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ORIGINAL ARTICLE

Comparison the Effectiveness of Oxytocin and Misoprostol in Prevention of Primary Post-Partum Haemorrhage

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ABSTRACT

Introduction: Postpartum haemorrhage is one of the leading causes of maternal mortality. Maternal Mortality globally is estimated as 599.00 deaths per year, a ratio of 400 maternal deaths per 10,000 live births. The aim of this study was to compare the effectiveness of oxytocin and misoprostol in prevention of primary post-partum haemorrhage

Material and Method: It was Randomized Controlled Trial, which was conducted in the department of Obstetrics and Gynaecology, Hospital, Peshawar, between 14th March 2020 to 22 April 2022). The sample size was 100(50 in each group) Using 4% of PPH in misoprostol group, 24% of PPH in oxytocin group, 95% confidence level and 90% power of test under WHO software for sample size determination.

Results: A total of 100 patients of primary post-partum haemorrhage were observed, which were divided in two equal groups A & B. Patients in Group A were managed with misoprostol while patients in group B will be subjected to oxytocin. Gravida wise distribution shows that out of 50 patients 22(44%) were gravid less than or equal to one,18(36) patient have 2-5 and 10(20%) were more than 5 while group B contains 25(50%) less than or equal to one, 17(34%) patients 2-5 and 8(16%) have gravid more than 5. Gravida distribution among the groups was insignificant with p-value=0.802. Average age was 27.82 years+4.56SD with range of 20-36 years. Group A contained 13(26%) patients in less than or equal to 25 years, 30(60%) patients 26-35 years and 7(14%) patients having ages of more than 35 years. While group B contained 18(36%) patients in less than or equal to 25 years, 28(56%) in 26-35 years and 4(8%) patients with age more than 35 years. The age distribution among the group was also insignificant with p-value 0.429. Efficacy wise distribution was significant with p-value = 0.021. Group A showed 47(94%) efficacy while non-effective in 3(6%) patients. Similarly, Group B showed 39 (78%) efficacy while non effective in 11(22%) patients. The misoprostol has greater efficacy than oxytocin. Age wise distribution of drug-efficacy shows that efficacy was almost same in all age groups. The patients having less than or equal to 25 years of age have shown efficacy in 12(92.3%) patients while 1(7.7%) patients being non-effective. Patients with 26-35 years of age have shown efficacy in 28(93.3%) of patients and 2(6.7%) have shown no efficacy. Similarly, 7(100%) patients have shown efficacy and no patients have no efficacy, with age more than 36 years of age. The same pattern was followed in group B, although age wise efficacy was insignificant in both the groups with p-value=0.765 and 0.987 respectively. The prevention of PPH, particularly in resource poor settings, where PPH is the leading cause of maternal mortality The enormity of postpartum haemorrhage and the limitations in the use of oxytocin for the adequate preventive therapy were the basic rationales 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.

Conclusion: Misoprostol is more effective as compared to oxytocin in prevention of primary postpartum hemorrhage.

Keywords: Primary Postpartum haemorrhage, Cervical tears, Vaginal tears, oxytocin, Misoprostol, efficacy

INTRODUCTION

Post-partum haemorrhage (PPH) is an important cause of maternal morbidity and mortality especially in developing countries. PPH leads to severe post-natal anemia and hemorrhagic shock requiring blood transfusion and major surgical interventions. There are some measures and interventions to minimize postpartum hemorrhage. The primary cause of PPH is uterine atony [in] 70% of cases.[1] It occurs in up to 18% of births, causing deaths in 25-43% of pregnant women or 20 million deaths each year worldwide.[2] Active treatments of the third stage of labour[3] includes administration of uterotonic drugs, early cord clamping, controlled cord traction for placental delivery and fundal massage.[3] Compared to expectant management, active management decreases the incidence of PPH by 68%. Oxytocin is often not available in low resource settings due to parenteral administration and maintenance of cold chain which is necessary for their potency, which is not always possible in some peripheral centers due to non-availability of sterile needles, syringes or refrigerating equipment's. Misoprostol is prostaglandin E1 analogue first introduced as an anti-inflammatory drug for peptic ulcer disease. Later on it gained popularity as an effective modality for cervical ripening. It is also an active uterotonic agent as an option for pph prevention in low-resource settings because of its thermos stability, cost-effectiveness and ease of administration.[4] Compared with conventional oxytocic's for prevention of PPH, oral misoprostol was associated with a higher risk of severe PPH (RR 1.32; 95% CI 1.16 to 1.51).[5]

