

Body mass index is an independent risk factor for the development of endometrial polyps in patients undergoing in vitro fertilization

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Objective: To determine the subgroup of patients in whom office hysteroscopy should be routinely performed before an in vitro fertilization (IVF) program.

Design: Retrospective cohort analysis.

Setting: Tertiary education and research hospital.

Patient(s): Two hundred twenty-three patients who underwent a uterine evaluation by office hysteroscopy before the IVF and embryo transfer cycle.

Intervention(s): The office hysteroscopy was performed in the follicular phase of the menstrual cycle before the IVF cycle.

Main Outcome Measure(s): The office findings: number of polyps, number of multiple polyps, and polyp size.

Result(s): Patients with polycystic ovary syndrome (PCOS) had a higher number of endometrial polyps, but the difference was not statistically significant (28.9% vs. 18.3%). When comparing the patients according to BMI, patients with BMI ≥ 30 had a statistically significantly higher number of endometrial polyps versus BMI <30 (52% vs. 15%). On the other hand, obesity was positively correlated with the occurrence of polyps, size of the polyps, and occurrence of multiple number of polyps in the correlation analysis. In addition, logistic regression analysis using age, obesity, duration of infertility, and estradiol levels revealed that obesity was an independent prognostic factor for the development of endometrial polyps.

Conclusion(s): Office hysteroscopy should be performed in patients with BMI ≥ 30 because obesity may act as an initiator for the pathogenesis of endometrial polyps. (Fertil Steril® 2009;91:1056–60. ©2009 by American Society for Reproductive Medicine.)

Key Words: Hysteroscopy, polyp, obesity, PCOS, IVF, ICSI

Although a satisfactory improvement in the success rate of in vitro fertilization (IVF) is gained by tailored stimulation protocols, pure gonadotropins, standardized laboratory conditions, and culture mediums, uterine receptivity is still an enigma. In daily clinical practice, evaluation of the microenvironment of the endometrial cavity is impossible; however, a morphologic assessment of uterine receptiveness can be made confidently by hysteroscope (1). Using a hysteroscope, intra-uterine abnormalities such as endometrial polyps that might adversely affect endometrial receptivity and implantation in infertile patients can be inclusively, precisely identified and efficiently treated in the same setting, thus improving conception/fecundity rates over shorter intervals (2).

The lesion found mostly frequently with office hysteroscopy is endometrial polyp (2). Hormonal factors related to

estrogen excess have been implicated in the pathogenesis of endometrial polyps such as heavier weight, late menopause, and unopposed estrogen in either hormone replacement therapy or polycystic ovary syndrome (PCOS) (3). Nowadays, it is still a matter of debate whether hysteroscopy should be used as part of a routine diagnostic work-up for infertile women (1, 4–9), particularly before IVF with embryo transfer (IVF-ET) programs (2, 10–12). Although retrospective studies have found statistically significant merits, there are no guidelines on the use of office hysteroscopy for routine infertility assessment (13, 14). Thus, hysteroscopy has not been widely established as a routine diagnostic tool for assessment of infertility and preceding IVF despite its advantage of allowing cost-effective and more precise evaluation of the uterine cavity (5). Our study investigated whether hysteroscopy before an IVF program could be recommended as a routine procedure in a specially selected subgroup of patients.

MATERIAL AND METHODS

Patients who had undergone three cycles of intrauterine insemination after gonadotropin treatment with indications of

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unexplained infertility and PCOS were compared by hysteroscopy preceding IVF-ET for incidence of endometrial polyps. A total of 395 patients who were admitted to Zekai Tahir Burak Women's Education and Research Hospital IVF Clinic between January 2002 and May 2007 were examined, and 233 primary infertile were patients included and retrospectively evaluated in our current study. Institutional review board approval was obtained for the review of patient charts and clinical records, and informed consent in writing was obtained from each patient.

A total of 223 infertile patients were retrospectively evaluated. Their causes of infertility were as follows: unexplained ($n = 109$) and PCOS ($n = 114$). Unexplained infertility refers to the absence of a definable cause after thorough evaluation and standard tests for a couple's failure to achieve pregnancy after 12 months of attempting conception (15). The Rotterdam criteria were used to diagnose PCOS, in which a woman must have two of the following three manifestations: irregular or absent ovulation, elevated levels of androgenic hormones, and/or enlarged ovaries containing at least 12 follicles each (16). Demographic (age, duration of infertility) and laboratory (follicle-stimulating hormone [FSH], and estradiol [E_2]) findings were obtained from the patients' files. Body mass index (BMI) was calculated according to the generally accepted formula $\text{Weight}/\text{Height}^2$, where weight is in grams and height is in centimeters. The patients were divided into three classes: <25 normal body mass, 26 to 29.9 overweight, and ≥ 30 obese. Exclusion criteria were history of IVF/intracytoplasmic sperm injection (IVF-ICSI) treatment, patient age older than 40 years, secondary infertility, history of myomectomy involving hysterotomy, intrauterine adhesion, hysteroscopic adhesiolysis, and lack of histopathologic diagnose of polyp.

