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Original article

# Comparison of rectal misoprostol's effect when used before and after a cesarean section on post-cesarean bleeding



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## ABSTRACT

**Objective.** – Cesarean section is a common surgery in women. Different drugs are used to control its bleeding. This study compared the effect of using rectal misoprostol before and after surgery on the amount of post-cesarean bleeding.

**Materials and Methods.** – A number of 120 women who were admitted to our hospital because of elective cesarean section entered this clinical trial. They were divided into two groups. The first (before surgery) group received 400 µg of rectal misoprostol before the cesarean section and the second (after surgery) group after the surgery. The amount of bleeding was measured in both groups. The data were recorded and analyzed.

**Results.** – Their mean of age was 29.1 ± 6.1 years old. The mean of blood loss volume was 283 ± 147 mL in the before-surgery group and 294 ± 108 mL in the after-surgery group ( $P = 0.6$ ). There was no significant difference in the level of post-operation hemoglobin between the two groups. However, the frequency of need for additional uterotonics was 47% in the first group and 85% in the second group ( $P < 0.001$ ).

**Conclusion.** – There seems to be no significant difference in administering rectal misoprostol before or after the surgery, but the need for additional uterotonics is reduced if it is used before the surgery.

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## 1. Introduction

Cesarean section is a common surgery in women. Postpartum hemorrhage or bleeding is defined as losing more than 500 mL of blood after the third stage of delivery [1]. In developing countries, postpartum hemorrhage is still a cause of maternal mortality. Bleeding accounts for 50% of the maternal mortality causes in developing countries [2]. Every year, 14 million women suffer from postpartum hemorrhage of which about 140 000 of them die [3]. Different drugs are used to treat postpartum hemorrhage, including oxytocin, methyl-ergonin, and prostaglandins [1–8].

Misoprostol is a synthetic analogue of prostaglandin E1 that acts as a uterine contractile agent. It is effective in preventing and treating post-partum bleeding [4]. Using misoprostol in the form of prophylaxis reduces postpartum anemia and reduces the need for uterotonic agents [5,6].

The advantages of misoprostol are low cost, safety, stability, ease of use (including oral, vaginal, buccal or rectal), fast absorption, and its effect on the uterus [7]. Previous studies show

that misoprostol is effective in reducing postpartum hemorrhage, but there are not many studies on the best time to use this drug [8,9]. Hence, this study compared the effect of using rectal misoprostol before and after cesarean section on the amount of bleeding after the cesarean section.

## 2. Method

This clinical trial was done 120 pregnant women who had referred to our hospital in 2016. They were candidates for elective cesarean section with spinal anesthesia. The study protocol was approved by the ethics committee of our university (IR.ZAUMS.-REC.1396. 29).

The exclusion criteria were having or using: 1) placenta previa, 2) any kind of hypertension in pregnancy (preeclampsia, chronic hypertension, etc.), 3) diabetes mellitus, 4) active labor, 5) anticoagulant drugs, 6) history of cesarean section more than two times, 7) history of postpartum hemorrhage or hemorrhagic disorders, 8) hypersensitivity to prostaglandin compounds, 9) maternal chronic diseases, 10) history of any adhesions due to previous cesarean section, 11) contraindication of misoprostol use, 12) epilepsy, and 13) maternal heart disease.

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The study conditions were fully explained to all participants. All participants signed an informed consent before entering the study. They were examined before the surgery for the absence of active labor. Then, they were randomly divided into two groups (60 participants in each group). In the first group, 400 µg of rectal misoprostol (Cytotech, Pfizer, USA) was prescribed rectally in the operating room, after the spinal anesthesia and before starting skin incision. In the second group, the participants received 400 µg of rectal misoprostol (Cytotech, Pfizer, USA) at the end of surgery after skin closure.

Both groups received 1 L of normal saline with 30 units of oxytocin after clamping the umbilical cord. In cases that the bleeding was not enough controlled and additional uterotonic agents were needed, the amount of prescribed medication was recorded. The blood loss volume during the operation was measured by counting the small and large size surgical sponges before and after operation as well as measuring the amount of blood inside the suction device (the amount of blood in each blood-filled large sponge was counted as 50 cc and each blood-filled small sponge as 20 cc).

