Benefit of Misoprostol with oxytocin for prevention of postpartum hemorrhage in cesarean section

Hala Yahya AlShamalie, Saoura Ahmad Naiseh

Department of Obstetrics and Gyncology, Tishreen University, Faculty of Medicine,
Lattakia, Syria.

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Abstract:

Background: The commonest surgical procedure for women is cesarean delivery. Postpartum hemorrhage and intra-operative blood during cesarean delivery is a major concern to all obstetricians.

Aim: This study aims at comparing the efficacy of combined use of rectal misoprostol and oxytocin infusion with oxytocin in the prevention of PPH in cesarean delivery.

Materials and Methods: This was a prospective comparative observational study including 180 term pregnant woman scheduled for cesarean section at Tishreen University Hospital, Lattakia, Syria, between December 2020 and December 2021. Participants were divided into two equal groups. One group was treated with 20-IU oxytocin IV infusion alone while the other group was treated with Tab. Misoprostol 800mcg, rectal route plus 20-IU oxytocin IV infusion. The main outcome measure was postoperative blood loss.

Results: Both groups were comparable with regard to the age, parity, gravidity, and gestational age as well as hemoglobin and hematocrit levels. The combined use of rectal misoprostol plus oxytocin, compared with the use of oxytocin alone, was associated with a significant reduction in the mean blood loss (418 ± 150 ml vs. 649 ± 214 ml, respectively, P<0.0001), and a significant reduction in the mean decrease in hemoglobin and hematocrit. Moreover, the needs for a blood transfusion or extra uterotonics were significantly lower in the combination group than in oxytocin group (p<0.05). The use of rectal misoprostol combined with oxytocin was associated with a statistically significant increase in the rates of fever.

Keywords: Misoprostol, Oxytocin, Post-Partum Hemorrhage, Cesarean section, prevention

Introduction

The most common surgical procedure all over the world is Cesarean section and it was found as an independent and important risk factor for post-partum hemorrhage (PPH)(1). PPH is a major cause for mortality and morbidity in women (2).It is defined as any blood loss ≥ 1000 mL or accompanied with symptoms \signs of hypovolemia within 24 hours after birth regardless of delivery way (3). Its incidence is about 1 to 3 percent of births (4). The efficacy of giving oxytocin to reduce the frequency of postpartum hemorrhage is well known but it has many maternal side effects such as tachycardia and hypovolemia(5).

Misoprostol is a prostaglandin, E1 analogue that has strong uterotonic properties, was suggested as an alternative to oxytocin for preventing PPH following CD(cesarean delivery), but it has more side effects like fever and was found to cause more PPH(6). The use of misoprostol in addition to oxytocin hasn't received much interest, and because there aren't any syrian studies that evaluate this relation we decided to do thissearch.

Material and methods:

This study was designed to be prospective comparative observational study. We included 180 full term pregnant women

who undergone an elective CD(cesarean delivery) in the Department of Obstetrics and Gynecology in Tishreen University Hospital, Lattakia, Syria ,from December 2020 to December 2021. Women with known risk factors for PPH such as multiple gestation, polyhydramnios, fetal macrosomia, severe pre-eclampsia and eclampsia, two or more previous cesarean deliveries were excluded. Women with cardiovascular ,respiratory, hematological or renal disorders or with known hypersensitivity to prostaglandin or oxytocin, were also excluded. We obtained age, parity, medical and surgical history, hemoglobin before and after CD from all participants. Participants were divided into two equal groups. One group was treated with 20-IU oxytocin IV infusion alone while the other group was treated with Tab. Misoprostol 800mcg, rectal route plus 20-IU oxytocin IV infusion. We estimated mean blood loss and hemoglobin after CD and the need of additional uterotonics .In addition we observed incidence of side effects in the two groubs. We approved this study by institutional ethical approval committee and after obtaining verbal consent from all women subjected to the current study following full illustration of the purpose and methodology of current study. Data were then transferred into an SPSS (version 20) spread sheet for statistical analysis .Microsoft Office Excel 2010 was also used for this purpose. We expressed variables were as mean, standard deviation
,whereas, categorical variables were expressed by number and percentage .To evaluate association between categorical variables ,Chi-square and Fischer exact tests were used. Difference in mean between two groups was evaluated using independent sample t- test.

