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Original Research Article

Sublingual misoprostol to reduce blood loss at caesarean delivery

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ABSTRACT

Background: Caesarean section is the most common obstetrical procedure performed worldwide. Sometimes oxytocin alone is not sufficient to prevent postpartum haemorrhage and additional uterotonics may be required. We attempted an additional uterotonic misoprostol by sublingual route to evaluate the role of it to reduce blood loss at caesarean delivery.
Methods: This prospective clinical study was done on patients of S. S. G. Hospital, Baroda; 138 patients who underwent lower segment caesarean section (elective or emergency). The primary outcome was less intra/peri operative blood loss, need for additional uterotonic agents and perioperative haemoglobin (Hb) fall. The secondary outcomes studied were incidence of shivering, pyrexia, nausea, vomiting, operating time, blood transfusion, endomyometritis and hospitalization period. Average blood loss after normal vaginal delivery is 500 ml and after caesarean delivery is around 1000 ml.
Results: Mean postoperative Hb was high with misoprostol group and perioperative Hb fall was less. Perioperative Hb fall of 1 g or more was lesser in this group.
Conclusions: Sublingual misoprostol reduces intraoperative blood loss, perioperative blood loss and the need for additional uterotonic agents and blood transfusions at caesarean delivery.

Keywords: Lower segment caesarean section, Post-partum haemorrhage, Sublingual misoprostol

INTRODUCTION

Delivery by caesarean section is by far one of the most commonly performed obstetric operations all over the world. Nevertheless, it exposes women to the inherent risk of abdominal surgery; injury to the pelvic structures, infection and the need for blood transfusion. Obstetric blood loss is a major cause of maternal mortality. Caesarean section is specially associated with varying degree of blood loss.[1]

Postpartum haemorrhage is a leading cause of preventable maternal mortality all over the world. The average blood loss during a normal vaginal delivery is widely described as 500 ml; on the other hand, caesarean deliveries are associated with an average estimated blood loss of 1000 ml.[2] Atony is the main cause of postpartum hemorrhage (PPH) and is responsible for about 80% of PPH.[3] Therefore, uterotonics are administered.

Oxytocin is routinely used to prevent uterine atony and excessive uterine bleeding during caesarean delivery. However, despite its effectiveness, 10-40% of women need additional uterotonic therapy. Secondary uterotonic agents such as methyl ergometrine or 15-methyl prostaglandin F2 are associated with adverse effects when administered within a dose range likely to be effective.

Misoprostol is a prostaglandin E1 analogue with good uterotonic properties and few adverse effects as therapeutic dose. Because of its uterotonic properties, misoprostol has been evaluated for both the prevention and the treatment of PPH.[4] It is readily absorbed when given by oral, sublingual, buccal, vaginal or rectal route. Its easy availability, relatively low cost, thermo stability, long shelf life and ease of administration, all of which appear to make it particularly suitable for use in low resource settings in developing countries.

Despite routine use of oxytocin during caesarean section (CS), a number of women especially those at high risk may develop uterine atony and PPH intra or post operatively, with serious consequences. Any modality of treatment which helps in its prevention will be useful in reducing maternal morbidity and mortality. Misoprostol is an evidence-based alternative to other uterotonic agents.

Aims and objectives

Aims

Aim of the study was to assess the efficacy of sublingual misoprostol in decreasing intraoperative blood loss; and the need for additional uterotonic agents at caesarean delivery.

Objectives

Objectives of the study were to do prospective study to find difference in intraoperative blood and perioperative blood loss in two groups; and to know perioperative haemoglobin (Hb) fall in the two groups

METHODS

Study design

It was a prospective clinical study.

Study setting

The study was conducted at Baroda Medical College, SSGH affiliated to MS University.

Study population

Study was carried out on women at S. S. G. Hospital, Vadodara, department of obstetrics and gynaecology who met inclusion criteria mentioned below.

Study duration

The duration of the study was for one year.

Sampling and sample size

A total of 138 patients were included as sample size, 69 per group.

Inclusion criteria

Patients with lower segment caesarean section (elective and emergency) were included.

Exclusion criteria

Patients with abruptio placenta, placenta previa, severe pre-eclampsia, eclampsia, hypersensitivity to prostaglandin, temperature >38 ^{0}C, previous caesarean delivery or any other uterine surgery, non-reassuring fetal heart rate, polyhydramnios, and need for general anaesthesia were excluded.

