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## Effect of Hysteroscopy Before Intra Uterine Insemination on Fertility in Infertile Couples

Farideh Moramezi, Mojgan Barati, Razieh Mohammadjafari, Sara Barati and Masoud Hemadi  
Fertility, Infertility and Perinatology Research Center, School of Medicine,  
Ahvaz Jundishapour University of Medical Sciences (AJUMS), Ahvaz, Iran

**Abstract:** Uterine disorders like usual infertility factors (male factor, ovarian and tubal problems of women) may affect the outcome of infertility treatment in infertile patients. In our clinical trial, 110 couples diagnosed with infertility were candidate for Intra Uterine Insemination (IUI). The patients were divided randomly into two equal groups (n = 55): In group one (control group), patients without hysteroscopy underwent ovulation induction by clomiphene citrate and hCG followed by intrauterine insemination. The second group (experiment group), patients were undergoing hysteroscopy before intra uterine insemination on the day 21 of the cycle and due to abnormal findings, going under surgical treatment if they needed. The rates of pregnancy complications in patients were evaluated. The age, BMI, kind of infertility, duration of infertility, number of previous trial, duration of stimulation, the type of procedures used and semen analysis (TMC, Motility and morphology of sperm) were similar for both groups and no statistically significant differences emerged at all between them. In experimental group, hysteroscopy revealed pathology in the uterine cavity in 26 out of 55 cases. The overall rates of clinical pregnancy were higher in experimental group compared to the control group. The findings from this study showed that the use of hysteroscopy as a diagnostic or therapeutic procedure before IUI, can increase the rate of pregnancy and finally decrease the failure rate of infertility treatment and perinatal complications in infertile couples.

**Key words:** IUI, hysteroscopy, infertility, pregnancy, intra uterine malformations

### INTRODUCTION

Since the implantation is most important step in the pregnancy, any uterine anatomic abnormalities, i.e., adhesions, septa, polyps, submucous myomas, adenomyosis, endometritis, anomalies of the cervical canal and lesions of the uterotubal junction in the uterine can create negative influences on the fertility of female (Merviel *et al.*, 2000). Therefore, the appropriate diagnosis and healing of these disorders are most essential to get well result in restoring fertility of women. The exact examination of the uterine cavity often is not easy by the transabdominal and the endovaginal sonography (Valenzano *et al.*, 2006). These methods may offer insufficient data or even provide numerous false-positives and false-negatives on the uterine cavity (Merviel *et al.*, 2000).

Hysteroscopy, however, is a diagnostic procedure that makes available direct demarcation of endometrial, submucosal, intrauterine cavity deformity and even the cervical canal (Isaacson, 2002).

In addition, it helps avoid invasive diagnostic procedures as well as optimize the preoperative process for the women requiring therapeutic intervention. It is easily and rapidly carried out at an outpatient basis, without sedation, by proper small-caliber instruments and irrigation with physiological saline (Breitkopf *et al.*, 2003). Furthermore, it is well tolerated and is virtually devoid of complications (Breitkopf *et al.*, 2003). In addition, both hysteroscopic examination and ART procedure can be also doing at the same time (Merviel *et al.*, 2000; Hucke *et al.*, 2000). Therefore, it seems that if the high diagnostic accuracy of hysteroscopy for intrauterine pathologies can be a causes for the reduced fertility in women potentially, then, it may also initiate growing consensus towards its use in the routine investigation of infertile women prior to ART procedure (Isaacson, 2002; Hucke *et al.*, 2000; Campo *et al.*, 2005), as well as in the management of hysteroscopy in place of laparoscopy (Darwish and El-Saman, 2007; Hitkari *et al.*, 2007; Mijatovic *et al.*, 2010). The aim of this study was to assess the diagnostic value and usefulness of

hysteroscopy in primary assessment before Intra Uterine Insemination (IUI) on fertility in infertile couples.

### MATERIALS AND METHODS

This is a prospective study that carried out through the period from June 2011 to April 2012 in the Fertility, Infertility and Perinatology Research Center in Ahvaz. One hundred and ten healthy women between the ages of 22 and 44 years candidate IUI cycles were randomly assigned to one of two groups from the start of the cycle. Group 1 (experiment, n = 55) for the treatment of possible uterine disorder causes infertility underwent hysteroscopy before entering the IUI and depend on finding candidate for surgery. Group 2 (control, n = 33) took IUI without hystroscopy. It worth mentioning in group 1 if the patient had normal hysteroscopy, IUI was done at next cycle but if surgery had the IUI was done after 2 or three cycle.

The Ethics Committee of Jundishapour Ahvaz University of Medical Sciences approved this study. Patient assessment included demographic information as well as medical and gynaecologic histories with physical examination and routine laboratory screening (including BMI, CBC, Pap smear, TSH, PRL and viral serology).

The inclusion criteria were healthy women and absence of sexually transmitted disease, pelvic inflammatory disease or pregnancy. Patients with active vaginal bleeding were also excluded.

