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ARTICLE

Concurrent oocyte retrieval and hysteroscopy: a novel approach in assisted reproduction freeze-all cycles

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Kemal Ozgur M.D. completed his residency training in Obstetrics and Gynecology in 1993 at the Akdeniz University, Turkey, after which he completed a 3-year fellowship in Reproductive Endocrinology and Infertility at Tygerberg Hospital, South Africa and Jones Institute, Norfolk, USA. He returned to Akdeniz University in 1997 and established the IVF unit at the university. Two years later, Dr Ozgur founded Antalya IVF, the largest IVF centre in southern Turkey. His major areas of interest are assisted reproduction, andrology and hysteroscopic surgery. He has published extensively in these fields in peer-reviewed journals.

Abstract In this matched-controlled study (n = 300), the effect of hysteroscopic surgery performed concurrently with oocyte retrieval on the reproductive outcomes of intracytoplasmic sperm injection (ICSI) freeze-all cycles was investigated in patients screened for intrauterine anomalies. Conventionally, hysterscopic surgery is performed in a different cycle from IVF, delaying treatment completion and increasing patient anxiety. One hundred and fifty patients who had hysteroscopic surgery concurrently with oocyte retrieval (hysteroscopy group) in ICSI freeze-all cycles were matched according to age and oocyte number with 150 ICSI freeze-all cycles, in which the patients required no hysteroscopy (control group). In the hysteroscopy group, hysteroscopy was performed for diagnostic (n = 5) and therapeutic (n = 145) purposes. Blastocyst culture and Cryotop vitrification was performed in both groups. Frozen embryo transfer (FET) was successfully performed in the hysteroscopy group from 35 days after oocyte retrieval. No significant differences were observed for implantation, pregnancy, clinical pregnancy and early pregnancy loss rates in the hysteroscopy and control groups (48.9%, 72.0%, 61.3% and 14.8% versus 48.3%, 75.3%, 64.7% and 14.3%, respectively). Performing hysteroscopic surgery concurrently with oocyte retrieval in a segmented-IVF programme has no negative impact on reproductive outcomes, increases efficiency, and provides patients with low-risk treatment.

KEYWORDS: concurrent, freeze-all, hysteroscopy, oocyte retrieval, pregnancy

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Introduction

In assisted reproduction populations, the incidence of female genital tract anomalies (i.e. endometrial polyps, submucous myomas, intrauterine adhesions and intrauterine septa), inflammatory disease and lesions may be as high as 50%. The incidence is highly population-dependent and may increase with increasing age, duration of infertility, number of pregnancy losses and number of previous assisted reproductive treatment failures (Fatemi et al., 2010; Karayalcin et al., 2010; Kasius et al., 2013a, 2013b; Pundir et al., 2014). Each genital tract anomaly has a different risk rating for adverse reproduction and consequently infertility, and a different risk–benefit rating for surgery (Bosteels et al., 2013). There is a general agreement that surgery to repair or remove anomalies benefits reproduction and fertility, especially for patients with long-standing infertility or recurrent pregnancy losses (Bosteels et al., 2013); controversially, the therapeutic beneficial associations are based on retrospective, observational and non-randomized study trials (Smit and Mol, 2014).

Hysteroscopy has revolutionized female genital tract diagnostic and therapeutic procedures and is generally considered the gold standard procedure, due to its relative simplicity, its "see and treat" capabilities, its low operative and postoperative complications, and its high patient tolerance (Pundir et al., 2014). Recent technology improvements, leading to the miniaturization of hysteroscopes and ancillary instrumentation, as well as studies confirming the value of operative hysteroscopy in improving reproductive outcomes (Pundir et al., 2014) have promoted the use of hysteroscopy in routine infertility work-up by an increasing number of assisted reproductive treatment programmes. In a review by Pundir et al. (2014), the use of routine hysteroscopy in asymptomatic women in the cycle before their first IVF cycle was found to significantly increase the relative risk (RR) of clinical pregnancy (RR = 1.44) and live birth (RR = 1.30). Moreover, there have been reports that simply performing endometrial "scratching", i.e. intentional damage to the endometrium through biopsy or curettage in the cycle preceding IVF treatment might have a positive iatrogenic effect on reproductive outcomes (El-Toukhy et al., 2012; Potdar et al., 2012). Although research has continued in the use of hysteroscopy to generate positive iatrogenesis, its true value is still a matter of controversy, with a number of authors cautioning the acceptance of any clinical benefit from the available evidence (Simon et al., 2014; Smit and Mol, 2014).

