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ORIGINAL ARTICLE

Effect of Preoperative Misoprostol for reducing blood loss during Myomectomy

Ahmed Morsy Saad Abdel-Rahman [*1]

[1] Department of Obstetrics and Gynecology, Damanhour Educational Hospital, Damanhour, Egypt

Corresponding author*
Ahmed Morsy Saad Abdel - Rahman

E-mail:
dr.mero_2014@hotmail.com

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ABSTRACT

Background: Misoprostol is a synthetic version of prostaglandin E1, unlike its naturally occurring counterpart. Prostaglandins enhance the contractions of the myometrium, resulting in a decrease in bleeding from the myometrium.

Objective: To assess the effect of preoperative sublingual misoprostol versus a placebo on intraoperative blood loss during abdominal myomectomy.

Patients and methods: This case control study conducted on 100 patients at Damanhour Medical National Institute from October 2023 until March 2024.

Results: There was no discernible disparity in the use of Vasopressin among laparoscopic & open myomectomy (p-value = 0.15) or Tranexamic Acid (p-value = 0.39). In terms of postoperative complications, in the misoprostol group, 8% of patients had nausea, 4% had vomiting, and 8% had shivering, while in the control group, 4% of patients had nausea, 6% of patients had vomiting, and 4% of patients had shivering. There was no discernible disparity in complications between the groups.

Conclusions: Our study concluded that there was a significant disparity in blood loss during surgery amongst the two groups. Our findings also indicate that administering sublingual misoprostol before surgery is an easy, easily implemented, and comfortable approach to decreasing intraoperative blood loss throughout abdominal myomectomy.

Keywords: Misoprostol;Myomectomy; Sublingual;Blood loss; Leiomyoma

INTRODUCTION

Uterine leiomyomas are the predominant noncancerous growths found in females. Although the majority do not show any symptoms, around twenty to fifty percent of them result in menorrhagia, pelvic pain or pressure, and complaints related to the colon or urinary system **[1]**. Abdominal hysterectomy is most performed to treat uterine leiomyomas **[2]**.

For symptomatic leiomyomas, myomectomy —an open or laparoscopic procedure—is a successful surgical option. The surgery is frequently accompanied by intra-operative bleeding, which might cause anemia and necessitate a blood transfusion and a lengthy hospital stay **[3]**.

Due to the significant issue of hemorrhage in myomectomies, various techniques have been devised to decrease bleeding. The methods employed consist of the administration of

preoperative GnRH agonists, the use of tourniquet techniques, the clamping of both uterine and/or ovarian arteries, and the injection of intraoperative vasopressin into the myometrium **[4, 5]**.

Prostaglandins enhance the contractions of the myometrium, resulting in a decrease in the bleeding of the myometrium. Research has demonstrated that misoprostol, which is an analog of PGE1, effectively decreases blood flow in the uterine artery when administered during the early stages of pregnancy **[6]**.

Misoprostol is a replacement for the naturally occurring prostaglandin E1 that is utilized in obstetric and gynecological therapy. It is an essential medication. Within the context of surgical excision of leiomyomas, it has been found to reduce intraoperative hemorrhage **[7]**.

Misoprostol is thought to work through uterine vasoconstriction and decreased uterine arterial blood flow following myomectomy. Studies have been done to evaluate the efficiency and safety of misoprostol delivered vaginally and rectally to minimize intraoperative bleeding during myomectomy. Investigations have shown that misoprostol significantly decreases blood loss during open & laparoscopic myomectomies when given vaginally or rectally **[8]**.

The rectal & vaginal methods offer greater levels of sustained plasma than the sublingual route, although they may be perceived as more intrusive and less acceptable by certain individuals. Pharmacological research indicates that administering medication through the sublingual method leads to the highest peak plasma concentration, or systemic bioavailability. No trials have assessed the efficiency of sublingually delivered misoprostol to reduce blood loss during surgery. As a result, we sought to determine if sublingual misoprostol was useful in minimizing intraoperative blood loss throughout open & laparoscopic myomectomy **[9]**.

