Original Article

Effects of Misoprostol in Reducing Blood Loss during Abdominal Myomectomy in Nigeria

JE Nnagbo, CC Dim[1], MI Eze[1], SG Mba[2]

Department of Obstetrics and Gynaecology, University of Nigeria Teaching Hospital, Ituku-Ozalla, Enugu State, [1]Department of Obstetrics and Gynaecology, College of Medicine, University of Nigeria/University of Nigeria Teaching Hospital, Ituku-Ozalla, Enugu State, [2]Department of Obstetrics and Gynaecology, Enugu State University Science and Technology, College of Medicine/Teaching Hospital, Parklane, Enugu, Nigeria

Received: 07-Aug-2022;
Revision: 06-Mar-2023;
Accepted: 23-Mar-2023;
Published: 15-May-2023

Abstract

Background: Despite using a tourniquet to reduce bleeding during abdominal myomectomy, the procedure is still complicated by significant intraoperative bleeding. **Aim:** To determine whether misoprostol and tourniquet compared with tourniquet alone would significantly reduce bleeding during abdominal myomectomy at two tertiary hospitals in Enugu. **Materials and Methods:** This study is an open-label randomized controlled trial. A total of 126 consenting participants were recruited from women booked for abdominal myomectomy at the study centers over 7 months. They were randomized into groups A (vaginal misoprostol 400 μg) and B (no misoprostol) one hour before surgery. Intraoperatively, all participants had a tourniquet application. Intraoperative and postoperative blood loss was compared between the two groups. Descriptive and inferential analyses were carried out using IBM SPSS Version 22.0. A *P*- value of < 0.05 was considered statistically significant. **Results:** An intention-to-treat analysis was carried out. All 63 participants (100%) and 56 (90%) completed the study according to the protocol in groups A and B, respectively. Socio-demographic characteristics were not significantly different in both groups. The mean intraoperative blood loss in the "misoprostol group" (522.6 ± 127.91 ml) was significantly lower than in the "no-misoprostol group" (583.5 ± 186.20 ml), with $P = 0.028$. The difference in mean hemoglobin (g/dl) was lower in the "misoprostol group" than in the "no-misoprostol group" (1.3 ± 0.79 vs. 1.9 ± 0.89, $P < 0.001$). The mean 48 hours postoperative blood loss (ml) between the two groups was 323.8 ± 221.44 vs. 549.4 ± 519.72), with $P = 0.001$. **Conclusion:** Among women receiving tourniquet during myomectomy in Enugu, the additional use of vaginal misoprostol 400 μg significantly reduced intraoperative blood loss.

Keywords: *Abdominal myomectomy, blood loss, misoprostol*

Background

Abdominal myomectomy remains an essential surgical option, particularly in low-and-middle-income countries where there is a strong aversion to hysterectomy.[1] It has been identified as the mainstay of treatment in patients with symptomatic uterine fibroid in various studies in Nigeria.[2-4] The procedure has undergone several modifications over the years to make it safer. This is due to the significant hemorrhage associated with the procedure, which occasionally could be life-threatening, requiring blood transfusion, or may lead to hysterectomy if specific preventive measures to occlude uterine arteries are not taken.[1-3,5] For many years, various techniques of occluding uterine arteries have been in practice, such as Bonney's clamp, sutures, and rubber tubing, including the Foleys catheter. However, the use of rubber tubing as a tourniquet was popularized by Rubin in 1953,

Access this article online

Quick Response Code:

Website: www.njcponline.com

DOI: 10.4103/njcp.njcp_526_22

Address for correspondence: Dr. JE Nnagbo, Department of Obstetrics and Gynaecology, University of Nigeria Teaching Hospital, Ituku-Ozalla, Enugu State, Nigeria.
E-mail: jesp7200@yahoo.co.uk

How to cite this article: Nnagbo JE, Dim CC, Eze MI, Mba SG. Effects of misoprostol in reducing blood loss during abdominal myomectomy in Nigeria. Niger J Clin Pract 2023;26:454-62.

which replaced Bonney's clamp and ushered in trials on Foley's catheter thereafter.[6-9] Today, it has almost become a standard for preventing blood loss during an open abdominal myomectomy.[9-12] Despite this, an abdominal myomectomy is still associated with significant intraoperative and postoperative blood loss, causing postoperative anemia and requiring transfusion.[1] This stimulated a search for various techniques that could be combined with a tourniquet to significantly reduce blood loss during and after abdominal myomectomy.[10] Though tourniquet and misoprostol can independently cause a decrease in intraoperative blood loss,[11-16] it is still not documented that a combination of the two would result in a significant reduction in blood loss. However, in a more recent vaginal misoprostol versus tourniquet study, higher mean intraoperative blood loss of 931.89 ml vs. 848.40 ml (P = 0.532) and transfusion rates of 60 vs. 55% (P = 0.651), respectively, were reported in the misoprostol group.[6] However, those who lost between 500 and 1000 ml of blood were higher in the tourniquet compared with the misoprostol group, and it was concluded that the effectiveness of the two methods was comparable.[6] This suggests that using a tourniquet or misoprostol alone during myomectomy may not be sufficient to minimize blood loss and, by extension, its complications.

