P-763 Neonatal outcomes of the first 65 infants delivered after IVF treatment with progestin-primed ovarian stimulation using dienogest in patients with endometriosis

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Study question: What is the perinatal outcome of pregnancies resulting from a controlled ovarian hyperstimulation (COH) regimen of progestin-primed ovarian stimulation (PPOS) protocol using dienogest (DNG) in patients with endometriosis?

Summary answer: No difference in mean birth weight, however preterm and low birth weight babies are significantly more in the group treated with PPOS using DNG.

What is known already: Dienogest is an oral progestin effective for the treatment of endometriosis, such as reduction of endometrial lesion and control of pain intensity with safety profile and good tolerability. We reported for the first time in the world that DNG was better than dydrogesterone (DYG) for PPOS in terms of the mature oocytes rate and the fertilization rate in patients with endometriosis. Although there have been several reports of infants born with PPOS using DYG, it is essential to report on the perinatal outcome of embryos transferred after treatment with PPOS using DNG from now on. Study design, size, duration: We prospectively investigated the perinatal outcomes of 65 newborns which were the result of using a new COH regimen; PPOS with DNG. The results were compared with perinatal outcome data of babies born between 2018 and 2020 to 815 patients who underwent assisted reproductive technology (ART) treatment at our fertility center. As for the congenital malformation rate, the data was also compared with the 2017 Japanese data bank of babies born after ART treatment.

Participants/materials, setting, methods: We studied the perinatal data of all babies born after transfer of frozen embryos acquired by COH using PPOS protocol with DNG. The rate of maternal complications during pregnancy, pregnancy duration, birth weight, congenital malformations and method of delivery were investigated. We compared the perinatal outcomes of infants born after *in vitro* fertilization (IVF) and frozen embryo transfer at our center during the same period.

Main results and the role of chance: Perinatal data of 65 babies (study group) were compared with the perinatal data of 840 babies born after IVF at our center, and 47807 babies born after ART in Japan, 2017. We found 3 twin and 59 singleton pregnancies in the study group, compared to 23 twins, 1 triplet and 791 singleton pregnancies during the same period at our center. Considering singletons, there was no difference in mean birthweight (study group; 2893.2±652g vs. total at our center; 3001.2±425g, respectively, p=0.102). Preterm births (<37 weeks) were significantly more frequent in the PPOS using DNG treatment group than in total at our center (19.2% vs. 9.7%, p=0.016). The percentage of infants with a birth weight < 2.5 kg was also significantly higher in the PPOS treatment group compared to the total at our center (22.6% vs.11.9%, p= 0.015). The Caesarean section rate was 53.2% in the study group vs. 47.1% control group of our center respectively (p=0.353). One babies in

the study group had malformations in the ocular region. There was no significant difference in congenital malformations between the study group and ART data bank in Japan, 2017 (OR 0.67, 95% CI 0.093: 4.836).

Limitations, reasons for caution: The number of babies is still low, further prospective studies including larger populations are needed to confirm the efficacy of PPOS protocol with DNG.

Wider implications of the findings: This is the first report on the perinatal outcome of babies born by a new COH method using PPOS with DNG, which is a combination of endometriosis treatment and COH for IVF. The association of endometriosis with preterm birth and low birth weight needs to be further investigated.

Trial registration number: UMIN000031111