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Study question: Do serum progesterone or LH levels better predict the optimal timing for embryo transfer in true natural cycle frozen-thawed embryo transfers (NC-FET)?

Summary answer: Performing embryo transfer according to serum progesterone levels (PL) had similar ongoing pregnancy rates compared to embryo transfer according to serum LH levels.

What is known already: With efficient and safe embryo vitrification techniques, there is an increasing trend in frozen-thawed embryo cycles (FET) over fresh cycles. FET protocols are programmed cycle, NC-FET and modified NC-FET. NC-FET is increasing in popularity, since it is associated with favourable obstetric and perinatal outcomes. In NC-FETs, ovulation time is the critical parameter for synchronization of embryo and endometrium. In the literature, LH surge is the most commonly used test to define ovulation time.

Study design, size, duration: This prospective cohort study included 183 NC-FET cycles in an IVF clinic between March 2022 and November 2022.

Main outcome measure is ongoing pregnancy.

Participants/materials, setting, methods: 183 subfertile women aged between 18-40, having regular menstruation with a cycle length between 24-38 days are included. Protocol for NC-FET included serial hormone measurements and ultrasound monitoring when the dominant follicle reached the diameter of 15-16 mm. Serum LH level $\geq$ 15 IU/l defined as 'ovulation -1' in Group 1 and blastocyst embryo transfer was performed after 6 days. Serum PL > 1 ug/ml was defined as the 'ovulation day' in Group 2.

Main results and the role of chance: There were no significant differences in baseline characteristics including female age, female body mass index, infertility duration, infertility diagnosis and number of failed IVF cycles between two groups. Also, cycle characteristics regarding endometrial thickness, number of embryos transferred, embryo quality and PLs at transfer day were similar. The overall clinical pregnancy was 59.6% and ongoing pregnancy was 50.8%. The implantation rate was 61.7%. The clinical pregnancy and ongoing pregnancy of Group 1 and Group 2 were 49.5%, 50.5% and 47.3%, 52.7%, respectively (p > 0.05). PLs in order to detect ovulation time were calculated according to a mathematical modelling (PL(Ov)=a1 eb1 Ov)(Ov:ovulation day; a1,b1:regression coefficients; e:euler number$\cong$2.718) described in our previous study. Embryo transfer timing was planned after 5,4 or 3 days based on PLs calculated by modelling.

Limitations, reasons for caution: Since this is the first study planning embryo transfer in NC-FET based on progesterone levels, sample size should be increased and also serial change of progesterone levels were unknown in women >40 years of age.

Wider implications of the findings: Progesterone has a particular increasing pattern that enables ovulation day prediction accurately and may be used instead of serum LH levels in timing of embryo transfer.

Trial registration number: NCT05690360

O-296 Progesterone level is an alternative marker to detect ovulation time in natural cycle frozen-thawed embryo transfers

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