Uterine Evacuation before Operative Hysteroscopy in Patients with Active Uterine Bleeding: A randomized controlled trial

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Uterine Evacuation before Operative Hysteroscopy in Patients with Active Uterine Bleeding: A randomized controlled trial

Manizheh Sayyah-Melli, Maryam Kazemi-Shishavan, Nooshin Behravan, Parvin Mostafa Gharabaghi, Vahideh Rahmani

Abstract

Background: Concurrent bleeding or existing clots usually obscure the vision field and decrease the hysteroscopy success rate. Therefore, any efforts made to have a clear view during the hysteroscopy will improve the diagnostic or treatment outcomes. In this study, we examined the effect of preoperative clot evacuation on hysteroscopy and patient outcomes.

Methods: In this parallel-group clinical trial conducted from December 2018 to September 2019 at the Oncology Center of Alzahra Teaching Hospital in Tabriz, Iran, 114 patients with uterine bleeding were randomly assigned to receive either clot evacuation before standard operative hysteroscopy or standard hysteroscopy alone. The investigated endpoints were the clarity of vision, the volume of used distension media, duration of the procedure, amount of bleeding, and postoperative complications.

Results: All 114 participants completed the study. There were statistically significant differences in the frequency of the clear vision ($p<.001$), the severity of bleeding ($p=.0006$), mean serum volume used ($p<.001$), mean procedure time ($p<.001$), and the postoperative hematocrit levels ($p<.001$) between groups, in favor of women with preprocedural intrauterine evacuation. There was no difference in in-hospital stay ($p=0.081$) and anesthetic complications among the patients ($p=0.182$). The procedure was successfully performed on all patients of both groups with zero postoperative complications.

Conclusion: Removal of clots and other uterine contents before inserting hysteroscope rendered better and faster access to the uterine wall to observe existing abnormalities and reduce the hysteroscopy time. This additional surgical step could take a significant impact on surgical and clinical outcomes.

Trial registration:

Clinical trial registry name: Iranian Registry of Clinical Trials

Url: <https://en.irct.ir/trial/33369>

The registration number: IRCT20101130005283N13

Date of trial registration: 2018-11-16

Keywords: Hysteroscopy, Abnormal Uterine Bleeding, Metrorrhagia, Endoscopy, Mini-Invasive Surgery

Background

Abnormal uterine bleeding (AUB) seriously impacts women of childbearing age [1, 2] and postmenopausal women [3]. Depending on the underlying etiology, the surgeon may decide on a non-surgical treatment or a less invasive surgical procedure. Diagnostic, operative hysteroscopy is the practice of choice to evaluate intrauterine pathologies in patients with premenopausal [4, 5] and postmenopausal bleeding [6]. Direct visualization of the entire uterine cavity provides an opportunity to perform a biopsy of suspicious lesions or performing a surgical resection [7]. However, operative hysteroscopy may be associated with some complications such as fluid overload, bleeding, and uterine perforation [8]. Several strategies have been used to facilitate the procedure and improve the prognosis [9-11]. There is evidence on using gonadotropin agonists [12, 13] and letrozole [14] as a preoperative intervention. However, besides the insufficiency of this evidence's strength, the summary of the results was inconclusive. Other interventions, such as the administration of epsilon aminocaproic acid [15], oxytocin [16], or an intrauterine balloon, are proposed to reduce the amount of bleeding and the rate of complications during and after the hysteroscopic procedures [17]. Suction curettage in operative hysteroscopy has efficiently facilitated removing relatively large, multiple, or single endometrial polyps and submucous uterine myomas [18]. Likewise, a hysteroscopic direct visualization has expedited a more efficient vacuum aspiration of the retained conception tissue and reduces surgical complications [19]. This study was designed to evaluate intrauterine contents' evacuation before operative hysteroscopy to optimize visual quality and decrease procedure time.

