P-630 Progesterone levels using pessaries of 400 mg of vaginal progesterone (Cyclogest®) in artificial cycles for frozen embryo transfer

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Study question: Does the use of pessaries of 400 mg of micronized progesterone provide comparable results as pessaries of 200 mg x2, in terms of progesterone levels?

Summary answer: The administration of pessaries of Cyclogest® 400 mg reduces the probability of presenting suboptimal level of progesterone on the day of the embryo transfer.

What is known already: The endometrial preparation for frozen embryo transfer (FET) in Artificial Cycle (AC) with vaginally-administered progesterone, is one of the most common IVF procedures nowadays. Now, it has been shown that suboptimal progesterone levels on the day of the embryo transfer compromise the results of FET treatments. Recently, a new preparation of 400 mg vaginal pessaries has been introduced in the market of European countries. Efficacy of this new preparation has been studied in "fresh" IVF cycles but we lack the comparative studies in AC making it necessary to further investigate this area.

Study design, size, duration: Non-inferiority retrospective case-control trial based on 347 embryo transfer treatments with endometrial preparation in AC

carried out at Instituto Bernabeu between January 2019 and July 2020. 153 patients received 1 pessary of 400 mg every 12 hours (group A) and 194 received 2 pessaries of 200 mg every 12 hours (group B). Sampled size calculation resulted in 182 patients required to detect a minimum difference of 2 ng/ml so sample was powered for the purpose.

Participants/materials, setting, methods: Patients receiving embryos in AC preparation were included. All embryo transfers were performed at blastocyst stage after 5 days of progesterone administration. Progesterone levels were assessed the day of the embryo transfer by an electrochemiluminescence immunoassay.Primary outcome was the incidence of suboptimal progesterone levels according with the cutoff value stablished in the literature at 8.8 ng/mL. Secondary outcomes were pregnancy rates (PR), clinical pregnancy rates (CPR), ongoing pregnancy rates (OPR) and miscarriage rates (MR).

Main results and the role of chance: Incidence of suboptimal levels of progesterone was significantly lower in the group of 400 mg (9,8% in Group A vs 19,7% in the Group B, p=0.011). Given that there was an imbalance between groups in the body weight (66.9 +/- 14 vs. 61.9 +/- 13.165 kg, p<0.001) and BMI (24.63 +/- 4.861 vs. 22.54 +/- 3.092, p<0.001), we decided to perform a binary logistic regression setting patient's weight and BMI as confounding variables. The result confirms a higher risk of suboptimal progesterone levels (<8.8) with the 2x200 mg regimen (OR: 2.52 95%CI: 1.28-4.96; p=0.007). Mean progesterone levels were similar in both groups (13,8035 ng/mL +/- 4.62159 vs. 13.9799 ng/mL +/- 7.73243 respectively, p=0.146). No differences were observed in clinical outcomes: PR (52.3% vs. 53.1%, p=0.881), BM (14.7 % vs. 17.6 %, p=0.597), CM (20% vs. 18.6 %, p=0.819) and OPR (33.1 % vs. 33.7 %, p=0.912). The subjective medical decision to administer additional progesterone from the day of the embryo transfer onwards (taking values other than 8.8 ng / mL as a reference), was significantly lower in the group of 400 mg (24,3% vs 37,3%, p=0.009).

Limitations, reasons for caution: The inherent limitations of a retrospective analysis. The study was not powered to detect differences in clinical outcomes. Therefore, results other than progesterone levels should be interpreted with caution.

Wider implications of the findings: A single pessary of 400 mg minimizes the necessity of additional medication (usually subcutaneous progesterone). Presentation of 400 mg is superior to 2x200 providing adequate progesterone levels and patient comfort. Dose finding and pharmacokinetics studies of the vaginal administration will be necessary for the future to optimize FET under AC.

Trial registration number: NCT04722471