Method for randomization

Closed envelope technique by residents present in the labor room.

Group 1

It would consist of women who received 400 mcg of misoprostol sublingually after giving spinal anaesthesia preoperatively.

Group 2

It consisted of women who didn't receive any drug.

Primary outcomes

It included: intraoperative blood loss; perioperative blood loss; need for additional uterotonic agents; and perioperative Hb fall.

Secondary outcomes

It included: shivering, pyrexia, nausea, vomiting; operating time; postpartum haemorrhage; blood transfusion; endomyometritis and hospitalization period.

Data collection

Participant data including demographic characteristics, medical and pregnancy history, labor course and outcomes were collected.

Data analysis

Selected baseline characteristics and quantitative variables were compared using the independent t test for continuous variables and χ^2 test with Fishers exact test for categorical variables. Significance level was fixed at 5%.

All data was entered into a Microsoft excel. Statistical analysis was performed using Medcalc version. 12 or other equivalent software. Unpaired t test, mean, standard deviation (SD), confidence interval was used to find out level of significance and p value.

RESULTS

For this one-year study period, a total of 138-69 in each group were recruited.

69 were randomly assigned to cases and 69 to control group. All women received allocated intervention,

completed follow up and were analyzed according to group assignment.

There was no significant difference between two groups with respect to age, parity, gestational age, maternal weight and preoperative Hb (Table 1).

Operating time was similar in both the groups (Table 2).

Mean intraoperative blood loss was significantly less in misoprostol group as compared to placebo. Proportion of women with blood loss between 500 and 1000 ml was lesser with cases compared to control. However, there was no difference in proportion of women with blood loss of 1000 ml or more (Table 3).

Fewer women in misoprostol group needed additional uterotonic agents. Fewer women in misoprostol group needed blood transfusions (Table 4).

$$VL = EBV \times ln\,(Hct1/Hct2)$$

$$EBV: Bodyweight \times 70\ ml/kg$$

$$EBV = Estimated\ blood\ volume$$

Shivering and pyrexia were significantly more with case group. PPH was more in control group but the difference was not significant. There was no significant difference in incidence of nausea and vomiting.

Similarly, there was no difference in hospitalization period. None of the patients had chorioamnionitis in the case group as well as control group (Table 6).

This table shows that in comparison to control group, in case group there are more side effects because of use of misoprostol.

Table 1: Comparison of both groups for age, parity, gestational age, maternal weight and preoperative Hb.

Parameters	Cases	Controls	P value
Maternal age (year)	24.8±4.4	24.6±4.4	Ns p=0.75
Parity	1.27±0.6	1.23±0.6	Ns p=0.696
Gestational age (week)	38.92±1.45	38.75±1.24	Ns p=0.46
Preop Hb (g/dl)	9.93±1.04	9.8±1.07	Ns p=0.47
Weight (kg)	51.2±5.5	52.2±6.4	Ns p=0.326

Table 2: Comparison of operative time between both groups.

Parameter	Cases	Controls	P
Operating time	50.4±6.9	52.6±7.5	Ns p=0.075

Table 3: Comparison of mean intraoperative blood loss between two groups.

Estimated intraoperative blood loss (ml)	Cases	Control	P value
Total	487±174	689±189.7	S p<0.0001
<500	41 (59.4)	10 (14.5)	S p<0.0001 Chi square value: 25.18
500-1000	26 (37.7)	56 (81)	
>1000	2 (2.9)	3 (4.3)	

Table 4: Comparison of additional uterotonic agents and blood transfusions between both groups.

Parameters	Cases	Controls	P
Additional uterotonic therapy	7 (10.1)	20 (29)	P=0.0098 highly significant
Blood transfusion	3 (4.3)	12 (17.4)	P=0.0278 significant

Table 5: Comparison of postoperative Hb and perioperative Hb fall.

Parameters	Cases	Controls	P
Postoperative hb (g/dl)	9.27±1.06	8.78±1.16	P=0.0106 s
Perioperative hb fall (g/dl)	0.6±0.26	1±0.41	P<0.0001 hs
1 g/dl or more	13 (18.8)	40 (58)	P<0.0001 hs
Perioperative blood loss volume (ml)	571.4±173	769±193	P<0.001 hs

Mean postoperative Hb was significantly higher in the cases; perioperative Hb fall was significantly less in misoprostol group; peri-operative Hb fall of 1 gm or more was lesser in cases; perioperative blood loss volume calculated by differential equation originally described by Bourke and Smith in 1975 was significantly less in the case group

Table 6: Comparison of perioperative morbidity between two groups.

