ORIGINAL ARTICLE

Study of Per-rectal Misoprostol as a Method of prophylaxis of post-partum hemorrhage.

Naher M[1], Billah A[2], Sultan R[3], Jabbar T.S[4], Urmi S.J[5], Dolon F[6], Sultana J[7]

Abstract:

Objective: The aim of the study was to find out the effectiveness of per-rectal Misoprostol in the prevention of post-partum hemorrhage and to compare the effectiveness between per-rectal Misoprostol and intramuscular Oxytocin. **Materials and Methods:** This comparative prospective study was conducted in the Department of obstetrics and gynecology of Sir Salimullah Medical College & Mitford Hospital (SSME & MH) during the period of January 2016 to December 2016. One hundred pregnant patients were admitted in the labour ward having third stage of labour included population for this study. In group I (50 patients) received 600 µgm per-rectal Misoprostol after the delivery of baby. In group II (50 patients) received intramuscular 10 I.U. Oxytocin at 3rd stage of labour. The outcome measured by collecting information of duration of stage, amount of blood 1oss, comparison of change in hemoglobin level, blood transfusion required and cause of P.P.H. **Results:** It was found that cause of P.P.H in both groups are retained placenta, genital trauma and uterine atony. Most of the patients had anemia in both groups. The mean amount of Postpartum bleeding was 42.6±20.8 ml (±SD) in group I and 34.5±35.2 ml (±SD) in group II. No patient of group I required blood transfusion but 10% patient from group II required blood transfusion. There was no serious morbidity and bleeding was controlled effectively all the cases. **Conclusion:** This procedure is very safe, easy, cheap & does not require any logistic support. Routine use of Misoprostol analogue 600 µgm effective in blood loss after delivery. The study recommends the regimen for 100 resources, busy obstetric settings.

Key words: Postpartum hemorrhage, Per-rectal, Misoprostol, Prophylaxis Oxytocin.

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Introduction:

Obstetric hemorrhage is one of the most common causes of major maternal morbidity and mortality and most recent studies show that these deaths have increased (from 7 in 1997-1999 to 17 in 2000 - 2002) due to a rise in postpartum hemorrhage.[1,2]

The third stage of labour is defined as the duration from the birth of the baby until the complete expulsion of placenta and membranes. It is a period during labour when both the patients and obstetricians may be relieved with the safe arrival of a healthy baby.[5]

Complications may occur unexpectedly at third stage and unless prompt action is taken to control the situation, serious maternal morbidity and sometimes

1. Dr. Mahmuda Naher, Junior consultant, Department of Obstetrics and gynecology, Shaheed Tajuddin Ahmed Medical College, Gazipur. **(Corresponding Author)** Email: mah.naher@gmail.com,,Phone: 01712073991
2. Dr. Afrin Billah, Junior Consultant, Department of Obstetrics and gynecology, Shaheed Tajuddin Ahmed Medical College, Gazipur. Email: drafrin311@gmail.com
3. Dr. Rifat Sultana, Assistant Professor, Department of Obstetrics and gynecology, Shaheed Tajuddin Ahmed Medical College, Gazipur. Email: dr.rifat.sultana@gmail.com
4. Dr. Tahira Salwa Jabbar, Assistant Professor, Department of Obstetrics and gynecology, Shaheed Tajuddin Ahmed Medical Col1ege, Gazipur.
5. Dr. Sharmin Jahan Urmi, Junior Consultant, Department of Obstetrics and gynecology, Shaheed Tajuddin Ahmed Medical College, Gazipur.
6. Dr. Most. Fahima Dolon, Senior Consultant, Department of Obstetrics and gynecology, Shaheed Tajuddin Ahmed Medical College, Gazipur. Email: fahimadolon@gmail.com
7. Dr. Jubaida Sultan, Assistant Professor, Department of Obstetrics and gynecology, Shaheed Tajuddin Ahmed Medical College, Gazipur. Email: jubaidasultana01@gmail.com