Misoprostol is a prostaglandin E_1 analog that causes regular uterine contraction within 1 to 2 hours following vaginal administration, lasting up to 6 hours.[17] Hence, postoperative blood loss due to uterine relaxation could be prevented for up to 6 hours. In addition, misoprostol is cheap, readily available, and stable at room temperature; therefore, its use may be highly favored in developing countries. In Nigeria where intraoperative and postoperative hemorrhages complicate this commonly performed abdominal myomectomy, requiring blood transfusion, there is a need to combine misoprostol and tourniquet to avert these complications.[3,4,18] Nigeria remains a low-and-middle-income country where patients still pay out of pocket for health care, suggesting that blood transfusion and morbidity due to hemorrhage put more financial burden on the patient. Hence, this study determined the additional effect of misoprostol on blood loss when combined with a tourniquet.

Methodology

Trial design

A two-center, open-label, parallel design (1:1) randomized controlled study was conducted from February to August 2019.

Participants

All consenting women of reproductive age diagnosed with symptomatic uterine fibroids and booked for abdominal myomectomy were recruited proportionally from the two study centers. Exclusion criteria included a history of previous abdominal surgeries except for previous myomectomy, suspected genital tract malignancy, personal or family history of bleeding disorders, history of systemic disease that may increase the risk of complications during surgery such as diabetes mellitus, cardiovascular disease, and thyroid disease, and women on anticoagulant therapy.

Study settings/locations

The study was conducted at the gynecology units of the two teaching hospitals in Enugu State, Nigeria; University of Nigeria Teaching Hospital (UNTH), Ituku/Ozalla; and Enugu State University Teaching Hospital (ESUT-TH), Parklane, Enugu. Enugu State is located in the southeastern region of Nigeria with a total area of about 7,161 km^2 and a population of approximately 3.3 million.[19] UNTH and ESUT-TH are major referral centers for gynecological cases in southeastern Nigeria. The gynecology units of both institutions are very functional, with consultant-led clinics held from Monday to Friday. Gynecological admissions are typically elective cases from gynecology clinics and emergency cases from the accident and emergency unit, which functions daily. The abdominal myomectomy rate in UNTH and ESUT-TH was about 12 and 11 myomectomies per month, respectively. The main method of achieving hemostasis during myomectomy in both centers was the tourniquet method (use of Foleys catheter). The gynecological surgeons (consultants and senior registrars) in the two institutions obtained certification from the same postgraduate examination bodies (National Postgraduate College of Medicine or West African College of Surgeons), therefore were assumed to have acquired similar skills in performing an abdominal myomectomy.

Interventions

The intervention (400 micrograms of misoprostol (Cytotec, Pfizer, United Kingdom) tablets) was given to group A (n = 63), while those in group B, control (n = 63) received no misoprostol. However, all participants in both groups A and B received a tourniquet. Vaginal misoprostol was administered by a trained junior resident doctor 1 hour before the abdominal incision, while a tourniquet was applied as soon as the uterus was delivered, intraoperatively by the surgeon (consultant or senior registrar).

Outcomes

Primary: The volume of estimated intraoperative blood loss in the two groups was obtained by converting the difference in weights of the mops, gauze, surgical drapes, and towels after use to volume plus the volume of blood in the suction bottle at the end of surgery.

Secondary: The difference in preoperative and postoperative hemoglobin (g/dl) (postoperative hemoglobin was carried out 48 hours after surgery via venous blood and subtracted from the preoperative hemoglobin) was found.

The rate of nausea, vomiting, or shivering (the number of patients who developed any or all in the first 24 hours of surgery) was determined.

The volume of postoperative blood loss (blood collected in the drain from the end of surgery to the time the effluent is no longer macroscopically bloody) was measured.

Sample size calculation

The sample size was calculated using the formula[20]

$$n = \frac{2SD^2\left(Z_{a/2} + Z_b\right)^2}{d^2}$$

$Z_{a/2}$ = 1.96 (from Z table) at type 1 error of 5%. Z_b = 0.84 (from Z table) at 80% power. d (effect size); calculated as standardized effect size = (0.3) multiplied by the standard deviation (SD) = 0.3x 286 of the mean blood loss in the control group of a previous study.[12] d = 85.8.

$$n = \frac{2\,x286^2\left(1.96 + 0.84\right)^2}{85.8^2}$$

n = 62.2 approx. to 63. The total sample size was 126: 63 in group A and 63 in group B.

