



**PREVENTION OF POST PARTUM HAEMORRHAGE BY RECTAL
MISOPROSTOL. A RANDOMISED CONTROLLED TRIAL**

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Abstract

Objective: To assess the effectiveness of rectally used misoprostol in the prevention of postpartum hemorrhage compared with oxytocin.

Materials and Methods: 402 women underwent analysis and were randomized to receive either two 200 micrograms rectal misoprostol tablets (study group) or 20 units oxytocin in 50 cc normal saline intravenously (control group). Primary outcome measures were the incidence of postpartum hemorrhage or a change in hematocrit or hemoglobin from admission to day one post delivery.

Results: The incidence of postpartum hemorrhage was 7% in the study subjects and 6% in the control subjects ($P>0.05$). 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 labour were similar in both groups.

Conclusion: Rectal misoprostol is as effective as intravenous oxytocin in preventing postpartum hemorrhage with the same incidence of side effects and is recommended to be used as a uterotonic agent for the routine management of third stage of labour.

Introduction

Postpartum hemorrhage complicates 4-6% of vaginal deliveries and is regarded as a major cause of maternal mortality and morbidity, causing deaths in 25-43% of pregnant women or 20 million deaths each year worldwide. (1-3)

This calls us to consider measures and interventions to minimize postpartum hemorrhage. Active treatment of the third stage of labour which includes early cord clamping, controlled cord traction for placental delivery and intravenous oxytocin therapy is an effective measure to prevent postpartum hemorrhage. In our hospital the active management of third stage of labour is practiced routinely.(4,5)

Recently, oral misoprostol has been used to prevent postpartum hemorrhage. (6-10) It has many advantages over oxytocin because it is inexpensive (\$1.3 for each 200 microgram tablet), heat stable at room temperature and does not require parenteral administration.

More recent studies reviewed the use of rectal misoprostol for the prevention of postpartum hemorrhage, but available data about the pharmacokinetics of rectal misoprostol and its use in preventing postpartum hemorrhage are still controversial.

We underwent this study to test the effects of rectal misoprostol in preventing postpartum hemorrhage compared to oxytocin and to add to the other measures that help to decrease the incidence of postpartum hemorrhage.

Materials And Methods

This study was undergone from February 1, 2002, to February 2003 at Prince Rashid Bin Al Hassan Hospital where the incidence of postpartum hemorrhage was ~7%, causing ~20% of maternal deaths.

Women included in the study were in active labour or undergoing induction of labour when vaginal delivery was anticipated. During randomisation, 450 women were divided into two groups: (1) the study group: 198 women, were given two 200 micrograms misoprostol tablets plus 500 cc intravenous normal saline and, (2) the control group: 204 women, were given two 330 mg lactose rectally as placebo plus 20 units oxytocin in 500 cc normal saline.

48 women were excluded from the study because they had gestational age of <34 weeks or caesarean delivery or were hypersensitive to prostaglandins or had anaemia at the start of the study.

Information included in the study was: maternal age, parity, episiotomy, perineal tear and birth weight. Expected side effects as nausea, vomiting, diarrhoea, hot flushes, headache, shivering, and hyperthermia were assessed. Blood loss was assessed either by weighing blood collected in bed pan and that collected from the gauze and pads or by obtaining the difference between Hb and hematocrit values between admission and day one post delivery or estimated by the person attending the delivery.

Primary outcome measures were the incidence of postpartum haemorrhage and drop in Hb or hematocrit. Secondary outcome measures were the length of third stage of labour and severe post partum haemorrhage. Post partum haemorrhage was defined as blood loss

in excess of 500 cc or 10% drop in Hb or hematocrit from admission to day one post delivery.

Results

450 women were randomised, 218 to the misoprostol group and 232 to the oxytocin group. 48 women were excluded from the study due to either caesarean section or hypersensitivity to prostaglandins or had initial haemoglobin <8mg %. After exclusion, 198 women received the study medication and 204 women received the control medication.

Table 1 describes the demographic characteristics of subjects while Table 2 describes the intrapartum characteristics.

