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Rectal Misoprostol versus Intravenous Oxytocin in the Active Management of the Third Stage of Labour

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ABSTRACT

Objectives: Postpartum hemorrhage (PPH) at third stage of labour may cause maternal morbidity. This study compared efficacy of rectal misoprostol and intravenous oxytocin in the active management of third stage of labour. **Methods:** The study involved 188 subjects in two groups. Group A was given Misoprostol 800µg rectally and group B was given oxytocin 10IU intravenously at the delivery of anterior shoulder of the baby. **Results:** The amount of blood loss was >500 ml in 12 patients in which 8 (8.5% from group A) were from group A and 4 (4.3%) were from group B. The frequency of PPH was statistically same in both study groups (P value = 0.62). The mean change of Hb in group A was 2.71 ± 0.15 g/dl and in group B 9.10 ± 1.23 g/dl. **Conclusion:** Results suggested that I/V oxytocin is more effective compared to rectal misoprostol for the active management of the third stage of labour.

Keywords: Postpartum hemorrhage **(**PPH), Rectal Misoprostol, I/V Oxytocin.

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INTRODUCTION

Pregnancy and childbirth involve significant health risks, even for women with no pre-existing health problems. Approximately 40 percent of pregnant women experience pregnancy-related health problems, and 15 percent of all pregnant women suffer long-term or life-threatening complications.[1] According to World Health Organization in 1995, nearly 515,000 women died from complications of pregnancy and childbirth.[2] Most of these deaths occur in developing countries, often because women lack access to life-saving care. Severe bleeding, or hemorrhage, is the single most important cause of maternal death worldwide.[3] At least one-quarter of all maternal deaths are due to hemorrhage; the proportions range from less than 10 percent to nearly 60 percent in various countries.[4,5] Even if a woman survives postpartum hemorrhage (PPH), she can be severely anemic and suffer from continuing health problems.

The third stage of labour is from delivery of the baby to the complete expulsion of the placenta and membranes.[6] It takes normally 5-15 minutes. If extends beyond 30 minutes, it is regarded as prolonged third stage. A major complication associated with third stage of labour is post partum hemorrhage which is the blood loss more than 500 ml.[7] It is one of the leading causes of maternal mortality in developing countries.[8] Women who survive PPH are likely to suffer from anemia and other complications.[9] Massive postpartum hemorrhage refers to the loss of 30–40% of the patient's blood volume resulting in changes in the hemodynamic parameters. Complications include hemorrhagic shock, disseminated intravascular coagulopathy (DIC), adult respiratory distress syndrome, renal failure, hepatic failure, loss of fertility, pituitary necrosis and maternal death.[10] Postpartum Hemorrhage after delivery is reported as being responsible for 25% of the 515,000 maternal pregnancy-related deaths reported by the World Health Organization.

Postpartum hemorrhage is often unpredictable, although many risk factors have been identified.[10] Abnormalities in one or a combination of four basic processes (Four T's): uterine atony (Tone); retained placenta, membranes, or blood clots (Tissue); genital tract trauma (Trauma); or coagulation abnormalities (Thrombin) usually account for PPH.[11] As a

conservative estimate, some 140,000 deaths each year could be prevented, if the women themselves had been given an understanding of the possible warning signs of bleeding, the knowledge and ability to seek skilled maternity care, at least at delivery, and had access to functioning emergency obstetric services.[12]

Active and physiological management are two different and well-studied strategies used in the management of the third stage of labour. The basic mechanisms of the active management include uterotonics with delivery of the anterior shoulder of the baby, gentle downward cord traction with counter traction of the uterine body, and early cord clamping. Physiological management does not recommend uterotonics until after delivery of the placenta (if at all) and no cord traction, and the timing of cord clamping varies, usually after pulsation of the cord has ceased.[13] The prophylactic administration of an injectable medicine oxytocin is an integral part of the active management of the third stage of labour. It has its own side effects. It reduces the blood loss up to 40%, postpartum anemia and need for blood transfusion.[14,15] Misoprostol tablet stimulates uterine contraction rapidly and powerfully.[16] It is a synthetic analogue of prostaglandin E1. Like other uterotonics, misoprostol causes the uterus to contract, and thus can reduce postpartum bleeding. Misoprostol has a range of potential benefits including ease of administration (oral or rectal), low cost, and stability.[5]

