One at a time

Eric Flisser, M.D., and Frederick Licciardi, M.D.

New York University Program for In Vitro Fertilization, Reproductive Surgery and Infertility, New York University School of Medicine, New York, New York

Review of abstracts presented at the 2004 Annual Meeting of the American Society for Reproductive Medicine clearly demonstrate that good prognosis patients should be given the option of a single embryo transfer. (Fertil Steril® 2006;85:555–8. ©2006 by American Society for Reproductive Medicine.)

Key Words: Embryo transfer, in vitro fertilization, single embryo transfer

The incidence of multifetal gestation is substantial in the IVF population, but the application of techniques to reduce the frequency of multiple gestations has not been universally accepted. This is despite ample evidence that delivery rates can be preserved after implementing protocols that reduce the number of embryos transferred per patient (Table 1). Although the implantation rate per embryo in the United States has risen to impressive levels, the number of embryos per transfer has not fallen to or below that of many of our European counterparts.

Generally, to patients, twin pregnancy is a favored outcome (1) and twinning is often viewed as a benign complication of fertility treatment, even a favored complication by some. When cost of treatment is an issue, twinning essentially becomes a "two-for-one" deal. In addition, fresh embryo transfer cycles outperform thawed, cryopreserved embryo cycles, creating bias toward the application of measures that increase initial success. Certain sectors of the IVF community have not seized on the results presented by its own members at its annual national conference. Abstracts presented at the 2004 Annual Meeting of the American Society for Reproductive Medicine (ASRM), October 16–20, 2004, in Philadelphia, Pennsylvania, demonstrated what had been proposed in theory: reducing the number of embryos transferred resulted in fewer multiple gestations without compromising high pregnancy rates (PR) (Table 2).

In abstracts describing young patients and patients receiving donor oocytes, investigators continued to have successful transfers when embryo number was limited. In patients less than 36 years using autologous oocytes, the ongoing PR for single blastocyst transfer was not significantly different from patients receiving two blastocyst transfer (67.4% vs. 78.4%, $P=.25$) (2). No significant difference was seen in ongoing PR of patients receiving single embryos generated from donor oocytes vs. those receiving two donor oocyte-generated embryos (70.6% vs. 65.5%, $P=.88$). As expected, twin pregnancy was all but eliminated when single embryo transfer (SET) was performed; a statistically significant reduction in the twinning rate was reported when accounting for fresh and frozen cycles undertaken by these patients compared to patients who received two blastocysts (2% vs. 64.9%, $P<.05$).

When SET was expanded to all patients at a particular clinic, the reduction in the number of embryos transferred from two to one in a significant percentage of transfers (25.1% vs. 71.3%, $P<.0001$) did not significantly affect PR (33.3% vs. 33.8%, $P=.3$) (3). The reduction in number of embryos transferred was achieved in Sweden by removing patient choice from the transfer algorithm by legal mandate. A retrospective comparison of embryo transfers from the period after new regulations showed a significant reduction in the twinning rate (22.6% vs. 8.8%, $P<.0005$). Exemptions from the mandated restrictions account for the higher twinning rate compared to other SET studies.

In a retrospective comparison of patients receiving elective single blastocyst transfer and patients who met the same criteria for SET but opted for two blastocyst transfer, a significant reduction in the twinning rate was observed in the SET group, with no statistical decrease in the PR (4). In patients receiving one vs. two embryos, the PR was 77.4% vs. 82.5% ($P=.75$), whereas the twinning rate was 4.2% vs. 69.2% ($P<.0001$). Similarly, in another study, 89 cases of SET were compared to 215 two embryo transfers. The resulting multiple gestation rate was significantly different (3.3% vs. 42.2%, $P<.01$), whereas the clinical PR were not (49.4% vs. 59.1%, $P>.05$) (5).

Received April 21, 2005; revised and accepted August 9, 2005.

The opinions and commentary expressed in Editor's Corner articles are solely those of the author. Publication does not imply endorsement by the Editor or American Society for Reproductive Medicine.

Reprint requests: Eric Flisser, M.D., New York University Program for In Vitro Fertilization, Reproductive Surgery and Infertility, New York University School of Medicine, 660 First Avenue, 5th Floor, New York, New York 10016 (FAX: 212-263-8827; E-mail: flisse02@med.nyu.edu).