The amount of hemoglobin was measured 6 and 24 h after the cesarean section in all participants. Demographic information such as maternal age, gestational age, need for uterotonic agents and blood loss volume were also recorded. One surgeon did all the cesarean sections. We did the analysis with the statistical package for social sciences (SPSS) software version 21.

### 3. Results

The mean of age for all participants was  $29.1 \pm 6.1$  years old. There was no significant difference between the two groups in terms of average age, gestational age, hemoglobin level before surgery, neonatal Apgar score, and parity based on independent *t*-test (Table 1).

The mean of blood loss volume was  $283 \pm 147$  mL in the first (before-surgery) group and  $294 \pm 108$  mL in the second (after-surgery) group ( $P = 0.6$ ). There was no significant difference in the level of post-operation hemoglobin between the two groups (Table 2). However, the frequency of need for additional uterotonic agents was 47% in the first group and 85% in the second group. Based on Chi-square test this difference was significant ( $P < 0.001$ ).

The most common complication was abdominal pain (15.5%) in the first group and diarrhea (16.7%) in the second group which was not significant based on Chi-square test ( $P = 0.238$ ; Table 3). Apgar score of newborns was not significantly different between the two groups. No neonatal complications or admission to the intensive care unit occurred in both groups (Table 1).

**Table 1**

Comparing different parameters between the two studied groups.

Parameter	Before-surgery group (mean ± standard deviation)	After-surgery group (mean ± standard deviation)	<i>P</i> value
Maternal age	29.2 ± 6.3	29.0 ± 5.9	0.45
Gestational age	38.0 ± 1.0	37.8 ± 1.0	0.53
Hemoglobin level before cesarean	11.9 ± 1.0	12.0 ± 1.2	0.32
Neonatal Apgar score	9.3 ± 0.5	9.4 ± 0.5	0.607
Parity	3.4 ± 1.4	3.3 ± 1.4	0.757

**Table 2**

Comparing hemoglobin level before and after surgery in between the two groups.

	Before-surgery group (mean ± standard deviation)	After-surgery group (mean ± standard deviation)	<i>P</i> value
Mean of hemoglobin level 6 h after surgery	11.1 ± 1.37	11.2 ± 1.36	0.6
Mean of hemoglobin level 24 h after surgery	11.0 ± 1.31	10.9 ± 1.29	0.7

### 4. Discussion

In 2015, more than 300 thousand women died of peri- and postpartum events in the world. Postpartum hemorrhage or bleeding was a main cause. Most of these deaths could have been prevented and many of them happened because of the long distance to the hospital when the problem had occurred. Patients living in rural and urban areas suffer from severe anemia due to their lack of proper nutrition, which poses a greater risk of postpartum bleeding [10,11].

Misoprostol is a cheap and affordable drug that does not have specific requirements to be kept and its administration does not require special skills. This drug quickly became approved for postpartum hemorrhage in rural areas around the world. Many studies have shown that misoprostol is effective in reducing blood loss, but the best time to administer this drug has not been studied enough [8,9,12–14].

In our study, the mean of blood loss was not significantly different between the group that received rectal misoprostol before the surgery and the one that received it after the surgery ( $P = 0.6$ ). Also, the post-operation hemoglobin level was not significantly different between the two groups. In a study in Egypt, Borg and colleagues did the same investigation on 180 pregnant women.

In our study, a group of patients received 400 µg of misoprostol before and after the surgery. Both groups received 10 units of oxytocin after embryo removal and during surgery. The means of blood loss volumes were  $372 \pm 25$  and  $722 \pm 34$  mL in the groups that received misoprostol before and after the surgery, respectively. They concluded that using rectal misoprostol before surgery is significantly more effective than using it after the surgery [15]. This is not consistent with our findings.

In another study with the same structure on 300 pregnant women, Abd-Ellah and colleagues arrived at the same conclusion. The means of blood loss volumes were  $620 \pm 291$  and  $898 \pm 321$  mL in the groups that received the drug before and after the surgery, respectively [16]. They administered 600 µg of misoprostol in two groups: before and after the cesarean section. They did not administer oxytocin. Their patients lost more blood which might be the result of not administering oxytocin during the surgery.

