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Original Article

Effect of Rectal Misoprostol in Reducing Intra-Operative Blood Loss During Myomectomy - A Randomized Controlled Trial

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ABSTRACT

Objective: To determine the effect of administration of pre-operative rectal misoprostol in reducing intra-operative blood loss during abdominal myomectomy in comparison to no treatment.

Study design: Randomized controlled trial (single blind) (NCT05108597 at Clinicaltrials.gov)

Place and Duration of the Study: Obstetrics and Gynecology department, Pak Emirates Military Hospital, Rawalpindi from March 2019 to March 2020.

Methodology: A total of 200 women for elective abdominal myomectomy were randomly allocated into two groups. In the experimental group, 100 women were administered 400ug Misoprostol through the rectal route prior to surgery and 100 were in the control group, in which no drug was administered. The surgical procedural elements, the surgeon or surgeons performing the procedure and the use of antibiotics as well as anesthetic agents was standardized to remove any bias. Intraoperative blood loss was recorded by a single trained doctor and calculated using visual scale for the abdominal sponges and chest swabs/gauzes used during surgery and blood collected in suction bottle.

Results: The mean age was 30.45±4.58 years. The mean blood loss was significantly low in experimental groups as compare to control groups [523±97.3 vs. 815.9±117.93 $p<0.001$]

Conclusion: In conclusion, administration of rectal misoprostol appears to be effective in reducing intra-abdominal blood loss during abdominal myomectomy.

Keywords: Intraoperative Complications, Leiomyoma, Misoprostol, Uterine Myomectomy.

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INTRODUCTION

The most prevalent benign gynecological tumors are uterine leiomyomata (fibroids).[1] Uterine fibroids affect 20-40% of women in their reproductive years, and their prevalence rises to nearly 70% by the age of 50.[2] Fibroids are usually asymptomatic, but they can cause abnormal uterine bleeding, heavy menstrual bleeding, pressure symptoms, pelvic pain, anemia, and infertility, all of which impact one's quality of life and necessitate treatment.[3] Medical, surgical, and radiological guided procedures are all available to treat symptomatic leiomyomata. Medical options,[4] like NSAIDS, Tranexamic acid, contraceptives, GnRH analogues, and selective progesterone receptor modulators (SPRM) can be helpful in relieving symptoms but these options do not remove fibroids and symptoms return after cessation of medical treatment.

Radiological interventions like uterine artery embolization, myolysis and ablations are also temporary.[5] Surgical options include myomectomy and hysterectomy, hysterectomy being the only definitive treatment option at the expense of loss of future fertility in a woman. In women who want to keep their fertility preserved, myomectomy is the most common conservative surgical choice among the uterine sparing techniques.[6] However, major problem with myomectomy is excessive blood loss during surgery (due to excessive blood supply to fibroids), which can be life threatening and may need blood transfusion and can lead to potential loss of reproductive capability through hysterectomy.

A variety of trials have been conducted to evaluate the effectiveness of various strategies to limit intraoperative blood loss during myomectomy, including intravenous oxytocin,[7] use of tourniquets, clamping/ligation of bilateral uterine arteries,

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vasopressin, misoprostol,[8-10] bupivacaine and epinephrine,[11] etc.

Misoprostol, being a synthetic analogue of prostaglandin E1, is frequently used in obstetrics and gynecology because of its uterotonic (causes powerful uterus contraction, resulting in vascular structure constriction and reduction in the blood flow) and cervical priming effects,[12] It is being used for evacuation of uterus in missed and incomplete abortion, induction of labor and management as well as prevention of postpartum hemorrhage.[13] Because of its wide-ranging applications and uses in reproductive health, misoprostol is on the World Health Organization's Model List of Essential Medicines. It can be administered through different routes i.e. orally, vaginally, sublingually or through rectal route.[14] Rectal route has longer duration of action as compared to oral route or sublingual route, with less side effects observed.[15] This drug has gained wide popularity as it is stable at room temperature, inexpensive, and generally available.

A study published in the Australian and New Zealand Journal of Obstetrics and Gynecology by Abdel-Hafeez *et al*., 2015,[1] found that a single dosage of misoprostol taken via the rectal route preoperatively reduced intraoperative blood loss and surgical time in abdominal myomectomy. Intraoperative blood loss in the study (misoprostol) group was significantly lower (574±194.8ml) than in the placebo group (874±171.5 ml).

