

# Combination of Misoprostol and Oxytocin for Effective Control of Postpartum Hemorrhage During Cesarean Section

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**Abstract:** *Objective:* This study is to analyze the value of combining misoprostol and oxytocin in the prevention and control of postpartum hemorrhage during cesarean section. *Methods:* 82 cesarean section patients from July 2023 to July 2024 were selected as samples and randomly divided into two groups. Group A received misoprostol combined with oxytocin treatment, while Group B received only misoprostol treatment. The amount of postpartum hemorrhage, coagulation indicators, postpartum recovery indicators, and adverse reactions were compared between the two groups. *Results:* The intraoperative, 2-hour postpartum, 2-24-hour postpartum, and total blood loss in Group A were all lower than those in Group B ( $P < 0.05$ ). The activated partial thromboplastin time (APTT), plasma prothrombin time (PT), fibrinogen (FIB), and thrombin time (TT) in Group A were all lower than those in Group B ( $P < 0.05$ ). The first exhaust time, first time out of bed, and hospital stay after cesarean section in Group A were all shorter than those in Group B ( $P < 0.05$ ). The adverse reaction rate in Group A was lower than that in Group B ( $P < 0.05$ ). *Conclusion:* The application of misoprostol combined with oxytocin during cesarean section can optimize coagulation indicators, reduce blood loss, shorten postpartum recovery time, and is highly effective and feasible.

**Keywords:** Oxytocin; Misoprostol; Cesarean section; Postoperative bleeding

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## 1. Introduction

Cesarean section has become a commonly used assisted delivery technique for difficult births, referring to the assisted delivery technique of removing the fetus through the abdomen. However, postpartum bleeding can easily occur, which can increase the risk of maternal death. In recent years, the number of cesarean sections has increased year by year, but how to prevent and control postoperative bleeding remains a hot research topic in clinical practice. There are many inducements for postoperative bleeding after cesarean section, such as uterine atony, incision laceration, and placental abruption, which can increase the amount of postoperative bleeding

and prolong the recovery period of the mother. Intramuscular injection of oxytocin is a commonly used method to prevent and control postpartum hemorrhage. The active ingredient stimulates uterine contraction, which can reduce uterine bleeding. However, the risk of side effects of oxytocin alone is high, and combining it with misoprostol can further enhance uterine contraction, resulting in reduced postoperative bleeding <sup>[1]</sup>. Based on this, this article explores the effect of misoprostol combined with oxytocin using 82 cesarean section patients from July 2023 to July 2024 as samples.

## **2. Materials and methods**

### **2.1. Materials**

A sample of 82 pregnant women who underwent cesarean section from July 2023 to July 2024 were selected and randomly divided into groups.

### **2.2. Inclusion and exclusion criteria**

- (1) Inclusion criteria: (a) Meet the cesarean section standards in the “Expert Consensus on Cesarean Section Surgery” <sup>[2]</sup>; (b) Singleton pregnancy; (c) Primiparas.
- (2) Exclusion criteria: (a) Coagulation disorders; (b) Drug intolerance; (c) Mental disorders.

### **2.3. Treatment methods**

Group A received intravenous infusion of oxytocin injection (Shanghai Hefeng Pharmaceutical Co., Ltd.; National Medical Approval Number H31020850; 1 mL 10 units 10 vials) at a dose of 20 IU mixed with 500 mL of sodium chloride solution, administered within 1 hour, once; misoprostol tablets (Wuhan Jiulong Renfu Pharmaceutical Co., Ltd.; National Medical Approval Number H20073696; 0.2 mg × 3 tablets) were inserted into the anus. After observing the completion of delivery, 0.2 mg of misoprostol tablets were pushed into the anus 5 cm area through the rectum, administered once. The oxytocin method for Group B was the same as Group A.

### **2.4. Observation indicators**

- (1) Blood loss: Record the amount of blood loss during surgery, 2 hours postpartum, 2-24 hours postpartum, and total blood loss.
- (2) Coagulation indicators: Detect APTT, PT, FIB, TT and other indicators using the solidification method.
- (3) Postoperative recovery indicators: Record the time of first exhaustion, first time out of bed, and length of hospital stay after cesarean section.
- (4) Adverse reactions: Record vomiting, nausea, and skin itching.

