Original Article

Postpartum Haemorrhage

A Randomized Controlled Trial on Prevention of Postpartum Haemorrhage with Sublingual Misoprostol or Oxytocin

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ABSTRACT

Introduction: Failure of the uterus to contract adequately after child birth (a tonicity) is the most common cause of postpartum hemorrhage and misoprostol produces a rapid peak concentration, and is more effective than oral administration.

Objective: We compared the postpartum blood loss with 400µg sublingual misoprostol and after standard care using 10 iu intramuscular oxytocin.

Study Design: Randomized controlled trial.

Place and Duration of Study: This study was conducted in a Department of Obstetrics and Gynecology Ghulam Muhammad Mahar Medical College Teaching Hospital Khairpur Sindh during 2011.

Materials and Methods: 60 women for each group were assigned to receive the study medications with in 1 minute of clamping and cutting the cord. Chi-square and studentt-test were used to test categorical and continuous outcomes. Mean postpartum blood loss and PPH (>500ml), >10% pre- to postpartum decline in hemoglobin and reported side effects.

Results: The mean estimated blood loss with sublingual misoprostol was 200± 125ml (n=60) and 360±136ml with oxytocin (n=60) P-value ≤ 0.001.The incidence of PPH was 3.3% with misoprostol and 6.6% with oxytocin group. No women lost >1000 ml of blood. Hemoglobin decline of > 10% observed that 11.6% and 45.0% in women after receiving misoprostol and oxytocin (P≤ 0.001). Side effects were significantly greater in the misoprostol group than in the oxytocin group.

Conclusion: In this trial we found sublingual misoprostol more effective than intramuscular oxytocinin reducing PPH, with only transient side effects.

Key Words: Hemoglobin, misoprostol, oxytocin, Postpartum hemorrhage, sublingual.

INTRODUCTION

Postpartum hemorrhage (PPH), defined as a blood loss of > 500 ml after delivery, is the most common complication of the 3rd stage of labor and is the leading cause of maternal death in Africa and Asia.[1]

Although most women experiencing a blood loss of 500ml do not require additional treatment,[2]PPH can also exacerbate anemia and its consequences.[3]

The usefulness of misoprostol a synthetic prostaglandin E1 analog marketed for the prevention and/or treatment of peptic ulcer, also used in the active management of third stage of labor (AMTSL) in developing countries was first reported by EL-Rafaey.[4] Because of its uterotonic effects, misoprostol has been demonstrated to be effective for both the prevention and treatment of PPH.[5] With its ease of administration and storage, there has been increasing evaluation and promotion of misoprostol in developing countries.[6]

Compared with other routes of administration, sublingual and oral misoprostol have the shortest time to reach peak concentration (20 minutes), which is approximately one-third of the time of the vaginal route. Sublingual misoprostol also has the highest peak concentration and greatest bioavailability, 400µg administered sublingually approaches nearly twice the peak concentration of oral administration.[7] The avoidance of first-pass metabolism via the liver achieves a higher peak concentration by sublingual administration than by oral administration. Sublingual misoprostol more suitable than other routes of administration for clinical applications requiring a rapid onset of action, such as that required for the prevention of PPH.[8]

Oxytocin, long considered the gold standard of uterotonics, remains an efficient uterotonic , with a slightly more rapid onset of action, but has a shorter half-life than misoprostol.[9]

A study was conducted in India showed women receiving 600 and 400µg sublingual misoprostol had lower mean blood loss (96 and 26ml) than those receiving oxytocin (126ml).[10]

Our study's aim was to compare the effectiveness of a relatively low dose, 400µg of sublingual misoprostol with the standard care of 10 iu I/M oxytocin on measured postpartum blood loss.

MATERIALS AND METHODS

Women with a singleton pregnancy at >37 weeks of gestation, with cephalic presentation, anticipating a

normal spontaneous vaginal delivery and with hemoglobin > 10 g/dl at the time of presentation, who were admitted to the labor room of Obstetric Department of Ghulam Muhammad Mahar Medical College Teaching Hospital Khairpur Sindh during year of 2011 were included in the study.

Women with postdates pregnancy, medical disorders, instrumental deliveries, multiple gestation and still births were excluded from the study.

Subjectswere assigned to treatment with 1:1 ratio using simple randomization.

During one year of study period 120 women was included in the study. Sixty women for each group. One group received 2 tablets (400µg) misoprostol sublingual and other group received 10 iu I/M oxytocin within 1 minute of clamping and cutting the cord. Clinicians continued to monitor the patients.

As part of the standard of care, controlled card traction and uterine massage were provided to both groups.

Visual assessment of blood loss was measured for 2 hours after delivery, women's vital sign and side effects (nausea, vomiting, diarrhea, abdominal pain and fever) were monitored for 6 hours after delivery. A blood sample for hemoglobin and hematocrit estimation was obtained between 12 and 48 hours after delivery.

The primary outcomes are mean blood loss and postpartum hemorrhage. Secondary outcomes include side effects and > 10% postpartum decline in hemoglobin, which is directly associated with blood loss.

SPSS version 15 was used for data analysis. Student t-test and Chi-square test were used for analysis of the study results.

RESULTS

A total of 120 women were eligible during the study period. Of these, 60 were randomly assigned to the misoprostol group and 60 were randomly for the oxytocin group.

