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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 sub fertile 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.¹ The endometrial polyp is mostly asymptomatic and sometimes diagnosed only during infertility investigation.² 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.³⁻⁵

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.^{6,7} There are an estimated 74.2 million infertile couples worldwide and 40.5 million couples would be looking for fertility treatment.^{8,9}

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.^{2,3,10} 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.¹ The endometrial polyp is mostly asymptomatic and sometimes diagnosed only during infertility investigation.²

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 glycodeline 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.^{2-5,11,12}

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.^{8,12-15} Therefore, because endometrial polyps may influence fertility, their removal is usually performed in women undergoing infertility treatment.¹²

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.¹²

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).¹⁶ 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).

	Included	Excluded
Population	Sub fertile women with endometrial polyps	<ul style="list-style-type: none"> • Women who did not have endometrial polyps • Women who had other uterine abnormalities
Intervention	Polypectomy	
Comparison	Expectant conduct	
Outcomes	<ul style="list-style-type: none"> • Clinical pregnancy rate • deployment fee • spontaneous abortion rate • live birth rate • chemical pregnancy rate 	
Study design	Case studies - control, prospective, randomized, quasi-randomized, prospective	Systematic review and meta-analyzes, case report

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.

Study	Random sequence generation	Allocation concealment	Blindness	Incomplete outcomes
Isikoglu et al	No	No	No	No
Pérez- Medina et al	Yes	No	No	No
Lass et al	No	No	No	No
Ghaffari et al	No	No	No	No

Table 3: Data extracted from the selected studies.

Article	Period	Country	Journal	Design
Isikoglu et al	From January, 2003 to December, 2004.	Turkey	Reproductive BioMedicine Online	Descriptive retrospective controlled study
Lass et al	From January, 1991 to May, 1997, 2004	United Kingdom	Journal of Assisted Reproduction and Genetics	Retrospective Study
Ghaffari et al	From January, 2011 to December, 2013	Iran	European Journal Obstetrics and Gynecology and Reproductive Biology	Cross-sectional study
Pérez-Medina et al	From January, 2000 to February, 2004	Spain	Human Reproduction	Prospective randomized study
Article	Group 1	Group 2	N Group 1	N Group 2
Isikoglu et al	Included endometrial polyps - hysteroscopic polypectomy	Endometrial polyps - expectant conduct	40	15
Lass et al	Treated endometrial polyps - hysteroscopic polypectomy	Endometrial polyps - expectant conduct	21	49
Ghaffari et al	Treated endometrial polyps - hysteroscopic polypectomy	Endometrial polyps - expectant conduct	43	43
Pérez-Medina et al	Treated endometrial polyps - hysteroscopic polypectomy	Endometrial polyps - expectant conduct	101	103
Isikoglu et al	Patients with endometrial polyps and patients with unchanged uterine cavity		Unclarity	
Lass et al	Patients with endometrial polyp diagnosed by transvaginal ultrasound		Patients with polyps greater than 20 mm	
Ghaffari et al	Patients with incidental diagnosis of endometrial polyp during oocyte removal stimulation phase		Patients' partners with Azoospermia Patients with uterine cavity alterations distinct from endometrial polyp	
Pérez-Medina et al	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		Patients over 39 years old Anovulation patients Patients' partners with Azoospermia Patients with uncorrected tubal disease Prior failed patients to r-FSH use	

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).

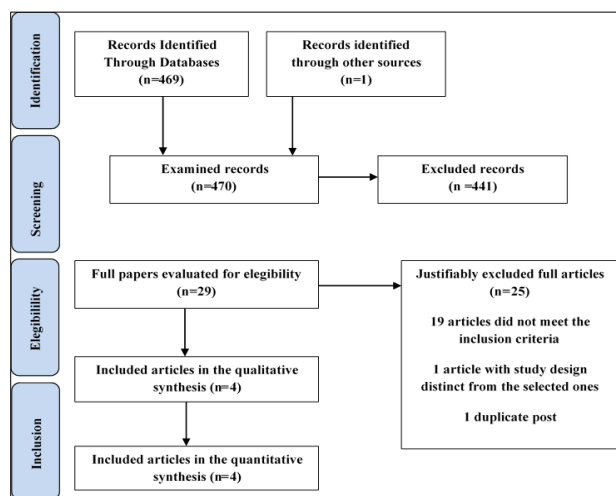


Figure 1: Study selection.

