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

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Abstract

Background

Concurrent bleeding or existing clots usually obscure the vision field and decrease the success rate in hysteroscopy. Therefore, any effort to have a clear view during the hysteroscopy will meliorate the diagnostic or treatment outcomes. We examined the effect of preoperative clot evacuation on hysteroscopy and patient outcomes.

Methods

In this parallel-group trial, 114 patients with uterine bleeding were randomly assigned to receive either clot evacuation before standard operative hysteroscopy or standard hysteroscopy alone. The primary endpoints were the clarity of vision, amount of bleeding, the volume of consumed media, duration of the procedure, and postoperative complications.

Results

All 114 participants completed the study. There were statistically significant differences in the frequency of the clear vision ($p < 0.001$), the severity of bleeding ($p = 0.0006$), mean procedure time ($p < 0.001$), mean serum volume used ($p < 0.001$), and the postoperative hematocrit levels [95% CI (-3.00, -1.88)] ($p < 0.001$) between groups. There was no difference related to 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 the insertion of the hysteroscope rendered better and faster access to the uterine wall to observe existing abnormalities. This method of starting the hysteroscopy procedure has a significant impact on surgical 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 registration: 2018-11-16

Background

Abnormal uterine bleeding (AUB) has a significant impact on women of childbearing age [1, 2] and postmenopausal women [3]. Depending on the underlying etiology, the surgeon may decide on a less invasive surgical procedure or not a surgical treatment. Diagnostic and operative hysteroscopy is the practice of choice for evaluation of intrauterine pathology 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 surgical resection [7]. However, operative hysteroscopy may be associated with complications such as fluid overload, uterine perforation, and bleeding [8]. Several strategies have been used to facilitate the procedure and improve prognosis [9–11]. There is evidence on using gonadotropin agonists [12, 13], selective progesterone receptor modulators such as ulipristal acetate [14], and letrozole [15] as a preoperative intervention. However, the quality of the evidence in some of these studies was low. Other interventions, such as the administration of epsilon aminocaproic acid [16], oxytocin [17], or an intrauterine balloon, are used to reduce the amount of bleeding and the rate of complications during and after the hysteroscopic procedures [18]. The efficiency of suction curettage during operative hysteroscopy has facilitated the removal of relatively large multiple or single endometrial polyps and submucous uterine myomas [19]. Direct visualization in operative hysteroscopy renders a more efficient vacuum aspiration of the retained conception tissue and reduces surgical complications [20]. However, to our knowledge, there is no evidence regarding optimizing visual quality during hysteroscopy procedures in nonpregnant women with uterine bleeding at the starting of the procedure. This study was designed to evaluate the effects of intrauterine contents evacuation before starting the operative hysteroscopy on efficient hysteroscopic procedures.

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.

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. By 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 for as the final recruitment sample size considering a 10% probability of nonparticipant or loss to follow-up.

Patients with active uterine bleeding due to a uterine pathology or misoprostol use were eligible to participate in the study during the enrolment period. Patients who had coagulopathy disorders, known cervical or uterine malignancy or marked cervical stenosis, genital tract infections, 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 find out the assigned procedure for the participant 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.

The surgeon dilated of the uterine cervix with the Hegar dilator and removed clots and contents of the uterine cavity with ring forceps when the grouping was A. Then, the resectoscope was inserted to examine the entire uterine cavity and remove visible lesions. Glycine 1.5% was used as a distension medium. In the absence of a lesion, uterine curettage was performed. In the case of B grouping, the surgeon started with resectoscope insertion regardless of uterine bleeding, and other procedures were the same as group B. The amount of bleeding during surgery was recorded using a Likert scale [zero (no bleeding) to 5 (severe bleeding)] as agreed by both the surgeon and the circulating nurse. The clarity of the view during the procedure, duration of surgery, amount of bleeding, hematocrit levels at six hours after surgery, and early complications were documented.

