

Management of endometrial polyps diagnosed

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12/11/22

Introduction

- Successful pregnancy requires
 - good-quality embryos
 - appropriate uterine receptivity
- Pregnancy rates of
 - Selective single embryo transfer cycle : <30%
- Implantation - most important step
 - requiring maternal-embryonic talk, complex endometrial protein synthesis and

Introduction

- Endometrial thickness, structure and texture are crucial for uterine receptivity.
- Any structural pathology in the uterine cavity -> subfertility or implantation failure
 - Ex: fibroids, polyps, intrauterine adhesions, endometritis or decreased endometrial thickness
 - Most common intrauterine -> endometrial polyps
 - proven to interfere with fertility

Introduction

- Management of endometrial polyps
 - cycle cancellation and polypectomy
 - removal of the endometrial polyp and embryo freezing with embryo transfer after a few months
 - ignoring the polyp and continuing treatment; and lastly
 - Hysteroscopic polypectomy during the ICSI cycle before oocyte retrieval without cycle cancellation

Introduction

- There are only a few reports assessing the effect of endometrial polyps on IVF/ICSI cycles
 - Isikoglu et al.(2006)
 - endometrial polyps <1.5 cm discovered both before or during IVF/ICSI cycles did not seem to affect implantation and pregnancy rates
 - Lass et al. (1999)
 - polyps <2 cm did not decrease pregnancy rates but increased miscarriage rates
 - There are possible beneficial approach of performing

Introduction

- About this study
 - retrospective analysis of 8359 cases.
 - analysis of all fresh ICSI cycles performed at the Anatolia IVF Center between July 2005 and January 2009.
- Frozen cycles were not included in this study.
- Institutional Review Board approval was not obtained in this study, because it is a retrospective analysis of standard

Materials and methods

- Group 1

- 47 patients with an endometrial polyp before their ICSI cycle and underwent hysteroscopic polyp resection, subsequently followed by ICSI treatment.

- Group 2 (n = 47)

- without endometrial polyps as a control group for group 1 matched for demographic characteristics
- selected from 8359 patients in a way they would be matched with patients of group 1

M a t e r i a l s a n d m e t h o d s

- Group 3
 - 128 patients with an endometrial polyp during stimulation in their ICSI cycles
- Group 4 (n = 128)
 - without endometrial polyps as a control group for group 3 matched for demographic characteristics
 - selected from 8359 patients in a way they would be matched with patients of group 3 with regard to age, BMI, cause and duration of infertility, control follicle count, number of

Materials and methods

- All patients diagnosed with an endometrial polyp by transvaginal ultrasonography before the ICSI cycle underwent hysteroscopic polyp resection.
- All hysteroscopic polyp resections were performed under general anesthesia using a 2.9-mm 30 degree hysteroscope (Storz, Germany). Polyps were removed by scissors and sent for pathological examination.
- All pathology examinations verified the diagnosis of the endometrial polyp.

M a t e r i a l s a n d m e t h o d s

- Major trauma to the endometrium was avoided.
- D&C were not performed for any of these patients.
 - Obtain no pathological results, such as endometritis or hyperplasia, transvaginal ultrasonographic examinations of patients did not raise suspicion of any other uterine pathologies.
- These patients underwent ICSI treatment in the next cycle

Materials and methods

- Gonadotrophin dose was individualized and monitored according to **follicular growth and serial plasma oestradiol** determinations.
- HCG to achieve final follicular maturation and to trigger ovulation
 - When >3 follicles reached a diameter of 17 mm
 - human chorionic gonadotrophin (HCG) was administered

Materials and methods

- Oocytes were inseminated 4–6 h after retrieval by ICSI using fresh ejaculates and cultured for 3 days.
- Embryo transfer on day 3.
- Usually two or three embryos were replaced according to patient age, indication of IVF, number of previous attempts and number and quality of embryos available.
- The embryos were all loaded into Wallace

Materials and methods

- One day after oocyte retrieval, all patients began to receive luteal-phase support by vaginal progesterone (Crinone gel 8%; Serono).
- Pregnancy was diagnosed by increasing serum concentrations of b-HCG 14 days after oocyte retrieval and a serum b-HCG concentration 45 mIU/ml was considered as positive.
- Cases with b-HCG concentrations <45 mIU/ml were considered negative for pregnancy.

Materials and methods



Figure 1 Transvaginal ultrasonographic view of an endometrial polyp.

