ORIGINAL ARTICLE

Effectiveness of Per Rectal Misoprostol Versus Intramuscular Oxytocin for Prevention of Primary Postpartum Haemorrhage

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Abstract

Objective: To compare the effectiveness of per rectal misoprostol over oxytocin in primary postpartum haemorrhage (PPH).

Study Design: Randomised controlled trial study.

Place and Duration of Study: Gynaecology and Obstetrics Department, Unit IV, Bolan Medical Complex Hospital, Quetta, from September 2013 to February 2014.

Methodology: Emergency obstetric patients receiving per rectal misoprostol (800 µgm) were named as group 'A' and those receiving 10 units oxytocin intramuscularly were labelled as group 'B'. The patients were followed within 24 hours of spontaneous vaginal deliveries. Pads soaked were used to assess the amount of blood loss.

Results: A total of 1,678 patients were included in the study. The mean age of patients in group-A was 29.11 years while the mean age of patients in group-B was 29.16 years. One hundred and twenty-three (14.66%) patients in group-A and 120 (14.31%) patients in group-B had PPH. Among the total 1,678 patients, 243 (14.49%) had postpartum haemorrhage among whom 24 (9.88%) had major haemorrhage with a blood loss ≥1000 mL. Among the sub-group (839 patients) administered misoprostol had 123 (14.66%) patients with blood loss greater than 500 mL and the rest 716 patients (85.34%) had blood loss less than 500 mL. The sub-group administered oxytocin have 120 (14.31%) out of 839 patients with postpartum haemorrhage while 719 (85.69%) had blood loss less than 500 mL.

Conclusion: Active management of 3rd stage of labour with per rectal misoprostol administration was as effective as intra-muscular oxytocin. Both were equally effective to reduce PPH and the subsequent need for surgical interventions.

Key Words: *Postpartum haemorrhage. Misoprostol. Oxytocin.*

INTRODUCTION

Postpartum haemorrhage (PPH) is arguably the most preventable but still a major cause of maternal death in low-income countries.[1] PPH occurs in almost 4% of vaginal deliveries, and leads significant morbidity of about 1/4th of all the maternal deaths.[2,3] Blood loss of 500 mL or more in first 24 hours after child birth is defined as PPH by the WHO.[4] In developing countries like Pakistan, especially in Balochistan province, most women are anaemic. Poor health conditions are further aggravated by increased blood demand during pregnancy and blood loss during the third stage of labour.[5] Active management of the third stage with 10 units of intramuscular oxytocin, controlled cord traction, and uterine massage are standard care by the WHO.[6] Execution of WHO guidelines in Pakistan is difficult, owing to a lack of proper refrigeration for storing parenteral uterotonics, shortage of skilled personnel to administer, and non-availability of sterile syringes and needles. There is a need for safer, more effective and affordable, thermo-stable, and non-parenteral uterotonics.[6]

Misoprostol is an analog of prostaglandin E1 (PGE1) and has potent uterotonic action. Misoprostol is economical, easy to store without refrigeration, and has nominal adverse effects. The administration of misoprostol per rectal route has attracted the interest of researchers owing to its pharmacokinetic advantage of achieving the highest serum peak concentration.[7]

In most developing countries, 50% or more of deliveries are attended by unskilled providers at home.[10]. In addition, health facilities are often not adequately staffed or lack medicines that can address PPH.[11] These structural barriers are further complicated by difficulties in predicting who will develop PPH. Many women who develop PPH do not present with any of the risk factors typically associated with the complications.[8] Consequently, PPH is an obstetric complication that requires effective preventive interventions, tailored to the diverse needs of women and providers in resource-poor settings.

The prevention of PPH, particularly in resource poor-settings, where PPH is the leading cause of maternal mortality.[9] The authors reviewed the current strategies being implemented to prevent PPH, ranging from active management of the third stage of labour (AMTSL) in health facilities. The enormity of postpartum haemorrhage and the limitations in the use of oxytocin for the adequate preventive therapy were the basic rationales

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behind this study. Secondarily, our cultural setups of home deliveries have a marked role in grave morbidity as well as lack a consensus protocol for the choice of adequate preventive treatment of haemorrhage. Keeping in view the above mentioned factors, this study was conducted to compare the effectiveness of the per rectal misoprostol medication to the intramuscular oxytocin to control the blood loss as adequate preventive therapy.

