

Hysteroscopic Evaluation of The Uterine Cavity After Intracytoplasmic Sperm Injection and Embryo Transfer Failure: Is It Rewarding?

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ABSTRACT

Objective: This study was performed to evaluate the role of hysteroscopy and directed biopsy in women after intracytoplasmic sperm injection (ICSI) and embryo transfer failure despite transfer of good-quality embryos. **Materials and Methods:** One hundred and twenty eighty women who failed to conceive after one trial of Intracytoplasmic sperm injection and embryo transfer due to male factor infertility despite transfer of good-quality embryos and met the inclusion criteria and completed the follow up period, were recruited in the study. All patients were subjected to diagnostic hysteroscopy with directed biopsy and any intrauterine abnormalities were corrected accordingly. Post-operative follow up was done monthly for a period of one year to detect pregnancy either spontaneous or after assisted trials. **Results:** Twenty five percent of patients demonstrated abnormal hysteroscopic findings. Uterine adhesion was the most common anatomical abnormalities and represented 10.2% of the patients. However, hyperplastic endometrium was the most common histopathological abnormalities and represented 3.9% of the patients. The clinical pregnancy rate was significantly higher in the operative hysteroscopy group (60%) when compared to the non-intervention diagnostic hysteroscopy group (14.3%). **Conclusion:** Hysteroscopic evaluation of the uterine cavity should be an essential step before a second trial of ICSI.

Key Words: Hysteroscopy, endometrial histopathological abnormalities, ICSI failure.

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INTRODUCTION

Although assisted reproductive technology (ART) had helped many couples to reproduce, the overall pregnancy rates are around 35% and only 29% result in a live birth. The unsuccessful pregnancy outcome of patients undergoing *in vitro* fertilization (IVF) or other reproductive technologies depends on several factors, namely: embryo quality, intra uterine environment and the laboratory quality control and technique of embryo transfer which play a major role for the achievement and further continuation of pregnancy¹.

Nevertheless, implantation failure is still considered one of the main limiting factors that prevent a further increase in pregnancy rates². Hysteroscopy is the gold standard method for evaluating the endometrial characteristics and treating uterine pathology. It can diagnose more accurately adhesions, polyps and myomata which are considered the most significant causes of implantation failure³.

Some publications had evaluated the uterine cavity by hysteroscopy among patients with recurrent IVF and

embryo transfer failures prior to commencing further IVF-embryo transfer cycles and concluded that it could serve as a positive prognostic factor for achieving a subsequent pregnancy^{3,4,5}. In this study we will try to address the role of hysteroscopy (diagnostic and operative) and directed biopsy after failure of the first trial of ICSI and embryo transfer due to male factor infertility despite transfer of good-quality embryos.

MATERIALS AND METHODS

One hundred and twenty eighty women who failed to conceive after one trial of Intracytoplasmic sperm injection and embryo transfer performed for male factor infertility, in which two or more good quality embryos were transferred and completed the follow up period, were recruited. The study had been carried out in the Endoscopic units of Qena and Sohag university hospitals during the period from January 2008 to October 2010 after the protocol was approved by the human research ethics committees of both hospitals and after fulfilling the following inclusion criteria:

- Age between 20-35 years.
- Normal female hormonal profile (FSH, LH, prolactin, estradiol, midluteal progesterone).
- Normal lupus anticoagulant and anticardiolipin antibodies.
- Normal paternal karyotyping.
- An informed consent was obtained from all patients before participation in the study.

The Exclusion Criteria Included:

- Paternal chromosomal abnormalities.
- Evident uterine pathology.
- Polycystic ovarian syndrome (PCOs).
- Endometriosis.
- Tubal pathology (hydrosalpinx).
- Thyroid dysfunction.
- Obese females with body mass index more than 25.

After clinical examination, all women were subjected to clinical pelvic ultrasonography, hysteroscopy (diagnostic and operative when indicated) and directed biopsy using a rigid 5.5 mm hysteroscope (Karl Storz GmbH & Co, Tuttlingen, Germany). All patients received two tablets (400 µg) misoprostol (Misotac®, Sigma Pharmaceutical Industries, Egypt) 4 hours before hysteroscopy as a cervical priming agent. One gram Cefotax® vials T3A, Pharma group, Assiut, Egypt was given IV to patients who were subjected to operative hysteroscopy immediately before induction of anesthesia and another 1 gram 6 hours after surgery. All procedures were done within the first 5 days postmenstrual.

