The Effect of Blastomere Number on Pregnancy and Implantation Rates Following Frozen Embryo Transfer in Donor-Oocyte Recipients

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Summary

Donor egg recipients tend to have high pregnancy rates (PRs) following transfer and are more prone to have multiple births. The decision on how many embryos to transfer from the retrieval cycle may depend on how likely is success of transferring frozen-thawed embryos. The present study evaluated pregnancy outcome based on the number of blastomeres of any given frozen-thawed embryos transferred. The ongoing/delivered PRs for 4, 5, 6, 7, and ≥8 cell embryos were 24.7%, 33.3%, 38.7%, 41.2%, and 43.7%. The implantation rates were 12.2%, 17.2%, 17.9%, 20.8% and 24.8%. There was a progressive increase in outcome with higher number of blastomers but even with a maximum of 4 cells still produced a respectable PR though about half of ≥8 cells.

Introduction

Implantation rates following transfer of day 3 embryos with 7 or 8 blastomeres derived from donor oocytes and transferred to recipients on estrogen/progesterone (P) replacement are frequently greater than 30%. This may be a sufficient outcome for a woman to transfer only 1 embryo to prevent multiple births.

However, the decision on whether to only transfer one embryo may hinge on how successful would be a subsequent frozen embryo transfer (ET).

The present study evaluated pregnancy rates (PRs) and implantation rates according to maximum number of blastomeres of any frozen-thawed embryos transferred. Knowledge of the potential chance of a frozen-thawed embryo derived from a donor oocyte implanting could influence a couple as to how many fresh embryos to transfer.

Materials and Methods

Donated eggs were available either from infertile women undergoing IVF-ET themselves and sharing half of the eggs with a recipient or paid donors who also frequently shared the oocytes between two recipients (1,2). Most donors were ≤35 years old; occasionally especially with family members, some donors were as old as 39 (3).

Women having frozen ETs either failed to get pregnant with the fresh ET or were trying for another child. In general the best embryos available were transferred.

The embryos were frozen using a simplified method in which a slow cooling program is started at the seeding temperature of -6°C in an alcohol-bath controlled-rate freezer. 1,2 propanediol was used as the cryoprotectant (4).

The thawing procedure used a one-step dilution of the cryoprotectant (4). Embryos were frozen at the 2 pronuclear or day 3 multi-cell stages.

Pregnancy rates and implantation rates were determined according to the maximum number of blastomeres of any embryo transferred. Though in general there was an attempt to choose embryos with the least fragmentation, nevertheless, these data were based entirely on blastomere number without any evaluation of fragmentation or symmetry.

Results

The clinical (ultrasound evidence of pregnancy) and ongoing (past 16 weeks)/delivered PRs and implantation rates according to maximum blastomere number of any frozen-thawed embryo transferred is seen in Table 1. The clinical and ongoing/delivered PRs and implantation rates was significantly lower ($p<.01$) for the group with maximum 4 cell embryos compared to the 4 other groups combined. The clinical, ongoing/delivered PRs and implantation rates were significantly higher ($p<.01$) in those having at least one 8-cell embryo transferred compared to the other 4 groups combined.

There appears to be a progressively higher pregnancy outcome with each group with progressively higher number of blastomeres but the results were not much different between 5-≥8 blastomeres. Though the ongoing/delivered PR for 4 cell maximum was only 60% of that with ≥8 cells, and the implantation rates for 4 cell was only 50% of ≥8 cell, the fact remains that the women still had a 24.7% ongoing/delivered PR.

Table 1 – Association of blastomere number of frozen-thawed embryos derived from donor oocytes and pregnancy outcome

	Maximum number of blastomere of any embryo transferred				
	≤4	5	6	7	8
# of transfers	85	158	155	136	126
# clinical preg.	26	60	65	58	64
% clinical preg/transfer	30.6	39.2	41.9	42.6	50.8
# ongoing/delivered preg.	21	51	60	56	55
% ongoing/delivered preg./transfer	24.7	33.3	38.7	41.2	43.7
# embryo transferred	288	541	547	451	387
# embryo implanting	35	93	98	94	96
% implanting/transfer	12.2	17.2	17.9	20.8	24.8

The miscarriage rates for the 4 groups were 19.2%, 20.0%, 12.3%, 6.9%, and 21.9%, respectively.

Discussion

The Cooper Center for IVF generally reports to the Society for Assisted Reproductive Technology (SART) PRs following frozen ET only slightly lower than fresh ET which would not be expected especially since the embryos used for frozen ET are frequently de-selected based on quality. However, we previously found that when evaluating donor oocyte cycles, where an infertile donor provides eggs for herself and an anonymous recipient, that the PRs for fresh ET in donors is similar to the PRs in the first frozen ET of donors who deferred fresh ET for various reasons (5). Interestingly, the PRs were significantly higher for recipients having fresh ET vs. those who deferred fresh ET and their first transfer was a frozen ET (5). These data were interpreted as supporting the contention that controlled ovarian hyperstimulation adversely affects implantation following IVF-ET (5).

In another presentation at the World Congress of In Vitro Fertilization, Istanbul, Turkey 2005, we presented the PRs and implantation rates according to blastomere number of embryos following fresh ET in donor egg recipients (6). The PRs and implantation rates from the present study following frozen ET demonstrated that the frozen-thawed embryos have about a 70% chance of implanting compared to a fresh embryo. Thus these data support the conclusions of the aforementioned study (5), but with a lot more cycles evaluated and using eggs from paid donors in addition to infertile ones.

With the knowledge of the chance of any given embryo implanting

based on blastomere number and whether it is a fresh or frozen-thawed embryo, a given couple can calculate the approximate risk of twins if 2 embryos are transferred vs. twins or triplets if 3 are transferred. This information can help a couple consider the likelihood of a single fresh embryo implanting and the down side of freezing the others; the couple's fear of multiple birth vs. financial benefits of achieving a pregnancy on the first transfer can help recipients decide on how many fresh embryos to transfer and how many frozen embryos to transfer.

One cannot be sure that the embryo with the greatest number of blastomeres was in fact the one that implanted. Nevertheless, since hormonal replacement is the same in all groups, the assumption is that most of the miscarriages would have been chromosomal abnormalities. Since the miscarriage rate was similar in the 8-cell group vs. 4 and 5 cell group, these data suggest that the risk of aneuploidy does not decrease with increasing blastomere number.

The patient should be aware that the quoted PRs per transfer according to blastomere number could actually be even a little higher since embryos with less blastomeres may have actually implanted. Thus these data are actually the minimum chance an embryo with a given blastomere number will implant. Many countries throughout the world are doing single embryo transfers and hopefully these data will encourage these IVF centers to analyze their data similarly. It would be interesting to evaluate whether the addition of pre-implantation diagnosis or transfers at blastocyst stage improves outcome vs. day 3 transfers of 8 cell embryos.

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