Zagazig University Medical Journal
www.zumj.journals.ekb.eg
https://doi.org/10.21608/zumj.2023.254608.3044 Volume 31, Issue 3, March. 2025
Manuscript ID ZUMJ-2312-3044
DOI:10.21608/zumj.2023.254608.3044
ORIGINAL ARTICLE

Intrauterine Misoprostol plus Oxytocin versus Oxytocin only in Prevention of Primary Postpartum Hemorrhage : Randomized Controlled Trial

Mostafa Abbas Ibrahim[1], Mona Mohamed Atta [2], Mostafa Salah Omara [3]
Obstetrics and Gynecology Department, Faculty of Medicine,Zagazig University,Zagazig, Egypt

Correspondingauthor:
Mona Mohamed Atta

Email
dr.mona.ata@gmail.com

Submit Date: 11-12-2023
Revise Date: 30-12-2023
Accept Date: 31-12-2023

ABSTRACT

Background: In low-resource regions of the world, misoprostol, with or without oxytocin, has recently emerged as an effective substitute for oxytocin for preventing postpartum hemorrhage by reducing intraoperative and postoperative blood loss (PPH). This study aimed to compare the intrauterine misoprostol plus oxytocin effects versus oxytocin only in the prevention of primary postpartum hemorrhage.

Methods: This double-blinded randomized controlled clinical trial involved 94 cases admitted for elective cesarian section at Zagazig University Maternity Hospital. Group (A): 47 pregnant women who received only 20 IU intravenous oxytocin in 500 mL of normal saline solution (infused at a rate of 125 mL/hour) immediately after delivery of the fetus. Group (B): 47 pregnant women who received 20 IU intravenous oxytocin added to 500 mL of normal saline solution (with an infusion rate of 125 mL/hour) immediately after fetal delivery plus intrauterine misoprostol tablets (800mcg) intrauterine after placental delivery. The amount of intra-operative post-operative blood loss and occurrence of PPH were assessed.

Results: The blood loss differed significantly between both groups (P<0.001), with higher blood loss either intraoperative, postoperative, and total blood loss in Group A (Mean ± SD 85.1±8.6) than in Group B (Mean ± SD 62.3±9.1). Hemoglobin and HCT differed significantly between both groups postoperatively in the two studied groups (p=0.045 for each), which was more among Group A (Mean ± SD 10.07±0.77) than Group B (Mean ± SD 10.37±0.65).

Conclusion: Reduced intraoperative blood loss and prevention of primary postpartum hemorrhage could be achieved by intrauterine misoprostol combined with oxytocin infusion during cesarean section.

Keywords: Misoprostol, Oxytocin, Intrauterine, Postpartum Hemorrhage

INTRODUCTION

Bleeding after giving birth that exceeds 1000 milliliters is known as postpartum hemorrhage (PPH). In cesarean section (CS) deliveries, the typical blood loss due to postpartum hemorrhage is (1000 ml or more). One-quarter of all female fatalities are attributed to it [1]. In Africa and Asia, PPH accounts for about a third of maternal mortality rates [2]. Prevalence estimates for PPH fall around between 0.6 and 6.4% [3]. Atony of the uterus, which occurs following placental delivery in both vaginal and cesarean deliveries, is the leading cause of postpartum hemorrhage. It accounts for about 80% of PPH occurrences [4].

The rise in PPH has been attributed primarily to cesarean deliveries. Developed and emerging nations are seeing an increase in the percentage of surgeries performed by cesarean section [5].

With a rate of 55%, Egypt is among the countries with the greatest cesarean delivery rates. The rate is two to three times higher than the optimal rate, between 10% and 15% [6].

The uterotonic drug most commonly prescribed during pregnancy is oxytocin. Patients with preeclampsia, extended labor, or heart illness may not be good candidates for oxytocin as a PPH preventive medication due to the risks of tachycardia as well as hypotension [7]. Furthermore, developing nations lack the infrastructure to store oxytocin in the cold, as it is both heat and light-sensitive. On top of that, further uterotonic medications may be necessary to induce a good uterine contraction in 10–40 percent of cases while using it [8]. The addition of misoprostol as an alternative to oxytocin to PPH preventative measures was the culmination of many years of study and development [9].

The prostaglandin E1 (PGE1) analog misoprostol attaches itself specifically to the EP-2/EP-3 prostanoid receptors. Numerous studies have demonstrated its effectiveness as a stimulant of the myometrium in a pregnant woman's uterus. At room temperature, misoprostol remains stable, has a lengthy half-life, is cheap, and exhibits substantial uterotonic action. A new, less invasive option for reducing intraoperative and postoperative blood loss in low-resource nations is misoprostol, with or without oxytocin [10]. Using misoprostol intrauterine during CS is not widely discussed in the literature [11].