mortality may occur.[6] The 3rd stage is perhaps the most dangerous part of labour for the mothers are in the main risk of being postpartum hemorrhage.[5] Postpartum hemorrhage is defined as an estimated blood loss in excess of 500 ml or any bleeding causing deterioration of the patient's hemodynamic condition (evidenced by rising pulse rate and falling blood pressure). Research has demonstrated that normal blood loss in a vaginal delivery may exceed 500 ml and can range from 500 to 1000 ml.[6] Prendiville et al. suggested that blood loss in excess of 1000 ml would be a more useful clinical definition.[4] However, the problem of blood loss at delivery could remain notoriously inaccurate because it is a subjective visual observation of the obstetrician rather than an objective management. Therefore, a decline in hematocrit or hemoglobin is a more reliable estimation of blood loss.[7] Although risk factors may increase a woman's chances of developing postpartum hemorrhage, 2/3rd of the cases of postpartum hemorrhage occurs without any predisposing factors. Hence all pregnant women remain 'at risk' for this catastrophic event. Postpartum hemorrhage is the leading cause of maternal death in developing world's accounting for 14.9% of such death in areas where maternal mortality is high and less than 10% in advanced countries.[8] Various comparative trials have been conducted to study the reduction of blood loss through active versus expected management of labour. They have predominantly focused on blood loss originating from the placental bed. As a part of the physiological adaptation to pregnancy the spiral arteries of the placental bed are denuded of their muscular layer. Active management promptly initiates uterine contractions which compress these spiral arteries as they run among uterine smooth muscle fibers. Adequate management of the third stage is crucial for the prevention of postpartum bleeding in patients undergoing vaginal delivery. Prendiville et al. in the Bristol showed third stage trial and found an incidence of postpartum bleeding of 5.9% in the actively managed group and 17.9% in the physiologically managed group. They concluded that though active management had definitely reduced third stage blood loss, even then PPH is a big problem.[3] Drugs used for prophylaxis against postpartum hemorrhage include Oxytocin, Ergometrine and Syrtrometrine (a combination of Oxytocin and Ergometrine), Prostaglandins F2α . The most commonly used agents are injectable Oxytocin and/or Ergometrine. They both require parenteral administration and ergometrine require refrigeration. Parenteral Prostaglandins have shown promise but their use has been limited by side effects. In dire situations intramyometrial injection of prostaglandin F2α has been used with apparently dramatic effects but this method has not been assessed in controlled trial and serious side effects have been reported. Misoprostol is a prostaglandin El analogue and is a potent uterotonic agent. It has gastric antisecretory properties. It has clinical application in peptic ulcer, induction of abortion, cervical ripening and induction of labour. The disadvantage of using Oxytocin in the management of the third stage of labour is the requirement for a trained and qualified person to administer this drug, it also requires a readily available supply of sterile syringe and needle that must be handled and disposed of properly. This drug must be handled and stored properly because it is unstable when exposed to light and high temperature. Misoprostol offers several advantages over Oxytocin including a shelf life of several years, stability at high temperature (i.e., it does not require refrigeration), rectal administration (i.e., it does not require needle or syringe), minimal side effects such as nausea and vomiting, it can be administered to hypertensive patients. The advantage of Misoprostol can make it a feasible drug to be used in the routine management of the third stage in developing countries.4,5 The rectal route for Misoprostol has been considered to have several practical advantages. Gastrointestinal side effects are reduced. The per-rectal administration of Misoprostol is possible to patients who are vomiting, who are unable to take oral medication, or who are under anesthesia. Because the side effects of oral Misoprostol are essentially gastrointestinal and dose dependent, the rectal route may be chosen for fewer side effects. The effect of Misoprostol on the postpartum uterus has been shown to be rapid. Therefore, Misoprostol may be a potential alternative to standard oxytocic in preventing atonic postpartum hemorrhage in both low risks and high risks pregnancies. Indeed, the majority of the deliveries (90%) in our country take place at home and trained personnel do not attend many of them. Lack of access

to skilled birth attendant who are able to administer parenteral oxytocin, the high incidence of anemia in pregnancy, non-availability of safe blood transfusion services and lack of refrigeration to store Oxytocin, worsen the outcome of postpartum hemorrhage in our country.

Several recent studies have examined the use for oral and rectal Misoprostol in the third stage of labour. Potential advantages of Misoprostol include well tolerance of the drug, its stability in light and room temperature, its low cost and easy administration as well as its less side effects.

This study of per-rectal administration of Misoprostol would be an alternative to Oxytocin for the prevention of postpartum hemorrhage. It is used as a dose of 600 µg per-rectal in our country, even in tertiary hospital as a prophylaxis for postpartum hemorrhage. This study is to assess the effectiveness of per-rectal Misoprostol on prevention of postpartum hemorrhage in a tertiary hospital.

Materials and Methods:

This prospective study was conducted in the Department of obstetrics and gynecology of Sir Salimullah Medical College and Hospital (SSMCH) during the period of January 2016 to December 2016. Total 100 cases of pregnant women & at 3rd stage of labour ware selected and divided by two groups.

