Archives of Women's Health & Gynecology

doi: 10.39127/AWHG:1000101

Noureldin EH. Arch Women Heal Gyn: 101.

Research Article

Combined Use of Misoprostol Plus Oxytocin Versus Oxytocin Alone to Reduce Blood Loss During Cesarean Section

Elsayed Hamdi Noureldin*

Obstetrics and Gynecology Department, Faculty of Medicine; Zagazig University. Zagazig, Egypt

***Corresponding author**: Dr Elsayed Hamdi Noureldin, Lecturer of Obstetrics and Gynecology, Obstetrics and Gynecology Department, Faculty of Medicine, Zagazig University. Zagazig, Egypt.

Citation: Noureldin EH (2018) Combined Use of Misoprostol Plus Oxytocin Versus Oxytocin Alone to Reduce Blood Loss During Cesarean Section. Arch Women Heal Gyn: 101.

Received Date: 08 May, 2018; **Accepted Date:** 15 May, 2018; **Published Date:** 22 May, 2018

Abstract

Introduction: Post-partum hemorrhage (PPH) continues to be a leading cause of maternal morbidity and mortality worldwide. According to the world health organization estimates, more than 585.000 women die every year from pregnancy related cause, of which 25% were due to severe bleeding.

Post-partum hemorrhage is defined as a blood loss of than 1000 ml in the first 24 hr following delivery. The incidence of cesarean delivery is increasing and the average blood loss during cesarean delivery (1000ml) is double the amount lost during vaginal delivery (500ml), active management of third stage of labor by administration of uterotonic drugs reduced risks of postpartum hemorrhage, reduced post-partum anemia and the need for blood transfusion. Therefore, active management should be the routine management of choice.

Misoprostol has become a valuable agent in the treatment of PPH. The sublingual route has the advantage of ease administration and rapid absorption. The transient Side effects of misoprostol appear to be dose and route related. **The aim of the study** is to compare the effect of combined oxytocin– misoprostol versus oxytocin alone in reducing blood loss at cesarean delivery. **Methods:** One hundred and two women included in this study were divided into two groups: -

The misoprostol oxytocin group*:* included fifty-one cases received 200 mcg sublingual misoprostol plus 5 IU bolus intravenous oxytocin that was adminstered slowly immediately after delivery of the fetus.
The oxytocin group: included fifty-one cases received 5 IU bolus intravenous oxytocin followed by I.V drip of 15 units' oxytocin in 500mL of Ringer lactate solution over 1 hour at a flow rate 120 drops per minute.

After delivery of the placenta, additional uterotonic has been adminstered in the form of slow injection of oxytocin 20 IU. The frequency of additional uterotonic used since administration of study dose till 24 hours after surgery was reported result significant difference between misoprostol oxytocin group and oxytocin group as regarding the need for additional uterotonics (in misoprostol oxytocin group was 21.6% (11 cases), in oxytocin group: was 2.0% (1 cases) (p-value0.002)). Significant difference between misoprostol oxytocin group and oxytocin group as regarding the need for uterine massage (in misoprostol oxytocin group was 54.6% (28 cases), in oxytocin group: was 15.7% (8cases)). Significant difference between misoprostol oxytocin group and oxytocin group as regarding uterine tone score after treatment (misoprostol oxytocin group: the median of tone score was 2.74, IQR (0.44), oxytocin group: the median of tone score was 3.48, IQR (0.7). NO Significant difference between misoprostol oxytocin group and oxytocin group as regarding the estimated blood loss (in misoprostol oxytocin group: was 585.1ml, in oxytocin group: was 562.4ml.

Conclusion: Based on the data found in our study, it was concluded that administration of a low dose of misoprostol plus oxytocin fail to show any significant difference regarding estimated blood loss and cases of misoprostol-oxytocin group needed more additional uterotonic and more need for uterine massage during cesarean section compared to oxytocin when given alone but use of them was not associated with any serious side effects.