The present work aimed to compare the effect of the intrauterine misoprostol added with oxytocin versus oxytocin only in preventing primary postpartum hemorrhage.

METHODS

This was a double-blinded, randomized controlled clinical trial that was carried out on 94 pregnant females at term (38-40 weeks of gestation) who were scheduled for elective cesarean section in the duration from February 2022 to February 2023.

Verbal and written informed consents were obtained from all participants after an explanation of the procedure and medical research. The research was conducted under the World Medical Association's Code of Ethics (Helsinki Declaration) for human research. This study was carried out after the approval of the Institutional Review Board (IRB) (#9198).

Cases with the following criteria were included; Pregnant females aged 18 years or above who were at term (38 - 40) weeks with singleton pregnancy who were scheduled for elective cesarean section under spinal regional anesthesia.

Cases with the following characteristics were excluded: who undergone general anesthesia, morbidly obese patient BMI >40, anemic patients who had Hb lower than 8gm/dl, multiple gestations, polyhydramnios, ante partum hemorrhage, and previous rupture uterus. Also we excluded any case who had suspected placenta accrete previa, thrombocytopenia, coagulopathies or taking anticoagulant therapy, medically complicated pregnancies, hyper sensitivity to oxytocin, or contraindication to receive prostaglandins.

Pregnant women meeting all the inclusion criteria was allocated into two equal groups (group A and group B) and each group involved 47 cases.

Methods of randomization:

Before the trial, there are 94 opaque and sealed envelopes which contain a slip of paper allocating the patients into two equal study groups 47 for each group (group A, group B) that indicate their medication , patient take an envelope and surgeon open the randomization envelope in the operating theater. The allocation will be blind to both recruiter and participant.

All cases who met the inclusion criteria were subjected to the following: Full history taking with special emphasis on obstetric history including parity, mode of delivery and menstrual history. General examination was done including vital data (e.g., Blood pressure, pulse and temperature). Abdominal examination was done including fundal height, abdominal and pelvic grips. Fetal viability, biometry, and the location of the placenta were

all evaluated by ultrasound. We performed standard laboratory tests, including a full blood count, hemoglobin A1c, Rh, and coagulation profile, to establish a baseline.

Intra operatively: Group A (Oxytocin group): 20 IU of intravenous oxytocin added to 500 ml of Normal saline solution was administered (with rate of infusion of 125 mL/hour) directly after delivery of the fetus. Group B (Misoprostol group): 20 IU of intravenous oxytocin added to 500 ml of Normal saline solution was administered (with rate of infusion of 125 mL/hour) directly after delivery of the fetus plus two tablets of misotac, each containing 800 mcg of misoprostol, were placed near the corneas after the placenta was delivered, and two tablets were injected into the uterine cavity at the fundus. A 1500 mL crystalloid iv bolus was administered to patients in both groups during CS. By combining the suction bottle capacity with the pre- and post-operative weight difference of the operating towels, we were able to approximate the volume of blood loss during CS (weighting method).

Postoperatively: Intravenous crystalloids were continued after surgery 500 ml every 8hours until the patient was able to tolerate oral fluids, Vital signs were assessed (blood pressure and pulse) were recorded every half an hour for two hours. Postoperative hemoglobin level was measured 2 hours postoperative. The amount of bleeding was calculated in the first 2 hours post CS by weighting the used napkin.

There were different ways used to assess total blood loss: A mathematical computation was used to estimate the blood loss during the operation and in the two hours following the procedure. The hematocrit level was measured both before the operation (preoperative) and two hours after the procedure (postoperative). The estimated blood loss (EBL) for every patient was measured using the following formula [12]: $\mathrm{EBL} = EBVx\frac{(HCT1-HCT2)}{HCT1}$ estimated blood volume, measured in milliliters (mL) is EBV=weight in kg × 85, the initial pre-operative hematocrit is Hct 1, and 2-hours post-operative hematocrit is Hct 2.

Primary outcome included: Assessment of amount of intra-operative (from start of skin incision to skin closure) , estimated post-operative blood loss (2h after CS) and total blood loss either by summation of intra-operative plus post-operative blood loss or by using mathematical method using the formula:

$$\mathrm{EBL} = \mathrm{EBVx}\frac{(\mathrm{HCT1\text{-}HCT2})}{\mathrm{HCT1}}$$

Secondary outcome included: Occurrence of post-partum hemorrhage (loss of blood ≥) 1000 ml), the necessity of transfusing blood during the initial twenty-four hours following surgery, the need for additional doses of uterotonics either intra or postoperative, and side effects of the drugs (vomiting, nausea, shivering and pyrexia).

