

The Effect of Injectable Hyoscine and Vaginal Misoprostol on Cervical Preparation before Hysteroscopy

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Abstract

Introduction: Hysteroscopy is the gold standard in identifying endometrial and uterine cavity pathologies. With the advancement of technology and the creation of a mini-hysteroscopes, this operation can be easily performed in the doctor's office. Complications of this operation are often related to the difficulties of entering the hysteroscope, which can lead to damage to the cervix, the creation of a false canal, bleeding, uterine perforation or difficulty in entering the hysteroscope. Considering the systemic side effects of prostaglandins, researchers are looking for less complicated drugs. Therefore, the aim of this study is to compare the effect of injectable hyoscine with vaginal misoprostol in preparing the cervix before hysteroscopy.

Materials and Methods: This double-blind clinical trial was conducted on patients who underwent hysteroscopy at Mahdijeh Hospital in Tehran, Iran. Patients were randomly divided into two groups and received vaginal misoprostol or injectable hyoscine 2-3 hours before surgery. Then, variables such as the ease of entering the hysteroscope, the need for Bougie for cervical dilatation, and hysteroscopy complications (damage to the cervix or uterus, pain, and bleeding), as well as the side effects of drugs were investigated and statistically analyzed.

Results: According to the analysis, two groups are similar in terms of confounding variables. The results of hysteroscopy complications and drug complications showed that the use of injectable hyoscine, such as vaginal misoprostol, not only reduces complications of hysteroscopy, but also has fewer drug complications. In the current study, the overall prevalence of complications of hyoscine and misoprostol were 24% and 32%, respectively.

Conclusion: Hyoscine can be a suitable drug for preparing the cervix before performing dilatation and curettage, it will also cause the cervix to dilate more easily. Using vaginal hyoscine before surgical hysteroscopy reduces the need for cervical dilatation and facilitates surgical hysteroscopy.

Keywords: Hyoscine, Hysteroscopy, Misoprostol, Cervical Preparation.

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INTRODUCTION

Hysteroscopy is the gold standard method in diagnosing and sometimes treating intrauterine pathologies (1). A hysteroscope is an intraluminal endoscope similar to a cystoscope. In this minimally invasive method, the hysteroscope enters the cervix through the vagina and shows the inside of the uterus through a camera on the monitor. Using a hysteroscope, it is possible to detect localized lesions and take samples from the right place (2). Although the first report of the use of a hysteroscope was in 1869 in

polypectomy, many operations are performed using a hysteroscope, such as diagnostic hysteroscopy with or without simultaneous laparoscopy, hysteroscopy-polypectomy, hysteroscopy-myomectomy, hysteroscopy for removal of the intra-uterine device (IUD) and Removal of uterine septum (3). Hysteroscopy is an important and valuable method for managing and treating intrauterine lesions. This method is the least dangerous and invasive for the patient compared to laparotomy methods. Cervical dilation is one of the problems that surgeons face during hysteroscopy.

This problem attracts more attention in nulliparity, menopause and cervical stenosis patients. Also, when performing myomectomy with a hysteroscope, sufficient cervical dilation is needed for the resectoscope to enter and the mass to exit (4). Therefore, some of the hysteroscopy complications are related to cervical dilation. These symptoms include tearing of the cervix, entering through an unnatural route and creating a false way, bleeding and tearing of the uterus. If the cervix is soft and prepared before hysteroscopy, the number of complications will be minimal (5-7).

Misoprostol is an analogue of prostaglandin E1, which is widely used to prevent and treat stomach ulcers caused by long-term use of non-steroidal anti-inflammatory drugs. The amount of medicine available in vaginal administration is three times that of oral administration (9). In studies, it has been shown that vaginal misoprostol is more effective in medical induction of abortion compared to oral misoprostol (10). Recently, misoprostol is used to prepare the cervix for induction of labor, termination of pregnancy in the first trimester, and treatment of missed abortion (11). Misoprostol has been used to prepare the cervix before hysteroscopy in non-pregnant women (12, 13), so the aim of this study was to compare the effect of injectable hyoscine with vaginal misoprostol in preparing the cervix before hysteroscopy.