For active management of 3rd stage of labour in group I (50 cases) after delivery of baby, received 600 µgm parental Misoprostol, but some indicated cases also received Oxytocin drip on intramuscular. But in group II (50 cases) received intramuscular 10 I.U Oxytocin (2 ampules).

After delivery of baby. linen soiled with amniotic fluid was removed and a fresh disposable absorbent line saver sheet with plastered backing under women was introduced and also a wedge-shaped bedpan was placed under the women's buttock.

The blood in the bed pen was measured in a measuring jug. When active bleeding had stopped, any blood clots was applied in a plastic bag, were weighed in grams. The known dry width of the linen savers and sanitary pads was applied in a plastic bag, were weighed in grams. The known of the linen savers and sanitary pads were subtracted to give the approximate volume of blood in milliliters. This was added to measured blood volume from the bed pan to give the total blood.

Severity of postpartum hemorrhage was defined as total measured blood volumes from the bed pan, sanitary pads and linen savers less them 500 ml mild, more than 500 ml death and more than 1000 ml collection are severe form.

Collected data was compiled and tabulated according to key variables and calculated by using 't' test. Students' "t" test was reformed using software like SPSS and a P value <0.05 was considered statistically significant.

Results:

During the study period, out of the 100 patients, 50 patients who were given Misoprostol was taken in the group I and 50 patients who were given Oxytocin was in the group II.

Table I: Basic data of the patient (n = 100)

Parameters	Group I (n = 50) Mean±SD	Range (Years)	Group II (n = 50) Mean±SD	Range (Years)
Age (Year)	28.7±5.0	20 - 42	28.4±4.9	19 - 36
Gestation (Weeks)	38.7±1.5	36 - 41	38.7±2.2	36 - 42

Table I. Shows that in group I (n = 50) mean±SD of the patients was 28.7±5.00 and range of the age was 20 - 42 years. In group II (n = 50) mean±SD age of the patents was 28.4±4.9 and the range of the age was 19-36 years. It also shows us group I mean±SD gestation age to the patient was 38.7±1.5 and range 36 – 41 weeks. In Group II mean±SD gestation age in 38.7±2.2 and range 36 - 42 weeks.

Table II: Outcome of the study patients (n =100)

Parameters	Group I (n = 50) n	%	Group II (n = 50) n	%
Third stage duration (min) Mean±SD	10.2±6.8		9.3±3.7	
Range (min-max)	(2 – 30)		(4 – 17)	
Blood Loss (ml)				
> 500 ml	6	12.0	11	22.0
< 500 ml	4	88.0	39	7.8
Mean±SD	341.8±238.2		219.5±115.7	
Range (min-max)	(100 – 700)		(120 -500)	

The mean±SD duration of third stage was 10.2±6.8 minutes which ranged from 2 to 30 minutes in group I and 9.3±3.7 with minutes ranged from 4 to 17 minutes in group II. The mean±SD blood loss was 341.8±238.2 ml varied from 100-700 ml in group I and 219.5±115.7 ml varied from 120-500 ml in group II.

Table III: Immediately after delivery amount of bleeding (ml) of the study patients (n =100)

Amount of bleeding (ml)	Group I (n = 50) Mean±SD	Group II (n = 50) Mean±SD	P value
	42.6±20.8	34.5±35.2	0.208ns

ns = not significant

P value reached from unpaired t-test

Table III shows the mean amount of bleeding (ml) of the study subjects and found the mean (±SD) amount of bleeding (ml) was 42.6±20.8 ml varied from 20 -100 ml in group 1 and 34.5±35.2 ml varied from 12 - 200 ml in group II. The mean amount of bleeding difference was not statistically significant (p >0.05) between two groups.

Table IV: Comparison of changes in hemoglobin levels between groups (n = 100)

Hemoglobin (gm/dl)	Group I (n = 50) Mean±SD	Group II (n = 50) Mean±SD	P value
Pre-delivery	9.9±1.7	10.5±0.6	0.002s
Range (min-max)	(9-11)	(9-12)	
Post-delivery	9.8±0.9	9.9±0.1	0.781ns
Range (min-max)	(9.2-11.5)	(9.3-12.3)	

S = significant, ns = not significant

P value reached from unpaired t-test

Table IV shows the mean hemoglobin level during pre-delivery of the study subjects and found the mean±SD hemoglobin level was 9.9±1.7 gm/d1 varied from 9-11 gm/dl in group I and 10.5±0.6 gm/dl varied from 9-12 gm/dl in group II. The mean post-delivery was found 9.8±0.9 gm/dl with range from 9.2 to 11.5 gm/dl in group I and 9.9±0.1 gm/dl with range from 9.3 to 12.3 in group II. The mean hemoglobin (gm/dl) level difference during pre-delivery was statistically significant (p <0.05) between two groups and the mean hemoglobin (gm/dl) level difference during post-delivery was not statistically significant (p >0.05) between two groups in unpaired-t-test.