The Following Outcome Parameters were Recorded During The Procedure:

- Morphological evaluation of the uterine cavity which recorded whether normal or having pathological abnormalities.
 - Congenital uterine defects (septate uterus, bicornate uterus).
 - Acquired uterine defects (endometrial adhesion, fibroid or endometrial polyp).

Surgical correction was carried out for cases with anatomical defects either congenital or acquired.

Hysteroscopic incision, polypectomy and adhesiolysis was done for patients with uterine septum, endometrial polyp and intrauterine adhesions at the same sitting under laparoscopic guidance. Directed biopsies of the endometrium and histopathologic examination of the samples were done in all patients in order to evaluate the endometrial pattern. All patients were followed up monthly for a period of 1 year for the occurrence of pregnancy. If pregnancy did not occur within this period of time, patients were scheduled for a second ICSI trial.

Conventional methods for microinjection of oocytes. (ICSI) and *in vitro* culture of oocytes and embryos were used. Immediately before uterine replacement, the embryos were examined using an inverted microscope. Embryos that had seven or more cells, symmetric blastomeres and less than 10% cytoplasmic fragmentation on day 3 after oocyte retrieval were scored as good embryos. Uterine replacement of embryos was performed transcervically 72 hours after oocyte retrieval with a Wallace catheter (Wallace Embryo Replacement Catheter, Ref. 1816N; Smiths Medical International Limited, Kent, UK) under ultrasonographic guidance. Luteal support was performed with micronized progesterone, 400 mg vaginally daily (Cyclogest®, Multipharma, Egypt), starting on the day of oocyte retrieval. Clinical pregnancy was diagnosed when fetal heartbeats were visualized on transvaginal ultrasonography

Statistical Analysis:

Collected data were represented by number and percentage, Z test and chi-squared (χ^2) test had been used to compare between percentages and proportions where indicated. A P-value < 0.05 was considered statistically significant. Results were expressed as relative risk (RR) with 95% confidence interval (CI) using fixed effects models.

RESULTS

Demographic characteristics and variables of the studied patients is shown in Table (1). The majority of the studied group had history of primary infertility. Most of the secondary infertility patients had history of abortion and previous surgical evacuation.

Table 1: Patient characteristics of the study group.

	Study group (N= 128)
Age (years)	
• Range	20-35
• Mean	28 ± 3.6
Infertility	
• Primary infertility	92 (71.87%)
• Secondary infertility	36 (28.1%)
▪ Abortion	28 (87.6%)
▪ Prior delivery	8 (21.4)
Previous surgical evacuation	8 (6.25%)

Variables were presented as mean ±SD, number and percentage

The overall hysteroscopic findings of patients in the study group is shown in Table (2). Uterine adhesion and septate uterus were the most common anatomical abnormalities.

The histopathological findings of the endometrium among the studied group is shown in Table (3). Hyperplastic endometrium was the most common type

of histopathological abnormalities and tuberculous endometritis was the least common.

Table (4) compares the clinical pregnancy rates among the hysteroscopic intervention group and the diagnostic hysteroscopy group during the follow up period. The clinical pregnancy rate was significantly higher among the operative hysteroscopy group when compared to the non-intervention diagnostic hysteroscopy group.

Table 2: Hysteroscopic findings of patients of the study group.

Total number 128 (100%)	
Normal hysteroscopic finding	96 (75%)
Pathological abnormalities	32 (25%)
□ Uterine adhesions	13 (10.2%)
□ Septate uterus	12 (9.4%)
□ Polyp	5 (4.6%)
□ Bicornate uterus	1 (0.8%)
□ Fibroid	1 (0.8%)

Values were presented as number and percentage.

Table 3: Histopathological findings of the endometrium among the study group.

N= 128(%)	
Normal histopathological findings	112(87.5%)
Abnormal histopathological findings	16(12.5%)
• Hyperplastic endomtrium	10 (7.8%)
• Chronic non specific endometritis	4 (3.1%)
• Tuberculous endometritis	2 (1.6%)

Values were presented as number and percentage.

