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Title:

OPTIMIZING GONADOTROPIN STIMULATION TO MAXIMIZE THE LIKELIHOOD OF OBTAINING EUPLOID EMBRYOS

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Objective:

In order to optimize the number of viable oocytes retrieved for IVF, reproductive endocrinologists alter gonadotropin (Gn) dosage and duration of stimulation. The ultimate measure of a successful IVF cycle is a euploid embryo. Here we aimed to understand the relationship between commonly adjusted Gn stimulation parameters and the likelihood of obtaining euploid embryos. These insights better enable data-driven personalization of protocols for patients undergoing fertility treatments.

DESIGN:

Retrospective cohort study

MATERIAL AND METHODS:

Patients who underwent fresh IVF with embryo screening (pre-implantation genetic screening (PGS)) from 2009 - 2015 were included. Binomial regression with generalized estimating equations (GEE) was utilized to understand factors that impact the likelihood of embryos from a given patient being aneuploid.

RESULTS:

Overall, aneuploidy was detected in 47% of the embryos resulting from 1190 fresh IVF cycles in which PGS was performed. As expected, higher aneuploidy rates were observed with increased maternal age (2% with each unit increase in patient's age ($p=0.012$)). After controlling for age and FSH levels, we observed that the likelihood of aneuploid embryos decreased with greater numbers of oocytes retrieved



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(2% decrease in likelihood per unit increase in retrieved oocytes) ($p < 0.0001$). Antagonist and Estrogen priming protocols were associated with increased aneuploidy rates (20% ($p = 0.0016$) and 23% ($p = 0.02$), respectively) compared to Down Regulation and MicroFlare protocols. We also observed that increasing Gn dosage was only associated with a significant increase in aneuploidy rates in patients who were stimulated past day 12 (mean surge day = 12, 95% CI = 10-15), with every 1000 unit increase in the cumulative Gn dosage past day 12 [mean dose = 3320, 95% CI = 1350 - 5550] corresponding with a 15% increase in the aneuploidy rate ($p = 0.0003$).

CONCLUSION:

Protocols relying on minimal or no Gn stimulation have gained traction in the US and abroad. We demonstrated that higher dosages of Gn correlate with higher numbers of oocytes retrieved, but not with increased likelihood of a resultant embryo being aneuploidy in most patients. A small increase was seen in low responding patients who received increasing dosages for more than 12 days of stimulation, but this effect may be related to the patient population and not the stimulation protocol. For most IVF patients, standard stimulation protocols do not seem to result in diminished embryo quality.

SUPPORT:

None