

Matched controlled study to evaluate the effect of endometrial polyps on pregnancy and implantation rates following in vitro fertilization-embryo transfer (IVF-ET)

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Summary

Purpose: To determine if endometrial polyps negatively effect outcome following in vitro fertilization-embryo transfer (IVF-ET) and whether hysteroscopic resection improves pregnancy and implantation rates and/or decreases miscarriage rates. **Methods:** Retrospective study with two matched controlled groups (polyps vs no polyps) based on age and previous number of IVF failures. The polyp group was further stratified by whether polypectomy was performed or not. **Results:** There was no difference or even trend for lower pregnancy rates or higher miscarriage rates with the presence of endometrial polyps. **Conclusions:** These data do not support the recommendation for hysteroscopic resection of endometrial polyps to aid conception rates.

Key words: Endometrial polyp; Hysteroscopic polypectomy; In vitro fertilization-embryo transfer; Endometrial irritation.

Introduction

A previous study found no difference in implantation rates or miscarriage rates following in vitro fertilization-embryo transfer (IVF-ET) in women with endometrial polyps ($n = 33$) vs those without ($n = 280$) [1]. This study was a retrospective observational study [1].

Generally speaking, there is more credence given to a prospective rather than a retrospective study. Indeed a prospective randomized study was performed to determine if hysteroscopic polypectomy before intrauterine insemination (IUI) achieved better pregnancy outcomes than no intervention [2]. These data did demonstrate that hysteroscopic polypectomy prior to performing several cycles of IUI did improve the pregnancy rate for that group [2].

The data strongly suggesting that hysteroscopic polypectomy improves pregnancy rates does not necessarily indicate that endometrial polyps are associated with infertility. There are data suggesting that any irritation of the endometrium, such as an endometrial biopsy can cause an increase in adhesion proteins, e.g., connexin protein 43 [3]. The objective of the study by Perez-Medena *et al.* was to see if polypectomy could improve pregnancy rates following IUI. In fact 42 of the 64 (65%) pregnancies in the hysteroscopic resection of the polyp group conceived prior to the IUI cycle (there was a 3 month delay). Thus if the 42 pregnancies were eliminated prior to the IUI cycles, the pregnancy rate in the group with polyps removed would be 22 of 59 (37.2%) vs 29 of

103 (28.2%) for controls ($p = \text{NS}$). None of the controls became pregnant during the 3-month study delay.

Thus the study of Perez-Medena [2] is important because it suggests that either the presence of any size polyp can negatively affect pregnancy rates, or irritating the endometrium by polypectomy can improve subsequent pregnancy rates. This is an important distinction because the possibility exists that a simple endometrial biopsy could suffice to irritate the endometrium in lieu of the more invasive, more risky, and more expensive hysteroscopy.

Before submitting a proposal to the Institutional Review Board of Cooper Hospital University Medical Center the proposed study of repeating the study by Perez-Medena *et al.* [2] with the variation of performing an endometrial biopsy rather than polypectomy on the controls, we first presented the study to the ethics committee for the Cooper Institute for Reproductive Hormonal Disorders. The panel suggested that a retrospective study of the patients at Cooper Institute for Reproductive Hormonal Disorders first be performed to determine – based on our own data – if the presence of endometrial polyps impacts either conception rates or miscarriage rates. If a relationship was found, the committee suggested that the aforementioned prospective study with the control without polyps having an endometrial biopsy performed prior to IVF-ET would be appropriate. If no retrospective data supported hysteroscopic polypectomy the committee would not support this surgically invasive procedure.

Thus the present study retrospectively evaluated the reproductive impact of endometrial polyps on pregnancy and miscarriage rates following IVF-ET using matched controls.

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Materials and Methods

Infertile women at the Cooper Institute for Reproductive Hormonal Disorders having either a hysterosalpingogram or sonohysterogram prior to undergoing IVF-ET were evaluated. Those demonstrating endometrial polyps were advised that there is a conflict in the literature as to the benefit of performing hysteroscopic resection of the polyp. Thus the option of having a polypectomy performed or not was left up to the patient. All polypectomies were performed at Cooper Hospital University Medical Center and not in the office. It was recommended to the couple to delay IVF-ET two months following a polypectomy.

