Does the time interval between hysteroscopic polypectomy and start of in vitro fertilization affect outcomes?

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Objective: To investigate whether the time interval between hysteroscopic polypectomy and the start of IVF-ET cycles affect IVF cycle outcomes.
Design: Retrospective cohort.
Setting: Academic center.
Patient(s): All patients diagnosed with endometrial polyps undergoing hysteroscopic polypectomy before fresh IVF-ET.
Intervention(s): Hysteroscopic polypectomy.
Main Outcome Measure(s): Patients were divided into three groups based on the time interval between hysteroscopic polypectomy and the start of a fresh IVF-ET cycle. Group 1 consisted of patients who underwent IVF-ET after their next menses, group 2 after two or three menstrual cycles, and group 3 after more than three menstrual cycles. Demographics, baseline IVF characteristics, controlled ovarian stimulation response, and pregnancy outcomes after ET were compared among the groups.
Result(s): A total of 487 patients met inclusion criteria: 241 in group 1 (49.5%), 172 in group 2 (35.3%), and 74 in group 3 (15.2%). There were no differences in the baseline characteristics of the three groups. Ovarian stimulation outcomes, specifically total stimulation days, total gonadotropins administered, and number of oocytes retrieved, were similar between groups. There were no differences in the mean number of embryos transferred. The overall pregnancy outcomes were similar for groups 1, 2, and 3: implantation rate (42.4%, 41.2%, and 42.1%, respectively), clinical pregnancy rate (48.5%, 48.3%, and 48.6%), spontaneous miscarriage rate (4.56%, 4.65%, and 4.05%), and live birth rate (44.0, 43.6%, and 44.6%).
Conclusion(s): Because waiting for two or more menstrual cycles after hysteroscopic polypectomy does not necessarily yield superior outcomes, patients can undergo ovarian stimulation after their next menses without affecting IVF-ET outcomes. (Fertil Steril® 2016;105:539–44. ©2016 by American Society for Reproductive Medicine.)
Key Words: Endometrial polyps, hysteroscopy, polypectomy, in vitro fertilization, timing

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Endometrial polyps are benign localized lesions of the endometrium that are commonly seen in women of reproductive age (1). Endometrial polyps, as well as other intrauterine lesions, such as leiomyomata or septae, can affect implantation of a healthy embryo (2–4) and are implicated in the pathogenesis of subfertility and early pregnancy loss, though the association is controversial (5, 6). Although isolated uterine-associated infertility can be found in 2%–3% of infertile women (7), intrauterine lesions may be found in ~40%–50% of subfertile or infertile women (5–7). Previous observational studies have suggested that resection of endometrial polyps can help to increase natural conception rates as well as increase pregnancy rates with the use of assisted reproduction (8–13). Although current evidence suggests that endometrial polyp resection is beneficial before pursuing assisted reproduction, there

Received September 11, 2015; revised October 18, 2015; accepted October 27, 2015; published online November 18, 2015.
N.P. has nothing to disclose. S.A. has nothing to disclose. J.L.E. has nothing to disclose. J.P.L. has nothing to disclose. R.T.E. has nothing to disclose. P.H.C. has nothing to disclose. Z.R. has nothing to disclose.
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Fertility and Sterility® Vol. 105, No. 2, February 2016 0015-0282/$36.00

http://dx.doi.org/10.1016/j.fertnstert.2015.10.028

are almost no data regarding the optimal time interval between polyp resection and start of assisted reproduction treatment (14). In this context, we sought to investigate whether the time interval between hysteroscopic polypectomy and the start of in vitro fertilization–embryo transfer (IVF-ET) cycles affect IVF cycle outcomes.

MATERIALS AND METHODS

Inclusion and Exclusion Criteria

The Weill Cornell Medical College Institutional Review Board approved the study protocol. All patients diagnosed with endometrial polyps undergoing hysteroscopic polypectomy before fresh IVF-ET cycles from January 2010 to June 2013 were analyzed for potential inclusion. Endometrial polyps were diagnosed with the use of criteria described by Pérez-Medina et al. (13). A polyp was usually suspected when a hyperechoic endometrial mass with regular contours occupied the uterine cavity either partially or fully (13, 15). Two-dimensional measurements of the polyp were performed, with the mean of these measurements recorded as the definitive measurement (16). Two-dimensional transvaginal ultrasonography, in experienced hands, can detect endometrial polyps accurately (17). All of the hysteroscopic polypectomies (1) were performed in the operating room in the follicular phase of the menstrual cycle. After cervical dilatation to 8 mm, a 22-F monopolar resectoscope with 1.5% glycine as the distention media was used. An automated Stryker fluid management system was also used. Patients did not receive intrauterine balloons or postoperative estrogens after the hysteroscopic polypectomies. All endometrial polyps were confirmed histologically. Exclusion criteria included IVF cycles cancelled before ET, frozen-thawed embryo cycles, donor oocyte cycles, and patients with recurrent IVF failure.

