

# Blastomere number and pregnancy rates in the succeeding in vitro fertilization cycle in women who formed all embryos with $\leq 5$ blastomeres

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## Summary

**Purpose:** To determine the likelihood of pregnancy following the transfer of embryos all with slow cleavage to day 3. Furthermore to determine the likelihood that if slow cleavage happens once, it is likely to repeat. **Methods:** A 10-year retrospective review of in vitro fertilization-embryo transfer (IVF-ET) cycles was performed to identify day 3 embryo transfers where none of the embryos had  $> 5$  blastomeres. The pregnancy rate was then determined. If pregnancy did not occur and another IVF-ET cycle was performed it was determined what percentage of those cycles also showed 100% slow cleavage. **Results:** The ongoing delivered pregnancy rate was 22.3% and the implantation rate was 15.6%. Of the 90 women trying another cycle 82.2% had at least one embryo with six blastomeres. The implantation rate for cycle number 2 for those with at least one 6-cell embryo was 18% (34/187) but was zero (0/17) for those not having at least a 6-cell embryo in cycle number 7. **Conclusions:** These data can help a couple decide whether to pursue a second cycle following an IVF-ET cycle with 100% slow cleavage embryos.

**Key words:** Blastomere number; Slow cleavage; Embryo transfer.

## Introduction

A study of single-embryo transfer in women with diminished egg reserve found the following pregnancy rates according to the blastomere number of a day 3 embryo: 4 cell - 3.8%, 5 cell - 9.5%, 6 cell - 37.8%, 7 cell - 40.0% and 8 cell - 42.4% [1]. The present study evaluated pregnancy rates in a larger series of women not necessarily with diminished egg reserve following transfer of all embryos (not reduced to one) with  $< 6$  blastomeres.

The study also aimed to determine what the chance was of having at least one embryo with six blastomeres in the next cycle if the preceding one did not have any. In addition if a 6 cell embryo was present vs none in the second embryo transfer, would it have an effect on the pregnancy rate.

## Materials and Methods

A 10-year retrospective study of IVF-ET cycles was carried out to identify first embryo transfers where the maximum number of blastomeres in any embryo transferred was 5.

All types of controlled ovarian hyperstimulation regimens were used including luteal phase leuprolide acetate with high-dose gonadotropins, an antagonist protocol using cetrorelix or ganirelix, or mild stimulation protocol [2].

All embryo transfer cycles were counted including those with only one embryo transferred and including female partners to age 39.9.

The viable pregnancy rate from 8-12 weeks and live delivered

pregnancy rates were determined in cycle 1 when no embryos had six blastomeres. These same parameters were also determined in cycle 2 and comparisons were made between those cycles where again there were no embryos with six blastomeres vs those which did not have at least one embryo with six cells.

## Results

The first cycle results of transferring day 3 embryos with a maximum of five blastomeres were 24.8% (60/242) for 8-week viable pregnancy rates and 22.3% for 12-week viable pregnancy rates (Table 1). The implantation rate was 15.6%.

The number of women not having a live delivered pregnancy in the first cycle where no embryos had six blastomeres trying a second cycle was 90/191 (47.1%).

The majority of women attempting a second IVF-ET cycle did have an embryo with six or more blastomeres transferred: 74 of 90 (82.2%). Sixty-seven of these 90 women had two or more embryos transferred and 60 of these 67 women (89.6%) with two or more embryos transferred had at least one day 3 embryo with six blastomeres. The seven women in cycle 2 with  $\leq 5$  blastomeres and  $\geq 2$  embryos transferred had 17 embryos transferred and not one implanted (implantation rate 0%). A total of 16 women (single embryo transfers included) in cycle 2 had 16 embryo transfers of 26 embryos and none implanted. The 60 women with at least one embryo with six blastomeres had 187 embryos transferred and 34 implanted (implantation rate 18% per embryo) (Table 1).

The live delivered pregnancy rates in cycles 3 and 4 are shown in Table 1 according to whether there were any

Table 1. – Pregnancy outcome according to blastomere size (based on patient age  $\leq 39$  from 1/1/97 to 12/31/07).

	Cycle 1		Cycle 2		Cycle 3		Cycle 4
Blastomere size	≤ 5	≤ 5	≥ 6	≤ 5	≥ 6	≤ 5	≥ 6
# transfers	242	16	74	7	29	5	26
# pregnancies (beta-hCG > 200 mIU/ml)	74	0	29	2	11	0	17
% pregnant/transfer	30.6	0.0	39.2	28.6	37.9	0.0	65.4
# 8-week viable	60	0	22	2	9	0	14
% 8-week viable pregnancy rate	24.8	0.0	29.7	28.6	31.0	0.0	53.8
# 12-week viable	54	0	21	2	8	0	13
% 12-week viable pregnancy rate	22.3	0.0	28.4	28.6	27.6	0.0	50.0
# miscarriages	9	0	1	0	1	0	1
% miscarriages/ 8-week viable	15.0	0.0	4.5	0.0	11.1	0.0	7.1
# deliveries	51	0	21	2	8	0	13
Delivered pregnancy rate/transfer	21.1	0.0	28.4	28.6	27.6	0.0	50.0
# embryos transferred	486	26	201	18	80	6	75
Avg. # embryos per transfer	2.0	1.6	2.7	2.6	2.8	1.2	2.9
# sacs implanted	76	0	35	2	11	0	21
Implantation rate (%)	15.6	0.0	17.4	11.1	13.8	0.0	28.0

day 3 embryos with six blastomeres or more: the group with six or more blastomeres: 42/129 = 32.4%, implantation rates: 18.8% (67/356), mean number embryos transferred: 2.8. In contrast the group with a maximum of five blastomeres: 2/28 = 7.1%, implantation rate: 4% (2/50), mean number of embryos transferred: 1.8, number of patients (1<sup>st</sup> cycle) with only 4 cell embryos: 128, number of patients (cycles 2-4) with only 4 cell embryos: 16 ( $p < 0.01$ , Fisher's exact test).

## Discussion

Based on these data transferring more than one embryo with only four or five blastomeres does seem to more than double the chance of a successful live delivery when compared to single embryo transfers of similar numbers of blastomeres [1]. The difference could also be some-

what related to a better oocyte quality since in the aforementioned study all patients had diminished oocyte reserve with a mean serum FSH of 20 mIU/ml whereas in this study the IVF-ET cycle included – but were not limited to – females with diminished egg reserve.

Since the live delivered pregnancy rate was 50% higher for women with at least one 6 cell embryo in succeeding cycles compared to the first cycle with a maximum of five cells it seems that blastomere number is an important criteria for prediction of pregnancy rates, especially with 5 cells as the cut-off.

The study suggests that possibly slight variation in subsequent controlled ovarian hyperstimulation cycles or just fortuitously that most women who do not achieve a 6 cell embryo on their first IVF-ET cycle do not necessarily have a condition that would predispose them to always forming embryos with fewer blastomeres. However, those who have slow cleavage in two consecutive cycles seem to have some type of genetic defect that leads to a high likelihood of failure. This group should probably be discouraged from trying a third cycle. They should possibly consider a change in gametes.

The average number of blastomeres in the first cycle group not making a 6 cell embryo was 4.2 and there were 128 (52.9%) cycles where there were only 4 cell embryos. In the persistent group of  $< 6$  blastomeres the average number of blastomeres was 4.2 and the number with only 4 cell embryos was 16 (57.1%).

## References

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