Materials and methods

- During ovarian stimulation, serial transvaginal ultrasound examinations were performed (Toshiba Medical System Corporation 1385; Shimoishigami, Japan).
- An endometrial polyp was diagnosed by the presence of a hyperechogenic endometrial mass confirmed by two expert ultrasonographers (Figure 1).
- Measurements of the endometrial polyp was always performed on two dimensions and the average was recorded as the

Materials and methods

- It is a well-known fact that two-dimensional ultrasonographic diagnosis of endometrial polyps may be problematic.
- However, in this study, the diagnosis was made by the common opinion of two expert ultrasonographers. The diagnosis of endometrial polyps in group 3 was not verified by sonohysterogram or hysteroscopy as these patients continued treatment and the embryo transfer was performed at the same cycle. Such invasive

Materials and methods

- Female and male ages, BMI, length of ovulation induction, total dose of gonadotrophin used, endometrium thickness on the day of transfer, number of retrieved oocytes and number of embryos transferred were recorded for all patients in each group. The main outcome measure was clinical pregnancy rate based on ultrasound visualization of fetal heartbeat and biochemical pregnancy rate was also calculated.

Statistical analysis

- Statistical analysis was performed using Statistical Package for Social Sciences (SPSS, Chicago, IL, USA) version 12.0.
- The chi-squared test and Fisher's exact test were used to analyze nominal variables in the form of frequency tables.
- Normally distributed (Kolmogorov-Smirnov test) parametric variables were tested by independent Student's t-test.
- Non-normally distributed metric variables

Results - Demographic characteristics

- Patients diagnosed with an endometrial polyp before ICSI cycles (group 1) were similar to their controls (group 2) with regard to demographic, stimulation and transfer characteristics (Table 1).
- Patients diagnosed with an endometrial polyp during ovarian stimulation (group 3) were similar to their controls (group 4) with regard to demographic, stimulation and transfer characteristics (Table 2).
- The impact of BMI on prevalence of

Results - Demographic characteristics

- BMI of patients diagnosed with an endometrial polyp before ICSI treatment was 26.65 ± 5.65 kg/m² and BMI of patients diagnosed with an endometrial polyp during treatment was 26.09 ± 4.68 kg/m². BMI of patients who did not have endometrial polyps was 26.20 ± 5.48 kg/m². These three groups were similar to each other.
- BMI did not seem to have an effect on prevalence of endometrial polyps in this

Impact of polyp presence

- Patients diagnosed with an endometrial polyp before ICSI cycles (group 1) were similar to their controls (group 2, both n = 47) with regard to pregnancy rates and pregnancy outcomes (Table 3).
- In groups 1 and 2, respectively, the implantation rates were 31.9% versus 46.8% and the clinical pregnancy rates were 29.8% versus 38.3%.
- Patients diagnosed with an endometrial polyp during ovarian stimulation (group 3)

Impact of polyp presence

Table 1 Demographic and cycle characteristics of patients who underwent polyp resection prior to ICSI (group 1) and matched controls with no polyps (group 2).

Characteristic	Group 1 (n = 47)	Group 2 (n = 47)
Female age (years)	32.9 ± 5.0	33.8 ± 5.8
Male age (years)	36.4 ± 5.5	37.9 ± 6.9
BMI (kg/m ²)	27.6 ± 6.5	26.9 ± 5.3
Length of ovulation induction (days)	9.9 ± 1.8	9.9 ± 1.5
Total dose of gonadotrophins (ampoules)	37.3 ± 18.3	33.8 ± 16.9
Endometrial thickness on transfer day (mm)	11.5 ± 2.8	11.2 ± 2.3
Oocytes retrieved	11.9 ± 7.4	12.0 ± 7.0
2 PN oocytes	6.9 ± 5.1	7.0 ± 4.6
Embryos transferred	2.8 ± 1.0	2.8 ± 1.0

Values are mean ± SD. There were no statistically significant differences between the two groups. BMI = body mass index; ICSI = intracytoplasmic sperm injection; PN = pronuclei.

Impact of polyp presence

Table 2 Demographic and cycle characteristics of patients diagnosed with an endometrial polyp during ovarian stimulation (group 3) and their matched controls with no polyps (group 4).