According to a study by Fauzia Anbreen in 2010, a low rate of PPH was demonstrated with misoprostol as determined by blood loss >1000ml which was 4% in misoprostol group and 24% in oxytocin group (p<0.001).[6]It is, however, as yet unclear which gives the best balance of efficacy and safety Given the relative effectiveness of misoprostol for PPH, the tendency has been to use high doses. There are, however, potential dangers in this. Further research is needed to assess the potential beneficial and harmful effects of misoprostol and to determine safe and effective dose.[7] A recent study shows that misoprostol might be a first line treatment alternative for post-partum haemorrhage in cases where use of oxytocin is not feasible.[8]The risk factors for cervical and vaginal tears in cases of primary postpartum haemorrhage are, foetal macrosomia (26%)[9],cervical cerclage (14%)[10],vacuum vaginal deliveries(18.7%), forceps deliveries (15.9%) and induction of labour(68.7%)[11].Obstetric hemorrhage remains one of the major causes of maternal death in both developed and developing countries. In the 2003-2005 report of the UK confidential enquiries into maternal deaths, hemorrhage was the third highest direct cause of maternal death (6.6 deaths/million maternities with a rate similar to previous triennium.[12]Hemorrhage emerges as the major cause of severe maternal morbidity in almost all near miss audits in both developed and developing countries.[13]Primary postpartum hemorrhage involving an estimated loss of 500-1000ml of blood (and in the absence of clinical signs of shock) should prompt basic

measures (close monitoring, group and screen) to facilitate resuscitation should it become necessary.[13]Maternal deaths specifically from lower genital tract bleeding as the cause of post-partum hemorrhage are rare in developed countries. The 2000-2002 United Kingdom confidential enquiries reported only one death from this cause. Worldwide, no accurate figures exist but it is likely that the numbers are significant, particularly where there is significant co-morbidity and a poorly resourced maternity infra structure.[14]Cervical and vaginal lacerations are a known cause of primary post-partum hemorrhage. Although cervical lacerations occur in more than half of the vaginal deliveries. They are less than 0.5 cm in length and rarely require repair.[15]Increase bleeding when persists in the presence of a firmly contracted uterus in a case of PPH, laceration of cervix, lower uterine segment or vagina is highly suspected.[16]This study aims to compare the effectiveness of oxytocin and misoprostol in prevention of primary post-partum hemorrhage and will highlight the one more effective. This study will provide us with the better method of prevention of primary post-partum hemorrhage in our region. If it is found that misoprostol is more effective, then we will recommend it for prevention of primary post-partum haemorrhage.

MATERIAL AND METHODS

It was Randomized Controlled Trial, which was conducted in the department of Obstetrics and Gynaecology, Hospital, Peshawar, between 14th March 2020 to 22 April 2022). The sample size was 100(50 in each group) Using 4% of PPH in misoprostol group, 24% of PPH in oxytocin group, 95% confidence level and 90% power of test under WHO software for sample size determination. All labouring patients a ge 19 to36 years having spontaneous onset of labour, with normal duration of labour and having normal vaginal delivery were included in the study. All the Patient having preterm labor, Patient having chorioamnionitis and lower segment C-section, Patient having polyhydramnios, Multiple pregnancies, Induction of labour and Prolonged labour were excluded from the study.

The study was conducted after approval from hospital's ethical and research board. The purposes of the study were explained to all subjects and written informed consent was obtained. All subjects meeting the inclusion criteria were included in the study. Detailed history and clinical examination was done for all subjects followed by routine investigations. All subjects were followed under supervision of an expert obstetrician to determine the effect of misoprostol and oxytocin in preventing primary PPH. PPH was measured by blood loss estimated by pad test, Pre weighed pads were given to the patient for next 24 hours. All the soaked pads were weighed in the weighing scale which were then subtracted from the initial weight of dry pads. A hundred-gram increase in weight were considered to be equivalent to 100ml of blood loss (assuming specific gravity of blood equivalent to 1gm/ml). m hemoglobin concentration. All above mentioned information were recorded in designed preform. Strictly exclusion criteria were followed to control confounders and bias in the study results.

