hysteroscopic tubal occlusion in management of hydrosalpinx prior to ICSI

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Abstract: Patients with hydrosalpinges have significantly lower implantation and pregnancy rates than patients with other tubal pathologies. An increased risk for early pregnancy loss and increased risk for ectopic pregnancies was reported, and many studies confirmed that the presence of hydrosalpinx significantly impairs in vitro fertilization (IVF) outcome as well. The lowered efficacy of IVF led to the concept that fallopian tube surgery prior to IVF might improve results. In the current study we investigated the treatment efficacy of three options for the management of hydrosalpinx prior to ICSI cycles. The study is designed as an *equivalence* clinical trial assuming that the three techniques are almost equally effective. The ultimate goal of the trial is to reach multiple alternatives in this context, with comparable success rate of ICSI cycles. Three options for hydrosalpinx treatment were tested; laparoscopic disconnection of the hydrosalpinx, hysteroscopic occlusion of the cornual end of the affected tube and hydrosalpinx aspiration. The study involved 60 women with tubal factor of infertility in the form of unilateral or bilateral hydrosalpinx divided into three equal groups. All women were prepared for ICSI cycles with controlled ovarian hyperstimulation (COH) using hMG. There was no significant difference between the three groups regarding the response to COH, endometrial thickness, total number of retrieved oocytes, the number of MII oocytes, and the embryo number or grade. The three treatment options resulted in comparable pregnancy rates ($p = 0.765$). However, aspiration group had the lowest rate of clinical pregnancy (40%) compared to 50% in laparoscopic disconnection group and hysteroscopic occlusion groups with no significant difference. This confirms the assumption of this equivalence trial giving a chance to adapt the way of management according to the circumstances of each individual case. In conclusion, surgical treatment of hydrosalpinx prior to ICSI cycles can be done through laparoscopic disconnection of the hydrosalpinx, hysteroscopic occlusion of the cornual end of the affected tube or hydrosalpinx aspiration. The three techniques are generally safe with comparable outcome regarding clinical pregnancy rate. The management can be individualized according to the patient's general condition and status of the abdominal wall and pelvis pelvic regarding adhesions and complications of previous surgery.

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1. Introduction

Tubal factor infertility resulting from various forms of tuboperitoneal damage remains an extremely common 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. Hydrosalpinx is a Greek word that means a Fallopian tube filled with water or fluid. Patients with hydrosalpinges have been identified as a subgroup with significantly lower implantation and pregnancy rates than patients with other tubal pathologies. An increased risk for early pregnancy loss and increased risk for ectopic pregnancies was reported, and many studies confirmed that the presence of hydrosalpinx significantly impairs in vitro fertilization (IVF) outcome as well **(Strandell et al., 1994, 1999; Andersen et al., 1994; Vandromme et al., 1995).**

Surgical management of hydrosalpinx improves pregnancy rates but patient selection is an important factor for successful surgery. Prognostic factors include the extent of adhesions, the nature of adhesions, the diameter of the hydrosalpinx, the macroscopic condition of the endosalpinx, and tubal wall thickness **(Boer-Meisel et al., 1986).**

The success of pregnancy depends on the pathoanatomic condition of the tube, particularly on the degree of epithelial destruction, the flattened folds, the absence of cilia on the ciliated cells, and the deficiency of secretory cells particularly in the ampulla. These findings were confirmed obtaining microbiopsies before salpingostomy, which were studied by scanning and transmission by electron microscopy **(Bontis et al., 1996).**

According to the previous criteria most authors suggest four stages for the classification of

hydrosalpinx: stages I, II, III, and IV. The success of pregnancy is higher in stages I and II but disappointing in stages III and IV. Also, ectopic pregnancies are more often reported in patients with stages III and IV **(Bontis & Dinas, 2000).**

Microsurgical and laparoscopic salpingostomy results in the same conception rates but minimal access surgery has advantage over laparotomic microsurgery as shorter hospital stay, less postoperative pain, and less adhesion formation are reported after laparoscopy **(Marana & Quagliarello, 1988; Winston & Margara, 1991; Tarlatzis & Grimbizis; Milingos et al., 2000).**

The association of hydrosalpinx with decreased pregnancy and implantation rates in IVF cycles has been confirmed by overwhelming scientific evidence **(Camus et al., 1999; Zeyneloglu et al., 1998)**. It has been suggested that the retrograde spillage of hydrosalpinx fluid into the uterine cavity could adversely affect embryo development, reduces endometrial receptivity by decreasing the expression of endometrial receptivity markers (HOXA10, β-integrin and leukemia inhibitory factor), prevents the contact of embryos with endometrial surface or simply wash-out the embryos **(Meyer et al., 1997; Andersen et al., 1996)**.

In 2010, a meta-analysis of various prospective randomized studies revealed that laparoscopic salpingectomy or proximal tubal occlusion increases the odds of clinical pregnancy, ongoing pregnancy and live birth **(Johnson et al., 2010)**. However, salpingectomy or proximal tubal occlusion requires hospitalization, general anesthesia and may be associated with operative complications particularly in patients with dense adhesions. Moreover, bilateral salpingectomy precludes any possibility of future unassisted conception or tubal repair.

