Rectal Misoprostol versus Intramuscular Oxytocin for Prevention of Post Partum Hemorrhage

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ABSTRACT

Background

Postpartum hemorrhage (PPH) is an important cause of maternal morbidity and mortality especially in the developing countries. Compared to expectant management, active management decreases the incidence of PPH.

Objective

To compare the effectiveness of rectal misoprostol with intramuscular oxytocin in the prevention of postpartum hemorrhage.

Methods

This is a prospective, randomized and analytical study from 1st September 2009 to 28th February 2010 at Department of Obstetrics and Gynecology, Dhulkhel Hospital - Kathmandu University Hospital, Dhulikhel, Nepal. A total of 200 women were included to receive either 1000 micrograms rectal misoprostol tablets or 10 units of oxytocin intramuscularly. Primary outcome measures were the incidence of postpartum hemorrhage or a change in hematocrit or hemoglobin from admission to day two post delivery. Secondary outcome measures including severe postpartum hemorrhage and the duration of the third stage of labor were noted. Also the side effects of both misoprostol and oxytocin were recorded.

Results

The frequency of postpartum hemorrhage was 4% in the misoprostol subjects and 6% in the control subjects (P=0.886) There were no significant difference among the groups in the drop of hematocrit (P>0.05). Secondary outcome measures including severe postpartum hemorrhage and the duration of the third stage of labor were similar in both groups. Similarly, the side effects between the misoprostol and oxytocin group within 6 hours was statistically significant (p=0.003) whereas the side effects within 24hours was statistically not significant (p=0.106).

Conclusion

Rectal misoprostol is as effective as intravenous oxytocin in preventing postpartum hemorrhage with the similar incidence of side effects and is worthwhile to be used as a uterotonic agent for the routine management of third stage of labor.

KEY WORDS

misoprostol, oxytocin, postpartum hemorrhage

INTRODUCTION

Postpartum hemorrhage (PPH) is an important cause of maternal morbidity and mortality especially in the developing countries.[1] Postpartum hemorrhage, the loss of more than 500ml of blood after delivery occurs in upto 18% of births.[2] The primary cause of PPH is uterine atony which accounts for 70% of cases leading to severe postnal anaemia and hemorrhagic shock requiring transfusions and surgical interventions.[3,4]

The best preventive strategy is the active management of third stage of labor which involves administering an uterotonic drug soon after delivery of the anterior shoulder, controlled cord traction and fundal massage.[5] Compared to expectant management, active management decreases the incidence of PPH by 68%.[5]

Most of the uterotonics require parental administration and maintenance of cold chain which is necessary for their potency, which is not always possible in some peripheral centres due to non availability of sterile needles, syringes

or refrigerating equipment.[5] Misoprostol a prostaglandin E1 analogue first introduced as an anti inflammatory drug for peptic ulcer disease. Later on it gained popularity as an effective modality for cervical ripening.[4] It is also an active uterotonic agent and allows the uterus to contract within few minutes.[6,7,8] It is stable at room temperature, inexpensive and rapidly absorbed into the circulation after rectal administration.

The purpose of the study was to compare the efficacy and safety of rectal misoprostol with intramuscular oxytocin in prevention of postpartum hemorrhage.

METHODS

This is a randomized, prospective and analytical study from 1st September 2009 to 28th February 2010 at Department of Obstetrics and Gynecology, Dhulikhel Hospital - Kathmandu University Hospital. A total of 200 women having singleton pregnancy and low-risk vaginal deliveries were included in the study.

Women with chorioamnionitis, preterm labor, polyhydramnios, and lower segment cesarean section in previous pregnancy were excluded from the study. All condition which were a contraindication to the use of prostaglandin and uterotonics like asthma, heart disease or hypersensitivity reaction were also excluded from the study.

Written consent was taken from the woman at the admission to the labor room and purpose of the study was explained. The women were randomly allocated as per the lottery technique to receive either intramuscular (IM) oxytocin 10 units or 1000mcg of tablet misoprostol rectally at the delivery of anterior shoulder. Randomization was carried out when vaginal delivery was imminent.

Hemoglobin was measured at the time of admission. At the time of delivery of anterior shoulder, either IM oxytocin or rectal misoprostol was administered depending on the lottery. Placenta was delivered by controlled cord traction. Preweighed sterile drapes were used and blood collected in calibrated bucket. Preweighed pads were given to the patient for next 48 hours. All the soaked drapes and pads were weighed in the weighing scale which was then substracted from the initial weight of dry drapes and pads. A hundred gram increase in weight was considered to be equivalent to 100ml of blood loss (assuming specific gravity of blood equivalent to 1gm/ml).[9] The woman was encouraged to breast feed the baby. Strict record of her vital signs was maintained and uterine contractility was noted every thirty minutes for first four hours. Any heavy bleeding was noted for next 48 hours. Hemoglobin values were carried out after 24 hours of delivery. In our study, difference in pre and post delivery hemoglobin was estimated to calculate the blood loss. Side effects of uterotonics i.e. fever, shivering and abdominal pain were noted.

