Potentially important variables identified by transvaginal ultrasound-guided embryo transfer

Robert Woolcott1 and Jim Stanger

Lingard Fertility Centre, 23 Merewether Street, Newcastle, NSW 2291, Australia

1To whom correspondence should be addressed at: Suite 12, Eastpoint, 50 Glebe Road, The Junction, NSW 2291, Australia

Transvaginal ultrasound-guided embryo transfer was performed on 121 consecutive patients. Observation was made of guiding cannula and transfer catheter placement in relation to the endometrial surface and uterine fundus during embryo transfer. The position and movement of a transfer-associated air bubble and the impact of sub-endometrial myometrial contraction leading to endometrial movement was observed. Results indicate that tactile assessment of embryo transfer catheter placement is unreliable: in 17.4% of transfers the outer guiding catheter inadvertently abutted the fundal endometrium. The outer guiding cannula indented the endometrium in 24.8% and the transfer catheter embedded in the endometrium in 33.1%. Unavoidable sub-endometrial transfers occurred in 22.3% of transfers. Ultrasound-guided transfer avoided accidental tubal transfer in 7.4% of transfers. Transfer catheter withdrawal did not significantly affect embryo transfer-associated air bubble position. Endometrial movement due to sub-endometrial myometrial contraction was obvious in 36.4% of cases, with active motion of the transfer-associated air bubble occurring in 28.1%. Pregancies occurred in 45.5% of transfers with endometrial movement compared to 15.6% (P < 0.001) without.

Key words: embryo transfer/ultrasound-guided/variables

Introduction

Embryo transfer is a common and little studied clinical aspect of the treatment of infertility with assisted reproductive technology. It is almost universally performed as a blind procedure without any significant attempt being made to document variables of the transfer process which might have an adverse impact on pregnancy rates. A limited number of small studies have been undertaken in order to assess whether ultrasound guidance might improve results from in-vitro fertilization (IVF; Hurley et al., 1991; Al-Shawaf et al., 1993). While ultrasound guidance alone may be unlikely to affect the outcome of IVF, there is a variety of assessable variables which could be of importance. The main aim of the present study was to determine variables which could be documented by transvaginal ultrasound-guided embryo transfer and to assess suitability for further study.

Materials and methods

Transvaginal ultrasound-guided embryo transfers were performed in 121 consecutive patients. Of these patients 55 underwent transfer of fresh embryos and 66 of cryostored embryos. The stimulation regimen employed used luteal phase down-regulation with intra-nasal nafarelin followed by follicular phase Pergonal, Metrodin or Metrodin HP 150–450 IU (Seronon, Sydney, Australia) together or in combination depending on the clinical circumstance of each patient. The transfer of fresh embryos was on day 2 post egg collection. The transfer of cryopreserved embryos was in a natural menstrual cycle 4 days after the onset of the luteinizing (LH) surge.

In all cases a Jansen–Anderson K-JITS 2000 catheter set was employed for embryo transfer which uses an outer guiding cannula and a soft 2 French transfer catheter, both of which are readily visible by transvaginal ultrasonography. A bivalve Graves speculum was placed into the vagina and the cervix visualized. Any excess cervical mucus was removed by wiping with a small gauze swab. The outer guiding cannula was placed through the cervix to a position where the operator believed it to be within the endometrial cavity. The speculum was then removed and then replaced by a 5 or 6 MHz transvaginal ultrasound probe (Toshiba 250, Sydney, Australia) to obtain a view of the outer guiding catheter and to assess its position within the endometrial cavity. Should this cannula have been either laterally abutting or near the Fallopian tube orifice or conversely within the cervical canal then it was repositioned under ultrasound guidance. A satisfactory position of the outer guiding cannula for embryo transfer was arbitrarily deemed to be one which allowed placement of the embryo transfer catheter centrally within the uterine cavity and 5 to 15 mm from the fundal surface of the endometrium. Once the optimal position for each particular patient was obtained, notification was given to the embryologist to load the embryos. The embryo transfer catheter was loaded with 5 l of air proximal to 15–25 ml of human tubal fluid medium (HTF; Irvine, San Francisco, CA, USA) with 50% patient serum, containing the embryos to be transferred. The catheter was then placed into the outer guiding cannula and its movement into the endometrial cavity observed till the catheter was within 15 mm of the fundal endometrial surface. The embryos were then injected over 5–10 s allowing observation of the movement of the transfer-associated air bubble into the uterine cavity. Observation was made of the process of transfer catheter withdrawal. The air bubble was observed until movement ceased, while the embryologist checked the transfer catheter for unexpelled embryos. Observation of the impact of endometrial wave-like movement on the position of the air bubble was made during this time. The ultrasound probe was then removed and the patient allowed to leave.

Results

Tactile assessment of catheter position was unreliable: in 17.4% (21/121) the guiding cannula was inadvertently abutting the fundal endometrium (Figure 1; Table I).

