

## Administration of Misoprostol versus Hyoscine Butylbromide Prior to Hysteroscopy as a Cervical Priming Agent

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### ABSTRACT

**Background:** A treatment called hysteroscopy is used to examine and treat a number of gynecological issues.

**Objective:** To compare misoprostol versus hyoscine butylbromide as a cervical priming agent in patients underlying hysteroscopy.

**Patients and methods:** This randomized controlled clinical trial was carried out on 82 participants who were scheduled for operative hysteroscopy at Obstetrics and Gynecology Department, Zagazig University Hospitals. All participants in our study were divided randomly for cervical ripening prior to hysteroscopy into two groups; Group (A): Misoprostol was administrated (n=41), Group (B): Hyoscine butylbromide was administrated (n= 41). All patients were subjected to full history taking, routine clinical examination and laboratory investigations. The cervical priming agent was administrated 2 hours before the scheduled hysteroscopy.

**Results:** There was no statistically significant difference between the two studied groups regarding age, height, weight, BMI, the mean parity, previous history of CS, history of abortion, the diagnosis, the procedure time, and anesthesia. Cervical dilatation width was significantly higher among group A while cervical dilatation time was significantly lower among group A than group B. The self-reported pain was significantly higher among group A than group B. Nearly 44% of the participants of group A needed postoperative analgesia administration, while only 12.2% of group B needed postoperative analgesia administration.

**Conclusion:** Hyoscine butylbromide is as effective as misoprostol as a cervical priming agent in patients undergoing operative hysteroscopy with less need for postoperative pain medication and postoperative complications.

**Keywords:** Hysteroscopy, Misoprostol, Hyoscine Butylbromide, Cervical Priming Agent.

### INTRODUCTION

A treatment called hysteroscopy is used to diagnose and treat a variety of gynecological issues, most notably irregular menstruation, endometrial biopsy, polyp removal, fibroid removal, and infertility (1). Hysteroscopy has a number of advantages over other procedures since it is minimally invasive, cheap, easy to perform, and well-liked by patients. As a result, it is regarded as the absolute benchmark for both diagnosis and therapy. A slender telescope-like instrument with a tiny camera called a hysteroscope is inserted through the cervix to examine the uterus' inside (2).

Cervical dilatation is necessary for bigger tools used in surgery but is not necessary for diagnostic mini-hysteroscopes with tiny instrument diameters less than 5 mm (3).

Misoprostol (PG E1) usage prior to surgical hysteroscopy allowed for simple cervical dilatation and fewer difficulties, but it also comes with a long list of adverse effects, including fever, diarrhoea, nausea, and stomach cramps, in addition to being costly (4).

Hyoscine butylbromide has a peripheral anticholinergic effect that causes a spasmolytic effect on the smooth muscles of the female genital tract. It has demonstrated its effectiveness by shortening the first stage of labour by facilitating cervical dilatation. It also has another benefit in that it lessens pain and muscle cramping with fewer complications, is readily available, and is inexpensive (5).

Therefore, this study aimed to compare misoprostol versus hyoscine butylbromide as a cervical

priming agent in patients underlying operative hysteroscopy.

### PATIENTS AND METHODS

This randomized controlled clinical trial (RCT) was carried out on 82 participants who were scheduled for operative hysteroscopy at Obstetrics and Gynecology Department, Zagazig University Hospitals during of period from February 2022 to February 2023.

**Inclusion criteria:** Females of reproductive age between 18-50 years who were scheduled for operative hysteroscopy.

**Exclusion criteria:** Post-menopausal patients, incompetent cervix, stenotic cervix, previous history of cervical surgery, patients suffering from asthma, hypertension, myasthenia gravis and glaucoma were excluded from the study.

### Selected patients were divided into two groups:

**Group (1):** included 41 patients who took misoprostol 400 mcg oral 2 hours before the hysteroscopy. **Group (2):** included 41 patients who took hyoscine butylbromide 20 mg/ml 1 cm intramuscular 2 hours before the hysteroscopy.