Table 1 Demographic Characteristics

Characteristic	Misoprostol group n= 198	Oxytol in group n= 204	p
Maternal age *(y)	23.5+/-4.3	23+/-4.9	0.280
Parity Primipara* Multyara*	93(47%) 105(53%)	98(48%) 106(52%)	0.830
Gestational age# (d)	277+/-28.7	272+/-31.2	0.059
Predelivery tib level# (g/dl)	11.1+/-2.3	11.2+/-2.7	0.344
Predelivery hematocrit #(%)	35+/-3.5	35.2+/-3.4	0.281
Anteparam blood transfusion*	2(1%)	3(1%)	0.173

Data are presented as mean + SD, unless otherwise indicated

*Not statistically significant deference among groups (p > 0.05) X2 (chi- square test)

#Not statistically significant deference among groups (p > 0.05) t-test (student test)

Table 2 Intrapartum Characteristics

Characteristic	Misoprostol group n= 218	Oxytol in group n= 232	p
Admitted in spontaneous Labour*	131(60%)	151(65%)	0.274
Required induction*	87(40%)	81(35%)	0.460
Route of delivery*			
Vaginal	196(90%)	207(89%)	0.812
cls	22(10.1%)	252(11%)	
Episiotomy#	11.1+/-1.3	11.2+/-2.6	0.301

Data are presented as mean + SD, unless otherwise indicated
 *Not statistically significant deference among groups (p > 0.05) X2 (chi- square test)
 #Not statistically significant deference among groups (p > 0.05) t-test (student test)

There were no significant differences between the groups with respect to their demographic or intrapartum characteristics. The outcome measures of the trial treatment are described in Table 3.

Of the 402 women, 7% of the study subjects and 6% of the control subjects had postpartum haemorrhage (P=0.628). A comparison of the drop in Hb and hematocrit indicated that 1.4% of the study group and 1.3% of the control subjects had 10% drop in Hb from admission to day one postpartum (P=0.675).

Table 3 Outcome measures among the two groups

Variable	Misoprostol group n= 198	Oxytol in group n= 204	p
Postpartum Haemorrhage (= 500)*	14(7%)	12 (6%)	0.628
Drop in Hematocrit Level (%)#	4.6%+/- 4.2	4.5%+/-4.1	0.675
Drop in Haemoglobin level (%)#	1.4+/-1.3	1.3+/-1.2	0.674

Data are presented as mean + SD, unless otherwise indicated
 *Not statistically significant deference among groups (p > 0.05) X2 (chi- square test)
 #Not statistically significant deference among groups (p > 0.05) t-test (student test)

A 10% drop in hematicrit was observed from admission to day one postpartum occurred in 4.6% of the study subjects and in of 4.5% of the control subjects (p=0.674).

There were no significant differences in the number of women who required additional oxytocin to control bleeding after delivery. The length of the third stage of labour was similar in both groups 10 and 8 minutes respectively.

Regarding the side effects, shivering was observed with equal frequencies in both groups ~10%. Other side effects as nausea, vomiting and diarrhoea were the same in both groups. Similar neonatal outcomes (birth weight and Apgar score) were observed in both groups.

Discussion

In developing countries postpartum haemorrhage is regarded as one of the major causes of maternal mortality and morbidity. Consequently, the active management of the third stage of labour should be practiced along with the routine use of intravenous oxytocin. 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.

The rectal route has been chosen because of the ease of administration, and can avoid the gastrointestinal side effects of nausea, vomiting, and diarrhoea, so it can be given to a nauseated women. The results of our study met the our expectations where the blood loss did not exceed the incidence in our hospital ~7% where we use the routine method of active management of third stage of labour along with oxytocin intravenously.

Recent studies has shown that rectal misoprostol is useful in the treatment of third stage of labour and may be effective in the treatment of postpartum haemorrhage (11-13) Karkanis et al. studied 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. No difference in Hb was observed between the groups. The duration of the third stage of labour did not differ between the two groups.(13)

In a trial done by Bugalh et al., 663 women with uncomplicated vaginal delivery were randomised to receive 400 micrograms rectal misoprostol or oxytocin 10 IU IM after delivery of the infant. No significant differences were observed between groups, before and 72 hours after delivery. He concluded that rectal misoprostol appears to be effective as parenteral oxytocin in preventing postpartum haemorrhage.(10) Bamigboye et al. (12) 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). His results showed that he incidence of postpartum hemorrhage, duration of third stage of labour and the drop in Hb were similar.

Rectal misoprostol in one tablet was used by Shoja et al. (13) to stop severe delivery induced haemorrhage on uterine atony after failure of syntocinon. In all the five patients

studied haemorrhage ceased in less than 5 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.

No difference in shivering between rectally administered misoprostol and oxytocin was observed in our trial, findings that are consistent with other studies.

In comparing the side effects of rectal to oral misoprostol used for prevention of postpartum hemorrhage, Khan et al. (14) has shown that the relative risk of shivering in the rectal group was 73% that of oral group (95% CI 61%, 86%). Our study along with the available literature on rectally administered misoprostol illustrates that rectal misoprostol seems to be effective in reducing the likelihood of postpartum haemorrhage after vaginal delivery at a dose of 400 micrograms.

Conclusion

Rectal misoprostol seems to be safe and effective in preventing postpartum haemorrhage and is recommended for use in managing the third stage of labour.

References

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