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**Title:**

SLOWER BLASTOCYSTS DEMONSTRATE LOWER IMPLANTATION RATES DUE TO EMBRYO-ENDOMETRIAL ASYNCHRONY AND NOT BY REDUCED EMBRYONIC COMPETENCE

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**Objective:**

Delayed embryo blastulation (Gardner grade <4) observed at day 5 is correlated with lower implantation rates (IR). It is commonly believed that this decrease is the result of impaired reproductive competence of the embryo. Recent data on frozen embryo transfers with these embryos has not entirely support the hypothesis, thus further analysis of the relationship between the embryonic projection and the endometrial advancement is now under greater scrutiny, particularly with regard to the timing of the progesterone increase. We undertook this study to compare IRs of slow versus normal blastulating embryos both under a synchronous and asynchronous endometrium.

**Design:**

Retrospective analysis

**Materials and Methods:**

Patients undergoing a fresh IVF cycle with a single embryo transfer (SET) in 2010 – 2015 were included. Patients were segregated according to the degree of blastocelic expansion (Slow Gardner <4; Normal Gardner ≥4) and subdivided based on the level of progesterone (P<sub>4</sub>) on surge day (Group A: P<sub>4</sub><1.5; Group B: P<sub>4</sub>>1.5). Patients with peak endometrial thickness at time of embryo transfer of <6 mm were excluded. The main outcome measure was IRs. Bivariate associations were examined using Pearson's Chi-square test, independent samples t-test, as



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appropriate. All statistical tests were two-sided and P value <0.05 was considered statistically significant.

**Results:**

We identified 458 sacs from 1075 patients that underwent a fresh SET in the study period. The IR in normal developing blastocysts was 47.0% and in slow blasts was 14.0% (p<0.05), irrespective of P<sub>4</sub> level at surge; and when divided by P<sub>4</sub> level at surge regardless of degree of blastulation, the IR was 43.3% vs. 19.4% (p<0.05), respectively. The observed IR from a normal developing blastocyst transfer was statistically lower if the P<sub>4</sub> was ≥1.5 ng/mL when compared to a P<sub>4</sub> <1.5 ng/mL (24.0% vs. 47.8%, p<0.05). Slow blastocysts had also lower IR when transferred with a P<sub>4</sub> ≥1.5 ng/mL when compared to a P<sub>4</sub> <1.5 ng/mL, although statistical significance was not reached because of a small sample size.

**Conclusions:**

Premature progesterone elevation appears to signal the onset of the window of implantation. IR may be decreased if the embryo is not advanced enough to implant during the narrow window. An early opening of the WOI and poor embryonic-endometrial synchrony combine to severely diminish outcome. Active laboratory and clinical management could enhance IR by cryopreserving late developing embryos and prolong thaw/transfer until a more controlled and receptive uterine environment exists. Further prospective studies and a more detailed real time molecular analysis of the transcriptome may further elucidate the optimal synchronization parameters.

**Support:**

None.

**Table:**

	Slow Blastocysts		Chi-Square
	<1.5	≥1.5	
<38	22.2% (14/63)	0% (0/2)	NS
≥38	8% (6/75)	0% (0/3)	NS
	Normal Blastocysts		
<38	52.2% (333/634)	31.6% (6/19)	p<0.05
≥38	36.4% (99/272)	0% (0/7)	p<0.05



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