Table 4: Pregnancy rates with and without use of operative hysteroscopy in the studied group.

	Hysteroscopic intervention Group (N=30)	Diagnostic hysteroscopy Group (N=98)	
Patients get pregnant	18(60%)	14(14.3%)	P-value < 0.05

Values were presented in number, percentage and proportions. Z test had been used to compare between proportions. P-value of < 0.05 was considered statistically significant.

The pregnancy rates after correction of individual uterine abnormalities is shown in Table (5). Highest rate was among patients with intrauterine adhesolysis. After

correction of uterine abnormalities, an equal number of patients conceived spontaneously and after a second trial of ICSI.

Table 5: Pregnancy rates after correction of individual uterine abnormalities.

	Uterine adhesions N=(13)	Septate Uterus N=(12)	Endometrial polyp N=(5)	P.value
Spontaneous pregnancy	4 (30%)	4 (33.4%)	1 (20%)	NS
Pregnancy after ICSI	5 (40%)	2 (16.6%)	2 (40%)	NS
	9 (70%)	6 (50%)	3 (60%)	NS

Values were presented in number and percentage. (X²) test had been used to compare between percentages. P-value of < 0.05 was considered statistically significant. NS= Non Significant.

DISCUSSION

Despite the rapid developments in the field of assisted reproduction, the implantation and pregnancy rates remain un-expectantly low. It was estimated that up to 85% of embryos transferred into the uterine cavity do not implant⁶. Although endometrial receptivity is considered one of the three major pillars that play a major role for achievement of pregnancy. Most in-vitro fertilization programs are still using hysterosalpingography and/or ultrasonography as a routine investigational tool to document the presence of a normal uterine cavity and endometrial pattern⁷.

Apart from the clear concept of hysteroscopy as a gold standard tool for evaluating the endometrial cavity⁸, hysteroscopy can also offer great assistance for the interpretation of uncertain findings from other diagnostic modalities⁹. Furthermore, it enables direct visualization of the cervical canal and uterine cavity in addition to obtaining a directed biopsy from any suspicious pathology which will increase the diagnostic accuracy of endometrial histopathological lesions³. Many studies reported that small lesions may be missed by US⁸.

In the current study, abnormal hysteroscopic findings had been reported in 25% of women scheduled for second trial of ICSI and embryo transfer. Uterine adhesions and septate uterus were the most common anatomical abnormalities among the studied group and represented (10.2% and 9.4%), respectively. This agreed with the results of Rama, who reported that the most common anatomical abnormality in their study was uterine adhesions that was identified in 11.6%³.

Using hysteroscopy to treat these two prevalent findings resulted in a pregnancy rate of 70% among patients treated by hysteroscopic adhesolysis within the year of follow up and a pregnancy rate of 50% among participants for whom incision of a uterine septum had been done which is comparable to the results of Colacurci², who reported 70% pregnancy rate after incision of a uterine septum using either hysteroscopy with versapoint versus resectocopy with unipolar knife⁴.

Spiewankiewicz and Tirso, reported that pregnancy rates after hysteroscopic polypectomy were (76%) and 64%, respectively^{9,10}. These results nearly agree with our results. We found that 4.6% of patients with endometrial polyps which could not be diagnosed with either TVS or HSG. Sixty percent of them conceived after polypectomy within one year.

In this study, the high pregnancy rate after correction of intrauterine lesions 60% compared to 14.3% in the non-intervention diagnostic hysteroscopy group. This result was generally accepted with the study of Oliveira et al. 2003, who reported that women with abnormal hysteroscopic finding⁹s should be treated properly before

going on to IVF because ignoring it would increase the risk of spontaneous abortion and poor endometrial receptivity¹¹.

In our study, hyperplastic endometrium was the most common histopathological finding and tuberculous endometritis was the least abnormality among our studied group. These findings are comparable with results of Talia, who reported one patient diagnosed as tuberculous endometritis out of 100 patients subjected to diagnostic hysteroscopy and endometrial biopsy¹².

CONCLUSION

Hysteroscopic evaluation of the uterine cavity should be an essential step before a second trial of ICSI.

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