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## O-292 Comparison of effect of two different trigger regimens; single (hCG) versus dual (hCG + Leuprolide) on outcome of fresh IVF cycles: A randomized controlled trial

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**Study question:** Does adding gonadotropin-releasing hormone agonist (GnRHa) to hCG trigger increases the number of high-grade embryos in GnRH antagonist protocol in fresh non-donor IVF?

**Summary answer:** Final oocyte maturation triggered by dual trigger increases the number of MII oocytes thus transferring good-quality embryos and cryopreserving surplus embryos compared to hCG trigger.

**What is known already:** hCG has been conventionally used as a 'faux' LH surge to bring about final oocyte maturation due to structural similarity between the two. GnRH agonist, on the other hand, induces a more physiological gonadotropin surge for follicular maturation, but is associated with luteal phase deficiency. Recent studies have shown that combining GnRHa with hCG trigger improves oocyte maturation and embryo quality with the added benefit of a luteal phase support, thereby improving IVF outcomes in terms of both embryological and reproductive outcomes.

**Study design, size, duration:** A single-center, open labelled, randomized controlled trial including 100 normal responder patients between 21-38 years undergoing IVF using GnRH antagonist protocol between January 2020 to August 2021. The study excluded patients with the presence of other variables of adverse outcomes like diminished ovarian reserve (AFC < 5 or AMH < 1.2 ng/ml), endocrine disorders, thin endometrium (<6mm), previous history of uterine surgeries, and high responders.

**Participants/materials, setting, methods:** 100 patients undergoing fresh IVF cycle using GnRH antagonist protocol were randomized after informed consent to receive either dual trigger (Leuprolide acetate 1 mg + rhCG 250 mcg, n = 50) or single hCG trigger (rhCG 250 mcg, n = 50). Oocyte retrieval was done 35-37 hours after trigger followed by IVF/ICSI, as indicated. Oocyte and embryo grading was done using Istanbul consensus. Analysis was done by ITT. Outcomes were analyzed using Independent t-test and Chi-square test.

**Main results and the role of chance:** The baseline characteristics were comparable in both arms. the number of MII oocytes retrieved (7.82 versus 5.92, $p = 0.003$) and the number of day-3 grade-1 embryos (4.24 versus 1.8, $p < 0.001$) were higher in the dual trigger group, whereas fertilization rates between the two groups (91.82% versus 88.51%, $p$=*NS*) were comparable. Consequently, the number of embryos cryopreserved (2.68 versus 0.94, $p < 0.001$) were significantly higher in the dual trigger group. However, the implantation rate between the two groups (21% versus 19.6%, $p = 0.770$) was comparable. The serum LH levels 12 hours post trigger were measured in both the arms and as expected, high serum LH values were documented in the dual trigger group (46.23 mIU/ml vs 0.93 mIU/ml, $p < 0.0001$).

**Limitations, reasons for caution:** Due to the impact of the Covid-19 pandemic causing an intermittent pause in IVF services at our center, a smaller sample size of 100 patients could be enrolled in the study, and reproductive outcomes in terms of live births and cumulative live births could not be assessed

**Wider implications of the findings:** This study, though small, has contributed to some evidence of redesigning the dual trigger in all antagonist cycles, with the exception of high responders and PCOS patients. The addition of GnRHa to hCG trigger has led to the possibility of cryopreserving surplus embryos thereby increasing the cumulative live births.

**Trial registration number:** CTRI/2020/08/027030