Meta-Analysis

Hysteroscopic polypectomy versus expectant management in endometrial polyps in asymptomatic infertile women: a meta-analysis

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ABSTRACT

Background: Endometrial polyp is a hyperplastic structural abnormality of the uterine cavity and is one of the most commonly found intrauterine abnormalities. The endometrial polyp is mostly asymptomatic and sometimes diagnosed only during infertility investigation. The influence of endometrial polyps on female infertility is not completely understood, however, due to the possibility of endometrial polyps influencing fertility, their removal is usually performed in women undergoing infertility treatment.

Methods: This meta-analysis was performed through an electronic search using MEDLINE, PubMed in October 2017, bringing together the terms of interest in order to select studies that would compare polypectomy and expectant management for endometrial polyps in subfertile women. Four articles were selected according to the inclusion and non-inclusion criteria.

Results: Five variables were collected from the selected articles to be compiled and analyzed (rate of live births per transferred embryo, chemical pregnancy rate, spontaneous abortion rate, implantation rate and clinical pregnancy rate), none of which showed any difference statistically significant in conduct.

Conclusions: The data concluded that there is no statistical significance between expectant management and polypectomy.

Keywords: Endometrial polyps, In-vitro fertilization, Intrauterine insemination, Marital infertility, Ovulation induction, Ovarian stimulation, Polyp, Sub fertile

INTRODUCTION

Endometrial polyp is a hyperplastic structural abnormality of the uterine cavity and is one of the most commonly found intrauterine abnormalities. The endometrial polyp is mostly asymptomatic and sometimes diagnosed only during infertility investigation. The influence of endometrial polyps on female infertility is not completely understood, however, due to the possibility of endometrial polyps influencing fertility, their removal is usually performed in women undergoing infertility treatment.

Marital infertility, according to the World Health Organization and the International Committee for Monitoring Reproductive Technology (ICMART), is defined as the couple's inability to naturally conceive after 12 months of unprotected regular sexual intercourse. There are an estimated 74.2 million infertile couples worldwide and 40.5 million couples would be looking for fertility treatment.

The presence of endometrial polyps has often been associated with infertility. About 25% of women with this condition had endometrial polyps identified through hysteroscopic evaluation. Endometrial polyp is a hyperplastic structural abnormality of the uterine cavity located in the endometrium that surrounds one or more spiral arteries and contains endometrial glands and stroma in its composition. It is one of the most commonly found intrauterine abnormalities.
found intrauterine abnormalities. The endometrial polyp is mostly asymptomatic and sometimes diagnosed only during infertility investigation.

The influence of endometrial polyp on female infertility is not completely understood, but some mechanisms that may be involved are: endometrial inflammatory response, interference with endocrine function pattern, increased glycolic acid concentration, which inhibits sperm binding to the pellucida zone, decreased HOXA10 and HOXA11 mRNA expression, hormonal disorders and influence on ovulation and irregular endometrial bleeding.

Endometrial polyps can be diagnosed by hysterosalpingography or transvaginal ultrasound; however, the gold standard for diagnosis is hysteroscopy, an exam that can diagnose and treat endometrial polyps at the same surgical time. Therefore, because endometrial polyps may influence fertility, their removal is usually performed in women undergoing infertility treatment.

Polypectomy, as well as any procedure, has risks associated with its performance such as infection, bleeding, uterine perforation and risks associated with anesthesia. However, there is no statistically significant evidence to prove the superiority of polypectomy over expectant management.

The aim of this meta-analysis is to gather comparative articles and to evaluate if there is statistical significance that proves the superiority of polypectomy compared to the expectant management in women with infertility.

METHODS

Evidence acquisition

To report the results of this meta-analysis we used the PRISMA report indices (preferred reporting items for systematic reviews and meta-analysis). This systematic review is registered in the PROSPERO database with registration number: CRD42017081370.

**Researched question**

In order to determine the focus of this meta-analysis we have established clinical questions considering five components: the population to be studied, the intervention and comparison, results and design of each study included in the meta-analysis. The present study was structured in the “PICOS” format: population, intervention, comparative, outcomes, study design.

**Eligibility criteria**

Authors used as criteria to select the articles of interest studies that only included women with diagnosed endometrial polyp and that compared the expectant management versus polypectomy performed by any surgical technique evaluating the outcome pregnancy. Due to the scarcity of randomized controlled trials found, other study designs such as case-control, prospective and retrospective and quasi-randomized trials were also included in the study selection.

**Non-inclusion criteria**

Articles that did not compare expectant management and polypectomy were not included, as well as articles that the control group was not composed of patients with diagnosed endometrial polyp.

Articles in which patients had other abnormalities than endometrial polyps or whose patients had symptomatic endometrial polyps were not included to avoid selection bias or confounding information.

Articles that had the study design distinct from those described in Table 1 were also not included.

Table 1: Selection criteria of the included studies (PICOS).