Methods

We performed a parallel-group randomized trial involving patients with abnormal uterine bleeding recruited from December 2018 to September 2019 at the Oncology Center of Alzahra Teaching Hospital in Tabriz, Iran.

Patients with active uterine bleeding due to a uterine pathology or misoprostol use were eligible to participate in the study. Patients with coagulopathy disorders, genital tract infections, patients with diagnosed cervical or uterine malignancy, or significant cervical stenosis, and patients who received treatment affecting endometrium growth were excluded. Withdrawal criteria were surgical or anesthetic complications during the hysteroscopy procedure.

The study was fully described for the participants, and verbal and written informed consent was obtained from each patient. All patients had undergone Pap smear, transabdominal and transvaginal ultrasonography, hematological assessments, and endometrial Pipelle sampling before the operation. Patients information was recorded in the data collection forms before the procedure. One of the researchers generated the blocked random allocation sequence using RandList Version 2.1 (DatInf GmbH, Tübingen, Germany) with sequentially-numbered envelopes. Intervention and control group was labeled as A and B, respectively. The leading researcher used the sequence to determine the participant's assigned procedure right after the patient went under general anesthesia. All patients underwent general anesthesia with the same protocol, and the same surgeon performed all the procedures. The statistician was blind to the grouping until the final report.

In group A, the surgeon dilated the uterine cervix with the Hegar dilator and removed accessible clots and uterine cavity contents with ring forceps. Then, she inserted the resectoscope to examine the entire uterine cavity and remove visible lesions. In group B, the surgeon started the procedure with resectoscope insertion regardless of uterine bleeding, and later procedures were the same as group A. Monopolar hysteroscopy device and Glycine solution (1.5%) as a distending medium were used in all procedures. We used a Likert scale [zero (no bleeding) to 5 (severe bleeding)] to measure the amount of bleeding during surgery. Both the surgeon and the circulating nurse agreed on the scale selected for each participant. The clarity of the

view during the procedure, duration of surgery, amount of distension medium, hematocrit levels at six hours after surgery, and early complications were also documented.

Statistical analysis

Due to the lack of similar studies, Cohen's estimate of medium effect size (0.3) considered desirable for calculating the sample size required to reject the null hypothesis of 0.05 with a power of 0.8. Using the G-power 3.0.10 software, we computed the required sample size using 2 degrees of freedom *Chi-Square Test*, that at least 54 people were needed in each group. We estimated 114 as the final recruitment sample size considering a 10 % probability of not participating or losing follow-up.

Intention to treat analysis was performed. Independent samples t-test, paired t-test, and Mann Whitney U test was used for data analysis. Pearson Chi-Square was used for comparison of categorical variables. Data analysis was performed using IBM SPSS (IBM Corp, Armonk, NY, USA) version 25 at the significance level of 0.05.

Results

The participants' baseline characteristics and their indications for hysteroscopy are presented in Table 1. We approached 125 eligible participants, six declined to participate, and five did not meet the study's inclusion criteria. One hundred and fourteen were randomly allocated to intervention and control groups. None of the participants were lost to follow-up; therefore, all the participants were included in the analysis. The consort flow diagram is demonstrated in figure 1.

We used a χ^2 test with adjusted standardized residuals and corresponding adjusted significance levels to compare bleeding categories in the intervention and control groups. The intervention group experienced less "Severe bleeding" ($p=.0006$) and "Moderate bleeding" ($p<.001$). "None bleeding" occurred more in the

intervention group ($p < .001$). There was no statistically significant difference between the two groups in the "Mild bleeding" category ($p = .635$) (figure 2).

Vision quality was significantly more favorable in intervention group [$\chi^2(2) = 50.61$, ($p < .001$) ($\phi = 0.66$, $p < .001$)]. The "clear vision" depicted in figure 3 was observed more in the intervention group (91.2%) than the control group (26.3%) ($p < .001$). Compared to the controls (64.9%), "blurred view" was significantly less frequent in the intervention group (5.3%) ($p < .001$). The rate of "no clear view" was not statistically different between the two groups ($p = 0.241$) (figure 3).