MATERIALS AND METHODS

This double-blind clinical trial was conducted on patients who underwent hysteroscopy in the years 2017 to 2019 at Mahdiah Hospital in Tehran-Iran. Inclusion criteria include: having hysteroscopy and having informed consent. Exclusion criteria include: sensitivity to prostaglandins or hyoscine, history of injury or surgery on the cervix, having an active infection of the cervix, suffering from glaucoma, history of cardiovascular diseases and tachycardia, being treated with estrogen and pregnancy.

Sample size

Between 2017 and 2019, a total of 200 patients underwent hysteroscopy in Mahdia Hospital, of which 140 were non-pregnant women who were included in the study.

Procedure

At first, people were randomly divided into two groups. The first group received misoprostol and the second group received hyoscine. The randomization was such that people with odd file numbers were in the misoprostol group and people with even file numbers were in the hyoscine group. All patients were examined by the gynecology resident at the beginning of hospitalization. Individuals in the misoprostol group received 200 micrograms of vaginal misoprostol 3 hours before the operation. People in the hyoscine group received 20 mg of hyosin intramuscularly 2 hours before the operation. In order to blind the study,

patients in the misoprostol arm were prescribed 20 mg of intramuscular placebo (Vitamin B Complex Injection).

Patients were referred to the infertility operating room for hysteroscopy. Then, the demographic information of the patient, gravidity, parity and the method and number of deliveries, hysteroscopy indication, the need to use a Bougie dilator, and hysteroscopy complications (pain, bleeding, and cervical laceration) were recorded in the questionnaire. Also, the use of misoprostol or hyoscine and the complications of each These drugs (diarrhea, vomiting, fever, and abdominal pain related to the use of misoprostol, dry mouth, heart palpitations, blurred vision, urinary retention, constipation, and abdominal distension related to the use of hyoscine) have been questioned.

DATA ANALYSIS

SPSS 16 software was used for statistical analysis. We used chi-square test to compare two quantitative variables in two groups. A significance level of 0.05 was considered.

Ethical considerations

Before patients participated in the study, their parents were given sufficient explanation that participation in this study was completely voluntary. Informed and voluntary consent was obtained from the parents of the study participants. It should be noted that no additional costs were imposed on the patients in the process of conducting this study. Also, the information of the checklists is considered confidential and the results were published only as a group. The ethical principles of Helsinki were observed. The study was approved by the ethics committee of Iran University of Medical Sciences.

RESULTS

A total of 140 patients were included in this study, consisting of 70 patients in the misoprostol group and 70 patients in the hyoscine group, and it was difficult for 18 patients to pass the hysteroscope through the cervix. The average age of people in the hyosin group was 36.2 ± 6.71 and in the misoprostol group was 36.07 ± 7.32 years ($P=0.8$; Figure 1). In both groups, 8 patients had vaginal delivery. In addition, 68 people in the hyoscine group and 67 individuals in the misoprostol group had not yet reached menopause.

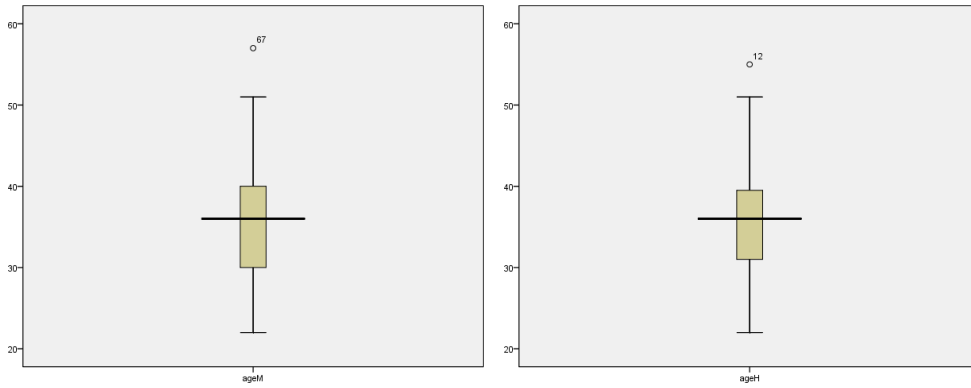


Figure 1: Age distribution of two groups

The use of a Bougie as a mechanical intraoperative dilator has been considered variable. This variable was investigated using Chi-square statistical test, 7 patients in the hyoscine group and 11 people in the misoprostol group had to use a mechanical dilator, the difference was not found to be statistically significant ($P>0.05$), (Table 1 and figure 2).