Data were entered and analyzed using SPSS 22.0. Categorical variables were described in terms of frequencies and percentages. Quantitative variables were described as mean ± standard deviation. Chi square test were applied to compare effectiveness. A p-value ≤ 0.05 will be considered statistically significant. Effectiveness were stratified among age, parity and gravid to see modifications. Post stratification Chi-square test was applied. All results were presented in tables and charts.

RESULTS

A total of 100 patients of primary post-partum haemorrhage were observed, which were divided in two equal groups A & B. Patients in Group A were managed with misoprostol while patients in group B will be subjected to oxytocin. Gravida wise distribution shows that out of 50 patients 22(44%) were gravid less than or equal to one,18(36) patient have 2-5 and 10(20%) were more than 5 while group B contains 25(50%) less than or equal to one, 17(34%) patients 2-5 and 8(16%) have gravid more than 5. Gravida distribution among the groups was insignificant with p-value=0.802. (Table 2)

Table 1: Gravida Wise Comparison of Both the Groups

Gravida	Group		Total	P-value
	A	B		
<= 1.00	22	25	47	0.802
	44.0%	50.0%	47.0%	
2.00 - 5.00	18	17	35	
	36.0%	34.0%	35.0%	
6.00+	10	8	18	
	20.0%	16.0%	18.0%	
Total	50	50	100	
	100.0%	100.0%	100.0%	

Average age was 27.82 years+4.56SD with range of 20-36 years. Group A contained 13 (26%) patients in less than or equal to 25 years, 30(60%) patients 26-35 years and 7(14%) patients having ages of more than 35 years. While group B contained 18(36%) patients in less than or equal to 25 years, 28(56%) in 26-35 years and 4(8%) patients with age more than 35 years. The age distribution among the group was also insignificant with p-value 0.429. (Table 3)

Table 2: Age Wise Distribution in Both the Groups

Age (in years)	Group		Total	p-value
	A	B		
<= 25.00	13	18	31	0.429
	26.0%	36.0%	31.0%	
26.00 - 35.00	30	28	58	
	60.0%	56.0%	58.0%	
36.00+	7	4	11	
	14.0%	8.0%	11.0%	
Total	50	50	100	
	100.0%	100.0%	100.0%	

Efficacy wise distribution was significant with p-value = 0.021. Group A showed 47(94%) efficacy while non-effective in 3(6%) patients. Similarly, Group B showed 39(78%) efficacy while non effective in 11(22%) patients. The misoprostol has greater efficacy than oxytocin. (Table 4).

Table 3: Efficacy Wise Distribution of Patients in Both the Groups

Efficacy	Groups		Total	P-value
	A	B		
Yes	47	39	86	0.021
	94.0%	78.0%	86.0%	
No	3	11	14	
	6.0%	22.0%	14.0%	
Total	50	50	100	
	100.0%	100.0%	100.0%	

Table 5: Gravida Wise Distribution of Efficacy in Both the Groups

Groups	Efficacy	Gravida		
		<= 1.00	2.00 - 5.00	6.00+
A	Yes	21	17	9
		95.5%	94.4%	90.0%
	No	1	1	1
		4.5%	5.6%	10.0%
	Yes	20	13	6
B		80.0%	76.5%	75.0%
	No	5	4	2
		20.0%	23.5%	25.0%
	P-Value	0.2507	0.3021	0.8235

Age wise distribution of drug-efficacy shows that efficacy was almost same in all age groups. The patients having less than or equal to 25 years of age have shown efficacy in 12(92.3%) patients while 1(7.7%) patients being non-effective. Patients with 26-35 years of age have shown efficacy in 28(93.3%) of patients

and 2(6.7%) have shown no efficacy. Similarly, 7(100%) patients have shown efficacy and no patients have no efficacy, with age more than 36 years of age. The same pattern was followed in group B, although age wise efficacy was insignificant in both the groups with p-value=0.765 and 0.987 respectively. (Table 5).