STATISTICAL ANALYSIS

Data was analyzed statistically with IIBM SPSS, version 20.0 (IBM Corporation, Armonk, New York). Numbers and percentages were used to communicate qualitative data, whilst standard deviations and means were used to describe quantitative data. Two sets of normally distributed variables were compared using the t-test. We used the Chi-square test to compare percentages of categorical variables when it was applicable. In cases where a single cell was fewer than 5, the Fisher exact test was substituted for the chi-square test. A p-value < 0.05 is considered significant.

RESULTS

We found that all of age, gravidity, body mass index (BMI), parity as well as gestational age were insignificantly different between the studied groups (Table 1).

The group that received intravenous oxytocin in addition to intrauterine misoprostol (Group B) had a significantly lower rate of blood loss intra and postoperatively, as well as total estimated blood loss compared to the only intravenous oxytocin group (Group A) (P value <0.001) (Table 2).

Postoperative Hb was significantly increased in group B than in group A (P value =0.045). In both groups, Hb 2 hours postpartum significantly dropped postoperative than preoperative (P value= 0.004 in only

intravenous oxytocin group and 0.013 in intravenous oxytocin plus intrauterine misoprostol group) (Table 3).

Postoperative HCT was significantly increased in group B than in group A (P value =0.045). In both groups, HCT 2 hours postpartum significantly dropped postoperative than preoperative (P value <0.001) (Table 4).

Preoperative and postoperative pulse, systolic blood pressure (SBP) and diastolic blood pressure (DBP) were insignificantly different between the studied groups (Table 5). Shivering was significantly increased in group B than in group A (P value =0.040). Nausea, vomiting, and headache were insignificantly different between the two studied groups (Table 6, Figure 1).

Table (1): Demographic data of the studied groups.

		Group A (n=47)	Group B (n=47)	t-test or X^2 test	P value
Age (years)	**Mean ± SD**	28.04 ± 4.61	27.79 ± 4.88	**t=** 0.261	0.795
	Range	20 – 36	20 – 35		
BMI (kg/m^2)	**Mean ± SD**	31.25 ± 2.62	30.65 ± 2.02	**t=** 1.231	0.221
	Range	26 - 36.2	28 – 35		
Gravidity	**Mean ± SD**	2.8±1.3	2.6±1.2	X^2= 5.217	0.266
	Range	(1-4)	(1-5)		
Parity	**Nullipara**	12 (25.53%)	19 (40.43%)	X^2= 2.358	0.125
	Multipara	35 (74.47%)	28 (59.57%)		
Gestational age (weeks)	**Mean ± SD**	38.94 ± 0.7	38.87 ± 0.97	**t=** 0.365	0.716
	Range	38 – 39	38 – 39		

BMI: body mass index

Table (2): Intra and postoperative blood loss of the studied groups

		Group A (n=47)	Group B (n=47)	t-test	P value
Intraoperative blood loss (ml)	**Mean ± SD**	390.64 ± 36.2	348.62 ± 31.36	6.015	**<0.001 ***
	Range	350 – 470	300 - 400		
Postoperative blood loss (ml)(2hours)	**Mean ± SD**	75.85 ± 11.44	63.72 ± 12.13	4.986	**<0.001 ***
	Range	60 – 100	40 - 80		
Total blood loss summation intra+postoperative blood loss (ml)	**Mean ± SD**	465.64 ± 36.2	423.62 ± 31.36	6.015	**<0.001 ***
	Range	425 – 545	375 - 475		
total blood loss using formula (ml)	**Mean ± SD**	642.33 ± 162.2	338.98 ± 131.01	9.975	**<0.001 ***
	Range	303.5 – 965	115 - 518		

*: significant as P value ≤0.05

Table (3): Hb of the two studied groups.

		Group A (n=47)	Group B (n=47)	t-test#	P value#
Preoperative Hb (g/dL)	**Mean ± SD**	10.53 ± 0.73	10.69 ± 0.59	1.210	0.229
	Range	9.2 - 11.9	9.3 - 11.7		
Postoperative Hb (g/dL)	**Mean ± SD**	10.07 ± 0.77	10.37 ± 0.65	2.036	**0.045***
	Range	8.2 – 11	8.6 - 11.3		
t-test##		2.946	2.531		
P value##		**0.004***	**0.013***		

Hb: hemoglobin, *: significant as P value ≤0.05, #: comparison between group A and group B, ##: comparison between preoperative and postoperative Hb

Table (4): HCT of the studied groups

		Group A (n=47)	Group B (n=47)	t-test#	P value#
Preoperative HCT (%)	**Mean ± SD**	32.18 ± 2.41	32.67 ± 1.95	1.072	0.286
	Range	28.2 – 36	29.2 - 35.7		
Postoperative HCT (%)	**Mean ± SD**	28.73 ± 1.71	29.58 ± 2.3	2.032	**0.045***
	Range	26.8 – 35	26 - 33		
t-test##		8.009	7.035		
P value##		**<0.001***	**<0.001***		

HCT: hematocrit, *: significant as P value ≤0.05, #: comparison between group A and group B, ##: comparison between preoperative and postoperative HCT

Table (5): Vital signs of the studied groups.

