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Effect of misoprostol on cervical transition pain in office hysteroscopy: Results of a tertiary center

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Abstract

Objective: Office hysteroscopy is a method that has become increasingly popular because of its low complication rate, rapid recovery, and cost-effectiveness. Pain is the biggest obstacle to the successful completion of office hysteroscopy procedures. Thus, the present study aimed to investigate the efficacy of misoprostol in providing cervical ripening, and thus reducing pain during the cervical transition of hysteroscopy.

Methods: This research was conducted as an observational case-control study. Seventy-nine patients who underwent office hysteroscopy were included. Twenty-nine patients were administered 200 µg of vaginal misoprostol 4 h before office hysteroscopy, whereas the control group consisting of 50 patients was not provided with premedication for cervical dilatation. Patients were asked to rate their pain between 0 and 10 using the visual analog scale (VAS) 30 min after the procedure.

Results: VAS pain scores after diagnostic office hysteroscopy (3.61 ± 0.61) and operative office hysteroscopy (4.45 ± 0.82) were significantly lower in the misoprostol group than in the control group patients. None of the patients experienced serious side effects caused by misoprostol and requested to end the procedure.

Conclusion: A significant reduction in the VAS pain score was detected in patients who were administered 200 µg of vaginal misoprostol 4 h before office hysteroscopy. Misoprostol facilitated transition by providing cervical maturation and reduced the risk of pain-related unsuccessful hysteroscopy.

Keywords: Office hysteroscopy, misoprostol, visual analog scale, pain

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Misoprostolün ofis histereskopide servikal geçiş ağrısı üzerine etkisi: Tersiyer bir merkezin sonuçları

Öz

Amaç: Ofis histereskopi düşük komplikasyon oranı, hızlı iyileşme ve düşük maliyet nedeniyle gittikçe daha fazla tercih edilmektedir. Ağrı, ofis histereskopi prosedürünün başarıyla tamamlanabilmesi önündeki en büyük engeldir. Bu nedenle, bu çalışmada misoprostolün servikal olgunlaşmayı sağlamadaki ve böylece histereskopinin servikal geçişi sırasında ağrıyı azaltmadaki etkinliğinin araştırılması amaçlandı.

Yöntemler: Gözlemsel vaka kontrol araştırması şeklinde yürütülen çalışmamızda ofis histereskopi uygulanan 79 hastaya yer verildi. Hastaların 29 tanesine ofis histereskopiden 4 saat önce 200 µg vajinal misoprostol uygulanırken 50 hastadan oluşan kontrol gruba servikal dilatasyon amaçlı premedikasyon uygulanmadı. Hastalardan işlemden 30 dakika sonra VAS (Visual Analog Skala) yardımıyla ağrılarını 0-10 puan arası derecelendirmeleri istendi.

Sonuçlar: Misoprostol uygulanan hastalarda hem diagnostik ofis histerskopi sonrası VAS ağrı skoru (3,61 ± 0,61) hem de operatif ofis histereskopi sonrası VAS ağrı skoru (4,45 ± 0,82) kontrol grubu hastalar göre anlamlı düşük bulundu. Hiçbir hastada misoprostolün neden olduğu ciddi yan etki görülmedi ve işlemin sonlandırılması talep edilmedi.

Tartışma: Ofis histreskopiden 4 saat önce 200 µg vajinal misoprostol uygulanan hastalarda VAS ağrı skorunda anlamlı azalma saptanmıştır. Misoprostolün servikal olgunlaşma sağlayarak geçişi kolaylaştırdığı ve başarısız histereskopi sayısını azalttığı görülmüştür.

Anahtar kelimeler: Ofis histereskopi, misoprostol, visuel analog skala (VAS), ağrı.

