

Mini Review

Late Rise Human Chorionic Gonadotropin after Embryo Transfer: Causality and Significance! A mini review

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Abstract

The reliable detection of hCG in maternal blood usually coincides with the embryonic implantation phase which is around 7 days post fertilization. It is believed that hCG levels taken post embryo transfers have a diagnostic and prognostic value when it comes to reproductive outcomes. Very low initial hCG levels predict a higher risk of chemical pregnancies, miscarriages and ectopic pregnancies. A review of the literature was performed so as to understand the mechanisms leading to late hCG rises as well as significance of such findings.

Introduction

Human chorionic gonadotropin (hCG) is produced by the placental syncytio-trophoblasts as early as 7–8 blastomere stage of the embryonic development i.e. before actual implantation takes place (M.-L.Bonduelle et al. 1988). The reliable detection of hCG in maternal blood usually coincides with the embryonic implantation phase which is around 7 days post fertilization (Ahmed et al. 1983). While serial hCG levels aren't usually monitored in spontaneous pregnancies, women undergoing assisted reproductive technologies (ART) treatments usually necessitate such an approach especially after embryo transfer (ET). It is believed that hCG levels taken post ET have a diagnostic and prognostic value when it comes to miscarriages, ectopic pregnancies, predicting multiple gestations as well as live births (Schmidt et al., 1994, McCoy et al. 2009).

Discussion

Despite the lack of consensus on the hCG cutoff values that correlate with the best ART outcomes, a bulk of the studies use a value of 70 mIU/ml on day 14 post ovum pickup as an acceptable reference value (Sung et al. 2016). Values equivalent to 5 mIU/mL or below are judged as negative pregnancy tests (Sung et al. 2016, Maslow et al. 2016). It is believed that the amount of hCG produced reflects the mass of the trophoblast tissue as well as its function (Porat et al. 2007). Despite the discrepancies in the literature, there is a certain agreement that very low initial hCG levels are associated with adverse pregnancy outcomes and intra-uterine growth restriction. This can be explained by the small placental mass with a suboptimal function thus preventing normal fetal growth (Haddad et al. 1999, Krantz et al. 2004, Porat et al. 2007). A possible explanation for the latter might be that some embryos have a division lag, thus a later or abnormal implantation

due to variances in trophoblast differentiation (invasive/extravillous versus hCG-producing/ villous phenotype) in an endometrium of decreased receptivity (Bolton et al. 1989, Woodward et al. 1993, Smith et al. 2004, Morse et al. 2016). Jukic et al. found out that smoking status and age at menarche affected the time of implantation by almost 24 hours and thus a late hCG rise. Current active or passive smoking status was significantly associated with delayed implantation. Younger age at menarche (younger than 12 years of age) was also found to be associated with a slow initial hCG rise (Jukic et al.2011). On another note, low initial hCG levels from 1.0 to 5.0 mIU/mL might be due to a false negative result related to laboratory methodology used for the hCG titration (Maslow et al. 2016). It's worth mentioning that it's not only the initial hCG value but the doubling time as well as the hCG-rise curve is more correlated with the pregnancy outcome (Shamonki et al. 2009, Maslow et al. 2016, Morse et al. 2016). A doubling time of 2 days has been set as the best predictor of live birth rate although an increase rate as low as 53% can also predict a viable pregnancy (Shamonki et al. 2009, Seeber et al. 2012). Initial hCG value post ET is important to diagnose a possible pregnancy, however it doesn't correlate alone with the possibility of a live birth. Serial hCG levels are important especially when the initial values are lower than the cut-off value.

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