ROLE OF 400 MCG INTRAOPERATIVE SUBLINGUAL MISOPROSTOL FOR REDUCTION OF CAESAREAN BLOOD LOSS

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ABSTRACT

BACKGROUND

Lower segment caesarean section is a common surgical procedure. Postpartum haemorrhage incidence after LSCS is 4%. Misoprostol is a prostaglandin E1 analogue with good uterotonic properties, easy availability, low cost, thermostability, long shelf life, easy administration and few adverse effects at therapeutic dose. It is readily absorbed by oral, sublingual, buccal, vaginal or rectal route. Sublingual route attains quickest concentration. Dose of 400 mcg was chosen in this study to minimise adverse effects with optimal therapeutic benefit.

The aim of the study is to determine the efficacy of sublingual misoprostol in reducing caesarean blood loss.

MATERIALS AND METHODS

It is a prospective experimental study done in VSSIMSAR, Burla. Women undergoing LSCS were randomly assigned to study and control groups of equal strength of 100 each. In all cases, preoperative Hb%, haematocrit, pulse, BP was noted. Study group were given 400 mcg misoprostol at the time of cord clamping. In control group, nothing was given. In all patients, active management of third stage of labour was done by using oxytocin 10 IU (IV) along with uterine massage. Blood loss soaked by tetra was calculated using formula, blood loss = wet weight-dry weight/1.05 (1.05 is constant). Amount of blood loss, postoperative Hb%, haematocrit, pulse rate, BP was noted in both groups and compared. BP and pulse were noted after 1 hour and Hb%, haematocrit were noted after 24 hours.

RESULTS

Study group showed significant decrease in total blood loss (around 117.9 mL) as compared to control group. There was significant decrease in the postoperative fall in Hb in the study group as compared to control, the mean difference being 0.631 gm%. Study group also showed decrease in postoperative fall in haematocrit as compared to control, the mean difference being 0.055.

CONCLUSION

Misoprostol significantly reduced caesarean blood loss and doesn't affect foetal outcome without significant adverse effect.

KEYWORDS

Sublingual, Misoprostol, Intraoperative, Caesarean.

HOW TO CITE THIS ARTICLE: Nayak L, Pradhan K, Mishra S. Role of 400 mcg intraoperative sublingual misoprostol for reduction of caesarean blood loss. J. Evid. Based Med. Healthc. 2017; 4(10), 573-577. DOI: 10.18410/jebmh/2017/112

BACKGROUND

Caesarean delivery is the most common major surgical procedure performed in women worldwide. The rates of caesarean section in industrialised countries and developing countries from 1996 to 2006, about 46% has increased.[1] Some developing countries such as Chile, Brazil, Korea, China, Iran, Pakistan, Turkey and India have rates of caesarean section of 25-40%.[2] Delivery caused by caesarean section can cause more complications than normal vaginal delivery and one of the most common complications is primary or secondary haemorrhage (20%).[3] Postpartum haemorrhage remains a leading cause of early maternal death accounting for about 3,00,000 deaths worldwide every year and of morbidity related to anaemia, blood transfusion and haemorrhage-related ischaemic complications.[4,5] Rates of postpartum haemorrhage is more after caesarean section (4% v/s 0.6%) than vaginal delivery.[6] Among these, 6% need blood transfusion[7,8] and 11% suffer from postpartum anaemia.[9] According to WHO recommendations for PPH prevention (2012) oxytocin 10 IU (intravenous) is recommended uterotonic drug of choice. The efficacy of

Financial or Other, Competing Interest: None.
Submission 24-01-2017, Peer Review 27-01-2017,
Acceptance 31-01-2017, Published 02-02-2017.
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DOI: 10.18410/jebmh/2017/112

routine administration of oxytocin to reduce the frequency of postpartum haemorrhage after vaginal delivery is well established. It has been assumed that benefits of injectable uterotonic agents observed for vaginal birth also apply to caesarean deliveries, yet not rigorously demonstrated. Oxytocin use in the setting of caesarean delivery may result in maternal adverse effects such as hypotension and tachycardia. Despite its effectiveness, 10%-40% women need additional uterotonic therapy.[10,11] Secondary uterotonic agents such as methylergometrine or 15-methyl prostaglandin $F_2\alpha$ are associated with adverse effects when administered within a dose range likely to be effective.

These drugs also need parenteral administration. Oxytocin and methylergometrine also need refrigeration between 2° to 8°C to maintain potency. Prostaglandin $F_2\alpha$ causes gastrointestinal side effects, bronchospasm and also has high cost, which restrains its use in developing countries like India.