The outer guiding cannula was seen to abut the internal
tubal ostia in 7.4% (9/121) of cases prior to embryo transfer allowing adjustment of its position for correct placement of embryos (Table I), and thus preventing inadvertent tubal embryo transfer.

The outer guiding cannulas of catheters which indented the endometrium or embedded beneath the endometrial surface were identified in 33.1% of cases (40/121). In 8.3% of cases (10/121) the outer guiding cannula was seen to indent the endometrium. In 24.8% of cases (30/121) the embryo transfer catheter was seen to be embedded within the endometrium (Figure 2; Table II). Pregnancies occurred in 30.0% (12/40) of these transfers.

Sub-endometrial embryo transfer was identified in 22.3% (27/121) of cases where the air bubble was seen to remain below the endometrial surface on removal of the catheter (Figure 3). Pregnancies occurred in 22.2% (6/27) of these cycles.

Identification could be made of possible withdrawal of embryos with the embryo transfer catheter. The embryo transfer-associated air bubble was seen to be withdrawn between 2 and 5 mm towards the cervix in 5.0% of cases (6/121), but in no case was it seen to be withdrawn into the cervix, and no embryos remained in the catheter on post-embryo transfer check.

Endometrial movement was obvious in 36.4% (44/121) of cases. Active motion of the embryo transfer-associated air occurred in 28.1% (34/121) of cases with back and forth motion of 2–5 mm. In one case there was air bubble movement of 4 cm towards the cervix in a patient with very active endometrial movement. Pregnancies occurred in 45.4% (20/44) of the transfers with obvious endometrial movement compared to 15.6% (12/77) ($P < 0.001$, Fisher’s exact test) of those without. Of patients achieving pregnancy 62.5% (20/32) had endometrial movement and 43.8% (14/32) had active air bubble movement due to endometrial motion (Table III). There were no differences in the age, aetiology of infertility, number or quality of embryos transferred between those patients with identifiable endometrial movement and those without (Table IV).
Table III. The presence and effect of endometrial peristalsis

<table>
<thead>
<tr>
<th>Peristalsis</th>
<th>n</th>
<th>%</th>
<th>Pregnant (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absent</td>
<td>77</td>
<td>63.6</td>
<td>15.6</td>
</tr>
<tr>
<td>Present</td>
<td>44</td>
<td>36.4</td>
<td>45.4</td>
</tr>
<tr>
<td>Bubble motion</td>
<td>34</td>
<td>28.1</td>
<td>43.8</td>
</tr>
</tbody>
</table>

Table IV. Comparison of patients with and without identifiable endometrial movement

<table>
<thead>
<tr>
<th>Endometrial movement</th>
<th>Present (n = 44)</th>
<th>Absent (n = 77)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years)</td>
<td>32.3</td>
<td>32.7</td>
</tr>
<tr>
<td>No. embryos transferred (mean)</td>
<td>1.95</td>
<td>1.97</td>
</tr>
<tr>
<td>Embryo quality (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A grade</td>
<td>74.5</td>
<td>73.9</td>
</tr>
<tr>
<td>B grade</td>
<td>22.8</td>
<td>23.3</td>
</tr>
<tr>
<td>C grade</td>
<td>1.7</td>
<td>1.8</td>
</tr>
<tr>
<td>Causes of infertility (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tubal</td>
<td>41</td>
<td>39</td>
</tr>
<tr>
<td>Endometriosis</td>
<td>25</td>
<td>22</td>
</tr>
<tr>
<td>Male factor</td>
<td>47</td>
<td>45</td>
</tr>
<tr>
<td>Other</td>
<td>9</td>
<td>10</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>14</td>
<td>13</td>
</tr>
</tbody>
</table>

Discussion

With the widespread acceptance of embryo cryopreservation into the practice of assisted reproduction units embryo transfer has become the single most common procedure performed by medical practitioners in this field. It is remarkable therefore that there is a dearth of published literature on both technical aspects of performing transfers and the identification of variables which might affect the outcome of the procedure. Moreover, the published data on the biophysical factors which affect the possibility of pregnancy in the time between embryo transfer and expected next menses in patients treated for infertility with IVF are limited. Various authors have attempted to address biophysical variables of embryo transfer which might affect the outcome of IVF therapy (Mansour et al., 1990; Gonen et al., 1991; Kato et al., 1993; Sharif et al., 1995a,b). Hurley et al. (1991) in a small randomized prospective trial failed to demonstrate any significant benefit from ultrasound-guided embryo transfers, nor did Al-Shawaf et al. (1993) in a non-randomized study. Krampl et al. (1995) have demonstrated that the use of embryo transfer-associated air bubbles does not affect pregnancy rates adversely in IVF therapy and has some potential advantages of minimizing capillary action within the narrow diameter catheters used for embryo transfer. This might reduce the chance of embryos being expelled from the catheter should it come in contact with fluid within the guiding catheter at embryo transfer. Others have used radiological methods in an attempt to assess via mock embryo transfer of radio-opaque contrast what happens during and after embryo transfer. Indeed Knutzen et al. (1992) demonstrated a potential risk of contrast medium being expelled from the uterine cavity along the path of a transfer catheter. It was unfortunate, however, that the volume of contrast medium injected in this study was substantially more than is usually used. Such methods have the limitation of not actually being within a treatment cycle and not tracking the movement and position of embryo-associated phenomena. They are valuable, however, in adding to our understanding and it would seem appropriate for further study to be done in this field.