The characteristics of the study subjects and the birth weights of the newborns were comparable (Table: 1). On average all women were aged <25 years and delivered between 38-39 weeks of gestation.

Women receiving oxytocin were slightly younger (22± 3.0 years old) and more had first pregnancy (53.3%) compared with womenreceiving misoprostol (23±3.2 years old and 55% were parity more than one). Un booked women were equally more in both groups of study population. More women in the misoprostol group received antenatal iron supplementation (41.6%) compared with those receiving oxytocin (33.3%), P=0.06. The average birth weight of newborn in both groups was nearly identical (Table: 1).

Regarding complications and blood loss in third stage of labor, estimated mean blood loss was 200±125 ml in women receiving misoprostol compared with 360ml ±136 ml in women receiving 10 iu intramuscular oxytocin (P=<0.001) shown in (Table: 2). Only 2(3.33%) of women experienced PPH in misoprostol group, compared with 5(8.33%) in women who receiving oxytocin (P=0.002). There was no blood loss of >1000ml or maternal death occurred in both study groups (Table: 2).

Table No.1: Characteristics of study population

variable	Misoprostol N=60 %	Oxytocin N=60 %
-Age	23±3.2	22±3.0
-Parity -Nuliparous -Multiparous<5	 27 45% 33 55%	 32 53.3% 28 46.6%
-Gestation at delivery	38.6 weeks	38.5 weeks
-Received antenatal care	20 33.3%	18 30%
-Un booked women	40 66.6%	42 70%
-Received antenatal iron	25 41.6%	20 33.3%
-Duration of Ist stage labor	9-10 hours	8-9 hours
-Duration of 2nd stage labor	20-45 minutes	35-50 minutes
-Episiotomy	32 53.3%	30 50.0%
-Birth weight (g)	2.6-2.9 kg	2.8-3.1 kg

Table No. 2 Blood loss, Hb changes and side effects

Variables	Misoprostol N:60	Oxytocin N:60	P-value
Mean blood loss (ml)	200±125ml	360±136ml	< 0.001
PPH	2(3.33%)	5(8.33%)	<0.002
Hb decline >10%	7(11.6%)	27(45%)	<0.001
Duration of 3rd stage	10-22 minutes	10-25 minutes	<0.05
Nausea	4(6.66%)	-	-
Vomiting	3(5.0%)	1(1.6%)	<0.02
Shivering	32(53.3%)	3(5.0%)	<0.001
Fever (>38◦c)	2(3.33%)	-	-
Additional uterotonic	1(1.6%)	3(5.0%)	<0.02
Blood transfusion	1(1.6%)	1(1.6%)	<0.98
Maternal death	-	-	-

Women receiving misoprostol and oxytocin had a similar duration of third stage of labor.

More than 10% decline of postpartum hemoglobin in women receiving misoprostol and oxytocin, 11.6% and 45% respectively.

Minor type of side effects like nausea, vomiting and fever was more seen in misoprostol group as compared to oxytocin group. Shivering was more seen in misoprostol group 32(53.3%) as compared to 3(5.6%) in oxytocin receiving women. In more cases additional utero-tonic required in oxytocin group 3(5.0%) as

compared to 1(1.6%) in misoprostol group. One woman in each group required a blood transfusion.

DISCUSSION

The WHO recommends oxytocin as the preferred treatment for managing PPH due to uterine atony but oxytocin has a slower onset of action,[11]or in situation where skilled health worker are not able to provide AMTSL,WHO recommends either oxytocin or misoprostol for prevention of PPH.[12]

In 2011, the WHO added misoprostol (600µg) orally to its Model list of essential Medicines for the prevention of PPH.

This study found 400µg sublingual misoprostol, with more rapid bioavailability than oral misoprostol, to be significantly superior to 10 iu intramuscular oxytocin in reducing mean postpartum blood loss. The Cochrane review found virtually no difference in mean blood loss in its comparisons of sublingual misoprostol and injectable uterotonics.[13]

Women receiving oxytocin required additional uterotonics than sublingual misoprostol for PPH treatment in our study, consistent with Vimalaet al.[14]

The incidence of PPH in this study is higher in those receiving oxytocin I/M (8.33%) where as those receiving sublingual misoprostol had a PPH rate (3.33%), it is correlate with study of Vimalaet al.[14]

Consistent with studies comparing 600µg oral misoprostol or 400µg sublingual misoprostol with injectable oxytocin, the incidence of side effects in women receiving 600µg oral misoprostol or 400µg sublingual misoprostol is similar and may be attributable to the group and sustained bioavailability of sublingual misoprostol.[13,14] In those studies, more women receiving misoprostol experienced side effects, although, as in this study, transient shivering has often been the side effects with substantially greater incidence than that associated with oxytocin 32(53.3%), 3(5.6%) women who experienced shivering and other side effects in misoprostol group cure with simple supportive measures, all side effects, including fever, were short lived and required no medical interventions.

CONCLUSION

The transient and self-resolving nature of the side effects associated with misoprostol and the effectiveness and ease of the administration of sublingual misoprostol particularly useful in buzzy and low resource setting labor room.

This trial found sublingual misoprostol more effective than intramuscular oxytocin in reducing PPH, with only minorand transient side effects.

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