Several studies have suggested that 400 to 600 mcg of misoprostol (administered orally) may be as effective in reducing postpartum hemorrhage as oxytocin or syntometrine; another found it less effective.[17,18,19] A WHO multi-center study found that misoprostol was not as effective as oxytocin in reducing maternal bleeding when administered as part of active management of the third phase of labour in hospital settings. Compared with women who received oxytocin, women receiving misoprostol (600 mcg orally) immediately after delivery had a higher rate of blood loss of 1,000 ml or more (4 vs. 3 percent), required additional uterotonics more frequently, and had a higher incidence of shivering and elevated temperature.[20, 21] Rationale of this study is to determine whether misoprostol is as effective as oxytocin in the active management of the third stage of labour and to promote its use in areas where facilities for administration of intravenous oxytocin are not available especially in remote areas.

METHODOLOGY

Study Design

The study design was Randomized Control Trial (RCT). The study was conducted at Obstetrics and Gynecology department of Holy Family Hospital, Rawalpindi and its duration was six months.

Sample Collection

Purposive sampling technique was used for sample collection. Sample size was calculated by using WHO sample size calculator taking

Confidence level = 95 %, Absolute Precision = 0.05, Power of test 80%

Population proportion = P1 2.7 % [6], Population proportion = P2 1.4 % [7]

Sample size n = 188 (94 in each group).

Two criteria were used to collect samples:

a) Inclusion Criteria:

It included all women having singleton uncomplicated term (37-42 weeks) pregnancy with vertex presentation and spontaneous onset of labour with the anticipation of vaginal delivery admitted in Holy Family hospital.

b) Exclusion Criteria:

It included all women having medical disorders (hypertension, cardiac diseases, renal disorders and known cases of bleeding disorders), women with previous history of the third stage complications and women with any contraindication to drug.

Efficacy

The efficacy of the two drugs was measured by following parameters:

- Duration of the third stage of labour < 30 min
- Blood loss < 500ml
    - Blood loss was measured by collecting blood into bed pan. All tampons, gauze pieces, sanitary pads were pre-weighed and then 1 hour after the delivery of placenta. 1g increase was equal to 1ml.
- Hemoglobin concentration before delivery.
    - Hemoglobin concentration 12 hours after delivery.

Data Collection

All the patients admitted in first stage of labour through outdoor and emergency fulfilling the inclusion criteria were selected for study. Approval from hospital ethical committee and informed consent from patients was taken. Exclusion criteria were strictly followed to limit the confounding

variables (hydramnios, chorioamnionitis, grand multiparity, macrosomia, multiple gestations and any episode of antepartum hemorrhage in the current pregnancy) and bias. Patients were randomly allocated to two groups; group A (odds numbers) and group B (even numbers) by using random number table. Misoprostol 800 ug rectally was given to group A and oxytocin 10IU intravenously was given to group B at the delivery of anterior shoulder of the baby. If intravenous oxytocin is used during the second stage of labour, it was immediately stopped after delivery.

In all cases, the third stage of labour was managed by early cord clamping and controlled cord traction until placental expulsion (Brandt-Andrew's method). During the third stage of labour patient was observed for general conditions, blood pressure, pulse, respiratory rate, size and consistency of the uterus and amount of vaginal blood loss. This observation was continued until 24 hours after delivery. If placenta is not delivered within 30 minutes of delivery it was removed manually under general anesthesia and urogenital trauma will also be looked for. Immediately after birth, the blood loss was measured by collecting into a bedpan. All soaked pads were. The difference in weight before and 12 hours after the delivery was calculated. 1g increase in weight was considered to be equivalent to 1ml blood. Irrespective of the allocation of the medication, an additional dose of intravenous syntometrine (5IU oxytocin, 0.5mg ergometrine) was given if the uterus was not well contracted or if vaginal bleeding was more than 500ml. Blood was transfused if vaginal bleeding was more than 1000ml.

