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SHORT COMMUNICATION

Novel protocol for scheduling oocyte retrieval in IVM cycles in PCOS patients: a case series

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Abstract In-vitro maturation (IVM) is associated with a longer egg-collection procedure in the operating room and a longer oocyte-handling time in the IVF laboratory than standard IVF. Hence, if the designated day of oocyte retrieval could be planned in advance, the workload pressure on that specific day can be planned in advance. This study presents a simple method for advance scheduling of IVM in patients with polycystic ovary syndrome (PCOS). A fixed protocol of oral contraceptive pill administered prior to gonadotrophin priming and based on the days of the week enable the exact dating of the oocyte retrieval day, thereby increasing patient convenience and improving control of the IVF-unit workload. This protocol was compared with immediate-start IVM and resulted in a similar pregnancy rate (43.8% and 40.0% per cycle, respectively).

KEYWORDS: IVF, IVM, oral contraception, PCOS, scheduling, protocol

Introduction

In-vitro maturation (IVM) cycles are associated, in this study centre's experience, with a longer time for the egg-collection procedure in the operating room and a longer oocyte-handling time in the IVF laboratory than standard IVF. By timing the egg-collection day in advance, clinicians can better plan the workload of both the operating room and the IVF laboratory. This study group previously reported the use of oral contraceptive pills (OCP) for advanced scheduling of IVF cycles (Pinkas et al., 2008). The aim of this study was to evaluate the effectiveness of OCP administration for scheduling in advance the oocyte retrieval date in IVM cycles in patients with polycystic ovary syndrome (PCOS).

Materials and methods

The study was approved by the local Institutional Review Board. In a case series, the study population included only women with PCOS, based on Rotterdam criteria (Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group,

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2004) assigned for IVF treatment. All selected patients had at least 12 small antral follicles in each ovary. These patients may benefit from IVM in terms of preventing ovarian hyperstimulation syndrome and cycle cancellation due to hyperresponse on the one hand and at the same time maintain a high pregnancy rate (Cha et al., 2005; Chian, 2004; Chian et al., 1999; Child et al., 2003; Mikkelsen and Lindenberg, 2001).

To schedule IVM, the study centre used a fixed protocol based on the days of the week and then oocyte retrieval in these cycles was planned for a Monday. The decision to administer OCP (or not) was determined by the planned workload of IVM and IVF cycles in the IVF unit.

Oral contraceptive pill and IVM protocol

OCP administration was started on the second day of spontaneous or induced menstrual bleeding and continued for at least 10 days, to the following Wednesday (**Figure 1**). Six days later, on the following Tuesday, a 3-day course of gonadotrophin stimulation was administered for priming follicular growth. The daily dose of gonadotrophins was selected according to the daily effective dose in a previous ovulation induction or IVF cycle, if available: first-time patients were administered 112.5 IU FSH (Gonal F; Merck Serono, Switzerland) or 125 IU FSH (Puregon; Organon, Schering-Plough Corporation, The Netherlands). Oestrogen supplementation (Estrofem, 2 mg twice daily; Novo Nordisk, Denmark) was added simultaneously with the gonadotrophins and continued throughout the treatment cycle. Estrofem was administered with the aim of establishing endometrial growth for improving the implantation potential because of the relatively short time between menstruation and embryo transfer during IVM treatment. Estrofem probably has an inhibitory effect on endogenous FSH secretion, but this effect was negated by the administration of exogenous FSH given at the same time for priming follicular growth. This was followed by injection of human chorionic gonadotrophin (Ovitrelle, 250 μg; Merck Serono) on Saturday, followed by egg collection 2 days later on Monday. Matured oocytes were fertilized by intracytoplasmic sperm injection (ICSI). Embryo transfer was performed 3 days later. Surplus embryos were cryopreserved by vitrification. Progesterone supplementation was routinely started on the day of ICSI, via the vaginal route (Endometrin, 100 mg twice daily; Ferring, Germany) and the intramuscular route (Geston, 50 mg/48 h; Nordic Pharma, UK). The use of combined vaginal and intramuscular progesterone was decided empirically with the aim of securing the exposure of the endometrium to progesterone in the absence of any ovarian production.

Immediate-start protocol

In cycles with immediate assignment for treatment, the 3-day priming course with gonadotrophin was started on days 5–9 of spontaneous or induced menstrual bleeding, using the same day-of-the-week-based protocol described above. All other treatment and follow-up parameters were similar to the above. The measured oestradiol concentrations reflect the combined contribution of ovarian oestradiol and of the absorbed oral Estrofem treatment. In the data, the coefficient of variance of oestradiol concentration was 5.5–11%. Specific oestradiol metabolites were not measured.

Oocyte retrieval and insemination

Oocyte retrieval was performed under general anaesthesia using ultrasound guidance with a 19-G, single-lumen aspiration needle (Cook, Queensland, Australia). The aspiration pressure was reduced to 90 mmHg. The follicular fluid was collected into pre-heated test tubes containing heparin-supplemented human tubal fluid and filtered through a 70-μm nylon-mesh cell strainer. All cumulus–oocyte–complexes identified were cultured in commercial maturation medium supplemented with 75 mIU/ml of both FSH and LH, at 37°C, 5% CO_2 and denuded 24–30 h later. Matured oocytes were inseminated by ICSI and embryo transfer was performed on day 3 post oocyte retrieval. Surplus embryos were cryopreserved by vitrification. Clinical pregnancy was defined as the presence of a gestational sac with an embryonic pole.

Results

Outcome was compared between cycles that were OCP-deferred or immediately assigned for treatment. A total of 26 IVM cycles were performed. Cycle timing with OCP was applied in 16 cycles and immediate assignment in

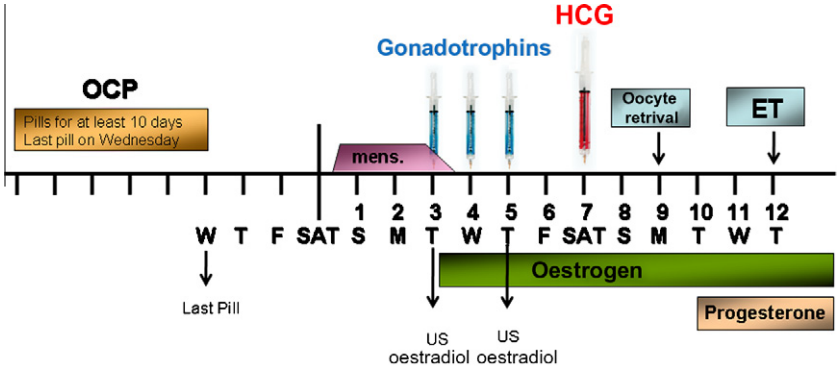

Figure 1 Protocol for scheduling oocyte retrieval day using oral contraception, based on the days of the week. ET = embryo transfer; HCG = human chorionic gonadotrophin; OCP = oral contraceptive pill.