<table>
<thead>
<tr>
<th>Included</th>
<th>Excluded</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Population</strong></td>
<td>Sub fertile women with endometrial polyps</td>
</tr>
<tr>
<td><strong>Intervention</strong></td>
<td>Polypectomy</td>
</tr>
<tr>
<td><strong>Comparison</strong></td>
<td>Expectant conduct</td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td>• Clinical pregnancy rate</td>
</tr>
<tr>
<td></td>
<td>• Deployment fee</td>
</tr>
<tr>
<td></td>
<td>• Spontaneous abortion rate</td>
</tr>
<tr>
<td></td>
<td>• Live birth rate</td>
</tr>
<tr>
<td></td>
<td>• Chemical pregnancy rate</td>
</tr>
<tr>
<td><strong>Study design</strong></td>
<td>Case studies - control, prospective, randomized, quasi-randomized,</td>
</tr>
<tr>
<td></td>
<td>prospective</td>
</tr>
</tbody>
</table>

P: Subfertile women with endometrial polyps, I: Polypectomy, C: Expectant conduct, O: Effectiveness, S: Case studies - control, prospective, randomized, quasi-randomized, prospective
Table 2: Quality assessment of included studies.

<table>
<thead>
<tr>
<th>Study</th>
<th>Random sequence generation</th>
<th>Allocation concealment</th>
<th>Blindness</th>
<th>Incomplete outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isikoglu et al</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Pérez- Medina et al</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Lass et al</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Ghaffari et al</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

Table 3: Data extracted from the selected studies.

<table>
<thead>
<tr>
<th>Article</th>
<th>Group 1</th>
<th>Group 2</th>
<th>N Group 1</th>
<th>N Group 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isikoglu et al</td>
<td>Included endometrial polyps - hysteroscopic polypectomy</td>
<td>Endometrial polyps - expectant conduct</td>
<td>40</td>
<td>15</td>
</tr>
<tr>
<td>Lass et al</td>
<td>Treated endometrial polyps - hysteroscopic polypectomy</td>
<td>Endometrial polyps - expectant conduct</td>
<td>21</td>
<td>49</td>
</tr>
<tr>
<td>Ghaffari et al</td>
<td>Treated endometrial polyps - hysteroscopic polypectomy</td>
<td>Endometrial polyps - expectant conduct</td>
<td>43</td>
<td>43</td>
</tr>
<tr>
<td>Pérez-Medina et al</td>
<td>Treated endometrial polyps - hysteroscopic polypectomy</td>
<td>Endometrial polyps - expectant conduct</td>
<td>101</td>
<td>103</td>
</tr>
<tr>
<td>Isikoglu et al</td>
<td>Patients with endometrial polyps and patients with unchanged uterine cavity</td>
<td>Unclarity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lass et al</td>
<td>Patients with endometrial polyp diagnosed by transvaginal ultrasound</td>
<td>Patients with polyps greater than 20 mm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ghaffari et al</td>
<td>Patients with incidental diagnosis of endometrial polyp during oocyte removal stimulation phase</td>
<td>Patients’ partners with Azoospermia Patients with uterine cavity alterations distinct from endometrial polyp</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pérez-Medina et al</td>
<td>Patients with infertility greater than or equal to 24 months who were diagnosed with endometrial polyp by sonography and who were candidates for intrauterine insemination</td>
<td>Patients over 39 years old Anovulation patients Patients’ partners with Azoospermia Patients with uncorrected tubal disease Prior failed patients to r-FSH use</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Research strategy

An electronic search was performed using MEDLINE, PubMed in October 2018. No language restriction was performed for the articles. The search combined relevant terms and descriptors from the Medical Subject Headings of the National Library of Medicine (MESH) related to "polyp" OR "uterine disease" OR "watchful waiting" OR "general surgery" OR "endoscope" OR "endoscopy" OR "hysteroscopy" OR "reproductive history" OR "pregnancy maintenance" OR "pregnancy outcome" OR "pregnancy complications" OR "pregnancy complications, infectious" OR "pregnancy complications, neoplastic" OR "pregnancy" OR "time to pregnancy" OR "uterine hemorrhages."

Articles selection

The selection of articles was made by 2 authors (TBM and SAO). Initially, all articles found through the search strategy were evaluated by title and abstract. Subsequently, all articles for which sufficient information...
was not obtained in consideration of the inclusion and exclusion criteria by title and abstract were evaluated in their entirety. Only articles that met the inclusion criteria and did not meet the non-inclusion criteria were included in the meta-analysis (Table 1).

Authors compiled and tabulated data extracted from the selected studies (Table 3).

RESULTS

Some questions were elaborated for the construction of this meta-analysis

- Is polypectomy more effective compared to expectant management regarding clinical pregnancy outcome?
- Can polypectomy increase the rate of embryonic implantation?
- Do patients undergoing polypectomy have a higher rate of spontaneous abortion?
- Is chemical pregnancy greater in patients who underwent polypectomy?
- Is there a significant difference between the rate of live births in women undergoing polypectomy and patients with expectant management?

