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The Effect of Oral and Vaginal Misoprostol use for Cervical Ripening in Patients Undergoing Office Hysteroscopy

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ABSTRACT

Objective: This study aimed to evaluate the effectiveness of oral and vaginal misoprostol in reducing pain levels in patients undergoing office hysteroscopy.

Methods: The study included 225 patients scheduled for office hysteroscopy. The demographic data of the participants were collected. Using the sealed envelope method, patients were allocated into three groups of 75 each: one group received no misoprostol, the second group received oral misoprostol, and the third group received vaginal misoprostol. Oral and vaginal misoprostol (200 mcg) were administered 1 hour before the procedure. Pain levels were evaluated using visual analogue scale (VAS) scores among the groups.

Results: The pre-procedural VAS scores were significantly higher in patients who received either form of misoprostol than in those who did not receive it ($p<0.01$). The procedure duration was notably shorter for the groups receiving misoprostol ($p<0.05$). Post-procedural VAS scores were elevated in the non-misoprostol group in contrast to the misoprostol groups, with the vaginal misoprostol group showing higher scores than the oral group ($p<0.05$).

Conclusion: Our findings indicate that both vaginal and oral misoprostol administered before diagnostic hysteroscopy reduce pain and shorten the procedure duration. Further studies are necessary to determine the optimal dosage and timing for minimizing side effects while maximizing efficacy.

Keywords: Misoprostol, hysteroscopy, servical ripening

INTRODUCTION

Hysteroscopy is a minimally invasive technique used to diagnose and treat different uterine conditions, including endometrial polyps, fibroids, and uterine anomalies. During the procedure, complications such as cervical laceration, pain, excessive bleeding, infection, and uterine perforation can occur (1-3). These risks can be mitigated by preprocedural cervical ripening. Misoprostol, which is known for its cervical ripening properties, can be used for this purpose (4-6).

This study aimed to assess the effects of misoprostol on cervical ripening and its potential to reduce complications during office hysteroscopy. The impact on pain levels was assessed using the visual analogue scale (VAS).

METHODS

This randomized, controlled, single-blind, prospective study was conducted between May and September 2019 at the Health Sciences University Türkiye, Gaziosmanpaşa Taksim Training and Research Hospital. The study included 225 patients with various gynecological complaints who underwent office hysteroscopy. The Taksim Training and Research Hospital Clinical Research Ethics Committee approval was obtained (approval no: 54, date: 08.05.2019). All participants provided informed consent. The study groups were determined using the sealed envelope method, and all procedures were conducted by a single operator who was unaware of the administration of misoprostol.

Demographic data, such as age, parity, cervical length, weight, height, delivery method, procedure duration, and hysteroscopy

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indication, were recorded. The participants were divided into three groups: no misoprostol, oral misoprostol, and vaginal misoprostol, with 75 patients in each group. Then, misoprostol (200 mcg) was administered 1 h before the procedure.

Transvaginal ultrasonography was performed using a Mindray DC-7 series ultrasound machine. Diagnostic office hysteroscopies were performed using an Olympus CV-170 series hysteroscope. Procedures were ideally scheduled for premenopausal patients postmenstruation and for menopausal patients during amenorrhea. The procedure began with the patient in the dorsal lithotomy position, using a no-touch technique to traverse the cervical canal. The uterine cavity was distended using an isotonic solution at an intrauterine pressure of 80 mmHg.

Inclusion criteria comprised patients aged 18-80 years with indications for office hysteroscopy, such as abnormal uterine bleeding, infertility, postmenopausal bleeding, and increased endometrial thickness. The exclusion criteria were age under 18 years, suspected pregnancy, active infection, severe bleeding, advanced malignancy, current intrauterine device use, cervical stenosis, vaginal septum, and uterine anomaly.

Statistical Analysis

Data analysis was conducted using SPSS software version 15 for Mac-iOS. Descriptive statistics are provided for categorical and numerical variables. For numerical variables, the mean, median, and standard deviation were used, whereas frequency and percentage were used for categorical variables. Homogeneity was assessed using the Levene test, and the Shapiro-Wilk test was used to check for normal distribution of continuous variables. One-way ANOVA and Kruskal-Wallis tests were used for group comparisons based on distribution. Pearson's chi-square test was used for categorical variables. p-value less than 0.05 was considered statistically significant.

RESULTS

Table 1 presents the demographic data of the patients and comparisons according to the administration route of misoprostol, which did not reveal any statistically significant differences between groups.

When we compared the delivery methods according to the administration route of misoprostol, there was no statistically significant difference between groups ($p>0.05$) (Table 2). Indications for hysteroscopy included endometrial polyps (54.7%), abnormal uterine bleeding (25.3%), submucosal fibroids (6.2%), infertility (4.4%), postmenopausal bleeding (4.4%), amenorrhea (3.6%), and others (0.4%) (Table 3).