A thorough history was gathered, which included a full examination of the patient's complaint and any symptoms that needed treatment at the time. It also included information about any known sexually transmitted diseases and prior gynecological illnesses, and determining the risk of contracting HIV and hepatitis B. The obstetric history, included parity, the

number of children, pregnancy details, delivery mode, birth weights, complications, miscarriages, and terminations, as well as any postpartum issues including depression and subfertility. The regularity of the cycle and its lengths, dysmenorrhea and its main or secondary types, the timing of the previous menstrual period, and the presence or absence of intermenstrual bleeding were all part of the menstrual history.

Each case underwent a general examination that included taking their vital signs, determining their level of awareness and sickness, looking at their posture, attitude, gait, and BMI. Checking for rash, bruises, pallor, jaundice, edema, and surgical scars on the head, neck, chest, abdomen, upper limbs, and lower limbs. Palpating the abdomen for ascites, peritonitis, anomalies of the umbilical cord, and abnormal masses such as enlarged liver, spleen, uterus, bladder, and lymph nodes.

#### **Local clinical examination:**

- a) Examining the perineum to evaluate the external genitalia, urethra, and rectum. Basic vulvar anatomy, symmetry, and any swelling, bruising, erythema, rashes, lesions, discharge, or growths were all examined.
- b) A pelvic exam to check for masses and pain.
- c) Bimanual examination: The dominant hand's fingers are slowly introduced into the vagina to locate and assess the cervix. Tenderness in the cervical motion was induced. Pushing the uterus between the hands with the non-dominant hand allowed us to feel its size, location, and examination of both adnexa for masses and pain.
- d) Cusco's speculum: This instrument was greased (with lubricating jelly) and put into the vagina to examine the cervix. Colour, lesions, ulcers, abnormal lumps, discharge, blood, and whether the external os seemed open or closed were all checked on the cervix.

#### **Laboratory investigations:**

Participants underwent routine preoperative laboratory examinations, including complete blood counts, complete urine analyses, liver function tests, kidney function tests, fasting blood sugar levels, and testing for hepatitis markers.

#### **Ultrasonographic Examination:**

A convex probe was used for the preoperative abdominal ultrasound examination and a vaginal probe for the transvaginal ultrasound. to determine the lesion's location and examine the health of the genital tract.

#### **I. Administration of the cervical priming agent: -**

In group A: Misoprostol 400 mcg were taken orally 2 hours before the hysteroscopy. In group B: Hyoscine

butylbromide 20 mg/ml intramuscular was administered 2 hours before the hysteroscopy

#### **II. Intervention (intraoperative steps):**

Elective surgery for hysteroscopy was anticipated. The same surgeon performed each operation. Spinal anesthesia was administered to all patients. With bipolar surgical hysteroscopy, isotonic solution such as normal saline was used as the fluid distension medium, while with monopolar surgical hysteroscopy, hypotonic solution such as glycine 1.5% was employed. By evaluating the opening of the cervical canal using the reversed dilator method and Hegar dilators, as follows, the effectiveness of the cervical priming agent was evaluated: The largest dilator that went through the cervical canal was utilised as the outcome parameter after using Hegar number 8 first, and smaller dilators were used in succession if the larger dilator didn't pass through the cervical canal. The length of the procedure and any complications during or after it were noted.

#### **III. Postoperative care:**

Monitoring the patient's vital signs, airway patency, neurologic state, pain management, fluid and electrolyte balance assessment, maintenance, and detailed reporting of the patient's status to the receiving nurse on the unit as well as the patient's family were all part of the postoperative care. Monitoring and evaluation of vaginal bleeding, discomfort, and potential medication adverse effects. keeping an eye out for any indications of potential postoperative problems.

#### **IV. Outcome measures:**

Main outcomes included cervical dilatation width and cervical dilatation time. Secondary outcomes included procedure time and postoperative pain and need of analgesics.