Randomization

Simple randomization was performed by an independent statistician who prepared a random allocation schedule using computer-generated random numbers.[19] This was carried out using the computer to randomize numbers 1–126 into two sequences (A and B), which were concealed using serially arranged sealed opaque envelopes.

Allocation concealment

Allocation into interventions, group A = misoprostol and group B = no misoprostol, could not be concealed, so participants knew who received misoprostol. Thus, once eligible patients gave their informed consent, a research assistant contacted the researcher, and an envelope was opened. The first envelope was opened for the first patient, the second for the second patient, etc., until all the envelopes were opened for treatment allocation. Once the allocation of intervention was confirmed, they received it accordingly. Each recruited and randomized participant had their identification number (generated numbers) written on their case notes.

Blinding

This was an open-label study. The participants knew whether they received misoprostol or not because we did not have a placebo similar to misoprostol. So, the participants were not blinded. Since the intervention (misoprostol administration) occurred 1 hour before surgery, the surgeons were not aware of who received the misoprostol or who did not. Researchers (PI and assistants) could not be blinded since they allocated patients and also measured the outcome variables.

Ethical considerations

Ethical clearance was obtained from the Ethical Research Committee of the University of Nigeria Teaching Hospital, Ituku/Ozalla, before the commencement of the study. The certificate number is NHREC/05/01/2008B-F WA0002458-IRB00002323.

Protocol

The myomectomies were performed by the consultants and senior registrars in Obstetrics and Gynaecology at the two study centers. The senior registrars were retrained on the abdominal myomectomy technique with the help of the supervisors (consultants), for the purpose of this study. This ensured uniformity in the procedures. Five research assistants were selected from each center and trained. They assisted the researcher in collecting data using the pro forma designed for the study. A research assistant (junior resident doctor) in each gynecology unit helped insert 400 μg misoprostol into the posterior fornix 1 hour before surgery and weighed the gauze, mops, and abdominal drapes before and immediately after the surgery.

Procedure for myomectomy

The technique of abdominal myomectomy used in this study was originally described by Bonney and modified by Hudson[21,22] and adapted to our practice in the two study centers. All participants received prophylactic antibiotics (intravenous ceftriaxone 1 gram statim and metronidazole 500 mg statim 30 minutes before the procedure).

Anesthesia: Anesthesia was administered mainly through the epidural route. However, those with very large uterine sizes (28 weeks and above) had general anesthesia.

Weighing of materials: Before the commencement of surgery, all the mops (each of 50 x 50 cm), gauze (each

of 10 x10 cm), and drapes were weighed using a standardized weighing scale. The weighing process was such that asepsis was maintained. A sterile bowl was weighed first to record its empty weight before the mops, gauze, and drapes were weighed. The same research assistant who measured the weights before surgery was responsible for reweighing these materials after the surgery in the centers. Otherwise, the researcher carried out the measurements. The weighing scales used in both centers were from the same company (Camry Industries Company Limited, Hong Kong) and model (EK5350). They were standardized before use. Batteries were changed when it was necessary.

Abdominal skin incision: The type of abdominal incision used depended on the size of the uterus. Transverse incisions were used when the uterine size was less than or equal to 20 weeks, and midline incisions were used when the uterine size was >20 weeks. Some abdominal incisions were extended above the umbilicus when it was necessary.

Application of tourniquet: A size 24-gauge Foley catheter provided for each participant was applied to the lower part of the uterus by the surgeon, being careful not to damage the fimbria, ovaries, and intestines or the infundibulopelvic ligament. Traction was exerted on the two ends of the catheter to occlude the two uterine arteries. The traction was maintained with one strong Kocher's forceps applied anteriorly. Tourniquet time, the time interval from application to release of tourniquet intervals of 30 minutes,[23] was carried out for all patients. The tourniquet was released to enable reperfusion at 30-minute intervals and reapplied till the fibroid nodules are removed. Points of bleeding were noted, and the figure of eight stitches was applied accordingly.

Surgical technique: As many fibroid nodules as possible were enucleated via an anterior incision on the uterus, while those not accessible through the anterior incision were enucleated via separate incisions. After the enucleation of all visible and palpable myoma masses, Vicryl 2/0 was used for the endometrium when it was breached; otherwise, Vicryl 2 suture was utilized in closing dead spaces and achieving hemostasis. This prevented hematoma formation.

Wound Drain: An improvised closed drain was placed into the Pouch of Douglas using a size 24-gauge Foleys catheter with five fenestrations created on it, each measuring about 1 cm in diameter and 2 cm apart. A urine bag was attached to form a closed drain. The drain enabled complete egress of blood that could have collected after abdominal closure.