Intrauterine anomaly diagnoses are most commonly made during fertility work-up for IVF treatments, but are frequently discovered during ovarian stimulation, as endometrial proliferation often may accentuate intrauterine anomalies. Hysteroscopic surgery for an anomaly diagnosed in the fertility work-up phase has generally been scheduled for the proliferation phase of a menstrual cycle preceding IVF treatment. If, however, the anomaly was diagnosed during procedures preceding embryo transfer the cycle has been discontinued, or the embryo transfer postponed (i.e. cohort freeze-all) until a cycle following surgery. Inevitably, the need for hysteroscopic surgery, therefore, has meant a delay in the completion of treatment (Berkkanoglu et al., 2008). By choosing to perform segmented-IVF in all patients, based on previously reported promising frozen embryo transfer (FET) peri-implantation and perinatal outcomes (Ozgur et al., 2015a, 2015b), one has the opportunity to perform intrauterine surgery proactively within the segmented-IVF cycle. In this study, the impact on reproductive outcomes of performing oocyte retrieval and hysteroscopy during the same operation theatre time in segmented-IVF cycles of a fully segmented-IVF programme was investigated.

Materials and methods

Cycle and patient characteristics

This retrospective matched-controlled single-centre study was conducted on assisted reproductive treatment cycles performed between June 2014 and September 2015. Elective segmented-IVF was performed routinely at the assisted reproductive treatment centre from March 2014. Ethics committee approval was not sought for this retrospective study as patients provide informed consent before treatment, which includes agreement to the use of their anonymized data for research, in accordance with the clinic's patient data protection guidelines. Anonymized patient cycles were extracted from the clinic's assisted reproductive treatment database. The cycle extraction excluded patient cycles with no informed consent for the inclusion of their data in research. The study group (hysteroscopy group) consisted of the first 150 consecutive intracytoplasmic sperm injection (ICSI) freeze-all with FET cycles extracted in which patients had undergone hysteroscopy surgery at the time of oocyte retrieval. The control group ($N = 150$) consisted of matched ICSI freeze-all with FET cycles in which patients did not require hysteroscopic surgery based on their diagnosis (i.e. no intrauterine anomalies found by transvaginal ultrasound).

The cycles were matched according to female age (≤±0.7 years) and oocyte number (≤±7.0), with body mass index (BMI) and infertility duration taken into consideration (**Table 1**). Control cycles were only matched once with a study cycle and no duplicate patient cycles were used in the matching. In this study, the hysteroscopic surgery was performed immediately after oocyte retrieval during the same operation theatre time slot. Hysteroscopies were perfomed for diagnostic ($n = 5$) and therapeutic ($n = 145$) purposes; adhesions ($n = 1$), partial uterine septa ($n = 70$), submucosal myomas ($n = 7$), endometrial polyps ($n = 43$) and a combination of anomalies ($n = 24$). The basic fertility work-up of all infertile patients of the assisted reproductive treatment centre included a 2D transvaginal ultrasound scan to examine the uterine cavity. If needed, a saline-infused sonography or hysterosalpingography was performed to confirm the existence of an anomaly before surgery. The decision to perform hysteroscopic surgery on the day of the oocyte retrieval was based on the findings of the fertility work-up.

Ovarian stimulation, oocyte retrieval and embryo culture

Conventional ovarian stimulation was performed using a gonadotrophin-releasing hormone (GnRH) antagonist (Cetrotide, 0.25 mg, Merck Serono, Istanbul, Turkey)

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