### **2.5. Statistical analysis**

Data was processed using SPSS 21.0. Chi-square ( $\chi^2$ ) test was used to compare counting data (% recorded), and *t*-test was used for measurement indicators (mean ± standard deviation, SD recorded). There was a statistically significant difference with  $P < 0.05$ .

### 3. Results

#### 3.1. Baseline data

Comparing the data of Group A with Group B,  $P > 0.05$ . As shown in **Table 1**.

**Table 1.** Baseline data analysis table ( $n$ , mean  $\pm$  SD)

Group	Age (years)	Gestational weeks	Body mass index (kg/m <sup>2</sup> )
Group A ( $n = 41$ )	29.11 $\pm$ 0.81	38.11 $\pm$ 1.05	23.74 $\pm$ 1.61
Group B ( $n = 41$ )	29.09 $\pm$ 0.79	38.09 $\pm$ 1.06	23.71 $\pm$ 1.63
$t$	0.1132	0.0858	0.0838
$P$	0.9102	0.9318	0.9334

#### 3.2. Blood loss

The blood loss during surgery, 2 hours postpartum, 2-24 hours postpartum, and total blood loss in Group A were all lower than those in Group B, with  $P < 0.05$ . As shown in **Table 2**.

**Table 2.** Blood loss (mL, mean  $\pm$  SD)

Group	Intraoperative blood loss	2h postpartum blood loss	2-24h postpartum blood loss	Total blood loss
Group A ( $n = 41$ )	207.44 $\pm$ 8.09	150.44 $\pm$ 3.82	147.41 $\pm$ 2.89	451.44 $\pm$ 10.25
Group B ( $n = 41$ )	309.81 $\pm$ 9.44*	190.36 $\pm$ 4.41*	175.44 $\pm$ 4.06*	550.69 $\pm$ 12.19*
$t$	52.7246	43.8111	36.0145	39.9023
$P$	0.0000	0.0000	0.0000	0.0000

Note: \*Indicates a statistically significant difference compared to Group A with  $P < 0.05$ .

#### 3.3. Coagulation indicators

At 24 hours postoperatively, APTT, PT, FIB, and TT in Group A were all lower than those in Group B, with  $P < 0.05$ . As shown in **Table 3**.

**Table 3.** Coagulation indicators (mean  $\pm$  SD)

Group	APTT(s)		PT(s)		FIB(g/L)		TT(s)	
	Pre-operation	24h Post-operation	Pre-operation	24h Post-operation	Pre-operation	24h Post-operation	Pre-operation	24h Post-operation
Group A ( $n = 41$ )	41.29 $\pm$ 1.42	27.49 $\pm$ 1.06	13.18 $\pm$ 1.12	7.21 $\pm$ 0.48	5.39 $\pm$ 1.02	2.61 $\pm$ 0.46	16.41 $\pm$ 1.21	11.25 $\pm$ 0.48
Group B ( $n = 41$ )	41.31 $\pm$ 1.38	30.21 $\pm$ 1.15*	13.19 $\pm$ 1.11	8.52 $\pm$ 0.69*	5.41 $\pm$ 1.04	3.62 $\pm$ 0.57*	16.39 $\pm$ 1.19	12.62 $\pm$ 0.57*
$t$	0.0647	11.1359	0.0406	9.9795	0.0879	8.8293	0.0755	11.7720
$P$	0.9486	0.0000	0.9677	0.0000	0.9302	0.0000	0.9400	0.0000

Note: \*Indicates a statistically significant difference compared to Group A with  $P < 0.05$ .

#### 3.4. Postoperative recovery indicators

The time of first exhaust, first time out of bed, and length of hospital stay after cesarean section in Group A

were all shorter than those in Group B, with  $P < 0.05$ . As shown in **Table 4**.

