The Effect of Intra-Catheter Air Volume on the Outcome of Intrauterine Insemination (IUI): A Clinical Trial Study

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ABSTRACT

Background & Objective: The presence of air in the catheter was found to affect the success of embryo transfer into the uterine cavity. This study determined the chances of achieving pregnancy using the intrauterine insemination (IUI) method with different air volumes inside the IUI catheter.

Materials & Methods: This clinical trial study was performed on 521 IUI cycles among 270 couples from 2013 to 2014. The patients were divided into three groups (each group of 90 patients), based on three volumes of air inside the catheter (0.0 ml, 0.5 ml, and 1 ml). Other variables, include the woman’s age, menstrual cycle status, duration of infertility, type of infertility, sperm morphology, total motile sperm count (TMSC), number of motile sperm inseminated (NMSI), and pregnancy rate or the success rates of IUI were evaluated.

Results: The mean age of women and men were 33 and 30 years, respectively. Based on three volumes of air inside the catheter (0.0 ml, 0.5 ml, and 1.0 ml), the pregnancy rates were 5%, 9.4%, and 16.5%, respectively. TMSC of more than 5.6x10^6 and NMSI of more than 3.4x10^6 were associated with the chance of IUI achievement. At the same time, there was no significant relationship between the woman’s age, irregular menstrual cycles, and duration of infertility with the success rate of IUI. We found that the air volume of 1.0 ml inside the IUI catheter significantly increased the pregnancy rate compared to other groups.

Conclusion: The volume of air within the catheter had a significant relationship with the success rate of IUI.

Keywords: Infertility, Intrauterine Insemination, Pregnancy Rate

Introduction

Infertility is the failure to get pregnant after at least one year of regular unprotected intercourse (1, 2). Infertility has physical and emotional effects on infertile couples, which leads to social problems, personal suffering, mental illness, sexual disability, and divorce (3, 4). The overall incidence of female infertility varies from 10 to 20% and almost 15% of all women are infertile (5, 6). However, in high-income countries, the prevalence of primary infertility had a decreasing trend of -9.3 and -11.6 in men and women, respectively (7). Recently, assisted reproductive technology (ART) has opened a new window to treat infertility (8, 9). Intrauterine insemination (IUI) is a procedure in which a high motile sperm concentration is injected into the uterine using a thin and flexible catheter (10-13). There are different indications for the IUI procedure, including male factors (14, 15), ovulation (16-18), endometriosis with a normal fallopian tube (19), and unexplained infertility (20, 21). IUI may be used as a first-line treatment for couples with infertility due to its cost-effective and non-invasive properties compared with other ART procedures (20, 22). The successful pregnancy rates for IUI vary widely from less than 5% to more than 70% (23) and depend on etiologic factors (24). Several factors, including maternal age (25), the length of infertility, type of infertility, and the number of sperms in the initial evaluation or through an insemination catheter may influence on the IUI outcome (26, 27). Besides, the number of mature follicles (17, 28), estradiol (E2) levels following human chorionic gonadotropin (HCG) injection (29), the speed of IUI (30), and the type of catheter (hard tip or soft tip) (31) have been reported to affect the chances of pregnancy with IUI (32-34). One of the main problems during an IUI procedure is that the whole semen sample does not
discharge to the uterine cavity and a part of the semen remains inside the catheter. It was shown that the presence of air accelerated the chances of embryo transfer from the catheter into the uterine cavity (35, 36). We assumed that adding some air after insemination reduced the residual sample in the catheter and may influence the IUI outcome. No study has examined the effect of air volume within the catheter during the IUI procedure. This study aimed to assess the impact of air volume in the catheter during the sperm injection on the chance of IUI success.