This research aimed to evaluate the influence of preoperative sublingual misoprostol in contrast to a placebo on intraoperative blood loss throughout abdominal myomectomy.

PATIENTS AND METHODS

This case control study conducted on 100 patients at Damanhour Medical National Institute from October 2023 until March 2024. The trial was accessible to any woman who visited the unit's outpatient clinic & qualified for a laparoscopic or open myomectomy.

Inclusion criteria

Women who are 18 years or older and do not have any conditions that would prevent them from using misoprostol are eligible. Women diagnosed with uterine myomas measuring three to eight centimeters must undergo a myomectomy. cases who have one or two grades of submucous fibroids, suffer symptoms after menstruation, & have been confirmed with fibroids using ultrasonography.

Exclusion criteria

A history of prostaglandin allergy. Any surgical case, including bleeding that requires surgical or medical intervention to decrease hemorrhaging, excessive menstrual hemorrhage caused by a pelvic infection, intrauterine contraceptive device, allergic reaction to misoprostol or asthma, pregnancy, medical conditions such as high blood pressure, lung and heart illness, chronic hormonal & metabolic disorders like diabetes,

hormonal therapy before treatmentfor exampleoral contraceptives or GnRH analogs, broad &cervical ligament abnormalities, blood clotting disorders, anemia with a level of hemoglobin below ten g/d, & any myomectomy procedure that had to be changed to a hysterectomy.

Methods

All patients underwent a pelvic ultrasound examination to determine the location &number of uterine myomas, & the best strategy of surgery. All patients received preoperative hemoglobin up to 72 hours before their procedure.Each research individual received a special trial participant number, which was utilized to assign each patient to a research arm on the day of operation.

Cases were separated into two groups (misoprostol 200 mm vs. placebo 206 mm). In total, 67 open and 33 laparoscopic myomectomies were performed.

Randomization

The research drug was provided in an opaque, sealed envelope & delivered sublingually to the case right before their surgery, at least 30 minutes before the planned surgery, but it had to happen exactly 10 minutes before intubation.

According to the standard operating procedure at the facility, each patient got a vasopressin injection into the uterine myometrium consisting of 20 IU diluted in forty milliliters of normal saline. The length of the procedure, as well as the time between drug administration and the start, were noted.Open or laparoscopic myomectomy in female patients under the age of 18. Preoperative sublingual 400mcg misoprostol or placebo was given to women having open myomectomy or laparoscopic for symptomatic uterine leiomyomas. By accurately recording the postoperative volume in the suction canister & weighted packs, minus any irrigation fluid utilized, intra-operative blood loss was calculated.

Data collection

Any preoperative side effects from drug administration, such as nausea, vomiting, headaches, and shivering, were noted. At least 12 hours after surgery, serum hemoglobin and any problems or blood transfusions were noted.

Procedures

Both a monopolar spade and a bipolar Harmonic Scalpel were utilized in the process of performing laparoscopic myomectomies. Following the creation of an oval incision on the front surface of the fibroid, it was dissected.Morcellation of the myoma was performed in an Espinar bag while the individual was under anesthesia, and the uterus was sutured using V-lock to create layers. The Pfannenstiel, or midline incision, was generated during open myomectomies, & a transverse incision was made across the anterior surface of the myoma using either monopolar diathermy or a scalpel. Both incisions were performed in order to remove the myoma. The size and position of the myomas were taken into consideration when making these incisions. Similar layering and V-lock sutures were used to close the uterus.

OUTCOMES

Primary outcomes

This research investigation aimed to evaluate the impact of preoperative sublingual misoprostol on intraoperative hemorrhage during a myomectomy operation.