Measurement of blood loss

This was carried out by the researcher or a research assistant (junior resident doctor in Obstetrics and Gynecology). The blood volume in the suction-calibrated bottle was read, and the used mops, gauze, and drapes were counted and reweighed (in gram) as described above. The difference in weight (in grams) was converted to milliliter using the gravimetric method,[24,25] which assumed that the density of water at room temperature is similar to blood, that is, 1 g/ml (1 g difference in weight is equivalent to 1 milliliter of blood).[26] Therefore, the total intraoperative blood loss was the total difference in weight (grams) of mops, gauze, and drape converted to milliliter plus the blood volume in the suction-calibrated bottle. Both preoperative weighing and postoperative weighing of the drapes, gauze, and mops were conducted by the same person during each procedure at the two hospitals with the same type of weighing scales, which were standardized before use.

Intraoperative monitoring of the onset of nausea, vomiting, or shivering was carried out by the researcher or the assistants. This commenced immediately after the abdominal incision was made.

Postoperative care

Postoperative care was the same in the two centers. Participants received intravenous antibiotics (ceftriaxone and metronidazole) for 48 hours and then converted to orals; received intramuscular analgesics (pentazocine and diclofenac) for 48 hours; and then converted to orals, and vital signs were monitored from the immediate postoperative period till discharge. They were commenced on graded oral sips as soon as bowel sounds were established within the first 24 hours of surgery. The wound drain was monitored every 24 hours, and the volume of effluent was recorded in milliliter. It was removed when the effluent became macroscopically non-bloody. Participants received a blood transfusion intraoperatively when they had hypovolemia or when the volume of allowable blood loss (ABL) was exceeded.[18] ABL was calculated using the formula[18] ABL = (EBVx (Hi-Hf))/Hi, where EBV is estimated blood volume calculated as body weight in (kg) x average blood volume (ml/kg), assuming an adult woman has an average blood volume of 65 ml/kg, Hi is initial hemoglobin, and Hf is the final hemoglobin. ABL = 65(Hi-Hf)/Hi. Postoperatively, a participant also received a blood transfusion if there was symptomatic anemia or hypovolemia[18] or when the 48 hours postoperative Hb was less than 8 g/dl. After discharge, they were seen two weeks later with the histology results. Preoperative Hb was recorded

before surgery, while postoperative hemoglobin was recorded from estimation done on the second day postoperative in gram/dl using a standardized HemoCue machine (Hb 201+, Danaher Company, Brea, CA, USA) in the hematology laboratory of UNTH.

Data collection

Data collection was carried out with the designed pro forma by the researcher and the trained assistants.

Data analysis

The data analysis was an intention-to-treat. It was both descriptive and inferential with Statistical Package for Social Science (IBM SPSS) statistics for Windows, version 20.0, Armonk, NY: IBM Corp. Descriptive statistics, which include frequency and percentages, which were used to summarize categorical variables such as type of incision, indications for surgery, and marital status. Age, parity, and body mass index (BMI) were dichotomized and analyzed as categorical variables using the Chi-square or Fisher's exact test. Means and SDs were obtained for continuous variables such as age and preoperative hemoglobin and compared using Student's t-test. A *P* value less than 0.05 was regarded as significant.

Results

An intention-to-treat analysis was performed. One hundred and twenty-six participants were recruited for the study, but 119 (94.4%) completed it, but all data were analyzed; 63 (50%) were in the misoprostol group, while 63 (50%) were in the no-misoprostol group. The details of the study flow are shown in Figure 1.

Participants' basic characteristics

Table 1 shows that the basic characteristics of participants were similar for the misoprostol group and the control (no-misoprostol) group. Participants' mean age was 34.1 ± 4.30 vs. 33.4 ± 4.44 years for the misoprostol and control groups, respectively (P = 0.087). A majority of the participants in both groups were nullipara (50/63, 79.4% vs. 49/63, 77.8%).

Comparison of blood loss and hemoglobin difference between the misoprostol and control groups

Table 2 shows that when compared between the two groups, the mean intraoperative blood loss was significantly lower in the misoprostol than the "no-misoprostol" groups (522.6 ± 127.91 vs. 583.5 ± 186.20, *P* = 0.028). Likewise, the mean total volume of blood lost after 48 hours postoperative and the difference in mean Hb (g/dl), that is, preoperative Hb–Hb 48 hours postoperative, was lower in the misoprostol group than in the no-misoprostol group (1.3 ± 0.79 vs. 1.9 ± 0.89, *P* < 0.001). The details of the results are shown in Table 2.

