The effect of low dose hCG/GnRH agonist dual-trigger on pregnancy outcomes

Shapiro MA, Romanski PA, Thomas A, Farland LV, Yanushpolsky E

Obstetrics & Gynecology, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, USA

OBJECTIVE: The use of a GnRH agonist (GnRHa) to trigger final oocyte maturation has been shown to eliminate ovarian hyperstimulation syndrome (OHSS) but is also associated with lower pregnancy and live birth rates compared to hCG triggers due to inadequate luteal phase support. The use of a dual-trigger with both low-dose hCG and GnRHa can help provide the necessary luteal phase support, but the optimal hCG dose is unknown. Our objective was to assess pregnancy and OHSS rates following dual-trigger with GnRHa and low-dose hCG compared to hCG-only trigger. A secondary objective was the assess pregnancy outcomes in subsequent frozen cycles for the same patient population.

DESIGN: Retrospective cohort study

MATERIALS AND METHODS: Fresh IVF/ICSI GnRH antagonist cycles from 1/1/2012 to 5/31/2017 were reviewed. Patients who received a dual-trigger with a GnRHa (2 mg) and low-dose hCG (1,000u) were compared to women who received an hCG-only trigger (10,000u hCG/250u Ovidrel). Freeze-all cycles and predicted poor responders (≥41 years old, BMI <18 or >40 kg/m^2, AMH <2.0) were excluded. Demographics, stimulation and pregnancy outcomes were analyzed. Logistic and Poisson regression were used to estimate the odds ratio (OR) and relative risk (RR).

RESULTS: The dual-trigger group was younger (mean 33.6 vs 34.7 years), had a higher AMH (6.2 vs 4.9 ng/mL,) and a higher rate of day 5 embryo transfer (74.7% vs 44.4%) compared to the hCG-only trigger group. The dual-trigger group had more oocytes retrieved (18.1 vs 13.6) and a better blastocyst conversion rate (54.8% vs 39.6%). Yet, the dual-trigger group was more likely to have an unsuccessful biochemical pregnancy (14.6% vs 9.9%) and a lower probability of clinical pregnancy (gestational sac, 43.5% vs 50.1%) and live birth (33.6% vs 42.9%), all which reached the threshold of statistical significance. There were 3 cases of OHSS, all in the hCG-only trigger group. In subsequent frozen cycles, pregnancy rates were comparable between the two groups and live birth rates for both groups were better than live birth rates for the fresh dual-trigger transfer.

CONCLUSIONS: The dual-trigger group had a better prognosis based on age and AMH levels, and had better stimulation outcomes. Despite this observation, pregnancy outcomes were significantly worse in this group, suggesting that the low dose hCG (1,000u) in the dual-trigger protocol may not have provided adequate luteal support, compared to an hCG-only trigger (10,000u hCG/250u Ovidrel). Interestingly, the pregnancy rates were comparable in subsequent frozen cycles, further supporting the hypothesis that the issue lies in inadequate luteal phase support. Further studies are needed to establish the optimal dose of hCG to both support early pregnancy development and offer an acceptably low risk for OHSS.