TABLE 1

Summary of abstracts involving single embryo transfer.

Abstract #	SET (n)	CPR[a]
O-89	43	67.4%
O-322	31	77.4%
P-182	89	49.4%
P-185	30	63.3%
P-193	30	50%
P-196	765	33%
P-206	108	44.0%
P-236	19	73.7%
P-238	187	32.3%

Note: SET = single embryo transfer; CPR = clinical pregnancy rate.

[a] Definitions of CPR vary according to the definitions of the original authors of the abstracts.

Flisser. Review of SET abstracts ASRM 2004. Fertil Steril 2006.

Improving embryo selection using blastocyst culture was demonstrated to reduce twinning while maintaining efficiency (2, 4–6). When SET of high quality embryos was performed the fifth day after retrieval, a similar PR to two embryo transfer was observed, with a significant reduction in the multiple PR (6). The on-going PR was 73.7% (14/19) vs. 68.9% (54/90), whereas the multiple gestation rate was 6.3% (1/16) vs. 58.8% (20/34) ($P<.001$).

Differentiating blastocyst potential based on grade is the key to successful SET (7). In SET of day 5 blastocysts, those with grade A inner cell mass had a statistically higher clinical PR than those with lower grades: 41.7% vs. grade B 24.1%, ($P<.05$), and vs. grade C 6.3% ($P<.001$).

However, the reproductive potential of embryos is difficult to predict even with current systems, and, consequently, two embryo transfer always carries a high risk of twin pregnancy. In one study, cultured embryos were graded A–D from best to worst in three categories: inner cell mass, trophoblast development, and blastocoele cavity development (8). In optimal cycles with excellent quality blastocysts (AAA, AAB, or ABA), 33 patients undergoing two-blastocyst transfer had a twinning rate of 61.5%. Patients with good, but lower grade (BAA, BBA, BAB, or BBB) two-blastocyst transfer in this program had a twinning rate of 33.3% with a total PR of 55.6%. An implantation rate of 42.6% in this group suggests that SET in these patients can still be highly successful, if the reproductive potential of embryos with these grades can be parsed out.

Similarly, in another abstract, in patients less than 38 years, when at least one excellent or good quality embryo was available for transfer, PR exceeded 72% (9). Although a statistically significant decrease in multiple pregnancies occurred when only one of the two embryos were transferred was top quality (64.8% vs. 38.7%, $P<.05$), the multiple pregnancy rate was high. The multiple PR remained high even when only fair or poor embryos were transferred (38.7% vs. 27.8%, $P>.05$).

Although extended culture is well suited for embryo selection, reduction of the twinning rate is not limited to SET of blastocysts. Careful selection of cleavage stage embryos can also lead to successful IVF cycles. The importance of embryo selection is highlighted by a study in which SET of four-cell cleavage stage embryos was performed on the second day after retrieval by evaluating the number of identifiable nuclei in blastomeres (10). When each blastomere of a four-cell cleavage stage embryo had one identifiable nucleus the SET clinical PR was 41%, compared to 26% when one nucleus was seen in zero, one, two, or three blastomeres ($P<.003$). Another study demonstrated similar results: a clinical PR of 44.0% for SET of four-cell embryos in 108 patients (11).

Even when the cohort of eggs retrieved yields only one viable embryo, PR remain acceptable. Fifteen patients underwent SET of high quality blastocysts and were compared

TABLE 2

Abstracts comparing single embryo transfer to two embryo transfer.

Abstract #	SET (n)	CPR	Multiple gestation rate	TET (n)	CPR	Multiple gestation rate
O-89	43	67.4%	0%	97	78.4%	60.0%
O-322	31	77.4%	4.2%	63	82.5%	69.2%
P-182	89	49.4%	3.3%	215	59.1%	42.2%
P-236	19	73.7%	6.3%	45	68.9%	58.8%
Total	182	61.0%	2.3%	420	68.1%	52.1%[a]

Note: SET = single embryo transfer; TET = two embryo transfer; CPR = clinical pregnancy rate.

[a] The pregnancy rate and twinning rate were calculated as the weighted average of the outcomes of these abstracts.

Flisser. Review of SET abstracts ASRM 2004. Fertil Steril 2006.