Misoprostol is a prostaglandin E1 analogue with good uterotonic properties and few adverse effects at therapeutic dose. It has been evaluated for both the prevention and treatment of PPH.[12] Its easy availability, relatively low cost, thermostability, 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. It is readily absorbed when given by oral, sublingual, buccal, vaginal or rectal route. A study by Tang et al showed that sublingual route of administration of misoprostol attains quickest concentration compared to other routes of administration. Most studies have found misoprostol as effective[10,13,14,15,16] and in one case more effective than oxytocin.[17]

Zhao et al[17] in their study comparing 600 µg oral misoprostol with oxytocin (20 U intrauterine plus 20 U IV) found misoprostol more effective in the reduction of postpartum bleeding. Acharya et al[10] comparing the effectiveness of 400 µg oral misoprostol with 10 U IV syntocinon found misoprostol to be as effective as intravenous syntocinon in the reduction of intraoperative blood loss. Lokugamage et al[13] compared 500 µg oral misoprostol with 10 U IV syntocinon and concluded that oral misoprostol could be used as an alternative oxytocic agent. Hamm et al[14] in a placebo-controlled study concluded that 200 µg buccal misoprostol reduced the need for additional uterotonic agents.

In another study, comparing 400 µg sublingual misoprostol versus 20 U oxytocin infusion, Vimala et al[15] found sublingual misoprostol to be as effective as oxytocin. In a placebo-controlled double-blind study comparing 800 µg oral misoprostol with 20 U oxytocin infusion after initial administration of 5 U of IV oxytocin, Lapaire et al[16] found misoprostol to be as effective as oxytocin in reducing postoperative blood loss.

Dose of misoprostol in various studies has ranged from 200 to 800 µg.[10,17,13,14,15,16] As the side effects are dose related, a dose of 400 µg was chosen in the present study to minimise maternal adverse effects with optimal therapeutic benefit. In a recent review, 400 µg of misoprostol was found to be safer than 600 µg and just as effective.[18]

So, this study was undertaken to determine the efficacy of 400 µg sublingual misoprostol in reducing caesarean blood loss.

MATERIALS AND METHODS

This prospective experimental study was done in VSSIMSAR, Burla. Term primigravida or multigravida with singleton pregnancy having normal or abnormal presentations delivered by caesarean section were included in the study. Patients having severe medical and surgical complications including the heart, liver, kidney, brain disease and blood disorders, any contraindication to misoprostol including mitral stenosis, glaucoma and diastolic blood pressure over 100 mmHg and known allergic to prostaglandins were excluded from the study. Patients having history of thromboembolic disorders, abnormal placentation such as placenta praevia, placental abruption and placental adhesions caused by repeated artificial abortions, pregnancy complications such as severe pre-eclampsia, multiple pregnancies, macrosomia and polyhydramnios. Complication with myoma and with any blood dyscrasia were also excluded from the study.

Informed consent was taken from all the patients. They were randomly assigned to study and control groups of equal strength of 100 each. In all cases, preoperative Hb%, haematocrit, pulse and BP was noted. Study group were given 400 µg misoprostol at the time of cord clamping. In control group, nothing was given. In all patients, active management of third stage of labour was done by using oxytocin 10 IU (IV) along with uterine massage.

The quantity of blood (mL) = (weight of (used material + unused material) after surgery-weight of all materials prior to surgery)/1.05 plus the volume included in the suction container after placental delivery. In addition, pads used after completion of caesarean section to 2 hours postpartum weighed.

Amount of blood loss, postoperative Hb%, haematocrit, pulse rate, BP was noted in both groups and compared. BP and pulse were noted after 1 hour and 2 hours and Hb%, haematocrit were noted after 24 hours.

Statistics

Numerical data like age, haemoglobin, amount of blood loss, haematocrit, vitals like BP, pulse, respiratory rate, e.t.c. were presented as mean scores and Student's t-test was used to compare the means between two groups (case and control). Entire data was calculated on 95% CI. A p value <0.05 was considered significant.

RESULTS

A total of 200 patients were included in the study. Study group received 400 µg sublingual misoprostol at the time of cord clamping. Control group patients who did not receive misoprostol after delivery of the neonate at the time of cord clamping, oxytocin 10 units in a pint of IV fluid is given by IV route over 30 minutes and 400 micrograms of misoprostol