Bias risk assessment

The guidance suggested by Cochrane collaboration was followed to assess the risk of bias in the included studies. Authors evaluated sequence generation, allocation concealment, blinding, and incomplete outcome data for each test included in the review. A low risk of bias was considered when a "yes" judgment for all domains was obtained, while a high risk of bias was considered when a "no" judgment for one or more domains was obtained (Table 2).

Analysis

The metanalytic measure of interest is the odds ratio, which was obtained by the Mantel-Haenszel method. In cases where the number of events in one of the groups is zero, Peto's method was applied. In addition to the odds ratios, the respective 95% confidence intervals (CI) as well as the funnel and forest plot were presented. To assess heterogeneity between studies, the Higgins and Thompson I² statistics and the Cochran Q test were used. The random effect model was applied when the I² statistic was greater than 50% or when the null hypothesis of the Cochran Q test was rejected. The statistical tests applied were bilateral and the adopted significance level was 5%. Meta-analyses were performed using the Cochrane collaboration's review manager software (Rev Man 5.3; <<http://tech.cochrane.org/revman>>).

Description of selected articles

After study selection, only four articles were included in the quantitative and qualitative synthesis (Figure 1). The

four included studies totaled 415 patients (205 in the group who underwent polypectomy and 210 patients in the expectant management group).

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=0.67; 95% CI: 0.14, 3.27; I²=0%; $p=0.62$), (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).

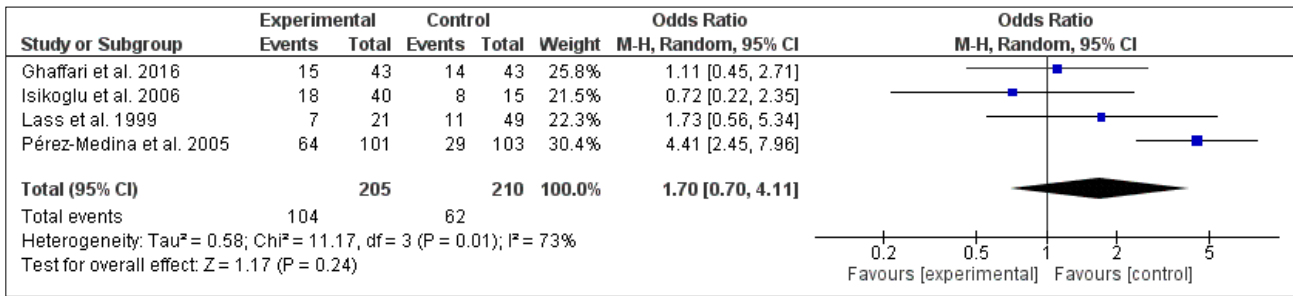


Figure 2: Forest plot for clinical pregnancy rate.

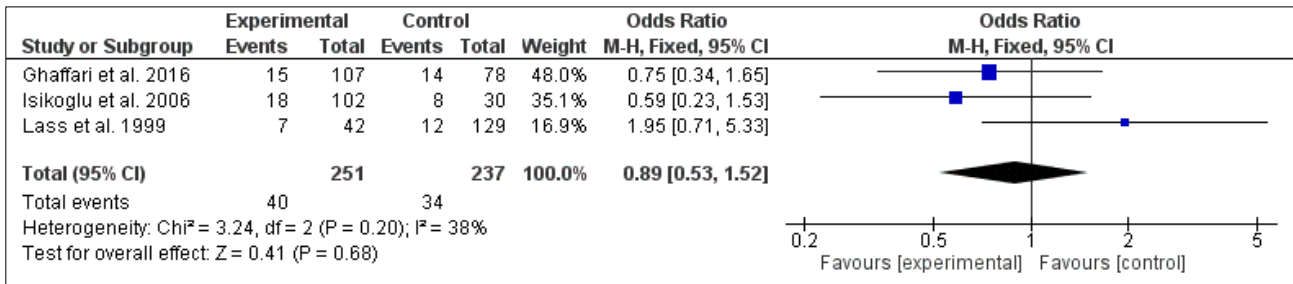


Figure 3: Forest plot for deployment rate.