Table 1: Failure of chemical dilator use and mechanical dilator use

Residual	Expected N	Observed N	hyoscine
28	35	63	0
28-	35	7	1
misoprostol			
24	35	59	0
24-	35	11	1
	misoprostol	hyoscine	
	32.914	44.8	Chi-square
	1	1	df
	0.000	0.000	Asymp. sig

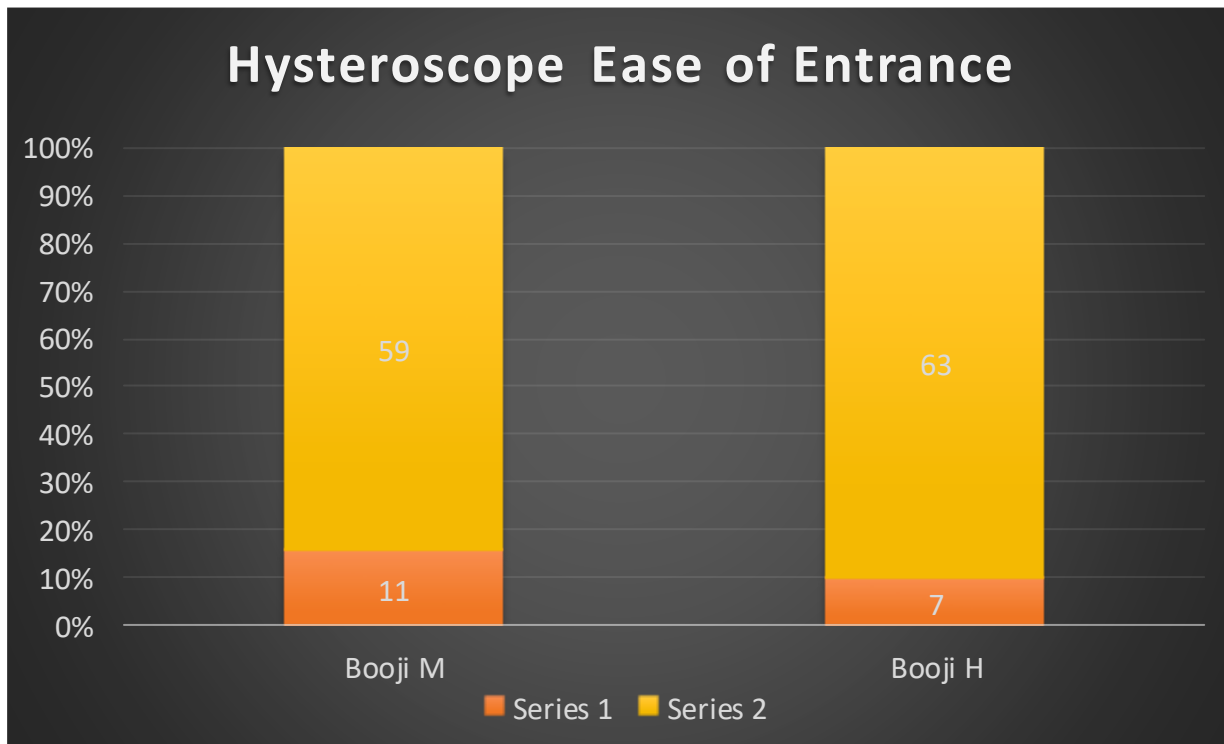


Figure 2: Checking the ease of entering the hysteroscope, an indicator of the proper functioning of the chemical dilator

In this study, 4 postoperative pain complications that require painkillers were investigated. Rupture of the uterus and cervix during surgery and bleeding during surgery were analyzed (Figure 3). In the statistical population, there were no cases of bleeding or rupture of the uterus and cervix, but 8 people in the hyosin group and 10 people in the misoprostol group had pain after hysteroscopy. The chi-square test showed no statistically significant difference in complications after hysteroscopy using hyoscine or misoprostol ($P>0.05$).