Table V: Blood transfusion required between the groups (n = 100)

Blood transfusion	Group I (n = 50) n	%	Group II (n = 50) n	%	P value
Required	0	0.0	5	5	
Not required	50	100	45	9.0	

Table V shows that no patients of group I required blood transfusion but 5(10%) patients from group II required blood transfusion.

Table VI: Cause of PPH of the study patients (n = 100)

Causes of PPH	Group I (n = 50) n	%	Group II (n = 50) n	%
Uterine atony	2	4.0	0	0.0
Retained placenta	6	12.0	2	4.0
Retained product of conception	0	0.0	0	0.0
Genital tract trauma	6	12.0	2	4.0

Table VI shows the cause of PPH of the study subjects. It was observed that the cause of PPH developed due to uterine atony 2(4.0%), retained placenta 6(12.0%) and genital tract trauma 6(12.0%) in group I patients. In group II, PPH developed due to retained placenta 2(4.0%) and genital tract trauma 2(4.0%).

Discussion:

Postpartum hemorrhage is an important cause of maternal morbidity and mortality worldwide, accounting for at least 150,000 maternal deaths every year.

The decreased prevalence of postpartum hemorrhage in most developed parts of the world probably is due to better management of the third stage of labor.[10] However, it is prevalent in those countries where high multiparity, prolonged labour, fibroids and severe

anemia (probably caused by close spacing of pregnancies, poor diet or parasitic infections) are common, although most cases of postpartum hemorrhage occur without such predisposing factors.[10] The risk of dying from postpartum hemorrhage depends on the amount and rate of blood loss and also on the health status of the mother. When women already are compromised by severe anemia and intercurrent illnesses, maternal blood loss of as little as 250 ml may be fatal.[11]

This cross-sectional descriptive type study was carried out with an aim to find out the effectiveness of per-rectal Misoprostol in the prevention of postpartum hemorrhage and to compare the effectiveness between per-rectal Misoprostol and other uterotonic agent for prevention of postpartum hemorrhage as well as to assess the incidence of side effects of Misoprostol. A total of 100 patients ranging from 36-42 weeks pregnancy having normal vaginal delivery, out of which 50 patients received 600 µgm Misoprostol per rectally after the delivery of the baby was considered as group I and 50 patients received 10 I.U. Oxytocin (2 amp) I/M for active management was considered as group II, were included in the study, in the Department of Obstetrics and Gynecology, Sir Salimullah Medical College and Mitford Hospital (SSMC and MH), Dhaka, during January 2016 to December 2016. The present study findings were discussed and compared with previously published relevant studies.

In this current study it was observed that the mean age of the patients 28.4±5.0 years and 28.4±4.9 years in group I and group II respectively, which is comparable with Bouwmeester et al. (2005) study, where the authors shown, the mean age of the patients was 30.4 years in group I and 29.8 years in group II. Similarly, Ozumba et al. (2006) and Wedisinghe et al. (2008) have observed identical mean age of the patients and thus, support the present study. ln another study Walraven et al. (2005) has observed lesser mean age in The Gambia, West Africa, which were 25.9±5.3 years and 25.8±5.3 years in group I and group II respectively. On the other hand, Chong et al. (2004) has observed higher mean age in Chinese women, which was 32.2 years. They have stated that the higher age range may be due to increased life expectancy in the Chinese women.

In this present study it was observed that the mean±SD parity was 0.8±0.15 and 1.1±0.14 in group I and group II respectively and the mean difference was not statistically significant ($p > 0.05$), Multigravida was found 44.0% in group I and 64.0% in group II in this study. Almost similar findings obtained by Nisa et al. (2009), Boucher et al. (2004) and Choy et al. (2002) in their series of studies. Higher mean parity was observed by Nasr et al. (2009), McDonald et al. (2004), Villar et al. (2002).