INTRODUCTION

Hysteroscopy is a procedure that allows the evaluation of the uterine cavity and endometrial biopsy/resection in the same session. Office hysteroscopy can be conducted in routine examination rooms without the need for general anesthesia and operating room conditions. It is a method that has become increasingly popular and preferred by both doctors and patients because of various benefits such as low complication rate, rapid recovery, and cost-effectiveness. The inability of patients to tolerate pain is the main reason for the unsuccessful completion of office hysteroscopy procedures[1]. Despite application by experienced surgeons, the procedure was reportedly painful[2]. The initial pain felt during the procedure is due to dilatation of the cervix and the uterine cavity distension. When operative endometrial interventions are added to the procedure, pain may also occur in the late period of the procedure following the triggering of uterine contractions[3].

There is no broad agreement in the literature on the most appropriate method available for reducing pain due to hysteroscopic examination[4]. Various pharmacological agents such as opioids, local anesthetics, and misoprostol, have been advocated to minimize the pain during office hysteroscopy. Inserting and guiding the hysteroscope through the cervical canal is severely painful, especially in patients with a narrow cervical canal. Therefore, cervical priming agents, including misoprostol, were suggested to effectively minimized pain during this procedure[5].

Prostaglandins are used for cervical dilatation in the management of birth induction, medical abortion, and early pregnancy loss[6,7]. Although there is no conclusive information suggesting routine cervical dilatation before office hysteroscopy, there is a particular focus on a hypothesis that the cervical maturation effect of misoprostol, a specific prostaglandin, may reduce pain due to hysteroscopy[6,8]. In contrast with publications in the literature that report that cervical preparation provided with

misoprostol reduces pain during office hysteroscopy, there are also publications reporting that it has no effect on pain[6,8-11].

In the present study, the effect of 200 µg vaginal misoprostol administered before office hysteroscopy on the severity of pain during the cervical transition was examined. The present study aimed to investigate the efficacy of misoprostol in providing cervical ripening, and thus reducing pain during the cervical transition of hysteroscopy.

METHODS

The study included patients who underwent office hysteroscopy between January 2020 and December 2020 at Gynecology clinic of Diyarbakır Gazi Yasargil Training and Research Hospital. This research was conducted as an observational case-control study. Ethical approval was obtained from the ethics committee of our hospital (21.04.2022/70). The articles of the Helsinki Declaration were adhered to during the design and conduct of the study. Informed consent was obtained from all participants.

All patients who were planned to experience office hysteroscopy alone or in combination with endometrial biopsy or septum resection at our gynecology clinic as a component of their routine medical care were enrolled in this study.

Pregnant women, patients with a history of cervical stenosis, patients whose cervix could not be clearly visualized, patients with cervical malignancies or suspected of malignancies, patients with severe vaginal bleeding, patients with active genital infection, patients with allergy or other medical contraindications of misoprostol using, patients under 18 years old, and patients with communication problems due to medical or sociocultural causes were excluded from the study.

A total of 89 patients who met the relevant criteria were included in the study. Routine gynecological vaginal examination and transvaginal ultrasound imaging findings, pre-procedure hemogram, coagulation parameters, and serum beta-human chorionic gonadotropin values were obtained through the medical archive system. Hysteroscopy procedures were performed by experienced surgeons during the proliferative period of the menstrual cycle. Thirty-one patients were administered 200 µg of vaginal misoprostol (Cytotec®, Pfizer, NY, USA) by a ward nurse 4 h before hysteroscopy. In contrast, no agents that caused cervical dilatation were administered to 58 patients. No patients were received non-steroidal anti-inflammatory drugs or local anesthetic gels before the hysteroscopy. Also, patients were not given analgesic medication before the procedure and cervical local anesthesia was not applied during the procedure. Patients who were administered misoprostol were questioned about undesirable side effects such as drug-related fever, chills, nausea-vomiting, and diarrhea. A vaginal speculum was used in patients who were asked to lie in the lithotomy position to visualize the cervix. The vagina was cleaned with an antiseptic solution (Povidone-iodine 10%). A tenaculum was used to straighten the cervical canal if needed. A 2.9 mm rigid hysteroscope with a 30° lens angle and a 3.5 mm external diagnostic sheath was used in all patients (Karl Storz, Germany). A sterile saline solution was used for uterine distension. Office hysteroscopy was performed under a maximum pressure of 60–80 mm Hg with the help of a manual sleeve. The cervical transition could not be achieved in 10 patients (11.4%), with 2 patients in the misoprostol group and 8 patients in the control group, and these patients were not included in the study. Seventy-nine patients who underwent the successful completion of hysteroscopy were included in the study.