Cervical canal passage time was markedly extended in the non-misoprostol group compared with the vaginal and oral groups ($p<0.05$), with no notable variation among the latter two ($p>0.05$) (Table 4).

VAS scores post-procedure were higher in the non-misoprostol group than in the misoprostol group, with higher scores in the vaginal group than in the oral group ($p<0.05$) (Table 4). Pre-procedural VAS scores were higher in patients receiving misoprostol than in those who did not ($p<0.01$), with no notable difference among the vaginal and oral groups ($p>0.05$) (Table 5).

Table 1. Comparison of demographic characteristics according to the route of misoprostol administration

Misoprostol	Absent (n=75) Mean ± SD	Vaginal (n=75) Mean ± SD	Oral (n=75) Mean ± SD	p-value
Age(years)	42±9.40	41.25±8.50	42.19±8.70	0.793
Parity	2.63±1.73	2.35±1.16	2.91±1.83	0.105
Cervical length (mm)	32.32±5.74	31.49±5.25	30.36±7.72	0.104
Body mass index	28.14±5.49	28.68±3.76	29.31±4.78	0.320

One-way ANOVA, SD: standard deviation

Tablo 2. Comparison of delivery methods according to the route of administration of misoprostol

			Misoprostol		
		Absent Frequency(%)	Vaginal Frequency(%)	Oral Frequency(%)	p-value
Delivery Method	Normal vaginal delivery	37 (49.3)	41 (54.7)	41 (54.7)	0.980
	Normal vaginal Delivery+C/ Section	13 (17.3)	10 (13.3)	11 (14.7)	0.980
	Nulliparous	18 (24)	17 (22.7)	18 (24)	0.980
	C/Section	7 (9.3)	7(9.3)	5 (6.7)	0.980
	Chi-square test				

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Table 3. Indications for hysteroscopy

Indications	Frequency(%)
Endometrial Polyp	123 (54.7)
Abnormal Uterine Bleeding	57 (25.3)
Submucosal Fibroid	14 (6.2)
Infertility	10(4.4)
Postmenopausal Bleeding	10 (4.4)
Amenorrhea	8 (3.6)
Bicornuate Uterus	1 (0.4)
Habitual Abortion	1 (0.4)
Non-visible Intrauterine Device	1(0.4)

When cervical length, cervical canal passage time, and postoperative VAS score were evaluated according to the delivery method in the groups in which no misoprostol was administered, oral misoprostol was administered, and vaginal misoprostol was administered, no statistically significant differences were found between the delivery methods for any of the three parameters (p>0.05) (Table 6).

DISCUSSION

Misoprostol is an effective treatment for cervical ripening. Our study demonstrated that administering vaginal or oral misoprostol

Table 4. Evaluation of postprocedural VAS, cervical length, and passage time through the cervix according to the administration route of misoprostol

Misoprostol				
	Absent	**Vaginal**	**Oral**	**p-value**
Cervical length (mm) Median (min-max)	30(20-55)	30(23-45)	30(17-45)	p1,p2,p3=0.277
Cervical canal passage Time (sec) Median (min-max)	40(8-130)	10(1-60)	10(3-65)	p2=1, p1,p3=0.001
Postoperative VAS Score Median (min-max)	4(2-8)	2(0-8)	1(0-7)	p1,p2,p3=0.001

Kruskal-Wallis testi, Min: minimum, Max: maximum, P1: vaginal absent, P2: vaginal oral, P3: oral absent, VAS: visual analogue scale

Table 5. Preoperative VAS scores before office hysteroscopy

Preoperative VAS Score	Absent	Vaginal	Oral	p-value
Median(min-max)	0(0-0)	0(0-6)	0(0-4)	p1, p2=0.001, p3=0.360

Kruskal-Wallis testi, Min: minimum, Max: maximum, P1: vaginal absent, P2: vaginal oral, P3: oral absent, VAS: visual analogue scale

Table 6. Evaluation of VAS, cervical length, and cervical passage time based on the method of misoprostol administration and delivery mode

Misoprostol		Normal vaginal delivery	Normal vaginal delivery+C/Section	Nulliparous	C/Section	p-value
Absent	Cervical lenght(mm) Median(min-max)	30(20-42)	32(27-49)	31.5(25-42)	37(30-55)	0.058
	Cervical canal passage time(sec) Median(min-max)	40(8-115)	45(15-130)	40(10-128)	55(18-130)	0.058
	Postoperative VAS score Median(min-max)	4(2-7)	6(2-7)	5,5(2-8)	5(2-8)	1
Oral	Cervical lenght(mm) Median(min-max)	30(20-45)	28(17-42)	31(25-40)	35(31-37)	0.940
	Cervical canal passage time(sec) Median(min-max)	8(3-65)	10(5-15)	10(6-60)	13(7-15)	0.241
	Postoperative VAS score Median(min-max)	1(0-6)	3(0-5)	1(0-7)	2(0-5)	0.194
Vaginal	Cervical lenght(mm) Median(min-max)	30(23-43)	32.5(25-42)	30(24-35)	30(23-45)	0.084
	Cervical canal passage time(sec) Median(min-max)	9(1-60)	11(7-30)	12(5-19)	9(7-13)	0.083
	Postoperative VAS score Median(min-max)	2(0-7)	2.5(1-8)	2(0-6)	3(2-7)	0.474