Though some authors have found similar Bouwmeester et al. (2005), Ozumba et al. (2006), Wedisinghe et al. (2008), Ngan et al. (2007), Leung et al. (2006) gestational age range in their studies and majority of the findings are in agreement with the present study regarding the gestational age. The mean gestational age of the study subjects was found 38.7±1.5 weeks varied from 36-41 weeks in group I and 38.8±2.2 weeks varied from 36-42 weeks in group II and the difference was not significant ($p > 0.05$).

In this present study, it was observed that labour occurred spontaneously 90% and induced 10% in group I. In group II labour occurred spontaneously 94% and induced 6%. More than eighty percent (84%) patients required no augmentation and 16% patients had undergone augmentation of labour, where as in group II more than two third (68%) patients required no augmentation and 32% patients undergone augmentation.

In this present series, it was observed that the mean±SD duration at third stage was 10.2±6.8 minutes in group I and 9.3±3.7 with minutes in group II, which were almost similar in both groups. Nasr et al. (2009) observed the mean duration of third stage of labor were 8.25±2.31 minutes and 7.97±2.82 minutes in group I and group II respectively, which is consistent with the current study.

The mean±SD blood loss was found significantly ($p < 0.001$) higher in group I in this study. The mean blood loss was 341.8±238.2 ml, which varied from 100 -700 ml in group I and 219.5±115.7 ml varied from 120-500 ml in group II in this study. Majority (88%) of the group I patients had blood loss less than 500 ml and 78% in group II. Similarly, Walraven et al. (2005) has observed less than 500 ml blood loss 89%

and 88% in group I and group II respectively. Nisa et al. (2009), Boucher et al. (2004) and Choy et al. (2002) have also made almost identical observations.

In this current series it was observed that 14% of group I patients had required additional Oxytocin, whereas 24% of group II patients had required additional Oxytocin, which was higher in group II but not statistically significant ($p > 0.05$).

The mean hemoglobin level during pre-delivery of the present study subjects was found 9.9±1.7 gm/dl varied from 9 - 11 gm/dl in group I and 10.5±0.6 gm/dl varied from 9-12 gm/dl in group II. However, post-delivery the mean hemoglobin level was found 9.8±0.9 gm/dl varied from 9.2 – 12.3 gm/dl in group II. The mean hemoglobin (gm/dl) level was significantly ($p < 0.001$) higher in group II patients during pre-delivery but almost similar during post-delivery. Nasr et al. (2009) observed the mean hemoglobin level was 10.62±0.2 gm/dl in group I and 10.7±0.6/dl in group II. Similarly, Walraven et al. (2005) have showed the mean hemoglobin level was 10.0±1.4 gm/dl in group I and 10.2±1.3/dl in group II, which are comparable with the present study. Similar observations also made by Norstro et al. (1990), Su et al. (2007) and Ngan et al. (2007).

In this present study it was observed that no patients of group I required blood transfusion but 10% patients from group II required blood transfusion.

Regarding the cause of PPH of the study subjects it was observed in the present study that PPH developed due to uterine atony 4%, retained placenta 12% and genital tract trauma 12% in group I patients. In group II, PPH developed due to retained placenta 4% and genital tract trauma 4%. Similar observations made by Nasr et al. (2009), Bouwmeester et al. (2005), McDonald et al. (2004), Villar et al. (2002), Choy et al. (2002), Boucher et al. (2004).

The mean amount of bleeding of the current study was found 42.6±20.8 ml varied from 20-100 ml and 34.5±35.2 ml varied from 12-200 ml in group I and group II respectively, which is consistent with Wedisinghe et al. (2008), Ozumba et al. (2006) and Nasr et al. (2009).

Moreover, in a recent systematic review, Carroli et al. (2008) found that the overall prevalence of PPH (blood loss >500 ml) in different publications from 2003 to 2006 was 6.09% when the outcome was measured objectively, 7.23% when it was assessed subjectively and 5.4% when it was not specified. Nasr et al. (2009) reported in their study that patients needed blood transfusion 3.1% in group I and 1.6% in group II, which is lesser with the present study.

Conclusion:

This study concludes that Misoprostol has the potential, effective rectally stable drug with a rapid onset of action for prevention of postpartum hemorrhage. It has predictable side effects and a good safety profile. It is as effective as standard oxytocic drugs in preventing atonic postpartum hemorrhage. Though the study was limited to low-risk patients. However, Misoprostol has scope for use even in high-risk patients like Rh-negative blood groups where other oxytocics are contraindicated. Moreover, it holds promise for the obstetrician in rural areas to tide over, the "Third stage of labour" by effectively controlling blood loss.

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