International Journal of Reproduction, Contraception, Obstetrics and Gynecology
Upadhyay P et al. Int J Reprod Contracept Obstet Gynecol. 2022 Apr;11(4):1220-1224
www.ijrcog.org
pISSN 2320-1770 | eISSN 2320-1789

DOI: https://dx.doi.org/10.18203/2320-1770.ijrcog20220908

Original Research Article

Randomised controlled study to compare preoperative and postoperative effectiveness of rectal misoprostol for preventing blood loss in elective caesarean delivery

Priyanka Upadhyay[1]*, Iram Wani[1], Ruhina Khan[2]

[1]Department of Obstetrics and Gynaecology, Indraprastha Apollo Hospitals, Delhi, India
[2]Department of Obstetrics and Gynaecology, Geetanjali Hospital, Udaipur, Rajasthan, India

Received: 20 February 2022
Accepted: 14 March 2022

***Correspondence:**
Dr. Priyanka Upadhyay,
E-mail: drpriyankaupadhyay2703@gmail.com

ABSTRACT

Background: Comparison between pre-operative and post-operative effectiveness of rectal misoprostol for preventing blood loss in elective caesarean delivery.
Methods: A single-blind randomized controlled study of 180 full-term pregnant women were scheduled for elective caesarean delivery. Computerized random allocation of women were done in group 1 to receive 400µg rectal misoprostol at urinary catheter insertion plus 400µg rectally after abdominal closure (preoperative group i.e. group 1, n=90) and group 2 who received 800µg of rectal misoprostol after abdominal closure (postoperative group i.e. group 2, n=90). Primary result was intraoperative blood loss.
Results: Intraoperative blood loss was significantly lower in the preoperative misoprostol group who was compared with the postoperative group (526.3±112.8 ml versus 735.4±135.7 ml; p<0.001). Postpartum hemorrhage (PPH) during the first 24 hours after delivery was also lower in the preoperative group against the post-operative group (205.1±77.4 ml versus 289.5±130.1 ml; p<0.001). Fewer women in the preoperative group needed additional uterotonics (8 versus 19; p<0.001) and after delivery, the decrease in haemoglobin levels was also significantly less in the preoperative group (−6.25 versus −14.28%; p<0.001).
Conclusions: Preoperative rectal administration of misoprostol significantly reduced intraoperative and postoperative blood loss during and after elective caesarean delivery.

Keywords: Elective caesarean delivery, Intraoperative blood loss, Misoprostol, Postpartum haemorrhage, Randomized controlled trial, Rectal route

INTRODUCTION

The incidence of caesarean delivery is increasing in developed and developing countries.[1] There is two times more blood loss in caesarean delivery when compared to normal delivery.[1] Also, in developing countries, postpartum hemorrhage (PPH) is the culprit for maternal mortality in 50% of cases.[3]

In caesarean section, different uterotonic agents are used to decrease blood loss intraoperatively and postoperatively like oxytocin, methylergometrine and prostaglandins.[4]

Misoprostol, which is aprostaglandin E1 analog, is an easily available, affordable drug which is extensively used in management of PPH everywhere. It helps in uterine contractions and dilation of cervix but may also cause fever, chills, nausea and vomiting. It is safe and can be used vaginally or rectally or orally or even sublingually hence, it is an uterotonic agent of choice for controlling blood loss.[5,6]

Misoprostol rectally has low peak concentration and slow absorption & has minimal adverse effects while other routes like vaginal administration depends on pH and

microflora of vagina and other route like sublingual route has maximum bioavailability as well as maximum side-effects because it avoids first pass metabolism leading to fastest maximum peak concentration and thus fastest onset of action.[7-9]

Previous studies mainly investigated misoprostol use in PPH after vaginal delivery but only few recorded evidence on its role in intraoperative blood loss during caesarean.

Objective

In our study, we compare effectiveness of rectal misoprostol before and after caesarean with the aim to minimise blood loss during and after caesarean delivery.

METHODS

A single-blinded randomized controlled trial (RCT) of full-term pregnant women who attended Indraprastha Apollo Hospital, Delhi, India, during November 2018 to November 2019 after ethical committee approval. Informed written consent was taken from all patients included in study and were informed about the risks and benefits of this study. Randomly 190 pregnant women were selected among those who were planned for elective caesarean section under spinal anaesthesia. But later 4 in group 1 and 5 in group 2 refused later and hence dropped out of our study and we continued our study with 90 patients in each group according to our inclusion and exclusion criteria.

Inclusion criteria

The study included women with: maternal age 20–35 years, body mass index 25–30, normal coagulation profile, and normal amniotic fluid volume (assessed using the amniotic fluid index).

Exclusion criteria

The study excluded women with: hepatic, renal, cardiac disorders; hypertensive or diabetic patients; history of allergy to misoprostol or any contraindication to use of misoprostol; any previous uterine surgery; haemoglobin levels less than 9 g/dl, antepartum hemorrhage, history of PPH; and fibroids.

