RESEARCH ARTICLE

A comparative study on rectal misoprostol versus intramuscular oxytocin to prevent postpartum haemorrhage

Bijoy Kumar Dutta, Komal Rani Gupta

Correspondence: Dr. Bijoy Kumar Dutta, Assistant Professor, Department of Obstetrics and Gynaecology, FAAMC, Barpeta. Pin-781301

ABSTRACT

Objective: To see the efficacy of rectal misoprostol in comparison to intramuscular oxytocin in prevention of postpartum haemorrhage in low risk patient. **Methodology:** A prospective, double-blind study carried out for a period of 1 year. 400 cases had been taken for the study, which were divided randomly into two groups containing 200 cases each. ie. Group A (600 µgm misoprostol rectally given immediately following delivery of baby) and Group B (10 IU of oxytocin given intramuscularly immediately after delivery). The personal information and medical data of the selected cases were collected in structured proforma. Statistical analysis was done using SPSS version 15.0. **Results:** The mean third stage blood loss was 185±84.42 ml and 168±68.38ml in misoprostol group and oxytocin group respectively with significant difference ($p<0.05$). Mean change in Hb% (gm/dl) pre and post delivery was 0.89±0.32SD (gm/dl) in misoprostol group and 0.83±0.28SD (gm/dl) in oxytocin group ($p>0.05$). Incidence of PPH was 3% and 2% in group A and group B respectively ($p>0.05$). Shivering, pyrexia was found more in misoprostol group than oxytocin with the incidence being 20.5% versus 2% (shivering) and 8.5% versus 0.5% (pyrexia) respectively. **Conclusion:** It is observed that the misoprostol 600µg rectally is less effective than intramuscular oxytocin 10 IU when used as prophylactic uterotonic during the active management of third stage of labour.

Keywords: Rectal misoprostol, intravenous oxytocin, third stage of labour, postpartum haemorrhage.

Postpartum haemorrhage (PPH) is the most common cause of maternal death worldwide. Most cases of morbidity and mortality due to PPH are in the first 24 hours following delivery and these are regarded as primary PPH whereas any abnormal or excessive bleeding from the birth canal occurring between 24 hours and 12 weeks postnatally is regarded as secondary PPH [1, 2]. Although medical advances have dramatically reduced the dangers of childbirth, death from haemorrhage still remains a leading cause of maternal mortality in both developed and developing countries. Uterine atony or diminished myometrial contractility, accounts for 80% of PPH. Certain factors are associated with developing PPH, such as prolonged third stage of labour; pregnancy induced hypertension; previous PPH; twins or previous multiple pregnancies;

Received: 20th September 2015; **Accepted**: 22nd October 2015.

Dutta BK, Gupta KR. A comparative study on rectal misoprostol versus intramuscular oxytocin to prevent postpartum haemorrhage. The New Indian Journal of OBGYN. 2016; 2(2): 98-103

early detachment of placenta from the uterus; soft tissue laceration; instrumental delivery; infection and obesity [3]. However, most of cases of PPH take place in women with no known risk factors. That is why all women must have access to prevention during pregnancy and to emergency treatment at the time of delivery for severe blood loss.

There are several different types of uterotonic drugs (oxytocin, ergometrine, prostaglandins) that play a critical role in both prevention and treatment of PPH. The relative advantages and disadvantages of these different drugs and potential side effects have been an important topic of research for prevention and treatment of PPH. For centuries, the uterotonic agent of choice has been oxytocin with or without supplemental ergot preparations. Both oxytocin and ergometrine are unstable at room temperature and thus require special temperature and light storage conditions to remain effective. These storage requirements are a major hurdle to the widespread use of oxytocin in the developing countries.

Misoprostol is a prostaglandin E_1 (PGE_1) analogous which stimulates pregnant uterus through prostanoid EP2 and EP3 receptors [4]. It is an active uterotonic agent and allows the uterus to contract within few minutes. It is stable at room temperature, inexpensive and rapidly absorbed into the circulation after administration. In addition it can be administered by various routes eg. orally, sublingually, vaginally or rectally. For this reason, misoprostol has attracted considerable attention as an alternative to oxytocin for prevention of PPH in resource poor settings [5, 6, 7]. The present study was carried out with objectives to see the efficacy of rectal misoprostol in comparison to intramuscular oxytocin in prevention of postpartum haemorrhage in low risk patient.