Introduction

Postpartum hemorrhage (PPH) describes excessive bleeding after delivery of a fetus. It is the leading cause of maternal death responsible for approximately 68,500 deaths a year, 99.7% occurring in developing regions**.** It occurs in approximately 6% of deliveries when defined as a blood loss equal to, or greater than 500 ml, or 1–2% when a 1000 ml is used (1). It therefore represents a significant global health burden, disproportionately affecting those in the world's poorest countries.

Postpartum hemorrhage is the consequence of several different pathologies that can occur in isolation or combination: uterine atony, genital tract trauma, retained placental tissue and coagulation dysfunction. In severe cases of postpartum hemorrhage often pathologies co-

exist, with intractable hemorrhage often leading to coagulopathy (2).

Uterine atony is regarded as the most common cause of PPH. It occurs when inadequate myometrial tone results in unchecked blood flow to the placental bed. An individual's risk of excessive blood loss will be influenced by numerous pre-existing, pregnancy-related and obstetric factors. Risk factors for PPH include: Asian ethnicity; obesity; previous PPH; multiple pregnancy; anemia; large baby; placenta previa; age over 40 years; induction of labor; prolonged labor; intrapartum pyrexia; placental abruption; episiotomy; operative vaginal delivery; retained placenta; and delivery by caesarean section (3).

Nowadays, the incidence of fatal PPH has decreased because of active management of third stage of labor which includes controlled cord traction, uterine fundal massage, and administration of a pharmacological uterotonic (4). Although surgeon experience has a great role in reducing the occurrence of primary postpartum hemorrhage at cesarean section, the administration of uterotonics, sometimes in high doses, helps in preventing or stopping excessive blood loss from an atonic uterus. These include oxytocin, ergometrine, and prostaglandins.

Oxytocin and ergometrine are light- and heat-sensitive and require cold-chain storage. Prostaglandins E2 and F2a are used as second- or third-line agents but they are heat-labile and too expensive for use in developing countries (5). Misoprostol, a synthetic prostaglandin E1 analog, has been emerged to prevent and treat gastroduodenal damage induced by nonsteroidal anti-inflammatory drugs (NSAIDs) (6).

Oxytocin is a short amino-acid polypeptide hormone, released from the posterior lobe of the pituitary gland. It is widely used to stimulate uterine contractions to accelerate labor progress (7).

Although oxytocin is the gold standard drug for prevention and treatment of PPH, it requires cool storage, sterile equipment, and trained personnel, so that routine use of oxytocin in low-resource settings may be difficult (8).

Misoprostol offers many advantages over oxytocin in such settings. It is heat-stable, costs lower, and has variable routes of administration: orally, rectally, vaginally, or sublingually.

Also, it is formulated as a tablet, stable at room temperature, widely available and affordable, and does not require any special skills, equipment, or facilities for its use (9).

After oral administration, the plasma concentration increases rapidly, peaks at 30 min, and then declines rapidly. The sublingual route allows fast absorption of drug and more sustained therapeutic effect than oral administration as it avoids first-pass effect. Misoprostol stimulates uterine contractions by selectively binding to myometrial proteinoid receptors, and it has a long half-life and minimal adverse effects, such as gastrointestinal symptoms, shivering, pyrexia, fatigue, and headache (10).

Aim of The Study

The aim of this study is to compare the effectiveness of combined sublingual misoprostol and oxytocin infusion administered immediately after delivery of the neonate at cesarean section versus intravenous oxytocin infusion alone in the prevention of uterine atony and thereby reducing blood loss.

Patients and Methods

This was a cross-sectional observational clinical study, done on patients scheduled for elective cesarean section at term at Al Zahraa hospital, Jeddah. KSA, between period from December 2017 to May 2018.

Inclusion criteria:

- Pregnant at term (37 – 40) weeks.
- Elective Cesarean section under regional anesthesia.
- No history of medical disorder.
- No history of coagulation abnormalities.

Written and informed consents were obtained from each subject following a detailed explanation of the objectives of the study.

