Influence of Embryo Transfer Distance on Pregnancy Rate in ICSI Cycles

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Abstract

Purpose: To investigate the influence of transfer distance to the fundus on pregnancy rate.

Method: Retrospective single center study, including 674 consecutive cycles of ICSI done at Adam International Clinic between January 2005 and December 2005.

All patients were included and data examined regarding; their age, endometrial thickness at day of HCG, endometrial pattern at day of HCG, number and quality of embryos transferred, difficulty of embryo transfer as reported by the transferor, transfer distance to the fundus as measured by trans-abdominal ultrasound and if the ejection of the media inside the inner sheath of the transfer catheter was seen or not.

Results: Our data indicate that the actual distance to the fundus did not affect the pregnancy rate.

Conclusion: Our data proves that the exact position of embryo deposition from the fundus does not influence pregnancy rate, however the use of trans-abdominal ultrasound can be of help in visualizing the catheter in the more difficult transfer and air bubbles can be documented, also ultrasound guidance adds to the confidence in the procedure by both the physician and the patient.

Key Words: Embryo transfer distance – Pregnancy rate – ICSI cycles.

Introduction

EMBRYO transfer is a very important final step in ICSI treatment. About 85% of all couples undergoing ICSI reach this stage, but only one-third of them achieve ongoing pregnancy. The pregnancy rate after embryo transfer is dependent on multiple factors such as embryo quality [1,2], endometrial receptivity and the technique of the transfer itself [3].

Numerous methods, including the use of ultrasound guidance for proper catheter placement in the endometrial cavity, have been suggested as a means of improving the technique of embryo transfer.

This study was carried out to investigate the influence of transfer distance from the fundus on pregnancy rate and hence if there is a best site for embryo deposition during embryo transfer.

Material and Methods

This is a retrospective single center study, including 674 consecutive cycles of ICSI done at Adam International Clinic between January 2005 and December 2005.

All patients were included and data examined regarding; their age, endometrial thickness at day of HCG, endometrial pattern at day of HCG, number and quality of embryos transferred, difficulty of embryo transfer as reported by the transferor, transfer distance to the fundus as measured by trans-abdominal ultrasound and if the ejection of the media inside the inner sheath of the transfer catheter was seen or not.

The ovulation protocols used were the long luteal phase agonist protocol and the short protocol (as judged by patient's age, ovarian reserve judged by day 3 FSH and antral follicular count and previous history of ovarian response). Ovarian response was monitored by vaginal ultrasound and HCG was given when there was >=1 follicle >=18 mm and >=3 follicles >=16mm. ultrasound guided oocyte retrieval was carried out 35 hours later. Embryo transfer was performed on day 2 or day 3 after oocyte retrieval according to number and quality of embryos.

Embryo transfer was carried out under trans-abdominal ultrasound guidance and transfer distance to the fundus (TDF) was measured between the high echogenic transfer dot and the surface of
the fundal endometrium. Also if the ejection of the transfer media inside the inner sheath of the catheter was seen or not.

The ultrasound used was General Electric (Logiq 180). The transfer catheter used was Cook (Cook OB/GYN Spenser, Indiana, USA).

Pregnancy test in blood was done 2 weeks after transfer.

**Statistical evaluation:**

Data were statistically described in terms of mean ± standard deviation (± SD), frequencies (number of cases) and relative frequencies (percentages) when appropriate. Comparison of quantitative variables between different groups in the present study was done using Student \( t \) test for independent samples in comparing 2 groups when normally distributed and Mann Whitney U test for independent samples when not normally distributed. For comparing categorical data, Chi square \( (\chi^2) \) test was performed. Exact test was used instead when the expected frequency is less than 5. A probability value \( (p \) value) less than 0.05 was considered statistically significant. All statistical calculations were done using computer programs Microsoft Excel version 7 (Microsoft Corporation, NY, USA) and SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) statistical program.

**Results**

Patients were segregated into the pregnant group (275 cases) and the non-pregnant group (399 cases) and the following parameters were studied in order to detect the influence of TDF and if there were other variables that significantly affected the pregnancy rate.

1- **Age:**

In the pregnant group age ranged between 17 and 45 ys with a mean of 28.73 while in the non-pregnant group it ranged between 17 and 46 ys with a mean of 31.51 which is statistically significant higher.

<table>
<thead>
<tr>
<th>Table (1).</th>
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<tbody>
<tr>
<td><strong>Age (years)</strong>(^*)</td>
</tr>
<tr>
<td>28.73±5.31</td>
</tr>
<tr>
<td><strong>Number of embryos</strong>(^*)</td>
</tr>
</tbody>
</table>

\(^*\) Data are described in mean ± SD.

