Where does the embryo implant after embryo transfer in humans?

Kazunori Baba, M.D., Ph.D., Osamu Ishihara, M.D., Ph.D., Naoki Hayashi, M.D., Masahiro Saitoh, M.D., Junko Taya, M.A., and Katsuyuki Kinoshita, M.D., Ph.D.

Department of Obstetrics and Gynecology, Saitama Medical Center, Saitama Medical School, Kawagoe, Japan

Objective: To investigate where human embryos implant after ET.

Design: Prospective analysis.

Setting: University hospital.

Patient(s): Sixty infertile women without uterine fibroids, a major uterine anomaly, or a history of cesarean section.

Intervention(s): Transabdominal and transvaginal three-dimensional ultrasound examinations.

Main Outcome Measure(s): The location of ET-associated air bubbles in the uterine cavity and the location of the resultant gestational sac.

Result(s): Sixty ETs resulted in 22 pregnancies, and 32 gestational sacs were located. Twenty-six of the 32 embryos were within or between the area in which the catheter tip was situated and the area over which air bubbles had spread immediately after ET.

Conclusion(s): In cases of pregnancy achieved through ET, approximately 80% of embryos implant in areas to which they initially are transferred and approximately 20% implant in other areas. (Fertil Steril 2000;73: 123–5. ©1999 by American Society for Reproductive Medicine.)

Key Words: Embryo transfer, implantation, three-dimensional ultrasound, gestational sac

In vitro fertilization and ET are used throughout the world as an indispensable means of treating infertility. Embryo transfer is the most critical step that affects the success rate of IVF-ET, and procedures for ET have changed little since IVF-ET first was described 21 years ago. There are indications that transferred embryos may be relocated and even expelled from the uterine cavity (1). In cases of pregnancy, however, it remains unknown where embryos implant after transfer and how many move before implantation.

We identified the locations of embryos in the uterine cavity immediately after ET and the locations of gestational sacs (GSs), indicating the sites of implantation, with the use of three-dimensional ultrasound, which depicts the entire uterine cavity in a frontal view of the uterus (2).

MATERIALS AND METHODS

The study included 60 patients who were undergoing IVF-ET. The patients ranged in age from 26–40 years and did not have uterine fibroids, a major uterine anomaly, or a history of cesarean section. Indications for IVF-ET included tubal factor infertility, male factor infertility, idiopathic infertility, and endometriosis.

Informed consent was obtained from each patient. Institutional review board approval was not obtained because IVF-ET and ultrasonography were routine clinical procedures and the three-dimensional ultrasound scanner had been fully approved by the Ministry of Health and Welfare of Japan. The study was conducted in accordance with the Helsinki Declaration of 1975 on human experimentation.

Ovulation induction, oocyte retrieval, and embryo culture were performed according to standard procedures (3). Embryo transfer was performed 2 days after oocyte retrieval using a uterine catheter (Fuji System, Tokyo, Japan) loaded first with 5–10 μL of air, then with 5–10 μL of a medium that held 1–3 embryos, and then with 5–10 μL of air again. The catheter
was soft and comprised a single piece; it was identical to an inner cannula of the Edwards-Wallace Embryo Replacement Catheter (SIMS; West Sussex, Chichester, United Kingdom).

The patient was placed in the modified lithotomy position on a bed, and the catheter was inserted into the uterine cavity through the cervix. The tip of the catheter was directed into the midfundal area of the uterus using a three-dimensional ultrasound scanner (Combison 530D; Kretztechnik-Medison, Zipf, Austria) applied transabdominally for guidance. The medium containing the embryo(s) was injected gently into the uterine cavity along with air on each side.

Immediately after withdrawal of the catheter, ET-associated air bubbles in the uterine cavity were located transabdominally with the three-dimensional ultrasound scanner. The patient remained in the supine position on the bed for 2 hours after ET and then was released.

The luteal phase was supported with 50 mg of progesterone (Progehormon; Mochida Pharmaceuticals, Tokyo, Japan) administered daily for 14 days starting on the day of oocyte retrieval. In cases of pregnancy, GSs were located by an expert ultrasound technician (K.B.) using the three-dimensional ultrasound scanner applied transvaginally.

### Table 1

Relation between the location of air bubbles immediately after ET and the location of the gestational sac after implantation in 22 pregnancies (32 gestational sacs).

<table>
<thead>
<tr>
<th>Location of air bubbles immediately after ET</th>
<th>Location of gestational sac (no. of gestational sacs)</th>
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</thead>
<tbody>
<tr>
<td>Midfundal area</td>
<td>midfundal area (8), left fundal area* (1), middle of the uterine cavity* (1)</td>
</tr>
<tr>
<td>Midfundal to right fundal area</td>
<td>midfundal area (4), right fundal area (3), right fallopian tube* (1)</td>
</tr>
<tr>
<td>Midfundal to left fundal area</td>
<td>midfundal area (4), left fundal area (2), left fallopian tube* (1)</td>
</tr>
<tr>
<td>Midfundal to right and left fundal areas</td>
<td>right fundal area (2), left fundal area (3), middle of the uterine cavity* (2)</td>
</tr>
</tbody>
</table>

* Location of the gestational sac in cases where no air bubbles were seen immediately after ET.

RESULTS

Sixty ETs (167 embryos) resulted in 22 pregnancies, and 32 GSs were located 18–28 days after ET. In 7 of the 22 pregnancies, air bubbles had remained in the midfundal area immediately after ET. Air bubbles had spread from the midfundal to right fundal areas (Fig. 1A) in 5 cases, from the midfundal to left fundal areas in 4 cases, and from the midfundal to both fundal areas in 6 cases. In no case did air bubbles spread toward the internal os immediately after ET.

Thirty GSs were located in the midfundal, right fundal (Fig. 1B), or left fundal areas, or in the middle of the uterine cavity, and 2 GSs were located in the fallopian tube. The relation between the location of air bubbles immediately after ET and the location of GSs is shown in Table 1. Six GSs were found in areas where no air bubbles were present immediately after ET.

DISCUSSION

Although the human embryo at the time of ET was too small to be observed by ultrasound, we believe that the transferred embryos were situated somewhere within or between the midfundal area in which the catheter tip was placed and the area over which air bubbles spread immediately after ET (4). It appeared that 81% (26/32) of the embryos that implanted successfully did so in the areas to which they initially were transferred. Nineteen percent (6/32) of the embryos, including two tubal pregnancies, appeared to have moved before implantation, probably through wavelike movements of the endometrium (1).

There were two cases of tubal pregnancy in which air bubbles had spread from the midfundal area to the right or left fundal area. The embryos implanted in the fallopian tube on the same side to which the air bubbles had spread. No tubal pregnancies occurred in the cases in which air bubbles remained in the midfundal area immediately after ET.

Thus, it should be possible to avoid tubal pregnancies by transferring embryos only to the midfundal area. Asymmetry of the endometrial cavity may determine the direction in which air bubbles spread. Further studies should be conducted to clarify the factors that control this phenomenon.

Three-dimensional ultrasound has proved useful for monitoring the site of ET. As more ETs are performed with three-dimensional ultrasound guidance, it may be possible to identify an optimal transfer area for increased success and to avoid the occurrence of ectopic pregnancies. Three-dimensional ultrasound should prove to be indispensable for ET.

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References