The use of misoprostol in fields other than pregnancy has been fairly limited therefore requiring the need of further studies. It has been used through the oral, sublingual and vaginal route in many randomized controlled trials; however, the rectal administration has been far less studied thereby providing the aim and innovation for this study.

METHODOLOGY

This randomized controlled trial was undertaken in Pak Emirates Military hospital Rawalpindi from 4th March 2019 to 4th March 2020. Approval was taken from hospital's ethical committee (IRB No. A/28/EC/369). NCT05108597 was the national clinical trial number at Clinicaltrials.gov. On the basis of study conducted by Abdel Hafeez published in Australian and New Zealand Journal of Obstetrics and Gynecology,[1] using WHO sample size calculator a sample size of 200 was calculated taking 5% Level of significance, 80% Power of test, Anticipated population mean±SD (Misoprostol) = 574±194.8 and test value of population mean (Placebo group) Mean±SD = 874±171.51.

Inclusion Criteria: Patients admitted for elective abdominal myomectomy eligible for the study included healthy females, 18-50 years of age, diagnosed with intramural or sub-serosal fibroids on ultrasound, of American Society of Anesthesiologists (ASA) physical status class I-II.

Exclusion Criteria: Patients having other systemic or metabolic diseases or having pre-operative Hemoglobin <10 g/dl, and prior history of receiving Danazol or GnRH analogues before surgery were excluded.

All eligible patients were randomized into equal strength experimental and control groups using the lottery technique after obtaining informed written consent. Patient's detailed history including biodata, parity & BMI was recorded. Bimanual pelvic examination of each patient was done to assess the size of the uterus. In experimental group Misoprostol 400ug was administered through the rectal route one hour prior to surgery. In the control group, no drug was administered. The surgical procedural elements, the surgeon or surgeons performing the procedure and the use of antibiotics as well as anesthetic agents was standardized to remove any bias. The primary outcome measure was intra-operative blood loss, which was determined by adding the blood collected in the suction bottle and the blood absorbed in the sponges and gauzes at the end of operation. Intraoperative blood loss was recorded by a single trained doctor and calculated using visual scale for the abdominal sponges and chest swabs/gauzes used during surgery and blood collected in suction bottle. He was unaware of the patients' randomization and medication use i.e., blinded. The absorptive capacity of two types of gauzes used in myomectomy (Surgical Sponges/ Chest gauzes) was determined when the gauze had absorbed the blood. Completely soaked/saturated surgical gauzes (abdominal sponges) had the absorptive capacity of 100 ml while partially soaked (50% saturated) surgical gauzes had absorptive capacity of 50 ml. Similarly, fully soaked chest gauzes had the absorptive capacity of 30 ml while partially soaked (50% saturated) surgical gauzes had absorptive capacity of 15 ml.

Data was analyzed by using Statistical Package for the Social Sciences (SPSS) version 21.00. The mean and standard deviation were calculated for quantitative factors such as age, weight, parity, BMI,

uterine size, and fibroid size. An independent sample t-test was employed to compare intraoperative blood loss in both groups. The *p*-value≤0.05 was considered statistically significant.

RESULTS

The primary outcome measure was intra-operative blood loss. The mean blood loss was significantly low in experimental group as compared to control group [523±97.3 vs. 815.9±117.93, *p*<0.001] as visualized in Table-I. The mean age of the patients included in the study was 30.45±4.58 years. Patients' demographics, height, weight and BMI as well as the number of fibroids and size of the uterus are reported in Table-II. Most of the women had nulliparity in both groups. 69 of the 100 patients in experimental group were nulliparous and 4% were multiparous while 27% were primiparous (had delivered once). In the control group, 64% were nulliparous, 25% were primiparous and 11% were multiparous.

Stratification analysis with respect to age of the women showed that mean blood loss was significantly lower in the experimental group (Table-III). Similarly, stratification analysis with respect to BMI and size of the uterus revealed that mean blood loss was significantly lower in the experimental group as shown in Table-IV and V respectively.

