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Title

Interpreting Early hcg Dynamics in the Era of the Thawed Euploid Single Embryo Transfer: How Important is Doubling?

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Objective:
The often quoted minimal serum HCG doubling time of early gestations (66% rise in 2 days) is based on a study with an 85% confidence interval in a cohort of only 20 female patients. More recent studies examining HCG dynamics in ART pregnancies are often confounded by multiple embryo transfer, replacement of unscreened embryos, and variation in the day of embryo development and normalization of endometrial transformation. The minimal HCG rise in early pregnancies conceived after single, euploid, frozen-thawed blastocyst transfer (FET) that correlates with good reproductive outcome has yet to be determined.

Design:
Retrospective cohort analysis

Materials and Methods:
Patients that underwent single, euploid FET, from June 2011 to March 2016, were included. Oocyte donor cycles were excluded. Serum HCG levels were monitored on day 9 post FET, and if positive, on day 11. The rise was then correlated with implantation and ongoing pregnancy rates. Data was analyzed by student's t-test, Chi-square, Kruskal-Wallis, linear and binary logistic regression.

Results:
A total of 458 single, euploid FETs were included. HCG rise of ongoing pregnancies (mean: 158.74 ± 57 %; range: 9.5-698.32%) did not differ by maternal age (x2=1.55, p=0.82), BMI (x2=7.13, p=0.13) or blastocyst expansion grade (x2=0.69, p=0.71). The degree of HCG rise significantly correlated to successful implantation (OR 4.101 [95% CI 2.39-7.21], P<0.0001) and ongoing pregnancy (OR 3.51 [95% CI 1.83-6.74], P=0.0002), with a minimal threshold of 10.8% rise conferring a 50% probability of ongoing pregnancy (Table 1). This association was not

influenced by maternal age (x2=5.09, p=0.28), BMI (x2=1.78, p=0.78) or blastocyst expansion stage (x2=0.03, p=0.98).

Conclusions:

This is the largest study to date which establishes thresholds for initial HCG rise in normal pregnancies resulting from single, euploid FET. HCG dynamics have long been used to establish prognosis. By using SET of euploid embryos in a synthetically prepared endometrium, we eliminated confounding variables and demonstrated that HCG doubling confers a 75% probability of clinical pregnancy. Furthermore, this data points to the need for continued luteal support, even in pregnancies with only a 10% initial HCG rise.

Support:

None.

Table:

Probability of ongoing pregnancy	Percent HCG rise over 48 hours
50%	10.8%
75%	106.5%
80%	131.4%
90%	202.2%
95%	272.9%