Also, a study by Ragab and colleagues on 384 pregnant women concluded that using rectal misoprostol before surgery is significantly more effective than after surgery. They administered 400 µg of misoprostol without oxytocin. The mean of blood loss volumes in their study were  $570 \pm 240$  and  $844 \pm 270$  mL in the groups that received before and after the surgery, respectively [17].

The inconsistency between our results and the results of these studies might be because of faster administration of uterotonic

**Table 3**  
Comparing the complications between the two groups.

	Complications			
	None	Headache	Diarrhea	Abdominal pain
Before-surgery group	38 (65.5%)	3 (5.2%)	8 (13.8%)	9 (15.5%)
After-surgery group	44 (73.3%)	0	10 (16.7%)	6 (10%)

drugs. According to our results, the amount of used uterotonic drugs in the after-surgery group was significantly higher than the before-surgery group. If a uterotonic drug is more used, the uterus becomes more contracted and the bleeding is reduced. This can be a reason of our different result. Also, the number of participants might have been influential on this non-significant difference. We have used a higher dosage of oxytocin during the embryo removal which can be a reason of lower blood loss in our participants.

Our findings show a significant difference in the frequency of need for uterotonic drugs between the two studied groups. In this regard, our results are consistent with the other mentioned studies. In our study, these frequencies were 47 and 85% for the before-surgery and after-surgery groups. In Abd-Ellah and colleagues, these percentages were 30 and 53% [16], in Ragab and colleagues they were 22 and 40% [17], and in Borg and colleagues they were 0 and 30% [15].

The most common complications of our study were abdominal pain and diarrhea which were not significantly different between the two groups. This is in agreement with the other studies [16,17].

In a study, Garag and Hadi compared the effect of rectal misoprostol and oxytocin on the amount of blood loss after cesarean section. Their participants included 200 pregnant women who were undergoing elective cesarean section. They administered 400 µg rectal misoprostol before the surgery in one group and oxytocin after the surgery in the other group. They found out that the amount of blood loss and the decrease of post-operation hemoglobin level in the misoprostol group was significantly less than the oxytocin group. But there was no significant difference between the two groups in terms of neonatal hospital admission at intensive care unit [18].

Also, Nankali and colleagues compared the effect of misoprostol with placebo on the bleeding after hysterectomy. Their results showed that the blood loss volume had decreased significantly in the group that received misoprostol [19]. These studies confirm that misoprostol is effective on decreasing post-surgery blood loss.

We observed no neonatal complications in our study. The Apgar score was not significantly different between the two groups. Other studies have also shown that administering 25 and 50 µg of misoprostol does not result in any neonatal complications [20]. Some studies have reported that using misoprostol plus oxytocin reduces the amount of bleeding during cesarean section compared to using oxytocin alone. This combination has had no neonatal complications [21,22]. In our study, although the misoprostol dosage was higher, the skin was incised in a short period after administering misoprostol and the embryo was removed in less than two minutes. So, there was no tachysystolia, fetal asphyxia, or neonatal complication.

A limitation of our work was the low number of participants because this report is based on the residency program thesis of one of the authors. The advantage of this report was that all the surgeries were done by one surgeon and the studied population were homogenous. The amount of lost blood was lower in our study compared to the previous similar studies. We did not use weighing gauze sponges to estimate the amount of blood loss which might be a limitation. We only estimated the amount of

blood loss during the surgery, not the blood loss until 24 h after the surgery.

## 5. Conclusion

There seems to be no significant difference in post-cesarean bleeding and post-operative hemoglobin when we administer rectal misoprostol before or after the surgery, but the need for additional uterotonics is reduced if it is used before the surgery. Because misoprostol is accessible in most cities, and it can be kept or transported at room temperature, we recommend it to be used more in the rural areas to reduce postpartum bleeding. It is suggested that the same study be done with a large-scale population to arrive at more sound results on the best time to administer misoprostol.

Since misoprostol is more accessible and easier to keep compared to oxytocin and it seems to be quite effective in decreasing blood loss after cesarean section, replacing it with oxytocin in elective cesarean sections can be a possible option which needs further research.

## Conflicts of interest

The authors report no conflicts of interest.

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