#### **Ethical Consideration:**

**The Faculty of Medicine at Zagazig University gave its ethical approval for this investigation (IRB: # 9176 at 19/12/2021). After receiving all the facts, every patient gave her signed approval. The Helsinki Declaration was upheld throughout the course of the investigation.**

#### **Statistical analysis**

SPSS version 20.0 was used to analyse the data. Quantitative data were grouped and represented by mean  $\pm$  standard deviation (SD), whereas qualitative data were represented as numbers and percentages. P value less than 0.05 was considered significant.

#### **RESULTS**

There was no statistically significant difference between the two studied groups regarding age, height, weight, and BMI (**Table 1**).

**Table (1): Basic characteristics of the two studied groups**

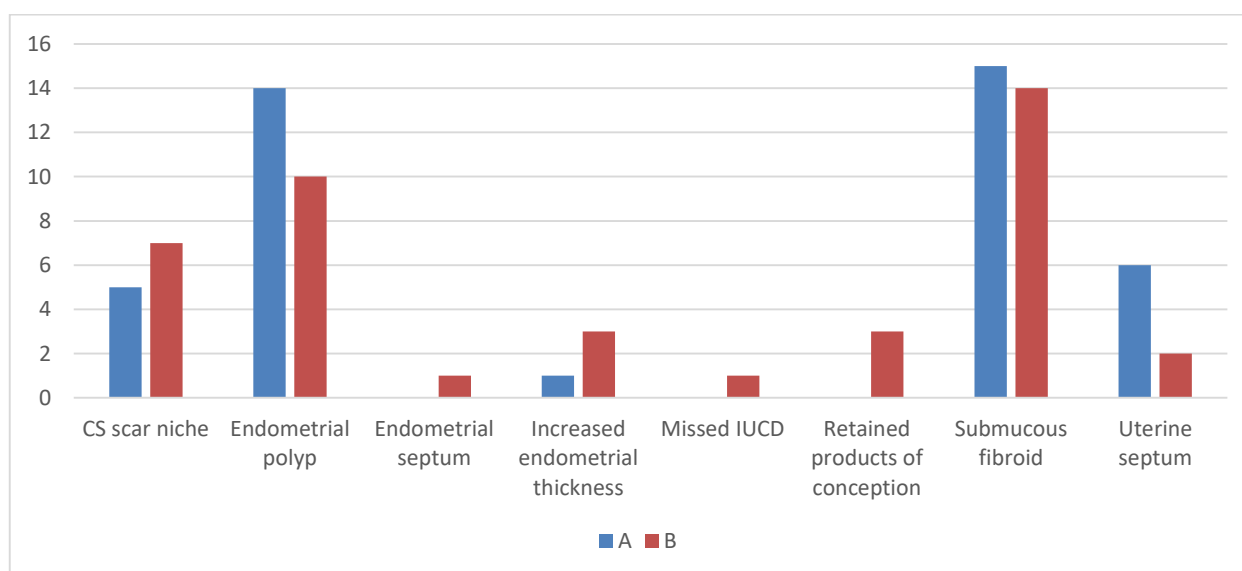
Variable		Group A n= 41	Group B n= 41	P value
Age (years)	Mean ± SD	29.3± 6.9	29.1± 6.5	0.895
Height	Mean ± SD	164.3± 7.3	164.4± 7.3	0.928
Weight	Mean ± SD	78.0 ± 13.8	74.1 ± 12.5	0.531
BMI	Mean ± SD	28.1 ± 4.7	27.5 ± 4.9	0.566

There was no significant difference between both groups regarding parity, previous CS, and previous abortion (Table 2).

**Table (2): Obstetric history among the two studied groups**

Variable		Group A n= 41	Group B n= 41	P value
Parity	Mean ± SD	1 ± 1.1	1.1 ± 1.2	0.566
Previous CS	No, n (%)	26 (63.3)	23 (56)	0.676
	Once, n (%)	9 (22)	9 (22)	
	> 1, n (%)	6 (14.7)	9 (22)	
Previous abortion	No, n (%)	29 (70.7)	25 (61.0)	0.839
	Once, n (%)	4 (9.8)	8 (19.5)	
	> 1, n (%)	8 (19.5)	8 (19.5)	

Regarding the diagnosis of the participated patients, there was insignificant difference between the 2 groups (Figure 1).