Complete history and physical examination was done with ultrasonography, complete blood count, liver and kidney function tests and coagulation tests.

Randomization was done to make two groups: group 1 received 400 µg rectal misoprostol just after spinal anaesthesia at insertion of the urinary catheter, and another 400 µg rectally after closure of the abdomen (preoperative group); and group 2 received 800 µg of rectal misoprostol after closure of the abdomen (postoperative group).

5 IU oxytocin intravenously and 0.2 mg of ergometrine intramuscularly were given to both groups. Alsointravenous infusion of 20 IU oxytocin in 500 ml, Ringer lactate at a rate of 120 ml per hour was also given.[2]

The participants, outcome assessor, and statistician were blinded to the randomization.

Caesarean was conducted by a senior experienced gynaecologist while ensuring all precautions to prevent any intraoperative or postoperative blood loss.

Two methods were used to obtain blood loss during surgery. One method was done by using a formula given.

$$Blood\ loss = estimated\ blood\ volume\ (EBV) \times [\{preoperative\ hematocrit - postoperative\ hematocrit\} \div preoperative\ hematocrit]$$

Estimated blood volume was the weight in kilograms multiplied by 85.[2]

Another method was by pre and post operatively weighing the towels and dressings and also by adding suctioned fluid during surgery. Main outcome parameter was intraoperative blood loss. Secondary outcomes were occurrence of primary PPH (defined as bleeding >1000 ml during the first 24 hours after the operation), need of any extra uterotonics, and blood transfusion.

Statistical analysis

The mean±standard deviation (SD) blood loss at caesarean was 324±167 ml as per Chaudhuri et al.[10] The main outcome of study is volume of blood loss at caesarean, so the sample size was calculated as minimum sample size needed to be 86 patients in each group to be able to reject the null hypothesis with 90% power at α=0.05 using one-way analysis of variance and a test ratio between the two groups of 1:1. We recruited 90 women in each group. Sample size calculation was done using G*Power software version 3.1.2.[11] We coded and entered the data with statistical package for the social sciences (SPSS) version 25, data summarization was done by mean±SD, median, minimum and maximum for numerical data, and frequency (count) and relative frequency (percentage) for categorical data. We used Kruskal-Wallis and Mann-Whitney tests to compare between numerical variables. The χ^2 test was used to compare categorical data. Whenever the expected frequency obtained was less than 5, we used the exact test $p<0.05$ was considered statistically significant.

RESULTS

Baseline characteristics of the study patients were similar in terms of age, parity, body mass index (BMI), gestational age, and number of caesarean for previous caesarean deliveries (Table 1).

Table 1: Particulars of group 1 (70) and group 2 (70).

Particulars	Group 1 (pre-op)	Group 2 (post -op)	P value
Age (years)	25.8±5.6	25.3±6.2	0.6174
Parity	2.1±0.7	2.3±0.6	0.0717
BMI (kg/m²)	26.7±3.1	27.1±2.7	0.417
Period of gestation (weeks)	38.5±1.5	38.7±1.4	0.4162
Previous caesarean	1.8±0.4	1.7±0.6	0.248

No significant difference amongst the two groups was found regarding duration of the surgery (Table 1).

The women who were given misoprostol before caesarean, blood loss during surgery was significantly less when compared to the postoperative group (526.3±112.8 ml versus 735.4±135.7 ml, p<0.001). Preoperative group had significantly less blood loss during the first 24 hour after delivery (205.1±77.4 ml versus 289.5±130.1 ml, p<0.001). Some patients in each group needed additional uterotonics which is compared to group 1 versus group 2 (8 versus 19, p<0.001) (Table 2).

Table 2: Comparison of results between 2 groups for misoprostol administration.

Results	Group 1	Group 2	P value
Estimated blood loss (ml)	526.3±112.8	735.4±135.7	<0.0001
PPH (within 24 hours)	205.1±77.4	289.5±130.1	<0.0001
Pre-op Hb (gm/dl)	11.2±1.5	11.4±1.2	0.3852
Post-op Hb (gm/dl)	10.5±1.3	9.8±1.7	0.007
% Hb change	6.25	14.28	<0.0001
Extra uterotonic utilised	8	19	<0.0001
Blood transfusion	2	3	0.718

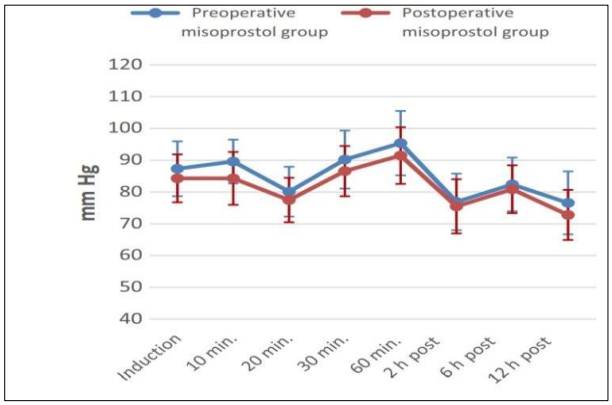

Figure 1: Change in mean arterial blood pressure in the preoperative and postoperative rectal misoprostol groups.