Data Analysis

Data was analyzed with SPSS-10 Mean $\pm$ SD and was calculated for quantitative variables like age and Hb concentration before and after delivery. Frequency and percentage was calculated for qualitative variables i-e duration of third stage, blood loss. Chi square test was used to compare duration of third stage and blood loss in misprostol group and oxytocin group because both parameters in this study were measured on qualitative scale. P-Value <0.05 was considered significant.

RESULTS

In group A the mean age of subject was 26.44 ± 3.3 years (Range: 20 – 40 years). The mean age in group B was 27.2 ± 4.6 years (Range: 21 – 38 years). Overall mean age of all 188 subjects was 26.82 ± 3.95 with over all age range of 18 years (Table 1).

Table 1: Descriptive Statistics of Age of Subjects (years) Among study groups

	Study Groups		Total
	A	B	
N	94	94	188
Mean	26.44	27.2	26.82
Std. Deviation	3.3	4.6	3.95
Minimum	20.00	21.00	20.00
Maximum	40.00	38.00	38.00

Key words: Study Group A: Rectal Misoprostol Study Group B: Intravenous Oxytocin Rectal Misoprostol versus intravenous Oxytocin in the Active Management of the Third Stage of Labour

According to their socioeconomic status 82 (43.6%) were Rs. 5,000-10,000 income group in which 42 (44.7%) were from group A and 40 (42.6%) from group B. 65 (34.6%) were from Rs. 10,000-20,000 income group in which 34 (36.2%) were from group A and 31 (33%) were from group B. There were 41 (21.8%) subjects who were from Rs. > 20,000 income group, in which 18(19.1%) were from group A and 23 (24.5%) were from group B (Table 2).

Table 2: Frequency Distribution of Socio Economic Groups Among study groups

	Study Groups		Total
	A	B	
Rs. 5,000-10,000	42 (44.7%)	40 (42.6%)	82 (43.6%)
Rs. 10,000-20,000	34 (36.2%)	31 (33%)	65 (34.6%)
Rs. > 20,000	18 (19 1%)	23 (24.5%)	41 (21.8%)
Total	94 (100%)	94 (100%)	188 (100%)

Key words: Study Group A: Rectal Misoprostol Study Group B: Intravenous Oxytocin Rectal Misoprostol versus Intravenous Oxytocin in the Active Management of the Third Stage of Labour

There were total 176 (93.6%) subjects who's amount of blood loss during delivery was < 500 ml, in which 86 (91.5%) were from group A and 90 (95.7%) were from group B. The amount of blood loss > 500 ml was in 12 patients (frequency of PPH) in which 8 (8.5%) were from group A and 4 (4.3%) were from

group B. The frequency of PPH or blood loss > 500 ml was statistically same in both study groups having the P value = 0.62 (Table 3).

Table 3: Frequency Distribution of Amount of Blood loss Among study groups

	Study Groups		Total
	A	B	
< 500 ml	86 (91.5%)	90 (95.7%)	176 (93.6%)
> 500 ml	8 (8.5%)	4 (4.3%)	12 (6.4%)
Total	94 (100%)	94 (100%)	188 (100%)

Chi-Square = 0.24 p-value = 0.62

Key words: Study Group A: Rectal Misoprostol Study Group B: Intravenous Oxytocin Rectal Misoprostol versus Intravenous Oxytocin in the Active Management of the Third Stage of Labour

The duration of third stage of labour was < 30 minutes in 170 (90.4%) subjects in which 81 (86.2%) were from group A and 89 (94.7%) were from group B. There were 18 subjects who's durations of labour were > 30 minutes, in these 18 subjects, 13 (13.8%) were from group A and 5 (5.3%) were from group B. The duration of third stage of labour was statistically significant in group B as compare to group A having the P value=0.047 (Table 4).