The comparisons for procedure duration, media volume use, and admission duration between the two groups are summarized in Table 2. The procedure continuation was considerably shorter in the intervention group ($U = 765.5$, $p < .001$). The Glycine volume used in the intervention group was significantly lesser than the amount used in the control group ($U = 754.0$, $p < .001$).

The postoperative hematocrit reduction was higher in the control group [95% CI (-3.00, -1.88)] (Table 2). There were no complications associated with general anesthesia or surgery in either of the groups. However, 4 (7.0%) of participants in the intervention group, and 1 (1.8%) in the control group reported nausea after recovery ($p = 0.182$).

Discussion

Hysteroscopy is a standard method for evaluating abnormal uterine bleeding. [20-22] So, clear vision during hysteroscopic procedures is crucial for favorable outcomes. When the surgeon uses forceps to remove polyps without a fair vision, malignant cells may remain after the excision [23]. On the other hand, flushing out the clots needs the usage of a large amount of medium, and it also lengthens the procedure duration.[24] Several researchers used notable interventions to reduce hysteroscopic complications, such as oxytocin, misoprostol, vasopressin, bupivacaine and epinephrine, mesna, and intrauterine injection of aminocaproic acid. Some studies used pericervical tourniquet, cervical balloon catheter, and Foley balloon

tamponade in this matter. However, these interventions' effectiveness has not been fully clarified [16, 17, 25].

Researchers have also intended to modify standard hysteroscopic procedures for better outcomes. Murakami et al. safely used vaporization and prostaglandin F-2 alpha to reduce the operation time and hysteroscopic complications in patients with submucosal myoma [26]. In another study, curettage suctioning use during myomectomy has reduced the complication rates [18]. Moreover, the successful use of the hysteroscopy to evacuate pregnancy remnants is reported in various studies. Zhu et al. used forceps to remove the placenta and clots' remnants before hysteroscopy to reduce thermal and electrical damage during the procedure [27]. Multiple factors also affect the amount of fluid absorption. For instance, utilizing bipolar electrical equipment with isotonic distension fluids has minimized fluid overload [28]. Our results indicate that evacuating accessible clots and the uterine cavity contents with ring forceps leads to more efficient and practical hysteroscopy procedures in patients with concurrent active uterine bleeding, which provides an optimal clear view of the inner uterine wall, considerably reduces the time of hysteroscopy, and the amount of fluid use and subsequently fluid absorption.

Furthermore, A clear hysteroscopic view increases the probability of locating more lesions in a shorter duration; thus, the success rates of hysteroscopy clinical outcomes such as intraoperative bleeding will improve. Our study had some limitations: Bleeding categories were created based on the surgeon and operating nurse's estimation on the bleeding volume; however, it was clinically valuable. The size, type, and accurate numbers of leiomyoma and endometrial polyps were not evaluated in the study; this information may affect the amount of bleeding. Future studies may provide more information using quantitative estimates of bleeding and details about leiomyoma and endometrial polyps.

Conclusion

This study showed that removing clots and other uterine contents before inserting the hysteroscope in patients with active uterine bleeding results in better and faster access to the uterine wall to detect the

abnormalities and perform the appropriate procedure. This method is efficient and practical. This method's success rate and effectiveness could be retested with different clinically important outcomes such as incomplete lesion resection and intrauterine adhesions.

List of abbreviations;

None

Declarations;

Ethics approval and consent to participate;

The ethics committee of Tabriz University of Medical Sciences approved the study. The ethics board approval number is 60019, and all participants provided written informed consent with guarantees of confidentiality.

Consent for publication;

'Not applicable.'