Table 1: Participants' basic and gynecological characteristics

	Misoprostol. (group A) No misoprostol (group B)		χ^2/t	*P*
	n=63 (%)	*n*=63 (%)		
Age group				
20–24	0 (0.0)	4 (100.0)	8.114	0.087
25–29	10 (55.6)	8 (44.4)		
30–34	15 (36.6)	26 (63.4)		
35–39	32 (60.4)	21 (39.6)		
40–44	6 (60.0)	4 (40.0)		
Parity				
0	50 (50.5)	49 (49.5)	0.257	0.968
1	6 (42.9)	8 (57.1)		
2–4	7 (53.8)	6 (46.2)		
Preoperative Hb mean±SD	11.4±0.86	11.5±1.12	1.771	0.178
BMI group				
<30	46 (46.9)	52 (53.1)	1.780	0.182
≥30	17 (60.7)	11 (39.3)		
Mean±SD	27.32±4.27	26.40±3.79	1.307	0.194
Uterine size				
≤24 weeks	17 (42.5)	23 (57.5)	0.941	0.332
>24 weeks	46 (55.4)	40 (44.6)		
Mean±SD	23.26±5.69	23.73±7.04	0.428	0.669
Number of fibroids				
Mean±SD	9.100±3.788	9.413±4.145	0.455	0.650
Type of incision				
Midline	24 (50.0)	24 (50.0)	0.003	0.955
Transverse	39 (50.0)	39 (50.0)		
Type of anesthesia				
General	14 (43.8)	18 (56.2)	0.907	0.494
Regional	49 (52.1)	45 (47.9)		

Comparison of misoprostol-associated side effects among participants

Concerning the side effects associated with misoprostol, Table 3 shows that though the incidence of intraoperative nausea did not differ in the two groups, six (10.0%) participants in the misoprostol group had intraoperative vomiting, compared with the control group where there was no incidence of vomiting intraoperatively. The observed difference was statistically significant (P = 0.014). Also, intraoperative shivering occurred more in the misoprostol participants when compared with the control group (P < 0.001). However, the incidence of 24 hrs postoperative nausea and vomiting was independently higher in the no-misoprostol (control) group compared with the misoprostol group. There was no difference in the

Table 2: Comparison of mean blood loss and hemoglobin difference between the misoprostol and no-misoprostol groups

	Misoprostol (group A) Mean±SD	No misoprostol (group B) Mean±SD	*t*-test	*P*
Mean volume of intraoperative blood loss	522.6±127.91	583.5±186.20	2.218	0.028
Mean volume of blood loss 48 hrs postoperative	323.8±221.44	549.4±519.72	3.314	0.001
Difference in preoperative and postoperative Hb	1.3±0.79	1.9±0.89	3.618	< 0.001

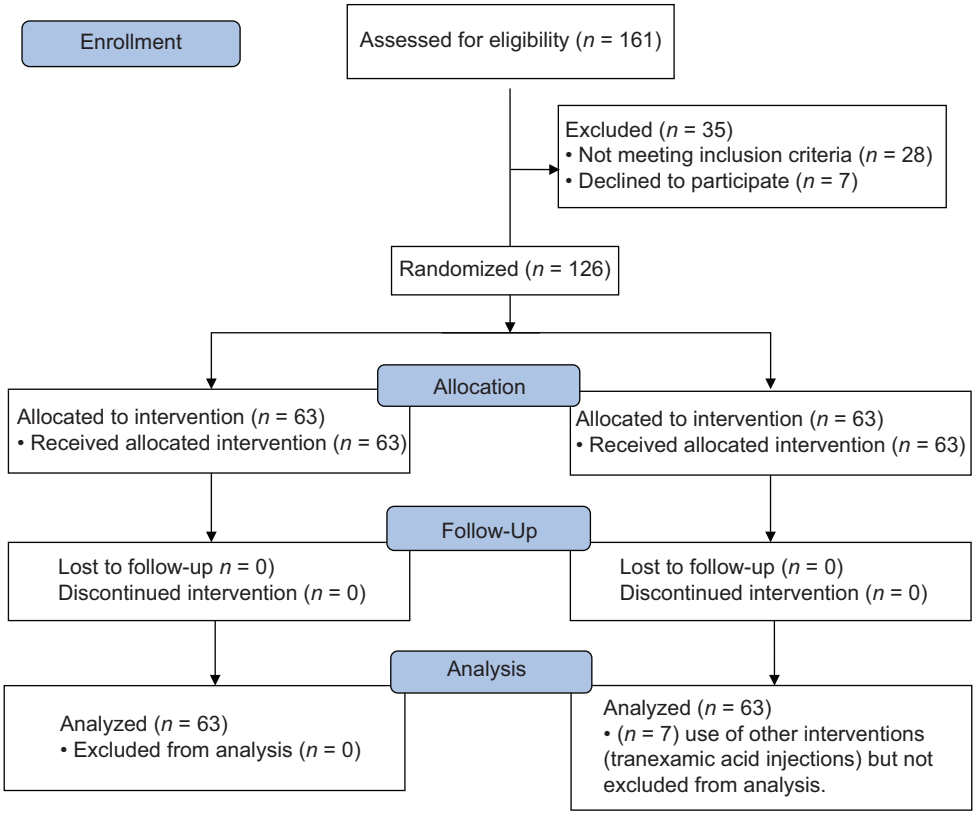

Figure 1: Flow Diagram of the study

incidence of 24 hrs postoperative shivering between the two groups.

