

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 of hysteroscopy. Therefore, any efforts made in order to have a clear view during the hysteroscopy will improve 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 investigated endpoints were the clarity of vision, amount of bleeding, the volume of distension 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 ($p<.001$), the severity of bleeding ($p=.0006$), mean procedure time ($p<.001$), mean serum volume used ($p<.001$), and the postoperative hematocrit levels ($p<.001$) between groups, in favor of women with preprocedural intrauterine evacuation. 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 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

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, operative hysteroscopy is the practice of choice for evaluation of 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 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] and letrozole [14] 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 [15], oxytocin [16], or an intrauterine balloon, are used to reduce the amount of bleeding and the rate of complications during and after the hysteroscopic procedures [17]. The efficiency of suction curettage during operative hysteroscopy has facilitated the removal of relatively large, multiple, or single endometrial polyps and submucous uterine myomas [18]. Direct visualization by a hysteroscope could facilitate a more efficient vacuum aspiration of the retained conception tissue and reduces surgical complications [19]. In a randomized controlled trial study, carbon dioxide was used as a

distension media in patients without excessive bleeding at the time of hysteroscopy [20]. Furthermore, a balloon catheter has been used successfully for cervical ripening in young women before operative hysteroscopy [21]. However, to our knowledge, there is no evidence regarding optimizing visual quality during hysteroscopic procedures in nonpregnant women with uterine bleeding at the starting of 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 not participant 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 enrollment period. Patients who had coagulopathy disorders, known cervical or uterine malignancy or marked cervical stenosis, genital tract infections, received treatment affecting endometrium growth, have been 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 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. All procedures were performed with glycine 1.5% as a distension medium, monopolar instrumentation, and during the follicular phase in the case of the fertile patients. In the case of B grouping, the surgeon started with resectoscope insertion regardless of uterine bleeding, and later procedures were the same as group A. 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 and Mann Whitney U 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 figure 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 [#]
*Hysteroscopy indication				3.92	.140 ^a
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 \pm IQR, †mean (SD) and *frequency(percentage)
Mann-Whitney U test or † independent samples t-test or à chi-square test was performed

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).

There was a significant association between the intervention group and the vision quality categories [$\chi^2 (2)=50.61, (p <.001) (j=0.66, p <.001)$]. 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 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 ($U = 765.5$, $p < .001$). 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 blood 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 ($p = 0.182$).

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

	Groups(N=57)	Median		IQR	P-Value*
		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(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)	(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 \pm 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; (%)

Discussion

Hysteroscopy is a standard method for the evaluation of abnormal uterine bleeding. This procedure is vastly used for removing intrauterine polyps, submucosal myoma, pregnancy remnants, and cesarean-induced pathologies [22-24]

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 [25]. The findings of our study showed that removal of the clots and uterine contents before hysteroscopy facilitates the procedure efficiency by providing a clearer view resulting in a shorter duration of surgery ($p < .001$), a considerable reduction in used distension media ($p < .001$) and less blood loss ($p < .001$). In order to reduce hysteroscopic complications, several researchers used notable interventions, such as oxytocin, misoprostol, vasopressin, bupivacaine and epinephrine, mesna, and intrauterine injection of aminocaproic acid. Furthermore, some studies used pericervical tourniquet, cervical balloon catheter, and Foley balloon tamponade in this matter. However, the effectiveness of these interventions has not been fully clarified [16, 17, 21].

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 the remnants of pregnancy is reported in various studies. Zhu et al. used forceps to remove remnants of the placenta and clots before hysteroscopy to reduce thermal and electrical damage during the procedure [27].

Our results indicate that with concurrent active uterine bleeding, it is reasonable to remove intrauterine contents to have a clear view of the inner uterine wall. Based on the findings for shorter procedure duration and reduction in Glycine volume use, this procedure, resulting in an efficient and practical method. A clear hysteroscopic view increases the probability of locating lesions; thus, the success rates of hysteroscopy outcomes such as duration of surgery, intraoperative bleeding, and distending media use 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. What is more, 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. Thus future studies may provide more information by using quantitative estimates of bleeding and details about leiomyoma and endometrial polyps.

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.

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 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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Competing interests

None declared.