Kruskal-Wallis testi, Min: minimum, Max: maximum, VAS: visual analogue scale

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before diagnostic hysteroscopy lessened the pain associated with the procedure and also reduced the time required for completion.

In a 2017 study by Tasma et al. (7), the impact of misoprostol on pain during diagnostic hysteroscopy was assessed in 149 nulliparous premenopausal and postmenopausal women, with 74 receiving misoprostol and 75 in the placebo group. The misoprostol group received 400 mcg of oral misoprostol 24 hours before and 12 hours before the office hysteroscopy. Pain levels were evaluated using VAS scores in the misoprostol and placebo groups post-procedure. The study revealed a considerable decrease in pain in premenopausal women who received misoprostol compared with the placebo group ($p<0.05$). However, for postmenopausal women, no significant difference in VAS scores was observed between the misoprostol and placebo groups ($p>0.05$). Based on these findings, the authors recommended the use of misoprostol in premenopausal women because of its efficacy in reducing procedural pain, but cautioned against its use in postmenopausal women because of its ineffectiveness and potential side effects (7). Our findings on the effect of misoprostol on pain are consistent with those of Tasma et al. (7), although our limited postmenopausal sample size meant that the effect of misoprostol on this subgroup could not be statistically validated.

Fabiana et al. (2018) examined the impact of misoprostol on pain during diagnostic hysteroscopy in 158 postmenopausal women, with 79 receiving misoprostol and 79 receiving placebo. Participants in the misoprostol group were administered 200 mcg oral misoprostol 6 hours prior to hysteroscopy. VAS scores were used to measure pain in both groups after the procedure. The study observed no notable variation in VAS scores among the groups receiving misoprostol and placebo. in postmenopausal women ($p>0.05$). Furthermore, no difference in procedure duration was noted, although the misoprostol group experienced higher rates of side effects such as diarrhea and bleeding. The study concluded that misoprostol should not be recommended for postmenopausal women because of its ineffectiveness in reducing pain and the increased risk of side effects (8). The difference between our study and Fabiana's study might be attributed to the fact that their study included only postmenopausal women.

In 2008, da Costa et al. (9) investigated the impact of misoprostol on procedure duration and pain during diagnostic hysteroscopy in 120 postmenopausal women, with 60 women receiving oral or vaginal msoprostol and 60 women receiving placebo. Participants in the misoprostol group received misoprostol before the office hysteroscopy, and cervical passage time was measured during the procedure. The study reported that those who received misoprostol experienced significantly lower pain levels compared with the group receiving plasebo ($p<0.05$), with no significant difference in pain levels between the different misoprostol groups ($p>0.05$). The researchers concluded that misoprostol administration before office hysteroscopy effectively reduced pain severity in postmenopausal women (9). Our findings on misoprostol's effect on pain levels were in line with those of da Costa et al. (9)

Ngai et al.'s (10) 2001 study focused on the effect of misoprostol on procedure duration in diagnostic hysteroscopy among 34 postmenopausal women, with 18 in the 400 mcg oral misoprostol group and 16 in the placebo group. The group receiving misoprostol received 400 mcg of the drug 12 hours before the procedure. The study found no notable difference in procedure duration between the misoprostol and placebo groups ($p>0.05$). The authors concluded that preprocedural administration of misoprostol did not significantly affect cervical ripening in postmenopausal women (10). Our study's findings on procedure duration differed from those of Ngai et al. (10) possibly because of the extended administration time of 12 hours before the procedure and the exclusive selection of postmenopausal women as participants.

In 2008, Singh et al. (10) explored the effect of misoprostol on pain during diagnostic hysteroscopy in 100 women and divided them into a misoprostol group of 50 and a placebo group of 50. Participants assigned to the misoprostol group received 400 mcg vaginal misoprostol 6 and 4 hours prior to hysteroscopy. Pain levels were evaluated using VAS scores in both groups after the procedure. The study found that misoprostol recipients experienced significantly lower pain levels compared to those in the placebo group ($p<0.05$). The authors concluded that using misoprostol before office hysteroscopy effectively reduced pain (11). Our findings regarding the effect of misoprostol on pain were in agreement with those of Singh et al. (10).

