



## Hysteroscopic polypectomy without cycle cancellation in IVF/ICSI cycles: a cross-sectional study



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### ABSTRACT

**Objective(s):** To evaluate the effect of hysteroscopic polypectomy during ovarian stimulation phase on in vitro fertilization and/or intracytoplasmic sperm injection (IVF/ICSI) cycles outcomes.

**Study design:** This cross sectional study was performed in female infertility department of Royan Institute from January 2011 to December 2013. In total, 160 patients who were diagnosed incidentally polyp/polyps less than 20 mm during the stimulation phase for oocyte recoveries were recruited; of these, fifty eight cases underwent hysteroscopic polypectomy without cycle cancellation non-randomly. Polyp resection was performed through hysteroscopic polypectomy during ovarian stimulation. The interval between polypectomy and embryo transfer (ET) was 3–17 days. The women who did not undergo hysteroscopic polypectomy and matched for polyp size were selected as control group. The outcomes of IVF/ICSI cycles were compared between groups.

**Results:** The data analysis showed the two groups were comparable in terms of patients' characteristics and stimulation outcomes. The implantation rate was not significantly different between groups ( $P=0.3$ ). The clinical pregnancy and live birth rates were similar between groups (%34.9 vs. %32.5 and %30.2 vs. %27.9,  $P=0.9$  and  $P=0.8$ ). No pregnancy was observed in patients who had the interval between hysteroscopic polypectomy until ET less than 5 days and the multivariable logistic regression analysis revealed that the interval between polyp resection and ET was significant predictor for live birth rate (odds ratio: 1.2, confidence interval: 1.01–1.5,  $P=0.04$ ).

**Discussion(s):** For the management of the polyps less than 20 mm which have been diagnosed during the stimulation phase, the performance of hysteroscopic polypectomy without cycle cancellation does not improve the pregnancy and live birth rates. Therefore, it seems that the continuation of the treatment cycle and ignorance of these polyps is the appropriate treatment choice and the performance of hysteroscopic polypectomy and frozen embryo transfer program could be the next treatment option.

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### Introduction

Despite recent progress in assisted reproduction technologies such as development of new protocols to improve the oocyte yield as well as advances in culture medium, in most infertility centers, the highest pregnancy rate does not usually exceed 30–50% per embryo transfer [1] and a relatively low percentage of the transferred embryos actually implant [2]. The impaired endometrial receptivity resulting from some structural pathology such as

fibroids, polyps and intrauterine adhesions has been evaluated in many studies [3].

One of the most common intrauterine pathologies is endometrial polyp [4]. Although endometrial polyps may be detected during evaluation of abnormal bleeding, most of polyps are asymptomatic and discovered only during the infertility workup [5]. Endometrial polyps have been detected in up to 25% of women with unexplained infertility on hysteroscopic evaluation [5]. The incidental appearance of a polyp during ovarian stimulation, in either IVF or intracytoplasmic sperm injection (ICSI) cycles is challenging. However, their effect on endometrial receptivity and fertility remains obscure. In some retrospective studies, polyps have been associated with recurrent abortion and infertility [6,7].

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Different strategies have been reported including: (1) giving up stimulation and hysteroscopic polypectomy, (2) continuing stimulation, all embryo freezing and then frozen embryo transfer after hysteroscopic polypectomy, (3) continuing stimulation and ignoring the polyp, (4) hysteroscopic polypectomy without cycle cancellation before oocyte retrieval [2,8]. In a recent study, Tiras et al. [3] suggested further studies be needed to identify the most appropriate management of endometrial polyps.

Some studies showed that discovered endometrial polyps smaller than 1.5 cm during IVF/ICSI cycles, did not have adverse effect on implantation and pregnancy rates [3,9], but a trend toward increased miscarriage has been demonstrated in some studies [1]. In two studies, hysteroscopic polypectomy was performed during stimulation before oocyte retrieval without cycle cancellation [2,8]. Adverse effects have not detected in neither of them; however, the sample sizes of these case-series studies were limited to draw a definite conclusion. The aim of this cross-sectional study is to assess the impact of hysteroscopic polypectomy during ICSI cycles on the pregnancy outcomes in women who are affected with polyps smaller than 2 cm.