		Group A (n=47)	Group B (n=47)	t-test	P value
Preoperative pulse (beats/min)	**Mean ± SD**	74.04 ± 3.74	74.72 ± 2.14	1.082	0.282
	Range	67 – 79	70 - 78		
Postoperative pulse (beats/min)	**Mean ± SD**	77.4 ± 4.19	78.66 ± 3.76	1.528	0.130
	Range	70 – 85	70 - 82		
Preoperative SBP (mmHg)	**Mean ± SD**	107.19 ± 5.41	105.32 ± 5.76	1.624	0.108
	Range	100 – 118	95 - 115		
Postoperative SBP (mmHg)	**Mean ± SD**	116.34 ± 4.79	115.85 ± 5.25	0.472	0.638
	Range	105 – 122	110 - 125		

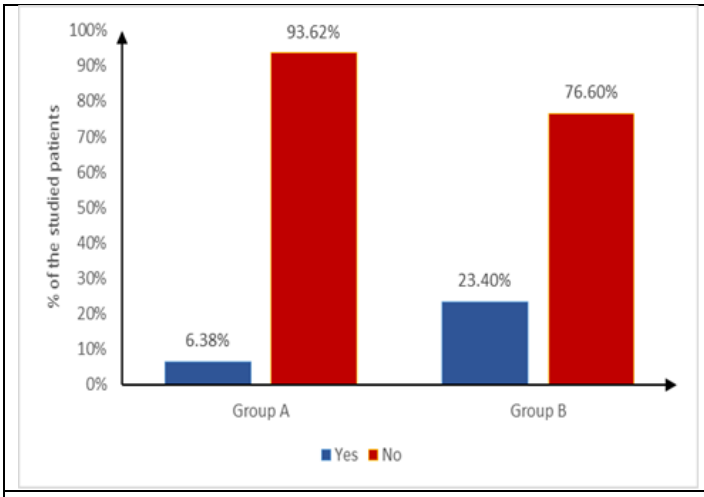
		Group A (n=47)	Group B (n=47)	t-test	P value
Preoperative DBP (mmHg)	**Mean ± SD**	72.47 ± 4.28	73.72 ± 2.45	1.746	0.084
	Range	57 – 78	70 - 78		
Postoperative DBP (mmHg)	**Mean ± SD**	77.53 ± 4.7	78.68 ± 4.07	1.268	0.208
	Range	70 – 88	73 - 88		

SBP: systolic blood pressure, DBP: diastolic blood pressure

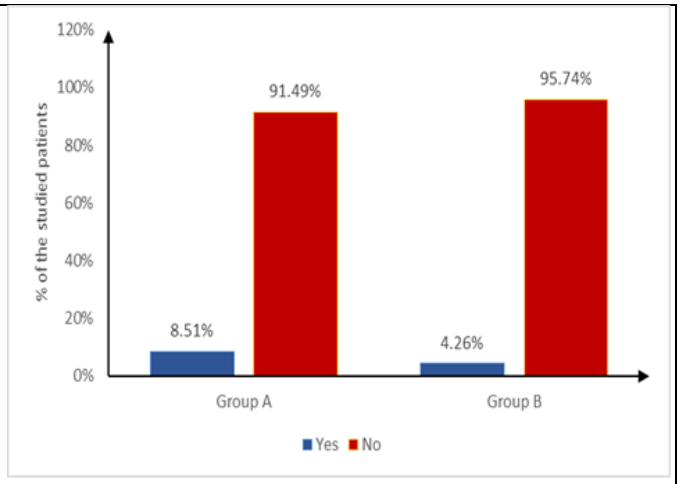
Table (6): Side effects of the studied groups.