\(^‡\) Statistically significant difference.

2- **Endometrial thickness:**

In the pregnant group endometrial thickness measured on HCG day ranged between 5 and 16mm with a mean of 10.66 while in the non-pregnant group it ranged between 5 and 18mm with a mean of 10.36 with no statistically significant difference.

<table>
<thead>
<tr>
<th>Table (2).</th>
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<tbody>
<tr>
<td><strong>Endometrial thickness (mm)</strong>(^*)</td>
</tr>
<tr>
<td>10.66±1.75</td>
</tr>
</tbody>
</table>

\(^*\) Data are described in mean ± SD.

\(^†\) Data are described in number of cases (%).

\(^‡\) Statistically significant difference.

3- **Endometrial pattern:**

In the pregnant group trilaminar endometrial pattern on HCG day was found in 172 cases (83.5%) and 34 cases showed hyperechogenic endometrium. In the non-pregnant group trilaminar endometrium was found in 217 cases (75.87%) and hyperechogenic endometrium in 69 cases with statistically significant difference.

<table>
<thead>
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<th>Table (2).</th>
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<tr>
<td><strong>Pregnancy</strong></td>
</tr>
<tr>
<td>Tri laminar endometrium</td>
</tr>
</tbody>
</table>

\(^*\) Data are described in number of cases (%).

\(^‡\) Statistically significant difference.

4- **Quality of embryos transferred:**

In the pregnant group the number of good embryos transferred per cycle ranged between 0 and 5 with a mean of 1.97 and that of fair embryos ranged between 0 and 6 embryos with a mean of 0.98 and that of bad embryos ranged between 0 and 5 with a mean of 0.42.

While in the non-pregnant group the number of good embryos transferred per cycle ranged between 0 and 6 embryos with a mean of 1.4 and that of fair embryos ranged between 0 and 5 with a mean of 1.26 and that of bad embryos ranged between 0 and 6 embryos with a mean of 0.53.

There were statistically significant more good embryos transferred per cycle in the pregnant group while statistically significant more fair embryos were transferred per cycle to the non-pregnant group and no statistically significant difference between the 2 groups in the number of bad embryos transferred.

<table>
<thead>
<tr>
<th>Table (3): Number of embryo by quality.</th>
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<tbody>
<tr>
<td><strong>Pregnancy</strong></td>
</tr>
<tr>
<td>Good (^*)</td>
</tr>
<tr>
<td>Fair (^*)</td>
</tr>
<tr>
<td>Bad (^*)</td>
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</tbody>
</table>

\(^*\) Data are described in mean ± SD.

\(^‡\) Statistically significant difference.

5- **Rate of difficult transfer:**

In the pregnant group difficult transfer was reported in 64 cases Vs 210 easy cases (23.36%)
while in the non-pregnant group difficult transfer was reported in 179 cases Vs 219 easy cases (44.97%) which is statistically significant higher rate.

6- Transfer distance to the fundus:
In the pregnant group TDF ranged between 0 (at fundal endometrium) and 2.4mm with a mean of 0.81 while in the non-pregnant group it ranged from 0 to 2.5mm with a mean of 0.84 with no statistically significant difference between the 2 groups.

7- Evidence of ejection flow:
In the pregnant group the flow of media inside the inner catheter sheath was seen in 217 cases and could not be seen in 51 cases (80.97%) while in the non-pregnant group it was seen in 297 cases and could not be seen in 90 cases (76.74%) with no statistically significant difference between the 2 groups.

Table (4).

<table>
<thead>
<tr>
<th>Transferer</th>
<th>Pregnancy</th>
<th>No pregnancy</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transferer 1</td>
<td>64 (23.36)</td>
<td>179 (44.97)</td>
<td>&lt;0.001‡</td>
</tr>
<tr>
<td>Distance to fundus</td>
<td>0.81±0.83</td>
<td>0.84±0.82</td>
<td>0.731</td>
</tr>
<tr>
<td>Laminar flow †</td>
<td>217 (80.97)</td>
<td>297 (76.74)</td>
<td>0.184</td>
</tr>
</tbody>
</table>

* Data are described in mean ± SD.
† Data are described in number of cases (%).
‡ Statistically significant difference.

8- Transferor:
Embryo transfer was performed by 3 transferors with no statistically significant difference between the pregnancy rate of each.

Discussion
Implantation of the embryos is said to involve an interaction between the embryo and endometrium. The quality of the embryo [1,2] and uterine receptivity [3] are certainly important factors in determining the success of implantation. The technique of embryo transfer itself may also be important.