**Hysteroscopy procedure:** The patients of group 1 underwent hysteroscopy to rule out pathology of the endometrial cavity. During this procedure the endometrial cavity was examined for the presence of polyps or submucosal myoma or other pathologic conditions. Any projection inside the uterine cavity was observed with special attention to its shape and echo whether it was of polypoid like structure or type of myomas.

**Ovarian stimulation:** In order to ovarian stimulation in both groups, Clomifen (50-100 g day<sup>-1</sup>) and then after 5 days HMG (75 unit per day) were given. Between 12th and 14th day, trans vaginal sonography was done; if follicles were about 18-20 mm, single dose of HCG was used to induce ovulation.

**IUI procedure:** Semen specimens were washed using the swim up method and a single IUI using a volume of 0.3 mL was performed 36 h after rhCG injection. Pregnancy was documented by the serum hCG level 2 weeks after the insemination. If pregnant, a vaginal ultrasound was carried out 2-4 weeks later. The outcome of the pregnancy rate was determined by comparison of the pregnancy rate between two groups.

Comparison of the pregnancy rates between the two groups.

**Statistical analysis:** All data are expressed as the means±SEM. Chi-square test and t-test were used for comparison of the data of the infertile group versus the fertile group. P-value less than 0.05 were considered as significant difference.

### RESULTS

A total of 110 cycles were randomized and available for investigation. None of the women refused to participate in the study. Fifty five patients were undergoing directly IUI and other women underwent hysteroscopy in the cycle before done IUI. The mean age of all of the patients was 32.3±4.5 years with a range of 22 to 44 years. The median duration of infertility of women was 4.7±1.4 years with a variety of 1.4 to 6.1 years. The two groups were found to be identical in the age, BMI, kind of infertility, duration of infertility, number of previous trial, duration of stimulation, the type of procedures used, the total dose of gonadotropin injected and semen analysis (TMC, Motility and morphology of sperm) (Table 1). Recorded no complications or difficulties in the performance of the hysteroscopy was recorded (none of the women had abdominal pain or nausea and no problems in insertion of the intrauterine insemination catheter into the cervical canal).

Table 1: Comparison of characteristics of women in two groups

Parameter	Control group	Experiment group	p-value
Age (years)	28.8±3	29.8±3	0.858
BMI (kg m <sup>-2</sup> )	23.99±0.59	24.01±0.69	0.949
Kind of sterility (male factor)	45 (80%)	36 (69.1%)	0.097
Kind of sterility (female factor)	2 (3.6%)	4 (7.3%)	0.871
Kind of sterility (idiopathic)	8 (14.8%)	15 (27.3%)	0.098
Duration of infertility	3.7±0.49	4.4±0.57	0.950
Number of IUI	114±2.07	106±1.92	0.045
Number of IUI positive	21±1.90	43±1.95	0.001
Number of OHSS	2 (3.6%)	3 (4.4%)	0.881
Non response to treat	3 (4.4%)	3 (4.4%)	0
Pregnancy Rate	11 (23.6%)	22 (40%)	0.05
Abortion Rate	2 (3.6%)	1 (1.8%)	0.887

Table 2: Comparison of findings from uterine evaluation experiment group

Findings	Experiment group	
	No.	%
Normal	31	56.4
Utens polyp	5	9.1
Stenosis cervix	5	9.1
Asherman's syndrome	1	1.8
Uterus septum	13	23.6
Hysteroscopy surgery	26	49.9
Hysteroscopy diagnostic	29	51.1

**Table 3: Comparison of characteristics of women in two groups**

Characteristics	Clinical pregnancy		Abortion		p-value
	No.	%	No.	%	
Hysteroscopy surgery (N = 26)	11	42.3	1	38.4	0.001
Hysteroscopy diagnostic (N = 29)	11	37.9	0	0.0	0.001
Non hysteroscopy (N = 55)	11	2.0	2	3.63	0.001

In control group, three women had the failure in treatment and two abortions happened too but in experiment group, three women had a failure in treatment, and one abortion happened. No significant relation was found (Table 1).

In experimental group, hysteroscopy revealed no pathology in the uterine cavity in 29 out of 55 patients. Oviduct tubes also were opened in all of patients. In the remaining 26 (47.27%), hysteroscopy evidenced, that surgery is needed due to some uterine disorder such as common pathologies: 13 (23.6%) abnormalities (uterine septum) related to the uterine cavity, 5 (9.3%) endometrial polyps, 5 (9.1%) cervical stenosis and 1 (1.8%) Asherman's syndrome (Table 2). In addition, we observed two patients presented more than one polyp lesion. No significant relation was found between pregnancy and type of pathology ( $p > 0.835$ ).

In the order of the clinical pregnancy between these two groups, the overall clinical pregnancy rates were lower for the control group 11(23.6%) compared to experimental group 22(23.6 %) ( $p < 0.05$ . Table 1).