**Figure (1): Diagnosis of the participated groups**

There was no statistically significant difference between both group A and B regarding the procedure and anesthesia (Table 3).

**Table (3): Procedure and anesthesia among the two studied groups**

Variable		Group A n= 41	Group B n= 41	P value
Procedure	Biopsy, n (%)	1 (2.4)	3 (7.3)	0.373
	IUCD removal, n (%)	0 (0)	1 (2.4)	
	Myomectomy, n (%)	15 (36.6)	14 (34.1)	
	Polypectomy, n (%)	14 (34.1)	10 (24.4)	
	Endometrial Resection, n (%)	5 (12.2)	10 (24.4)	
	Septectomy, n (%)	6 (14.6)	3 (7.3)	
Anesthesia	General, n (%)	1 (2.4)	1 (2.4)	1
	Spinal, n (%)	40 (97.6)	40 (97.6)	

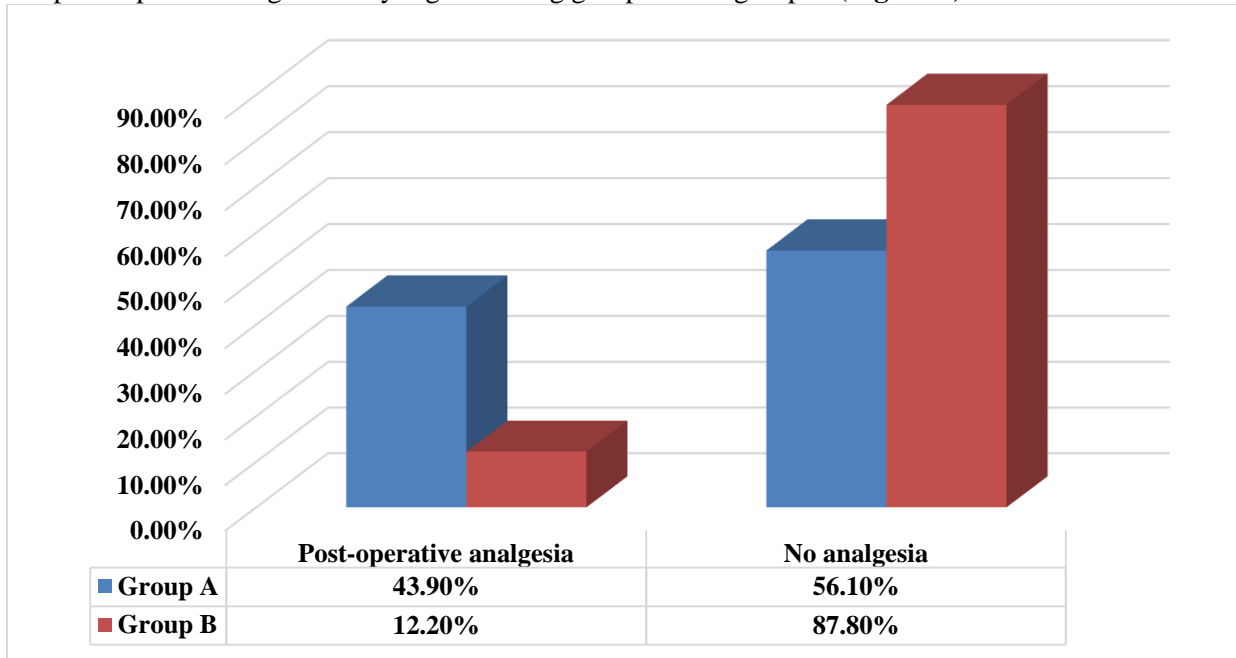
Cervical dilatation width was significantly higher among group A while cervical dilatation time was significantly lower among group A than group B. No significant difference was found among both groups regarding procedure time (Table 4).

