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Combined Use of Misoprostol Plus Oxytocin versus Oxytocin Alone to Reduce Blood Loss during Cesarean Section

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ABSTRACT

Background: Misoprostol is thought to present several improvements over oxytocin for preventing and treating of Post-Partum Hemorrhage (PPH). **Objective:** This study aimed to evaluate the efficacy of oxytocin alone versus combination of oxytocin–misoprostol in preventing excessive blood loss after caesarean section.
Subjects and Methods: One hundred and two women were included in this study who were attending the Obstetrics and Gynecology Departments, Zagazig University Hospitals and Benha Teaching Hospital. Misoprostol 200 mcg sublingually and oxytocin 5 IU bolus intravenously were administered to 51 patients. The other 51 cases received 5 IU bolus intravenous oxytocin followed by I.V drip of 15 units' oxytocin in 500 mL of Ringer lactate solution over 1 hour.
Results: There was a statistically significant difference between the misoprostol oxytocin group and the oxytocin group in terms of the requirement for more uterotonics, need for uterine massage, and the uterine tone score following therapy.
Conclusion: There was no significant difference in estimated blood loss between the groups that received either oxytocin alone or a low dosage of misoprostol. However, the misoprostol-oxytocin group required more uterotonic and uterine massage during Caesarean section than the oxytocin group.
Keywords: Misoprostol, Oxytocin, Post-partum hemorrhage.

INTRODUCTION

Excessive bleeding after giving birth is referred to as postpartum haemorrhage (PPH). About 68,500 deaths a year can be attributed to it, and 99.7% of those deaths occur in developing nations [(1)]. Roughly 6% of births experience excessive bleeding, defined as blood loss of 500 ml or more; about 1%-2% of births experience excessive bleeding of 1000 ml or more [(2)]. As a result, it poses a serious threat to global public health, particularly harming the poorest people everywhere. Due to improvements in third-stage labour treatment such as controlled cord traction, uterine fundal massage, and pharmacological uterotonics, the rate of fatal PPH has decreased in latest decades [(3)]. Because of their sensitivity to heat and light, oxytocin and ergometrine must be kept in a refrigerated supply chain. Since prostaglandins E2 and F2a are heat-sensitive and prohibitively expensive, they are only utilized as a secondary or tertiary treatment option [(4)]. Misoprostol, a synthetic prostaglandin E1 analogue, has gained prominence as a therapeutic and preventative measure against gastroduodenal damage brought on by nonsteroidal anti-inflammatory drugs [(5)].

Misoprostol has multiple applications in obstetrics and gynaecology, inducing childbirth, preparing the cervix for surgery, stopping bleeding after delivery, and preventing miscarriage. In comparison with other synthetic prostaglandin analogues, misoprostol has many benefits, including its inexpensive price, long half-life, stability at high temperatures, and widespread availability [(6)]. When compared to oxytocin, misoprostol has various benefits. It can be taken orally, rectally, vaginally, or sublingually, and it doesn't degrade when heated. It's in tablet form, so it won't spoil if you leave it out, it's cheap and easy to find, and it doesn't call for any specialised training or expensive equipment to use [(6)]. The goal of this study was evaluation of the efficacy of oxytocin alone versus combination oxytocin–misoprostol in preventing excessive blood loss after caesarean section.

PATIENTS AND METHODS

One hundred and two women were included in this cross-sectional observational clinical study. They were attending the Obstetrics and Gynecology Departments, Zagazig University Hospitals and Benha Teaching Hospital.

Inclusion criteria: Pregnant at term (37 – 40) weeks, regional anesthetic for a planned elective caesarean delivery, no history of medical disorder, and no history of coagulation abnormalities.
Exclusion criteria: Any cesarean section under general anesthesia, and women at high risk for postpartum hemorrhage were not included.
On day of surgery all cases had obstetric ultrasonography for assurance of diagnosis and evaluation of fetal condition and blood sample for complete blood counting was taken. 102 Parturient were allocated into 2 equal groups each group involved 51 cases.
Group 1: After foetal delivery, women were given a combination of misoprostol (200 mcg sublingually) and oxytocin (5 IU bolus intravenously), which was slowly infused.