Table 4: Frequency Distribution of Duration of Third Stage of Labour

Among study groups			
	Study Groups		Total
	A	B	
< 30 minutes	81 (86.2%)	89 (94.74%)	170 (90.4%)
> 30 minutes	13 (13.8%)	5 (5.3%)	18 (9.6%)
Total	94 (100%)	94 (100%)	188(100%)

Chi-Square = 3.93 p-value = 0.047

Key words: Study Group A: Rectal Misoprostol Study Group B: Intravenous Oxytocin Rectal Misoprostol versus Intro venous Oxytocin in the Active Management of the Third Stage of Labour

The mean Hb in group A was 9.01 ± 1.23 g/dl and after delivery 11.43 ± 0.89 g/dl. The mean change of Hb in group A was 2.33 ± 0.87 g/dl. The mean Hb in group B was 9.07 ± 1.34 g/dl and after delivery was 11.78 ± 1.01 d/gl. The mean change of Hb in group B was 2.71±0.15 g/dl (Table 5).

Table 5: Descriptive Statistics of Hb (g/d1) Among study groups

		Study Groups	
		A	B
Mean t 3.D	Mean Hb	9.10 t 1.23	9.07t1 .34
	After Delivery	11.43 t 0.89	11.78 t 1.01
	Change in Hb.	2.33 t 0.87	2.71 ± 0.15

Key words: Study Group A: Rectal Misoprostol Study Group B: Intravenous Oxytocin Rectal Misoprostol versus Intravenous Oxytocin in the Active Management of the Third Stage of Labour

DISCUSSION

Most cases of PPH occur during the third stage of labour. During this time, the muscles of the uterus contract and the placenta begin to separate from the uterine wall. The amount of blood loss depends on how quickly this occurs. The third stage typically lasts between 5 and 15 minutes.[22,23] After 30 minutes, the third stage of labour is considered to be prolonged, indicating a potential problem. If the uterus is atonic and does not contract normally, the blood vessels at the placental site do not adequately constrict and severe bleeding results. Active management of the third stage of labour consists of interventions designed to speed the delivery of the placenta by increasing uterine contractions and to prevent PPH by averting uterine atony. Active management of the third stage of labour is commonly used in the United Kingdom, Australia, and several other countries.[24]

In contrast to active management, expectant management (also known as conservative or physiological management) of the third stage of labour involves waiting for signs that the placenta is separating from the uterine wall (for example, observing a gush of blood), and allowing it to deliver spontaneously. Expectant management is the common practice in parts of Europe, the United States, and Canada. Expectant management also is the norm in the majority of home births in developing countries.[22] Several large-scale, randomized, controlled studies (carried out in well-equipped maternity hospitals) have compared the effects of active and expectant management. Although the studies used different protocols and definitions of active management, their results are informative. The trials found decrease incidence of PPH and

fewer cases of low hemoglobin among women actively managed.[25,26]

A meta-analysis of several studies, available through the Cochrane database and WHO's Reproductive Health Library, confirmed that active management was associated with reduced maternal blood loss (including PPH), reduced incidence of postpartum anemia, and decreased need for blood transfusion.[22] Active management also was associated with a reduced risk of prolonged third stage labour, and less use of additional therapeutic uterotonic drugs.[25]

From literature it is evident that the injection of a uterotonic drug immediately after delivery of the baby is one of the most important interventions used to prevent PPH. The most commonly used uterotonic drug, oxytocin, has proven to be very effective in reducing the incidence of PPH and prolonged third-stage labour.[27,28] In this study we also noted similar findings. The frequency of PPH in groups A was 8.5% and in group B it was 4.3%. More over the duration of third stage of labour was < 30 minutes in 170 (90.4%) subjects in which 81 (86.2%) were from group A and 89 (94.7%) were from group B. There were 18 subjects who's duration of labour was > 30 minutes, in these 18 subjects, 13 (13.8%) were from group A and 5 (5.3%) were from group B. The duration of third stage of labour was statistically significant in group B as compare to group A having the P value = 0.047.

In a study conducted by Nodstorm which was double blind study and they used intravenous oxytocin 10 I.U versus saline solution in the management of postpartum hemorrhage instead of misoprostol. They measure blood loss, frequency of PPH, additional use of methylergonovine, difference in Hb pre and post delivery. The frequency of PPH was 7.8% vs 13.8%. They proved oxytocin more effective in the management of PPH.[27]

In a study conducted by Siddique, it was reported that 36% patients in misoprostol group, while 30% in oxytocin group developed PPH. They also measured the duration of third stage of labour which was not prolonged in any group.[28] while in current study duration of third stage of labour was statistically significant in group B as compared to group A.