## Materials and methods

### Subjects

This cross-sectional study was performed in the infertility department of the Royan Institute Research Center between January 2011 and December 2013. In the present study, all the women who had been diagnosed incidentally polyp/polyps during the stimulation phase for oocyte recoveries were recruited. Patients with co-existence of other uterine pathologies such as fibroids, intrauterine adhesions, endometriosis and severe male factor (azoospermia) were excluded. Prior to starting stimulation for evaluation of the uterine cavity, the basic work-up consists of two-dimensional transvaginal sonography (TVS) with or without the use of saline as contrast media. Diagnostic hysteroscopy was performed only for selected cases, such as those with repeated implantation failure. In the target population, the polyps were not detected before starting the stimulation. A polyp was diagnosed if an echogenic endometrial structure was detected by transvaginal sonography. Each polyp was measured in two longitudinal and transverse levels and the average diameter was calculated. The presence of polyps was always approved by Doppler sonography. Furthermore, our previous trial revealed that hysteroscopic polypectomy during ovarian stimulation is a harmless procedure [8]; therefore, the decision making about two treatment options including: (1) to proceed the cycle and ignore the polyp and (2) hysteroscopic polypectomy without cycle cancellation were performed on the basis of physician and patients' preference. The hysteroscopic polypectomy during stimulation was approved by the Institution Review Board and Ethics committee of the Royan Institute. The study was conducted according to the Helsinki Declaration and it was in compliance with the guidelines of the Committee of Publication Ethics. All participants were guaranteed of the confidentiality of the medical records and then written consents were obtained.

### Ovulation stimulation protocol

The patients received either the standard long protocol as described elsewhere [8] or antagonist protocol. Ovulation induction was performed by the application of Human Chorionic Gonadotropin (HCG) (Pregnyl<sup>®</sup>; Darou Pakhsh Pharmaceutical, Tehran, Iran) 10,000 IU, was injected intramuscularly, 34–36 h after hCG injection, oocyte retrieval was performed by trans-vaginal ultrasound guidance. Intracytoplasmic sperm injections for retrieved MII oocytes with or without insemination were

performed in accordance with standard general guidelines. The appearance of two pronuclei and of the second polar body 16–19 h after insemination or microinjection revealed normal fertilization. A maximum of three embryos were transferred 2–3 days after oocyte retrieval. After embryo replacement, hormonal supplementation was provided with vaginal progesterone (Aburaihan Co., Iran), 400 mg twice a day until the day of the  $\beta$ -HCG assay. Patients with a positive test continued with vaginal progesterone supplementation until 12 weeks pregnancy. The monitoring was performed by using transvaginal ultrasonography (Aloka-Alpha 10, Japan) during ovarian stimulation.

### Hysteroscopic polypectomy

Hysteroscopies to resect a polyp were performed under general anesthesia and direct visualization by using a hysteroscope (Karl Storz, Germany), with a 30° view with 2.9 mm BETTOCCHI<sup>®</sup> continuous flow sheath. None of the women needed cervical dilatation. Normal saline solution was used as the distension medium. Polypectomy was successfully performed in all of the patients by using a grasping forceps. The “grasping forceps” were guided under direct visualization by using an operating channel. After removing the polyp/polyps, the hysteroscope was inserted again to ensure complete removal of all polyps. The endometrial cavity was divided into the following locations: uterotubal junction (right and left), anterior uterine wall, posterior uterine wall, lateral uterine wall (right and left), and multiple. Multiple polyps were defined as the presence of two or more polyps. All the samples were fixed in formaldehyde and sent for pathology examination. The interval between polypectomy and embryo transfer was 3–17 days. All polypectomies were performed by a gynaecological surgeon.

### Pregnancy monitoring

The serum hCG level was measured 14 days after the embryo transfer. Clinical pregnancy was defined as a positive pregnancy test followed by the presence of gestational sac on transvaginal ultrasound 4 weeks after the embryo transfer. Biochemical pregnancy refers to transient rises in hCG without evidence of a gestation sac. Ongoing pregnancy was defined as the presence of gestational sac with fetal heartbeat detection at 12 weeks of gestation.

### Statistical analysis

Data are presented as mean  $\pm$  standard deviation (SD), proportion and odds ratio (OR). Statistical analysis was made by using SPSS 20 (SPSS Inc., Chicago, IL). The obtained data were analyzed by using the Student's *t*-test for continuous variables and Chi-square test for categorical variables. Multivariable logistic regression was used to assess the predictive variables for clinical pregnancy and live birth rates. Two-tailed *P*-value  $<0.05$  determined the statistical significance.

## Results

In total, 160 patients affected with polyps were detected during ovarian stimulation in ICSI cycle. Of these, fifty eight patients have undergone hysteroscopic polypectomy without cycle cancellation (Fig. 1). All the patients were found to have endometrial polyp/polyps in diagnostic hysteroscopy. A pathology examination revealed that all of the pathology samples were polyps. The mean average diameter of the polyps in the polypectomy group was higher than that of in the control group ( $10.0 \pm 4.0$  vs.  $13.3 \pm 5.7$  mm;  $P=0.001$ ), although none of the polyps were larger than 20 mm (size range 5–20 mm). This

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