Group 2: Just following caesarean section delivery of a newborn: Initially, a 5 IU bolus of oxytocin was infused intravenously, and then a 1-hour drip of 15 units of oxytocin was administered through intravenous drip in 500 mL of Ringer lactate solution at a flow rate of 120 drops per minute.

There was uniformity in the procedures used during surgery, and all patients were given spinal anesthetic. Patients were given an intravenous bolus of 500-1000 mL of crystalloid prior to spinal anesthesia

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administration. Not until the morning following the operation, 1 L of intravenous crystalloids were administered every 8 hours unless the patient could not tolerate oral fluids. According to hospital policy, doctors had performed a conventional technique that called for controlled cord traction to facilitate placenta delivery following medication administration and two-layer uterine incision closure.

Before, during, and after CS, the patients' vital signs (blood pressure, heart rate, and temperature) were recorded. After the placenta has been delivered, the woman's uterine tone is checked every 5 minutes in the postpartum ward and subsequently every 10 minutes until abdominal closure has begun. Tone of the uterus has been measured by how deeply a finger can be pressed into the tissue, with a score of 0 indicating a soft, swampy uterus and a score of 4 indicating a rock-hard, tetanic uterus.

An additional 20 international units (IU) of oxytocin were injected slowly as a uterotonic. Patients who received an extra uterotonic between the time of study dose delivery and 24 hours following surgery were asked to report their use frequency.

Blood loss during CS was often evaluated by the surgeon as minor (less than 500 ml), moderate (500-1000 ml), or major (>1000 ml) after placental delivery using the standard methods.

$$\text{Estimated blood loss} = \text{EBV X } \frac{\text{Preop hematocrit} - \text{Postop hematocrit}}{\text{Preop hematocrit}}$$

Estimated blood volume (EBV) in milliliters equals mother weight kilograms multiplied by 85 [7].

Excessive bleeding was defined as blood loss greater than or equal to 1000 mL during the procedure. After CS and again 24 hours later, a full blood count was taken both times. Regular medical attention was provided to new mothers in the postpartum ward. Up to 24 hours after surgery, data were collected on the necessity for uterine massage and other vital indicators.

The researcher kept a log of any unintended consequences they saw or heard about through in-depth interviews. In the first 24 hours after giving birth, patients were observed for adverse pharmacological reactions to the chosen medication.

Outcomes:

Primary outcome: The need for additional doses of uterotonics.

Secondary outcome:

- Severe postpartum hemorrhage (PPH) (blood loss 1000 ml or more).
- Hemoglobin drop in 24 hours postpartum.
- Uterine contraction.
- Need for uterine massage.
- Fundal positioning relation to umbilicus in 24 hours.
- Amount of intraoperative blood loss following delivery of the fetus.
- Blood transfusion.
- The appearance of adverse outcomes from a medicine (nausea, vomiting, shivering and pyrexia).

Ethical consent:

An approval of the study was obtained from Zagazig University Academic and Ethical Committee (ZU-IRB #5330). Every patient signed an informed written consent for acceptance of participation in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

In order to analyze the data acquired, Statistical Package of Social Services version 20 was used to execute it on a computer (SPSS). In order to convey the findings, tables and graphs were employed. The quantitative data was presented in the form of mean, median, standard deviation, and confidence intervals. The information was presented using qualitative statistics such as frequency and percentage. The student's t test (T) was used to assess the data while dealing with quantitative independent variables. Pearson Chi-square and Chi-square for Linear Trend (X^2) were used to assess qualitatively independent data. The significance of a P value of 0.05 or less was determined.

RESULTS

There were also no statistically significant differences between the groups in terms of age, weight, height, BMI, or gestational age **(Table 1)**.

