A comparison of clinical pregnancy rates and multiple gestation rates with 2 vs 3 embryos transferred with pairs matched for embryo quality

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Summary

Purpose: To determine the impact of embryo quality on multiple birth rates. *Materials and Methods:* A retrospective review of in vitro fertilization-embryo transfer (IVF-ET) cycles over ten years was performed. The data was stratified by number of embryos transferred (two vs three) and by percentage of embryos with < 6 vs ≥ 6 blastomeres. *Results:* Pregnancy rates (PRs) increase with the greater number of embryos with a higher blastomere count. However transferring more embryos with less blastomeres does not lower the risk of multiple births. *Conclusions:* Couples should consult the table, e.g. presented here, so they can make their best choice of how many embryos to transfer considering the importance of a higher pregnancy rate vs the risk of the complication of multiple births.

Key words: Blastomere number; Embryo quality; Multiple birth; In vitro fertilization-embryo transfer.

Introduction

One of the greatest challenges of the use of assisted reproductive technology is to avoid multiple pregnancies without compromising pregnancy rates. Multiple pregnancies are associated with increased risks for both the mother and fetus. Maternal risks include miscarriage, hemorrhage, preeclampsia, diabetes, anemia, polyhydramnios, and Caesarean section. Fetal complications include preterm delivery, low birth weight, and various birth defects.

Therefore the key question for every woman undergoing in vitro fertilization (IVF) is how many embryos to transfer? It has been shown that blastomere number is a better predictor of achieving pregnancy than fragmentation [1]. In a previous study of single embryo transfer (ET), the clinical pregnancy rate (CLPR) for six to eight cell embryos was 40.4% whereas the CLPR for four to five cell embryos was only 6.6% [1]. In contrast, in this same study, although embryos with < 25% fragmentation resulted in a 35% PR per transfer, those with > 50% fragmentation showed a 25% CLPR per transfer [1].

The objective of the present study was to evaluate PRs and multiple gestation rates (MGRs) according to the number of ETs and the number of embryos with ≥ 6 blastomeres. Because previous studies have looked at these two factors individually, this study also aims to look at these factors together by matched cohort comparison.

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Materials And Methods

IVF cycles from January 1997 to May 2007 were reviewed according to whether two or three embryos were transferred in women aged < 38. CLPR (live fetus on ultrasound eight weeks from conception) and MGR were compared according to blastomere number. In addition, comparison was done for women receiving two vs three embryos but matched according to embryo quality based on blastomere number. Chi-square analysis was used for statistical analysis.

Results

For patients younger than 38 years transferring two of their own embryos, there is a statistically significant difference in the CLPRs by cell stage of ETs ($p < 0.001$). The highest PR of 46.1% was obtained in cycles where both embryos had six or more cells.

In cycles where at least one of the two embryos had less than six cells, the CLPR were lower (21.6% for both < 6, 26.7% for 1 < 6 cell). These last two rates did not differ significantly for each other but combined they were significantly lower than the group with all embryos with > 6 blastomeres ($p < 0.05$).

In cycles where both embryos had six or more cells, 35.7% of the pregnancies had multiple sacs as compared to only 10.5% of pregnancies where both embryos had less than six cells ($p \leq 0.025$). However there was not a significant difference in the multiple rates between cycles where one of the two embryos or both embryos were at least six cells (32% vs 35.7%, respectively).

For patients younger than 38 years transferring three of their own embryos, there is a significant difference in PRs

Table 1. — *A comparison of pregnancy and multiple birth rates according to whether two or three embryos were transferred and percentage of embryos transferred with < 6 blastomeres.*

	Two embryos transferred			*Three embryos transferred*			
Blastomere	All embryos < 6	1 embryo < 6	All embryos ≥ 6	All embryos < 6	2 embryos < 6	1 embryo < 6	All embryos ≥ 6
Clinical pregnancy rate/transfer	21.6% (19/88)	26.7% (50/187)	46.1% (235/510)	30.2% (26/86)	39.7% (90/227)	46.3% (136/294)	54.6% (482/882)
% with multiple births	10.5% (2/19)	32% (16/50)	35.7% (84/235)	38.5% (10/26)	31.1% (28/90)	40.4% (55/136)	52.7% (254/482)

by cell stage (p = 0.044). The highest PR of 54.6% was obtained in cycles where all three embryos transferred had six cells or more. This rate was significantly higher than the 46.3% rate for cycles with only two embryos with six or more cells ($p < 0.05$).

The lowest PRs when three embryos were transferred were found in cycles with two or more embryos of less than six cells (39.7% for two and 30.2% for all three). These two rates were not statistically different from each other but were significantly lower than the group transferring all embryos with > 6 cells ($p < 0.01$).

The percentage of pregnancies with multiple gestations also differed by cell stage ($p < 0.001$). In cycles where all three embryos transferred had six or more cells, 52.7% of the pregnancies had multiple sacs as compared to only 38.4% of pregnancies where all embryos were less than six cells, 31.1% with at least two embryos less than six cells, and 40.4% with only one embryo with less than six cells.

The CLPRs per transfer with none of the embryos with ≥ 6 blastomeres was 21.6% (19/88) vs 30.2% (26/86) for two vs three ETs (p = 0.26). The respective MGRs were 10.5% (2/19) vs 38.5% (10/26) (p = 0.08) [but four of 26 (15.3%) were triplets].

For transfers having only one embryo with ≥ 6 blastomeres, the CLPRs per transfer were 26.7% (50/187) vs 39.7% (90/227) (p = 0.008) for two vs three ETs and the incidence of multiple gestations were 32% (16/50) vs 31.1% (28/90) (p = NS) with triplets in five (17.8%).

For transfers having two embryos with ≥ 6 blastomeres, the CLPRs per transfer were 46.1% (235/510) vs 46.3% (136/294) (p = NS) for two vs three ETs. The respective MGRs were 35.7% (84/235) vs 40.4% (55/136) with triplets in eight (5.8%) (p = NS).

When all three embryos had ≥ 6 blastomeres, the CLPRs per transfer was 54.6% (482/882) which was significantly higher than when transferring two embryos of similar quality (46.1%, 235/510) (p = 0.0025).

The MGR with all three ETs having ≥ 6 blastomeres was 52.7% (254/482) vs 35.7% (84/235) when only two embryos were transferred ($p < 0.0001$). The triplet rate was 32.3% (82/254).

Discussion

There is an improved chance of a clinical pregnancy with more embryos transferred especially when there is a greater percentage with six or more blastomeres which supports conclusions from previous studies [2-4]. However, there does not seem to be safety in preventing multiple gestations if there are less quality embryos being transferred.

This suggests that quantity rather than quality is more predictive of MGR. We suggest that each IVF center present their data in a similar fashion as in Table 1 to the couple seeking pregnancy by IVF-ET, so that after being properly counseled on the risk of multiple gestations and PRs they can decide on a two vs three ETs based on embryo quality as determined by blastomere number. For example by evaluating the Table, a couple would see that if none of the embryos have six blastomeres then transferring three embryos vs two raises the PR by 50% (30.2% vs 21.6%), but also more than triples the MGR (38.5% vs 10.5%). If a multiple birth rate of almost 40% is acceptable to the couple, they should have the right to have a greater chance of pregnancy from an expensive IVF-ET procedure.

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