Of the patients, 46 underwent only diagnostic office hysteroscopy, whereas 33 patients also underwent endometrial biopsy, polyp resection,

uterine synergism, or septum resection, in addition to office hysteroscopy. Patients were informed about the stages of office hysteroscopy before the procedure. Patients were verbally warned about pain just before entering the cervical canal during hysteroscopy. Patients were visited in their rooms 30 min after the procedure and asked to rate the severity of pain they felt during the cervical transition between 0 and 10 points (0 = no pain; 10 = most severe pain) using the visual analog scale (VAS). The groups were compared concerning age, parity, body weight, history of cesarean section, type of procedure (diagnostic or operative), and severity of pain felt.

VAS was preferred in the present study because it is a safe, easy to apply, well-designed, and accepted method for assessing pain severity. Patients were asked to rate their pain between 0 (no pain) and 10 (most severe pain) on a visual scale that could be answered either vertically or horizontally, with a length of 10 cm divided at equal intervals, and was easy to understand[12,13]. VAS is more precise and reliable in measuring pain intensity than other one-dimensional scales. Patients over the age of 5 years describe this method as easy to understand and apply[12].

Statistical Analysis

The VAS score was the primary outcome variable in the present study, which was conducted to examine the effect of misoprostol on pain sensation during the cervical transition due to office hysteroscopy. The minimum sample size, where a 1-unit difference in terms of mean VAS score between patient groups (misoprostol vs. control) could be statistically significant was calculated as 22 for a two-tailed t-test in independent groups with 0.05 error level (alpha error level-type I error) and minimum 0.80 power (type II error maximum: 0.20).

The data were statistically analyzed by using IBM SPSS Statistics for Windows, Version 20.0. package program (IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp). Mann Whitney U test was used for independent group comparisons, depending on the distributional properties of the VAS variable based on groups (according to results of the Shapiro Wilk test). We summarized the data as mean ± standard deviations and median (minimum-maximum) for continuous variables. Any p-value less than 0.05 was considered statistically significant.

RESULTS

Vaginal misoprostol was administered to 36.7% (n= 29) of the patients. The control group (n= 50) was not administered a cervical dilatator agent before hysteroscopy. There was no significant difference between the misoprostol and the control groups concerning age, gravida, parity, and body weight. History of cesarean delivery was detected to be significantly higher in the misoprostol group than in the control group (Table 1).

Table I: Demographic characteristics of the participants

	Misoprostol group (n = 29)	Control group (n = 50)	P-value
Age (Mean ± S.Dev)	39.7 ± 8.3	38.7 ± 9.9	**0.65**
Gravida (Mean ± S.Dev)	3.8 ± 2.0	3.5 ± 2.6	**0.64**
Parity (Mean ± S.Dev)	3.4 ± 2.0	3.1 ± 2.5	**0.50**
Bodyweight (kg)	70.5 ± 9.8	65.7 ± 11.3	**0.13**
C-section history n (%)	15(51.7%)	13 (26%)	**0.02**

Of the control group patients who did not receive premedication with misoprostol, 28 underwent diagnostic office hysteroscopy and 22 underwent operative office hysteroscopy. VAS scores were significantly higher in the operative office hysteroscopy group (5.27 ± 0.83/4.46 ± 0.92) than in the diagnostic office hysteroscopy group (Table 2).