	Group A (n=47)	Group B (n=47)	P value
No	34	32	
Shivering	3 (6.38%)	7 (14.89%)	**0.040***
Nausea	4 (8.51%)	2 (4.26%)	0.677
Vomiting	3 (6.38%)	4 (8.51%)	1.000
Headache	3 (6.38%)	2 (4.26%)	1.000

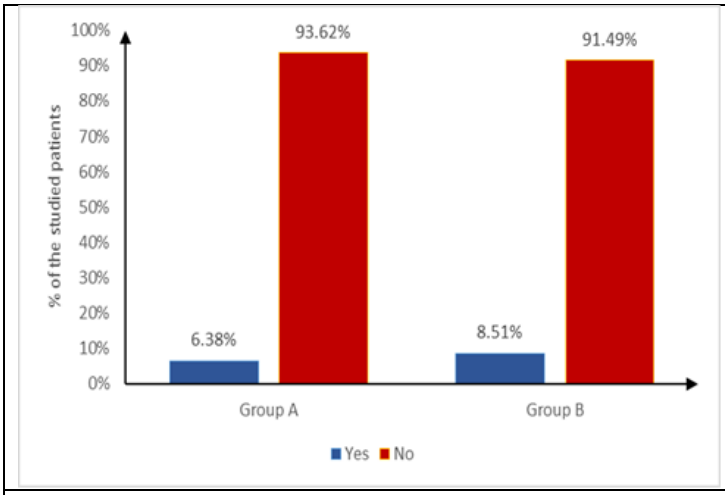
*: significant as P value ≤0.05



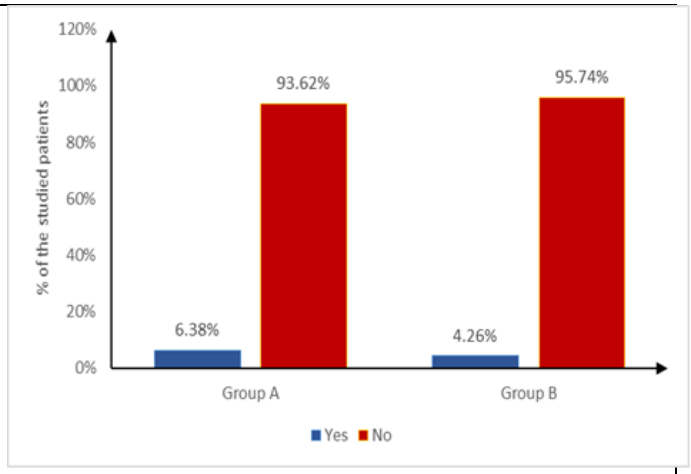
Shivering



Nausea



Vomiting



Headache

Figure 1: Effects of medication adverse events in both groups

DISCUSSION

According to national statistics. [13] Most maternal deaths in Egypt were caused by postpartum hemorrhage, however bleeding before and after delivery accounted for 43% of all maternal deaths. For every 100,000 live births, 32 mothers died from hemorrhage.

Compared to other routes—oral, sublingual, buccal, or rectal—the intrauterine route of misoprostol was deemed simpler and easier to use in the event of a caesarean section, hence it was selected for this study. It offers a safer alternative to the rectal route for spinal anaesthesia and might be utilised in any situation where contamination is a concern. In case you were wondering, misoprostol is a prostaglandin analogue that, when bound to myometrial cells, triggers powerful contractions that travel from the fundus, which is located near the cornea, all the way down to the uterine body, ultimately leading to tissue expulsion and a decrease in postpartum hemorrhage. Therefore, we assumed that inserting the pills at the uterine cornu was an easy and straightforward process. It has the potential to facilitate their uptake by myometrial cells.

The purpose of this research was to evaluate the efficacy of oxytocin alone vs intrauterine misoprostol with oxytocin in preventing major postpartum haemorrhage. No statistically significant differences were found between the two groups when comparing the mothers' ages, gravidities, parities, maternal body mass indexes, and gestational ages in this study. The two groups differed significantly in terms of blood loss, with the former experiencing significantly more blood loss during the operation and the latter experiencing significantly more blood loss overall. The results demonstrate that the group given intravenous oxytocin alone led to more blood loss than the group given intravenous oxytocin and intrauterine misoprostol.

In the present study statistical comparison between both groups, showed high significant differences as regards blood loss; P value is ($P \leq 0.001$).The intraoperative blood loss in the oxytocin group was 390.64±36.2 ml, while in the misoprostol plus oxytocin group it was 348.62±31.36 ml. The blood loss 2 hours after the operation was 75.85±11.44 ml, and the total blood loss when adding the intraoperative and postoperative blood losses was 465.64±36.2 ml, compared to 63.72±12.13 ml in the misoprostol plus oxytocin group it was 423.62±31.36 ml. Total blood loss using formula in oxytocin group show 642±162.2 ml,Vs 338.98±131.01 in misoprostol plus oxytocin group.