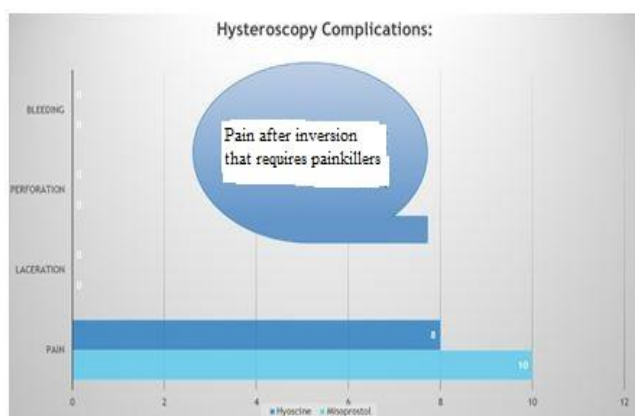


Figure 3: Examination of complications after hysteroscopy in the two groups of misoprostol and hyoscine

Figure 4 shows the distribution of the side effects of hyoscine. The results showed that among the 6 complications mentioned for **hyoscine** drug, only 3 cases exhibited dry mouth, tachycardia and blurred vision. A total of 17 people suffered from hyoscine complications, including dry mouth (16 cases; 22%), tachycardia (15; 21%) and blurred vision (4; 5%). The prevalence of hyoscine side effect was found to be 24% and the most observed side effect was dry mouth.

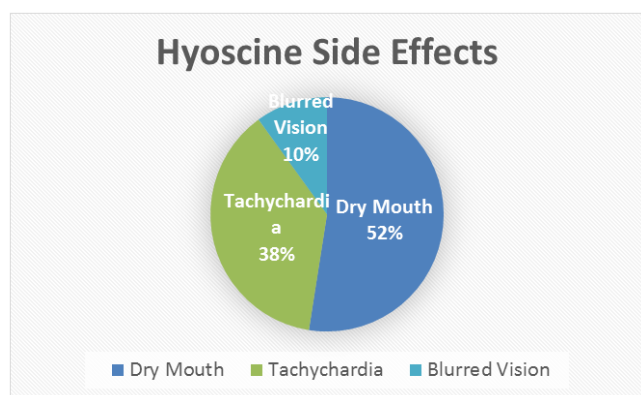


Figure 4: Distribution of side effects of hyoscine

Figure 5 shows the distribution of misoprostol side effects, only 3 side effects of diarrhea and vomiting and abdominal pain were observed in patients. A total of 23 people had

misoprostol drug complications, including abdominal pain (20 cases; 28%), vomiting (12 cases; 17%) and diarrhea (7 cases; 10%). Therefore, the prevalence of misoprostol complications was 32%, and the most common complication was abdominal pain.

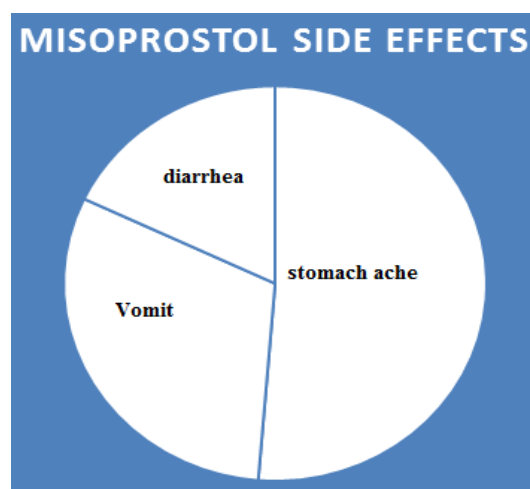


Figure 5: Distribution of misoprostol side effects

DISCUSSION

Considering the increasing role and importance of using hysteroscopy, researchers intend to make hysteroscopy easier and reduce its complications for patients by using an easier entry of the hysteroscope (14). One of these solutions is narrowing the diameter of the hysteroscope, which can be used in diagnostic hysteroscopy (15). Among the chemical dilators, misoprostol has been investigated and used to soften and prepare the cervix, especially in the labor process. Many studies have been done to determine the optimal time and dose of misoprostol. Considering the side effects of misoprostol drug and the relatively long time between drug administration and hysteroscopy, researchers thought of replacing another drug (16). Therefore, the aim of this study is to compare the effect of injectable hyoscine with vaginal misoprostol in preparing the cervix before hysteroscopy.

