

P-675: Serum progesterone measurement and optimization reduce pregnancy loss in frozen-thawed embryo transfer cycles with hormone replacement therapy

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Study question: Does progesterone (P) optimization by measuring and correcting its serum levels when appropriate reduce pregnancy loss following in vitro fertilization-embryo transfer cycles?

What is known already: Progesterone has been consistently associated with pregnancy achievement and development. A significant number of biochemical pregnancies following in vitro fertilization – embryo transfer cycles (IVT-ET) might be due to progesterone deficiency. Previous studies have shown that serum progesterone values lower than 9.2 to 10.64 ng/ml are detrimental to achieve optimal reproductive results in cycles with artificial endometrial preparation for frozen-thawed embryo transfer. However, the best approach in daily practice combining both efficiency and patient convenience is yet to be established.

Study design, size, duration: Retrospective cohort study from march 2018 to December 2019 in a private fertility care center. We included 153 frozen-thawed embryo transfer cycles, with a conventional hormone replacement therapy (HRT) for endometrial preparation.

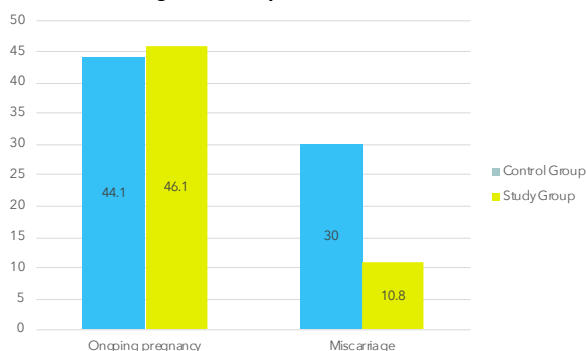
Table 1. Patients characteristics divided by groups (n = 153)

	Study Group (n = 89)	Control Group (n = 64)	P
Age (years/SD)	36.7 (3.25)	36.2 (4.53)	0,5
IMC (kg/m ²) (median [IQR])	21.38 [19.5 - 24.9]	23.37 [21.2 - 25.4]	0,049
Embryo morphology A or B (%)	59 (71.9)	40 (68.9)	0,75
Endometrial thickness (mm), median (IQR)	8.30 [7.6 - 9.1]	8.00 [7.5 - 9.3]	0,67
Estrogen therapy (days*), median (IQR)	13.0 [11.0 - 14.0]	12.0 [11.0 - 14.0]	0,68

*days of exogenous estrogen administration until the first day of the treatment with vaginal progesterone.

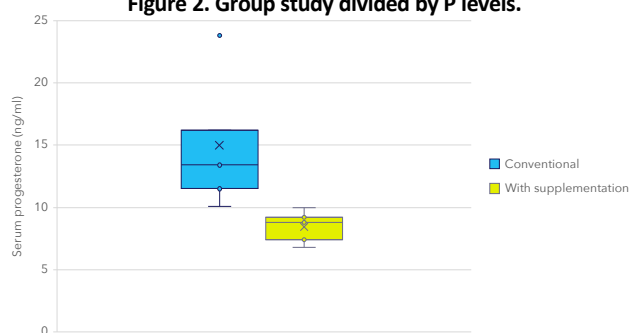
Participants/materials, setting, methods: Patients undergoing HRT in order to transfer frozen-thawed embryos. All women were treated with a sequential combination of 6 mg/day of oral estradiol valerate (EV) for 11 to 15 days followed by EV plus 200 mg/8h of vaginal micronized progesterone (P), for five days until the day of the ET (embryo at blastocyst stage).

Figure 1. Embryo transfer outcomes



The study population was divided into two groups, named by study group (n=89) and control group (n=64). In the study group, at the 4th day of P administration we determined serum progesterone values, in a morning blood sample. When these levels were lower than 10 ng/ml, we added 25 mg of daily subcutaneous progesterone, beginning in the evening of the day before the transfer performed. Conversely, patients from the control group were routinely treated, without any blood analysis. The primary outcome was ongoing pregnancy rate and the secondary was pregnancy loss.

Figure 2. Group study divided by P levels.



Main results and the role of chance: Age, BMI and embryo quality were equivalent between the study and control group (Table 1). The miscarriage rate was significantly lower in the study group (10.8% versus 30%; $P = 0.03$, 95% IC), without differences in ongoing pregnancy rates (46.1% versus 44.1%; $P = 0.86$). (Figure 1)

We determined serum P values in 89 patients. P levels under 10 ng/ml were found in 29.2% (26/89), with a median value of 8.8 ng/dl (7.4 – 9.2). In the rest of the group (70.8%), the median P levels was 13.39 ng/ml (11.5 – 16.2). (Figure 2). When comparing only the study group by progesterone levels, the outcomes did not show any difference, including ongoing pregnancy rate ($P = 1.0$) and pregnancy loss ($P = 0.3$).

Limitations, reasons for caution: As we want to combine both efficiency and patient convenience we do not perform a “second-look” in serum P levels after supplementation to verify if we achieved a better serum P concentration in these patients, so this missing data could be a limitation of the study group.

Wider implication of the findings: The present study suggests that with only one additional blood determination of additional subcutaneous progesterone in the luteal phase support in cycles of ET with HRT using their own oocytes, reducing the miscarriage rates.