The present study results agreed with Zhang et al. [14], who performed a research in China and discovered that intrauterine misoprostol effectively reduced blood loss throughout the operation and for two hours after the caesarean

section, with no negative side effects. There were no adverse effects in any of the two groups, and the results demonstrated that the misoprostol group had considerably less blood loss both during and after the surgery compared to the oxytocin group (P= 0.01). In terms of mean blood loss, the misoprostol plus oxytocin group showed significantly better results compared to the oxytocin group.

Also, In a study conducted by Bahadur et al. [8], the researchers found that women who received an intrauterine misoprostol dose of 800 mg followed by an oxytocin infusion of 20 IU had less blood loss and a lower hemoglobin differential compared to those who received only oxytocin.

According to Vimala et al. [15], women who took 400mcg of sublingual misoprostol (819± 236 ml) during CS had considerably less blood loss than those who took 20 IU of oxytocin (974± 285 ml, p = 0.004) shortly after the baby delivery.

There were no significant differences in the two groups in terms of estimated blood loss during the surgery, unlike in Owonikoko et al. [16], where two groups were given either 400 mcg of misoprostol sublingually or 20 IU of oxytocin intravenously shortly after the baby was born. In the initial two hours following surgery, the misoprostol group saw considerably lower mean blood loss compared to the oxytocin group (58.2 ± 20.7 vs 80.5 ± 26.8 mL; P-value=0.02).

Also, there was a statistically significant difference between the two groups following CS (p=0,004), suggesting that intravenous oxytocin infusion was more successful in minimizing blood loss than a little dosage of intrauterine misoprostol (400 mcg) [17].

The studies did find a decrease in blood loss, albeit to varying degrees. Those studying the topic who omitted women at high risk The studies conducted by Fekih et al. [18], Elsedeek [19], and Sood & Singh [20] showed a significant decrease in intraoperative blood loss, with the exception of the one that included women at high and low risk. Furthermore, misoprostol was given sublingually following intubation or rectally during catheterization in two of the trials that demonstrated a more significant decrease in blood loss. Results from a comprehensive review Additionally, when blood loss exceeded 1000 mL, Conde-Agudelo et al. [21] found no statistically significant difference among the three trials. In a meta-analysis, Hofmeyr et al. [22] found no evidence that greater doses of misoprostol were more effective in avoiding hemorrhage more than 1,000 cc.

Postoperative hemoglobin and HCT levels dropped significantly in both groups, according to the current research; however, the group that received intravenous oxytocin alone saw a greater drop than the group that received intrauterine misoprostol. While the misoprostol intrauterine plus oxytocin group had a hemoglobin level of 10.69±0.59 before CS, the oxytocin group had a level of 10.7±0.77 after CS. In contrast, the misoprostol plus oxytocin group had a mean of 10.37±0. 65.

Consistent with Abdelaleem et al. [17], the current investigation found a statistically significant difference between the two groups. Vimala et al. [15] revealed that in regards to the hemoglobin readings before and after delivery, there was no distinction between the two groups. The misoprostol group had a mean hemoglobin drop of 0.4 gm/dl, while the oxytocin group had a mean reduction of 0.6 gm/dl.

Both groups' Hct values dropped significantly, as seen by the extremely significant p-value ($p \leq 0.05$) when comparing their Hct levels before and after the operation. The postoperative Hct value of the oxytocin group was 28.73±1.71 more than that of the misoprostol plus oxytocin intrauterine group, which was 29.58±2.3 ($p \leq 0.045$). In both the Owonikoko et al. [16] and Alalfy et al. [2] studies, the two groups' pre- and postoperative hematocrit levels were not significantly different.

The current study found a statistically significant difference ($P \leq 0.05$) in the side effects of the drugs between the two groups. Specifically, the group given intra venous

oxytocin plus intra uterine misoprostol had a higher rate of shivering (14.89% versus 6.38%), while the group given intra venous oxytocin alone had a higher rate of headaches and nausea (l 6.38 percent and 8.51 percent versus 4.26 percent and 4.26 percent respectively).

The occurrence of side effects with misoprostol was found to be dosage dependent, according to Hofmeyr et al. [22]. Therefore, it is important to determine the smallest effective and safe amount of the medicine. In 30–70% of cases, shivering and pyrexia were reported as side effects of misoprostol use [23].

Adverse events such pyrexia, shivering, and metallic taste were more common in the misoprostol group than in the oxytocin group, according to Vimala et al. [15]. The oxytocin group had a considerably lower incidence of adverse effects including shivering/pyrexia (1/50 vs 27/50, P < 0.001) compared to the misoprostol group in Owonikoko et al. [16].