Several management options as hysteroscopic tubal occlusion, ultrasound guided aspiration of hydrosalpinx and medical treatment (antibiotics and/or corticosteroids) were suggested as alternatives to salpingectomy or proximal tubal occlusion. Several authors suggest that ultrasound guided aspiration of hydrosalpinx fluid is the best alternative because it is simple, safe, easy and inexpensive. Furthermore, there is evidence supporting its beneficial effect on the outcomes of IVF-ET from several prospective randomized controlled studies **(Hammadieh et al., 2008; Fouda & Sayed, 2011)**. On the other hand, the literature on using Essure micro-inserts for hysteroscopic tubal occlusion and antibiotics treatment was limited to small retrospective studies or prospective non-randomized studies **(Matorras et al., 2013; Hurst et al., 2001)**. Moreover, the occlusion of fallopian tube with Essure micro-inserts is expensive, delays IVF-ET cycle for 3 months and its risk to the patients who become pregnant and their fetuses is not known **(Arora et al., 2014)**.

A recent meta-analysis compared the pregnancy outcomes in hydrosalpinx patients treated with salpingectomy versus those treated with proximal tubal occlusion prior to in vitro fertilization (IVF). They reported no differences between the two procedures in the response days to controlled ovarian hyperstimulation, number of oocytes retrieved, embryos transferred per cycle, fertilized oocytes and rates of clinical pregnancy and implantation **(Zhang et al., 2015)**.

Aim of the Work

The aim of this work was to compare the efficacy of three different approaches in the management of hydrosalpinx prior to ICSI; namely laparoscopic proximal tubal occlusion, hysteroscopic tubal electrocoagulation and ultrasound-guided aspiration. The main objective is to assess their impact on ICSI cycle outcome.

2. Patients and Methods

Patients

This clinical trial was conducted at the Obstetrics and Gynecology Department ELAzhar University and EL Galaa Teaching Hospital from (2016 to 2019) The study involved 60 patients with tubal factor of infertility having hydrosalpinx and candidates for ICSI cycles.

Inclusion criteria

1) Age 20-30 years

2) Primary or secondary infertility

3) Tubal factor of infertility with unilateral or bilateral hydrosalpinx

4) Scheduled for ICSI cycle using long protocol for induction of ovulation

Exclusion criteria

1) Male factor of infertility

2) Uterine factor of infertility

3) Poor Ovarian reserve or poor responders

4) Obese patients with BMI > 30 kg/m2

5) Patients complaining of any medical disorders

Methodology:

All patients are subjected to the following:

A. History taking:

1) Full history taking with special interest to the case of infertility.

2) History of vaginal discharge.

3) History of abdominal surgeries.

4) History of pelvic inflammatory disease and Intra Uterine Device.

B. General examination

1) Vital signs, Weight (kg), Height (m)

2) Abdominal examination and presence of scars of previous operations

C. Local examination

1) 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.

2) Speculum examination for inspection of the cervix and visualization of the discharge.

D. Investigations

Hysterosalpingography: recent Hysterosalpingography (HSG) done within the last 6 months showing unilateral or bilateral fallopian tube dilatation with loss of rugal folds without or with decreased contrast in the peritoneal cavity. Some HSGs were already performed and some others were done during clinical evaluation .

Transvaginal Ultrasound: It was performed by the 7.5 MHz vaginal probe of the Sonoace X6 ultrasound machine before laparoscopic management and two weeks after the operation. The uterus was scanned in the sagittal plane for detection of any endometrial abnormality, visible hydrosalpinx in the form of elongated, diluted, tortuous tube containing fluid which is anechoic was recorded. In ultrasound image, hydrosalpinx looks as a tubular shape, echogenic wall, folded configurations and linear echos in the lumen of the fallopian tube **(Timor-Titsch and Rottem, 1987)**.

Hysteroscopic assessment of the uterine cavity: Patients were submitted to hysteroscopic examination under general anesthesia. The cervix was grasped by a tenaculum and the cervix was dilated to number 7 Hegar dilator. Then the hysteroscope was introduced into the cervix with normal saline used to distend the uterine cavity for optimal visualization. The appearance of the endometrium (atrophic or hyperplastic) and any abnormality (polyps, fibroid or malignant looking lesion) was recorded.

Laparoscopic assessment of the peritoneal cavity: and introduction pneumoperitoneum 2, CO anesthesia Under General of at least two ports was used to detect:

Presence or absence of endometriosis.

Peritoneal spill after cervical cannulation with methylene blue.

Tubal disconnection using bipolar diathermy or salpingectomy .

E. Induction of ovulation and embryo transfer at IVF unit:

1) The induction protocol was the long luteal phase agonist protocol. Participants received (GnRHa) long protocol, Decapeptyl 0.1 µg SC injection daily starting on day 21. After pituitary down regulation had been confirmed, by serum E2 <50 pg/ml, 225-300 IU of hMG per day was started on day 3 of the cycle, then the dose was adjusted according to the response, being monitored by ultrasound on day 8 or 9 to establish the number of ovarian follicles.

2) Triggering of ovulation was done by 10000 units of hCG IM when two or more follicles reach 18 mm in mean diameter.

3) Ovum retrieval using transvaginal ultrasound was scheduled 34-36 hours after hCG injection .

4) All grade embryos were transferred on day 3-5 after ovum retrieval.

