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Key Lectures

K-37
Cycle regimens for frozen-thawed embryo transfer

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Frozen–thawed embryo transfer (FET) enables the excess embryos generated by in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI) to be stored and utilized at a later date. This reduces wastage after IVF and increases the chance of conceiving after one cycle of ovarian stimulation and oocyte retrieval. In recent years, the number of FET cycles performed has increased dramatically due to the trend towards transferring fewer embryos after a fresh IVF cycle, and as a result of improved laboratory techniques. In contrast to the complex stimulation protocols employed to stimulate multiple follicular growth for IVF, frozen embryo transfer (FET) protocols are simpler, with the primary aim limited to adequate preparation of the endometrium to receive the thawed, transferred embryo(s). However, despite the growing importance of FET in the treatment of subfertility, there is little consensus on the best method for endometrium preparation in ovulatory women. In order to optimize pregnancy rates, the development of embryos and endometrium should be synchronized. This can be achieved in various ways. The simplest method of endometrium preparation is represented by natural cycle FET (NC-FET), in which the endocrine preparation of the endometrium is achieved by endogenous sex steroid production from a developing follicle. Timing of embryo transfer is determined by detecting the spontaneous luteinizing hormone surge or by administering human chorionic gonadotropin to initiate luteinization. A frequently employed alternative approach is represented by ‘artificial cycle protocols’ in which exogenous estrogens and progesterones are administered, with or without co-treatment with gonadotropin-releasing hormone agonists. In artificial cycle FET (AC-FET), estrogen and progesterone are administered in a sequential regimen that aims to mimick the endocrine exposure of the endometrium in the normal cycle. Initially, estradiol is given in order to cause proliferation of the endometrium, while suppressing the development of the dominant follicle. This is continued until the endometrium is observed to be 7-9 mm thick on ultrasound, at which time progesterone is added to initiate secretory changes. The physiological mid-cycle shift from estrogen to progesterone is thus emulated. The timing of embryo thawing and transfer is planned according to the moment of progesterone supplementation.

In conclusion, natural cycle treatment has a higher chance of live birth and lower risks of PIH, PPH and VPTB than AC for endometrial preparation in women receiving FET cycles. Ovarian stimulation with Gn/FSH or AI may be promising, but the evidence is scare and needs to be evaluated in future studiespregnancies after NCFET have a more favourable outcome compared with AC-FET, with lower rates of HDP, preeclampsia, LGA and macrosomia. The development of gestational hypertension in FET cycles seems not to be influenced by the mode of endometrial preparation. This is valuable information, as the number of FET cycles has increased, including the ‘freeze-all’ strategy. Future studies are required to clarify the underlying biologic mechanisms of our findings, and further randomized controlled trials are needed to improve the quality of evidence.