Discussion

Mechanical occlusion of the uterine arteries using a Foley catheter has almost become the standard for preventing intraoperative blood loss during abdominal myomectomy in Nigeria.[2,3,4,6,12,18] Despite this, the need for further reduction in blood loss during abdominal myomectomy has resulted in the search for other effective methods via various research works by different authors.[15,27-31] In the current study, the use of 400 µg misoprostol inserted vaginally 1 hour before myomectomy was demonstrated to be effective in significantly reducing the mean intraoperative blood loss compared with those who did not receive misoprostol. This finding is similar to results obtained from studies in other countries by Celik *et al.* in Turkey,[15] Abdel-Hafeez *et al.* in Egypt,[28] Vahdat *et al.* in Iran,[27] Rasheed *et al.* in Egypt,[29] and Mohamed *et al.* in Egypt.[30] In these studies, intraoperative blood loss was significantly reduced by misoprostol administered 1 hour before abdominal myomectomy. While these studies were misoprostol placebo-controlled studies, the current study was conducted on a population of women who also had tourniquet as another intervention for reducing blood loss during abdominal myomectomy. The implication of this finding is that giving vaginal misoprostol to women who would receive tourniquet during myomectomy can bring about a significant reduction in intraoperative blood loss. This finding is also in consonance with the result by Frederick *et al.*[31] in West Indies who showed that misoprostol plus vasopressin had a significant reduction in intraoperative blood loss compared with vasopressin alone. However, this study differs from the current study because all the participants received vasopressin rather than tourniquet as another active intervention. Be that

Table 3: Comparison of misoprostol-associated side effects among participants

	Misoprostol use		χ^2	*P* value RR (95% CI)	
	Yes *n* (%)	No *n* (%)			
Vomiting intraoperative					
Yes	6 (10.0)	0 (0.0)	NA	0.014	NA
No	57 (90.0)	63 (100.0)			
Nausea intraoperative					
Yes	5 (7.9)	10 (15.9)	1.670	0.196	0.69 (0.36-1.32)
No	58 (92.1)	53 (84.1)			
Shivering intraoperative					
Yes	14 (22.2)	0 (0.0)	NA	<0.001	2.17 (1.78-2.64)
No	49 (77.8)	63 (100.0)			
24 hrs postoperative vomiting					
Yes	2 (3.2)	14 (22.2)	11.750	<0.001	0.22 (0.06-0.79)
No	61 (96.8)	49 (77.8)			
24 hrs postoperative nausea					
Yes	2 (3.2)	14 (22.2)	10.473	0.001	0.14 (0.03-0.54)
No	61 (96.8)	49 (77.8)			
24 hrs postoperative shivering					
Yes	3 (4.8)	0 (0.0)	NA	0.246	NA
No	60 (95.2)	63 (100.0)			

NA=not applicable

as it may, this finding is at variance with the result of a study by Maneerat *et al*.[32] in Thailand who showed that 400 μg of misoprostol administered rectally 30 minutes before abdominal myomectomy had no significant reduction in intraoperative blood loss. This difference may be a result of different routes of administration of misoprostol and additional intervention used in this study.

This study also showed there was a significant reduction in the mean hemoglobin 48 hours postoperative in the no-misoprostol group compared with the misoprostol group. This finding was not surprising as both the mean intraoperative blood loss and the postoperative blood loss were significantly higher in the control group compared with the intervention group. This finding is in keeping with the result from investigators in other countries[15,27,29,30] who also demonstrated that misoprostol administered 30 minutes to 1 hour before abdominal myomectomy caused less reduction in postoperative hemoglobin compared with the placebo controls where it caused significantly more reduction. However, it is worthy of note that these studies were misoprostol placebo-controlled studies where no other active intervention such as tourniquet was used unlike this study. The implication of this finding is that vaginal misoprostol may be combined with another active intervention such as tourniquet to achieve a significant reduction in the mean postoperative hemoglobin.

Four hundred micrograms of misoprostol inserted vaginally has been reported to be associated with some dose-dependent side effects such as nausea, vomiting, and shivering.[33,34] In this current study, vaginal misoprostol (400 μg) administered 1 hour before abdominal myomectomy was significantly associated with intraoperative vomiting and shivering and 24 hours postoperative nausea and vomiting. Though these findings are known side effects of misoprostol, they could also be explained by the fact that some of these participants received opioid analgesics (pentazocine), which are known to cause similar side effects.[35] However, these side effects were minimal and managed with promethazine (nausea and vomiting) and tramadol (shivering). Furthermore, vaginal misoprostol has been demonstrated to have mild gastrointestinal side effects compared with other routes.[17,36] However, women who need misoprostol for reducing blood loss during an open abdominal myomectomy should be counseled on these treatable side effects before use.