5) Serum B-hCG test was done to confirm pregnancy two weeks after embryo transfer (chemical pregnancy).

6) Transvaginal ultrasound examination was done after 5 weeks from embryo transfer to confirm positive fetal pulsations (clinical pregnancy).

The Primary outcome was the success rates (Clinical pregnancy rate) of the ICSI cycles following the 3 lines of management of hydrosalpinx. The secondary outcome measure was the chemical pregnancy rate. We measured the following parameters to confirm the unity of distribution:

1) Number of oocytes collected in ICSI cycle

2) Maturity of oocytes collected in ICSI cycle

3) Endometrial thickness on day of triggering in ICSI cycle

4) Number and quality of embryos transferred

The studied sample was randomized into one of three groups:

• Group LD (n=20): In this group hydrosalpinx will be managed by laparoscopic proximal tubal disconnection.

• Group HO (n=20): In this group hydrosalpinx will be managed by hysteroscopic occlusion of the tubal ostia using the electrosurgical technique (using the roller ball.

• Group AS (n=20): In this group hydrosalpinx will be managed by vaginal ultrasound guided aspiration on the setting of the oocyte retrieval for the ICSI cycle.

• Patients of group LD and group HO had the tubal disconnection or occlusion the month prior to the ICSI cycle.

Surgical techniques:

Laparoscopic tubal disconnection (LD Group)

• Anesthesia: General anesthesia

• Position: low dorsal lithotomy position

• Sterilization and draping

Insertion of uterine manipulator. Entry closed umbilical entry 2starting with the insertion of Verres needle insufflation with CO followed by vertical umbilical incision, removal of the Verres needle and entry with a 10 mm port. Entry with 25 mm ports at the right and left lower quadrants. Identification of one or both affected fallopian tubes the fallopian tubes are grasped and the bipolar diathermy is applied on the fallopian tube 2-3 cm from the cornu followed by cutting of the diathermized point using scissors.

Hysteroscopic tubal occlusion (HO Group)

The patient is prepared by using 2 sublingual tablets of misoprostol preoperatively to facilitate cervical dilatation.

• Anesthesia: General anesthesia
• Position: lithotomy position

Sterilization and draping of the patient, evacuation of the bladder and dilatation of the cervix to Hegar number 7.

Rigid hysteroscopy was introduced using saline as a distention media, visualization of the uterine cavity to exclude any pathology and to visualize both tubal ostia. Coagulation of both tubal ostia using bipolar coagulation rod which is applied on each tubal ostia for 3 seconds.

Ultrasound Guided Aspiration (AS group)

• Anesthesia: General anesthesia
• Position: lithotomy position
• Sterilization: By saline and draping

Through transvaginal ultrasound with the use of the ovum pickup aspiration needle and after ovum pickup was finished the aspiration needle is washed from the inside using saline and the same needle is used to aspirate the hydrosalpinx either unilateral or bilateral.

Statistical methods

Data was analyzed using IBM SPSS Advanced Statistics version 22.0 (SPSS Inc., Chicago, IL). Numerical data were expressed as mean and standard deviation or median and range as appropriate. Qualitative data were expressed as frequency and percentage. Chi-square test was used to examine the relation between qualitative variables. For quantitative data, comparison between the 3 groups was done using ANOVA test or Kruskal-Wallis test followed by the suitable post-hoc test for pairwise comparison. All tests were two-tailed. A p-value < 0.05 was considered significant.

3. Results

The study included 60 women in three groups according to the treatment of hydrosalpinx in the context of ICSI. Group LD had laparoscopic disconnection of the hydrosalpinx, group HO had hysteroscopic occlusion of the cornual end of the affected tube and group AS had hydrosalpinx aspiration.

The three groups were comparable regarding age and body mass index (BMI) as shown in Table 1.

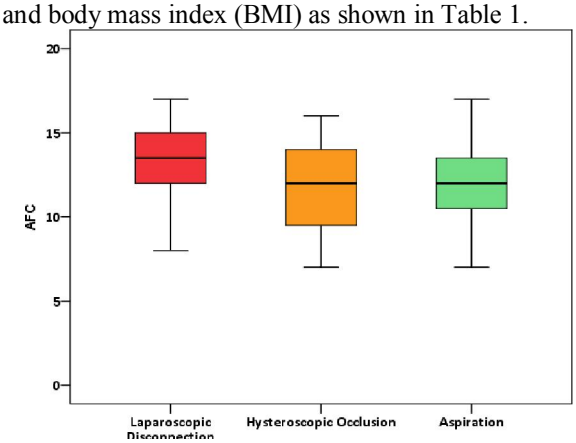

Figure 1: Antral Follicle Count (AFC) in the three studied groups

Table 1: Age and body mass index of the three studied group

Group LD n=20	Group HO n=20	Group AS n=20	p value
25.4±2.9	24.7±3.6	24.8±2.8	0.633
22.4±2.6	22.5±2.5	21.8±2.1	0.797

Data presented as mean±SD. LD: laparoscopic disconnection, HO: hysteroscopic occlusion, AS: hydrosalpinx aspiration.