Secondary outcomes

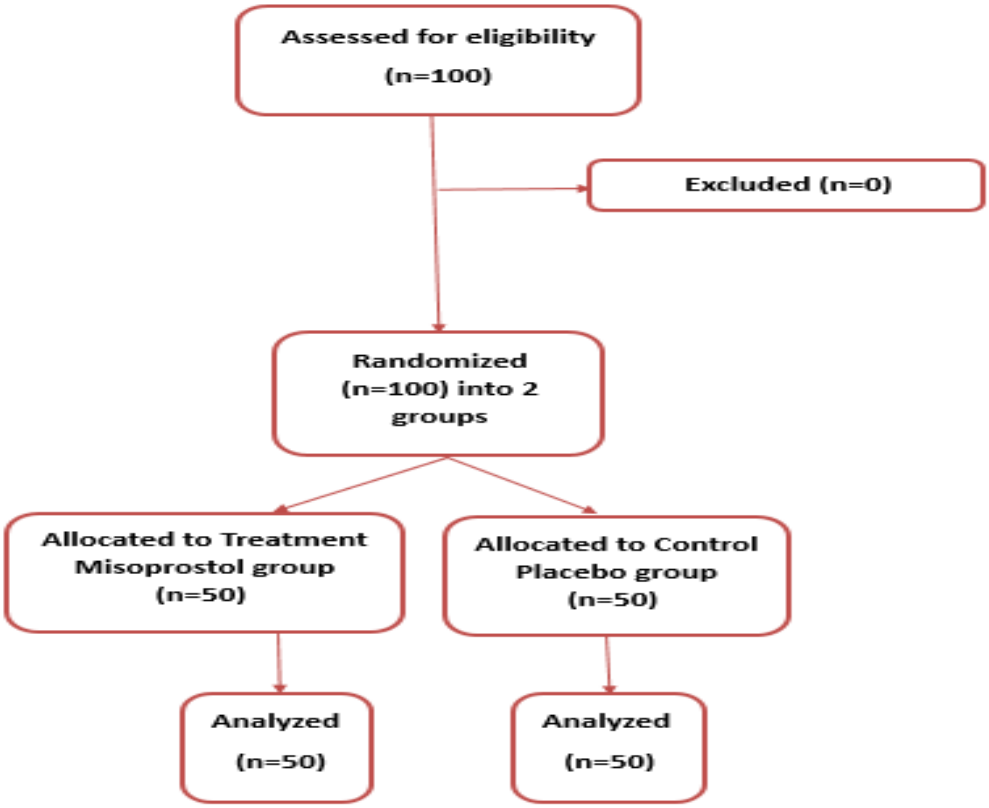
The variation in hemoglobin levels between before and after the operation, the length of the operation (in minutes), the rate of blood transfusion, the incidence of postoperative problems within thirty days (Clavien-Dindo system), & the usage of adjuvant blood loss-reduction techniques (such as tranexamic acid).

The power estimate was in accordance with earlier research that examined the effects of misoprostol given via the rectal and vaginal routes on intraoperative blood loss during myomectomy operations **[10, 11]**.

The placebo group had a mean anticipated blood loss of seven hundred milliliters, while the misoprostol group had a mean predicted blood loss of five hundred milliliters +/- three hundred milliliters. In order to identify a variance, seventy-two participants were required, thirty-six in each research arm, with a 1:1 enrollment ratio, a power of 0.8 (= 0.2), & a type one error rate of 0.05 (= 0.05). This was exploratory pilot research to determine the feasibility of the trail's concept.

STATISTICAL ANALYSIS

Interquartile Range (IQR) or Means Standard Deviation (MSD) was applied to reporting continuous variables. For discrete variables, reports included counts and percentages of the total. To analyze continuous information, the student's t-test, or Mann-Whitney test, was used. The chi-squared test assessed discrete variables. The significant P-values were 0.05 or less. Analysis utilized STATA 14 (StataCorp, 2015; Stata Statistical Software, Release 14, College Station, TX: StataCorp LP).



RESULTS

There was no discernible distinction among the misoprostol & placebo groups in the baseline demographics and features. The size of the largest myoma was comparable across the two groups (misoprostol 200 mm vs. placebo 206 mm). In total, 67 open and 33 laparoscopic myomectomies were performed. In the misoprostol group, there were more laparoscopic myomectomies than in the placebo group (52% vs. 14%, respectively), while in the placebo group, there were more open myomectomies **(Table 1)**.