Exclusion criteria:

- Any cesarean section under general anesthesia.
- Women with increased risk for post-partum hemorrhage will be excluded:

1-anemia Hb<8gm/dl
2-Multiple gestations
3-Polyhydramnios
4-Ante partum hemorrhage
5-Two or more previous cesarean section
6-Suspected placenta accrete
7-previous rupture uterus.
8- Women with thrombocytopenia, known coagulopathies, or receiving anticoagulant therapy.
9-Women with history of significant heart disease, hypertension requiring treatment, a history or evidence of liver, renal, vascular disease or endocrine disease.

- Women with history of hypersensitivity to oxytocin.
- Women with any severe allergic condition or severe asthma.
- Women with any contraindication to receiving prostaglandins, including known hypersensitivity to misoprostol or other prostaglandins (PGs) or glaucoma.
- Mental condition rendering the patients unable to understand the nature, scope and possible consequences of the study.

Methodology

For all patients included in the study the following was done: On day of surgery all parturient 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: 200 mcg sublingual Cytotec (Cytotec 200mg, Pfizer, USA) plus 5 IU bolus intravenous oxytocin (Syntocinon 5 I.U amp., Novartis, Switzerland) that was administrated slowly immediately after delivery of the fetus.

Group2: immediately after delivery of the neonate during caesarean section: 5 IU bolus intravenous oxytocin followed by I.V drip of 15 units' oxytocin in 500mL of Ringer lactate solution over 1 hour at a flow rate 120 drops per minute were given.

Surgical and anesthetic techniques had been standardized, with all patients undergoing spinal anesthesia. Patients received an intravenous bolus of 500-1000 mL crystalloid before spinal anesthesia. Intravenous crystalloids continued at 1 L every 8 hours until the morning after surgery, unless the patient was unable to tolerate oral fluids.

Surgeons had operated to a standard procedure, according to the guidelines at hospital, that specified controlled cord traction for delivery of the placenta after administration of the medicaments with two-layer closure of the uterine incision. The vital signs (baseline blood pressure and pulse rate) were recorded just before CS, average intraoperative and 2hours postoperative.

Uterine tone has been assessed immediately after delivery of the placenta and then every 5 minutes until abdominal closure begins and in the postpartum ward. Uterine tone has been rated according to the extent of indentation by finger pressure using a 5-point scale with 0 indicate soft boggy uterus and 4 indicate rock hard tetanic uterus (10). Additional uterotonic has been administered in the form of slow injection of oxytocin 20 IU. The frequency of additional uterotonic used since administration of study dose till 24 hours after surgery was reported.

Calculation of the quantity of blood loss:

After delivery of the placenta, the volume of blood loss during CS was estimated by the surgeon in the usual way (visual estimation, number of used swabs and amount of aspirated blood) as average (<500ml), mderate (500-1000 ml), and major (>1000 ml). Complete blood count has been done twice, just before and in 24 hours after CS. On the postpartum ward, patients received routine care. The need for uterine massage and vital signs were recorded up to 24 hours after the operation. fundal height in relation to umbilicus in 24 hours and the time took Fundal height to be below umbilicus in hours. Adverse effects were recorded by the researcher as they were observed or reported in response to direct questioning. The patients were monitored for side effects of the selected drug in the first 24 hours post-delivery. Patients had been questioned for side effects after drug administration, in the recovery room and in the postnatal ward. The patients were also monitored for signs of adverse effects. Any other symptoms volunteered, or signs observed by the attending doctor or nurse had been recorded. Adverse effects specifically looked for include abdominal pain, back pain, headache, nausea, feeling of warmth, and metallic taste.

Other adverse effects include shivering (mild and moderate/severe), pyrexia (body temperature at least 38°C) within 1 hour of taking the trial drug, vomiting, diarrhea, loss of appetite, abnormal heart beats(arrhythmias), heat sensation, , tremors, dizziness, dyspnea, difficulty in breathing, chest pain, pruritus, skin rash and flushing. Any blood transfusion, additional oxytocic therapy, incidence of PPH or any significant puerperal morbidity were recorded in the first 24 hours post-delivery. Serious adverse events were reported within 24 hours of the event.