Table 2: Hormonal profile and antral follicle count of the three studied group

	Group LD n=20	Group HO n=20	Group AS n=20	p value
FSH (IU/mL)	4.7±1.2	5.0±1.1	4.3±1.2	0.424
LH (IU/mL)	3.8±1.0	4.0±0.9	3.4±0.9	0.607
Prolactin (ng/mL)	16.3±4.5	15.6±4.2	15.9±4.1	0.617
Estradiol (pg/mL)	38.4±15.2	38.1±13.7	39.2±12.7	0.946
AMH (ng/mL)	4.6±1.5	4.5±1.3	4.5±1.6	0.903
(AFC)	14 (8-17)	12 (7-16)	12 (7-17)	0.065

Data presented as mean±SD or median (range).

FSH: follicular stimulating hormone, **LH**: luteinizing hormone **AMH**: anti mullerian hormone, **AFC**: antral follicle count.

Pretreatment hormonal profile showed no significant differences between the three groups in the levels of FSH, LH, prolactin, estradiol (E2) and anti-mullerian hormone (AMH) (Table 2) The antral follicle Ecount (AFC) was also comparable in the three groups (Figure 1).

All women had controlled ovarian hyperstimulation with human menopausal gonadotropin (hMG) in a daily dose between 225 and 300 IU. There was no significant difference in the total hMG dose between the three groups (p = 0.989) as shown in Table 3.

Table 3: Total dose of hMG used in the three studied group

	Group LD n=20	Group HO n=20	Group AS n=20	p value
Total HMG dose (IU)				
Mean±SD	3086±411	3079±472	3038±453	0.989
Median (Range)	3000 (2250-3600)	3300 (2250-3600)	3150 (2250-3600)	

HMG: human menopausal gonadotropoin.

Table 4 shows that there was no significant difference in the level of estradiol (p = 0.409) or endometrial thickness (p = 0.329) on the day of injection of hCG.

Table 4: Estradiol level at the day of hCG injection and endometrial thickness in the three studied group

	Group LD n=20	Group HO n=20	Group AS n=20	p value
Estradiol level (pg/mL)				
Mean±SD	2860±323	2759±431	2992±295	0.409
Median (Range)	2861 (2174- 3406)	2811 (2016- 3511)	2976 (2486- 3510)	
Endometrial Thickness (mm)				0.329
Mean±SD	10.2±1.5	10.7±1.8	10.5±1.6	
Median (Range)	10.0 (8.0- 13.0)	10.5 (8.0- 13.0)	10.5 (8.0- 13.0)	

Table (5) shows no statistically significant difference between three groups according to total number and phase of retrieved ova.

Table 5: Total number and phase of retrieved ova in the three studied group

	Group LD n=20	Group HO n=20	Group AS n=20	p value
Total No Ova Retrieved	13 (9-16)	12 (8-16)	13 (10-16)	0.403
No. of Atretic ova	0 (0-2)	0 (0-2)	0 (0-2)	0.724
No. of GV oocytes	0 (0-4)	0 (0-3)	1 (0-3)	0.947
No. of MI oocytes	4 (3-7)	5 (3-7)	5 (3-7)	0.878
No. of MII oocytes	6 (5-10)	7 (4-10)	7 (4-11)	0.407

GV: germinal vesicle phase, **MI**: metaphase I, **MII**: metaphase II Data presented as median (range)

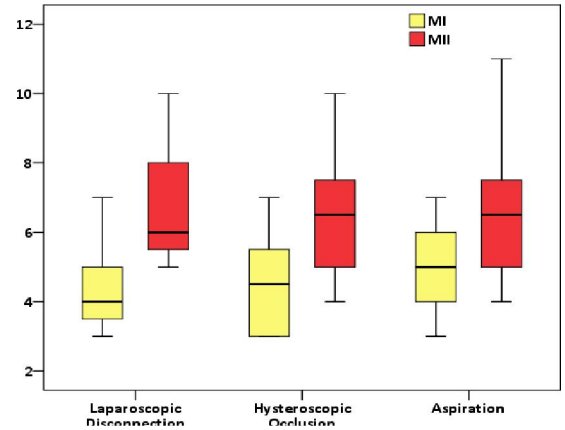

Figure 2: The number of MI and MII oocytes retrieved in the three studied groups

Table (6) shows the total number of embryos produced and their grades. There was no significant difference between the three groups in the total number of embryos (p = 0.666). The majority of embryos were of grade A. There was no significant difference between the three groups in the embryo grade.

Table (7) shows no statistically significant difference between three groups according to proportion of clinical or chemical pregnancy testing.

Figure 3 shows that there was no significant difference between the three studied groups regarding the proportion of clinical pregnancies (p = 0.765) or chemical pregnancies (p = 0.627). Eleven pregnancies were diagnosed chemically in laparoscopic disconnection group compared to 10 in hysteroscopic occlusion group and 8 in aspiration group. In laparoscopic disconnection group one pregnancy failed to continue clinically.