**Table (4): Outcome measures among the two studied groups**

Variable		Group A n= 41	Group B n= 41	P value
Cervical dilatation width	Mean ± SD	6.8± 1.1	6.0± 1.1	0.006*
Cervical dilatation time (seconds)	Mean ± SD	29.1 ± 15.2	39.3 ± 13.3	0.002*
Procedure time	Mean ± SD	23.3± 15.8	24.9± 16.0	0.659

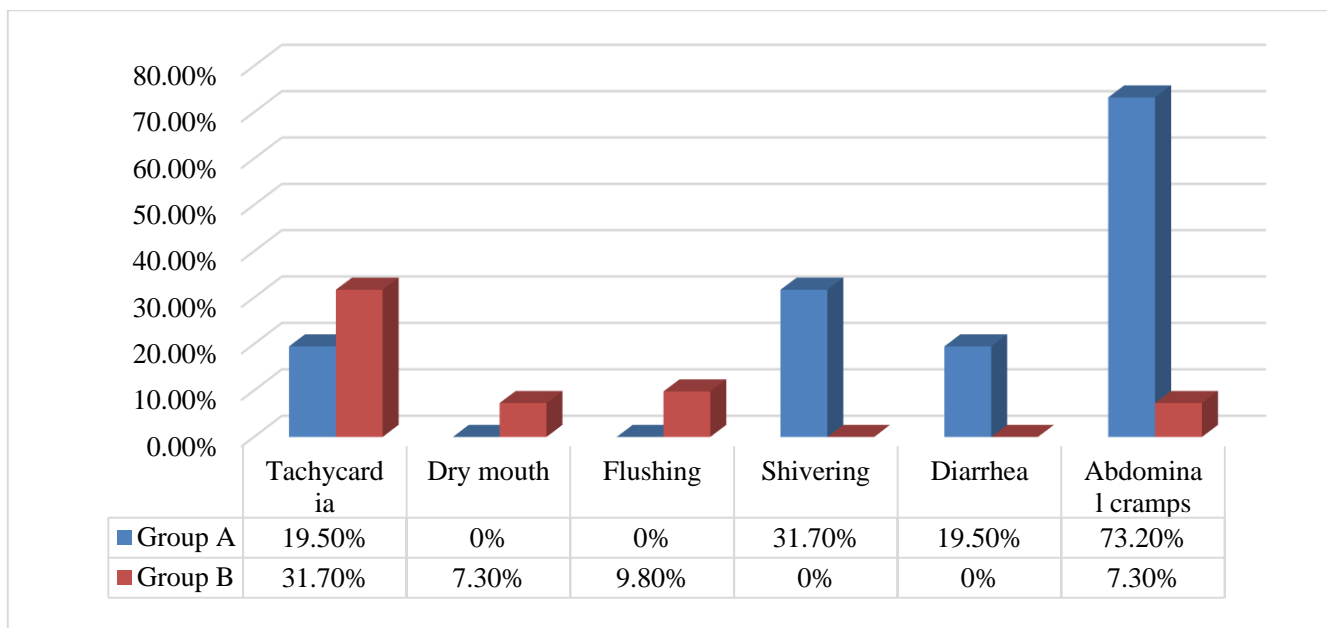
\*: Significant

The self-reported pain was significantly higher among group A than group B (Figure 2).



**Figure (2): Postoperative analgesia administration among the two studied groups**

Shivering, diarrhea and abdominal cramps were significantly higher among group A than group B. While there was no statistically significant difference between both groups regarding tachycardia, dry mouth and flushing (Figure 3).



**Figure (3): Postoperative complications among the two studied groups.**

## DISCUSSION

For diagnostic reasons, mini-hysteroscopes with less than 5 mm tool sizes are available; however, larger instruments for hysteroscopic surgery need that the cervix be dilated with laminaria japonica or mechanical dilators prior to operation. Prostaglandins are frequently used to soften and widen the cervical canal in order to allow the insertion of a hysteroscope (6).

According to **Inácio et al.** (7), misoprostol (prostaglandin E1) usage prior to surgical hysteroscopy has been associated with easier cervical dilatation, a quicker procedure, and fewer operational issues. However, side effects, including nausea, cramping in the stomach, diarrhoea, and fever, limit the medication's efficacy.