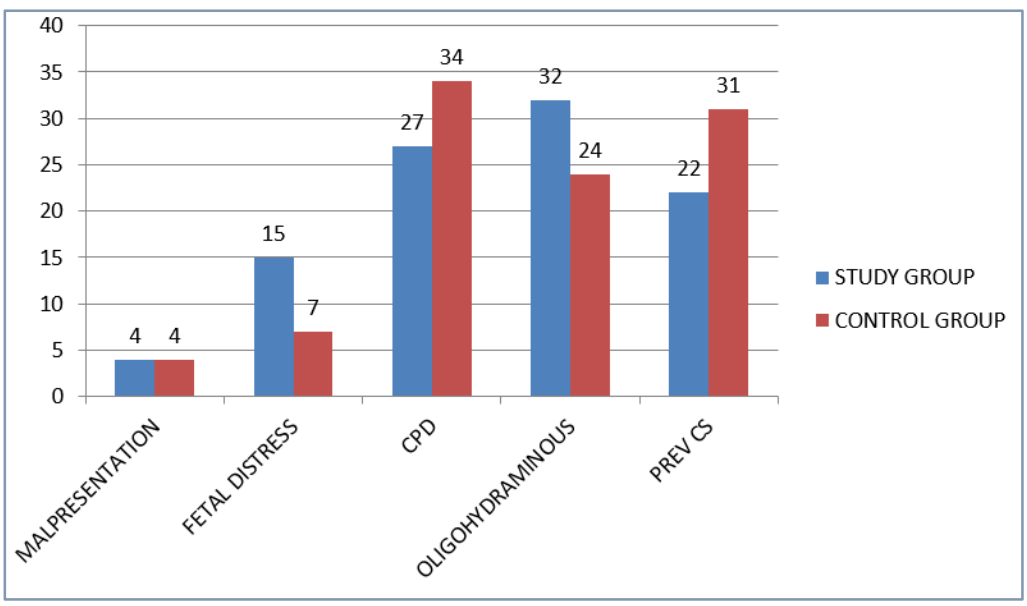
given sublingually in the study group. In the control group, no misoprostol was given. Oxytocin was administered as in the study group.

The possible confounding factors like age, BMI, gravida and gestational age were matched effectively in both the groups.

Parameters	Cases Mean	Control Mean	P Value
Age	24.3	24.9	0.778, NS
BMI	24.43	24.48	0.116, NS
Gravida	1.56	1.62	0.200, NS
Gestational age	39.29	39.32	0.552, NS

Table 1. Distribution of Patients According to Age, BMI, Gravida and Gestational Age

Both the groups were matched effectively in terms of indication of caesarean section.



Distribution of Patients According to Indication of Caesarean Section

The mean baby weight in study group was 2.875 kg and 2.928 kg in the control group (P value-0.238) suggesting that it was not statistical significant. The mean duration of caesarean section in study group was 42.15 mins. and 40.25 mins. in the control group (P value-0.387) suggesting that it was not statistical significant.

The mean blood loss from placental delivery to 2 hours postpartum was 363.40 mL in the study group and it was 481.30 mL in the control group (p<0.001) suggesting that there was statistically highly significant decrease in the blood loss in study group when compared to control. Patients who received 400 µg sublingual misoprostol had 117.9 mL less mean blood loss than patients who didn't receive sublingual misoprostol.

Total Blood Loss (in mL)	Cases		Controls		Mean Difference	P Value, Sig.
	Mean	SD	Mean	SD		
	363.4	77.73589	481.3	116.59872	117.9	<0.001,HS

***Table 2. Effect of* 400 µg Intraoperative Sublingual Misoprostol- Total Blood Loss in Both the Groups**

Difference in Hb% in the cases was 1.079%, difference in Hb in control was 1.71% with a mean difference is 0.631 gm%, which is highly significant, P value <0.001.

HB%	Cases		Controls		Mean Difference	P Value, Sig.
	Mean	SD	Mean	SD		
Before delivery	10.71	0.86305	11.039	0.98564	0.329	0.061, NS
After delivery	9.63	0.92260	9.32	1.01039	0.31	0.026, Sig.
Difference	1.079	0.36301	1.71	0.43462	0.631	<0.001, Sig.

***Table 3. Effect of* 400 µg Intraoperative Sublingual Misoprostol- Difference in Haemoglobin in Both the Groups**

There was decrease in postoperative fall in haematocrit in study group as compared to control. The mean difference being 0.055, but this was not found to be statistically significant (p value=0.145). There was no statistically significant difference in the vital signs (heart rate, respiratory rate, systolic and diastolic blood pressure) at the time of placental delivery, 1 hour postoperatively and 2 hours postoperatively in both the groups. 23 patients in control group required blood transfusion compared to which only 9 patients in the study group required the same. The result was found to be significant, p=0.007. Four cases in the study group required oxytocics as compared to seven in the control group. The difference was found to be statistically not significant.