Table 6: Total number and grade of produced embryos in the three studied group

	Group LD n=20	Group HO n=20	Group AS n=20	p value
Total No of embryos	7 (4-10)	7 (5-10)	8 (5-11)	0.666
Grade A	6 (3-9)	5 (3-7)	6 (4-8)	0.256
Grade B	1 (0-3)	1 (0-3)	1 (0-3)	0.060
Grade C	1 (0-3)	0 (0-2)	1 (0-3)	0.312

Data presented as median (range)

Table 7: Proportion of clinical and chemical pregnancies in the three studied groups

	Group LD n=20	Group HO n=20	Group AS n=20	p value
Clinical Pregnancy				
Positive	10 (50.0%)	10 (50.0%)	8 (40.0%)	0.765
Negative	10 (50.0%)	10 (50.0%)	12 (60.0%)	
Chemical Pregnancy				0.627
Positive	11 (55.0%)	10 (50.0%)	8 (40.0%)	
Negative	9 (45.0%)	10 (50.0%)	12 (60.0%)	

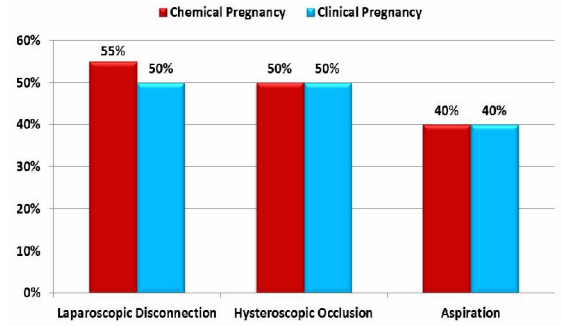

Figure 3: Proportion of clinical and chemical pregnancies in the three studied groups

4. Discussion

Tubal pathology ranks among the most frequent causes of subfertility accounting for 14% of cases. A spectrum of severity is 79 recognized at laparoscopy, ranging from peritubal adhesions, through damaged fimbriae or distorted tubal anatomy, tubal blockage to the most severe manifestation of tubal disease; *hydrosalpinx* ***(Evers, 2002)***.

The couple with tubal factor subfertility has two therapeutic options to overcome the mechanical obstructions present in tubal disease: in-vitro fertilization (IVF) or reconstructive surgery. The place of reconstructive surgery is a topic of debate, as selection of patients and the method for tubal surgery is challenging ***(Dechaud et al., 2004)***. IVF was primarily developed to treat tubal infertility and has been shown to be effective ***(Steptoe & Edwards, 1978)***.

However, a paradox emerged after recognition that IVF in patients with tubal disease was associated with lower implantation rates and an increased risk of early pregnancy loss than after IVF in other subfertile patients ***(Zeyneloglu, 1998; Camus et al., 1999)***. This deleterious effect of tubal disease on IVF outcome may be related to the severity of tubal damage. Disappointingly, the treatment was less effective in the patient group it was designed for than for subfertile patients with other causes for their subfertility ***(Vasquez et al., 1995; Csemiczky 1996)***.

There are several theories to explain the underlying mechanism by which hydrosalpinges exert a deleterious effect on IVF outcome. In these theories hydrosalpinx fluid seems to have a key role ***(Strandell & Lindhard, 2002)***. It has been proposed that the hydrosalpinx fluid may affect the transferred embryo; possibly by embryotoxic factors ***(Mukherjee et al., 1996)*** or a common factor deleterious to embryonic development and possibly by the lack of nutrients ***(Dickens et al., 1995; Tay et al., 1997)***. The bathing of the endometrial cavity in hydrosalpinx fluid may interfere with the endometrial interaction with the transferred embryo necessary for implantation ***(Fleming & Hull, 1996; Meyer et al., 1997)***.

Furthermore, mechanical effects exerted by hydrorrhoea (the leakage of hydrosalpinx fluid through the uterine cavity) ***(Andersen et al., 1996; Bloechle et al., 1997)***, the presence of a thin layer of fluid upon the endometrial surface ***(Sharara, 1999)*** and changes in endometrial peristalsis by the fluid ***(Eytan et al., 2001)*** may wash-out or hinder implantation of the transferred embryo. Moreover, it has been postulated that hydrosalpinges, during IVF stimulation, may exert a negative influence on oocytes in early follicular recruitment.

The lowered efficacy of IVF alone led to the concept that fallopian tube surgery prior to IVF might improve results. Suggested surgical interventions are: salpingectomy salpingostomy ***(Dechaud et al., 1998, Strandell et al., 1999)***, aspiration of hydrosalpinx fluid ***(Sowter et al., 1997; Van Voorhis et al., 1998)*** tubal ligation ***(Murray et al., 1998)*** and tubal occlusion by

means of Filshie clips ***(Darwish & El Saman, 2005, 2007)***, Essure micro-inserts ***(Kerin et al., 2005; Rosenfield et al., 2005)*** or electrocautery ***(Murray et al., 1998; Stadtmauer et al., 2000; Surrey & Schoolcraft, 2001)***.

In the current study we investigated the treatment efficacy of three options for the management of hydrosalpinx prior to ICSI cycles. The study is designed as an *equivalence* clinical trial assuming that the three techniques are almost equally effective. The ultimate goal of the trial is to reach multiple alternatives in this context, with comparable success rate of ICSI cycles. Three options for hydrosalpinx treatment were tested; laparoscopic disconnection of the hydrosalpinx, hysteroscopic occlusion of the cornual end of the affected tube and hydrosalpinx aspiration. The study involved 60 women with tubal factor of infertility in the form of unilateral or bilateral hydrosalpinx divided into three equal groups. All women were prepared for ICSI cycles with controlled ovarian hyperstimulation (COH) using hMG. The baseline criteria of the three groups were comparable including age, BMI, pretreatment hormonal profile and antral follicle count (AFC).