Table-I: Comparison of Mean Blood Loss Between the Experimental and Control Groups

Groups	Blood Loss Mean±SD	*p*-value
Control	815.9±117.93	*p*<0.001
Experimental	523±97.3	

Table-II: Pre-Operative Characteristics of Patients in Experimental & Control Group (n=200)

Variables	Experimental Mean±SD	Control Mean±SD	Total Mean±SD
Age (Years)	29.81±4.196	31.08±4.89	30.45±4.58
Weight (kg)	69.18±11.47	71.42±11.95	70.30±11.73
Height (cm)	157.28±6.148	157.07±6.94	157.17±6.54
BMI (kg/m^2)	28.00±4.60	29.09±5.45	28.54±5.06
No of fibroids	2.40±0.739	2.40±0.69	2.40±0.71
Uterine size	14.08±4.83	15.76±5.34	14.92±5.15
Largest fibroid	4.12±1.28	4.38±1.12	4.25±1.21

Table-III: Comparison of Mean Blood Loss Between Groups Stratified By age Groups

Age Groups (Years)	Experimental n	Experimental Blood Loss Mean±SD	Control n	Control Blood Loss Mean±SD	*p*-value
≤25	18	483.89±64.82	12	775.00±121.54	<0.001
26-30	39	544.87±106.86	40	825.00±119.29	<0.001
31 to 35	33	522.42±99.21	29	813.10±110.29	<0.001
>35	10	510.00±87.56	19	826.84±127.71	<0.001

Table-IV: Comparison of Mean Blood Loss Between Groups Stratified by BMI

BMI (kg/m^2)	Experimental n	Experimental Blood Loss Mean±SD	Control n	Control Blood Loss Mean±SD	*p*-value
≤25	30	504.67±108.42	26	821.15±102.15	<0.001
25.1-29.9	38	523.68±93.53	33	810.30±115.87	<0.001
>30	32	539.38±90.51	41	817.07±130.88	<0.001

Table-V: Comparison of Mean Blood Loss Between Groups Stratified By Uterine Size

Uterine Size (weeks)	Experimental n	Experimental Blood Loss Mean±SD	Control n	Control Blood Loss Mean±SD	*p*-value
≤10	31	523.87±96.42	16	786.25±136.71	<0.001
11-20	58	526.90±93.34	58	811.55±112.63	<0.001
>20	11	500.00±124.49	26	843.85±116.38	<0.001

DISCUSSION

Leiomyomas (fibroids) are hormone (estrogen) dependent and grow during the reproductive period. The demographics of childbearing have evolved, with many women delaying starting their families until they are in their 3rd or 4th decade of life. For many women in this generation, the old maxim "children, fibroids, and hysterectomy" no longer holds true, and there is a growing need of strategies that preserve fertility while treating the symptomatic leiomyomas.[16] Myomectomy is the surgical removal of uterine leiomyomas, while preserving the uterus. This surgery remains the main conservative treatment of uterine myomas, however, hemorrhage is often a problem in this surgery and can result in post-operative anemia, intraoperative hypovolemic shock, adhesions with infertility and pelvic infection. In myomectomy, there are several approaches for reducing intraoperative blood loss.[17] These can include peri-cervical tourniquets and uterine artery embolization, among various other surgical methods. Vasopressin, uterotonics such Oxytocin, Misoprostol, and

Tranexamic acid, and other medical therapies are used to minimize intraoperative blood loss.[18]

In our study, Misoprostol 400ug was administered per rectally one hour prior to surgery and in control group, no drug was administered. Rectal administration allows the medicine to be absorbed while avoiding the adverse effects of oral administration and has a longer half-life than oral administration.[19] The mean age of the patients was 30.45±4.58 years. Most of the women had nulliparity in both groups. The mean blood loss was significantly low in experimental group as compared to control group [523±97.3 vs. 815.9±117.93 p<0.001]. This finding is in line with the findings of Mostafa-Gharabaghi *et al*., who found that intraoperative blood loss, operation time, and the requirement for blood transfusion were all significantly lower in the misoprostol group than in the oxytocin group.[20] Misoprostol was found to be more effective than vasopressin in minimizing intra-operative blood loss in another trial comparing misoprostol to vasopressin in abdominal myomectomy.[21]

Naib *et al*., conducted research in Peshawar, Pakistan in which they observed that 6% of misoprostol group and 28% of no misoprostol group needed transfusion.[22] Similar finding was reported in studies,[23-24] published where there was decreased blood loss and hence lesser number of blood transfusions.