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Figures

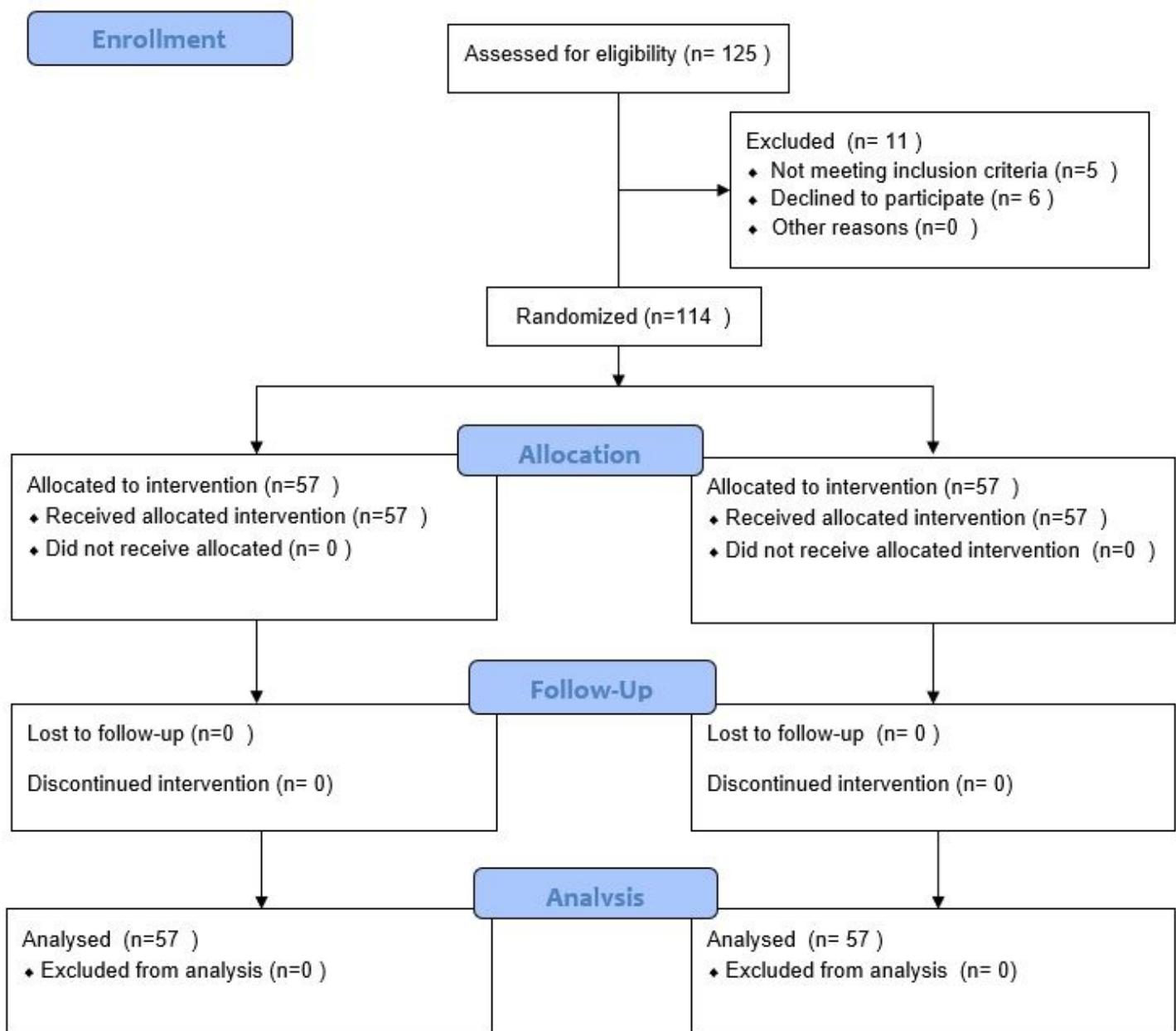


Figure 1

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

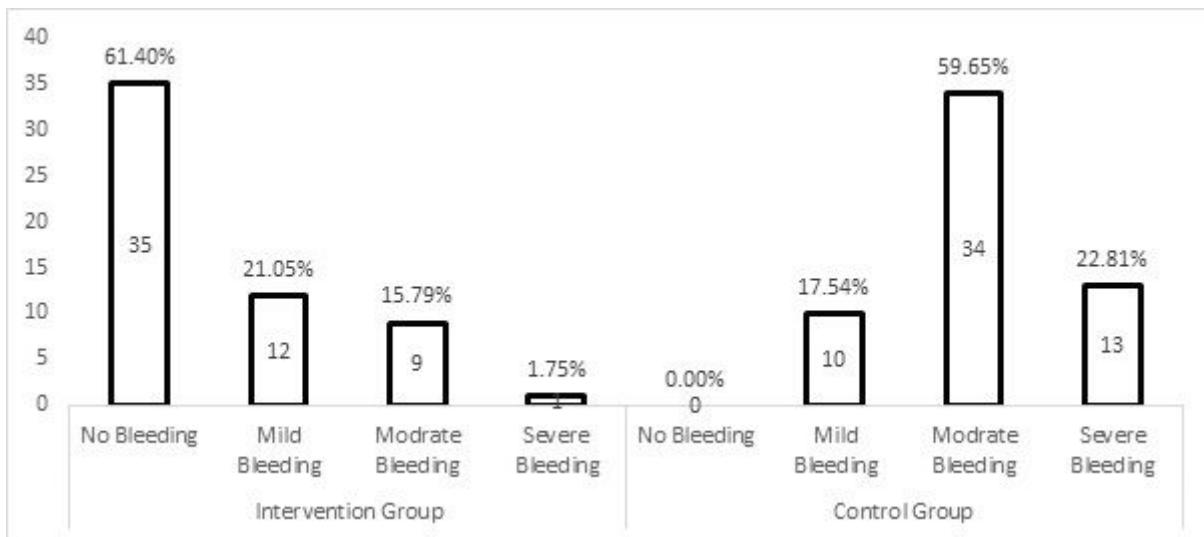