Statistical analysis

Intention to treat analysis was performed, and Independent samples t-test and paired t-test were 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 inclusion criteria of the study. 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 Fig. 1.

Table 1
Characteristics of the patients

	Total Sample (N = 114)	Intervention group (N = 57)	Control Group (N = 57)	t or Z or χ^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
Disease Duration	8.00 (5.00– 16.50)	6.00 (4.75– 24.00)	10.00 (6.00– 15.00)	-1.39	.164
Hysteroscopy indications				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%)		

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" ($p = 0.0006$) and "Moderate bleeding" ($p < 0.001$). "None bleeding" occurred more in the intervention group ($p < 0.001$). There was no statistically significant difference between the two groups in the "Mild bleeding" category ($p = 0.635$) (Fig. 2).

There was a significant association between the intervention group and the vision quality categories [χ^2 (2) = 50.61, ($p < 0.001$) ($\phi = 0.66$, $p < 0.001$)]. The "clear vision" depicted in Fig. 3, was observed more in the intervention group (91.2%) than the control group (26.3%) ($p < 0.001$). Compared to the controls (64.9%), "blurred view" was significantly less frequent in the intervention group (5.3%) ($p < 0.001$). The rate of "no clear view" was not statistically different between the two groups ($p = 0.241$) (Fig. 3).

The comparison of 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 ($U = 765.5$, $p < 0.001$). The Glycine volume used in the intervention group was significantly lesser than the volume used in the control group ($U = 754.0$, $p < 0.001$).

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 surgery (min)	Intervention	6.00	4.75	24.00	< 0.001
	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	Intervention	1.00	1.00	1.00	0.081
	Control	1.00	1.00	1.00	
Data are presented as median ± IQR, *Mann-Whitney U was performed					
	Groups (N = 57)	Mean (SD)	Mean Difference (95% Confidence Interval of the Difference)		P-Value**
‡Hct; Before procedure	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 differences (before-after)	Intervention	1.19 (0.82)	-2.44 (-3.00- -1.88)		< 0.001
	Control	3.64 (1.98)			
*Mann-Whitney U was performed, **independent samples t-test was performed, ‡Hct (hematocrit); (%)					

The postoperative blood hematocrit (Hct) 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, followed by curettage, is a standard method for the evaluation of abnormal uterine bleeding. Hysteroscopy is vastly used for removing intrauterine polyps, submucosal myoma, pregnancy remnants, and cesarean section ectopics [21, 22]

Clear vision during hysteroscopic procedures is crucial for favorable outcomes. When the surgeon uses forceps to remove polyps blindly, malignant cells may remain at the base of the polyp [23]. The findings of our study showed that removal of the clots, and uterine contents before hysteroscopy facilitate the procedure efficiency by providing a clearer view and results in a shorter duration of surgery ($p < 0.001$), a considerable reduction in used media ($p < 0.001$) and less blood loss ($p < 0.001$). Researchers have used notable interventions such as oxytocin, misoprostol, vasopressin, bupivacaine and epinephrine, mesna, intrauterine injection of aminocaproic acid, pericervical tourniquet, and Foley balloon tamponade regarding reducing hysteroscopy procedure complications. However, the effectiveness of these interventions has not been fully clarified [17, 18].

Researchers have also intended to modify standard hysteroscopy procedures for better outcomes. Murakami et al. safely used vaporization and prostaglandin F-2 alpha to reduce the operation time and hysteroscopy complications in patients with submucosal myoma [24]. In another study, curettage suctioning use during myomectomy has reduced the complication rates [19]. Furthermore, the successful use of the hysteroscopy to evacuate the remnants of pregnancy is reported in some studies. Zhu et al. used forceps to remove remnants of the placenta and clots before hysteroscopy to reduce thermal and electrical damage during hysteroscopy [25].