While it is impossible to assess what actually physically happens to embryos in the immediate post-transfer phase or to document their movement and final position, transvaginal ultrasonography offers the potential benefit of being able to document various phenomena which occurred immediately prior to, during and immediately after embryo transfer. Patient acceptability of transvaginal ultrasound as an intimate component of their embryo transfer was high. Both the patient and her partner have the opportunity to be involved and directly visualize the transfer of their embryos to the uterine cavity. It allows their involvement and commentary on the process and the psychological security of the satisfactory completion of the technical components of their treatment cycle. The use of ultrasound in the process does not add substantially to the time for embryo transfer as all transfers including the post-transfer standing ultrasound were completed within 15 min.

It is clear from the results of our study that tactile assessment of catheter position is unreliable. In 17.4% of embryo transfers the guiding catheter unintentionally abutted the fundal endometrium. This is of importance in that it may increase the risk of embryos being retained within the transfer catheter by preventing their free expulsion upon injection. Moreover, patients commonly report a sensation of pain or discomfort when the catheter touches the endometrial surface, which is obviously less than ideal. In 7.4% of cases the guiding catheter was not only abutting the endometrium but also adjacent to the internal orifice of the Fallopian tube, a phenomenon we have observed on numerous occasions in the performance of transvaginal gamete intra-Fallopian transfer (Woolcott et al., 1995a,b) and selective salpingography (Woolcott and Stanger, 1994; Woolcott et al., 1995) as a consequence of complete advancement of the guiding cannula to its maximal extent into the uterine cavity. Transvaginal ultrasound embryo transfer does not completely prevent this occurrence but does allow the identification of inappropriate catheter placement and for its re-positioning where necessary.

Catheters which indent the endometrium or embed beneath the endometrial surface were commonly identified. This has potential to affect the outcome of treatment. It more commonly occurred with the loaded embryo transfer catheter than the outer guiding catheter, and universally occurred in the posterior endometrium as a result of almost all patients in the group having uterine anteflexion (118/121). Essentially, despite the ability to mould the outer cannula to angles up to 60° it was common for the transfer catheter to be directed posteriorly rather than between the two endometrial surfaces. It has been our experience as a result of over 1000 ultrasound-guided embryo transfers that it is extremely difficult and usually impossible to reposition the outer guiding catheter to avoid a posterior path of the embryo transfer catheter toward or into the endometrium.

We believe we were able to differentiate between those cases where the catheter indented the endometrium and those
in which the catheter had penetrated the endometrial surface and embedded beneath the surface leading to intra-endometrial embryo transfers. With catheter indentation of the endometrium, the embryo-associated air was seen to be positioned after transfer between the anterior and posterior endometrial surfaces at their visible junction as identified by a central endometrial echo; however, with intra-endometrial transfer the hyper-echoic area of the air was seen to be positioned beneath the central endometrial echo. Whether intra-endometrial embryo transfer will be demonstrated to have any effect on pregnancy rates is debatable, although it would seem reasonable to adopt a practice of performing embryo transfer in the least traumatic method possible. On the other hand, Kato et al. (1993) have suggested that transvaginal transmyometrial embryo transfer may not only have advantages for those patients with severe cervical stenosis where transcervical transfer is impossible but may also in itself be beneficial in permitting intra-endometrial embryo transfers. This proposition has not been supported by follow-up studies by Kato or others but nevertheless indicates that pregnancy is possible following what might appear to be a relatively traumatic transfer methodology.

Movement of the embryo-associated air towards the cervix along the path of the transfer catheter on withdrawal uncommonly occurred in 5.0% (6/121) of cases and when it did occur was insignificant, being <5 mm in all cases. This is contrary to the results published by Knutzen et al. (1992) who suggest that embryos may be expelled in 32–52% of embryo transfers depending on the patient’s position. Their study, however, investigated mock transfers with 40 ml of radio-opaque contrast medium in non-treatment menstrual cycles. Knutzen, V., Stratton, C.J., Sher, G. (1990) Uterine endometrial peristalsis — a traumatic method possible. On the other hand, Kato et al. (1993) have suggested that transvaginal transmyometrial embryo transfer may not only have advantages for those patients with severe cervical stenosis where transcervical transfer is impossible but may also in itself be beneficial in permitting intra-endometrial embryo transfers. This proposition has not been supported by follow-up studies by Kato or others but nevertheless indicates that pregnancy is possible following what might appear to be a relatively traumatic transfer methodology.

References


Received on November 11, 1996; accepted on March 5, 1997