Batukan et al. (12) investigated the effect of misoprostol on the procedure duration during diagnostic hysteroscopy in 77 premenopausal women, with 39 in the group receiving oral misoprostol and 38 in the group receiving vaginal misoprostol. Participants received 400 mcg of oral or vaginal misoprostol 6 and 4 h prior to hysteroscopy, and cervical passage time was recorded. The study reported that vaginal misoprostol resulted in significantly shorter procedure durations than the oral route ($p<0.05$). The researchers determined that vaginal administration of misoprostol was more effective for cervical ripening than oral administration in premenopausal women (12). Our findings on the effect of oral misoprostol on the procedure duration differed from those of Batukan et al. (12), potentially due to variations in the dosage and timing of drug administration.

In 2008, Waddell et al. (13) studied the effectiveness of misoprostol on pain during diagnostic hysteroscopy in 101 women: 50 in the vaginal misoprostol group and 51 in the placebo group. Participants in the misoprostol group received 400 mcg vaginal misoprostol 24 and 12 h before the hysteroscopy. Pain levels were measured using VAS scores in both groups post-procedure. The study found that misoprostol recipients experienced significantly lower pain levels than the placebo group ($p<0.05$). However, the misoprostol group experienced cramps in the pelvic region. The researchers recommended the use of misoprostol for office hysteroscopy because of its ability to reduce pain (13). Our findings on vaginal misoprostol's effect on pain were consistent with those of Waddell et al. (13).

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Bastu et al. (14) examined the effect of misoprostol on pain during diagnostic hysteroscopy in 60 infertile women, with 20 in the 200 mcg misoprostol group, 20 in the 400 mcg misoprostol group, and 20 in the placebo group. Participants in the misoprostol group were administered vaginal misoprostol 12 hours before the hysteroscopy. Pain levels using VAS scores and procedure duration were assessed in the misoprostol and placebo groups post-procedure. The study reported that misoprostol recipients had significantly lower pain levels and shorter procedure durations compared with the placebo group ($p<0.05$), with no significant differences observed between the different dosage groups ($p>0.05$). The researchers concluded that vaginal misoprostol before office hysteroscopy effectively reduces pain and recommended a 200 mcg dose (14). Our findings on the effects of vaginal misoprostol on pain and procedure duration were consistent with those of Bastu et al. Since our study only used a single dosage, comparisons between different dosages were not possible.

In a 2011 meta-analysis of 17 studies, Gkrozou et al. (15) evaluated the effect of misoprostol on the procedure duration for diagnostic hysteroscopy in 707 women, with 359 in the oral or vaginal misoprostol group and 358 in the placebo group. Participants in the misoprostol group received the drug before hysteroscopy, and cervical canal passage time was measured during the procedure. The meta-analysis found that misoprostol recipients had significantly shorter procedure durations compared with the placebo group ($p<0.05$), no significant differences were observed among the various misoprostol groups ($p>0.05$).The authors advocated for the use of misoprostol before office hysteroscopy (15). Our findings regarding the impact of misoprostol on procedure duration are consistent with those reported by Gkrozou et al. (15) Furthermore, there are studies that claim to lower pain and duration with just some medications. For example, Gencer et al. (16) found that the position of Trendelenburg lithotomy reduced both the duration and pain of vaginoscopic office hysteroscopy. Another study conducted by Celik et al. (17) showed that bladder fulness by aligning the uterocervical angle reduced the pain scores of patients. These maneuvers are easy to perform and reduce pain; thus, combining misoprostol with some of these maneuvers may improve the pain scores further.

CONCLUSION

Misoprostol is a recognized agent for cervical ripening. The use of vaginal or oral misoprostol prior to diagnostic hysteroscopy effectively reduces pain and shortens the procedure duration. However, our current understanding of the biochemistry of the human cervix and the molecular mechanisms underlying cervical ripening is incomplete. Further studies are required to establish the ideal dose and timing of misoprostol for cervical ripening. Additionally, additional studies are needed to determine the most effective dosage, route of administration, and timing of misoprostol before diagnostic hysteroscopy to optimize its efficacy and minimize potential side effects.

Ethics

Ethics Committee Approval: The Taksim Training and Research Hospital Clinical Research Ethics Committee approval was obtained (approval no: 54, date: 08.05.2019).

Informed Consent: All participants provided informed consent.

Footnotes

Author Contributions: Surgical and Medical Practices - H.B.B.; Concept - H.B.B., S.S.; Design - S.S.; Data Collection and/or Processing - H.B.B., F.K.G., T.K.; Analysis and/or Interpretation - H.B.B., S.S.; Literature Search - F.K.G., T.K., G.S.; Writing - H.B.B., F.K.G., G.S.

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