The finding of a higher proportion of participants presenting with uterine sizes greater than or equal to 24 weeks in this study further strengthens the need for additional methods of preventing blood loss. This is because large fibroid masses have been reported to be associated with increased blood loss during myomectomy.[37]

The strength of this study lies in the fact that it is a randomized controlled trial, but it is limited by our inability to achieve blinding and relying on the participants' report of side effects of misoprostol. These are potentials for bias in the study. Additionally, previous myomectomy and duration of surgery are

possible confounders in this study but could not be controlled, thus may have affected the intraoperative and postoperative blood loss in this study. These may have affected the result of the study.

Conclusion

The administration of 400 µg vaginal misoprostol before myomectomy in addition to the standard practice of application of pericervical tourniquet significantly reduced intraoperative blood loss when compared to women that received only the standard practice.

Recommendations

We recommend the use of preoperative vaginal misoprostol as an additional intervention to the standard pericervical tourniquet during myomectomy in our environment characterized by a larger fibroid uterus to further reduce blood loss.

Acknowledgement

The authors acknowledge the financial grant offered by the African Research League in collaboration with the Directorate of Research and Training, College of Medicine, University of Nigeria, Ituku-Ozalla, Enugu State.

Trial registration number

PACTR202010757847686, URL: https://pactr.samrc.ac.za/Rearcher/ManageTrials.aspx/.

Financial support and sponsorship

This study was supported by the African Research League in collaboration with the Directorate of Research and Training, College of Medicine, University of Nigeria, Ituku-Ozalla, Enugu State.

Conflicts of interest

There are no conflicts of interest.

References

1. Ogedengbe OK. Uterine fibroids. In: Friday, editor. Contemporary Obstetrics and Gynaecology for the Developing Second Edition, Springer Publisher, USA. 2007. p. 202-13.
2. Ekine AA, Lawani LO, Iyoke CA. Review of clinical presentations of uterine fibroid and the effect of therapeutic intervention on fertility. Am J Clin Med Res 2015;3:9-13.
3. Ikeako LC, Ezegwui HU, Okeke TC, Ezenyeaku CCT, Umeobika J, Ezebialu U. Myomectomy in a secondary health centre in Awka, South-East Nigeria. Orient J Med 2012;24:1-5.
4. Okeke TC, Okezie OA, Obioha KC. Trends of myomectomy at the University of Nigeria Teaching Hospital (UNTH) Enugu, Nigeria. Niger J Med 2011;20:224-7.
5. Lumsden MA. Benign diseases of the uterus. In: Edmonds K, editor. Dewhurst Textbook of Obstetrics and Gynaecology. Wiley-Blackwell Publishers; 2007. Vol 7. p. 636-44.
6. Afolabi M, Ezeoke GG, Saidu R, Ijaiya MA, Adeniran AS. Comparing perioperative vaginal misoprostol with intraoperative pericervical haemostatic tourniquet in reducing blood loss during abdominal myomectomy: A randomized controlled Trial. J Turk Ger Gynecol Assoc 2019;20:23-30.
7. Ranney B, Frederick I. The occasional need for myomectomy. J Obstet Gynaecol 1979;53:437-42.
8. Rubin IC. The pericervical broad ligament tourniquet for preventive haemostasis in myomectomy. Obstet Gynaecol 1953;1:668-70.
9. Sanyal U, Ghosh S, Hiremath PB, Hiremath R. The role of tourniquet in myomectomy: An observational study. Int J Reprod Contracept Obstet Gynaecol 2019;13:154-8.
10. Kongnyuy EJ, Wisonge CS. Interventions to reduce haemorrhage during myomectomy for fibroids. Cochrane Database Syst Rev 2011;CD005355. doi: 10.1002/14651858.CD005355.pub4. Update in: Cochrane Dtabase Syst Rev.2014; 8: CD005355 PMID: 22071823.
11. Abdel-Fattah IH, Tharwat AA, Mohammad WEB, Ahmed MES, Aly Maaty AM. Vaginal misoprostol versus bilateral uterine artery ligation in decreasing blood loss in trans-abdominal myomectomy: A randomized controlled trial. Egypt J Hosp Med 2017;67:614-27.
12. Ikechebelu JI, Ezeama CO, Obiechina NJA. The use of tourniquet to reduce blood loss at myomectomy. Niger J Clin Pract 2010;13:154-8.
13. Taylor A, Sharma M, Tsirkas P. Reducing blood loss at open myomectomy using triple tourniquet: A randomized controlled trial. Br J Obstet Gynaecol 2005;112:340-5.
14. Niroomad N, Hajiha S, Tabrizi NM, Ghajarzadeh M. A single dose misoprostol for reducing haemorrhage during myomectomy: A randomized controlled trial. Arch Gynaecol Obstet 2015;292:155-8.
15. Celik H, Sapmaz E. Use of a single preoperative dose of misoprostol is efficacious for patients who undergo abdominal myomectomy. Fertil Steril 2003;79:1207-10.
16. Iavazzo C, Mamais I, Gkegkes D. Use of misoprostol in myomectomy: A systematic review and meta-analysis. Arch Gynaecol Obstet 2015;292:1185-91.
17. Gemzell-Danielsson K, Marions L, Rodriguez A, Spur BW, Wong PYK, Bygdeman M. Comparison between oral and vaginal misoprostol on uterine contractility. Obstet Gynaecol 1999;93:275-80.
18. Adesina TK, Owolabi BO, Raji HO, Olarinoye AO. Abdominal myomectomy: A retrospective review of determinants and outcomes of complications at the University of Ilorin Teaching Hospital, Ilorin, Nigeria. Malawi Med J 2017;29:37-42.
19. Nigeria Data portal. State population 2006. Available from https://nigeria.opendataforafrica.org/ifpbxbd/state-population-2006. [Last accessed on 2016 Jul 25].
20. Jaykaran C, Tamoghna B. How to calculate sample size for different study designs in medical research. Indian J Psychol Med 2013;35:121-6.
21. Bonney V. The modern scope and technique of myomectomy. J Obstet Gynecol Brit Emp 1922;29:591-607.
22. Hudson CN, Setchel ME. Fibroids and endometriosis: Myomectomy. In: Shaw's Textbook of Operative Gynaecology. 6th ed. Reed Elsevier Publishers India; 2011. p. 141-56.
23. Parker WH. Abdominal myomectomy: Patient and surgical technique considerations. OBG Manag 2017;29:23-8.
24. Nelson GH, Ashford C, Williamson R, Amburn SD. Method for calculating blood loss at vaginal delivery. South Med J 1981;74:550-2.
25. Ashraf AH, Hisham MR. Assessment of blood loss during caesarean section under general anaesthesia and epidural analgesia using different methods. Alex J Anaesth Intensive Care