Methodology

This was a prospective, double-blind study carried out in the department of 'Obstetrics and Gynaecology' of 'Gauhati Medical College and Hospital' for a period of 1 year from 1st June, 2012 to 31st May, 2013. The definition of postpartum haemorrhage for the present study was any amount of bleeding after delivery of baby that makes the patient symptomatic (eg. Light headness, vertigo, syncope) and/or results in signs of hypovolemia (eg. Hypotension, tachycardia, or oliguria) and quantitatively blood loss more than 500 ml in vaginal delivery. Women who were admitted into the labour room (booked or unbooked) had been taken for the study with the following inclusion criteria:

1. Patients who could give the proper history of time of onset of regular pain and general, systemic and pelvic examination demonstrated a term, live, singleton pregnancy with cephalic presentation and with an effaced cervix with 4cm or more dilation.

2. Patients belonging to age group in the range of 18-36 years and up to third gravida with history of regular menstrual cycle.

Exclusion criteria:

1. Caesarean section or instrumental delivery,
2. Haemoglobin less than 8 gm%,
3. History of antepartum haemorrhage,
4. Severe pregnancy induced hypertension,
5. Pre-eclampsia or eclampsia,
6. Prolonged labour or precipitate labour,
7. Foetal weight >3.5kg,
8. Polyhydramnios, and
9. Medical disorders (cardiovascular disease, diabetes mellitus, thyroid disorders and other coagulation abnormality etc.).

Informed written consent was obtained from the patient after proper counselling on admission to the labour room. The personal information and medical data of the selected cases were collected in structured proforma.

A total number of 400 cases had been taken for the study, which were divided randomly into two groups containing 200 cases each. ie. Group A and Group B. Group A patients were given 600 µgm misoprostol rectally immediately following delivery of baby. Group B patients were given 10 IU of oxytocin intramuscularly immediately after delivery. The third stage of labour was managed actively with delivery of placenta by controlled cord traction. Any blood clot which expressed from the uterus was measured in the

calibrated glass container. After delivery, the general condition was assessed at regular interval up to 2 hours. Maternal haemoglobin concentration was measured before delivery and repeated 24 hours after delivery. Comparison of quantitative variables between the study groups was done using 't' test for independent sample. P < 0.05 was considered statistically significant. Statistical analysis was done using SPSS version 15.0.

Results

The table-1 showing the baseline variables like antenatal registration, age, gravida, parity, gestational age, duration of labour, duration of third stage of labour, progress of labour and number of episiotomy of both study and control group where no significant statistical difference was observed between these two groups . The mean third stage blood loss was 185±84.42 ml and 168±68.38ml in group A and group B respectively with p-value being 0.025 suggested that there was significant difference (p<0.05) in the third stage between study (group A) and control (group B) group. The average blood loss during third stage of labour was found to be more in misoprostol group than the oxytocin group.

The mean change in Hb% (gm/dl) pre and post delivery in study population was 0.89±0.32SD (gm/dl) and 0.83±0.28SD (gm/dl) in group A and group B respectively. No statistical significant difference was found (p>0.05).

Incidence of PPH was 3% and 2% in group A and group B respectively and found to be 2.5% in whole study population. There was no significant difference in the incidence of PPH in both groups where the p>0.05 was not significant. Blood tran - sfusion was given to the patient who had blood loss >500ml and/or who developed signs and symptoms of shock. In misoprostol group out of 200 women only 5 patients and in oxytocin only 4 patients got blood transfusion.

Side effects were found to be more in study group A than the control group B. The incidence of shivering was significantly higher in the study group A (20.5%) than the control group B (2%). The degree of shivering was mild to moderate and subsided spontaneously within 4-5 hours without any treatment. Similarly, incidence of fever was significantly higher in group A than group B with the incidence being 8.5% and 0.5% respectively. Pyrexia was transient and did not require treatment, subsided spontaneously within 6-8 hours after delivery. Thus, the table-2 shows that

Table 1: Baseline characteristics of Group A(Study) and Group B (Control)