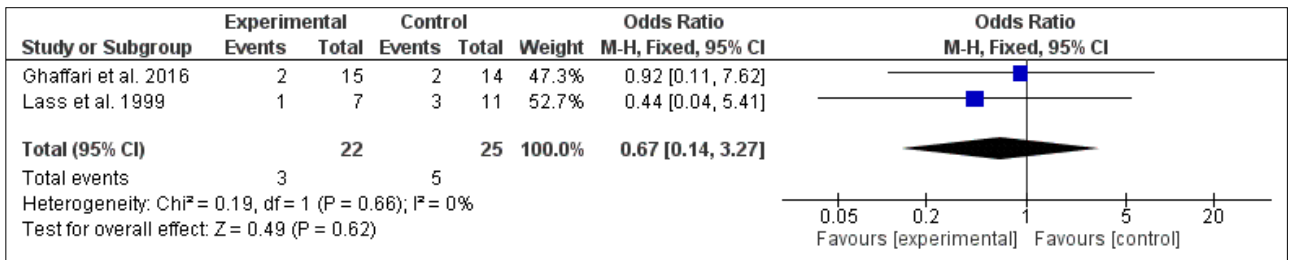


Figure 4: Forest plot for spontaneous abortion rate.

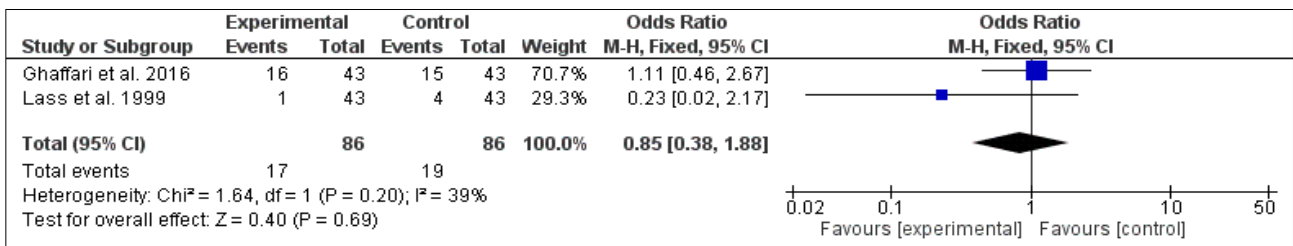


Figure 5: Forest plot for chemical pregnancy rate.

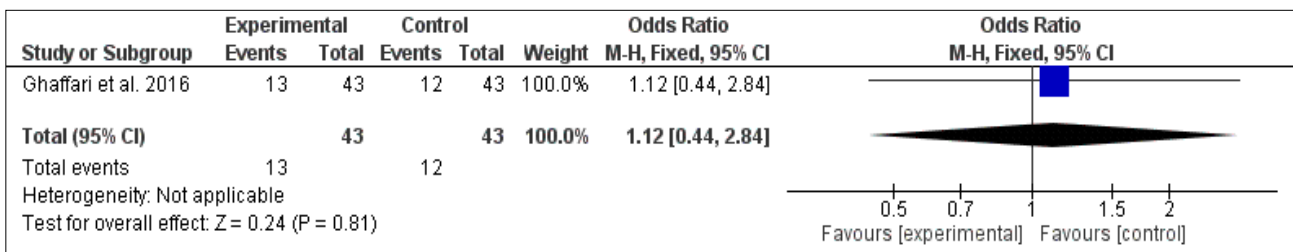


Figure 6: Forest plot for live birth rate per transferred embryo.