**Table 4.** Postoperative recovery indicators (mean  $\pm$  SD)

Group	First exhaust time after surgery (h)	First time out of bed after surgery (d)	Hospital stay (d)
Group A ( $n = 41$ )	17.15 $\pm$ 0.49	1.79 $\pm$ 0.42	5.05 $\pm$ 0.46
Group B ( $n = 41$ )	21.79 $\pm$ 0.68*	2.96 $\pm$ 0.51*	7.06 $\pm$ 0.69*
$t$	35.4476	11.3393	15.5199
$P$	0.0000	0.0000	0.0000

Note: \*Indicates a statistically significant difference compared to Group A with  $P < 0.05$ .

### 3.5. Adverse reaction indicators

The adverse reaction rate in Group A was lower than that in Group B, with  $P < 0.05$ . As shown in **Table 5**.

**Table 5.** Adverse reaction indicators ( $n$ , %)

Group	Vomiting	Nausea	Skin Itching	Incidence Rate
Group A ( $n = 41$ )	0 (0.00)	1 (2.44)	0 (0.00)	1 (2.44)
Group B ( $n = 41$ )	2 (4.88)	2 (4.88)	2 (4.88)	6 (14.63)*
$\chi^2$	-	-	-	3.9048
$P$	-	-	-	0.0481

Note: \*Indicates a statistically significant difference compared to Group A with  $P < 0.05$ .

## 4. Discussion

Cesarean section is often used in emergencies such as transverse or breech delivery, multiple pregnancy delivery, fetal distress delivery, preeclampsia, cephalopelvic disproportion, and labor stagnation. Additionally, a few women request a cesarean section due to fear of pain during childbirth. However, with the increasing number of cesarean sections, the incidence of postpartum hemorrhage, a common complication of cesarean section, has also increased, which can lead to increased blood loss and risk of maternal death. The causes of postpartum hemorrhage after cesarean section are related to the mother's factors. For example, excessive fear and anxiety of the mother can lead to endocrine disorders and uterine atony. During childbirth, long-term violent contraction of uterine muscles consumes a lot of physical strength, making it more prone to uterine muscle fatigue. Factors such as oversized fetuses or multiple pregnancies can cause excessive stretching of uterine muscle fibers during childbirth, reducing the uterus's ability to contract. Additionally, having too many births or preeclampsia can increase the risk of postpartum hemorrhage after cesarean section. The pathological feature of postpartum hemorrhage after cesarean section is a large amount of vaginal bleeding in a short period, which can cause symptoms such as tachycardia, hypotension, and paleness in the mother. As the amount of bleeding increases, it can also induce symptoms such as thirst, fatigue, and dizziness.

Currently, postpartum hemorrhage after cesarean section is treated with physical methods, medication, or surgical intervention in severe cases to ensure the mother's health and safety. Uterotonic agents are commonly used drugs to prevent post-cesarean bleeding, and oxytocin is often used to reduce the amount of bleeding after cesarean section and shorten the recovery time. However, due to individual differences among mothers, the

hemostatic effect of oxytocin is limited, and it should be combined with other drugs to enhance the hemostatic effect <sup>[3]</sup>. Additionally, oxytocin has a dose-dependent characteristic, and high-dose administration can increase the risk of uterine tetanic contraction and hypotension. Moreover, oxytocin can only prevent and control bleeding caused by uterine atony and has a poor effect on preventing postpartum hemorrhage caused by birth canal injury. Misoprostol is derived from prostaglandin E. After administration, it can excite the uterine muscle layer, accelerate uterine contraction, increase the contraction amplitude of the muscle layer, repair cervical damage caused by childbirth, increase intrauterine pressure, and enhance the hemostatic effect <sup>[4]</sup>. Compared with single oxytocin treatment, combined use with misoprostol can accelerate drug absorption and optimize the mother's coagulation function.