Variables		Group A N=200	Group B N=200	Group A N=200	Group B N=200	P value
		No (%)	No (%)	Mean	Mean	
Antenatal registration	Booked	89 (44.5%)	91(45.5%)	-	-	0.92
	Unbooked	111(55.5%)	109(54.5%)	-	-	
Parity	P_0	129(64.5%)	139(69.5%)			0.34
	P_1	53(26.5%)	50(25%)			
	P_2	18(9%)	11(5.5%)			
Age (Years)	15-20	56(28%)	38(19%)	23.89± 3.93SD	24.48± 3.76SD	0.12
	21-25	79(39.5%)	92(46%)			
	26-30	52(26%)	58(29%)			
	31-35	13(6.5%)	12(6%)			
Gestational age in weeks		-	-	38.34± 1.49SD	38.62± 1.65SD	0.76
Duration of labour in hours		-	-	5.49± 1.09SD	5.55± 1.03SD	0.058
Duration of 3rd stage of labour in minutes		-	-	6.25± 2.02SD	5.90± 1.60	0.056
Progress of labour	Spontaneous	152(76%)	145(72.5%)	-	-	0.4928
	Augmented	48(24%)	55(27.5%)	-	-	
Episiotomy	Done	145(72.5%)	148(74%)	-	-	0.8213
	Not done	55(27.5%)	52(26%)	-	-	
Blood loss in 3rd stage of labour (ml)		-	-	185.67± 84.42SD	168.47± 68.38	0.025
Change in Hb% in pre and post delivery (gm/dl)		-	-	0.895± 0.32SD	0.836± 0.28SD	0.523

overall there was no significant difference found in the incidence of side effects between study and control

Table 2: Side effects of uterotonic drugs		
Side effects	**Group A (N=200)**	**Group B (N=200)**
Headache	5 (2.5%)	3 (1.5%)
Nausea	16 (8%)	7 (3.5%)
Vomiting	4 (2%)	3 (1.5%)
Shivering	41 (20.5%)	4 (2%)
Diarrhoea	10 (5%)	5 (2.5%)
Pain abdomen	2 (1%)	0
Fever >38^{o} C	17 (8.5%)	1 (0.5%)

group, except in the incidence of shivering and pyrexia which was found to be more in misoprostol group.

Discussion

The number of unbooked cases was more in both study (55.5%) and control (54.5%) groups compared to booked cases. The maximum number of patients in both the study and control group was primigravida 64.5% and 69.5% out of 200 numbers in each group respectively. Due to difference in randomized selection of the patients by exclusion criteria, there was minimum difference in percentage.

The mean age was 23.89±3.93SD and 24.48±3.76SD in Group A and Group B respectively with p-value being P=0.12 (P>0.05) which suggest there was no significant difference in the mean age between two groups. The commonest age group involved in the study and control group was 21-25 years (39.5% and 46% in study and control group). The mean age group taken for the study was quite comparable to some other studies like Shrestha et al (2010) [8], Steven et al (2006) [9], Masoumeh et al (2009) [10] and Ibrahim et al (2003) [11].

Similarly, the patient taken for study were comparable in relation to their mean gestational age in weeks where 38.34±1.49SD and 38.62±1.65SD was observed in Group A and Group B respectively with p-value being P=0.763 (P>0.05). The mean gestational age taken for the study was comparable to some other standard trials [8-10, 12].

In the present study, the incidence of spontaneous labour and augmented labour was 76% and 24% (rectal misoprostol group) and 72.5% and 27.5% (oxytocin group) respectively. The cases, whose labour was induced, were not taken for the study. Comparing the incidence of spontaneous and augmented or accelerated labour with exclusion of induced labour, this study is found comparable to some other studies [11,12,13].

The mean duration of labour was 5.49±1.09SD and 5.55±1.03SD in misoprostol group (group A) and oxytocin group (group B) respectively with p-value being P=0.058 considered non significant (P>0.05). There was no significant difference (P>0.05) in the mean duration of labour between the study and control group.

However, the mean duration of third stage of labour in the present study was 6.25±2.02SD and 5.90±1.60SD in rectal misoprostol group and oxytocin group respectively. No statistical difference was noted in between two groups in relation to the mean duration of third stage of labour. Similarly, study performed by Karkanis et al in 2002 [14] among 240 women who ra - ndomly rece - ived 400 µgm rectal misopro- stol after delivery of the infants or parentral oxytocin (IM or IV) after delivery of anterior shoulder. No statistically significant difference found in mean duration of third stage of labour between two groups like that of our study.

