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Effects of a single rectal dose of misoprostol prior to surgery on intraoperative blood loss in total abdominal hysterectomy

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Abstract
Objective: To study the effectiveness of a pre-operative single dose rectal misoprostol for reducing blood loss of abdominal hysterectomy with or without salphingo – oophorectomy performed for uterine fibroid which are symptomatic and abnormal uterine bleeding.
Methods: This study conducted on patients planned for Total Abdominal Hysterectomy in the Department of Obstetrics and Gynaecology, RMMC&H during the period of October 2018 to October 2019. After the administration of 400 micrograms of Misoprostol to the case group A (n=48), they were compared with control group B (n=52) on blood loss.
Results: Amount of bleeding during the operation seems to be significantly lower in cases for whom Misoprostol was used. (Group A patients had a significantly lesser intra-operative blood loss (243.3 ± 27.3 ml) than their counterpart (323.5 ± 28.7 ml)). Our findings clearly indicates that both the Hemoglobin levels and Hematocrit values have declined at a significantly lower pace post-TAH (24hrs after surgery) in the group A than group B (p<0.05). The proportion of anemic patients has raised significantly in the group B following TAH than the increase of anemic patients found in the group A. This result further supports the beneficial role played by Misoprostol.
Conclusion: A single dose of rectal Misoprostol has positive effect on reducing intraoperative blood loss in women undergoing total abdominal hysterectomy due to fibroids and abnormal uterine bleeding.

Keywords: Misoprostol, haemorrhage, abdominal hysterectomy

1. Introduction
Fibroids are common benign tumours of smooth muscle of the uterus. During reproductive years, approximately 25-30% of women have symptoms due to fibroid [1].
These tumors consist of smooth muscle and extracellular matrix (collagen and fibronectin). Leiomyomas ae mostly multiple, round, and irregular. Fibroids are classified depending upon the location as sub mucosal, intramural, or sub serosal [2].
Abnormal uterine bleeding is an extremely common gynaecological complaint. It is estimated that 30% of women experience menorrhagia annually. It may display several patterns. Heavy menstrual bleeding defines prolonged or heavy cyclic menstruation. Objectively menses lasting longer than 7 days or exceeding 80 ml of blood loss are determining values [8]. Abdominal or vaginal hysterectomy may be needed in patients who have failed or declined hormonal therapy, who have symptomatic anaemia and who are experiencing a disruption in their quality of life from persistent, irregular bleeding.
TAH can be associated with several complications including major haemorrhage, thrombo embolism, bladder injury, etc. Severe haemorrhage of more than 400 mL which may need blood transfusion and infections are the commonest complications of TAH [9]. Shrinkage in the size of fibroids using hormones like gonadotropin-releasing hormone (GnRH) agonists for 3 months before surgery has been tried to decrease the blood flow to the fibroids. Vasopressin has also shown similar effects in clinical trials.
However, cost and side effects of these drugs render these therapies unavailable or not appropriate for most patients. Misoprostol, a prostaglandin E1 analog is economical and can be safely maintained at any temperature. This medication can be administered orally, rectally or sublingually. It has been showed that the pharmacokinetic in pregnancy and non pregnancy were not different [8].

It has been demonstrated that misoprostol stimulates uterine contractions and increases in myometrial contraction which leads to increase uterine artery resistance and reduce blood flow to uterus Misoprostol stimulates uterine contraction and reduce the blood flow to the uterus, here we hypothesized that pre-operative misoprostol may redistribute the blood flow from the diseased uterus back into the circulation.

We conducted this study to test the effect of misoprostol to reduce intra operative blood loss during total abdominal hysterectomy

Material and Methods

This study was conducted on patients planned for Total Abdominal Hysterectomy in the Department of Obstetrics and Gynecology, RMMC&H during the period of October 2018 to October 2019. The patient with symptomatic fibroids and abnormal uterine bleeding is hospitalized.

Age, parity, size of uterus, previous surgeries and BMI are registered. Pre-operative hemoglobin and hematocrit are measured. Patients who are planned for total abdominal hysterectomy are screened for eligibility according to the inclusion and exclusion criteria and are randomly assigned to study group A and control group B.

Exclusion criteria : Previous history of endometriosis, diabetes mellitus, obesity (BMI > 30 kg/m2), History of Myomectomy, Adnexal masses, Psychiatric disorders, Taking GnRH agonists before operation, invasive cancer of the cervix, endometrium or ovarian carcinoma, Any contraindication to misoprostol drug which includes mitral stenosis, cardiac diseases, diastolic BP of more than 100 mmHg, glaucoma, sickle cell anemia, severe hypertension, severe asthma, or major allergic reactions to prostaglandins were also excluded. In the study group, 400 micrograms rectal misoprostol is administered 30 minutes before surgery.

Outcomes are measured in terms of intraoperative blood loss, post-operative change in hemoglobin and hematocrit and the need for blood transfusion. Total blood loss is measured by adding up the blood volume in the suction container(a) and difference in weight between the wet (b) and dry(c) mop pads (1.09g equals to 1ml). Hence total blood loss is a+(b-c). Post-operative hemoglobin and hematocrit measured 24 hrs after the surgery. Record of blood transfusion maintained.

Postoperative period was monitored for any side effects of misoprostol like fever, vomiting, diarrhoea, chills and rigor etc…

Results

The prospective study was conducted on patients diagnosed with AUB and fibroid who were attending the Department of Obstetrics and Gynaecology for further evaluation and management. The participants were then randomly allocated into misoprostol group or group A (n=48) and control group or group B (n=52) before undergoing TAH. The mean age of the participants were comparable between the groups (Table 1) Control group averaged 43.9 ± 3.9 years & Misoprostol group averaged 43.5 ±5.0 years. Hemoglobin levels and Hematocrit values have declined at a significantly lower pace post-TAH in the group A than group B (p<0.05).

