# Endometrial polyps and their relationship in the pregnancy rates of patients undergoing intrauterine insemination

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**Summary**

*Purpose:* To evaluate the effect of the presence of endometrial polyps (EP) on pregnancy rates and how polypectomy could affect pregnancy rates in women scheduled for intrauterine insemination (IUI). *Methods:* The study included patients who had attended the Second Department of Obstetrics and Gynecology of the University of Athens from April 2003 to October 2008 for infertility treatment and were candidates for IUI. In these women the presence of an endometrial polyp had been already diagnosed during the infertility evaluation. The study group consisted of 86 women who, following the diagnosis of endometrial polyp, had agreed to have the polyps removed hysteroscopically prior to the IUI. The control group consisted of 85 women, who despite the fact that the presence of an endometrial polyp had been previously diagnosed and its removal suggested, elected not to have the polyp removed. We used statistical analysis to check what effect the removal of the polyp had on the total number of pregnancies. *Results:* There was a statistically significant difference in cumulative pregnancy rates between the two groups. The group that underwent polyp removal had higher pregnancy rates as compared to the one that the polyps were left intact. *Conclusions:* We propose that hysteroscopic polypectomy of any size appears to improve fertility in women with otherwise unexplained infertility.

*Key words:* Endometrial polyps; Intrauterine insemination; IVF.

## Introduction

Endometrial polyps are common findings during the reproductive years, occurring in up to 24% of women [1-3]. Those structures are benign tumors of the endometrium consisting of glands and endometrial stromal tissue whose blood supply is provided by branches of the endometrial spiral arteries [2]. The etiology for the development of endometrial polyps is not clear, but it seems that they are created by a localized anomaly of hormonal receptivity in certain areas of the endometrium with persistence of estrogen receptors and decrease of progesterone receptors leading to focal proliferation, and growth of the endometrium and the underlying stroma [4]. Disorders associated with prolonged unopposed exposure to estrogen such as oligo-anovulation, luteal phase insufficiency etc. are associated with the development of endometrial polyps [2].

The main presenting symptom related to an endometrial polyp (EP) is abnormal uterine bleeding [4, 5], but the majority are asymptomatic and often discovered during a routine sonographic evaluation or during the process of infertility investigation [6, 7].

The "gold standard" examination for diagnosing EPs is hysteroscopic evaluation of the endometrial cavity [4, 8-12].

The precise relationship of EPs and infertility or recurrent pregnancy loss remains obscure. It seems that the presence of endometrial polyps could cause an adverse effect in embryo implantation [4] although the exact mechanism that regulates implantation and/or other fertility problems is mostly unknown [13-15]. There are several reports indicating that the presence of EPs may adversely affect pregnancy rates in women undergoing IVF-ET [15-17]; thus, when an EP is discovered in the process of infertility evaluation and treatment, the therapeutic suggestion is removal and that rule is almost universally applied in women undergoing IVF [1-6]. To our knowledge, there is no established proof on how EPs affect implantation and furthermore the current litterature does not provide a clear answer to the question if a polypectomy could improve pregnancy rates in women undergoing COH and IUI.

The purpose of this study was to evaluate the effect of presence of EPs on pregnancy rates and how a polypectomy could affect pregnancy rates in women scheduled for IUI.

## Material and Methods

The study included patients who had attended the Second Department of Obstetrics and Gynecology of the University of Athens from April 2003 to October 2008 for infertility treatment and were candidates for ITI. In these women the presence of an EP had been already diagnosed during the infertility evaluation either by sonographic evaluation (including hysterosonogram) or by hysterosalpingogram (HSG). The study group consisted of 86 women who following the diagnosis of an endometrial polyp had agreed to have the polyp removed hysteroscopically prior to the IUI. The control group consisted of 85 women, who despite the fact that the presence of an EP had been previously diagnosed and its removal suggested, elected not to have the polyp removed. Those patients underwent a complete infertility inves-

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tigation that included a baseline transvaginal ultrasound (TVS), HSG, a midluteal phase serum progesterone concentration and basic hormonal profile which included a day 2 FSH. Patients with irregular cycles or any suggestion of PCOS had an additional hormonal evaluation which included in addition to FSH, LH estradiol, TSH, prolactin, 17 OH progesterone, Δ4 androstenedione and testosterone (free and total).

Couples were eligible for IUI if the female partner was younger than 38 years of age, day serum FSH was less than 10 mIU/ml and had at least the following: documented tubal patency by HSG or laparoscopy and a semen analysis indicating the absence of severe male factor (sperm count of at least 5 million/ml).