Methods

Study design

This clinical study was performed in the Fertility, Infertility and Perinatology Research Center, Imam Khomeini Medical Center, Ahvaz Jundishapur University of Medical Sciences, from 2013 to 2014. Diagnostic evaluation of all couples, including hormonal assay (FSH, L.H., Prolactin, and TSH), hysterosalpingography, semen analysis, density and motility of sperm (total, class A, B, A+B), and total motile sperm count (TMSC) were recorded and prepared the IUI samples. Patients with patent fallopian tube, with follicle-stimulating hormone (FSH) levels below 10 I.U./ml were entered into the study. IUI insemination was performed after 34-36 hours following HCG injection. All the IUI cycles underwent ovulation induction. Ovulation induction was started on the third day of the menstrual cycle with Clomiphene or Letrozole (5 mg) for five days. Two or more gonadotrophins (HMG) were added on the 7-8 days of processes (75 IU) (37). The patient was monitored until the time of ovulation. When at least one follicle with a diameter exceeding 17 mm was observed on vaginal ultrasonography, ovulation was triggered by 5,000–10,000 IU of HCG. The couples abstained from sexual activity for 3-5 days before insemination to help in concentrating semen. Sperm samples were collected via masturbation, within two hours before the IUI and were kept in a sterile container. Semen samples were prepared using density gradient centrifugation (20 min at 1300 rpm) and then washed in 2 ml of culture medium (Media Sperm wash, Company Sage, method swim up, Denmark). In this method, sperm cells were separated based on their density (38). Sperm cells with normal or abnormal shape had different densities. The density in normal cells was 1.10 g/mL and in abnormal cells was 1.06 to 1.09 g/mL. Sperm analysis was performed with both manual and computer-assisted procedures.

Performing IUI

In this section, 270 patients were enrolled into three groups (each including 90 patients) based on the volume of air inside the catheter (0.0 ml, 0.5 ml, and 1.0 ml) and during the sperm injection procedure. The three groups were matched according to age (less than 35 years). At first, a syringe (2 ml) was connected to the IUI catheter, and then the prepared semen sample was taken with the syringe. The sample was measured with eyes and added 0.0 ml, 0.5 ml, and 1.0 ml of air randomly. Then the sample stayed on the proximal of the catheter and followed by air with delicate hand motion. At the end, the catheter was entered to the uterus and the prepared samples (0.4 ml) were inseminated slowly. After two weeks, serum Beta-HCG levels were measured. Other variables include the woman’s age, menstrual cycle status, duration of infertility, type of infertility, sperm morphology, total motile sperm count (TMSC), number of motile sperm inseminated (NMSI), and pregnancy rate or the success rates of IUI were evaluated. In this study, the luteal phase didn’t stimulate progesterone.

Statistical analysis

All results were expressed as mean ± standard deviation (S.D.). By using the Tukey test as a post hoc test, different variables were evaluated. Finally, the comparison between the average of normal and abnormal variables was determined using the one-way ANOVA test. Statistical analyses were performed via SPSS 16.0 (IBM, USA). The results were considered significant with a P-value of less than 0.05.

Ethical statement

The study was approved by the Ethics Committee of Ahvaz Jundishapur University of Medical Sciences. Written informed consent was obtained from all participants in the study. This study was financially supported by the Vice chancellor for research, Ahvaz Jundishapur University of Medical Sciences (Grant Number: IRCT20201110049331N1).

Results

This study was performed on 521 IUI cycles among 270 couples from 2013 to 2014. The mean age of women and men was respectively 33±1.7 and 30±1.2 years (P=0.070) (Table 1). According to demographic characteristics, 55% of patients had regular menstrual cycles and 44% of women had a menstrual problem such as irregular menses. The distributions were the same in the three groups (P=0.80). Based on two types of infertility, 67% of couples had primary infertility (the inability to get pregnant) and 32% had secondary infertility (the ability to get pregnant at least once). The distributions were the same in the three groups (P=0.100). The mean duration of infertility was 4.1±2.8 years, with the same distributions in the three groups (P=0.120). Based on sperm morphology, the distribution of samples was the same in all three groups with the mean of 6.8% (P=0.130). There was no significant relationship between the woman’s age, irregular menstrual cycles, and duration of infertility with the success rate of IUI (P=0.100).