Table II: Comparison of VAS scores within the control group

		Diagnostic Office Hysteroscopy (n: 28)	Operative Office Hysteroscopy (n: 22)	p
VAS SCORE	**Mean ± S.Dev**	4.46 ± 0.92	5.27 ± 0.83	**0.002**
	Median (min–max)	4 (3–6)	5 (3–6)	

VAS: Visual analog scale

Approximately 58.2% of the patients (n = 46) underwent only diagnostic office hysteroscopy, whereas 41.8% (n = 33) also underwent an operative procedure (resection/biopsy) in the same session. Misoprostol and control groups were compared with respect to diagnostic and operative hysteroscopy procedures. In patients who underwent diagnostic office hysteroscopy, VAS scores were significantly lower in the misoprostol group than in the control group (p = 0.002). Similarly, in patients who underwent operative office hysteroscopy, VAS scores were significantly lower in the misoprostol group than in the control group (p = 0.014) (Table 3, Figure 1).

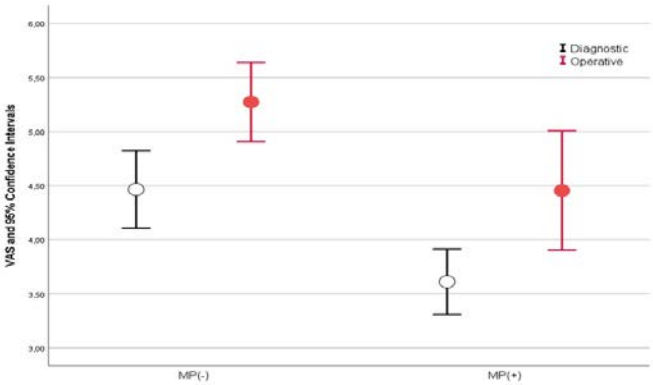

Figure 1. Misoprostol/VAS score evaluation

Table III: Comparison of VAS scores within the misoprostol group

		Diagnostic Office Hysteroscopy (n: 46)			Operative Office Hysteroscopy (n: 33)		
		Mp (+) (n: 18)	Mp (–) (n: 28)	p	Mp (+) (n: 11)	Mp (–) (n: 22)	p
VAS SCORE	**Mean ± S.Dev**	3.61 ± 0.61	4.46 ± 0.92	**0.002**	4.45 ± 0.82	5.27 ± 0.83	0.014
	Median (min–max)	4 (3–5)	4 (3–6)		4 (3–6)	5 (3–6)	

VAS: Visual Analog Scale, Mp: Misoprostol

In our study cohort, there were no reports of vasovagal reaction, uterine perforation, and severe vaginal bleeding during or after the office hysteroscopy procedure. The majority of participants in the misoprostol group (n=24, 82.8%) reported no side effects associated with misoprostol. The most frequently reported side effect related to misoprostol was abdominal cramping (n=3, 10.3%), followed by bleeding only (n=1, 3.45%), and both abdominal cramping and bleeding (n=1, 3.45%). However, these side effects were tolerable in these patients, and none of the patients requested to end the procedure.

DISCUSSION

As a result of recent developments in the field of minimally invasive surgery, office hysteroscopy has become a low-cost, reliable, and satisfactory method that can provide rapid results without the requirement of hospitalization or general anesthesia and allows simultaneous treatment when necessary[14,15]. A study reported a failure rate of 12% for office hysteroscopy and severe pain due to previous uterine surgery, severe cervical stenosis, postmenopause, no previous vaginal deliveries, and significant uterine flexion were stated as the cause of failure[16,17]. In addition to pharmacological agents, such as non-steroidal anti-inflammatory drugs, selective COX-2 inhibitors, opioids, local anesthetics, Sedo-analgesics, and spasmolytics, non-pharmacological methods, such as working with low uterine pressure during hysteroscopy, uterine tension provided by filling the bladder,