Unfortunately, research on the effectiveness of intrauterine misoprostol in reducing postpartum hemorrhage and severe intraoperative blood loss following caesarean sections is limited.Spanish researchers Quiroga et al. [24] focused on determining the benefits and risks of intrauterine misoprostol for preventing obstetrical bleeding. This study evaluated the effectiveness of intrauterine misoprostol with a placebo. Ten international units (IU) of oxytocin were administered intravenously to both groups. Patients at high risk of postpartum haemorrhage were excluded from the trial, whereas full-term women at low risk for PPH who underwent elective caesarean sections were included. The two groups were compared with respect to the side effects, haemoglobin and hematocrit decrease, and the need for further uterotonics. The results demonstrated that the use of intrauterine misoprostol reduced the need for extra uterotonics by 50%, reduced hemoglobin loss by 39.6%, and decreased the fall in hematocrit value by 40.6%. One possible limitation of the study by Quiroga et al. [24] was that both groups were given 10 IU of oxytocin intravenously following cord clamping, which could have affected the amount of blood lost during the operation. Few side effects are associated with the intrauterine combination of misoprostol and oxytocin, according to Quiroga et al. [24], which reduces post-cesarean blood loss.

The present study results were in accordance with the results of Ibrahim [25], who aimed for evaluation of the efficacy of oxytocin alone in Group 1 that included 51 women who had elective cesarean section at Obstetrics and Gynecology Departments, of Zagazig University Hospitals and Benha Teaching Hospital, compared to combination of oxytocin added to the misoprostol in Group 2 that included also 51 cases for prevention excessive blood loss after caesarean section, he revealed that shivering, vomiting and headache were more common in Group 1 (13, 6, and 6 cases respectively) compared to Group 2 (0,5 and 9 cases respectively).

The limitation of the study includes that it was a hospital-based study, this study did not represent any particular community, had a small sample size compared to the number of cases, and was not multicentric, all of which increase the likelihood of publication bias. Further studies on combining the intrauterine misoprostol and IV oxytocin infusion during CS may give best effect in reducing blood loss during and after CS to combine the benefits of both drugs using intravenous oxytocin to achieve faster initial effect with misoprostol for sustained uterine contraction. These studies needed to done on high risk patients and patients during emergency C.S to approve it is efficacy.

CONCLUSION

Reduced intraoperative blood loss and prevention of main postpartum hemorrhage could be achieved by intrauterine misoprostol combined with oxytocin infusion during cesarean section.

CONFLICT OF INTEREST:None
FINANCIAL DISCLOSURE:None

REFERENCES

1. Morfaw F, Fundoh M, Pisoh C, Ayaba B, Mbuagbaw L, Anderson LN, et al. Misoprostol as an adjunct to oxytocin can reduce postpartum-haemorrhage: a