Strickler et al., 1985 were the first to describe the use of trans-abdominal ultrasound in embryo transfer. They advocated that the use of ultrasound could help to position the catheter tip in the fundus of the uterus and ejection of the transfer bubble could be documented. This was reassuring to both the clinician and the patient [4]. Since then many studies documented the favourable effect of trans-abdominal ultrasound on pregnancy rates [5-8]. However other studies failed to prove the benefit of ultrasound guidance in terms of overall clinical pregnancy rates over clinical touch technique by experienced operator, in easy transfers and when uterine length was measured prior to transfer [9-13].

Furthermore studies started to address the best site for embryos deposition under ultrasound guidance. Our data indicate that the actual distance to the fundus did not affect the pregnancy rate. These results corroborated with those of Franco et al. [14] who found that the implantation and pregnancy rates were similar whether the embryos were deposited in the upper or lower half of the endometrial cavity also with the observations of Confino et al. [15] who observed that air bubbles move and split frequently post embryo transfer with the patient in the horizontal position, suggestive of active uterine contractions, this report challenges the common belief that a very accurate ultrasound guided embryo placement is mandatory. The very random bubble movement observed in this study suggests that a large "window" of embryo placement may be present. Also Oliveira et al. [16] placed catheter tip above and below the half point of the endometrial cavity length (ECL) and analyzed pregnancy according to absolute position of the catheter tip and relative position to ECL. Analysis based on relative distance revealed significantly higher implantation and pregnancy rates in more central areas of ECL, however analysis based on absolute position did not reveal any difference. Also in the meta-analysis done by Abou-Seta, 2007 [13] the systemic review showed that there is limited evidence of the superiority of lower cavity transfers (e.g.approx 20mm.) compared with the traditional high cavity (e.g. 10mm.) transfers.

On the other hand our data did not corroborate with Coroleu et al. [17] who found higher implantation rates when embryos are placed at 15mm + 1.5mm and 20mm ± 1.5mm than at 1 0mm + 1.5mm. Also Pope et al. [18] studied odds ratio examining relationship between embryo transfer depth and pregnancy rate and suggested that for every additional millimeter embryos are deposited away from the fundus, the odds of clinical pregnancy increased by 11% and after controlling for potential confounders, the clinical pregnancy rate is significantly influenced by the transfer distance from the fundus and Luo et al. [19] who found significantly higher pregnancy rates when transfer was at >0.75cm, but higher implantation rates with transfers at a distance.
<0.75 cm from the fundus which was not statistically significant.

We tried also to evaluate the endometrial receptivity factor and assessed it through 2 sonographic parameters viz. thickness and pattern. Our data failed to prove that endometrial thickness is a sensitive measure of receptivity, this corroborated with other investigators e.g. Schild et al. [20]; Schild et al. [21]; Aboulgahr et al. [22] and Ng et al. [23].

Zhang et al. [24] reported that increased endometrial thickness was associated with improved treatment outcome in IVF-ET, but this association was dependent on patient’s age, duration of ovarian stimulation and embryo quality. Amir et al. [25] studied the factors that contribute to endometrial thickness and assessed the impact of endometrial thickness on pregnancy rate. The main factor was age in addition to estrogen level, aetiology of infertility, induction of ovulation protocol and type of gonadotropine used and found that a thicker endometrium is correlated with higher pregnancy rate only for patients >35ys. of age.

As for endometrial pattern we found that the occurrence of triple line endometrium on the day of HCG was significantly higher in the pregnant group and thus can be of prognostic value evaluating the endometrial receptivity. This is in agreement with other investigators (Jarvela et al.) [26].

As for the embryo quality factor we confirmed its importance as our data revealed the pregnant group to be younger significantly (the factor that affects embryo quality via oocyte quality) and to have transferred significantly higher number of good embryos, this is in corroboration with other investigators (Roseboom et al., De Neubourge et al., Strandell et al.) [28,29].

Also our data confirmed difficulty of transfer to be a statistically significant factor harmful to pregnancy rate this is in corroboration with other investigators (Mansour et al., Lesny et al.) [28,29].

Conclusion:

Our data proves that the exact position of embryo deposition from the fundus does not influence pregnancy rate, however the use of trans-abdominal ultrasound can be of help in visualizing the catheter in the more difficult transfer and air bubbles can be documented, also ultrasound guidance adds to the confidence in the procedure by both the physician and the patient. To ensure that the catheter is positioned high enough without touching the fundus, a uterine length measurement is sufficient; also the beneficial effect of uterine straightening by passive bladder distention where full bladder is necessary for trans-abdominal ultrasonography can be obtained by advising to fill the bladder prior to embryo transfer.

We recommend that the influence of TDF on ectopic pregnancy rates and retained embryos in the catheter rates should be studied, that might show other benefits of TDF estimation.

References