Availability of data and materials;

The datasets generated and analyzed during the current study are available in the Mendeley repository, <https://data.mendeley.com/datasets/sdkmdzyrtb/1>

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Author contributions;

MS and MK designed the study. MS carried out the procedures as the leading surgeon. NB was the gynecology resident and aided in procedures. PG and VR contributed to sample recruitments. MK analyzed

the data. MS, MK, PG, and VR contributed to the interpretation of the results. MS and MK took the lead in writing the manuscript. All authors read and approved the final manuscript, provided critical feedback, discussed the results, and commented on the manuscript.

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Competing interests

None declared.

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figure legends

1. Flow diagram of clot evacuation before operative hysteroscopy vs. standard operative hysteroscopy
2. Frequency and percentages of bleeding categories during the hysteroscopy procedure in intervention and control groups
3. Frequency and percentages of hysteroscopy quality of vision categories in intervention and control groups

Tables and figures

Table 1: Characteristics of the patients						
		Total Sample (N=114)	Intervention group (N=57)	Control Group (N=57)	t or Z or x ²	p
Age(years)		44 (39-50)	44 (37-51)	46 (40-50)	-0.434	.664 [#]
†Married (years)		23.30 (10.12)	23.33 (11.46)	23.28(8.6)	0.025	.980 [‡]
Gravidity		2.00 (2.00-3.50)	2.00 (2.00-3.00)	3.00 (2.00-4.00)	-1.40	.159 [#]
Parity		2.00 (2.00-3.00)	2.00 (2.00-3.00)	2.00 (2.00-3.00)	-1.04	.295 [#]
*Hysteroscopy indication					3.92	.140 [◇]
leiomyoma		77 (67.5%)	35 (61.4%)	42 (73.7%)		
Endometrial polyp		29 (25.4%)	19 (33.3%)	10 (17.5%)		
Endometrial thickening		8 (7.0%)	3 (5.3%)	5 (8.8%)		
Data are presented as median ± IQR, †mean (SD) and *frequency (percentage)						
# Mann-Whitney U test or ‡ independent samples t-test or ◇ chi-square test was performed						

Table 2: Duration of surgery, distending media, duration of hospital stay and hematocrit levels in both groups

		Median	IQR		P-Value*
Groups(N=57)			Q1	Q3	
†Duration of Intervention		6.00	4.75	24.00	<0.001
surgery (min)	Control	10.00	6.00	15.00	

†Distending media (mL)	Intervention	1000.00	725.00	2000.00	<0.001
	Control	2500.00	1750.00	3750.00	
†Hospitalization(days)	Intervention	1.00	1.00	1.00	0.081
	Control	1.00	1.00	1.00	
		Groups (N=57)	Mean (SD)	Mean Difference (95% Confidence Interval of the Difference)	P-Value**
‡Hct. procedure	Before	Intervention	37.46 (3.62)	0.58 (-0.67-1.83)	0.360
		Control	36.88 (3.10)		
‡Hct; After procedure		Intervention	36.26 (3.68)	3.32 (2.09-4.55)	<0.001
		Control	32.93 (2.90)		
‡Hct.diff (before-after)		Intervention	1.19 (0.82)	-2.44 (-3.00- -1.88)	<0.001
		Control	3.64 (1.98)		

†Data are presented as median ± IQR ‡and as mean (standard derivation) and mean the difference

*Mann-Whitney U was performed, **independent samples t-test was performed, Hb; (mg/dL), Hct; (%)

Figure 1

Flow diagram of clot evacuation before operative hysteroscopy vs. standard operative hysteroscopy

Figure 2: Frequency and percentages of bleeding categories during the hysteroscopy procedure in intervention and control groups

Figure 3: frequency and percentages of hysteroscopy vision categories in intervention and control groups

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Figures

Figure 1

Flow diagram of clot evacuation before operative hysteroscopy vs. standard operative hysteroscopy

Figure 2

Frequency and percentages of bleeding categories during the hysteroscopy procedure in intervention and control groups

Figure 3

frequency and percentages of hysteroscopy vision categories in intervention and control groups