METHODOLOGY

This randomised controlled trial study was conducted at Gynaecology and Obstetrics Department, Unit IV, Bolan Medical Complex Hospital, Quetta, from September 2013 to Februar 2014. Randomisation was done by lottery method. Approval to conduct the research was taken from the Medical Superitendent of the Bolan Medical Complex Hospital, Quetta. A total of 1,530 sample size calculated was 1678 (839 for each group), keeping anticipated population proportion for taking misoprostol as 40.5%[6] and anticipated population proportion for taking oxytocin as 50%,[6] confidence level 95%, and power of test 90%. All the patients, whether primiparous or multiparous and of any age in third stage of labour with spontaneous vaginal deliveries, were included in the study except patients with C-section in third stage of labour. Patients with mal-presentations like transverse lie are absolute indication for caesarean section, breach presentation, compound presentation, twins and triplets pregnancy, patients with placenta previa like type III, IV, placenta accreta, placental abruption, scar rupture, myomectomy (uterine cavity opened), patients with any comorbid conditions like coagulation disorders, DIC, cardiac diseases, diabetes, and anaemia, were excluded from the study. All of the above mentioned are confounding factors and can cause a biasness during the study. Informed consent were taken from the patient. The patients fulfilling the inclusion criteria were included into the study. Baseline investigations like blood counts, blood grouping, coagulation profile was done to exclude any kind of bleeding disorder. Patients' comfort and temperature maintenance were kept in consideration.

Patients were given misoprostol per rectal and oxytocin intramuscularly by lottery method to remove the personal biasness. Patients receiving misoprostol were named as group 'A' and those receiving oxytocin were labelled as group 'B'. Misoprostol per rectal were given in a dose of 800 µgm and oxytocin as 10 units intramuscularly. The patients were followed for 24 hours after spontaneous vaginal deliveries. Pads soaked were used to asses the amount of blood loss. Any patient needing surgical intervention for control of haemorrhage, were considered as treatment failure.

The data were entered and analysed on SPSS version 17. The quantitative variable like age was calculated by taking mean and standard deviation. For parity, ratios were calculated. Amount of blood loss, major and minor haemorrhage, was assesed and chi-square test was applied. P-value of <0.05 was considered significant.

RESULTS

A total of 1,678 patients were included in the study. Eight-hundred and thirty-nine patients each were included in group-A and group-B. The mean age of patients in group-A was 29.11 ±5.580 years. Minimum age of patients was 18 years, maximum age of patients was 42 years, and range of age of patients was 21 years. The mean age of patients in group-B was 29.16 ±5.538 years. Minimum age of patients was 18 years, maximum age of patients was 42 years and range of age of patients, was 20 years as shown in Table I.

Among the total 1,678 patients, 243 (14.49%) had a postpartum haemorrhage.

Among these 243 patients, 24 (9.88%) had major postpartum haemorrhage with a blood loss ≥1000 mL while 219 (90.12%) patients had minor postpartum haemorrhage with a blood loss ranging ≥500 to <1000 mL (Figure 1).

Out of 1,678 patients, 143 patients were in < 20 years of age group, 1,385 patients were in the 20 - 40 years of age group and 150 patients >40 years of age group, as shown in Table II. Among the different age groups, 45 patients <20 years of age had postpartum haemorrhage while 114 patients in the 20 - 40 years age group had a significant amount of blood loss. At age >40 years, 84

Table I: Distribution pattern on the basis of patients' age in the study groups.