All women with primary infertility during a 1-year time period who were found to have endometrial polyps and who had an IVF-ET cycle in that year were the subjects. They were matched to a control group not found to have endometrial polyps who had also had an IVF-ET cycle. The women were matched as to age group (\leq age 39 and 40-43) and number of previous failed IVF-ET cycles. Clinical and live delivered pregnancy rates and implantation rates were then compared between the two groups with or without endometrial polyps. The data were further stratified according to whether the woman elected to have a polypectomy performed or not.

Since the Perez-Medina study found all sized polyps had the same negative impact there was no exclusion for polyp size and matching was not based on polyp size [2].

Results

Clinical and live delivered pregnancy rates per embryo transfer and implantation rates are shown in Table 1. The presence of endometrial polyps did not seem to adversely affect pregnancy and implantation rates. The oldest group (average age 38.5) included the 12 women with endometrial polyps that were not removed and yet there was a trend for higher clinical and live delivery rates in this older group than the group with endometrial polyps removed (average age 34.7) or the group without any polyps detected (average age 36.0). Interestingly the oldest group with the presence of endometrial polyps not undergoing hysteroscopy also had the least number of embryos transferred compared to those with hysteroscopic resection of endometrial polyps and those without polyps.

Table 1. — Retrospective matched control study to evaluate effect of endometrial polyps on pregnancy outcome following IVF-ET.

	Total polyps (present or removed)	Polyps removed	Polyps unremoved	Normal uterine cavity
No. retrievals	34	22	12	34
No. transfers	34	22	12	34
Average age	36.0	34.7	38.5	36.0
No. clinical pregnancies	14	9	5	11
% clinical preg./transferred	41.2	40.9	41.7	32.4
No. live/delivered	13	8	5	10
% live/delivered	38.2	36.4	41.7	29.4
Average # embryos transferred	3.1	3.3	2.7	3.3
Implantation rate (%)	22.1	23.6	18.8	15.3

Discussion

The present pilot retrospective matched-controlled study failed to corroborate previous findings of a prospective study indicating a link between polyp formation and lower pregnancy and implantation rates following IVF-ET, and more importantly pregnancy rates were improved following hysteroscopic resection [2].

The conclusions reached in the present study were similar to past retrospective studies, e.g., the one by Mastrominas *et al.* in 1996 concluding that polyps < 2 cm diameter do not require removal before IVF and do not affect the outcome of subsequent pregnancy [4] and the study by Lass *et al.* which concluded no effect of polyps < 2 cm on pregnancy rate but they could possibly increase miscarriage rate [5]. Subsequent to the article by Perez-Medina *et al.* [2] a retrospective study by Isikoglu *et al.* concluded that endometrial polyps < 1.5 cm do not affect pregnancy and implantation rates following IVF and intracytoplasmic sperm injection [6].

One hypothesized theory of the mechanism by which endometrial polyps could negatively affect pregnancy outcome was by their presence being associated with an increase in glycodeilin levels in the peri-ovulatory period in women [7]. Normally glycodeilin decreases during the peri-ovulatory period because it can inhibit sperm-oocyte binding. Thus the possibility exists that because fertilization occurs outside the body possibly studies with IVF-ET fail to show an association of endometrial polyps and pregnancy outcome, but possibly high levels of intratubal glycodeilin may inhibit fertilization following IUI. This could explain the conflicting conclusions from the study of Perez-Medina *et al.* [2] and the other retrospective studies including the present one that mostly involved IVF-ET [1, 5, 6].

However it should be recalled that 65% of the pregnancies recorded by Perez-Medina *et al.* occurred in the three months after the polypectomy but before the IUI study officially began. In fact no difference was found in the IUI cycles [2].

For these reasons the ethics committee decided against submitting the aforementioned proposal to re-evaluate prospectively the effect of hysteroscopic resection of endometrial polyps on IVF outcome with an endometrial biopsy control group. Instead, they recommended a study of endometrial biopsy for a study group and not for controls on IVF-ET outcome irrespective of the presence or absence of endometrial polyps with a possible evaluation of the subset of the population with endometrial polyps. The committee recommended that the decision to remove polyps or not be left up to the opinion of the consulting physician, and that the patients should be properly informed of the controversy, but they could not justify the random assignment to having hysteroscopic polypectomy or not.

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