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 position relation to umbilicus in24hours.
- Amount of intraoperative blood loss following delivery of the fetus.
- Blood transfusion.
- Occurrence of drug Side effects (nausea, vomiting, shivering and pyrexia).

Sample Size Justification

Sample size was calculated using STATA® version 11 program, setting the type-1 error (α) at 0.05 and the power (1-β) at 0.8. sample size estimation was based on the previous studies which reported that the mean amount of blood loss with the use of oxytocin during c.s is 600cc,and misoprostol can reduce it by 200cc (Vimala N and Kumar MS;2006)(Fazel MR et al;2013).thus, considering 90% power and 5%error,the sample size was determined to be 51 cases in each group. Results 47.

Results

One hundred and two women included in this study were divided into two groups: -

The misoprostol oxytocin group: included fifty-one cases received 200 mcg sublingual misoprostol plus 5 IU bolus intravenous oxytocin that was adminstered slowly immediately after delivery of the fetus.

The oxytocin group: included fifty-one cases received 5 IU bolus intravenous oxytocin followed by I.V drip of 15 units' oxytocin in 500mL of Ringer lactate solution over 1 hour at a flow rate 120 drops per minute.

After delivery of the placenta, additional uterotonic has been administrated in the form of slow injection of oxytocin 20 IU. The frequency of additional uterotonic used since administration of study dose till 24 hours after surgery was reported Significant difference between misoprostol oxytocin group and oxytocin group as regarding the need for additional uterotonics (in misoprostol oxytocin group was 21.6% (11 cases), in oxytocin group: was 2.0% (1 cases) (p-value0.002)). Significant difference between

misoprostol oxytocin group and oxytocin group as regarding the need for uterine massage (in misoprostol oxytocin group was 54.6% (28 cases), in oxytocin group: was 15.7% (8cases)). Significant difference between misoprostol oxytocin group and oxytocin group as regarding uterine tone score after treatment (misoprostol oxytocin group: the median of tone score was 2.74, IQR (0.44), oxytocin group: the median of tone score was 3.48, IQR (0.7). NO Significant difference between misoprostol oxytocin group and oxytocin group as regarding the estimated blood loss (in misoprostol oxytocin group was 585.1ml, in oxytocin group: was 562.4ml.

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/m2)	27.88±3.16	28.44±4.28	0.205
Gestational age (weeks)	38.0 ±0.9	38.0± 0.7	0.191

Table 1: The relation between study groups as regard age, weight, height, BMI and gestational age.

Variable	Misoprostol-Oxytocin group (n=51)	Oxytocin group (n=51)	p-value
Need for additional uterotonic	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 scores 5 min after 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 surgical intervention	0 (0.0%)	0 (0.0%)	

Table 2: Outcome measures 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±.9	0.975
Preoperative PCV (%)	32.6±3.02	32.59±2.7	0.975
Hemoglobin 24 h after delivery (g/dl)	10.08±.96	9.9±.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	

Table 3: Hemoglobin and hematocrit in both study groups.

Variable	**Misoprostol oxytocin group (n=51)**	**oxytocin group (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

Table 4: Hemodynamic variables in both study 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/or vomiting	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

Table 5: Incidence of drug-related side effects in both study groups.

Discussion

Cesarean delivery is the most frequently performed major surgical procedure worldwide. Compared with women delivering vaginally, women undergoing cesarean have an increased risk of high blood loss and so are more likely to need a blood transfusion. The global rise in the incidence of cesarean delivery has possibly contributed to the resurgence of postpartum hemorrhage (PPH) in high-income countries (10).

The risk of PPH is further increased in the presence of risk factors such as multiple pregnancy, polyhydramnios, grand multiparity, severe pre-eclampsia, prepartum hemorrhage, prolonged and obstructed labor, augmented labor, obesity, and anemia. Oxytocin-the gold standard oxytocic agent—is widely used during cesarean delivery to prevent PPH, even though some studies (11) have raised concerns about its efficacy and adverse effects. Misoprostol has been evaluated as an alternative to oxytocin during cesarean delivery and has also been used in combination with oxytocin (12).