There was a significant disparity in the intraoperative blood loss amongst the 2 groups (misoprostol group: 430.32± 140.2 ml, control group: 493.92± 145 ml). The variance in operating time among the placebo & misoprostol groups wasn't statistically significant. There was no discernible disparity in the time required for surgery or blood transfusion among laparoscopic and open myomectomy **(Table 2)**.

The disparity in postoperative hemoglobin among the 2 groups was different (misoprostol group: 11.23 ±1.93, control group: 10.12 ± 1.66) **(Table 3)**.

There was no discernible disparity in the use of Vasopressin among laparoscopic & open myomectomy (p-value = 0.15) or Tranexamic Acid (p-value = 0.39) **(Table 4).**

In terms of postoperative complications, in the misoprostol group, 8% of patients had nausea, 4% had vomiting, and 8% had shivering, while in the control group, 4% of patients had nausea, 6% of patients had vomiting, and 4% of patients had shivering. There was no discernible disparity in complications between the groups **(Table 5)**.

Table 1: Baseline demographics and patients' characteristics between the groups

	Treatment Misoprostol (n=50)	**Control Placebo (n=50)**	**P-value**
Age (yr) Median	30.19±7.22	30.36±5.53	0.89
BMI Mean (SD)	26.12±9.13	26.48±8.31	0.83
Occupational Status			
Employee	28(56%)	26(52%)	0.68
Unemployed	22(44%)	24(48%)	
Parity	1.5±0.5	1.6±0.6	0.36
Number of myomas excised	2±1.7	2.2±1.6	0.54
Site of myomas n (%)			
Subserosa	10(20%)	43(86%)	<0.001
Intramural	37(74%)	6(12%)	
Submucosal	3(6%)	1(2%)	
Size of largest myoma (mm) Mean (SD)	200±33	206±38	0.4
Laparoscopic Myomectomy (comparison group) n (%)	26 (52 %)	7 (14 %)	2.6 RR* (96 %CI: 1.0–6.2) P = 0.03
Open Myomectomy (baseline group) n (%)	23 (46 %)	44(88 %)	

*Laparoscopic Myomectomy was compared to abdominal Myomectomy to obtain this RR.

Table 2: Intra-operative data and blood loss between the groups

	Treatment Misoprostol (n = 50)	Control Placebo (n = 50)	P-value
Operative time (min)	109±14	120± 50	0.13
Estimated blood loss (ml)	430.32± 140.2	493.92± 145	0.02
Blood transfusion n (%)	2(4%)	5(10%)	0.23

Data presented as Mean +/- SD.

Table 3: Comparison of hemoglobin Pre& Post-operative between the groups

	Treatment Misoprostol (n = 50)	Control Placebo (n = 50)	P-value
Preoperative Hb Mean (SD)	13.52±1.83	13.55± 1.77	0.9
PostoperativeHb Mean (SD)	11.23 ±1.93	10.12 ± 1.66	0.002
P-value	<0.001	<0.001	_

Table 4: Postoperative outcome measures between the groups

	Treatment Misoprostol (n=50)	Control Placebo (n=50)	P-value
Use of Vasopressin (%)	48 (96%)	50 (100%)	0.15
Use of Tranexamic acid (%)	2(4%)	4 (8 %)	0.39

Data presented as Mean +/- SD or number of women (%).

Table 5: Comparison of Complications between the groups

	Treatment Misoprostol (n=50)	Control Placebo (n=50)	P-value
Complications			
Nausea	4(8%)	2(4%)	0.39
Vomiting	2(4%)	3(6%)	0.64
Shivering	4(8%)	2(4%)	0.39

DISCUSSION

The importance of uterus-protecting procedures such as myomectomies has grown due to the rising number of older women giving birth, the greater usage of assisted reproductive techniques, & the higher occurrence of dyspareunia & sexual dysfunction after hysterectomy **[12, 13]**.