DISCUSSION

In the present study, most of the patients (54.5%) were of the age group between 18-24 years with mean age of 24.3 years in study group and 24.9 years in control, which indicates that most of them were of middle age group and the difference between both the groups was not significant (P value = 0.778). Majority of the patients, 53.5% had a BMI between 18.5-24.9 kg/m^2, which was within normal range and the difference was found to be insignificant between both the groups (P value = 0.116). 54.5% of patients were primigravida and the difference was found to be insignificant (P value = 0.200). Majority of the patients (76%) were in the gestational age between 37-40 weeks. The mean gestational age was comparable in both the groups and the difference was not significant (P value = 0.552). So, the possible confounding factors like age, BMI, gravida were matched effectively in both the groups.

58.5% of the patients underwent caesarean section due to CPD and oligohydramnios. Indication of caesarean section can affect the amount of intraoperative blood loss, but the fact that they were matched adequately in both the groups removes the effect of these confounding factor and the difference was not statistically significant (P value = 0.270). Baby weight can affect the amount of blood loss. The mean baby weight in study group was 2.875 kg and 2.928 kg in the control group (P value-0.238) suggesting that it was not statistical significant. Both groups were comparable in terms of baby weight. Operating time can affect the amount of blood loss, but it was not a confounding factor in the present study. The mean duration was comparable in both the groups and the difference was not statistically significant (P value = 0.387).

When both the groups were compared according to the amount of blood loss from placental delivery to the end of caesarean section, an increase in the percentage of patients in control group (89%) had a blood loss of 300-500 mL as compared to 62% of patients in the study group. The present study showed that 400 µg sublingual misoprostol significantly reduces bleeding from time of placental delivery to 2 hours postpartum in caesarean section. Result showed that study group had mean blood loss of 363.40 mL ± 77.735 as standard deviation, while control group patients had a mean loss of 481.30 mL ± 116.598 as standard deviation. Thus, there is a reduction in total blood loss by about 25% and was found to be highly statistically significant (p value=<0.001). There was reduction in blood loss in both the parameters, i.e. from placental delivery to completion of skin closure (about 21% decrease) and from completion of skin closure to 2 hours postpartum (42% decrease) and both data were highly significant. When the blood loss from end of caesarean section to 2 hrs. postpartum was compared, 57% of the patients in the study group had blood loss of <50 mL as compared to 95% of the patients in the control group who had a blood loss of between 50-100 mL range. When the total blood loss was compared in both the groups, 86% of the patients in the study group had a blood loss between 300-400 mL as compared to 83% of the patients in the control group who had a blood loss of >400-500 mL.

400 µg sublingual misoprostol also reduced the incidence of postpartum bleeding (patients with blood loss ≥500 mL, but less than 1000 mL) in the study group as compared to control group. In present study, two cases in the study group had ≥500 mL total blood loss as compared to 9 cases in the control group and the data was found to be significant (P value = 0.03). The mean difference in fall of Hb% postoperatively between the case and control was found to be 0.631 gm%, which was highly significant (P value = <0.001), so there was relatively more fall in Hb in control as compared to case. When the difference in haematocrit was compared postoperatively in both the groups, it was seen that there was more decrease in haematocrit in the control group as compared to case with a mean difference of 0.055, but the result was insignificant (P value = 0.145). The difference in vitals pre and postoperatively (1 and 2 hrs.) when compared in both the groups was found to be insignificant in our study. The requirement of blood transfusion was seen to be significantly reduced in cases as compared to control (P value = 0.007). Additional oxytocics was required in four patients in the study group as compared to seven patients in the control group, but the difference was not significant (P value = 0.352).

Similar studies carried out by Vimala et al (2004), who conducted a randomised trial with 400 µg sublingual misoprostol with methylergometrine in active management of third stage of labour.[19] Sublingual misoprostol was found to be equally effective as intravenous ergometrine in preventing PPH. In another study comparing 400 µg sublingual misoprostol versus 20 U oxytocin infusion, Vimala et al[15] found sublingual misoprostol to be as effective as oxytocin. In a recent review conducted by Hofmeyr et al (2009), 400 µg of sublingual misoprostol was found to be safer than 600 µg and just as effective.[18] In a randomised-controlled trial by Vaid et al (2009) comparing the effectiveness of sublingual misoprostol 400 µg with methylergometrine 200 µg and PGF2α, sublingual misoprostol was equally effective.[20] A K Sood and Sanjay Singh (2012) in a prospective randomised-controlled study found out that 400 µg sublingual misoprostol reduces intraoperative blood loss in caesarean sections and the need for additional uterotonics at caesarean delivery.[21]

CONCLUSION

400 µg sublingual intraoperative misoprostol significantly reduced caesarean blood loss. Outcome of labour is always unpredictable, but there should be no attempt left to make it pleasant, comfortable and desirable as well. In this present study, trial of 400 µg of misoprostol sublingually for reduction of caesarean blood loss is an attempt to make the labour process comfortable and pleasant for the parturient and desirable for the healthcare providers.

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