Meta-analyses (13) concluded that misoprostol was as effective as oxytocin and that the combination of the misoprostol and oxytocin is better than is oxytocin alone for the prevention of PPH. However, women with known risk factors for PPH, who are expected to benefit from an alternative or additional oxytocic agent, were totally or partially excluded from other studies (12). Thus, the existing evidence on the optimal uterotonic agent during cesarean for high risk women is insufficient.

The present study was conducted to establish whether the combination of misoprostol and oxytocin more effectively reduces blood loss during and after cesarean delivery than does oxytocin alone with less side effects.

The study included 102 pregnant women undergoing elective lower segment cesarean section at term (completed 37 weeks of gestation or more) under regional anesthesia. 102 Parturient were allocated into 2 equal groups each group involved 51 cases.

a - Study group. I

200 mcg sublingual misoprostol plus 5 IU bolus intravenous oxytocin that was administrated slowly immediately after delivery of the fetus.

b – Study group. II
immediately after delivery of the neonate during caesarean section: 5 IU bolus intravenous oxytocin followed by I.V drip of 15 units' oxytocin in 500mL of Ringer lactate.
solution over 1 hour at a flow rate 120 drops per minute were given.
There was non-significant difference between misoprostol oxytocin group and oxytocin group as regards age, weight, height, BMI and gestational age.

According to the need for additional uterotonics for the women involved in this study, in misoprostol oxytocin group : was 21.6% (11cases), in oxytocin group : was 2.0% (1 cases) and That showed a significant difference between the two study groups as regard need for additional uterotonics (p-value0.002).

Increase requirement in the present study may be explained using small doses of uterotonics in misoprostol oxytocin group. Some previous studies have reported no difference (14). In a study woman who received 800 µg misoprostol by the intrauterine route there was no significant difference in the requirement for additional oxytocic therapy. Because the intrauterine route has not been evaluated elsewhere

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 (15).

Concerning the need for blood transfusion for the women involved in this study, in misoprostol oxytocin group: was 4.0% (2 cases), in oxytocin group: was 2.0% (1cases), that showed no Discussion 18 significant difference between the two study groups as regard the need for blood transfusion (p-value 0.46).

This finding is in accordance with previous studies (15). Concerning uterine tone after treatment for the women involved in this study, group of oxytocin significantly higher regard uterine tone score than misoprostol-oxytocin group.

According to blood loss in the present study, the combined use of misoprostol and oxytocin during cesarean delivery resulted in a no significant reduction in intraoperative blood loss compared with the use of oxytocin alone. (*Hamm J et al 2005)* did not report a significant difference in blood loss with the use of adjunct misoprostol. This agreed with the present study (16).

When combined with 20IU oxytocin drip, (200µg) Sublingual misoprostol was found to be as effective as intravenous oxytocin (20IU) in prevention of postpartum hemorrhage following cesarean delivery with less side effects (17).

However, the extent of the reduction in blood loss varied widely between the studies. The researchers who excluded high-risk women (,12) reported a greater reduction in intraoperative blood loss and the one that included both high- and low-risk women. Additionally, in two of the studies showing a greater reduction in blood loss, misoprostol was administered preoperatively (rectally during catheterization (18) or sublingually after intubation (12). Earlier administration of misoprostol could have had a role in reducing blood loss to a considerable extent in these study cohorts. the incidence of blood loss exceeding 1000 mL was similar in the two groups. A meta-analysis (13) of three studies also showed no significant difference in blood loss in excess of 1000 mL. I experienced no case with more than 1,000 cc blood loss, however, it occurred in 2 patients of Mansouri and Alsahly study (19). Hofmeyr et al. presented no more efficacy for higher dose of misoprostol in preventing hemorrhage more than 1,000 cc through a meta-analysis (20).

Concerning need for surgical intervention for the women involved in this study showed no surgical interventions was needed in both groups.