Misoprostol is used in obstetrics to induce birth, perform abortions, & treat and prevent postpartum hemorrhages. It has been found to reduce intraoperative hemorrhage in myomectomies, where excessive bleeding is a significant problem **[14]**.

Our results demonstrated that there wasn't discernible distinction among the misoprostol & placebo groups in the baseline demographics and features. The size of the largest myoma was comparable across the two groups (misoprostol 200 mm vs. placebo 206 mm). In total, 67 open and 33 laparoscopic myomectomies were performed. The misoprostol group underwent more laparoscopic myomectomies (52% vs. 14%,

respectively) than the placebo group. Myomectomies were more open.

This study is like the one by **El Maraghy et al. [15]**, whose goal was to find out how giving 400 µg of prostaglandin E1 under the tongue sixty minutes before abdominal myomectomy surgery affected blood loss. The study found no variance in age or body mass index among the misoprostol & placebo groups. However, there was a statistically significant distinction in the size of myomas among the groups that were analyzed.

Celik and Sapmaz [16] conducted a study to evaluate the efficacy of a single preoperative dose of misoprostol in abdominal myomectomies. They found that there wasn't a statistically significant variance among the misoprostol & placebo groups in terms of the sociodemographic characteristics of the cases.

Our current research demonstrated that there was a significant disparity in intraoperative blood loss amongst the 2 groups (misoprostol group: 430.32± 140.2 ml, control group: 493.92± 145 ml). The variance in operating time among the misoprostol & placebo groups wasn't statistically significant. Between laparoscopic and open myomectomy, there was no discernible disparity in the time required for surgery or blood transfusion.

Our results agreed with **El Maraghy et al. [15],** who reported that there wasn't statistically significant variance among the groups of study according to the period of the surgery& blood transfusion. Otherwise, they reported that there wasn't a statistically significant varianceamong the studied groups regarding intraoperative bleeding.

Kalogiannidis et al. [17] conducted research to determine if using misoprostol before surgery could decrease the amount of blood loss during minimally invasive surgeries such as laparoscopic or laparoscopically assisted myomectomy. They found that the group of cases who received misoprostol had significantly lower estimated blood loss (EBL) compared to the placebo group (126 +/- 41 vs. 217 +/- 74, respectively).

However, **Niroomand et al. [18]**discovered a statistically significant distinction in the period of operation among the misoprostol & placebo groups.

We found that the disparity in postoperative hemoglobin among the 2 groups was different (misoprostol group: 11.23 ±1.93, control group: 10.12 ± 1.66). There was no discernible disparity in the use of Vasopressin among laparoscopic & open myomectomy (p-value = 0.15) or Tranexamic Acid (p-value = 0.39).

Our results are supported by **El Maraghy et al. [15],** who stated that there was statistically significant variance among the groupsof study regarding postoperative hemoglobin.

In addition, **Kalogiannidis et al. [17]** stated that the decline of postoperative Hb was significantly greater in group II (1.6 +/- 0.43) compared to group I (1 +/- 0.33).

On the other hand, **Niroomand et al. [18]** reported that there wasn't statistically significant variance among the misoprostol and placebo groups regarding the mean postoperative HB level.

In terms of postoperative complications, our results showed that in the misoprostol group, 8% of patients had nausea, 4% had vomiting, and 8% had shivering, while in the control group, 4% of patients had nausea, 6% of patients had vomiting, and 4% of patients had shivering. There was no discernible disparity in complications among the groups.

Our results matched those of **Kalogiannidis et al. [17],** who reported that the rate of side effects was similar among groups.

CONCLUSION

Our study concluded that there was a significant disparity in intraoperative blood loss amongst the two groups. Our findings also indicate that administering sublingual misoprostol before surgery is an easy, easily implemented, and comfortable approach to decreasing blood loss during surgery throughout abdominal myomectomy.

Conflict of interest

No conflicts of interest have been claimed by the author.

Ethical approval

Ethical approval ID: HD000174

Authorship

The conception & design of the trail, data analysis, drafting, & revising manuscript were done by Dr**Ahmed.**

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Availability of data & materials

Data as well as materials were available.

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