applying heat to the lower abdomen, transcutaneous electrical nerve stimulation, hypnosis, and verbal suggestions, have also been proposed for treating office hysteroscopy-related pain[18]. Routine use of sedoanalgesia in office hysteroscopy is not recommended because of the lack of significant reduction in pain after the procedure and the high risk of side effects in particular[19]. Cervical local anesthesia, which is an invasive procedure, reduces the pain felt during the cervical transition and afterward, but it does not provide a significant reduction in the risk of hysteroscopy failure[20,21]. The use of misoprostol reportedly reduces pain due to both diagnostic and operative office hysteroscopy, increasing the dilatation of the cervix, making it simpler for the hysteroscope to enter the uterine cavity, and shortening the duration of the operation[10,22]. In another study, the use of misoprostol significantly reduced VAS pain scores only in office hysteroscopy procedure, but did not cause any significant changes in VAS pain scores in patients undergoing endometrial biopsy following hysteroscopy, and this was attributed to the increased use of tenaculum in operative procedures[11]. Studies have also reported that misoprostol use does not reduce pain due to office hysteroscopy or results in a decrease only in limited patient groups (postmenopausal women)[9,23]. These studies in the literature mostly used a dose of 200 μg of misoprostol. It has been reported that 400 μg misoprostol is not superior to its 200 μg counterpart in terms of pain sensation and ease of the procedure, and the use of 50 μg misoprostol can also considerably reduce VAS score in patients undergoing office hysteroscopy[6,11]. Compared with oral misoprostol, vaginally administered misoprostol has been reported to be superior in terms of cervical dilatation and has a lower complication rate[24]. In the present study, no additional pharmacological or non-pharmacological method was used in addition to 200 μg vaginal misoprostol. None of the patients experienced serious side effects caused by misoprostol and requested to end the procedure. Although the cesarean section rate was significantly higher in the misoprostol group (57.1%) than in the control cases (26%) (p= 0.02), mean VAS scores for both diagnostic and operative office hysteroscopy were significantly lower than those noted in the control group (p= 0.002, and p= 0.014, respectively). Consistent with the literature, the procedure failed in 11.23% (10/89) of all patients and the only reason for failure was the inability to achieve the cervical transition. The failure rates obtained in the present study were 6.4% (2/31) in the misoprostol group and 13.8% (8/58) in the control group. No patient experienced intolerable pain during the procedure, and no hysteroscopy procedures were interrupted due to pain. Based on these data, it can be suggested that the use of 200 μg vaginal misoprostol before office hysteroscopy in women with cervical stenosis is effective in reducing cervical transition pain. We believe that the cervical maturation effect provided by misoprostol will facilitate the transition, increasing doctor and patient comfort, and patient satisfaction by reducing pain.

New et al. stated that patients who experienced diagnostic office hysteroscopy only and patients who underwent endometrial biopsy in addition to hysteroscopy reported experiencing similar pain[25]. In the present study, higher VAS scores were reported by patients who experienced operative hysteroscopy only than patients who underwent diagnostic hysteroscopy only (p = 0.02). This may be because of the fact that operative hysteroscopy is a relatively long and challenging procedure, which may have led to bias in assessing the initial pain.

The present study only focused on cervical transition pain and does not include data on pain sensation during and after hysteroscopy. The strength of this study is that it provides clear statistical results on pain during the

cervical transition, which we believe is the most difficult step for the physician and patient for the successful completion of office hysteroscopy procedures, and the effect of misoprostol on this pain.

This research has demonstrated a further way that might assist clinicians to improve the performance of hysteroscopic procedures by reducing the reported pain of the patients during office hysteroscopy. Additional variables to examine include the cost-effectiveness of utilizing misoprostol and patient choice, not just pain score following office hysteroscopy.

CONCLUSION

A significant reduction in VAS pain score was detected in patients who were administered 200 μg vaginal misoprostol 4 h before office hysteroscopy. Misoprostol facilitated transition by providing cervical maturation and reduced the risk of pain-related unsuccessful hysteroscopy.

Ethics Committee Approval: Ethical approval was obtained from the ethics committee of Diyarbakir Gazi Yasargil Training and Research Hospital (21.04.2022/70). The articles of the Helsinki Declaration were adhered to during the design and conduct of the study. Informed consent was obtained from all participants.

Conflict of Interest: The author declares no conflict of interest.

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