According to drop in hemoglobin (g/dl) for the women involved in this study, that showed no significant difference between oxytocin and misoprostol group and oxytocin group in hemoglobin changes.

The present findings of a smaller postoperative drop in hemoglobin with the use of combined oxytocic's were in agreement with some of the previous studies (17).

In a study woman who received 800 µg misoprostol by the intrauterine route had smaller decreases in hemoglobin than did those given placebo, although there was no significant difference in the requirement for additional oxytocic therapy. Because the intrauterine route has not been evaluated elsewhere, it is difficult to say whether this finding is related to the unusual route of administration of misoprostol (18).

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-value0.00), which were statistically significant difference.
Additionally, the increased frequency of shivering in women who received sublingual misoprostol was in line with previous studies (12).

By contrast, researchers using the drug by the rectal (13), buccal (15), or intrauterine routes did not report a rise in the incidence of these adverse effects in women who received misoprostol. Administration of misoprostol by the sublingual route results in the highest peak concentration in the shortest time (30 minutes) and the greatest bioavailability compared with all other routes because of rapid absorption from the sublingual mucosa and the avoidance of first-pass metabolism by the liver (21). The duration of action has not yet been determined.

The unique properties of the sublingual route, although beneficial in terms of quick onset of strong uterine contractions, could also lead to more adverse effects.

According to Hofmeyr the incidence of side effects with misoprostol was dose-dependent and that efforts should be undertaken to establish the smallest effective and safe dose of the drug (20).

A large multi-country study which was conducted in collaboration with World Health Organization in five countries (Egypt, South Africa, Thailand, Vietnam and Argentina) showed no benefit of administering 600 mcg of sublingual misoprostol and same study conducted in (South Africa, Uganda, and Nigeria) evaluating adjunct use of misoprostol for prevention of PPH, also showed no beneficial effects in the both studies, misoprostol was associated with increased side effects **(20).**

A similar pattern was noted in one study that compared the side effect profiles of 200mcg, 400mcg, and 600mcg regimens of sublingual misoprostol for the management of PPH among Libyan women**.** In all three treatment groups, most women had shivering (75%-100%) and fever (83%-100%) confirmed by systematic temperature measurement (22).

In a study by wilfrido in Ecuador the incidence of side effects using *600µg* sublingual misoprostol was high (55%), however when they compared there with another study using higher dose (800µg) the incidence of side effects was lower in the 600µg group (23). The results provide further evidence of dose dependent nature of misoprostol-induced side effects.

Conclusion

Based on the data found in our study, it was concluded that administration of a low dose of misoprostol plus oxytocin fail to show any significant difference regarding estimated blood loss and cases of misoprostol-oxytocin group needed more additional uterotonic and more need for uterine massage during cesarean section compared to oxytocin when given alone, but use of them was not associated with any serious side effects.