Clinical and Laboratory Protocols

Controlled ovarian stimulation (COS) was carried out to maximize follicular response while minimizing the risk of ovarian hyperstimulation syndrome. COS, hCG trigger, oocyte retrieval, embryo culture, and ET were performed per our standard protocols (18). Gonadotropin doses were based on patient age, weight, antral follicle count, and previous response to stimulation, if any. After initiating COS with the use of gonadotropins (Follistim, Merck; Gonal-F, EMD-Serono; and/or Menopur, Ferring Pharmaceuticals), ovulation was suppressed with the use of 0.25 mg ganirelix acetate (Merck) or cetrotide (EMD-Serono).

hCG was used as the ovulation trigger based on a previously described sliding-scale protocol (15, 18). In general, the hCG trigger was given when two lead follicles attained a mean diameter $\geq$17 mm. Oocyte retrieval was performed under conscious sedation with the use of transvaginal ultrasound guidance 35–37 hours after hCG administration. Intramuscular progesterone was started the day after oocyte retrieval. Choice of insemination or intracytoplasmic sperm injection was based on the male partner's semen analysis. Embryos were cultured with the use of in-house culture media, and embryo transfers were performed with the use of Wallace catheters (Smiths Medical) at $\sim$1 cm below the uterine depth identified at a prior trial transfer.

Outcome Variables

Demographic characteristics recorded included age, gravidity, parity, and body mass index (BMI; kg/m^2). Baseline IVF characteristics recorded were FSH (mIU/mL) and E_2 (pg/mL) level at cycle start. COS parameters recorded were as follows: protocol type (GnRH antagonist vs. GnRH agonist), total days of ovarian stimulation, total dosage of gonadotropins administered (IU), peak E_2 level (pg/mL), peak endometrial stripe (mm), total number of oocytes retrieved, total number of mature oocytes, and mean number of embryos transferred (19). Pregnancy outcomes after ET were also recorded. Implantation rate was defined as the mean number of gestational sacs seen with the use of transvaginal ultrasonography divided by the number of embryos transferred for each patient. Clinical pregnancy rate was defined as the number of intrauterine gestations with fetal cardiac activity per IVF-ET cycle. A biochemical pregnancy was defined as positive hCG level without a gestational sac. Any pregnancy loss after visualization of an intrauterine gestation was considered to be a spontaneous miscarriage, and any birth after 24 weeks of gestation was considered to be a live birth.

Statistical Analyses

All statistical analyses were performed with the use of Stata version 13 (Statacorp). Continuous variables were checked for normality and expressed as mean $\pm$ SD. Categoric variables were expressed as n (%). By study design, patients were assigned to three groups based on the time interval between hysteroscopic polypectomy and the start of a fresh IVF-ET cycle: Group 1 consisted of patients who underwent IVF-ET after their next menses, group 2 after two or three menstrual cycles, and group 3 after more than three menstrual cycles. A sample size of 73 patients was estimated assuming an α error of 5% and a power of 80% to detect a 15% difference in clinical pregnancy rate (14). Analysis of variance and chi-square tests were used to compare means and percentages of recorded parameters among the three groups. Statistical significance was set at $P<.05$.

RESULTS

A total of 741 patients underwent hysteroscopies during the study period. Of the 609 patients who underwent hysteroscopic polypectomy, 487 (80%) underwent IVF treatment and 122 (20%) did not. The 487 patients who met inclusion criteria were grouped as follows: 241 (49.5%) in group 1, 172 (35.3%) in group 2, and 74 (15.2%) in group 3. Supplemental Figure 1 (available online at www.fertstert.org) summarizes the selection of the study cohort.

Table 1 compares the demographic and baseline IVF characteristics of patients undergoing fresh IVF-ET cycles after hysteroscopic polypectomy, stratified by number of menstrual cycles. The mean ages of patients in groups 1, 2, and 3 were 34.7 $\pm$ 4.91 years, 34.3 $\pm$ 4.79 years, and 34.9 $\pm$ 3.91 years, respectively. Similarly to mean age, there was no statistical difference in mean gravidity, parity, or BMI of