HBB, an anticholinergic substance, is known as hyoscine-n-butylbromide. The blood-brain barrier is not crossed by it. By preventing the transmission of neuronal impulses in the abdominal parasympathetic ganglia, HBB has peripheral anticholinergic action (8). HBB has a spasmolytic effect on the smooth muscles of the gastrointestinal, biliary, and urinary tracts as well as the female genital organs, particularly the cervico-uterine plexus, by suppressing cholinergic activity. It has been demonstrated that by promoting cervical dilatation, it can speed up the early stage of labour (9).

Our results cleared that there was no statistically significant difference between the two studied groups regarding age, height, weight, BMI, the mean parity, previous history of CS, history of abortion, the diagnosis, the procedure time, and anesthesia. On the other hand, there was statistically significant difference between the two studied groups regarding cervical dilatation width and cervical dilatation time. Cervical dilatation width was significantly higher among group A while cervical dilatation time was significantly lower among group A than group B.

Several findings were made using the same parameters as our investigation. In the same direction of our results, **Bastu et al.** (10) studied cervical priming before diagnostic operative hysteroscopy in infertile women by a comparison of 2 vaginal misoprostol doses 200 mcg and 400 mcg, vaginally administrated 12 to 15 hours before diagnostic office hysteroscopy and **Moro et al.** (11) studied the effect of antispasmodic drug 10 mg hyoscine-N-butylbromide oral tablets in reducing pain during hysterosalpingo contrast sonography (HyCoSy) in infertile patients. In terms of cervical dilatation breadth and cervical dilatation duration, **Bastu et al.** (10) and **Moro et al.** (11) discovered that there was a statistically significant difference between the groups they investigated.

In agreement with us, **Gokmen et al.** (12) examined the effects of rectal cytotec versus rectal buscopan administration prior to hysteroscopy and discovered no statistically significant differences between the groups they examined in terms of age, height, weight, BMI, mean parity, prior CS history, prior abortion history, diagnosis, procedure time, and anesthesia. Furthermore, they demonstrated a substantial difference in cervical dilatation breadth and time.

In our favour, **Marchand et al.** (9) investigated the effectiveness of hyoscine in pain management during hysteroscopy and showed that there was no statistically significant difference between the hyoscine and placebo group regarding the postoperative VAS score, need for postoperative analgesia, or procedure time.

In our study, the self-reported pain was significantly higher among group A than group B. Nearly forty-four percent of the participants of group A needed postoperative analgesia administration while only 12.2% of group B needed postoperative analgesia administration with significant difference.

The difficulty of inserting the hysteroscope into the internal cervical os, which causes discomfort, is one of the main issues with operational hysteroscopy. Patients might feel pain at various parts of the hysteroscopic process, in particular. There are a number of ways to lessen the discomfort associated with hysteroscopy, both pharmaceutical (such as paracetamol or NSAIDs) and non-pharmacological (such as intracervical block and paracervical block) <sup>(13)</sup>.

Studies suggest that using misoprostol or hyoscine butylbromide before to hysteroscopic surgery may provide a clearer view of the uterine cavity and so shorten the procedure's duration and even lower the risk of complications<sup>(14)</sup>.

Cervical priming and dilation techniques have been developed. Misoprostol is the most researched substance that has shown promise for cervical priming<sup>(10)</sup>.

In line with our findings, **Gokmen et al.** <sup>(12)</sup> investigated the administration of rectal 20 mg hyoscine-n-butyl bromide against rectal 200 mcg misoprostol two hours before to hysteroscopy and discovered that there was less need for analgesia in the HBB group. Although the HBB group experienced reduced postoperative discomfort, there was no change in the other investigated characteristics.

Even when carried out by skilled surgeons utilising an atraumatic approach, the discomfort associated with hysteroscopy remains to be its biggest drawback. Numerous studies have looked into potential pharmaceutical pain management for hysteroscopic procedures. The use of either misoprostol or hyoscine butylbromide resulted in decreased self-reported pain and less postoperative analgesia administration, according to **Riemma et al.** <sup>(15)</sup>.