Primary outcome measures were the incidence of postpartum haemorrhage and drop in Hb. Secondary outcome measures were the length of third stage of labor and severe post partum haemorrhage. Also, the safety of the drugs was assessed by adverse side effects.

The data were analysed by using SPSS version 15.0 for frequency and cross tabulation. Chi-square test was applied to compare the nominal and ordinal variables with Yates correction wherever necessary. Paired sample test was used to compare the differences between the count variables at 5 % level of significance.

RESULTS

The total number of patients enrolled during the study period was 200. Out of the study population 100 (50%) received rectal misoprostol and 100(50%) received IM oxytocin for the active management of third stage of labor. None of the women withdrew from the study. The comparison of demographic characteristics like age, gestational period and parity in both groups were similar as shown in table 1. The comparison of estimated blood loss between misoprostol and oxytocin was statistically significant (p=0.012, table 2). The severe PPH was 4% in misoprostol group whereas it was 6% in oxytocin group. Similarly, the mean pad changes on first day was statistically significant (p=0.001) whereas mean pad changes on day two between two groups was statistically not significant (p=0.16) as shown in table2. As shown in table 3, the pre and post delivery hemoglobin within misoprostol and oxytocin groups were statistically significant (p<0.001), whereas the pre-delivery and also the post-delivery hemoglobin between misoprostol and oxytocin was statistically not significant (p=0.222).

The table 4 showed that the fever with shivering was most frequent in misoprostol group within six hours and within 24 hours as compared to oxytocin group.(25% versus 10%, and 16% versus 4%). The side effects between the misoprostol and oxytocin group within six hours was statistically significant (p=0.003) whereas the side effects within 24 hours was statistically not significant (p=0.106).

The table 5 showed that the mean duration of labor (1st stage, 2nd stage and 3rd stage) between the misoprostol and oxytocin was statistically not significant.

DISCUSSION

The active management of the third stage of labor is traditionally performed with the routine use of intravenous oxytocin.[9] To substitute for oxytocin and to prevent postpartum haemorrhage misoprostol was chosen because it has similar advantages but with minimal side effects, low shelf life, inexpensive and easily available. It is easy to use and does not require special storage conditions (i.e., can be stored easily at room temperature; is thermostable and light stable; does not require specific conditions for

transfer) and has a shelf life of several years.[6,7] These advantages make it a useful drug in reducing the incidence of postpartum hemorrhage in developing countries.[8]

The misoprostal was administered rectally because the gastrointestinal side effects of nausea, vomiting, and diarrhea can be avoided, useable in nauseated women and easy to use.

Our study showed that there was incidence of PPH (blood loss > 500 ml) only in 4% in misoprostol group whereas it was 6% in oxytocin group. However the average blood loss, drop in haemoglobin concentration levels in both study groups were not statistically significant. This is similar to the findings in previous studies.[10-17]

The average duration of the third stage of labor was 5.7 minutes and 5.6 minutes for the misoprostol and oxytocin group, respectively. This was also not statistically significant (p = 0.824). The findings are comparable with those of several other studies comparing misoprostol with oxytocin.[18-26]

Table 1. Demographic characteristics.

Variables	Misoprostol (n=100) mean±SD	Oxytocin (n=100) mean±SD	p-value
Age (years)	22.8±4.18	23.05±3.52	0.692
Gestational weeks	38.6±1.82	38.7±2.5	0.668
Parity	1.55 ±0.96	1.56±0.83	0.936
Primigravida (n, %)	63 (63%)	62 (62%)	0.688
Multigravida (n, %)	37 (37%)	38 (38%)	

Table 2. Estimation of blood loss and mean pad changes in two days.

Variables	Misoprostol (n=100) mean±SD	Oxytocin (n=100) mean±SD	p-value
Blood loss	156.7±124.2	132.3±91.8	0.012
<500 ml (%)	96 (96%)	94 (94%)	0.886
>500 ml (%)	4 (4%)	6(6%)	
Pad for 1st day	3.1±1.1	4.0±2.1	0.001
Pad for 2nd day	2.1±1.0	2.3±1.2	0.164

Table 3. Comparison of pre and post delivery hemoglobin level.

Variables	Misoprostol (n=100) mean±SD	Oxytocin (n=100) mean±SD	p-value
Pre-delivery Hb level gm/dl	11.7±1.5	11.5±1.6	0.120
Post-delivery Hb level gm/dl	10.7±1.5	10.6±1.4	0.222
p-value	<0.001	<0.001	-

Table 4. Side effects within 6 and 24 hours.

Side effects	Misoprostol No (%)	Oxytocin No. (%)	p-value (with Yates correction)
Side effects within 6 hours			
no side effects	73(73%)	87(87%)	0.003
fever with shivering	25(25%)	10 (10%)	
pain abdomen	2(2%)	3(3%)	
Side effects within 24 hours			
no side effects	77(77%)	89(89%)	0.106
fever with shivering	16(16%)	4(4%)	
pain abdomen	7(7%)	7(7%)	
Total	100 (100%)	100 (100%)	

Table 5. Mean duration of labor.