There was no significant difference between the three groups regarding the response to COH measured by the level of estradiol on the day of injection of hCG was comparable in the three groups ($p = 0.409$). Also, endometrial thickness was comparable in the three groups ($p = 0.329$). The three groups were also similar in the total number of retrieved oocytes ($p = 0.403$) and the number of MII oocytes ($p = 0.407$). There was no significant difference in the embryo number or grade.

The primary outcome measure of the study was the rate of clinical pregnancy. The three treatment options resulted in comparable pregnancy rates ($p = 0.765$). However, aspiration group had the lowest rate of clinical pregnancy (40%) compared to 50% in laparoscopic disconnection group and hysteroscopic occlusion groups with no significant difference. This confirms the assumption of this equivalence trial giving a chance to adapt the way of management according to the circumstances of each individual case.

Salpingectomy remains the most frequently undertaken procedure. Despite guidelines recommending salpingectomy, there remained a wide variation in the methods offered and employed in surgical management, according to a French and an English survey. For example, laparoscopic salpingectomy was recommended and undergone in less than half of all French IVF centers ***(Ducarme et al., 2006)***. In IVF centers in the UK, laparoscopic salpingectomy was offered by 75% of clinicians ***(Hammadieh et al., 2004)***.

Each treatment has its own merits and drawbacks. Salpingectomy has the advantage that chronically infected tissue is removed in total; removing the risk of abscess formation or torsion and increasing the accessibility of the ovary during oocyte retrieval in IVF ***(Kontoravdis et al., 2006)***. Drawbacks however are the invasiveness of the procedure itself and the difficulty of the procedure in case of dense adhesions. Furthermore it has been suggested that salpingectomy may affect ovarian function by interfering with ovarian blood flow ***(Lass et al., 1998; Dar et al., 2000)***. There are however reassuring data to suggest that ovarian compromise does not occur after salpingectomy ***(Strandell et al., 2001)***.

In agreement with the results of the current study, a meta-analysis of randomized controlled trials reported similar outcomes of salpingectomy and proximal tubal occlusion for hydrosalpinx patients prior to IVF. Authors reported that there were no differences in the response days to controlled ovarian hyperstimulation, number of oocytes retrieved, embryos transferred per cycle, and fertilized oocytes between the patients receiving salpingectomy and proximal tubal occlusion. The pooled rates for clinical pregnancy (OR, 0.864; 95%CI: 0.53-1.40) and implantation (OR, 1.558; 95%CI: 0.81-3.00) were not significantly different between the hydrosalpinx patients with salpingectomy versus proximal tubal occlusion ***(Zhang et al., 2015)***.

Other possible adverse effects are interstitial pregnancy; which has been reported in two cases ***(Herman et al., 1991; Shariff et al., 1994)*** or ovarian pregnancy ***(Hsu et al., 2005)***. Formation of cornual fistulae ***(Hsu et al., 2005)*** and cornual rupture have been described ***(Inovay et al., 1999)*** in single cases after salpingectomy by electrocautery. Salpingectomy is the treatment with the most permanent character - any possibility of conceiving spontaneously is removed. This is a psychological burden for the patient and an important drawback as many gynecologists are aware of women who conceived spontaneously after being deemed to have hopeless tubal infertility.

In order to overcome the possible affection of ovarian function to compromising blood supply, laparoscopic proximal tubal division was suggested to preserve ovarian function. This was the type of laparoscopic salpingectomy adopted in the current study. Using 25 mm secondary ports at the right and left lower quadrants, we grasped the affected tube (s) 2-3 cm from the cornu to apply bipolar diathermy followed by cutting of the diathermized point using scissors. Laparoscopic proximal tubal division has been previously suggested as an optimal operation method for infertility patients with hydrosalpinges ***(Nakagawa et al., 2008)***. Other investigators reported

similar findings with no effect on ovarian reserve ***(Surrey ES, Schoolcraft, 2001; Sagoskin et al., 2003; Gelbaya et al., 2006)***.

Similar to the current study, ***Stadtmauer et al. (2000)*** investigated the effectiveness of proximal tubal cauterization for the treatment of hydrosalpinges before in vitro fertilization. They concluded that proximal tubal cauterization is effective in reversing the adverse effects of hydrosalpinges. Patients undergoing proximal tubal cauterization have achieved pregnancy and implantation rates comparable with patients with tubal factor infertility without hydrosalpinges and salpingectomy-treated patients. Compared to salpingectomy, aspiration, salpingostomy and tubal occlusion are thought to have the advantage of being less invasive, safer and easier to perform in the case of dense adhesions ***(Stadtmauer et al., 2000)***, with shorter hospital stays ***(Surrey & Schoolcraft, 2001; Taylor et al., 2001)***.

Aspiration of the hydrosalpinx fluid (HSF) was another choice we used in the current study. It is a rather simple procedure that can overcome some obstacles encountered when planning for open or laparoscopic salpingectomy. In addition to invasiveness of laparoscopic salpingectomy, it is not very safe or feasible in the presence of dense pelvic adhesions. Moreover – as shown above - some studies show that salpingectomy may have a negative effect on the ovarian blood flow and subsequently reduced ovarian response to gonadotrophin stimulation ***(Dechaud & Hedon, 2000)***. On occasions, a clinician may also be faced with the situation of identifying a hydrosalpinx for the first time in the period before oocyte collection, after IVF treatment had been commenced. In these situations, vaginal aspiration of HSF becomes a good alternative to salpingectomy. Vaginal ultrasound-guided aspiration of HSF is by far the simplest method of treating hydrosalpinges.