The work by **Rashwan et al.** <sup>(8)</sup> is innovative since it adds a pharmaceutical agent as an intervention that was previously disregarded. Their research suggests that HBB could be useful in reducing discomfort during hysteroscopic operations. Higher dosages and trials using alternative delivery methods might be useful study perspectives in the future.

In contrast to these studies, **Fernandez et al.** <sup>(16)</sup> examined the use of vaginal misoprostol for cervical ripening prior to operative hysteroscopy in premenopausal women with three dose regimens of misoprostol 200, 400, or 800 mcg misoprostol given vaginally 4 hours before surgery in comparison to a placebo group to evaluate cervical width using Hegar dilators and the time needed for. They discovered no discernible difference between misoprostol delivery and placebo administration. On the other side, misoprostol usage led to an increase in postoperative discomfort. Furthermore, **Healey et al.** <sup>(17)</sup> came to the conclusion that premenopausal women who took oral misoprostol prior to hysteroscopy did not benefit from doing so.

There was a statistically significant difference between the two analysed groups in terms of shivering, diarrhoea, and stomach cramps, which were

postoperative problems among our patients. In comparison to group B, group A experienced considerably more shivering, diarrhoea, and stomach pains. Tachycardia, dry mouth, and flushing were not statistically significantly different between the two groups.

Similar to our research, **Hadadian and Fallahian** <sup>(5)</sup> evaluated the effectiveness of vaginal hyoscine butyl bromide on cervical ripening prior to intrauterine procedures and found that there were fewer side effects such as shivering, diarrhoea, abdominal cramps, and tachycardia. There was a statistically significant difference between the tested groups in terms of diarrhoea, tachycardia, dry mouth, flushing, and abdominal cramps when **Gokmen et al.** <sup>(12)</sup> examined the surgical complications.

Contrary to our findings, the majority of randomised trials investigating the effectiveness of misoprostol in women having hysteroscopy discovered faster surgery times and simpler cervix dilatation. Misoprostol administration was linked to decreased pain in these trials <sup>(18)</sup>.

In contrast, **Jareethum et al.** <sup>(19)</sup> found a statistically significant difference in the levels of tachycardia and flushing among their individuals. Furthermore, **Marchand et al.** <sup>(9)</sup> showed that there aren't many side effects from using hyoscine butylbromide. Shivering, tachycardia, diarrhoea, dry mouth, flushing, and stomach pains were statistically significantly different amongst their study groups.

## CONCLUSION

Hyoscine butylbromide is as effective as misoprostol as a cervical priming agent in patients undergoing operative hysteroscopy regarding the need for pain medication or postoperative complications. The antispasmodic effects of HBB result in cervical dilatation and pain reduction.

We recommend considering hyoscine butylbromide as a golden cervical priming agent in patients undergoing operative hysteroscopy. In addition, further studies must be done to analyze this issue and trials of different routes of administration and higher doses of hyoscine butylbromide may be valuable future study perspectives.

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**Competing interests:** Nil.

## REFERENCES

1. **Bakour S, Jones S, O'Donovan P (2006):** Ambulatory hysteroscopy: evidence-based guide to diagnosis and therapy. *Best Practice & Research Clinical Obstetrics & Gynaecology*, 20(6): 953-975.
2. **Bosteels J, Kasius J, Weyers S et al. (2015):** Hysteroscopy for treating subfertility associated with suspected major uterine cavity abnormalities. *Cochrane Database of Systematic Reviews*, 12(12):CD009461. doi: 10.1002/14651858.CD009461.

