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Interventional embolization plays a role in hydrosalpinx resulting from fertilization and embryo transfer *in vitro*.

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Abstract

Objective: This research was aimed to explore the role of interventional embolization in hydrosalpin resulting from *In Vitro* Fertilization and Embryo Transfer (IVF-ET).
Methods: From 2013 to 2016, 130 patients were treated with IVF-ET in which 75 were treated with fallopian tube embolization followed by IVF-ET while others received IVF-ET without other treatments. Age, basal Estradiol (E2) value, basal Follicle-Stimulating Hormone (FSH) value, Gn dosage, antral follicle count, follicle count on the day of Human Chorionic Gonadotropin (HCG) administration, E2 value on the day of HCG administration, fertility rate, cleavage rate, clinical pregnancy rate, rate of abortion and ectopic pregnancy rate were tested.
Results: Pregnancy rate of the intervention group was significantly higher than that of the control group (P<0.05), while abortion and ectopic pregnancy rate of the intervention group was strikingly lower than that of the control group (P<0.05).
Conclusion: Interventional embolization plays a role in hydrosalpinx resulting from fertilization and embryo transfer *in vitro*.

Keywords: Hydrosalpinx, *In vitro* fertilization, Embryo transfer, Interventional embolization.

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Introduction

Fallopian tube plays an important role in reproductive process as the fertilization place of sperm and eggs and the transport channel of fertilized eggs [1]. Problems in any part of fallopian tube may lead to infertility. According to the survey data, fallopian tube diseases are the main reason of infertility (accounting for 40%), while hydrosalpinx accounts for 10%-30% of various fallopian tube diseases [2]. Since the success of first *In Vitro* Fertilization and Embryo Transfer (IVF-ET), the technology has brought good news for infertility patients. However, for patients with hydrosalpinx, the outcome of IVF-ET is disappointing. Statistical results show that hydrosalpinx can reduce implantation rate and clinical pregnancy rate of IVF-ET, while increasing early abortion rate and ectopic pregnancy rate [3]. Possible mechanism includes mechanical erosion action [4], toxic effect of embryo and gamete [5], and reduced endometrial receptivity [6]. Therefore, pre-treatment for hydrosalpinx before IVF-ET has significant value. Current treatments for hydrosalpinx mainly include ultrasound-guided hydrosalpinx aspiration, fimbria salpingostomy, proximal tubal ligation and tubectomy [7]. Hydrosalpinx aspiration and salpingostomy may cause high recurrence rate of hydrosalpinx and high ectopic gestation rate [8]. Tubectomy as a mature therapy can significantly improve the pregnancy outcome of patients with hydrosalpinx while easily injuring the arteries of fallopian tube-mesovarium which may affect ovarian blood flow and reduce ovarian reserve function and superovulation response [9]. Recently, with the development of interventional radiology, interventional embolization has been applied in the treatment for hydrosalpinx before IVF-ET and achieved a certain therapeutic effect. With advantages of convenient use, low cost, no anaesthetic risk and no effect on ovarian function, it significantly improves pregnancy rate and reduces ectopic gestation rate [10].

Materials and Methods

General data

From January 2014 to January 2016, a total of 130 patients with hydrosalpinx who were treated with IVF-ET were selected as objects. Enrolment condition: (1) regular menstrual cycle (23-32 days) with a period range of ± 3 days; (2) no other reasons for infertility except tubal factor (e.g. semen

abnormality); (3) no gynecological endocrinology diseases such as endometriosis, polycystic ovarian syndrome and pituitary-hypothalamic lesion; (4) no fibroid and history of ovarian operation; (5) no use of sexual hormones within 3 months before operation; (6) normal basal hormone level; (7) no interruption or discontinuity of treatment during assisted reproduction period of IVF-ET [9]. 75 patients in intervention group (unilateral hydrosalpinx: n=36, bilateral hydrosalpinx: n=39) were treated with fallopian tube embolization, which was followed by IVF-ET. 55 patients in control group (unilateral hydrosalpinx: n=22, bilateral hydrosalpinx: n=32) directly received IVF-ET without receiving any pre-treatment for hydrosalpinx. This research was approved by the Ethical Committee of Xingyuan Hospital of Yulin City and the research number is 2016-01-02.