In the current study, aspiration of HSF was statistically comparable to laparoscopic salpingectomy and hysteroscopic tubal occlusion regarding the pregnancy rate. However, it was associated with the lowest ongoing pregnancy rate (40%).

Aboulghar et al. (1990) described ultrasound-guided aspiration of hydrosalpinx 1 month before the IVF-ET cycle. They 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. ***Russell et al. (1991)*** reported a patient with bilateral hydrosalpinges who failed to conceive in the first IVF-ET cycle. The patient conceived after ultrasound-guided aspiration of hydrosalpinges which was performed 1 month before the second IVF-ET cycle. ***Sharara et al. (1996)*** reported seven women undergoing 11 IVF-ET cycles had their hydrosalpinges aspirated at the time of oocyte retrieval without any noted morbidity, resulting in two ongoing pregnancies and three pregnancy losses.

A comparative, controlled retrospective analysis was performed for women with infective tubal damage who were going to have surgical drainage of the hydrosalpinx at the time of oocyte collection for in-vitro fertilization. A total of 237 embryo transfer cycles in women with hydrosalpinges were compared with 705 embryo transfer cycles in women with tubal disease but no hydrosalpinx. Success rates were higher in the first cycle, but did not significantly influence overall differences. The study showed marked reduction in embryo implantation in the presence of tubal damage with distal occlusion, even in the absence of obvious fluid distension. The authors recommended surgical drainage of distended hydrosalpinges in these cases ***(Sowter et al., 1997)***.

Another study compared clinical pregnancy rate in women with hydrosalpinges with and without aspiration of HSF at the time of oocyte retrieval. It was found that aspiration of hydrosalpinges was associated with a higher clinical pregnancy rate, a higher ongoing pregnancy rate, and a higher implantation rate. This study confirms the association between the presence of hydrosalpinges and poor IVF outcomes ***(Van Voorhis et al., 1998)***. A randomized controlled trial was done on the effects of ultrasound-guided HSF aspiration of ultrasonically diagnosed hydrosalpinx during oocyte collection on IVF outcome including 66 women. Aspiration resulted in a greater biochemical pregnancy rate ***(Hammadieh et al., 2008)***.

More recently, 110 women with ultrasound-visible hydrosalpinges were enrolled in a study to test the effect of ultrasound-guided aspiration of HSF at the time of oocyte retrieval on the outcomes of IVF-ET. The authors reported that patients who underwent aspiration of hydrosalpinges demonstrated a significantly increased implantation and clinical pregnancy rates. In the aspiration group, re-accumulation of HSF within 2 weeks was associated with lower – but not statistically significant - implantation and pregnancy rates, compared to those with no reaccumulation ***(Fouda & Sayed, 2011)***.

A recent case report of a 36- year old nullipara with unilateral hydrosalpinx was published. The patient declined salpingectomy prior to IVF treatment and had two failed IVF cycles. Following transvaginal ultrasound scan guided aspiration of the hydrosalpinx fluid at the time of oocyte retrieval, she became pregnant with the third IVF attempt ***(Okohue & Ikimalo, 2015)***.

Bloechle et al. (1997) performed a study concerning a patient who developed bilateral hydrosalpinges during controlled ovarian stimulation in preparation for IVF treatment. In this patient, transvaginal aspiration of the tubal fluid was unsuccessful as the tubes refilled within 2 days. Additionally, on the day of embryo transfer a serometra developed which could not be seen on the day of oocyte retrieval. The uterine cavity was evacuated via an embryo transfer catheter and three embryos were transferred. The serometra reappeared 3 days after embryo transfer. A pregnancy could not be achieved.

There are concerns about the possible occurrence of infection after puncture of hydrosalpinx during aspiration of hydrosalpingeal fluid and that rapid re-accumulation of HSF may preclude any beneficial effect of aspiration. In the current study, we did not record any case of flaring of pelvic infection, peritonitis or fluid re-accumulation. These results are in accordance with previous studies reporting no infectious morbidity in patients after aspiration of hydrosalpinges ***(Sowter et al., 1997; Van Voorhis et al., 1998; Hammadieh et al., 2008)***.

The third option used in the current study was hysteroscopic bilateral tubal occlusion. We performed hysteroscopic tubal occlusion using diathermy. Coagulation of both tubal ostia was done with bipolar coagulation rod applied on each tubal ostia for 3 seconds. ***Darwish and El Saman (2007)*** performed a prospective comparative study to determine the efficacy and feasibility of hysteroscopic tubal occlusion of functionless hydrosalpinx prior to IVF/ICSI compared with laparoscopic tubal occlusion. They applied electro-coagulation of tubal orifices. Once the peritubal bulge was clearly seen, a roller ball electrode (size: 3 mm) was introduced inside it and activated at 50 Watts for about 8 s. They achieved complete occlusion in 9 cases out of 13. Pregnancy was achieved in 4 cases (31%).