3. **Guraslan H, Senturk M, Dogan K et al. (2022):** Diagnostic office hysteroscopy; why is it still painful procedure despite the surgical experience and mini-hysteroscope?. *Journal of Obstetrics and Gynaecology Research*, 48(6): 1418-1425.
4. **Zhuo Z, Yu H, Jiang X (2016):** A systematic review and meta-analysis of randomized controlled trials on the effectiveness of cervical ripening with misoprostol administration before hysteroscopy. *International Journal of Gynecology & Obstetrics*, 132(3): 272-277.
5. **Hadadian S, Fallahian M (2016):** Assessing the efficacy of vaginal hyoscine butyl bromide on cervical ripening prior to intrauterine procedures: A double-blinded clinical trial. *International Journal of Reproductive Biomedicine*, 14(11): 709-12.
6. **Paulo A, Solheiro M, Paulo C (2015):** Is pain better tolerated with mini-hysteroscopy than with conventional device? A systematic review and meta-analysis: hysteroscopy scope size and pain. *Archives of Gynecology and Obstetrics*, 292: 987-994.
7. **Inácio Q, Troncon J, Valério F et al. (2023):** misoprostol administration before hysteroscopy procedures—a retrospective analysis. *Brazilian Journal of Gynecology and Obstetrics*, 44: 1102-1109.
8. **Rashwan A, Alalfy M, Elkomy S et al. (2022):** Diclofenac potassium alone versus diclofenac potassium with hyoscine-N-butyl bromide (HBB) in reduction of pain in women undergoing office hysteroscopy: A double blind randomized, placebo-controlled trial. *The Journal of Obstetrics and Gynecology of India*, 72(1): 340-345.
9. **Marchand G, Kurdi W, Sainz K et al. (2022):** Efficacy of hyoscine in pain management during hysteroscopy: a systematic review and meta-analysis. *Journal of the Turkish German Gynecological Association*, 23(1): 51-56.
10. **Bastu E, Celik C, Nehir A et al. (2013):** Cervical priming before diagnostic operative hysteroscopy in infertile women: a randomized, double-blind, controlled comparison of 2 vaginal misoprostol doses. *International Surgery*, 98(2): 140-144.
11. **Moro F, Selvaggi L, Sagnella F et al. (2012):** Could antispasmodic drug reduce pain during hysterosalpingo-contrast sonography (HyCoSy) in infertile patients? A randomized double-blind clinical trial. *Ultrasound Obstet Gynecol.*, 39(3):260-5.
12. **Gokmen A, Aydin S, Ates S et al. (2022):** Administration of rectal cytotec versus rectal buscopan before hysteroscopy. *Minimally Invasive Therapy & Allied Technologies*, 31(1): 94-98.
13. **O'Flynn H, Murphy L, Ahmad G et al. (2011):** Pain relief in outpatient hysteroscopy: a survey of current UK clinical practice. *European Journal of Obstetrics & Gynecology and Reproductive Biology*, 154(1): 9-15.
14. **Kodama M, Onoue M, Otsuka H et al. (2013):** Efficacy of dienogest in thinning the endometrium before hysteroscopic surgery. *Journal of Minimally Invasive Gynecology*, 20(6): 790-795.
15. **Riemma G, Vitale S, Manchanda R et al. (2022):** The role of hysteroscopy in reproductive surgery: Today and tomorrow. *Journal of Gynecology Obstetrics and Human Reproduction*, 102350. doi: 10.1016/j.jogoh.2022.102350.
16. **Fernandez H, Alby J, Tournoux C et al. (2004):** Vaginal misoprostol for cervical ripening before operative hysteroscopy in pre-menopausal women: a double-blind, placebo-controlled trial with three dose regimens. *Human Reproduction*, 19(7): 1618-1621.
17. **Healey S, Butler B, Kum F et al. (2007):** A randomized trial of oral misoprostol in premenopausal women before hysteroscopy. *Journal of Obstetrics and Gynaecology Canada*, 29(8): 648-652.
18. **Preutthipan S, Herabutya Y (2000):** Vaginal misoprostol for cervical priming before operative hysteroscopy: a randomized controlled trial. *Obstetrics & Gynecology*, 96(6): 890-894.
19. **Jareethum R, Suksompong S, Petyim S et al. (2011):** Efficacy of mefenamic acid and hyoscine for pain relief during saline infusion sonohysterography in infertile women: a double blind randomized controlled trial. *European Journal of Obstetrics & Gynecology and Reproductive Biology*, 155(2): 193-198.