2006;9:25-30.
26. Vitello DJ, Ripper RM, Fettiplace MR, Weinberg GL, Vitello JM. Blood density is nearly equal to water density: A validation study of the gravimetric method of measuring intra-operative blood loss. J Vet Med 2015;2015:152730.
27. Vahdat M. The effects of misoprostol on intraoperative blood loss after myomectomy. Int J Reprod Contracept Obstet Gynecol 2015;4:776-9.
28. Abdel-Hafeez M, Elnaggar A, Ali M. Rectal misoprostol for myomectomy: A randomized placebo-controlled study. Aust NZJ Obstet Gynaecol 2015;55:363-8.
29. Rasheed MR. Effects of rectal misoprostol in myomectomy. Al-Azhar Assiut Med J 2014;12:270-9.
30. Mohamed SES, Mansour DY, Shaker AN. The effect of misoprostol on intra-operative blood loss during myomectomy operation: Randomized controlled trial. Evid Based Women Health J 2019;9:363-71.
31. Frederick S, Frederick J, Fletcher H, Reid M, Hardie M, Gardner W. A trial comparing the use of rectal misoprostol plus perivascular vasopressin with perivascular vasopressin alone to decrease myometrial bleeding at the time of abdominal myomectomy. Fertil Steril 2013;100:1044-9.
32. Maneerat P, Tongmai S. Rectal misoprostol in women undergoing myomectomy for intraoperative blood loss reduction: A double blinded randomized placebo- controlled study. Thai J Obstet Gynaecol 2019;27:88-99.
33. Goldberg AB, Greenberg MB, Darvey P. Misoprostol and pregnancy. Engl J Med 2001;344:38-47.
34. Elsheikh A, Antsalklis A, Mesogitis S, Papantoniou N, Rodolakis A, Vogas E. Use of misoprostol for the termination of second trimester pregnancies. Arch Gynaecol Obstet 2001;265:204-6.
35. Monstafa-Gharabaghi P, Alizadeh S, Atashkoye S, Sayyah-Melli M, Jafari-Shobieri M, Ouladsahebmadarek E, *et al*. Comparing the outcomes and side-effects of administration of a single preoperative dose of vaginal misoprostol with intraoperative oxytocin infusion in blood loss during abdominal myomectomy. Int J Womens Health Reprod Sci 2017;5:306-11.
36. Kuroiwa R, Handa S, Inomata K, Kato Y. The effect of pentazocine on nausea and vomiting following catheter ablation. Showa Univ J Med Sci 2020;32:103-11.
37. Takeuchi H, Kuwatsuru R. The indications, surgical techniques, and limitations of laparoscopic myomectomy. JSLS 2003;7:89-95.