Characteristic	Group 3 (n = 128)	Group 4 (n = 128)
Female age (years)	33.4 ± 5.0	33.2 ± 5.0
Male age (years)	36.7 ± 6.1	37.2 ± 6.0
BMI (kg/m ²)	26.1 ± 4.6	26.3 ± 4.9
Length of ovulation induction (days)	10.0 ± 1.9	9.9 ± 1.8
Total dose of gonadotrophins (ampoules)	38.8 ± 19.7	40.0 ± 20.0
Endometrial thickness on day of transfer (mm)	12.7 ± 2.7	11.0 ± 2.3
Oocytes retrieved	11.4 ± 6.1	11.1 ± 5.5
2PN oocytes	6.6 ± 4.5	6.7 ± 4.2
Embryos transferred	3.0 ± 1.2	2.9 ± 1.1

Values are mean ± SD. There were no statistically significant differences between the two groups. BMI = body mass index; PN = pronuclei.

Impact of polyp presence

Table 3 Comparison of pregnancy rates and outcomes in patients who underwent polyp resection prior to ICSI (group 1) and matched controls with no polyps (group 2).

Pregnancy outcome	Group 1 (n = 47)	Group 2 (n = 47)
HCG \geq 45 mIU/ml	15 (31.9)	22 (46.8)
Clinical pregnancies	14 (29.8)	18 (38.3)
Biochemical pregnancies	1 (2.1)	4 (8.5)
Miscarriages	2 (4.3)	3 (6.4)
Live births	12 (25.5)	15 (31.9)

Values are n (% per embryo transfer). There were no statistically significant differences between the two groups. HCG = human chorionic gonadotrophin; ICSI = intracytoplasmic sperm injection.

Impact of polyp presence

Table 4 Comparison of pregnancy rates and outcomes in patients diagnosed with an endometrial polyp during ovarian stimulation (group 3) and their matched controls with no polyps (group 4).

Pregnancy outcome	Group 3 (n = 128)	Group 4 (n = 128)
HCG \geq 45 mIU/ml	62 (48.4)	62 (48.4)
Clinical pregnancies	58 (45.3)	60 (46.9)
Biochemical pregnancies	4 (3.1)	2 (1.6)
Miscarriages	5 (3.9)	8 (6.3)
Live birth rate	1 (0.8)	1 (0.8)
Live birth %	52 (40.6)	51 (39.8)

Values are n (% per embryo transfer). There were no statistically significant differences between the two groups. HCG = human chorionic gonadotrophin.

Polyp localization

- Among all patients diagnosed with an endometrial polyp
- during ovarian stimulation (group 3, n = 128), localization of the endometrial polyp was recorded in 78 cases (60.9%).
- The polyp was located in the upper third of the uterine cavity in 36 cases (46.2%).
- Of these 36 patients, 16 patients (44.4%) achieved a serum b-HCG concentration 45 IU/ml after treatment.

Polyp localization

- The polyp was located in the middle third in 26 cases (33.3%) and 13 (50.0%) of these achieved a serum b-HCG concentration 45 IU/ml after ICSI.
- The endometrial polyp was located at the lower third in 16 cases (20.5%) and eight of these achieved a serum b-HCG concentration 45 IU/ml after treatment (50.0%).
- Thus, **localization of the endometrial polyp did not seem to affect pregnancy rates.**

Polyp size

- Polyp size was available in 98 cases of group 3 (76.6%).
- The smallest polyp was 4 mm in dimension and the biggest polyp was 14 mm in dimension. Most commonly, polyps were between 6 and 10 mm (n = 77; 78.6%).
- Polyps <6 mm and bigger than 10 mm were rare.
- Among these 98 patients of group 3 with a known polyp size, mean polyp dimension

Discussion

- A successful pregnancy is strongly dependent on an appropriate uterine receptivity.
- Any lesion leading to the distortion of the endometrial cavity, such as fibroids, synechia or polyps, may have a negative impact on uterine receptivity.
- The most common lesion of the endometrial cavity is an **endometrial polyp** (Doldi et al., 2005) defined as the overgrowth of endometrial glands and stroma covered by endometrial epithelium.

Discussion

- The exact mechanism by which endometrial polyps cause decreased uterine receptivity and subsequent infertility is not known.
- Possible inflammatory process caused by the polyp acting in a similar way as an intrauterine device (Ben-Nagi et al., 2009).
- Anatomical distortion of the endometrial cavity is another postulation and focuses mainly on the diminished volume of the endometrial cavity.