Results and discussion

There was no significant difference between the groups in terms of age,parity and average duration of surgery (Table 1).
The mean blood loss for the misoprostol with oxytocin group and oxytocin alone was 418±150 mL (mean+SD) and 649±214 mL (mean + SD) respectively.
There was significant less blood loss in misoprostol with oxcytocin group ($p<0.0001$). There was no significant difference between the two groups in the incidence of PPH (P=0.140) (table 2). There was no significant difference in the value of hemoglobin before CD between the two groups (11.6 ±0.89 vs 11.5 ± 1.2 g\dL [mean+SD] ,P=0.484). There was significant difference between the two groups in the value of hemoglobin after CD (11.15± 0.9 vs 10.3 ±1.2 g\dl [mean+SD] , P<0.0001). As for the postoperative drop of hemoglobin level we observed significant difference (0.45 ± 0.3 vs 1.2 ± 1.39 g\dL , p<0.0001) (table 3). We observed more need for additional uterotonics in group of oxytocin only compared to misoprostol with oxytocin (3.3% vs 11.1%, p=0.043). However, the incidence of fever was higher in the group of misoprostol (12.2% vs 3.45% , p=0.025) (table 4). These results confirm that combining misoprostol with oxytocin is better than using oxytocin only as it reduces blood loss and drop of hemoglobin after CD. In addition we observed a significant improvement in the hematological parameters with a better value of hemoglobin after birth. Many searches have studied combining misoprostol with oxytocin. A large study done by(Conde-Agudelo et al) included 3174 women showed that misoprostol reduces blood loss during and after CD (2) , which supports the findings in the current study. Another study in 2020 by (sure et al) (7), 200 women were devided into two groups : 100 patients were given 20 IU oxytocin IV alone after CD, and 100 patients were given 600 mcg, rectal route immediately after opening peritoneum plus 20 IU oxytocin IV. Intra and post-operative blood loss was significantly less when adding misoprostol (740 ±164 mL vs 790±185 mL
, p=0.04). there was no significant difference between in the incidence of PPH (1% vs 25 respectively),we agree with these results. In 2019, a systematic review and meta analysis were done by (Gallose et al) to evaluate uterotonic drugs for preventing PPH(8). The analysis included 137 randomized trials with 87466 women, they found that adding additional uterotonics to oxytocin is a better strategy for preventing PPH, with more side effects. These results support the results in this study. The reduction in caesarean section bleeding when misoprostol was combined with oxytocin may be explained by the initial rapid effect of oxytocin followed by the sustained effect of misoprostol on uterine contractility. Indeed, after a single intravenous injection, oxytocin appears in the circulation within 15 seconds, reaches its maximum concentration after 60 seconds and has a short half-life (4-10 minutes) (9). In contrast, the peak concentration after oral administration of misoprostol is about 40-65 minutes, with a duration of action of about 4 hours (10).

Conclusion:

Administration of misoprostol per rectal route plus oxytocin infusion after the cesarean section have shown, a better control of bleeding and maintenance of hemoglobin level when compared to oxytocin infusion alone. Thus, instead of oxytocin monotherapy combined use of misoprostol and oxytocin would be more effective in prevention of PPH.

*Variable	Misoprostol with oxytocin N=90	Oxytocin only N=90	P_value
Maternal age(year)	27.4 ± 4.1	28±4.5	0.351
Parity Nulliparous Multiparous	 35(38.9%) 55(61.1%)	 32(35.6%) 58(64.4%)	0.643
Duration of pregnancy(min)	38.5±6	40.1±5.9	0.072
*values are given as mean ± SD			

Table 1

*Variable	Misoprostol with oxytocin N=90	Oxytocin only N=90	P_value
Mean blood loss(mL)	418±150	649±214	<0.0001
Incidence of PPH(>1000mL)	2 (2.2%)	5(5.6%)	0.140
*values are given as mean ± SD			

Table 2

*Variable	Misoprostol with oxytocin N=90	Oxytocin only N=90	P_value
Hemoglobin before birth	11.6±0.89	11.5±1.02	0.484
Hemoglobin after birth	11.15±0.9	10.3±1.26	<0.0001
Drop of	0.45±0.3	1.2±1.39	<0.0001

hemoglobin			
*values are given as mean ± SD			

Table 3

Variable	Misoprostol with oxytocin N=90	Oxytocin only N=90	P_value
Need for additional uterotonics	3(3.3%)	10(11.1%)	0.043
fever	11(12.2%)	3(3.3%)	0.025

Table 4

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