

The Use of Ultrasound during Intrauterine Insemination in Unexplained Infertility May Improve Pregnancy Outcomes

Deniz Oztekin^a Emine Ozcinar^a Can Kose^a Ibrahim Gulhan^b
Mehmet Ozeren^a Sivekar Tinar^a

^aIVF Center, Ege Maternity and Gynecology Training and Research Hospital, and ^bDepartment of Gynecology, Izmir Bozyaka Education and Research Hospital, Izmir, Turkey

Key Words

Intrauterine insemination · Ultrasound · Pregnancy rate · Unexplained infertility

Abstract

Objective: To investigate the role of ultrasound guidance in intrauterine insemination (IUI). **Materials and Methods:** A retrospective study was conducted. The data was collected from the records of 197 couples with unexplained infertility who underwent IUI with a total of 267 IUI cycles in the in vitro fertilization center of our hospital between January 2009 and December 2010. **Results:** Of the 267 IUI cycles, 145 were carried out as US-guided, while 122 cycles IUI were performed with a blind procedure. In the US-guided IUI and blinded IUI groups, the pregnancy rates were 23.4 and 13.9%, respectively. The difference between the groups was statistically significant ($p = 0.049$), thereby indicating that US guidance improves pregnancy rates. In the US-guided IUI group, 9.7% of the cases were difficult, while in the blinded IUI group, 26.2% were difficult and the difference between the groups was also statistically significant ($p < 0.001$). **Conclusion:** US guidance in IUI improves pregnancy rates and reduces the frequency of difficult IUI.

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Introduction

Intrauterine insemination (IUI) with ovarian stimulation has been widely used as the primary therapeutic modality for infertility, especially that which is unexplained or caused by nonsevere male factor, anovulation or cervical mucus hostility. This method is less expensive and less invasive than in vitro fertilization (IVF).

Many studies focus on factors that affect the results of IUI, such as the length and type of infertility, sperm quality, ovarian stimulation protocols, number of follicles, time of insemination and type of catheter [1–3]. The IUI technique has been shown to be important; recent publications show that atraumatic and ultrasound (US)-guided embryo transfer improves the pregnancy outcomes of IVF cycles [4, 5]. Using US guidance during embryo transfer in IVF increases the frequency of ‘easy’ transfer and prevents the catheter from touching the uterine fundus, which may cause uterine contractions [6]. Similarly, using US guidance during IUI may improve results, but few studies have investigated the effect of US-guided IUI on pregnancy outcomes [7]. The aim of this study was to investigate whether or not the use of US guidance affects the clinical outcomes of IUI in unexplained infertility.

Table 1. Characteristics of patients

	US-guided IUI	Blinded IUI	p value
Age, years	31.2 ± 4.6	30.2 ± 4.6	0.08
BMI	25.4 ± 3.8	26.4 ± 3.8	0.62
Day 3 FSH, mIU/ml	7.3 ± 2.3	6.9 ± 2.3	0.13
Day 3 LH, mIU/ml	5.8 ± 2.5	6.3 ± 3.0	0.13
Day 3 E2, pg/ml	53.1 ± 34.7	47.5 ± 25.3	0.14
Number of cycles	145	122	
Number of patients	104	93	
Duration of infertility, months	56.71 ± 19.71	57.67 ± 19.61	0.73
Patent tube status (unilateral/bilateral)	7/97	4/89	0.54
Follicle count at hCG day (>16 mm)	2.5 ± 1.0	2.6 ± 1.1	0.64
Total motile sperm count (million)	67.38 ± 73.98	61.44 ± 72.19	0.50
Total hMG usage, IU	726.21 ± 170.63	713.73 ± 171.74	0.55
hMG induction duration, days	8.4 ± 1.9	8.4 ± 1.7	0.93

Materials and Methods

In this study, a total of 267 IUI cycles in 197 couples with unexplained infertility were evaluated retrospectively. Data were collected from the records of couples with unexplained infertility that underwent IUI in the IVF center of our hospital between January 2009 and December 2010. During the same period, a total number of 846 IUI cycles of 677 patients were performed in our IVF center. All patients received 3–6 cycles of clomiphene citrate before undergoing IUI with gonadotropins.

Unexplained infertility was defined as infertility for couples with no definite reason. Patients with at least one patent tube in hysterosalpingography or laparoscopy and husbands with normal sperm parameters according to World Health Organization classification were included. Women with myomas, endometriosis and uterine anomalies were excluded from the study. Patients with a basal follicle-stimulating hormone (FSH) level >12 mIU/ml, a maternal age >40 years, polycystic ovarian syndrome or a coexisting chronic disease such as hyper- or hypothyroidism, diabetes mellitus or any history of previous reproductive surgery were also excluded from the study.

Basal FSH, luteinizing hormone (LH) and estradiol (E2) were measured on the third day of the cycle. Ovarian stimulation was started on day 3 with 75–150 IU of human menopausal gonadotropin (hMG; Menogon, Ferring or Merional, IBSA), depending on the patient's situation. Patients were monitored by transvaginal folliculometry and doses of gonadotropin were adjusted according to their response. When at least one follicle reached ≥ 16 mm in diameter, 250 µg of recombinant human chorionic gonadotropin (hCG; Ovitrelle, Serono) was subcutaneously administered. IUI with the husband's semen was performed 36 h after the administration of hCG. Patients were not asked for a full bladder. If a patient preferred the full bladder position, US-guided (Sonoace X4, Samsung Medison) IUI was administered for the patient. If the patient preferred the empty bladder position, the blind procedure was used.