Table (1): The relation between study groups as regards age, weight, height, BMI and gestational age

Variable	Misoprostol-Oxytocin group (n=51)	Oxytocin group (n=51)	p-value
Age (years)	25.4 ± 3.2	26.48 ± 3.65	0.089
Weight (kg)	77.56 ± 9.85	81.2 ± 12.4	0.108
Height (cm)	166.76 ± 2.9	166.04 ± 3.3	0.256
BMI (kg/m^2)	27.88 ± 3.16	28.44 ± 4.28	0.205
Gestational age (weeks)	38.0 ± 0.9	38.0 ± 0.7	0.191

After medication delivery, the misoprostol-oxytocin group required significantly more uterotonic and uterine massage. Group of oxytocin significantly was higher regarding uterine tone score than misoprostol-oxytocin group (3.48 ± 0.7 vs 2.74 ± 0.44 respectively). When comparing the groups receiving oxytocin with those receiving misoprostol, there was no discernible difference in the amount of blood lost (mean of group 1= 585.1 ml vs. mean of group 2= 562.4 ml). Furthermore, the blood transfusion made no discernible difference **(Table 2).**

Table (2): Outcome measures in both study groups

Variable	Misoprostol- Oxytocin group (n=51)	Oxytocin group (n=51)	p-value
Need for additionaluterotonic	11 (21.6%)	1 (2.0%)	**0.002**
Need for uterine massage	28 (54.9%)	8 (15.7%)	**0.00**
Need for blood transfusion	2 (4.0%)	1 (2.0%)	0.46
Uterine tone score 5 minafter drug administration	2.74 ± 0.44	3.48 ± 0.7	**0.00**
Estimated blood loss	585.1 ± 195.12	562.4 ± 173.86	0.598
Need for surgicalintervention	0 (0.0%)	0 (0.0%)	

No statistically significant differences were found in HB or PCV changes between the misoprostol-oxytocin group and the oxytocin group (**Table 3).**

Table (3): Hemoglobin and hematocrit in both study groups

Variable	Misoprostol-Oxytocin group (n=51))	Oxytocin group (n=51	p- value
Preoperative hemoglobin(g/dl)	10.87 ± 1.0	10.86 ± 0.9	0.975
Preoperative PCV (%)	32.6 ± 3.02	32.59 ± 2.7	0.975
Hemoglobin 24 h afterdelivery (g/dl)	10.08 ± 0.96	9.9 ± 0.9	0.392
PCV 24 h after delivery (%)	30.27 ± 2.87	29.78 ± 2.76	0.385
Drop in hemoglobin (g/dl)	0.78 ± 0.04	0.93 ± 0.01	0.583
Drop in PCV (%)	2.33 ± 0.15	2.8 ± 0.03	0.59

In terms of heart rate, systolic blood pressure, and diastolic blood pressure, neither group differed significantly from the other **(Table 4).**

Table (4): Hemodynamic variables in both study groups

Variable	Misoprostol oxytocin group (n=51)	oxytocingroup (n=51)	p- value
Baseline heart rate (bpm)	95 ± 9.54	97 ± 8.5	0.085
Average intraoperative heart rate (bpm)	90 ±7.5	92 ±7.5	0.087
Heart rate 2 h after surgery (bpm)	86 ±7.5	87 ± 3.4	0.098
Baseline SBP (mmHg)	119.8 ±11.4	115 ± 11.2	0.112
Average intraoperative SBP (mmHg)	110 ± 10.7	105 ± 12.2	0.087
SBP 2 h after surgery (mmHg)	110.2 ±11.87	110 ± 12.54	0.98
Baseline DBP (mmHg)	60.2 ± 12.45	55 ± 12.2	0.098
Average intraoperative DBP (mmHg)	60.2 ±11.5	55 ± 12.5	0.089
DBP 2 h after surgery (mmHg)	70 ± 12.9	65 ± 13.2	0.23

The misoprostol-oxytocin group showed statistically significant difference as more women complained from shivering **(Table 5).**

Table (5): Effects of medication adverse events in both groups

Variable	Misoprostol oxytocin group (n=51)	Oxytocin group (n=51)	p-value
Heat sensation	5 (15.7%)	1 (2.0%)	0.09
Shivering	13 (25.5%)	0 (0.0%)	0.00
Nausea and/orvomiting	6 (11.8%)	5 (9.8%)	0.75
Headache	16 (31.4%)	9 (17.6%)	0.107
Abdominal pain	33 (64.7%)	27 (52.9%)	0.306
Palpitations	22 (43.1%)	17 (33.3%)	0.308
Fever	2 (3.9%)	1 (2.0%)	0.55

DISCUSSION

A woman's risk of postpartum hemorrhage increases if she has any of the following conditions during pregnancy: polyhydramnios, grand multiparity, severe pre-eclampsia, prepartum hemorrhage, delayed and obstructed labor, augmented labor, obesity, and anemia [8].