Discussion

- In their study, Spiewankiewicz et al. (2003)
 - 76% pregnancy rate in one year, after hysteroscopic removal of the endometrial polyp among 25 infertile patients.
- Varasteh et al. (1999)
 - 78% cumulative pregnancy rate after hysteroscopic polypectomy in cases of female infertility.
- Perez-Medina et al. (2005)
 - Studied subfertile women with sonographic

Discussion

- The polyps were detected in 452 of 2800 (16.1%) consecutive patients scheduled for IUI
- After hysteroscopic removal of endometrial polyps there was a 63% cumulative pregnancy rate compared with 28% in the control group (relative risk (RR) 2.3, 95% confidence interval (CI) 1.6–3.2) (Perez-Medina et al., 2005).
- Interestingly, 65% of all pregnancies in the polypectomy resulting in a **spontaneous pregnancy rate of 79% in the polypectomy**

Discussion

- Although studies in the literature point to a negative impact of endometrial polyps in natural conceptions and IUI cycles, the impact of endometrial polyps on pregnancy rates and pregnancy outcomes in IVF/ICSI cycles is rather obscure and there are few studies on the subject.
- Isikoglu et al. (2006)
 - implantation and pregnancy rates were similar for patients with endometrial polyps who proceeded with subsequent ICSI

Discussion

- Lass et al., 1999
 - 83 patients with endometrial polyps were divided into two groups.
 - The first group did not undergo hysteroscopic polyp removal and continued the standard IVF treatment.
 - The second group underwent hysteroscopic polypectomy just after oocyte retrieval and the embryos were frozen and transferred in a subsequent cycle.
 - The pregnancy rate of the first group was

Discussion

- They concluded that the presence of a small endometrial polyp before or through the stimulation for IVF should not alter the planned oocyte recovery and embryo transfer.
- Hereter et al., 1998
 - pregnancy rates and outcomes of 33 patients with endometrial polyps were compared with 280 controls and no difference was observed between the two groups with respect to implantation and miscarriage rates.

Discussion

- Recently, two studies have been published suggesting that hysteroscopic polypectomy before oocyte retrieval without cycle cancellation in IVF cycles might be possible (Batioglu and Kaymak, 2005; Madani et al., 2009).
- Their trial proposes that hysteroscopic polypectomy during ovarian stimulation may be a harmless procedure.
- However, their series is too small to be conclusive. with nine patients in one study

Discussion

- In most cases, the endometrial polyp presents itself as a single lesion and it is mostly located close to the uterine fundus.
- The question whether the localization of the endometrial polyp has an effect on pregnancy rates is also challenging.
- The current study failed to show any effect of the endometrial polyp localization on pregnancy rates.
- However, the observation from non-

Discussion

- Besides, polyps in the isthmocervical part of the uterus may preferentially interfere with sperm transport.
- These two different mechanisms could explain the differences in conception rates after hysteroscopic removal of polyps in different locations observed in non-controlled studies.
- However, this finding has not been verified in the current study, which had similar pregnancy rates for endometrial polyps

Discussion

- The size of the endometrial polyp is also an important factor affecting pregnancy rates.
- Most studies investigating the effect of endometrial polyps on pregnancy rates, both in natural conceptions and in cycles using assisted reproductive technologies, deal with small endometrial polyps, usually <2 cm in diameter. Similarly, the biggest endometrial polyp was 14 mm in this study.

Discussion

- The common endpoint of these studies (Isikoglu et al., 2006; Lass et al., 1999) and also the current study is that it is likely that **polyps <2 cm will not require treatment prior to assisted reproduction treatment.**
- However, the impact of polyps >1.5 cm on assisted reproduction outcomes does warrant further investigation.
- Polyp sizes in this study were <1.4 cm, probably because the study center mostly receives referred cases and patients with

Discussion

- This study presents data on the impact of endometrial polyps on pregnancy rates and outcomes in ICSI cycles and is unique, as far as it is known, as it involves the highest number of patients among all studies about the subject in the literature.
- The first finding is that endometrial polyps < 1.4 cm that occurred during ovarian stimulation did not affect pregnancy rates, miscarriage rates and live-birth rates in ICSI cycles.

Discussion

- Also, resection of an endometrial polyp <1.5 cm before oocyte retrieval without cycle cancellation or hysteroscopic polypectomy after oocyte retrieval with embryo freezing and transfer in a subsequent cycle does not seem appropriate with the available data, taking into consideration the possible harmful effect of the hysteroscopic resection on the endometrium just before embryo transfer and the relatively low pregnancy rates with frozen embryos as compared with fresh

Discussion

- As a result, the impact of endometrial polyps on pregnancy rates and outcomes in ICSI cycles is challenging to the assisted reproduction clinician.
- Although several management options exist, the most appropriate method is still a subject of debate and further studies are required.
- As far as is known, this study involves the highest number of patients in the literature in this field and it hopes it will help all