Perioperative morbidity	Cases	Control	P (significance value at 95% CI)
PPH	1 (1.4)	7 (10.1)	Ns p=0.067
Chorioamnionitis	0	0	Na
Shivering	43 (62.3)	27 (39.1)	S p=0.0106
Pyrexia	40 (58)	24 (34.8)	S p=0.0104
Nausea	37 (53.6)	27 (39.1)	Ns p=0.124
Vomiting	31 (45)	30 (43.4)	Ns p=0.95
Hospitalization period (days)	9.0±2.8	9.0±2.43	Ns P=1.00
Any other complication	1 (full length wound gap)	1 (full length wound gap)	Ns p=0.392
Any other medications given	6 (8.6)	9 (13)	Ns p=0.58

DISCUSSION

Misoprostol is an evidence-based alternative to other uterotonic agents which require a cold chain, skilled administration and have untoward effects in therapeutically effective doses.

Zhao et al in their study comparing 600 mcg oral misoprostol with oxytocin (20 U intrauterine plus 20 U IV) found misoprostol more effective in the reduction of postpartum bleeding.[5] Acharya et al comparing the effectiveness of 400mcg oral misoprostol with 10 U IV syntocinon found misoprostol to be as effective as intravenous syntocinon in the reduction of intraoperative blood loss.[6] Lokugamage et al compared 500 mcg oral misoprostol with 10 U IV syntocinon and concluded that oral misoprostol could be used as an alternative oxytocic agent.[7] Hamm et al in a placebo controlled study concluded that 200 mcg buccal misoprostol reduced the need for additional uterotonic agents.[8] In another study comparing 400 mcg sublingual misoprostol versus 20 U oxytocin infusion, Vimala et al found sublingual misoprostol to be effective as oxytocin.[9] Bahadur et al evaluated intrauterine misoprostol with oxytocin and oxytocin alone on blood loss during caesarean section and concluded that intrauterine misoprostol leads to decrease in intra and post-operative blood loss with side effect of transient shivering.[10] Kumari et al evaluated impact of pre-operative 200 mcg per rectal misoprostol on blood loss during and after caesarean delivery which resulted in significantly lower intra and post-operative blood loss in the misoprostol group as compared to placebo group.[11] Difference between pre and post-operative haematocrit values was also significantly lower in the study group compared to control group. Ahmed et al compared preoperative and postoperative per rectal misoprostol after elective cesarean section and concluded that preoperative per rectal misoprostol is linked with less blood loss as compared to postoperative per rectal misoprostol.[12] Ugwu et al did a randomized controlled trial for sublingual misoprostol to decrease blood loss after cesarean section and concluded that misoprostol plus oxytocin is superior to oxytocin alone.[13] Maged did 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 and result was that misoprostol minimized intraoperative blood loss.[14]

In a placebo-controlled double blind study, comparing 800 mcg oral misoprostol with 20 U oxytocin infusion after initial administration of 5 U of IV oxytocin, Lapaire et al found misoprostol to be as effective as oxytocin in reducing postoperative blood loss.[15]

The mean intraoperative blood loss in the present study was significantly less in misoprostol group, which is similar to that reported in two studies.[5,9] However, some studies have reported no difference.[6,8,15]

Mean intraoperative blood loss was significantly less in misoprostol group as compared to placebo (487±174 versus 689±189 ml). Proportion of women with blood loss between 500 and 1000 ml was lesser with cases compared to control (37.7% versus 81.0%).