Based on three volumes of air inside the catheter (0.0 ml, 0.5 ml, and 1.0 ml), total motile sperm counts were 7×10^6, 6×10^6, and 7×10^6, respectively (P=0.110). Also,
number of motile sperm inseminated were $7 \times 10^6$, $6 \times 10^6$, and $7 \times 10^6$, respectively ($P=0.120$). Our results showed that the pregnancy rates based on three volumes of air were $5\%$, $9.4\%$, and $16.5\%$, respectively ($P=0.040$). TMSC of more than $5.6 \times 10^6 \pm 4.3$ ($P=0.130$) and NMSI of more than $3.4 \times 10^6 \pm 1.9$ ($P=0.110$) were associated with the chance of IUI achievement (Table 2). We found that the air volume of 1.0 ml, inside the IUI catheter significantly increased the pregnancy rate in comparison with other groups ($P=0.001$) (Table 2).

### Table 1. Demographic and clinical characteristics of patients based on three volumes of air inside the catheter

<table>
<thead>
<tr>
<th>Variables</th>
<th>Air volume (cc)</th>
<th>Mean±SD/ Number (%)</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>0.0</td>
<td>30±1.2</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>0.5</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.0</td>
<td>31</td>
<td>P=0.070</td>
</tr>
<tr>
<td>Menstrual cycle status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regular</td>
<td>0.0</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.5</td>
<td>31.5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.0</td>
<td>33.5</td>
<td>P=0.080</td>
</tr>
<tr>
<td>Irregular</td>
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<td>30</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.5</td>
<td>31.5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.0</td>
<td>33.5</td>
<td>P=0.080</td>
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<tr>
<td>Type of infertility</td>
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<td></td>
</tr>
<tr>
<td>Primary</td>
<td>0.0</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.5</td>
<td>31.5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.0</td>
<td>33.5</td>
<td>P=0.100</td>
</tr>
<tr>
<td>Secondary</td>
<td>0.0</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.5</td>
<td>31.5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.0</td>
<td>33.5</td>
<td>P=0.100</td>
</tr>
<tr>
<td>Sperm morphology</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.0</td>
<td>6%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.5</td>
<td>6.7%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.0</td>
<td>6.7%</td>
<td>P=0.130</td>
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<tr>
<td>Duration of infertility (year)</td>
<td>0.0</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.5</td>
<td>3.5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.0</td>
<td>4.5</td>
<td>P=0.120</td>
</tr>
</tbody>
</table>

**Values are presented as mean±SD, Statistical analysis: One-way ANOVA test and the Tukey test as a post hoc test.

### Table 2. Comparing the IUI outcome using three air volumes

<table>
<thead>
<tr>
<th>Variables</th>
<th>Air volume (cc)</th>
<th>Mean±SD/ Number (%)</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>TMSC (ml)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.0</td>
<td>$7 \times 10^6$</td>
<td>$6 \times 10^6$</td>
<td>$7 \times 10^6$</td>
</tr>
<tr>
<td>0.5</td>
<td>$14 \times 10^6$</td>
<td>$16 \times 10^6$</td>
<td>$14 \times 10^6$</td>
</tr>
<tr>
<td>1.0</td>
<td>$5 \times 10^6$</td>
<td>$6 \times 10^6$</td>
<td>$6 \times 10^6$</td>
</tr>
<tr>
<td>NMSI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.0</td>
<td>$8.7 \times 10^6$</td>
<td>$8.1 \times 10^6$</td>
<td>$8.9 \times 10^6$</td>
</tr>
<tr>
<td>0.5</td>
<td>$2.7 \times 10^6$</td>
<td>$4 \times 10^6$</td>
<td>$3.5 \times 10^6$</td>
</tr>
<tr>
<td>1.0</td>
<td>$1.5 \times 10^6$</td>
<td>$2.2 \times 10^6$</td>
<td>$1.3 \times 10^6$</td>
</tr>
<tr>
<td>Pregnancy rate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.0</td>
<td>$7%$</td>
<td>$8%$</td>
<td>$7%$</td>
</tr>
<tr>
<td>0.5</td>
<td>$8%$</td>
<td>$8%$</td>
<td></td>
</tr>
<tr>
<td>1.0</td>
<td>$7%$</td>
<td>$7%$</td>
<td></td>
</tr>
</tbody>
</table>

**Values are presented as mean±SD, Statistical analysis: One-way ANOVA test and the Tukey test as a post hoc test. TMSC: Total motile sperm count; NMSI: Number of motile sperm inseminated; IUI: Intrauterine insemination.