Our results indicate that with concurrent active uterine bleeding, it is reasonable to remove intrauterine contents in order to have a clear view of the uterine wall. Based on the findings for shorter procedure duration and reduction in Glycine volume use, this method could be more efficient than the current standard method. A clear hysteroscopic view increases the probability of locating lesions; thus, the success rates of hysteroscopy outcomes will improve. Our study had some limitations: Bleeding categories were created based on the surgeon and operating nurse's estimation on the bleeding volume, which was clinically valuable. However, future studies may provide more information by using quantitative estimates of bleeding.

Conclusion

This study showed that the removal of clots and other uterine contents before insertion of the hysteroscope in patients with active uterine bleeding results in better and faster access to the uterine wall for observing the abnormalities and performing the appropriate procedure. This method is efficient and practical. No similar studies of uterine evacuation at the time of hysteroscopy in nonpregnant patients with active uterine bleeding have been done. The success rate and effectiveness of this method could be retested with different clinically important outcomes such as incomplete lesion resection rate and intrauterine adhesions.

List Of Abbreviations

Hct: hematocrit

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 used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests:

The authors declare that they have no competing interests.

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Author contributions:

Manizheh Sayyah-Melli (MS) and Maryam Kazemi-Shishavan (MK) designed the study. MS carried out the procedures as the leading surgeon. Nooshin Behravan was the gynecology resident and aided in procedures. Parvin Mostafa Gharebaghi (PG) and Vahideh Rahmani (VR) contributed to sample recruitment. 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, and discussed the results and commented on the manuscript.

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References

1. Munro MG, Critchley HOD, Fraser IS. The two FIGO systems for normal and abnormal uterine bleeding symptoms and classification of causes of abnormal uterine bleeding in the reproductive years: 2018 revisions. *Int J Gynaecol Obstet*. 2018;143(3):393–408.
2. Whitaker L, Critchley HOD. Abnormal uterine bleeding. *Best practice research Clinical obstetrics gynaecology*. 2016;34:54–65.
3. Munro MG. Investigation of women with postmenopausal uterine bleeding: clinical practice recommendations. *Perm J*. 2014;18(1):55–70.
4. Valentine LN, Bradley LD. Hysteroscopy for Abnormal Uterine Bleeding and Fibroids. *Clin Obstet Gynecol*. 2017;60(2):231–44.
5. Sinha P, Yadav N, Gupta U. Use of Hysteroscopy in Abnormal Uterine Bleeding: An Edge Over Histopathological Examination. *J Obstet Gynaecol India*. 2018;68(1):45–50.
6. Vilos GA, AlJasser R, Vilos AG, Oraif A, Abduljabar H, Abu-Rafea B. Histopathology and Clinical Outcomes of 151 Women with Postmenopausal Bleeding Treated with Resectoscopic Surgery. *J Minim Invasive Gynecol*. 2020;27(3):763–73.
7. Levy-Zauberman Y, Pourcelot AG, Capmas P, Fernandez H. Update on the management of abnormal uterine bleeding. *J Gynecol Obstet Hum Reprod*. 2017;46(8):613–22.
8. Cholkeri-Singh A, Sasaki KJ. Hysteroscopy safety. *Curr Opin Obstet Gynecol*. 2016;28(4):250–4.
9. Aas-Eng MK, Langebrekke A, Hudelist G. Complications in operative hysteroscopy - is prevention possible? *Acta Obstet Gynecol Scand*. 2017;96(12):1399–403.
10. Samy A, Raslan AN, Talaat B, El Lithy A, El Sharkawy M, Sharaf MF, Hussein AH, Amin AH, Ibrahim AM, Elsherbiny WS, et al: **Perioperative nonhormonal pharmacological interventions for bleeding reduction during open and minimally invasive myomectomy: a systematic review and network meta-analysis.** *Fertil Steril* 2020, **113**(1):224–233.e226.
11. Hoffman CR, Van Hal M, Tariq R, George S. Complications of fluid overload during hysteroscopic surgery. *Korean J Anesthesiol*. 2019;72(4):387–8.
12. Kamath MS, Kalampokas EE, Kalampokas TE. Use of GnRH analogues pre-operatively for hysteroscopic resection of submucous fibroids: a systematic review and meta-analysis. *Eur J Obstet Gynecol Reprod Biol*. 2014;177:11–8.
13. Lethaby A, Puscasiu L, Vollenhoven B. Preoperative medical therapy before surgery for uterine fibroids. *Cochrane Database Syst Rev*. 2017;11:Cd000547.
14. Vitale SG, Ferrero S, Caruso S, Barra F, Marin-Buck A, Vilos GA, Vitagliano A, Torok P, Ciebiera M, Cianci A. Ulipristal Acetate Before Hysteroscopic Myomectomy: A Systematic Review. *Obstet Gynecol Surv*. 2020;75(2):127–35.
15. Bizzarri N, Ghirardi V, Remorgida V, Venturini PL, Ferrero S. Three-month treatment with triptorelin, letrozole and ulipristal acetate before hysteroscopic resection of uterine myomas: prospective comparative pilot study. *Eur J Obstet Gynecol Reprod Biol*. 2015;192:22–6.