Before IVF cycles, all patients underwent office hysteroscopy for the complete evaluation of the uterine cavity, endometrium, and cervix. All procedures were performed in the early follicular phase of the menstrual cycle on an outpatient basis, without the use of a tenaculum or anesthesia, by three obstetrics/gynecology specialists with at least 10 years' experience in this field. Each patient was discharged within 60 minutes. A 5-mm continuous-flow mechanical office hysteroscope equipped with hysteroscopic scissors, grasping forceps, and a 30° rod lens (Karl Storz GmbH, Tuttlingen, Germany) was introduced blindly into the reduced uterine cavity. Intrauterine pressure was maintained at a constant 25 to 35 mmHg with saline distension medium using an electronic pump for irrigation and aspiration (Endomat; Karl Storz GmbH). All polyps and samples of endometrium were obtained for histologic examination by aspiration.

We were unable to calculate pretest power because to our knowledge there is no study in the literature on this subject. Hence, posttest power and actual power were calculated according to our results that for 99% power 61 patients were required. The differences between the mean of studied variables in two groups were analyzed by Student's *t*-test,

and the percentages of endometrial polyps in two groups were compared by using the chi-square tests; Pearson correlation analysis was used for univariate analysis. Logistic regression analysis was used for multivariate analysis. $P < .05$ was considered statistically significant.

RESULTS

When we compared the patients' ages (28.8 ± 4.1 vs. 28.5 ± 4.0 year), duration of infertility (4.9 ± 3.5 vs. 4.9 ± 3.0 year), FSH levels (5.5 ± 1.3 vs. 5.4 ± 1.2 IU/mL), and E_2 levels (51 ± 11.7 vs. 50.8 ± 13.1 pg/mL), there were no statistically significant differences between the PCOS and unexplained infertility groups, respectively. Although patients with PCOS had a higher number of endometrial polyps, the difference was not statistically significant (28.9% vs. 18.3%, $P = .08$). However, comparing the patients according to BMI found clinically significant relationships. Patients with $\text{BMI} \geq 30$ had a statistically significantly higher number of endometrial polyps compared with $\text{BMI} < 30$ (52% vs. 15%, $P < .001$). Obesity was positively correlated with the occurrence of polyps ($P = .001$, $r = 0.25$), size of the polyps ($P = .06$, $r = 0.27$), and occurrence of multiple number of polyps ($P = .006$, $r = 0.27$) in the correlation analysis. Furthermore, logistic regression analysis using age, obesity, duration of infertility, and E_2 levels revealed that obesity was an independent prognostic factor for the development of endometrial polyps ($P < .001$; $\text{RR} = 3.83$; CI , 1.68–5.77). Spotting was reported as the sole symptom by eight (24%) PCOS patients and four (20%) patients from the unexplained infertility group ($P > .05$). In addition, spotting was reported by six (23%) patients with $\text{BMI} > 30$ and six (23%) patients from the $\text{BMI} \leq 30$ group ($P > .05$) (Tables 1 and 2).

DISCUSSION

Despite the various advantages of office hysteroscopy—the convenience of the outpatient setting without any need for cervical dilatation or anesthesia in most cases, and the use of bipolar energy and normal saline rather than monopolar energy and nonionic distension media (17)—its use in the diagnostic work-up before expensive IVF-ET procedures is still controversial. Some investigators recommend routine hysteroscopy to evaluate the uterine cavity before IVF (2, 10–12), and others strongly recommend it as a part of the standard assessment of infertile women (1, 4–9). However, the ESHRE guidelines for infertility investigation (13) indicate that hysteroscopy is unnecessary unless for confirmation and treatment of suspicious endometrial pathology, and the Royal College of Obstetricians and Gynaecologists (14) states that hysteroscopy should not be performed as a routine test in infertility investigations because there is no evidence of fertility enhancement after treatment of uterine pathologies. Thus, no practice guidelines prescribe hysteroscopy as a mandatory diagnostic tool for infertility investigations.

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