Methods

Interventional embolization: Interventional embolization could be completed by outpatient procedure. After routine examination of chlamydia, mycoplasma and leucorrhea, patients with normal parameters received interventional embolization. Placed in lithotomy position, patients lay on the digital subtraction angiography with routine disinfection, draping and chamber testing. Then fluoroscopically-guided 7 F oviduct catheter was inserted into cornua uteri of hydrosalpinx across cervical canal. Under the guidance of 0.018 in guidewire, 3 F microcatheter was gently inserted into interstitial section and isthmus of fallopian tube, after which guidewire was slowly pulled out. According to the length of inserted microcatheter and the thickness of fallopian tube, proper microcoil was selected and released via 3F catheter in the drive of guidewire (trying to locate the near-end of microcoil in the cornua uteri next to interstitial section). Contralateral fallopian tube of patients with bilateral hydrosalpinx was treated with the same method. Finally, Hystero-Salpingography (HSG) was conducted to verify the effect of embolization. After a month, HSG was performed again to verify the embolization and patients without therapeutic effect need another embolization.

Therapeutic evaluation of embolism: (1) Significant effect: Microcoil located in fallopian tube with a length of near-end to oviduct aperture<10 mm;

(2) Effective: The length of near-end to oviduct aperture was 10-50 mm;

(3) Invalid: Contrast agent permeated to the far-end cross microcoil; microcoil shifted to the far-end or fallen off to uterine cavity.

IVF-ET assisted reproduction scheme: Routine long protocol of gonadotrophin releasing hormone agonists in controlled ovarian hyperstimulation was applied, and IVF and observation were conducted with routine method. ET (embryo transfer) was performed on the third day of *in vitro* culture, β-HCG detection 2 weeks after transplant and b ultrasonic examination 4 weeks after transplant. Fertilized egg and fetal heart beat were determined as clinical pregnancy which was followed by follow-up to delivery.

Observation index

Age, basal Estradiol (E2) value, basal Follicle-Stimulating Hormone (FSH) value, Gn dosage, antral follicle count, follicle count on the day of Human Chorionic Gonadotropin (HCG) administration, E2 value on the day of HCG administration, fertility rate, cleavage rate, clinical pregnancy rate, rate of abortion and ectopic pregnancy rate.

Statistical approach

Count data was described as case number or percentage and measurement data as mean ± SD. T test, χ^2 test and rank sum test were applied with statistical significant of $P<0.05$. Statistical software: SPSS 13.0 and Microsoft office excel.

Results

Effective rate of interventional embolization and HSG in re-examination a month after surgery

Among 73 patients in intervention group (unilateral hydrosalpinx: n=34, bilateral hydrosalpinx: n=39), 111 of 112 fallopian tubes had successful embolism. HSG reexamination after a month showed that microcoil of one patient shifted to ampullar region and remedial embolism was successful. Therefore, the total success rate was 100% and 97 fallopian tubes had significant effect, accounting for 86.6%. During therapeutic process, no serious complications occurred except abdominal pain and colporrhagia in few patients. 12 patients had severe abdominal pain without special treatment for spontaneous remission.

Comparison of general conditions in two groups

There was no statistical difference in general conditions such as age, antral follicle count, basal E2 value and basal FSH value between two groups ($P>0.05$), shown in Table 1.

Comparison of IVF-ET index in two groups

There was no statistical difference in Gn dosage, E2 value on the day of HCG administration, follicle count on the day of HCG administration, retrieved oocyte number, fertility rate, cleavage rate between two groups($P>0.05$), shown in Table 2.

Comparison of pregnancy outcome index in two groups

Compared with control group, the clinical pregnancy rate of intervention group was significantly higher with a statistical difference ($P<0.05$). The rate of abortion and ectopic

pregnancy rate of control group was significantly higher with a statistical difference (P<0.05) (Table 3).

Table 1. *General conditions between two groups.*

	Intervention group (n=75)	Control group (n=55)	t value	P value
Age	31.6 ± 3.8	32.4 ± 3.3	1.254	0.212
Basal FSH Value (U/L)	8.8 ± 1.9	8.5 ± 2.2	0.830	0.408
Basal E2 value (pmol/L)	168.2 ± 20.3	173.6 ± 24.6	1.365	0.175
Antral follicle count	10.7 ± 3.6	11.5 ± 4.1	1.178	0.241

Table 2. *Comparison of IVF-ET index in two groups.*

	Intervention group (n=75)	Control group (n=55)	t value	P value
Gn	26.7 ± 4.9	27.3 ± 5.2	0.671	0.503
E2 value on the day of HCG administration (pmol/l)	1228.5 ± 225.2	1276.4 ± 251.9	1.137	0.258
Follicle count on the day of HCG administration	14.3 ± 4.5	12.9 ± 5.1	1.653	0.101
Retrieved oocyte number	11.7 ± 4.6	10.6 ± 4.3	1.385	0.169
Fertility rate	72.6 ± 6.5	73.1 ± 7.8	0.397	0.692
Cleavage rate	95.4 ± 7.1	94.2 ± 8.6	0.868	0.387