Both groups had comparable haemoglobin levels with p value 0.3852, but the decrease to postoperative levels was significantly less in women of the preoperative misoprostol group as compared to the postoperative group for haemoglobin (−6.25 versus −14.28%, p<0.001) (Table 2).

Both groups were similar in mean arterial blood pressure and heart rate changes during intra and post-operative period, and few required blood transfusion (p=0.718), and no significant difference was found amongst the two groups (Figures 1 and 3 and Table 2).

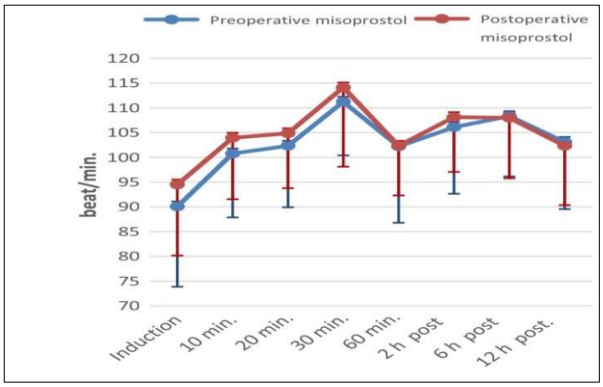

Figure 2: Change in heart rate in the preoperative and postoperative rectal misoprostol groups.

DISCUSSION

Blood loss was effectively reduced with the use of rectal misoprostol preoperatively (400µg after spinal anaesthesia or at time of catheterization and 400µg after abdominal closure). Blood loss during the first 24 hours of the procedure was also significantly less when compared with those who received equivalent doses postoperatively. Furthermore, there is significant reduction in the fall of haemoglobin in preoperative use of misoprostol group when compared to patients in the postoperative group who were given rectal misoprostol only after abdominal closure which justify our above findings indicating reduction of blood loss when misoprostol is given prior to surgery.

As per literature, misoprostol use via oral and sublingual routes allow rapid absorption and reach peak level within 12 minutes and have a half-life of 20–30-minutes,which explains the reason for less blood loss during intra-operative and post-operative period.[12,13] Since rectal and vaginal routes of misoprostol has a slow absorption rate, it's peak level would have been achieved by approximately 60 minutes indicating that misoprostol has reached its highest bioavailability and becomes the reason of reduced blood loss during and after operative procedure.[5]

Our study results were similar to the study conducted by Elsedeek who investigated the value of preoperative administration of rectal misoprostol during caesarean delivery and reported decreased intraoperative and

postpartum blood loss and resulted in higher haemoglobin and hematocrit levels in the study group which was compared with the placebo group.[8]

However, the use of only towel weight for blood loss estimation seems to be inadequate to study the whole aspect of blood loss.

Additional benefits of using misoprostol preoperatively is in the decreased need of additional uterotonic as shown in our study among the groups.[8,14,15]

In order to prevent any maternal and fetal side effects, a rectal route was chosen to administer misoprostol. Rectally, it is absorbed slowly & gives a prolonged effect with low peak levels, hence lesser side effects. Further, to decrease side effects we used a low dose of misoprostol i.e. 400 ug and administered it during catheterization prior to skin incision which allowed enough time for absorption since maximum levels are reached within 40–60 minute. Some studies have reported maximum levels reached in 20 minutes.[8,16]

Some studies have shown that preoperative misoprostol decreases blood loss more effectively rather than giving in postoperative period, .But also resulted in more side effects which are due to use of high dose mainly i.e. 600 ug.[14,17]

Few studies indicated effectiveness and safety of rectal misoprostol during preoperative and postoperative period.[5] There are other studies also where sublingual misoprostol was used but due to rapid peak and less sustained concentration either side-effects are more or adequate effect was not observed.

Although previous studies indicated preoperative misoprostol administration decreased bleeding at caesarean delivery, our study has several strengths: rectal administration was proved effective for the decreasing intraoperative bleeding without any beside effects; the administration dose was revised; and we used two methods of blood loss estimation for greater accuracy.

CONCLUSION

There are limitations in our study also like absence of double blinding and the relatively small sample size to demonstrate the benefits of misoprostol in minimising PPH. But we finally conclude that using misoprostol rectally effectively decreases intraoperative blood loss at caesarean, and hence, it should be recommended. But it should always be kept in mind if there is delay in delivery due to expected adhesions or abnormal lie or twins, it should be used with caution.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Upadhyay P, Wani I, Khan R. Randomised controlled study to compare preoperative and postoperative effectiveness of rectal misoprostol for preventing blood loss in elective caesarean delivery. Int J Reprod Contracept Obstet Gynecol 2022;11:1220-4.