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#### Title

凍結融解単一胚移植周期で D6 胚が出生児に与える影響

Delayed blastulation has no effect on neonatal outcomes in frozen-thawed single blastocyst transfer cycles.

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# Objective

生殖補助医療 (ART) において Day5 にて胚盤胞に至らない発育の遅い胚であっても、Day6 まで培養して 胚盤胞に到達すれば移植胚として用いられる。このような発育の遅い胚は、Day5 胚盤胞に比べ移植後の 妊娠率が低いことや、細胞分裂装置の異常を持つ細胞の割合が高くなるなどの報告がされているが、Day6 胚盤胞由来の出生児の詳細な報告は少ない。本研究では発育速度が遅い Day6 胚盤胞が出生児に与える影響について、単一胚盤胞移植から単児出産に至った児を対象として解析を行った。

Blastocysts formed on day 6 (D6BL) are available in embryo transfers though they are considered to be suboptimal for transfers due to delayed blastulation. Several reports revealed D6BLs have more abnormalities in mitotic apparatus and resulting poor clinical outcomes in transfers as compared with blastocysts formed on day 5 (D5BL). However, influences of delayed blastulation on neonatal outcomes after blastocyst transfers have not been investigated so far. The present study was conducted to clarify whether there is a difference in neonatal outcomes between singletons born after transfers of a frozen-thawed single blastocyst formed on Day 5 and Day 6.

### Design

後方視的研究

Retrospective cohort study.

## Materials & Methods

2008 年から 2016 年の間に Day5 あるいは Day6 にて Gardner 分類において BL3 以上に発育した胚盤胞の凍結融解単一胚移植から単児出産に至った Day5 胚盤胞由来の 1137 児、Day6 胚盤胞由来の 134 児を対象とした。両群間で出生児体重、出生児身長、在胎週数、性比、先天性異常率を T 検定もしくは $\chi$  二乗検定を用いて比較検討した。また、児の身体発育と性別、在胎週数、胚齢、母親の BMI の関係について重回帰分析を用いて解析した。

A total of 1137 neonates born after transfers of a frozen-thawed single D5BL and 134 neonates after D6BL transfers performed from 2008 to 2016 were analyzed. Blastocysts that reached grade 3 by the Gardner's score on day 5 or 6 are defined as D5BL and D6BL, respectively. Birth weight, birth height, gestational age at birth, sex ratio and congenital abnormalities were compared between singletons born after transfers of D5BLs and D6BLs by student's t-test or chi-square test. Multiple linear regression analysis was utilized to investigate the influential parameters in fetal development among gender, gestational age, day of blastulation and maternal BMI.

#### Results

出生児体重、身長、在胎週数、男児率および先天異常発生率は、それぞれ  $3057.3 \pm 477.7g$  対  $3041.2 \pm 447.8g$ ,  $48.7 \pm 2.6cm$  対  $48.7 \pm 2.9cm$ ,  $38.7 \pm 2.0$  週 対  $38.5 \pm 1.8$  週, 1.04 対 1.23, 3.5% 対 3.0%と両群間に有意な差は認められなかった。また、出生児の体重に対しては児の性別、在胎週数、母親の BMI が関与しており、身長に対しては児の性別、在胎週数が関与する結果となった。胚の発育の遅さは、出生児の体重と身長のどちらとも関与しない結果となった。

Birth weight (g), birth height (cm), gestational age (weeks), sex ratio (m/f) and congenital abnormality rates (%) of babies born after transfers of D5BLs vs D6BLs were  $3057.3 \pm 477.7$  vs  $3041.2 \pm 447.8$  (ns),  $48.7 \pm 2.6$  vs  $48.7 \pm 2.9$  (ns),  $38.7 \pm 2.0$  vs  $38.5 \pm 1.8$  (ns), 1.04 vs 1.23 and 3.5 vs. 3.0 (ns), respectively. Multiple linear regression identified gender (p<0.01), gestational age (p<0.01) and maternal BMI (p<0.01) as associated parameters with birth weight. Gender (p<0.01) and gestational age (p<0.01) were associated with birth height. Delayed blastulation was not identified as an associated parameter with either birth weight or height.

#### Conclusions

本研究では Day6 胚盤胞由来の出生児は Day5 胚盤胞由来と統計的な差はなく、発育の遅い胚は出生児に 影響を与えないことが示唆された。よって Day5 で胚盤胞が得られず Day6 でしか胚盤胞が得られない症 例でも、Day6 胚の移植は有効な選択になる。

The present study revealed neonatal outcomes were not statistically different between babies born after transfers of D5BLs and D6BLs. These results suggest that delayed blastulation has no effect on the neonatal outcomes. Therefore transfers of D6BLs are pragmatic options for females who cannot obtain blastocysts on day 5.

# Support

None.