Studies have been conducted regarding the use of drugs before hysteroscopy. Most of the studies on the preparation of the cervix are related to the progress of labor and on the pregnant cervix. In a study conducted by Hadadian et al. in Kerman in 2016, it was shown that the use of vaginal hyoscine before performing intrauterine procedures is a suitable choice for premenopausal women. In Hadadian's study, 60 women in the age group of 20-70 years were randomly divided into two groups. The control group received two doses of vitamin B6 as a placebo, and the intervention group received two doses of 10 mg hyoscine tablets. Tablets were inserted vaginally for the patients with an interval of 8 and 2 hours before the operation. The study was double-blind, and the patients and the researcher did not know the type of drug. The findings showed that the 8 mm

Hegar dilator easily passed through the cervix of 17 patients in the hyoscine group, but in the case of the control group, the Hegar dilator did not pass through the cervix of 20 patients. The side effects of using hyoscine, such as tachycardia, dry mouth, and hot flashes, had a low prevalence and were not statistically significant. In this study, the authors concluded that the vaginal use of hyoscine increases its local effects on the parasympathetic system, but it is ineffective on menopausal women, which can be explained by the histological changes of the cervix (17). In a multicenter study conducted by Elkins *et al.* in 2017, the effects of using misoprostol before hysteroscopy were investigated in nulliparous, premenopausal and menopausal women, where 149 patients referred for hysteroscopy in Dutch hospitals were investigated. Seventy-four people in the misoprostol group received two doses of misoprostol 800 micrograms orally 24 and 12 hours before the operation. Then, hysteroscopy was performed without using a tenaculum and speculum using a 5.5 mm hysteroscope and the pain level of the patients was evaluated three times. Two times were before hysteroscopy while receiving misoprostol and one time was immediately after hysteroscopy. The side effects of misoprostol, including nausea, diarrhea, abdominal pain, spotting, and gastrointestinal side effects were also investigated, which had a prevalence of 24%. In this study, the amount of hysteroscopy pain was reduced in premenopausal women, but it was not effective in menopausal women (18).

A double-blind study in France divided 48 patients of childbearing age undergoing hysteroscopy for submucosal fibroid or polyp into four groups and received 200, 400, or 800 µg vaginal misoprostol 4 hours before the procedure. The diameter of the hysteroscope is 10 mm, and the ease of entering the hysteroscope or Hegar dilator (3-8 mm) and the ease of dilating the cervix up to No. 10 of the Hegar dilator, as well as the patient's pain level, were checked. In the mentioned study, the participants who used misoprostol had more pain before the operation, and the duration of cervical dilatation and the ease of entering the hysteroscope and Hegar dilator were similar in the control groups with misoprostol. This study showed that the time interval of misoprostol administration is an important variable. In order to determine the optimal dose, it is necessary to allow more time for the effect of the drug.

In previous pharmacological studies, it was shown that the maximum bioavailability of vaginal misoprostol was 80±27 minutes, and then remains constant for several hours. In the mentioned study, the authors concluded that although the use of vaginal or oral misoprostol about 12 hours before the operation in previous studies made hysteroscopy easier, the incidence of misoprostol complications was about 25% and that hysteroscopy is an outpatient procedure, so every Surgery should calculate the risk-benefit ratio of using misoprostol according to the conditions (19).