In order to fulfill the criteria of idiopathic infertility, female partners had to have regular menstrual periods, proven spontaneous ovulation either by biphasic basal body temperature charts or by a midluteal serum progesterone concetration of at least 10 ng/ml.

Male partners had to have sperm count of more than 20 x $10^6$/ml, more than 50% motile spermatozoa, and more than 14% morphologically normal spermatozoa by Kruger criteria [18].

In couples with male infertility male partners had to have at least two semen evaluations obtained at least three months apart which should have been abnormal, according to WHO criteria [18].

Women in the study group were scheduled to have three cycles of COH combined with IUI three months after the removal of the polyps.

*Preparation of sperm and IUI*

Semen specimens were produced at the laboratory after 48-72 hours of sexual abstinence. After liquification in a 37°C incubator, semen was examined for sperm concentration and motility with the use of a Makler device (Sefi Medical Instruments Ltd., Haifa, Israel). Sperm preparation was carried out as previously described [18] and a final volume of 0.3-0.5 ml after processing was used for the IUI. A small aliquot was retained for a post-wash control and motility analysis .

Intrauterine insemination was performed with a use of Makler device (Sefi Medical Inc. ,Haifa, Israel). Women were requested to remain in bed for aproximately 10 minutes after the procedure.

*Ovarian stimulation*

Superovulation or ovulation induction, where needed, was initiated on the third day of a spontaneous menstrual cycle or the third day after progesterone-induced bleeding in women with ovulatory dysfunction with a fixed dose of recombinant FSH (Gonal F, Serono UK) dose of 50 IU daily. Ovarian response and follicular development were monitored by serial ultrasound and serum estradiol measurments.

When the leading follicle reached a diameter of at least 17 mm, ovulation was triggered by an intramuscular injection of 10000 IU HCG (Pregnyl, Organon). A single IUI was performed 34-36 hours after the injection.

Causes for cancellation included evidence of excessive ovarian response (more than 3 follicles larger than 15 mm), lack of cooperation at the time of IUI, male psychological reasons that caused difficulty of sperm-collection and couple preference.

All patients were asked to have a serum hHCG measured 14 days after the insemination. Clinical pregnancy was confirmed by a transvaginal ultrasound two weeks later which documented gestational sac with fetal pole and present cardial activity.

Table 1. — *Demographic characteristics of two groups*.

| | Study group | Control group |
|---|---|---|
| Mean age (years) | 31.22 | 29.94 |
| Mean standard error (age) | .335 | .349 |
| Ovulatory factor (%) | 23 (26.7%) | 21 (24.7%) |
| Cervical factor (%) | 10 (11.6%) | 8 (9.3%) |
| Endometriosis (%) | 8 (9.3%) | 10 (11.7%) |
| Male factor (%) | 20 (23.2%) | 23 (27%) |
| Idiopathic (%) | 25 (29%) | 23 (27%) |

Table 2. — *Polyp size*.

| Polyp | Study group (n = 86) | Control group (n = 85) |
|---|---|---|
| < 5 mm | 23 | 26 |
| 5-10 mm | 24 | 24 |
| 11-20 mm | 18 | 18 |
| > 20 mm | 21 | 17 |
| Mean | 13.67 | 12.01 |

Table 3. — *Pregnancy results according to IUI cycle - cancellation rates - Study group*.

| Study group | Patient number | Cycles | Cancellation | Pregnancies |
|---|---|---|---|---|
| 1st attempt | 86 | 81 | 5 | 15 |
| 2nd attempt | 71 | 61 | 10 | 11 |
| 3rd attempt | 60 | 50 | 10 | 9 |
| Totals | | 192 | 25 | 35 |

Table 4. — *Pregnancy results according to IUI cycle - cancellation rates - Control group*.

| Control group | Patient number | Cycles | Cancellation | Pregnancies |
|---|---|---|---|---|
| 1st attempt | 85 | 78 | 7 | 9 |
| 2nd attempt | 76 | 64 | 12 | 6 |
| 3rd attempt | 70 | 62 | 8 | 4 |
| Totals | | 204 | 27 | 19 |

Our statistical analysis was performed by the use of a commercially available SPSS program (SPSS Statistics 17.0). The Independent Groups t-test for means calculator tests the means of two independent groups to determine if they are significantly different from one another. We used confidence level: 95%.

The differences were considered to be statistically significant if $p < 0.05$.

## Results

Demographic characteristics of female patients were similar in the two groups (Table 1).

In Table 2 the polyp size in women of our sample is presented. There were no statistically significant differences in polyp sizes.

In women of the first group, there were 25 cancellations of IUI cycles, 192 completed cycles and among those, 35 women managed to conceive (Table 3).