In the current study, one group was managed by tubal occlusion through diathermy of the internal orifices through the hysteroscope. Hysteroscopic fulguration of internal orifice of fallopian tubes is designed to degenerate internal orifice tissue of diseased tube by electric heat energy to form tissue scar so as to prevent hydrosalpinx fluid reflux to uterine cavity, helping embryo's development and implantation and maximizing the protection of intra-mesosalpinx blood vessels and nerves theoretically. Experiments in vitro suggested that coagulation of tubal internal orifice at a hysteroscopic unipolar coagulation power of 50w within duration of 20s doesn't damage other fractions of endometrium and uterine serosa layer ***(Darwish & El Saman, 2007)***.

A recent study have concluded that hysteroscopic tubal occlusion of the proximal part of the hydrosalpinx can effectively prevent the hydrops backflow to endometrial cavity and benefit subsequent implantation in the course of assisted reproduction without significant complications. The study retrospectively analyzed data from 10 women with hydrosalpinx, who were unable to undergo laparotomy due to extensive pelvic adhesion and treated by operative hysteroscopy prior to IVF-ET. The total of 10 women underwent the fulguration of internal orifice of uterine tube. After their hysteroscopy operation, 5 out of 10 patients acquired clinical pregnancy ***(Bao et al., 2015)***.

Proximal tubal occlusion is recommended for patients with hydrosalpinx who cannot undergo laparoscopic surgery due to excessive fatness and extensive abdominal adhesions. It has been wildly utilized in clinics based on the benefits of this procedure as a simple operation, highly successful, rapid rehabilitation, minor injury, no requirement of general anesthesia as well as no severe complications happening like intestinal canals obstruction and blood vessels damage which are commonly occurred in operative laparoscopy or laparotomy ***(Rosenfield et al., 2005; Mijatovic et al., 2010)***.

Another way of hysteroscopic tubal occlusion is through insertion of the intratubal devices. The hysteroscopic insertion of the intratubal devices prior to IVF has been reported to be a reasonable option in cases of hydrosalpinx where laparoscopic salpingectomy is contraindicated ***(Mijatovic et al., 2010, 2012; Galen et al., 2011; Matorras et al., 2013; Legendre et al., 2013)***.

Ozgur et al. (2014) investigated the use of hysteroscopic Essure device placement for the treatment of hydrosalpinx in cases having ICSI and frozen embryo transfer procedures. Compared to laparoscopic tubal ligation, the hysteroscopic placement of Essure devices to isolate hydrosalpinx prior to assisted conception treatment produced comparable pregnancy outcomes.

A French survey involving 45 hospital centers was done to study the feasibility and results Essure microinserts before assisted reproductive technology treatment of women with hydrosalpinx when laparoscopy should be avoided. The study reported a retrospective analysis of 43 women who had 54 embryo transfers. The clinical pregnancy rate was 40.7%, implantation rate was 29.3% and the live-birth rate was 25.9% ***(Legendre et al., 2013)***.

A systematic review on the efficacy and safety of Essure in the management of hydrosalpinx before IVF involving 11 studies involving 115 women was done. Subsequent IVF resulted in 38.6% pregnancy rate, 27.9% live birth rate and 28.6% combined ongoing

pregnancy and live birth rate per embryo transfer ***(Arora et al., 2014)***.

However, hysteroscopic tubal occlusion devices such as Ovabloc, tubal screw, Essure and others have been declined by other authors. In such cases, these devices may be foreign bodies that can interfere with implantation by inducing uterine contractility ***(Darwish & El Saman, 2007)***.

Many studies have compared the different options for treatment of hydrosalpinx before IVF cycles. A prospective randomized study compared the clinical impact of proximal tubal occlusion and salpingectomy before IVF in patients with hydrosalpinges. Authors reported comparable rates of implantation, clinical-pregnancy, and ongoing-pregnancy in patients who underwent proximal tubal occlusion and those who underwent salpingectomy. They found that proximal tubal occlusion may be a valid alternative when salpingectomy is technically difficult or not feasible ***(Kontoravdis et al., 2006)***. Also, ***Stadtmauer et al. (2004)*** reported comparable effectiveness of proximal tubal cauterization compared to salpingectomy.

A more recent study compared the efficacy of ultrasound guided aspiration of hydrosalpinx fluid at the time of oocyte retrieval with salpingectomy in the management of patients with hydrosalpinx undergoing IVF-ET. In agreement with the results of the current study, the clinical pregnancy rate and the implantation rate were non-significantly higher in the salpingectomy group compared with the aspiration group (40% vs. 27.5%) and (18.95% vs. 12.82%), respectively ***(Fouda et al., 2015)***.

As an overall finding, surgical intervention - regardless of its type - had a beneficial effect on the pregnancy rate in patients with hydrosalpinx undergoing IVF. In a systematic review, surgical treatment for hydrosalpinges by laparoscopic salpingectomy versus non-surgical management significantly increased the odds of ongoing pregnancy (OR 2.20, 95%CI 1.26 to 3.82), and of clinical pregnancy (OR 2.31, 95%CI 1.48 to 3.62) ***(Johnson et al., 2010)***.

Recommendations

Further studies could be done regarding the same subject in order to recommend guidelines regarding the clinical situations in which each line of management could be used and proper assessment of the patients will help applying these guidelines and achieving better results.

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8/6/2019