Table 1: Parturient baseline characteristics

Groups	Age (in years)		t-value	p-value
	Mean	SD		
Control (n=52)	43.9	3.9	0.46	0.64
Misoprostol (n=48)	43.5	5.0		
Independent t- test used; p-value <.05 is significant.				

Group A patients had a significantly lesser intra-operative blood loss (243.3 ± 27.3 ml) than their counterpart (323.5 ± 28.7 ml) and this again unveils the protective effect of misoprostol. Among these patients all except three in the misoprostol group had blood loss less than 300 ml whereas 13.5% of those in the control group had the same. This difference was found to be statistically significant (p<0.05).

Table 2: Comparison of volume of blood loss

Variables	Groups				$\chi 2$	p-value
	Misoprostol (n=48)		Control (n=52)			
	No	%	No	%		
Blood loss						
<300 ml (n=93)	45	93.8	7	13.5	64.4	**<.001**
≥ 300 ml (n=7)	3	6.2	45	86.5		
Pearson's Chi square test used; p-value <0.05 is significant						

Table 3: Comparison of Pre- vs Post-interventional Blood parameters

		Misoprostol (n=48)		Control (n=52)		p-value [a]
		Mean	SD	Mean	SD	
Hemoglobin (in gm%)	Pre-intervention	12.4	0.8	12.3	0.8	.42
	Post-intervention	11.8	0.8	11.2	0.8	**.001**
	p-value [b]	**<.001**		**<.001**		
Hematocrit (in vol%)	Pre-intervention	36.0	2.4	35.7	2.7	.58
	Post-intervention	34.2	2.3	32.6	2.3	**.001**
	p-value [b]	**<.001**		**<.001**		
a- denotes unpaired t-test used; b- denotes paired t-test used; p-value<0.05 is significant.						

As per WHO classification of anemia Hb ≤ 10.9g% are anemic. The proportion of anemic patients has raised significantly in the group B following TAH than the increase of anemic patients found in the group A. This result further supports the beneficial role played by Misoprostol.

Table 4: Comparison of pre- & post-interventional anemia

Variables	Groups				$\chi 2$	p-value
	Misoprostol (n=48)		Control (n=52)			
	No	%	No	%		
Pre-interventional						
Hb ≥ 11g% (n=93)	47	97.9	46	88.5	3.4	.06
Hb ≤ 10.9g% (n=7)	1	2.1	6	11.5		
Post-interventional						
Hb ≥ 11g% (n=73)	42	87.5	31	59.6	9.8	**.002**
Hb ≤ 10.9g% (n=27)	6	12.5	21	40.4		
Pearson's Chi square test used; p-value <0.05 is significant						

In both the diagnosed groups, the highest proportion of anemic patients were represented in the control groups while those in the misoprostol groups remained much lower (p<0.05). This result strongly favors the sake of our study.

The need for blood transfusion has been assessed in the diagnosed groups and subgroup analysis were performed for its relation with the type of intervention given in our study. Pearson's chi-square test was used for the statistical analysis. Except one, hardly any patients needed blood transfusion in the misoprostol group whereas six patients of the control group required transfusions.

Discussion:

The effect of single dose of rectal misoprostol was compared on peri-operative bleeding in abdominal hysterectomy. Various drugs including progestin, androgens, GnRHa1, and mifepristone, have been tried, but, can be used for a short period due to side effects [3, 4].

Women with large fibroid which causes mennorhagia or pressure symptoms and who have completed her family can opt for Total abdominal hysterectomy (TAH). Excessive Bleeding, blood or iron transfusion following TAH are not uncommon [6] . Misoprostol which is a prostaglandin E1 has been in use in the field of obstetrics because of its low side effects. It causes contraction of the myometrial fibres thereby decreasing the blood flow to the uterus as a whole. Our study conducted on patients who underwent total abdominal hysterectomy for benign lesions of the uterus has shown that the drug misoprostol significantly decreases the intra operative blood loss in the case group when compared to the control group.

Both the Hemoglobin levels and Hematocrit values have declined at a significantly lower pace post-TAH in the group A than group B (p<0.05) [10]. This finding deepen the prongs in elaborating the beneficial role played by misoprostol.

The results are comparable to the study done by Chang *et al.* [5], where a single rectal dose of Misoprostol plus oxytocin was used prior to operation and significantly decrease in peri-operational bleeding and Hb changes were demonstrated. The study by Celik has demonstrated a significant difference in the post operative hemoglobin levels 9.7 vs 8.9 in the case and the control group following the use of pre operative vaginal misoprostol. Biswal *et al.* [7] demonstrated the same decrease in intra operative blood loss following the usage of sublingual misoprostol. These findings suggest that misoprostol in different routes of administration either alone or used along with some other drug like oxytocin has significantly reduced the blood loss in hysterectomy patients.

In our study, we opted for 400 micrograms of rectal dose of misoprostol based on the pharmacokinetics. Because of the douching of vagina in hysterectomy with antiseptics, we preferred to use rectal route which will not interfere with the surgery.

we observed minimal side effects like fever and vomiting in our study, which confirms the superiority of rectal administration to sublingual administration, which was studied by Biswas *et al.* [7]

Conclusions

Single rectal dose of misoprostol prior to surgery was effective in reducing blood loss volume, hemoglobin drop, need for blood transfusion in total abdominal hysterectomy

Conflict of Interest:

There is no conflict of interest to be declared.

Authors' contributions:

All authors contributed to this project and article equally. All authors read and approved the final manuscript.

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