In a study conducted by shafqat *et al*.,[25] in 2019, fifty women with a single intramural fibroid varying in size from 6 to 16 cm were included. 1 hour before surgery, group A received 400 mcg Misoprostol vaginally, while Group B received intravenous Tranexamic acid during operation. When compared to Tranexamic acid, intraoperative blood loss was considerably reduced (p<0.014) in the Misoprostol group, with a mean difference of 171.09 ml. In research conducted in Nigeria, the effectiveness of vaginal misoprostol administered peri-operatively was shown to be comparable to that of an intra-operative hemostatic peri-cervical tourniquet in decreasing blood loss during abdominal myomectomy.[26] In Myomectomy, Ragab A *et al*., compared a single dose of intra-vaginal Misoprostol to a double dose. They found that the women who received two dosages one and three hours before surgery had less blood loss intraoperatively (p<0.001).[9] Misoprostol, a safe and inexpensive medication, has mostly been studied and used in obstetrics. It has already demonstrated its effectiveness in the prevention and management of postpartum hemorrhage. However, further studies in gynecological (non-obstetric) procedures with larger sample sizes involving high-risk populations and other important factors should be carried out.

LIMITATION OF STUDY

Our research was conducted in a single blinded, single-center setting. To corroborate the findings of the current study, more research is needed, particularly multi-center double-blind randomized clinical trials.

CONCLUSION

Rectal misoprostol administration appears to be useful and is effective in reducing intra-operative blood loss during myomectomy.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

SN & MAQ: Study design, drafting the manuscript, data interpretation, critical review, approval of the final version to be published.

SN & SM: Data acquisition, data analysis, approval of the final version to be published.

AIM & QZ: Critical review, concept, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

1. Abdel-Hafeez M, Elnaggar A, Ali M, Ismail AM, Yacoub MJA, Obstetrics NZJo, et al. Rectal misoprostol for myomectomy: A randomised placebo-controlled study. Aust N Z J Obstet Gynaecol 2015; 55(4): 363-368.
2. Bulun SEJNEJoM. Uterine fibroids. N Engl J Med 2013; 369(14): 1344-1355.
3. Foth D, Röhl F-W, Friedrich C, Tylkoski H, Rabe T, Römer T, et al. Symptoms of uterine myomas: Data of an Epidemiological Study in Germany. Archives of Gynecology and Obstetrics 2016; 295(2): 415–426.
4. Bhagavath B, Lindheim S. Options for controlling blood loss during myomectomy. Fertility and Sterility 2019; 111(5): 894.
5. Das C, Rathinam D, Manchanda S, Srivastava D. Endovascular uterine artery interventions. Indian Journal of Radiology and Imaging 2017; 27(04): 488-495.
6. Monleón J, Cañete M, Caballero V, del Campo M, Doménech A, Losada M, et al. Epidemiology of uterine myomas and clinical practice in Spain: An observational study. European Journal of Obstetrics & Gynecology and Reproductive Biology 2018; 226: 59-65.
7. Ahmed M, Baqai S, Khushdil A, Ahmed F. Effect of oxytocin infusion on reducing blood loss during abdominal myomectomy: a randomized controlled trial. Journal of the Pakistan Medical Association 2019; (0): 1.