References

1. Carroli G, Cuesta C, Abalos E, Gulmezoglu AM. Epidemiology of postpartum hemorrhage: a systematic review. Best Pract Res Clin Obstet Gynaecol 2008; 22:999–1012.
2. Stafford I, Dildy GA, Clark SL and Belfort MA (2008): Visually estimated and calculated blood loss in vaginal and cesarean delivery. Am J ObstetGynecol; 199:519. e1.
3. RCOG Green-top Guideline no.52, (2009): How should PPH be managed? Minor revision November 2009.
4. Matsubara S, Yano H, Taneichi A, et al. Uterine compression suture against impending recurrence of uterine inversion immediately after laparotomy repositioning. J Obstet Gynaecol Res. 2009; 35:819–23.
5. Owonikoko KM, Arowojolu AO and Okunlola MA (2011): Effect of sublingual misoprostol versus intravenous oxytocin on reducing blood loss at cesarean section in Nigeria: a randomized controlled trial. Obstet Gynaecol Res 2011;37(7):715–21.
6. Park SC, Chun HJ, Kang CD, et al. Prevention and management of non-steroidal anti-inflammatory drugs-induced small intestinalinjury. World J Gastroenterol. 2011;17(42):4647–53.
7. RCOG. RCOG Green-top Guideline No 52(2011): prevention and management of postpartum haemorrhage; 2009, updated 2011.
8. Alfirevic Z, Blum J, Walraven G, et al. Prevention of postpartum hemorrhage with misoprostol. Int J Gynecol Obstet. 2007;99: S198–201.
9. Allen R and Barbara M and O'Brien (2009): Uses ofMisoprostol in Obstetrics and Gynecology.Reviews in obstetrics & gynecology. RevObstetGynecol; 2(3):159-168.
10. Ford JB, Roberts CL, Simpson JM, Vaughan J and Cameron CA (2007): Increased postpartum hemorrhage rates in Australia. Int J Gynecol Obstet 2007;98(3):237–43.
11. Thomas JS, Koh SH and Cooper GM (2007): Haemodynamic effects of oxytocin given as i.v. bolus or infusion on women undergoing Caesarean section. Br J Anaesth 2007;98(1): 116–9.
12. El Tahan MR, Warda OM, Rashad A, Yasseen AM, Ramzy EA, Ahmady MS, et al(2012): Effects of preoperative sublingual misoprostol on uterine tone during isoflurane anesthesia for cesarean section. Rev Bras Anestesiol 2012;62(5):625–35
13. Conde-Agudelo A, Nieto A, Rosas-Bermudez A and Romero R (2013): Misoprostol to reduce intraoperative and postoperative hemorrhage during cesarean delivery: a systematic review and metaanalysis. Am J Obstet Gynecol 2013; 209:40. e1.
14. Lopes T, Spirtos N, Naik R, Monaghan J (2011): opening and closing abdominal cavity: Bonney's gynecological surgery Blackwell publishing
15. Bamberg C, Dudenhausen JW, Bujak V, Rodekamp E, Brauer M, Hinkson L, Kalache Kand Henrich W (2016): A Prospective Randomized Clinical Trial of Single vs. Double Layer Closure of Hysterotomy at the Time of Cesarean Delivery: The Effect on Uterine Scar Thickness. Ultraschall Med. 2016 Sep 14. [Epub ahead of print].
16. Hamm J, Russell Z, Botha T, Carlan SJ and Richichi K (2005): Buccal misoprostol to prevent hemorrhage at cesarean delivery: a randomized study. Am J Obstet Gynecol; 192(5):1404–6.
17. Fekih M, Jnifene A, Fathallah K, Ben Regaya L, Memmi A, Bouguizene S, et al (2009): Benefit of misoprostol for prevention of postpartum hemorrhage in cesarean section: a randomized controlled trial. J Gynecol Obstet Biol Reprod (Paris) 2009;38(7):588–93.
18. Elsedeek MS (2012): Impact of preoperative rectal misoprostol on blood loss during and after elective cesarean delivery. Int J Gynecol Obstet 2012;118(2):149–52.
19. Mansouri HA, Alsahly N (2011): Rectal versus oral misoprostol for active management of third stage of labor: a randomized controlled trial. Arch Gynecol Obstet. 2011; 283:935–9.
20. Hofmeyr GJ, Gülmezoglu AM, Novikova N, Linder V, Ferreira S and Piaggio G (2009): Misoprostol to prevent and treat postpartum haemorrhage : a systematic review and meta-analysis of maternal deaths and dose – related effect . Bull world health organ. 2009; 87 :666-667.

21. Tang OS, Gemzell-Danielsson K and Ho PC (2007): Misoprostol: pharmacokinetic profiles, effects on the uterus and side-effects. Int J Gynecol Obstet 2007;99(Suppl. 2): S160–7
22. Elati A and Andrew Weeks (2011): Misoprostol for the management of postpartum haemorrhage. BMJ ;342: d2877.
23. Westhoff G, Cotter AM, Tolosa JE (2013): Prophylactic oxytocin for the third stage of labour to prevent postpartum haemorrhage. Cochrane Database Syst Rev; CD001808.