Mean duration of labor (in min.)	Misoprostol (n=100) mean±SD	Oxytocin (n=100) mean±SD	p-value
First stage	543.4±294.7	534.3±299.1	0.835
Second stage	24.8±22.1	27.2±24.9	0.459
Third stage	5.7±3.2	5.6±1.9	0.824

Recent studies has shown that rectal misoprostol is useful in the treatment of third stage of labor and may be effective in the treatment of postpartum haemorrhage. A recent study performed in South Africa compared a combination of intramuscular syntometrine injection and oxytocin infusion to rectal misoprostol and found that those who received misoprostol had a statistically significant reduction in bleeding and further medical cointerventions to control the bleeding (6% versus 34%) (RR, 0.18; 95% CI, 0.04-0.67) There was no record of maternal mortality or serious maternal morbidity. However, there was insufficient evidence for reliable conclusions about the possible effect on the need for surgical co-interventions (excluding hysterectomy). The use of misoprostol was noted to be superior to syntometrine/oxytocin in subjective cessation of haemorrhage within 20 minutes (64 women; RR 0.18,

95% 0.04 to 0.76) and significant reduction in the number of women who required additional uterotonics (one trial, 64 women; RR 0.18, 95% CI 0.04 to 0.76).[27] This is similar to our study as shown by mean pad changes within 1st day between misoprostol and oxytocin group which is statistically significant .

Similarly, study performed by Karkanis et al. among 240 women who randomly received 400 micrograms rectal misoprostol after delivery of the infant or parenteral oxytocin (5 units intravenously or 10 units intramuscularly) with the delivery of the anterior shoulder.[28] No difference in Hb was observed between the groups and also the duration of the third stage of labor did not differ between the two groups like that of our study.

Bamigboye et al. in his search for an effective, easily stored, affordable uterotonic agent to prevent postpartum haemorrhage, underwent a trial where he randomised 491 women to receive either 400 micrograms rectal misoprostol (241 women) or one ampule of syntometrin (250 women).[24] His results showed that the incidence of postpartum haemorrhge, duration of third stage of labor and the drop in Hb were similar like in our study. Rectal misoprostol in one tablet was used by Shoja et al. to stop severe delivery induced haemorrhage on uterine atony after failure of syntocinon.[29] In all the five patients studied, haemorrhage ceased in less than five minutes with no immediate side effects observed. This finding suggests that rectal misoprostol might be used for the control of severe postpartum haemorrhage, which failed to cease by the ordinary uterotonic agents.

In our study, an analysis of the side effects of the misoprostol and oxytocin revealed that fever with shivering was most frequent in misoprostol group (41%) as compared to oxytocin group (14%). However we noticed that abdomen pain was noted in both misoprostol as well as oxytocin group. This is in tandem with the results of other studies.[5,23,30] However, these undesirable side effects of misoprostol were found to be self-limiting, and shivering could be contained by simply covering the patient with blankets. Both fever and shivering with misoprostol are due to the prostaglandin E effect on central thermoregulatory centres and Lumbiganon et al have reported that although these symptoms may be of limited clinical concern. They can make one suspicious of infection or malaria, leading to unnecessary investigations and antibiotic or anti-malaria treatment.[30]

The frequency of fever with shivering was also found to be higher in our study incontrast with other studies using this dose of misoprostol.[30,31]

The side effects of rectal to oral misoprostol used for prevention of postpartum hemorrhage, Khan et al. has shown that the relative risk of shivering in the rectal group was 73% that of oral group (95% CL 61%, 86%).[32]

Our study along with the available literature on rectally administered misoprostol illustrate that rectal misoprostol seems to be effective in reducing the likelihood of postpartum haemorrhage after vaginal delivery at a dose of 1000 micrograms. Our study showed that there was not much difference in the rate of drop of hemoglobin in the misoprostol group as compared to oxytocin group. We also did not find much difference in the use of preweighed pads in both the groups. There was not much difference between the duration of different phases of labor in both the groups.

Taking into consideration that our country is a developing country and many centres do not have facilities for proper storage of oxytocin. As for its efficacy oxytocin needs to be stored at a temperature of two to eight degree Celcius, but many of our centres do not have refrigeration facilities. Hence misoprostol seems to be a better option for our low resource settings. Misoprostol is cheaper compared to oxytocin and its administration is much easier and no special training is needed to administer it. Again it does not require intramuscular administration like oxytocin and also the results are comparable to those of oxytocin use with an acceptable safety profile.

CONCLUSION

Misoprostol is an efficacious and safe alternative to conventional uterotonic agents like oxytocin in active management of third stage of labor especially in developing countries at community level and at the peripheral centres. It is as effective in prevention of postpartum hemorrhage as conventional uterotonic like oxytocin, with the same incidence of side effects. So, it is worthy to use rectal misoprostol as an alternative to oxytocin.

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