Another double-blind study conducted by Ahmad in 2011 in Egypt tested a single-dose regimen of 200 vaginal

misoprostol 3 hours before surgery on 150 patients. 200 µg misoprostol tablets were moistened with saline solution and then placed in the posterior fornix. The ease of 4mm hysteroscope insertion, the time required to start the procedure, the patient's pain, and the side effects of misoprostol and hysteroscopy were evaluated in both misoprostol and control groups. This study showed that the misoprostol was associated with transient side-effects, hysteroscope insertion was easier in the misoprostol group, the duration of the operation was shorter, and the patient experienced less pain. The side effects of misoprostol were found to be about 10% and there were similar side effects in the control group. Increasing the administration interval of misoprostol to more than 3 hours or increasing the dose to more than 400 micrograms increased the side effects of misoprostol, but did not improve the effects of misoprostol on the cervix (20).

In a double-blind study conducted by Issat in Turkey in 2015, the effects of using intravenous hyoscine in pregnant women in the active phase of labor were investigated. And a dose of 20 mg of hyoscine was administered intravenously. The results showed that the delivery occurred 57 minutes earlier and had no significant effects on the mother or the baby (21).

In the present study, misoprostol was inserted vaginally 3 hours before surgery and its effect was compared with the effect of hyoscine. Although there are complications such as abdominal pain in the misoprostol group as a drug complication, they are few and self-limiting. If abdominal pain exists before hysteroscopy and is accompanied by other symptoms such as nausea, diarrhea and vomiting, it is considered related to misoprostol, and if it occurs after hysteroscopy, it is considered to be related to hysteroscopy complications. Previous studies have shown that the use of misoprostol and hyoscine on the menopause cervix is ineffective, and this problem was attributed to the histological changes of the cervix tissue (13). In the current study, there were a total of 5 menopausal women who were in two groups of misoprostol and hyoscine, and only one of them had a history of one natural childbirth (in the hyoscine group). None of these 5 cases had serious hysteroscopy complications, but in one of them (from the misoprostol group), a bougie was used as a cervical dilator. The use of hyoscine and its effects on the menopause cervix require more studies with a large sample size. In this study, the overall prevalence of complications of hyoscine and misoprostol were 24% and 32%, respectively, which is almost similar to previous studies.

Further studies are needed in this population to compare the effect of hyoscine with misoprostol on multiparous cervix. Currently, with the advancement of technology and the construction of small hysteroscopes, which places this operation in the category of minimally invasive and outpatient surgeries, it is easy to use drugs such as hyoscine to prepare the cervix before hysteroscopy.

This study was conducted on a uniform population with a

similar age and parity distribution, which is one of the strengths of our study. Most of the women were referred from the infertility department and entered the study after confirming the indication of hysteroscopy by a specialist.

CONCLUSION

Hyoscine can be a suitable drug for preparing the cervix before dilatation and curettage. It will also dilate the cervix more easily. Using vaginal hyoscine before surgical hysteroscopy was capable of reducing the need for cervical dilatation and facilitating surgical hysteroscopy.