Groups	Misoprostol	Oxytocin
Total number of patients (n)	839	839
Mean age of patients in years ± Std. deviation	29.11 ±5.58	29.16 ±5.54
Median age of patients in years	28	28
Minimum age of patients in years	18	18
Maximum age of patients in years	42	42
Range of age of patients in years	21	22

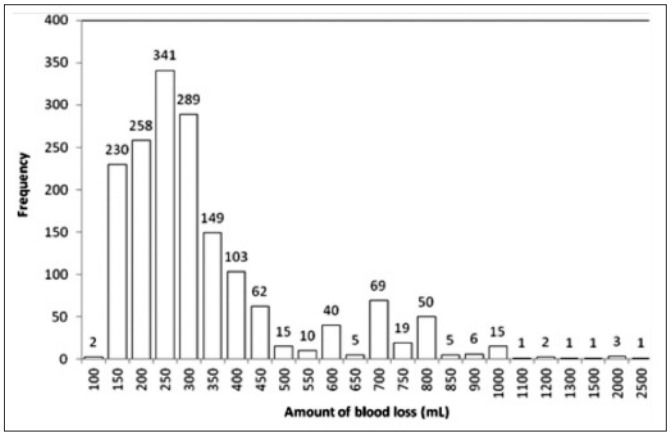

Figure 1: Sample frequency distribution amount of blood loss.

Table II: Comparison between mother parity with the risk of the occurrence of primary postpartum hemorrhage.

Parity	Blood Loss (mL)		Total	p-value
	<500	>500		
0-1	321 (84.25%)	60 (15.75%)	381 (100%)	<0.001
2-5	851(93.41%)	60 (6.59%)	911 (100%)	
>6	263 (68.13%)	123 (31.87%)	386 (100%)	
Total	1435 (85.52%)	243 (14.48%)	1678 (100%)	

patients had a significant blood loss with p-value of <0.001.

Effect of patient and risk associated for the occurance of PPH are given in Table II.

Total patient (1,678) were divided into two sub-groups with equal number of pateints (839 each). Amount of blood loss in sub-group administered with misoprostol, greater than 500 mL in 123 (14.66%), while 716 patients (85.34%) had blood loss, less than 500 mL. The sub-group administered with oxytocin had 120 (14.31%) patients with blood loss 500 mL, while 719 (85.69%) had no significant amount of blood loss.

In the sub-group administered with misoprostol, one out of 123 (1/123*100=0.81%) patient had eclampsia (tonic-clonic seizures). On the other hand, in the sub-group administered with oxytocin, 11 out of 120 (11/120*100=9.17%) patients had eclampsia (tonic-clonic seizures).

DISCUSSION

Maternal death is one of the most serious health problems for women of reproductive age in low-income countries. In Pakistan, almost 20,000 women died due to pregnancy and childbirth related issues.[15] WHO gives prevalence of PPH as 34% in Pakistan and cause of death in 27% with a home delivery in 65% of the cases. These figures are higher as compared to figures in industrialised countries, where it is quoted to be 2 - 11%. However, if blood loss is objectively measured, the incidence may rise to 20%. Postpartum haemorrhage (PPH) intensity and prevalence is severe in developing countries, especially in rural areas where women are malnourished and anaemic. Millennium Development Goals (MDGs), set by 189 countries in 2000, had the target to reduce the maternal deaths to three-quarters in 2015.[12] The leading cause of PPH are uterine atony, rupture uterus followed by genital tract tears, and retained placenta. Postpartum haemorrhage is preventable by the use of uterotonics.

Among the long list of uterotonics, oxytocin is preferred in hospital-based settings. Oxytocin is peptide chain hormone containing nine amino acids, discovered by Sir Henry Dale and was synthesised by Du Vigneaud, in 1953. The mechanism of the contraction of uterine smooth muscle during labour is enhanced by the action of oxytocin by changing the activity of the enzyme called myosin light chain kinase (MLCK). Intracellular calcium, the levels of which are controlled by voltage gated channels and releases the calcium from the sarcoplasmic reticulum that binds to the calmodulin and stimulates conversion of MLCK-P to MLCK, which in turn phosphorylates myosin and initiates smooth muscle contraction.[16] On the other hand, misoprostol is a methyl ester, a synthetic analogue of natural prostaglandin E1 additionally methylated at C16. After absorption, it undergoes rapid de-esterification to its biologically active metabolite, misoprostolic acid (MPA).