Table 3: Comparing mean third stage blood loss in ml			
Study	**Rectal misoprostol**	**Oxytocin IM/IV or others**	**p-value**
Shrestha et al 2010(1000µg) N-200	156±124.2	132.31±91.8	0.012
Gohil et al 2008 (400µg) N- 200	355±115.72	281±131.27	0.000089
Archana et al 2008 (400µg) N-200	237.48	152.34	0.001
Present study (600µg) N-400	185.67±84.42	168.47±68.38	0.025

In the present study as shown in the table-4, the difference in mean blood loss between rectal misoprostol group and oxytocin group is statistically

significant. Blood loss during third stage is found to be more in misoprostol group than oxytocin group. The results in the present study in relation to the third stage blood loss are similar or comparable to the other studies as shown in table-5 [8,12,15]. The wide range of third stage blood loss in different trails may be due to difference in the estimation of blood loss by subjective visual observation.

Considering PPH as a blood loss of ≥500 ml, in the present study, 3% of patients given misoprostol developed PPH as compared to 2% with oxytocin group which is statistically not significant ($p>0.05$). In some other trails also similar results was found [8,9,11,16]. Blood transfusion was given to the patients who had blood loss ≥ 500ml and developed symptoms of shock. In misoprostol group out of 200 women 5 patients and in oxytocin group 4 patients got blood transfusion.

As the blood loss at delivery is a subjective observation rather than an objective measurement, the more reliable estimation of blood loss will be decline in haematocrit or haemoglobin and clinical examination [17,18]. Thus, the difference in mean estimated blood loss between the groups will be better evaluated by difference in haemoglobin between pre-delivery and post-delivery haemoglobin level which is much more objective [19]. In the present study, the mean fall in haemoglobin pre-delivery and post-delivery was 0.895±0.32 gm/dl and 0.836±0.28 gm/dl in misoprostol group and oxytocin group respectively. There was no significant difference in mean fall in haemoglobin between two groups. In a trial done by Bugalho et al., 663 women with uncomplicated vaginal delivery were randomized to receive 400µg rectal misoprostol or oxytocin 10IU IM after delivery of the infant. No significant differences of haemoglobin level were observed between two groups, before and after delivery [20]. Bamigboye et al. in his search for an effective, easily stored, affordable uterotonic agent to prevent postpartum haemorrhage, conducted a trial where he randomized 491 women to receive either 400µg rectal misoprostol (241 women) or one ample of syntometrine (250 women). His results showed that the incidence of postpartum haemorrhage, duration of third stage of labour and the drop in haemoglobin level were similar [21].

The side effects of misoprostol are gastrointestinal, shivering, pyrexia, pain abdomen etc. In the present study, it was found that the misoprostol was associated with more side effects than the oxytocin. The incidence of nausea, vomiting, and diarrhoea was 8%, 2% and 5% respectively in misoprostol group.

The incidence of shivering, pyrexia was found to be more in misoprostol group than oxytocin with the incidence being 20.5% versus 2% (shivering) and 8.5% versus 0.5% (pyrexia) respectively. Shrestha et al. in their study among 200 cases found that the 16% patients developed shivering in misoprostol group and 4% developed in oxytocin group [8]. The degree of shivering was mild to moderate and subsided spontaneously within 4-5 hours without any treatment. Pyrexia was transient in nature, subsided spontaneously within 6-8 hours after delivery. Nasr et al. in study among 514 women who are randomly allocated to receive 800µg rectal misoprostol and oxytocin IV found that the incidence of fever was significantly higher in misoprostol group (18.7% verus 0.8%) [22].

Conclusion

In our study it is observed that the misoprostol 600µg rectally is less effective than intramuscular oxytocin 10 IU when used as prophylactic uterotonic during the active management of third stage of labour. Third stage blood loss found to be significantly more with misoprostol. But, duration of third stage of labour and mean fall in haemoglobin postpartum was similar. Overall there was no significant difference found in the incidence of side effects between both groups, except in the incidence of shivering and pyrexia which was found more in misoprostol. Most of the side effects were seen in the post delivery period within 2 to 3 hours following administration of drugs and subsided spontaneously within 4-5 hours.

Conflict of interest: None. **Disclaimer:** Nil.

References

1. Mousa HA, Alfirevic Z. Treatment for primary postpartum haemorrhage. Cochrane Database Syst Rev. 2007; (1): CD003249.

2. Alexander J, Thomas PW, Sanghera J. Treatments for secondary postpartum haemorrhage. Cochrane Database Syst Rev. 2002; (1): CD002867.

3. Combs CA, Murphy EL, Laros Jr RK. Factors associated with hemorrhage in cesarean deliveries. Obstetrics & Gynecology. 1991; 77: 77-82.

4. Kwast BE, Rochat RW, Kidane-Mariam W. Maternal mortality in Addis Ababa, Ethiopia. Studies in Family Planning. 1986; 17: 288–301.