Table 3. *Comparison of pregnancy outcome index in two groups.*

	Intervention group (n=75)	Control group (n=55)	χ^2 value	P value
Clinical pregnancy rat	39.7 (29/73)	21.4 (12/56)	0.671	0.503
Rate of abortion	6.9 (2/29)	33.3 (4/12)	1.137	0.258
Ectopic pregnancy rate	3.4 (1/29)	25.0 (3/12)	1.653	0.101

Discussion

Previous study showed that due to hydrosalpinx, IVF-ET reduced 50% clinical pregnancy rate, while doubling spontaneous abortion rate [3]. Possible mechanism includes (1) Mechanical erosion action generated by the backflow of hydrosalpinx to uterine cavity may affect normal implantation of embryon and cause hydrohystera which blocks the combination of embryo with intima; (2) As embryon is sensitive to pH, electrolyte, osmotic pressure and various growth factors in vegetation process, the hydrosalpinx may cause toxic effect on embryo and gamete; (3) Stimulated by microorganism, fragments of tissue and toxic substance in hydrosalpinx, uterine cavity will release cytokines, prostaglandin, leukocyte chemokines and other inflammatory substances, which reduces endometrial receptivity [11]. Our study shows that interventional embolization therapy followed by IVF-ET can effectively block the effect of hydrosalpinx on embryo and significantly increase clinical pregnancy rate of IVF-ET while reducing ectopic pregnancy rate.

Current treatments for hydrosalpinx before IVF-ET mainly include ultrasound-guided hydrosalpinx aspiration, fimbria salpingostomy, proximal tubal ligation and tubectomy. Simple hydrosalpinx aspiration fails to improve the clinical pregnancy rate, implantation rate and parturition rate of IVF-ET but causes relapsing hydrosalpinx [12]. Salpingostomy may cause high recurrence rate of hydrosalpinx in short period and high incidence of abortion and ectopic gestation [13]. Tubectomy and proximal tubal ligation can significantly improve clinical pregnancy rate and reduce ectopic pregnancy rate. However, they may easily injure mesovarium artery arches, which may affect ovarian blood flow and reduce ovarian reserve function and superovulation response [14]. In interventional embolization, microcoil is placed between interstitial section and isthmus of fallopian tube via interventional operation. Its mechanism of action is described as: (1) mechanically complete partition of tubular lumina; (2) alkaline phosphatase released by mild mechanical necrotic tissue can benefit lymphocytic aggregation and proliferation of vascular tissue, which increase the embolization of tubular lumina [15]. Mechanical method in interventional embolization of fallopian tube has no effect on ovarian function. Gn dosage and follicle count and E2 value on the day of HCG administration in two groups have no statistical difference, which proves the opinion above.

Reasons for ectopic gestation in patients with hydrosalpinx are unclear, possibly including: (1) Fallopian tube thickens due to hydrosalpinx, easily leading to ectopic gestation; (2) Mechanical erosion action generated by the backflow of hydrosalpinx to uterine cavity may affect normal implantation; (3) Hydrosalpinx reduces endometrial receptivity which influences embryo implantation; (4) Endometrium injure caused by retrograde infection affects endometrial receptivity [16]. In our study, ectopic pregnancy rate of control group is higher than that of intervention group, indicating that pre-treatment of interventional embolization for hydrosalpinx before IVF-ET can reduce ectopic pregnancy rate.

HSG re-examination of interventional embolization shows that 29 microcoils have mild shifts to far-end fallopian tube (range 5-30 mm). Possible reasons are: (1) For patients with linearization and thickening symptoms between interstitial section and isthmus, microcoil before fixation would have a shift under increased abdominal pressure; (2) Due to thick ampullar region of fallopian tube, the spring coil slides in the tractive force of crimped microcoil. In our study, patients with significantly effective treatment had no ectopic gestation while one patient with effective treatment had ectopic gestation locating between cornua uteri and spring coil. Therefore, proper microcoil is necessary in operation and placed near cornua uteri. Besides, propaganda and education after operation should be attached importance.

In conclusion, interventional embolization can significantly improve the success rate of IVF-ET and reduce ectopic gestation rate. As a new pre-treatment for hydrosalpinx, interventional embolization may further be applied for use in clinic with potential development prospect.

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