8. Tavana Z, Kordjamshidi P, Alborzi SJJoCR, Governance. The Efficacy of Misoprostol Plus Vasopressin Versus Vasopressin Alone on Surgical Outcomes Through Minimally Invasive Myomectomy: Research Protocol. J Clin Res Gov 2017; 5(2).
9. Ragab A, Khaiary M, Badawy AJJor, infertility. The use of single versus double dose of intra-vaginal prostaglandin E2 "misoprostol" prior to abdominal myomectomy: a randomized controlled clinical trial. J Reprod Infertil 2014; 15(3): 152.
10. Iavazzo C, Mamais I, Gkegkes IDJAog, obstetrics. Use of misoprostol in myomectomy: a systematic review and meta-analysis. Arch Gynecol Obstet 2015; 292(6): 1185-1191.
11. Nickol J, Berlit S, Lis S, Hornemann A, Tsagogiorgas C, Sütterlin M, et al. Hemodynamic effects of intramyometrial epinephrine injection for blood loss reduction in laparoscopic myomectomy. Arch Gynecol Obstet 2018; 298(5): 933-938. https://doi.org/10.1007/s00404-018-4891-5
12. Jeppson P. A systematic review on the use of misoprostol at the time of open myomectomy. BJOG: An International Journal of Obstetrics & Gynaecology 2020; 128(3): 484-484. https://doi.org/10.1111/1471-0528.16426
13. Allen R, O'Brien BMJRio, gynecology. Uses of misoprostol in obstetrics and gynecology. Rev Obstet Gynecol 2009; 2(3): 159.
14. Young D, Delaney T, Armson B, Fanning C. Oral misoprostol, low dose vaginal misoprostol, and vaginal dinoprostone for labor induction: Randomized controlled trial. PLOS ONE 2020; 15(1): e0227245.
15. Bulusu R, Ray P, Rani A, Handa PJJoEBM, Healthcare. Comparison of side effects of misoprostol by oral and rectal routes in active management of third stage of labour. Perspect Clin Res 2017; 4(3): 146-149.
16. Sirkeci RF, Belli AM, Manyonda IT. Treating symptomatic uterine fibroids with myomectomy: current practice and views of UK consultants. Gynecol Surg 2017; 14(1): 11. https://doi.org/10.1186/s10397-017-1014-4
17. Baird DD, Dunson DB, Hill MC. High cumulative incidence of uterine leiomyoma in black and white women: ultrasound evidence. Am J Obstet Gynecol 2003; 188: 100-107.
18. Samy A, Raslan A, Talaat B, El Lithy A, El Sharkawy M, Sharaf M et al. Perioperative nonhormonal pharmacological interventions for bleeding reduction during open and minimally invasive myomectomy: a systematic review and network meta-analysis. Fertility and Sterility 2020; 113(1): 224-233.e6.
19. Montis M, Tibaldi V, Santangelo G, Pajno C, Corno S, D'aniello D et al. The use of misoprostol and mifepristone in second trimester interruption of pregnancy: State of art. Clinical Obstetrics, Gynecology and Reproductive Medicine 2020; 6(2).
20. Mostafa-Gharabaghi P, Alizadeh S, Atashkhoye S, Sayyah-Melli M, JafariShobeiri 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. International Journal of Women's Health and Reproduction Sciences [Internet] 2016; 5(4): 306-311.
21. Protopapas A, Kathopoulis N, Chatzipapas I, Athanasiou S, Grigoriadis T, Samartzis K et al. Misoprostol vs vasopressin as a single hemostatic agent in laparoscopic myomectomy: Comparable, or just better than nothing?. Journal of Obstetrics and Gynaecology Research 2020; 46(11): 2356-2365.
22. Naib JM, Naveed P, Fatima S. Pre-operative use of misoprostol in major gynaecological surgeries. J Med Sci 2013; 21(4): 171-173.
23. Mohamed S, Mansour D, Shaker, A. The effect of misoprostol on intra-operative blood loss during myomectomy operation: Randomized controlled trial. Evidence Based Women's Health Journal 2019; 9(1): 363-371.
24. Khan QQ,Liaqat N, Shafqat T, Bawar S.Efficacy of preoperative misoprostol in reducing haemorrhage during abdominal myomectomy. J Ayub Med Coll Abbottabad 2020; 32(2): 198–203
25. Shafqat T, Yasmin S, Qazi Q, Rahim R. Comparison of efficacy of misoprostol vs tranexamic acid in reducing intraoperative blood loss in myomectomy. J Med Sci 2019; 27(4): 334-347.
26. Afolabi MA, Ezeoke GG, Saidu R, Ijaiya MA, Adeniran AS. Comparing perioperative vaginal misoprostol with intraoperative pericervical hemostatic tourniquet in reducing blood loss during abdominal myomectomy: A randomized controlled trial. J Turk Ger Gynecol Assoc 2019; 20(1): 23–30.