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 industrialized 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 anemic. 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 synthesized 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, misoprostol 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. WHO14 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.

CONCLUSION

Post-partum haemorrhage is a serious obstetrical emergency. Prompt resuscitation and identification of the causes of bleeding should be performed by a multidisciplinary team approach. Our study suggests that the use of misoprostol is more effective for decreasing the amount of blood loss, thereby avoiding a PPH, and is associated with mild and self-limiting side effects. Misoprostol is cost effective and easily administered and therefore may be considered for use in low resource areas when oxytocin is unavailable.

REFERENCES

1. Say L, Chou D, Gemmill A, Tunçalp Ö, Moller AB, Daniels J, et al. Global causes of maternal death: A WHO systematic analysis. Lancet Global Health 2014; 2: e323-e33.
2. Begley CM, Gyte GML, Devane D, McGuire W, Weeks A. Active versus expectant management for women in the third stage of labour. Cochrane Database Syst Rev 2015; 3.
3. 3. Gohil JT, Tripathi BA. Study to compare the efficacy of Misoprostol, Oxytocin, Methyl-ergometrine and ErgometrineOxytocin in reducing blood loss in active management of 3rd stage of labour. J Obstet Gynaecol India 2017; 61:408-12.
4. Ngwenya S. Postpartum hemorrhage: Incidence, risk factors, and outcomes in a low-resource setting. Int J Womens Health 2018: 2:647-50.
5. 5. Uncu Y, Karahasan M, Uyaniklar Ö, Uncu G. Prophylactic misoprostol for the prevention of postpartum hemorrhage: A randomized controlled trial. Eur Rev Med Pharmacol Sci 2019; 19:15-22.
6. World Health Organization (WHO). WHO recommendations for the prevention of postpartum haemorrhage. WHO, Geneva, Switzerland; 2017;19:15-22.
7. 7. Rajaei M, Karimi S, Shahboodaghi Z, Mahboobi H, Khorgoei T, Rajaei F. Safety and efficacy of misoprostol versus oxytocin for the prevention of postpartum hemorrhage. J Pregnancy 2018; 1-4 .
8. Hancock A, Weeks AD, Lavender DT. Is accurate and reliable blood loss estimation the “crucial step” in early detection of postpartum haemorrhage: An integrative review of the literature. BMC Pregnancy Childbirth 2019; 15:230.
9. Abdul-Kadir R, McLintock C, Ducloy AS, El-Refaey H, England A, Federici AB, et al. Evaluation and management of postpartum hemorrhage: Consensus from an international expert panel. Transfusion 2020; 54:1756-68.
10. Prata N, Bell S, Weidert K. Prevention of postpartum hemorrhage in low-resource settings: Current perspectives. Int J Womens Health 2017; 5:737-52.
11. Callaghan WM, Kuklina EV, Berg CJ. Trends in postpartum hemorrhage: United States 1994-2006. Am J Obstet Gynecol 2018; 202:353.
12. Cohen RL, Alfonso YN, Adam T. Country progress towards the millennium development goals: Adjusting for socioeconomic factors reveals greater progress and new challenges. Glob Health 2014; 10:67.
13. American College of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 76: Postpartum hemorrhage. Obstet Gynecol 2016; 108:1039-47.
14. World Health Organization. WHO guidelines for the management of postpartum haemorrhage and retained placenta. Geneva: WHO; 2019. Available at: http:// whqlibdoc.who int/publications/ 2019/9789241598514_eng.pdf.
15. Cook L, Roberts I. Woman trial collaborators postpartum hemorrhage and the woman trial. Int J Epidemiol 2019; 39: 949.
16. Dyer RA, Dyk D, Dresner A. The use of uterotonic drugs during caesarean section. Int J Obstet Anesth 2018; 19: 313-9.
17. Naz H, Sarwar I, Fawad A, Un-Nisa A. Maternal morbidity and mortality due to primary PPH-experience at Ayub Teaching Hospital Abbottabad. J Ayub Med Coll Abbottabad 2018; 20: 59-65.