REFERENCES

- Al-Fozan H, Firwana B, Al Kadri H, Hassan S, Tulandi T. Preoperative ripening of the cervix before operative hysteroscopy. *Cochrane Database Syst Rev.* 2015; 2015(4). doi:10.1002/14651858.CD005998.pub2.
- Robinson LLL, Cooper NAM, Clark TJ. The role of ambulatory hysteroscopy in reproduction. *J Fam Plan Reprod Heal Care.* 2013; 39(2). doi: 10.1136/jfprhc-2012-100375Jivraj.
- Critchley HOD, Warner P, Lee AJ, Brechin S, Guise J, Graham B. Evaluation of abnormal uterine bleeding: Comparison of three outpatient procedures within cohorts defined by age and menopausal status. *Health Technol Assess (Rockv).* 2004; 8(34). doi:10.3310/hta8340.
- Carneiro MM. What is the role of hysteroscopic surgery in the management of female infertility? A review of the literature. *Surg Res Pract.* 2014; 2014: 105412.
- Abdelhakim AM, Gadallah AH, Abbas AM. Efficacy and safety of oral vs vaginal misoprostol for cervical priming before hysteroscopy: A systematic review and meta-analysis. *Eur J Obstet Gynecol Reprod Biol.* 2019; 243:111-9.
- Song T, Kim MK, Kim ML, Jung YW, Yoon BS, Seong SJ. Effectiveness of different routes of misoprostol administration before operative hysteroscopy: a randomized, controlled trial. *Fertil Steril.* 2014; 102(2): 519-524.
- Saha M, Chakraborty A, Chattopadhyay S, Saha S, Paul J, Das A. Effect of misoprostol for cervical priming before gynecological procedures on nonpregnant premenopausal women. *J Nat Sci Biol Med.* 2015; 6(Suppl 1): S123.
- Hua Y, Zhang W, Hu X, Yang A, Zhu X. The use of misoprostol for cervical priming prior to hysteroscopy: a systematic review and analysis. *Drug design, Drug Des Devel Ther.* 2016; 10:2789.
- Gkrozou F, Koliopoulos G, Vrekoussis T, et al. A systematic review and meta-analysis of randomized studies comparing misoprostol versus placebo for cervical ripening prior to hysteroscopy. *Eur J Obstet Gynecol Reprod Biol.* 2011; 158(1):17-23.
- Mohammadian S, Tavana A, Tavana S, Mohammadian A, Fallahian M. Cervical Priming by Misoprostol before Diagnostic Dilatation and Curettage: A Randomized Clinical Trial. *J Reprod Infertil.* 2015; 16(3):162-166.
- Gilstrap M, Sciscione A, editors. *Induction of labor—Pharmacology methods.* Seminars in perinatology; 2015: Elsevier.
- Bakker R, Pierce S, Myers D. The role of prostaglandins E1 and E2, dinoprostone, and misoprostol in cervical ripening and the induction of labor: a mechanistic approach. *Archives of gynecology and obstetrics.* 2017; 296(2): 167-79.
- Chatsis V, Frey N. *Misoprostol for Cervical Ripening and Induction of Labour: A Review of Clinical Effectiveness, Cost-Effectiveness and Guidelines.* 2018.
- Lam CJ, Imudia AN. Novel uterine closure technique to prevent intrauterine adhesions. *Fertil Steril.* 2019; 112(3). doi:10.1016/j.fertnstert.2019.07.1318.
- Kumaresan S, Perumal D. A clinical study of diagnostic hysteroscopy in abnormal uterine bleeding and its histopathological correlation. *Int J Reprod Contraception, Obstet Gynecol.* 2018; 7(2). doi:10.18203/2320-1770.ijrcog20180057.
- Souza CAB, Genro VK, Tarrasconi D V., Oppermann MLR, Cunha Filho JSL. Diclofenac versus a combination of hyoscine and diclofenac for outpatient hysteroscopy: A placebo controlled randomized clinical trial. *Eur J Obstet Gynecol Reprod Biol.* 2020; 247. doi:10.1016/j.ejogrb.2020.01.030.
- Hadadian S, Fallahian M. Assessing the efficacy of vaginal hyoscine butyl bromide on cervical ripening prior to intrauterine procedures: A double-blinded clinical trial. *Int J Reprod Biomed.* 2016; 14(11). doi:10.29252/ijrm.14.11.709.
- Elkins N, Hunt J, Scott KM. Neurogenic Pelvic Pain. *Phys Med Rehabil Clin N Am.* 2017; 28(3). doi:10.1016/j.pmr.2017.03.007.
- Cicinelli E. Diagnostic minihysteroscopy with vaginoscopic approach: Rationale and advantages. *J Minim Invasive Gynecol.* 2005; 12(5).
- Ahmad G, Attarbashi S, O'Flynn H, Watson AJS. Pain relief in office gynaecology: A systematic review and meta-analysis. *Eur J Obstet Gynecol Reprod Biol.* 2011; 155(1). doi:10.1016/j.ejogrb.2010.11.018.
- Issat T, Beta J, Nowicka MA, Maciejewski T, Jakimiuk AJ. A Randomized, Single Blind, Placebo-Controlled Trial for the Pain Reduction During the Outpatient Hysteroscopy After Ketoprofen or Intravaginal Misoprostol. *J Minim Invasive Gynecol.* 2014; 21(5). doi:10.1016/j.jmig.2014.04.006