The double gradient method was used for semen preparation. The sperm sample was collected by masturbation after 2–5 days

of abstinence. The collected samples were then kept in an incubator at 37°C for 20 min for liquefaction. After liquefaction, samples were examined for sperm count, motility and morphology. They were then centrifuged with double-layer (upper 1 ml 45%, lower 1 ml 90% Pure Sperm) gradient medium, after which the filtrate was collected and washed. Samples were washed twice with sperm washing medium and during the washing process, centrifugation was performed at 1,600 rpm for 10 min. Supernatant was carefully removed and layered with 0.7 ml of G-sperm and kept in the incubator at 37°C, tilted at an angle of 45 degrees for 20 min. After 20 min, 0.5 ml of the upper layer, expected to contain highly motile spermatozoa, was gently aspirated using a soft catheter (Genetics). A total of 1 ml of sperm preparation was slowly injected into the uterine cavity. If a tenaculum application was needed to fix the cervix, the insemination was considered a difficult IUI.

Institutional review board approval was obtained for the study. For statistical analysis, SPSS software for Windows (version 13.0). χ^2 and a Student t test were used for comparing the groups. $p < 0.05$ was considered statistically significant.

Results

The mean age of the patients was 30.6 ± 4.0 years (range 21–40). Of the 267 cycles, 145 were carried out as US-guided and 122 were performed using the blind procedure. There were no statistically significant differences between the groups in terms of FSH, LH and E2 on day 3, age, BMI, duration of infertility, patent tube status, follicle count at hCG day, total motile sperm count, total hMG usage and hMG induction duration (table 1). Outcomes for the groups are shown in table 2. The overall pregnancy rate was 19.1% (51/267). Ten pregnancies were multiple pregnancies and 10 ended in abortion.

Table 2. Outcomes of US-guided and blinded IUI

	US-guided IUI	Blinded IUI	p value
Number of cycles	145	122	
Number of follicles ≥ 16 mm	2.5 ± 1.0	2.5 ± 1.1	0.64
Difficult IUI	14 (9.7)*	32 (26.2)	<0.001
PR	34 (23.4)	17 (13.9)	0.049
Multiple PR	8 (5.6)	2 (1.6)	0.09
Abortion rate	6 (4.1)	4 (3.3)	0.71

PR = Pregnancy rate.

There was no significant difference between the US-guided and blinded IUI groups regarding the multiple-pregnancy rate, abortion rate and the number of follicles ≥ 16 mm. The pregnancy rates were 23.4 and 13.9%, respectively (p value), and the difference was statistically significant ($p = 0.049$). In the US-guided group, 9.7% of the cases were difficult. In the blinded group, 26.2% were difficult. The difference was statistically significant ($p < 0.001$).

Discussion

In this study, we found that US guidance in IUI improved the pregnancy rates and reduced the frequency of difficult IUI. Use of US guidance during embryo transfer has been widely accepted as an important procedure in IVF. This study confirmed previous findings that US-guided embryo transfer is associated with higher pregnancy rates [4–6, 8], but how it actually improves the pregnancy outcome is not known. Avoidance of endometrial induction may be one of the underlying mechanisms. US guidance does reduce the frequency of ‘difficult’ transfers, which may lead to increased pregnancy rates [9].

Endometrial contractions may lead to the expulsion of semen from the uterus. Although some authors have suggested that intrauterine manipulations may initiate these uterine contractions [10, 11], van Gestel et al. [12] showed that no contractions or induction of unfavorable (fundus-to-cervix) endometrial wave-like activity were observed in patients undergoing IUI. Uterine contractions may occur as a result of touching the fundus during intrauterine manipulations. In our study, avoiding touching the fundus in the US-guided group may have led to a decrease of these unfavorable contractions.

Sometimes during transcervical insertion of a catheter, a teneculum is needed for correction of the cervico-uterine angle. This type of catheterization is called ‘difficult’ insemination. The number of difficult insemination in which we had to use a teneculum was higher in the blinded group than in the US-guided group.

A randomized controlled study comparing US guidance and blind intervention was performed by Ramón et al. [7]. In this study, 73 couples with 231 IUI cycles were evaluated. No tenaculum was used during catheterization and in both groups all patients had a full bladder. No difference between the groups with regard to pregnancy rates was found and the authors concluded that US-guided IUI did not produce better results than blind insemination. On the other hand, in general clinical practice, a full bladder is not necessary to perform IUI and it may not be raised as an issue in IUI without US guidance. All subjects in our blinded IUI group had an empty bladder, but in Ramón’s study [7], the subjects in the blinded IUI group had a full bladder like the US-guided group. A full bladder may improve the angle between cervix and uterus. A cervical manipulation like teneculum application to the cervix is not frequently required. If the clinician does not use US guidance during IUI, an empty bladder may result in a traumatic catheterization and may decrease success rates. In contrast to Ramón’s study, our results showed that US guidance during IUI improved pregnancy rates and that rates of ‘difficult’ IUI were decreased by US guidance.

Conclusions

In our study, US-guided IUI increased pregnancy rates. A prospective study with larger populations is recommended in order to understand how US guidance improves the pregnancy rate during IUI.

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