propensity score-matched retrospective chart review in Bamenda-Cameroon, 2015-2016. *BMC Pregnancy Childbirth*. 2019;19(1):257.
2. Alalfy M, Lasheen Y, Elshenoufy H, Elzahaby IM, Kaleem HW, El Sawah H,et al. The efficacy of intrauterine misoprostol during cesarean section in prevention of primary PPH, a randomized controlled trial. *J Matern Fetal Neonatal Med*. 2020;33(9):1459-65.
3. Royal College of Obstetricians and Gynecologists (RCOG). Prevention and Management of Postpartum Hemorrhage: Green-top Guideline No. 52. BJOG.;2016, 124: 106- 49.
4. Lisonkova S, Mehrabadi A, Allen VM, Bujold E, Crane JM, Gaudet L,et al. Atonic Postpartum Hemorrhage: Blood Loss, Risk Factors, and Third Stage Management. *J Obstet Gynaecol Can*. 2016;38(12):1081-90.
5. Rasri W: Intrauterine misoprostol plus intravenous oxytocin for reduction of blood loss in cesarean delivery. Thai J Obstetr Gynecol;2018, 26:237-45.
6. American College of Obstetricians and Gynecologists. ACOG practice bulletin: clinical management guidelines for obstetrician-gynecologists number 183. Postpartum hemorrhage. OBGYN,2017, 130:168-86.
7. Shady NW, Sallam HF, Elsayed AH, Abdelkader AM, Ali SS, Alanwar A,et al. The effect of prophylactic oral tranexamic acid plus buccal misoprostol on blood loss after vaginal delivery: a randomized controlled trial. *J Matern Fetal Neonatal Med*. 2019;32(11):1806-12.
8. Bahadur A, Khoiwal K, Bhattacharya N, Chaturvedi J, Kumari R. The effect of intrauterine misoprostol on blood loss during caesarean section. *J Obstet Gynaecol*. 2019;39(6):753-6.
9. Begley CM, Gyte GM, Devane D, McGuire W, Weeks A, Biesty LM. Active versus expectant management for women in the third stage of labour. Cochrane Database Syst Rev. 2019;2(2):CD007412.
10. Maged AM, Fawzi T, Shalaby MA, Samy A, Rabee MA, Ali AS, et al. A randomized controlled trial of the safety and efficacy of preoperative rectal misoprostol for prevention of intraoperative and postoperative blood loss at elective cesarean delivery [retracted in: Int J Gynaecol Obstet. 2023 Dec;163(3):1059]. *Int J Gynaecol Obstet*. 2019;147(1):102-7.
11. Ali Algadiem E, Aleisa AA, Alsubaie HI, Buhlaiqah NR, Algadeeb JB, Alsneini HA. Blood Loss Estimation Using Gauze Visual Analogue. *Trauma Mon*. 2016;21(2):e34131.
12. Shook PR, Schultz JR, Reynolds JD, Spahn TE, DeBalli P. Estimating blood loss for cesarean section: how accurate are we? Anesthesiology 2003;98(l):1.
13. The National Maternal Mortality Study Egypt. Ministry of Health and Population, Egypt.2013
14. Zhang J, Troendle J, Reddy UM, Laughon SK, Branch DW, Burkman R, et al. Contemporary cesarean delivery practice in the United States. Am J Obstet Gynecol. 2010;203(4):326.-6.
15. Vimala N, Mittal S, Kumar S. Sublingual misoprostol versus oxytocin infusion to reduce blood loss at cesarean section. Int J Gynaecol Obstet 2006; 92(2):106-10.
16. Owonikoko KM, Arowojolu AO, Okunlola MA. Effect of sublingual misoprostol versus intravenous oxytocin on reducing blood loss at cesarean section in Nigeria: a randomized controlled trial. *J Obstet Gynaecol Res*. 2011;37(7):715-21
17. Abdelaleem AA, Abdelaleem NA, Abbas AM. Intrauterine Misoprostol versus intravenous Oxytocin infusion during cesarean delivery to reduce intraoperative and postoperative blood loss: a randomised clinical trial. Int J Reprod Contracept Obstet Gynecol 2019;8:1662-7.
18. Fekih M, Jnifene A, Fathallah K, Ben Regaya L, Memmi A, Bouguizene S, et al. Intérêt du misoprostol dans la prévention de l'hémorragie du post-partum immédiat en cas de césarienne : essai prospectif randomisé [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.
19. Elsedeek MS. Impact of preoperative rectal misoprostol on blood loss during and after elective cesarean delivery. *Int J Gynaecol Obstet*. 2012;118(2):149-52.
20. Sood AK, Singh S. Sublingual misoprostol to reduce blood loss at cesarean delivery. *J Obstet Gynecol India*. 2012; 62(2): 162–7.
21. Conde-Agudelo A, Nieto A, Rosas-Bermudez A, Romero R. Misoprostol to reduce intraoperative and postoperative hemorrhage during cesarean delivery: a systematic review and metaanalysis. *Am J Obstet Gynecol*. 2013; 209(1): 1–17.
22. Hofmeyr GJ, Middleton K, Singata-Madliki M. Randomized feasibility study of suction-tube uterine tamponade for postpartum hemorrhage. *Int J Gynaecol Obstet*. 2019;146(3):339-43.
23. Kavle JA, Khalfan SS, Stoltzfus RJ, Witter F, Tielsch JM, Caulfield LE. Measurement of blood loss at childbirth and postpartum. *Int J Gynaecol Obstet*. 2006;95(1):24-8.
24. Quiroga Díaz R, Cantú Mata R, Tello Gutiérrez HE, Puente Villalobos M, Montemayor Garza R, Martínez Mendoza A. Misoprostol intrauterino para la prevención de la hemorragia postcesárea [Intrauterine misoprostol for the prevention of bleeding cesarean]. *Ginecol Obstet Mex*. 2009;77(10):469-74.
25. Ibrahim RAA. Combined Use of Misoprostol Plus Oxytocin versus Oxytocin Alone to Reduce Blood Loss during Cesarean Section. EJHM, 88(1), 3299-303.

Citation

Ibrahim, M., Atta, M., Omara, M. Intrauterine Misoprostol plus Oxytocin versus Oxytocin only in Prevention of Primary Postpartum Hemorrhage: Randomized Controlled Trial. Zagazig University Medical Journal, 2023; (1246-1256): -. doi: 10.21608/zumj.2023.254608.3044