Abstract citation ID: deaf097.941

P-635 Optimizing stimulation protocols: lower aneuploidy and higher pregnancy rates with r-FSH/r-LH

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Study question: Does the source of luteinizing hormone (LH) in controlled ovarian stimulation (COS) affect euploidy and clinical outcomes?

Summary answer: Aneuploidy rate was lower, while live birth and clinical pregnancy rates were significantly higher in embryos from women stimulated with r-FSH/r-LH than HP-HMG.

What is known already: Since the use of gonadotropin-releasing hormone (GnRH) analogues deprive growing follicles of LH, supplementation with this hormone is thought to improve reproductive outcomes. Currently, different LH sources are available, such as the menopausal gonadotropin hormone (HMG), and its highly purified version (HP-HMG); the recombinant LH (r-LH) and a combination of r-LH and human folliclestimulating hormone (r-FSH) in a single injection. However, there is no evidence to suggest the superiority of one of these LH preparations in terms of clinical outcomes and euploidy.

Study design, size, duration: This retrospective paired cohort study included the analysis of 588 embryos obtained from 141 women stimulated with r-FSH/r-LH and 456 embryos from 146 women who received HP-HMG. Videos of embryo development were acquaried during three months using time-lapse systems.

Participants/materials, setting, methods: Videos of embryo development from both stimulation groups were analyzed using EMBROYLY (ImVitro, France), an Artificial Intelligence (AI) tool which classified each embryo into a transfer confidence category based on its predicted implantation potential: very low, low, moderate, or high. Euploidy and clinical outcomes were compared across the four categories within each COS group.

Main results and the role of chance: No significant differences were found between the r-FSH/r-LH and HP-HMG groups in women's age (37.9 ± 4.0 vs. 37.9 ± 3.8, respectively), BMI (23.37 ± 3.95 vs. 23.17 ± 3.46, respectively) and AMH levels (7.65 ± 8.11, n = 69 vs. 9.93 ± 10.54, n = 88, respectively).

The HP-HMG group showed a significantly higher aneuploidy rate than the r-FSH/r-LH group across transfer confidence categories: low (69.1% vs. 54.8%*, respectively), moderate (60.8% vs. 22.2%*, respectively), and high (47.6% vs. 0.0%*, respectively). Logistic regressions revealed that AI-assigned categories significantly predicted aneuploidy in the r-FSH/r-LH group while comparing very low vs. low categories and moderate vs. high categories. In contrast, these transfer confidence categories did not predict aneuploidy in the HP-HMG group ($p > 0.05$). Regarding clinical outcomes, the r-FSH/r-LH group had higher live birth rates from embryos in the very low (27.6% vs. 12.5%, respectively) and low (47.2% vs. 26.7%, respectively) transfer confidence categories compared to the HP-HMG group, with statistical significance for low-quality embryos*. Similarly, the clinical pregnancy rate of low-quality embryos was significantly higher in r-FSH/r-LH patients than HP-HMG ones (49.4% vs. 28.3%*, respectively).

*p-value$<$0.05

Limitations, reasons for caution: This study is limited by its retrospective, descriptive and single-center nature. A multicenter study that also evaluates the embryo development and implantation potential of embryos from both COS protocols would be needed. In addition, prospective studies are necessary to confirm these findings and reduce potential biases inherent to retrospective analyses.

Wider implications of the findings: Our findings suggest that r-FSH/r-LH may reduce aneuploidy rates and improve live birth outcomes, particularly in low-quality embryos. This may indicate that the LH source used for COS influences embryo ploidy and implantation potential. Therefore, personalizing stimulation protocols could optimize clinical outcomes, especially for patients with higher aneuploidy risk.

Trial registration number: No