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O-130 Reproductive outcomes of normal ovarian reserve patients after progestin-primed ovarian stimulation with clomiphene acetate vs GnRH antagonist: A retrospective study with inverse-probability-of-treatment weighting

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Study question: To evaluate the effectiveness of clomiphene acetate (CMA) for preventing premature LH surge in patients with normal ovarian reserve compared to cetrelax.

Summary answer: In progestin-primed ovarian stimulation (PPOS) than GnRH antagonist (GnRH-ant), the incidence of premature LH surge was significantly lower, without significant difference in oocyte maturation rate.

What is known already: The GnRH-ant protocol is one of the conventional protocols which has some disadvantages including increased premature LH surge rate and cancelation rate. In recent years, the PPOS protocol has attracted attention as a new ovarian stimulation using progestin as an alternative to GnRH analog for suppressing a premature LH surge, however its efficacy is still controversial. In addition, many studies have investigated the reproductive outcomes of PPOS using medroxy-progesterone acetate or dydrogesterone; however, there are few reports of CMA, an oral progestin, which is inexpensive and widely used in Japan.

Study design, size, duration: This retrospective cohort study was performed in a reproduction center between March 2018 and October 2020 which included 977 Japanese patients with normal ovarian reserve undergoing PPOS (n = 299), or GnRH antagonist (GnRH-ant) with cetrelax.

(n = 608) in their first IVF cycle at the reproduction center. In subgroup analysis, pregnancy outcomes after frozen embryo transfers (FET) between PPOS (n = 284) and GnRH-ant (n = 579) were also compared.

Participants/materials, setting, methods: The inclusion criteria were patients aged < 40 years and AMH ≥ 1.1 ng/mL, who underwent autologous oocyte retrieval in their first IVF cycle with freeze-all strategy. The primary outcome was the incidence of premature LH surge, the secondary outcomes was oocyte maturation rate. To reduce the impact of treatment bias and potential confounding factors, we conducted logistic regression models with inverse-probability-of-treatment weighting (IPTW).

Main results and the role of chance: After IPTW, baseline clinical data were well-balanced between the two groups, including age, AMH, BMI, the duration, type, and cause of infertility, antral follicle count, the history of recurrent spontaneous abortion, and previous IVF attempts. The premature LH surge rate was significantly lower with PPOS (3.1%) compared to GnRH-ant (20.1%) (odds ratio, 0.21; 95% confidence interval, 0.11–0.36). No significant differences were found in total gonadotropin dose (2400IU for PPOS vs 2400IU for GnRH-ant, p = 0.136), the number of oocyte retrieval (n = 15 vs n = 15, p = 0.484), oocyte maturation rate (78.8% vs 77.8%, p = 0.275), fertilization rate (73.0% vs 72.0%, p = 0.412), viable embryo rate per oocyte retrieval (40% vs 40%, p = 0.890), and good quality blastocyst rate (72.0% vs 69.6%, p = 0.092). However, the good quality day-3 embryo rate was significantly lower with PPOS (37.2% vs 49.1%, p < 0.05). There were no differences in the incidence of moderate-to-severe OHSS (0.3% vs 0.7%, p = 0.481). In FET cycles, the pregnancy outcomes, such as implantation rate (43.1% vs 51.9%, p = 0.013) and clinical pregnancy rate (46.5% vs 54.7%, p = 0.027) were significantly lower with PPOS, however, no significant differences were found in ongoing pregnancy rate (75.6% vs 80.5%, p = 0.325), and live birth rate (72.4% vs 79.5%, p = 0.142).

Limitations, reasons for caution: This was a retrospective cohort study conducted in a single center. The participants in this study were limited to Japanese ethnicity. The results need to be validated across different centers and other ethnicities.

Wider implications of the findings: This is the first report assessing the reproductive outcomes on PPOS using CMA, widely used in Japan. The PPOS with CMA significantly suppressed the premature LH surge rate compared to GnRH-ant protocol, without decrease in oocyte maturation rate.

Trial registration number: N/A