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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Conflict of interest: None declared

Ethical approval: Not required

REFERENCES

1. Doldi N, Persico P, Di Sebastiano F, Marsiglio E, De Santis L, Rabellotti E, et al. Pathologic findings in hysteroscopy before in vitro fertilization-embryo transfer (IVF-ET). *Gynecol Endocrinol.* 2005;21(4):235-7.
2. Rackow BW, Jorgensen E, Taylor HS. Endometrial polyps affect uterine receptivity. *Fertil Steril.* Elsevier Ltd; 2011;95(8):2690-2.
3. Ghaffari F, Arabipoor A, Bagheri N, Hosseini F. Hysteroscopic polypectomy without cycle cancellation in IVF/ICSI cycles: a cross-sectional study. *Eur J Obstet Gynecol Reprod Biol.* Elsevier Ireland Ltd; 2016;205:37-42.
4. Pérez-Medina T, Bajo-Arenas J, Salazar F, Redondo T, Sanfrutos L, Alvarez P, et al. Endometrial polyps and their implication in the pregnancy rates of patients undergoing intrauterine insemination: a

- prospective, randomized study. *Hum Reprod.* 2005;20(6):1632-5.
5. Lass A, Williams G, Abusheikha N, Brinsden P. The effect of endometrial polyps on outcomes of in vitro fertilization (IVF) cycles. *J Assist Reprod Genet.* 1999;16(8):410-5.
 6. Zegers-Hochschild F, Adamson GD, de Mouzon J, Ishihara O, Mansour R, Nygren K, et al. The international committee for monitoring assisted reproductive technology (ICMART) and the world health organization (WHO) revised glossary on ART terminology, 2009. *Human Reprod.* 2009;24(11):2683-7.
 7. Kamel RM. Management of the infertile couple: an evidence-based protocol. 2010 [cited 2017 Nov 19]; Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2844387/pdf/1477-7827-8-21.pdf>
 8. Di Spiezio Sardo A, Di Carlo C, Minozzi S, Spinelli M, Pistotti V, Alviggi C, et al. Efficacy of hysteroscopy in improving reproductive outcomes of infertile couples: a systematic review and meta-analysis. *Hum Reprod Update.* 2016;22(4):479-96.
 9. Bosteels J, Kasius J, Weyers S, Broekmans FJ, Mol BW, illem J, et al. Hysteroscopy for treating subfertility associated with suspected major uterine cavity abnormalities. *Cochrane database Syst Rev.* 2015;2(2):CD009461.
 10. Varasteh NN, Neuwirth RS, Levin B, Keltz MD. Pregnancy rates after hysteroscopic polypectomy and myomectomy in infertile women. *Obstet Gynecol.* 1999;94(2):168-71.
 11. Cholkeri-Singh A, Sasaki KJ. Hysteroscopy for infertile women: a review. *J Minim Invasive Gynecol.* 2015;22(3):353-62.
 12. Jayaprakasan K, Polanski L, Sahu B, Thornton JG, Raine-Fenning N. Surgical intervention versus expectant management for endometrial polyps in subfertile women. *Cochrane Database Syst Rev.* 2014;(8):CD009592.
 13. Silva ACJS, Silva JC, Reis FJC, Nogueira AA, Ferriani RA. Routine office hysteroscopy in the investigation of infertile couples prior to assisted reproduction. *Int Congr Ser.* 2004;1271(C):255-8.
 14. Golan A, Eilat E, Ron-el R, Herman A, Soffer Y, Bukovsky I. Hysteroscopy is superior to hysterosalpingography in infertility investigation. *Acta Obstet Gynecol Scand.* 1996;75(7):654-6.
 15. Bakas P, Hassiakos D, Grigoriadis C, Vlahos N, Liapis A, Gregoriou O. Role of hysteroscopy prior to assisted reproduction techniques. *J Minim Invasive Gynecol.* 2014;21(2):233-7.
 16. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Int J Surg.* 2010;8(5):336-41.
 17. Batioglu S, Kaymak O. Does hysteroscopic polypectomy without cycle cancellation affect IVF?. *Reprod Biomed Online.* 2005;10(6):767-9.

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