The data presented in this article indicates that Group A had lower blood loss compared to Group B, with  $P < 0.05$ . This difference can be attributed to the intravenous infusion of oxytocin injection, a polypeptide hormone drug that stimulates rhythmic uterine contractions in the mother, increasing the frequency and intensity of contractions, thereby achieving excellent hemostatic effects. However, it's important to note that the active ingredient of oxytocin only acts on the upper segment of the uterus, and oxytocinase in the mother's body can dilute the concentration of oxytocin, while intestinal activity can deactivate it, limiting the hemostatic effect of oxytocin alone <sup>[5]</sup>. Additionally, due to the short half-life and duration of oxytocin, it should be combined with misoprostol for synergistic hemostatic treatment. This combination can regulate intrauterine pressure, increase uterine tension, restore rhythmicity of smooth muscle, soften the cervix, and stimulate uterine contractions. Administered through the anus, misoprostol takes effect within 2.5–20 minutes, and its half-life is up to 90 minutes, making the combined administration more effective in controlling postpartum hemorrhage <sup>[6]</sup>. Another set of data shows that 24 hours after surgery, Group A had lower APTT, PT, FIB, and TT compared to Group B, with  $P < 0.05$ . This can be explained by the use of oxytocin treatment, which stimulates smooth muscle contraction to stop bleeding, slowing blood loss and maintaining blood concentration. This reduces the adverse effects of blood loss on coagulation factor function, helping to stabilize coagulation indicators. However, long-term or excessive use of oxytocin can affect uterine smooth muscle function, leading to poor uterine contraction and even indirectly damaging coagulation function. Combination therapy with misoprostol enhances the uterus's sensitivity to oxytocin, improves hemostatic efficacy, protects vascular endothelial cells and platelet function, and indirectly improves coagulation indicators <sup>[7,8]</sup>.

Another set of data indicates that Group A had shorter times for first exhaust, first ambulation, and hospital stay after cesarean section compared to Group B, with  $P < 0.05$ . This is because during pregnancy, the expression of uterine receptors for contractions gradually increases in the myometrial region, reaching a peak during childbirth, enhancing the effect of oxytocin on stimulating uterine contractions. Therefore, injecting oxytocin before childbirth can effectively prevent and control bleeding. The active ingredient of misoprostol can bind to prostaglandin receptors in smooth muscle, activating calcium ion channels in cells and stimulating uterine contractions. It can also soften and dilate the cervix, reducing cervical resistance during childbirth <sup>[9,10]</sup>. Combined administration during cesarean section surgery results in synergistic effects, increasing uterine contractility and reducing blood loss in the myometrium. The complementary advantages of combined administration, with misoprostol's long-lasting and slow-acting properties, can compensate for the fast-acting and short-duration limitations of oxytocin alone. This combination can effectively relieve symptoms such as dizziness and fatigue, improve postoperative recovery, shorten early ambulation time, accelerate gastrointestinal motility, reduce the risk of deep vein thrombosis in the lower extremities after cesarean section, and help reduce cesarean section complications and

hospital stay<sup>[11,12]</sup>.

Finally, data shows that the adverse reaction rate in Group A was lower than that in Group B, with  $P < 0.05$ . This is because misoprostol administered through the anus results in a high local blood drug concentration, reducing systemic side effects of the drug. Additionally, misoprostol does not induce hypertension and has minimal damage to the cardiovascular system<sup>[13,14]</sup>. Furthermore, oxytocin can continuously exert its effect for 1.5–2 hours, with a drug half-life of 10–15 minutes. Combining it with misoprostol enhances hemostatic effects and ensures high safety. However, it's essential to prioritize wound care after cesarean section, maintaining dryness and cleanliness of the wound, observing for any fluid leakage or redness, and actively preventing postoperative wound infection. Encouraging early ambulation once the mother's vital signs are stable can help shorten the postoperative recovery period and prevent venous thrombosis in the lower extremities. Initially, strenuous or vigorous activities should be avoided. Providing a scientific diet for the mother, increasing vitamin and protein intake, and encouraging her to drink more water are also crucial. Breastfeeding should be arranged as soon as possible after cesarean section to stimulate uterine contractions and shorten the time for uterine involution<sup>[15]</sup>.

## 5. Conclusion

In summary, the combination of oxytocin and misoprostol for the prevention and control of postpartum hemorrhage after cesarean section can reduce drug side effects, improve coagulation indicators, shorten postoperative recovery time, and reduce perioperative blood loss. This approach has significant promotional value.

## Disclosure statement

The author declares no conflict of interest.

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