In a study conducted by Gerstenfeld, rectal misoprostol was used versus intravenous oxytocin for the active management of third stage of labour. One group received tablet misoprostol 200ug per rectal plus 2ml of saline in Ringer lactate intravenously. While other group received 2 lactulose tablets per rectal plus 20 unit oxytocin in ringer lactate intravenously. Blood loss measured for change in Hb concentration from admission to 1 day Post-delivery.[29] In current study the Hb was measured from pre-delivery to 12 hour post-delivery. Different studies conducted in different ways but all of them had same conclusions that oxytocin is more effective in reducing postpartum hemorrhage as compared to misoprostol. In addition to standard oxytocics, misoprostal was given for PPH management shows great potential in improving women's health outcomes after experiencing this obstetrical complication.[30]

Our results also suggests women who bleed less overall had a smaller drop in hemoglobin and did not require additional interventions, such as blood transfusion, additional oxytocics and uterine packing to manage their postpartum bleeding. Lastly, PPH is an unpredictable and rapid cause of maternal death worldwide. Current evidence indicates that where appropriately trained birth attendants, necessary equipment, and injection safety can be ensured active management of the third stage of labour (uterotonic drugs, cord clamping, and controlled cord traction) will significantly reduce the incidence of PPH.[31]

Together with the prevention and treatment of anemia and skilled attendance at all deliveries, active management can prevent PPH in thousands of women worldwide each year. Those cases that cannot be prevented require the immediate intervention of skilled, well-equipped providers. Ongoing operations research is helping to determine the best approaches for managing postpartum bleeding and its complications in various settings, including the service delivery requirements for safe and effective active management of the third stage of labour. As the information that providers need to prevent and manage PPH is disseminated through new national guidelines, more women will receive the obstetric care they need. When included in a continuum of pre- and post-natal care, appropriate management of the third stage of labour will improve the survival and quality of life of mothers and infants worldwide.[24]

CONCLUSION

According to this study I/V oxytocin is more effective as compared to rectal misoprostol for the active management of the third stage of labour.