Clinical pregnancy rate

All selected studies (Isikoglu et al; Pérez-Medina et al; Lass et al and Ghaffari et al) evaluated the rate of clinical pregnancy in the two groups involved.

When comparing the intervention versus control groups, there was no statistical significance (p<0.05) (OR=1.70; 95% CI: 0.70, 4.11; I²=73%; p=0.24), (Figure 2).

Deployment fee

The implantation rate was evaluated by three of the selected studies (Isikoglu et al; Lass et al and Ghaffari et al) and when compared the intervention group versus the control group there was no statistical significance. (OR=0.89; 95% CI: 0.53, 1.52; I²=38%; p=0.68) (Figure 3).

Spontaneous abortion rate

The rate of spontaneous abortion was assessed by two of the selected studies (Lass et al and Ghaffari et al) and when comparing the intervention group versus the control group no statistical significance was found. (OR=0.85; 95% CI: 0.38, 1.88; I²=39%; p=0.69), (Figure 4).

Chemical pregnancy rate

The rate of chemical pregnancy was assessed by two of the selected studies (Lass et al and Ghaffari et al) and no statistical significance was found between the intervention and the control group. (OR=0.85; 95% CI: 0.38, 1.88; I²=39%; p=0.69), (Figure 5).
Figure 2: Forest plot for clinical pregnancy rate.

Figure 3: Forest plot for deployment rate.

Figure 4: Forest plot for spontaneous abortion rate.

Figure 5: Forest plot for chemical pregnancy rate.

Figure 6: Forest plot for live birth rate per transferred embryo.
**Live birth rate per transferred embryo**

The rate of live births per transferred embryo was analysed by only 1 of the selected studies and no statistical significance was found (Ghaffari et al). (OR=1.12; 95% CI: 0.44, 2.84; I²=not applicable; p=0.81), (Figure 6).

**DISCUSSION**

The evaluation of the uterine cavity in women undergoing infertility investigation is an important step, since structural abnormalities can influence endometrial receptivity and consequently embryonic implantation.1,3,9,15

After compiling and analyzing the data, it was possible to realize that the meta-analysis did not show a statistically significant difference between polypectomy and expectant management, despite all possible mechanisms by which endometrial polyps may affect fertility mentioned in the introduction. However, characteristics of the included studies may have biased the sample group. For example, most of the studies included in this meta-analysis included polyps smaller than 20 mm and perhaps patients with larger polyps could benefit from polyp resection.

In the study by Lass et al, it was shown that the group of women with polyps smaller than 20 mm had no deleterious effects on the conception process, but the group undergoing expectant management was related to a higher rate of miscarriage (27.3%), versus 14.3%), although no statistical significance was demonstrated, a fact attributed by the author to the small group of patients.

Another variable to be analyzed is the possible complications that hysteroscopy and consequently polypectomy may cause. The endometrium may be injured during hysteroscopic polypectomy.3 However, the study Varesh et al, gathered a group of 78 patients and allocated these patients into 3 groups, patients with fibroids, patients with endometrial polyps and patients without any uterine abnormalities. Patients with fibroids and endometrial polyps underwent resection of these abnormalities.

Although this particular study does not compare expectant management versus polypectomy for endometrial polyps, it is important because it demonstrates in its results that patients who underwent polypectomy had rates of spontaneous abortion similar to those without uterine abnormality (31.5% spontaneous abortion rate, polypectomy 27.7% and no uterine abnormalities 37.5%) thus demonstrating the safety of the method.

In the study by Batioglu et al, 6 patients with endometrial polyps discovered during in vitro fertilization cycle underwent polypectomy and 3 of these patients were successful in becoming pregnant (two became single fetuses and one became pregnant with triplets). Despite the small sample size, the study demonstrates that hysteroscopy is a safe procedure.3,17

However, some studies demonstrate the positive value of polypectomy in the pregnancy outcome. Pérez-Medina et al, demonstrated that the group that underwent polypectomy achieved more than double the pregnancy rate compared to the expectant management group. (Polypectomy group 63.4%; expectant management group 28.3%; p<0.001). In addition, it was observed that most pregnancies after polypectomy occurred spontaneously during the period patients waited for treatment. This, according to Pérez-Medina et al suggests a strong cause-and-effect relationship of polyp presence and implantation process.4

**CONCLUSION**

The present meta-analysis did not identify superiority in performing polypectomy or proceeding with expectant management for endometrial polyps in sub-fertile women.

There are still a small number of randomized, blinded studies and a considerable sample size that propose to compare expectant management with resection for endometrial polyps.

Therefore, in order to guide clinical management based on the principles of beneficence and nonmaleficence, further studies are needed comparing expectant management with polypectomy and evaluating its various outcomes.

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**Ethical approval: Not required**

**REFERENCES**