Blood loss at caesarean is difficult to assess accurately. So in this study, perioperative change in Hb between preoperative and the second postoperative day was also done to assess the blood loss indirectly. We also found out the perioperative blood loss by the Bourke and Smith formula which was also significantly high in control group.[16]

The need for additional uterotonic agents was significantly less in the present study; this finding is similar to that reported in a similar study in which oxytocin infusion was given to all women.[8] Significant trend toward lesser perioperative Hb fall, which was found in this study, is similar to that reported in a recent study, in which concomitant oxytocin infusion was given to all women, as in the present study. In study reporting no difference, misoprostol was either compared with oxytocin, or a lower dose of misoprostol was used.[6,8,9,15,17]

Caesarean delivery is carried out in a setting where conventional oxytocics are available and active management of third stage of labor is invariably practiced. Misoprostol may have a role as an adjunct to oxytocin in prevention of postpartum hemorrhage in high-risk women,

where other uterotonic agents are either contraindicated or not available. In the present study, 400 mcg by sublingual route appears to be promising.

CONCLUSION

Sublingual misoprostol reduces intraoperative blood loss, perioperative blood loss and the need for additional uterotonic agents and blood transfusions at caesarean delivery. It may have a role as an adjunct to oxytocin in the prevention of postpartum hemorrhage in high-risk women, where other uterotonic agents are either contraindicated or not available.

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REFERENCES

1. Ashraf AH, Ramadani HM. Assessment of Blood Loss During Cesarean Section Under General Anesthesia and Epidural Analgesia Using Different Methods. AJAIC. 2006;9(1):25-34.
2. Siwatch S, Kalra J, Bagga R, Jain V. Sublingual vs Vaginal Misoprostol for Labor Induction. J Postgrad Med Edu Res. 2012;46(3):138-43.
3. Hayman RG, Arulkumaran S, Steer PJ. Uterine compression sutures: surgical management of postpartum hemorrhage. Obstet Gynecol. 2002;99(3):502-6.
4. Goldberg AB, Greenberg MB, Darney PD. Misoprostol and pregnancy. N Engl J Med. 2001;344(1):38-47.
5. Zhao Y, Li X, Peng Y. Clinical study on reduction of postpartum bleeding in cesarean section by misoprostol. Zhonghua Fu Chan Ke Za Zhi. 1998;33(7):403-5.
6. Acharya G, Al-Sammarai MT, Patel N, Al-Habib A, Kiserud T. A randomized, controlled trial comparing effect of oral misoprostol and intravenous syntocinon on intra-operative blood loss during cesarean section. Acta Obstet Gynecol Scand. 2001;80(3):245-50.
7. Lokugamage AU, Sullivan KR, Niculescu I, Tigere P, Onyangunga F, El Refaey H, Moodley J, Rodeck CH. A randomized study comparing rectally administered misoprostol versus Syntometrine combined with an oxytocin infusion for the cessation of primary postpartum haemorrhage. Acta Obstet Gynecol Scand. 2001;80(9):835-9.
8. Hamm J, Russell Z, Botha T, Carlan SJ, Richichi K. Buccal misoprostol to prevent hemorrhage at cesarean delivery: a randomized study. Am J Obstet Gynecol. 2005;192(5):1404-6.
9. 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.
10. 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.
11. Kumari KA, Swathi E, Saranu S. Impact of pre-operative 200 mcg (P/R0 per rectal misoprostol on blood loss during and after Cesarean delivery. IAIM. 2016;3(6):49-58.
12. Abd-Ellah AH, Tamam AAE, Khodry MM. Is the Time of administration of misoprostol of value? The uterotonic effect of misoprostol given pre- and post-operative after elective cesarean section. Middle East Fertility Soc J. 2014;19(1):8-12.
13. Ugwu IA, Enabor OO, Adeyemi AB, Lawal OO, Oladokun A, Olayemi O. Sublingual misoprostol to decrease blood loss after caesarean delivery: a randomised controlled trial. J Obstet Gynaecol. 2014;34(5):407-11.
14. Maged AM, Fawzi T, Shalaby MA, Samy A, Rabee MA, Ali AS, Hussein EA, Hammad B, Deeb WS. 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. Int J Gynaecol Obstet. 2019;147(1):102-7.
15. Lapaire O, Schneider MC, Stotz M, Surbek DV, Holzgreve W, Hoesli IM. Oral misoprostol vs. intravenous oxytocin in reducing blood loss after emergency cesarean delivery. Int J Gynaecol Obstet. 2006;95(1):2-7.
16. Bourke DL, Smith TC. Estimating allowable hemodilution. Anesthesiology. 1974;41(6):609-12.
17. Fekih M, Jnifene A, Fathallah K, Ben Regaya L, Memmi A, Bouguizene S, Chaieb A, Bibi M, Khairi H. 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.

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