In the second group (which consisted of 85 women each also having 3 cycles of treatment), there were 27 cancellations of IUI cycles, 204 completed cycles, and 19 women managed to conceive (Table 4).

Fifteen women of the 35 women in the first group managed to conceive from the first treatment cycle, 11 women

achieved from the second attempt and nine managed conception after the third cycle (Table 3).

In the control group, nine women managed to conceive from the first treatment cycle, six after the second cycle and four after the third cycle (Table 4).

There was a statistically significant difference in cumulative pregnancy rates between the two groups. The group that underwent polyp removal had higher pregnancy rates as compared to the one where the polyps were left intact.

It should be noted that in the period of three months after removal of the polyps and before the implementation of IUI, there was no pregnancy achieved in the study women.

More specifically, in Table 1 we examine the heterogeneity of the samples. For all variables we found statistically non-significant results. A level frequently quoted is $p < 0.05$ (type-1 error). Thus we could proceed with the analysis. In Table 2 we found statistically non-significant differences in the three categories (< 5 mm, 5-10 mm, 11-20 mm) while the fourth result (> 20 mm) ($p = 0.045$) was statistically significant. The correlation and t could not be computed because the standard error of the difference was 0, so we could not find a p value for pair 2 and pair 3. The mean comes out statistically non-significant ($p = 0.159$). In Tables 3 and 4 cancellation rates are shown; we found statistically non-significant differences in all three attempts. For cycle variables we found statistically significant results in the third attempt ($p = 0.001$) only. For pregnancy variables we found statistically significant differences in all attempts (1: $p = 0.045$, 2: $p = 0.024$, 3: $p = 0.024$) suggesting that the treatment group achieved more pregnancies and, therefore, treatment is recommended.

## Discussion

EPs are a common cause of intrauterine pathology, with a variety of symptoms ranging from unpredictable bleeding to infertility [4-7]. Management of EP is a doubtful decision, particularly because EPs are almost always benign and treatment may be conservative, with follow-up visits every six months to one year being sometimes the approach recommended [19].

Our study examined the effect of hysteroscopic polypectomy to intrauterine insemination success rates.

In a previous study investigators reported that hysteroscopic polypectomy in infertile women possibly increases pregnancy rates by three to four times [20]; the methodological problem is that in that study [20], EP coexisted with submucous myomas, so that the exact impact on infertility is difficult to calculate.

In our study, we found that after the removal of the endometrial polyp, 35 out of 86 women (40.69%) managed to conceive after IUI. On the other hand, in the group of women who did not have a polypectomy, respective results showed a 22.35% (19 out of 85 patients) conception rate.

Other authors have suggested that otherwise asymptomatic polyps, less than 2 cm in diameter, do not interfere with IVF/embryo transfer rates, but may increase risk of spontaneous abortion and, in general, increase pregnancy loss and thus hysteroscopic treatment is needed [15].

Persistent functional EPs, even if small, are likely to impair fertility and thus removal of these lesions tends to improve reproductive performance [4].

In another study it was suggested that hysteroscopic removal of even small polyps improves reproductive outcome and therefore should be recommended to infertile women undergoing assisted reproductive technology procedures [10, 21].

As for time of achieving conception after removal of endometrial polyps, findings of a study by Spiewankiewicz *et al*. reported that 19 out of 25 infertile patients in whom polypectomy was performed conceived in a 12-month-period 17.

In our study, 15 out of 35 women of the study group conceived after the first IUI effort, 11 after the second and nine after the third effort. Those numbers were nine, six, and four for the control group, respectively. Cancellation rates were similar in both groups (25 women cancelled their IUI cycle in the first group, and 27 in the second). Thus, we find an improvement (statistically important) in pregnancy rates of women of all groups.

Hysteroscopy is an effective and safe way to remove EPs because the procedure is done under direct vision (and so problems of blind dilatation and curettage, such as leaving residual tissue or missing even the whole polyp are avoided). Operative hysteroscopy is a reliable technique with low recurrence rates, especially for difficult cases; for example in cases of EPs larger than 2 cm [4]. In our study, we used hysteroscopic scissors or resectoscope to remove the polyps from the underlying endometrial tissue. No major complications (such as uterine rupture or severe blood loss) occurred in our study, a finding consistent with those of other authors [4, 10] who proposed that hysterectopy is a safe and effective diagnostic and therapeutic method.

In conclusion, hysteroscopic polypectomy for any size polyp appears to improve fertility in women with otherwise unexplained infertility. Nonetheless, further studies would be useful to confirm that EPs are not coincidental with infertility, because our study directly implies that EPs may have a causative effect in infertility.

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