However, the use of oxytocin has few limitations, especially in resource-poor conditions where the medical facilities are lacking and attendants are untrained. Moreover, oxytocin also requires cool storage and sterile equipment for its routine use. Another uterotonic, misoprostol, an E1 prostaglandin analogue, originally registered to prevent the ulcer, has also the prosperities to induce uterine contractions. From various studies, misoprostol has proven to be effective in preventing and treating postpartum haemorrhage (PPH) resulting from the failure of the uterus to contract fully after delivery. It is formulated as a tablet, stable at ambient room temperature, widely available and affordable; and does not require any special skills, equipment, or facilities for its use. WHO[14] and the American College of Obstetricians and Gynecologists (ACOG)[13] acknowledge that misoprostol is effective in treating PPH and recommend that it can be used for treatment in situations where standard uterotonics are unavailable or unfeasible to use.

Primary postpartum haemorrhage is defined as blood loss of more than 500 mL following vaginal delivery or caesarean woman while pregnant or within 42 days of section. The results of the present study showed that both the agents were equally effective in preventing the PPH as there was no significant difference between the drugs. The average blood loss in two groups was 322 ±6.9 and 337 ±7.3 mL in misoprostol and oxytocin, respectively. The preventive measures adopted by administering the agents were effective in women 14.66% and 14.31% in misoprostol and oxytocin groups, respectively. However, the prevalence of PPH was more frequent than a study conducted in Abbottabad where the frequency of PPH was calculated as 7.1%.[17] This difference may be due to difference in sample size, health of the women, preventive measures as well as other geographical factors. Side effect of misoprostol were not prominent in this study as per rectal misoprostol is known to have a steady serum rise with lower peak serum concentration and longer half-life. This may account for the low side effect profile. The longer half-life of rectally administered misoprostol equally has a beneficial effect of prolonging uterine contraction and preventing a delayed haemorrhage.

Another important factor that plays a major role in PPH is parity. Grand or multi-parity is linked with variety of complications due to depletion of nutrients such as Fe, Ca, vitamins, uterine damage, hypertension, unstable lie, mal-presentation, late engagement of fetal head, rapid labours, macrosomia, preterm labour, and post-partum haemorrhage (PPH). In Pakistan, multiparous and grand-multiparous is still common as the results of present study depict that 54% and 23% of the total women were multiparous and grand-multiparous, respectively. Moreover, the frequency of PPH increased within grand-multiparous mothers. There was also no significant difference among the two drugs to prevent PPH in relation to the parity. In terms of the minimal risk concept, the safest babies to have are the second, third and the fourth.[18] Similar results were observed in the given study that women with multi-parity (6.5%) risk of PPH. Studies investigating specific risk factors for PPH have demonstrated that nulliparous women have elevated rate of PPH compared to those who are multiparous.[19-21] In the present study, when primiparous women were compared with multiparous and grand-multiparus women, maximum PPH was observed in grand-multiparous (34%) followed by nulliparous (16%) and multiparous with minimum PPH (7%). Bais *et al.*[22] study revealed that in nulliparous women an abnormal third stage labour, retained placenta, and to some extent high birth weight and perineal damage were the contributing factors in PPH.

One of the other factors that can have an effect on PPH is age of the women. Moreover, age factor is related to the parity. Women with age ≥40 mostly belong to the group grand-multiparous, so these mothers are at high risk of PPH. The results of the present study showed that 56% mother in age group ≥40 years had marked PPH. A similar trend was observed as in parity that most nulliparous women belonged to group with age ≤20 years, as 31% of the women belonging to this group had more than 500 mL blood loss. The mother at minimum risk was to that aged between 20 - 40 years with 8% risk of PPH.

CONCLUSION

Active management of third stage of labour is associated with reduce risk of postpartum haemorrhage and subsequently reduce the need for surgical interventions.

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