REFERENCES

1. Starrs A. 2007. The Safe Motherhood Agenda: Priorities for the Next Decade.
2. World Health Organization. 2001. Global estimates of maternal mortality for 1995: results of an in-depth review, analysis and estimation strategy [statement]. Geneva: World Health Organization.
3. Nabila T, Mehnaz K, Rashida P. Effectiveness of misoprostol in the prevention of postpartum hemorrhage. PJMHS. 2015;9 (1):268-70.
4. Abouzahr C. 1998. Antepartum and Postpartum Hemorrhage. In: Murray CJL, Lopez AD. Health dimensions of sex and reproduction. Boston: Harvard University Press; pp 172–4.
5. Saima A, Sarah K, Gulfishan H, Nargis S. Oral misoprostol versus oxytocin in the management of third stage of labour. J Pak Med Assoc. 2014; 64:428-32.
6. Baker PN. 2006. Obstetrics by ten teachers. 18thed. London: Hodder Arnold.
7. Chong YS, Su LL, Arulkumaran S. Current strategies for prevention of postpartum hemorrhage in the third stage of labour. Curr Op Obs. & Gynecol. 2004;16:143-50.
8. Hofmeyr GS, Ferreir S, Nikedem VC, Sigata LM, Jafta Z, Maholwana B, et al. Misoprostol for treating postpartum hemorrhage: a randomized controlled trial. BMC Pregnancy and Child Birth 2004;4:16.
9. Tahseen F, Anwar A, Arfat Y. Intraumbilical Veinous injection Oxytocin in the Active Management of Third Stage of Labour. J Coll Physicians Surg Pak. 2008;18(9):551-4.
10. American College of Obstetricians and Gynaecologists. ACOG Practice Bulletin: Clinical Management Guidelines for Obstetrician–Gynaecologists. Postpartum Hemorrhage. Obstet Gynecol. 2006;108(4):1039-47.
11. Mishra N, Chandraharan E. 2009. Post partum hemorrhage (PPH). In: Warren R, Arulkumaran SS. Best practice in labor and delivery. Cambridge University Press; pp 160-70.
12. CEMACH. 2007. Saving Mothers' Lives – Reviewing Maternal Deaths to Make Motherhood Safer 2003–2005. London: CEMACH.
13. Rogers J, Wood J, McCandlish R. Active versus expectant management of third stage of labor: the Hutchingbrooke trial. Lancet. 1998;351:693– 7.
14. Pal SA. Hemorrhage and maternal morbidity and mortality in Pakistan. JPMA. 2007;57:576-7.
15. Parsons SM, Walley RL, Crane JM; Mathews K, Hutchens D. Rectal Misoprostol Versus Oxytocin in the Management of third stage of labour. J Obstet Gynaecol Can. 2007;29:711-8.
16. Sultana N, Khatun M. Misoprostol versus Oxytocin in the Active Management of the Third Stage of Labour. J Bangladesh Coll Phys Surg. 2007;25:73-6.
17. Cook CM, Spurrett B, Murray H. A randomized clinical trial comparing oral misoprostol with synthetic oxytocin or syntometrine in the third stage of labour. Aust N Z J Obstet Gynaecol. 1999;39(4):414-9.
18. Walley RL, Wilson JB, Crane JM, Matthews K, Sawyer E, Hutchens D. A double-blind placebo controlled randomized trial of misoprostol and oxytocin in the management of the third stage of labour. BJOG. 2000;107(9):1111-5.
19. Ng PS, Chan AS, Sin WK, Tang LC, Cheung KB, Yuen PM. A multicentre randomized controlled trial of oral misoprostol and i.m. syntometrine in the management of the third stage of labour. Hum Reprod. 2001;16(1):31-5.
20. Gülmezoglu AM, Villar J, Ngoc NT, Piaggio G, Carroli G, Adetoro L, et al. WHO multicentre randomised trial of misoprostol in the management of the third stage of labour. Lancet. 2001;358(9283):689–95.
21. Tuncalp O. Hofmeyr GJ, Gulmezoglu AM, Prostaglandins for preventing postpartum hemorrhage. Cochrane Data Syst Rev. 2012;8:494.
22. Prendiville WJ, Harding JE, Elbourne DR, Stirrat GM. The Bristol third stage trial: active versus physiological management of the third stage of labour. BMJ 1988;297:1295–300.
23. Bugalho A, Daniel A, Faúndes A, Cunha M. Misoprostol for prevention of postpartum hemorrhage. Int J Gynaecol Obstet. 2001;73(1):1-6.
24. WHO. 2001. Reproductive Health Library. Geneva: WHO/HRP.
25. Poeschmann RP, Doesburg WH, Eskes TK. A randomized comparison of oxytocin, sulprostone and placebo in the management of the third stage of labour. British J Obs & Gynecol. 1991;98;(6):528-30.
26. Elbourne DR, Prendiville WJ, Carroli G, Wood J, McDonald S. Prophylactic oxytocin for the third stage of labour. Cochrane Database Syst Rev. 2001;4:180-8.
27. Nordström L, Fogelstam K, Fridman G, Larsson A, Rydhstroem H. Routine oxytocin in the third stage of labour: a placebo controlled randomised trial. British J Obs & Gynecol 1997;104(7):781-6.
28. Siddiqui SM, Shaikh JM, Jillani KA, Siddiqui MA. Prevention of P.P.H: Oxytocin versus Misoprostol. Med Channel (Obstetrics and Gynecology) 2009;15(2):41-4.
29. Gerstenfeld TS, Wing DA. Rectal misoprostol versus intravenous oxytocin for the prevention of postpartum hemorrhage after vaginal delivery. Am J Obstet Gynecol. 2001;185(4):878-82.
30. Tahir S, Ghaffar S, Javed N. Comparison of The Efficacy & Safety Of Misoprostol For Termination

Of Pregnancy In Second Trimester In Scarred Versus Unscarred Uterus. APMC 2011:5(1):19-22.

31. Islam M. 2010. Managing Complications in Pregnancy and Childbrith: a Guide for Midwives and Doctors (MCPC).

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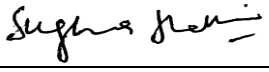
Dr. Sughra Shehzad	Interpretation and manuscript writing	
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