Figure 2

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

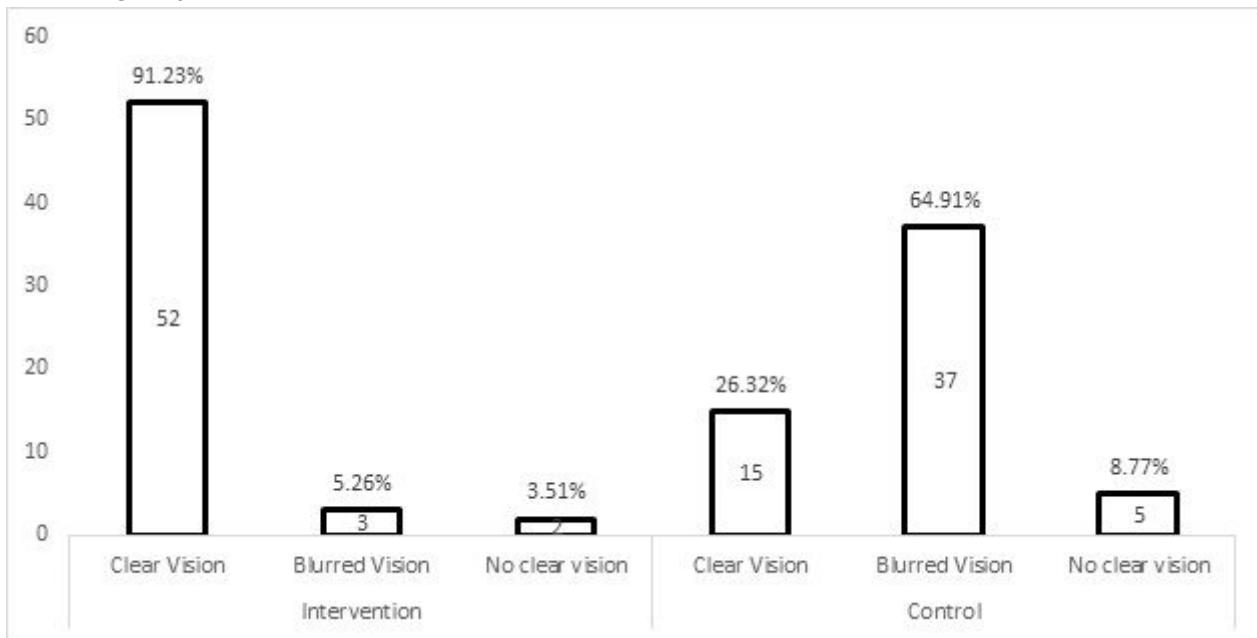


Figure 3

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