5. Chong YS, Su LL, Arulkumaran S. Misoprostol: a quarter century of use, abuse, and creative misuse. Obstetrical & Gynecological Survey. 2004; 59(2): 128–40.

6. Gupta B, Jain V, Aggarwal N . Rectal misoprostol versus oxytocin in the prevention of postpartum hemorrhage. a pilot study. International Journal of Gynecology & Obstetrics. 2006; 94(Suppl 2): S139–40.

7. Derman RJ, Kodkany BS, Goudar SS, Geller SE, Naik VA, Bellad MB et al. Oral misoprostol in preventing postpartum haemorrhage in resource-poor communities: a randomized controlled trial. Lancet. 2006; 368(9543): 1248–53.

8. Shrestha A, Dongol A, Chawala CD, Adhikari RK. Rectal misoprostol versus intramuscular oxytocin for prevention of postpartum haemorrhage. Kathmandu Univ Med J. 2011; 9(33): 8-12.

9. Steven MP, Robert L et al. Rectal misoprostol versus oxytocin in the management of third stage of labour. J Obstet Gynaecol Can. 2007; 29(9): 711-18.

10. Masoumeh M, Fatemeh T, Batool T, Nahid S, Afsaneh V. Efficacy of rectal misoprostol for prevention of postpartum haemorrhage. Iran J Pharm Res. 2013; 12(2): 469-74.

11. Ibrahim A, Adnan AO. Prevention of postpartum haemorrhage by rectal misoprostol; A randomized control trial. Middle East Journal of Family Medicine. 2004; 5(5).

12. Gohil JT, Tripathi B. A study to compare the efficacy of misoprostol, oxytocin, methyl ergometrine and ergometrine-oxytocin in reducing blood loss in active management of third stage of labour. The Journal of Obstertics and Gynaecology of India. 2011; 61(4): 408-12.

13. Gerstenfeld TS, Wing DA. Rectal misoprostol versus intravenous oxytocin for the prevention of postpartum haemorrhage after vaginal delivery. Am J Obstet Gynecol. 2001; 185(4): 878-82.

14. Karkanis SG, Caloia D, Salenieks ME, Kingdom J, Walker M, Meffe F, Windrim R. Randomized controlled trail of rectal misoprostol versus oxytocin in third stage management. J Obstet Gynecol Can. 2002; 24(2): 149-54.

15. Sharma A. A comparative study of efficacy of intramuscular oxytocin with controlled cord traction versus per rectal misoprostol in the management of third stage of labour. International Journal of Biological and Medical Research. 2013; 4(3): 3325.

16. Haque N, Bilkis L, Bari MS et al. Comparative study between rectally administered misoprostol as a prophylaxis versus conventional intramuscular oxytocin in postpartum haemorrhage. Mymensingh Med J. 2009; 18(1): 40-44.

17. Coombs CA, Murphy EL, Laros RK Jr. Factors associated with postpartum hemorrhage with vaginal birth. Obstet Gynecol. 1991;77:69-76.

18. Ratnam SS, Rauff M. In: Turnbull A, Chamberlain G (eds). Postpartum hemorrhage and abnormalities of the third stage of labour. London. Churchill Livingstone; 1989. p. 867-75.

19. Ng PS, Chan ASM, Sin WK, Tang LCH, et al. A multicentre randomized controlled trail of oral misoprostol and IM syntometrine in the management of the third stage of labour. Human Reproduction. 2001; 16(1): 31-35.

20. Bugalho A, Daniel A, Faúndes A, Cunha M. Misoprostol for prevention of postpartum hemorrhage. Int J Gynecol Obstet. 2001;73:1–6.

21. Bamigboye AA, Merrell DA, Hofmeyr GJ, Mitchell R. Randomized comparison of rectal misoprostol with syntometrine for management of third stage of labour. Acta Obstet Gynecol Scand. 1998; 77(2): 178-81.

22. Nasr A, Shahin AY, Elsamman AM, Zakherah MS, Shaaban OM. Rectal misoprostol versus intravenous oxytocin for prevention of postpartum haemorrhage. Int J Obstet Gynaecol. 2009; 105(3): 244-7.

---

[1]Bijoy Kumar Dutta, [2]Komal Rani Gupta

[1]Assistant Professor, Department of Obstetrics and Gynaecology, FAAMC, Barpeta; [2]PGT, Department of Obstetrics and Gynaecology Gauhati Medical College, Guwahati.