16. Rasheedy R, Makled A, Abou-Gamrah A, Giuma H. **Intrauterine Instillation of Tranexamic Acid in Hysteroscopic Myomectomy: A Double-Blind, Placebo-Controlled, Parallel-Group Randomized Clinical Trial.** *J Minim Invasive Gynecol* 2019.
17. Shokeir T, El-lakkany N, Sadek E, El-shamy M, Abu Hashim H. An RCT: Use of Oxytocin Drip during Hysteroscopic Endometrial Resection and Its Effect on Operative Blood Loss and Glycine Deficit. *Journal of Minimally Invasive Gynecology.* 2011;18(4):489–93.
18. Yu D, Li T-C, Xia E, Huang X, Zheng J. A prospective randomized controlled trial on the effectiveness of routine Foley balloon tamponade on the reduction of bleeding after hysteroscopic resection of myoma. *Gynecol Surg.* 2006;3(2):93.
19. Cheng C, Zhao T, Xue M, Wan Y, Xu D. Use of suction curettage in operative hysteroscopy. *J Minim Invasive Gynecol.* 2009;16(6):739–42.
20. Huchon C, Koskas M, Agostini A, Akladios C, Alouini S, Bauville E, Bourdel N, Fernandez H, Fritel X, Graesslin O, et al. Operative hysteroscopy versus vacuum aspiration for incomplete spontaneous abortion (HY-PER): study protocol for a randomized controlled trial. *Trials.* 2015;16:363.
21. Yendru KS, Yelamanchi SD, Vaddiraju GB. Hysteroscopic Resection of Submucous Fibroids in Symptomatic Women. *Journal of obstetrics gynaecology of India.* 2019;69(2):166–72.
22. Indraccolo U, Bini V, Favilli A. Likelihood of Accomplishing an In-Patient Hysteroscopic Myomectomy in a One-Step Procedure: A Systematic Review and Meta-Analysis. *Biomed Res Int.* 2020;2020:4208497.
23. Lee MMH. Endometrial Polyp Removed by a Manual Hysteroscopic Tissue Removal Device. *Gynecology minimally invasive therapy.* 2020;9(1):34–5.
24. Murakami T, Tamura M, Ozawa Y, Suzuki H, Terada Y, Okamura K. Safe techniques in surgery for hysteroscopic myomectomy. *Journal of Obstetrics Gynaecology Research.* 2005;31(3):216–23.
25. Xu D, Jamail G, Xue M, Guan X, Wang L. Removal of Retained Adherent Placental Remnants Using Hysteroscopy Endo-Operative System (HEOS). *Journal of Minimally Invasive Gynecology.* 2015;22(6):137.

Figures

Figure 1: Consort flow diagram of studied group.

Figure 1

Flow diagram detailing the study selection process

Figure 2

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

Figure 3

Frequency and percentages of hysteroscopy quality of vision categories in intervention and control groups

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