No significant undesirable reactions or surgical complication was reported in any of the patients. However, there were subjects of severe Ovarian Hyper Stimulation Syndrome (OHSS) in three patients in both groups and there was no significant difference (Table 3).

### DISCUSSION

In general, preventing infertility is not easy and does not assist the couple looking for therapeutic recommendation for infertility. Moreover, ART is time consuming costly and the success rate is low and the failure rate is high (Bamgbopa, 2010; Lorusso *et al.*, 2008). However, implementation of infertility care in low-resource settings includes simplification of diagnostic, i.e., hysteroscopy before ART procedures, can minimize the complication rate of interventions (Ombelet *et al.*, 2008; Madani *et al.*, 2009). Nonetheless, economic considerations and lack of capability are thought to contribute to the lack of enthusiasm to employ hysteroscopy as a routine investigative tool (Hinckley and Milki, 2004). Unfortunately, although

diagnostic and operative laparoscopy is well established in gynecology, diagnostic hysteroscopy specifically in ART is, however, not extensively employed in the ART clinic due to the unpleasantness created by the course of action. Nevertheless, most researchers reported that the diagnostic hysteroscopy is used in the extensive context of the infertility managing (Touboul *et al.*, 2009). However, Bozdogan *et al.* (2008) reported that the rates of incidence of uterine disorders in women undergoing IVF, and in patients with known IVF failures were 18-50% and 40-43%, respectively. Furthermore, endometrial polyps and uterine septum are more prevalent in the infertile female than in the fertile ones (De Placido *et al.*, 2007; Di Spiezio Sardo *et al.*, 2008; Surrey *et al.*, 2005). In the current examine endometrial polyps and submucous myomas were observed as protuberances into space of uterine through hysteroscopy as saying as well. This means that hysteroscopy is a high-performance tool in discriminating anatomy of uterine and in identifying congenital uterine disorders as well as in characterizing points that are very worthy information through managing hysteroscopic surgical of the lesions. Hucke *et al.* (2000) claimed that uterine anomalies performed the critical role in infertility and showed the uterine disorders that often lead to surgery are adhesion, uterine septum, endometrial polyp, myoma, adenomyosis and cervical defect (Hucke *et al.*, 2000). Oliveira *et al.* (2003) and La Sala *et al.* (1998) reported that of the 55 and 100 after IVF female undergoing diagnostic hysteroscopy, 25 (45%) and 18 (18%) cases respectively had abnormalities, which were treated (Oliveira *et al.*, 2003; La Sala *et al.*, 1998). Raju *et al.* (2006) also revealed that, in spite of similarities in the mean number of oocytes retrieved, fertilization rate and number of embryos transferred among IVF patients ruled in their study, the clinical pregnancy rates in IVF patients that had abnormal office hysteroscopy findings was lower than ones had normal hysteroscopy findings. Similarly, Demiroglu and Gurgan (2004) suggested that patients with normal hysterosalpingography but recurrent IVF-embryo transfer failure should be evaluated prior to commencing IVF-embryo transfer cycle to improve the clinical pregnancy rate. Thus, it seems that these studies along with the present study provide strong evidence for including diagnostic hysteroscopy as part of the primary investigation of infertile couple planned for assisted conception. modifications in the endometrial receptivity; or diminished cross-talk between embryo-endometrium resulting in hindered implantation and direct effect on the endometrium, leading to intrauterine fluid formation. Strandell (2007), Mollo *et al.* (2009) and

Garbin *et al.* (2006) suggested that the underlying mechanism explaining reduced implantation and embryo development awaits further research. Kolankaya and Arici concluded that myomas that compress the uterine cavity with an intramural portion and submucous myomas significantly reduce pregnancy rates and should be removed before assisted reproductive techniques and hysteroscopic myomectomy is the gold standard for the treatment of submucous myomas (Kolankaya and Arici, 2006). In a different scenario, Perez-Medina *et al.* (2005) reported that hysteroscopic polypectomy before Intrauterine Insemination (IUI) achieves better pregnancy outcomes than no intervention. (Perez-Medina *et al.*, 2005; El-Toukhy *et al.*, 2008). Contrary to the above-mentioned initiative results, some research declared that the hysteroscopic procedure (especially Hysteroscopy Surgery) was associated with a high prevalence of complications, i.e., perforation of the uterine, intestine or urinary bladder due to forceful manipulation of these organs, excess bleeding, increased fluid absorption from the uterine into the vessels, infection and also death (Bradley, 2002; Pasini and Belloni, 2001). However, in the current study, no notable undesirable reactions or surgical complication were observed in any of the patients.

### CONCLUSION

Hysteroscopy is efficacious as primary assessment in couples planned for ART. It is also the gold standard in the management of detected uterine anomalies. The application of hysteroscopy in assisted reproduction is rapidly evolving. There are, however many areas of hysteroscopy which require more research to enable the adoption of best practices in assisted reproduction.

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