Two meta-analyses by **Conde-Agudelo *et al.*** [9] and **Hua *et al.*** [10] both misoprostol and oxytocin were found to be beneficial in preventing PPH, and the combination was more successful than either drug used alone. Women at risk for PPH may benefit from an additional or alternative oxytocic medication.

The age, weight, height, body mass index, and geriatric age of the women in the misoprostol oxytocin group were not different from those in the oxytocin group.

This study found that women in the misoprostol-oxytocin group needed additional uterotonics based on their individual needs, it was 21.6% (11cases). In oxytocin group, it was 2.0% (1 case) and this demonstrated a statistically significant distinction between the study groups with respect to the requirement for supplementary uterotonics (p-value 0.002).

The use of low doses of uterotonics in the misoprostol-oxytocin group may account for the observed increase in need found in the present investigation. Some previous studies have reported no difference [11, 12]. In contrast, some prior research found that the need for extra uterotonic drugs was reduced when combination oxytocics were used [13, 14]. A research by **Quiroga *et al.*** [15] found no statistically significant difference in the need for further oxytocic medication among women who received 800 μg misoprostol via the intrauterine route. Due to the lack of data on the intrauterine route.

Concerning the need for uterine massage for the women involved in this study, there were higher significant difference in misoprostol oxytocin group than oxytocin group.

Concerning the need for blood transfusion for the women involved in this study, in misoprostol-oxytocin group, it was 4.0% (2 cases). In oxytocin group, it was 2.0% (1 case), that showed no significant difference between the two study groups as regards the need for blood transfusion (p-value 0.46). This result agrees with those of prior investigations [10, 13, and 15].

Concerning uterine tone after treatment for the women involved in this study, group of oxytocin was significantly higher regarding uterine tone score than misoprostol-oxytocin group. The current study found that compared to using oxytocin alone, combining misoprostol and oxytocin during caesarean delivery did not significantly reduce intraoperative blood loss.

The use of adjunct misoprostol was not associated with a significant reduction in blood loss, as reported by both **Chalermpolprapa** [13] and **Hamm *et al.*** [16]. The findings of the current investigation corroborated these findings.

When compared to intravenous oxytocin (20IU), misoprostol administered sublingually (200 g) was just as effective in preventing postpartum hemorrhage after caesarean birth with fewer adverse effects [17].

No surgical interventions were necessary for the women in either group, according to the results of this study.

There was no statistically significant difference between haemoglobin alterations in the oxytocin-misoprostol groups and the oxytocin group, as determined by the drop in hemoglobin (g/dl) for the women in this study.

The current results, which showed that combined oxytocics reduced the postoperative reduction in hemoglobin that were consistent with those of some earlier trials [13, 14].

Concerning hemodynamic effect for the women involved in this study, both study groups showed no significant differences.

As regard incidence of drug-related side effects for the women involved in this study, more women in misoprostol-oxytocin group complained from shivering 25.5% (13 cases) (p- value 0.00), which showed statistically significant difference. Shivering was also more common in women who took misoprostol sublingually, which is consistent with earlier research [10, 13, and 18]. Although the sublingual route had several advantages, such as a faster beginning of powerful uterine contractions, it also had some unique features that may increase the risk of side effects. **Hofmeyr *et al.*** [19] claimed that misoprostol's adverse effect frequency varied with dose and that researchers should work to determine the lowest effective and safe dose.

CONCLUSION

Our results suggested that low-dose misoprostol plus oxytocin did not significantly reduce estimated blood loss, and that the misoprostol-oxytocin group requires more uterotonic and uterine massage during caesarean section than the oxytocin group does; however, the use of these medications is not associated with any serious adverse effects.

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Author contribution: Authors contributed equally in the study.

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