### Discussion

IUI technique is a suitable fertility approach that frequently recommended to infertile couples to increase pregnancy rates (39). Several previous studies have shown that some specific factors can estimate the success rates of IUI (40, 41). The volume of air inside the catheter during sperm injection is one of the unknown factors that may influence the chance of IUI achievement. The results of the present study showed that the volume of air (1.0 ml) within the catheter had a significant relationship with the success rate of IUI. Moreno et al. examined the impact of air volume in the embryo transfer catheter through the in vitro fertilization (IVF) process. They compared the effect of air in the syringe, the proximal part of the catheter, and at the tip of the catheter with the syringe and the entire catheter without air. They found there was no relationship between the air loaded into the transfer catheter and the success of implantation and pregnancy rates (42). Christianson et al. used the results of a web-based survey and found that medium/air/embryo/air/medium, medium/embryo, medium/air/embryo, and low oxygen concentrations were used for embryo loading (43). Matitashvili et al. evaluated the influence of two embryo-loading techniques, including small droplets of air (15–20 μL medium/10 μL air/5–10 μL medium with embryo) or fluid inside the catheter (10...
μL of air) on the clinical pregnancy rate. They concluded that there were no significant differences between air-fluid (behind and in front of medium) and medium-only loading methods (44). Mo et al. assessed the effects of various parameters, including distance of the catheter tip to the fundus, uterine orientation, injection speed, and final embryo position during embryo transfer. They reported that embryo separation with the air bubble increased fast injection into a retroverted uterus (35).

We also displayed that the TMS count more than 5.6 ×10^6 was associated with the success rate of IUI (P>0.05). This result was consistent with other findings. Similarly, Merviel et al. demonstrated that the TMS count of more than five million among the 1088 IUI cycles had a positive effect on the outcome of the procedure (32). Jeong et al. suggested that the assessment of sperm motility more than TMSC could predict the chance of IUI success rate (45). Findeklee et al. demonstrated no significant association between the TMS count and the outcome of IUI (46). Hajder et al. evaluated the predictive value of TMSC in 98 couples with male factor and unexplained infertility. They found that couples with the TMSC> 5×10^6 were indicated for treatment with IUI (47). Nikbakht et al. reported that the TMS count of 5×10^6 to <10×10^6 was a useful prognostic factor in the IUI cycles (12). They showed that the rate of pregnancy following the IUI procedure with any air in the catheter of IUI was 9.9% per cycle. Kadour-Peero et al. assessed the impact of TMSC on the success of IUI. They reported that in women with 38–39 years, TMSC <5 million and in women with 40 years, TMSC ≤ 10 million had poorer outcomes (48).

In addition, we found that there was no relationship between the women's age and the chance of getting pregnant through the IUI technique. The recent survey by Soria et al. also showed that the woman's age had no significant effect on the success rate of IUI (49). Although the success rate of IUI decreased after the age of 37, IUI treatment can be a successful strategy in women older than 40 years of age (50). Finally, we found no correlation between the pattern of the menstrual cycle and the IUI success rate. Besides, the TMS count of greater than five million could be a predictor of IUI achievement among the infertile couples who participated in our study. These results may contribute to the higher predictive value of IUI outcome and better choices of indication for IUI.

The limitation of this study was that we didn’t measure the remaining sample in the IUI catheter after insemination in all three groups. Therefore, we couldn’t compare the result of IUI with the remaining sample in the IUI catheter. Although our study showed that the volume inside the catheter can assist the transfer of the entire sample through the uterus, more research is necessary to confirm these results.

### Conclusion

In conclusion, this study revealed clearly that the volume of air within the catheter affected the chance of a successful IUI outcome. It is recommended that predictors of IUI success should be separately investigated among the different indications for an IUI process through the upcoming studies.

### Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

### Acknowledgments

None.

### Conflict of Interest

The authors declare that there are no competing interests.

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