Research Article

Comparison of Sublingual & Per Rectal Misoprostol versus Oxytocin in the Prevention of Postpartum Hemorrhage

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Abstract:

Background: Postpartum Hemorrhage (PPH) is the most common reason of maternal death globally. Misoprostol and oxytocin are two first line and effective management protocols. But controversies exist in literature. For that matter, this study was conducted.

Objectives: To compare the frequency of postpartum hemorrhage with per rectal misoprostol in relation to intramuscular oxytocin in females undergoing normal vaginal delivery at term.

Methods: This randomized controlled trial was conducted in Department of Obstetrics & Gynaecology, Sheikh Zayed Hospital, Lahore from 01-01-2019 to 01-12-2019. Patients were divided randomly into equal halves through the lottery method. Group A received Misoprostol and group B received Oxytocin. Medications were administered within one minute of clamping and the cutting of cord. During 24 hours, soaked pads were evaluated for blood loss and total blood loss was calculated. If blood loss>500ml, then PPH was labeled.

Results: Mean age of women in Group A and in Group-B were 29.11±6.67 and 29.23±6.70 years. The mean gestational age for Group A came as 39.60±1.78 weeks and for Group-B, it was 39.53±1.72. In Group-A 24(15.7%) and in Group-B 59(38.6%) women suffered from PPH. PPH was significantly lower in comparison to the women in Group-B. P-value=0.000.

Conclusion: Results of this study showed that use of per rectal Misoprostol is more suitable and effective in the prevention of Post-partum hemorrhages compared to oxytocin in females undergoing normal vaginal delivery at term.

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Introduction:

In low-income countries, the major cause of death is postpartum hemorrhage, which is at the same time the most preventable complication[1]. Postpartum hemorrhage is defined as, loss of almost more than 500 ml to 1,000 ml of blood during the 1st 24 hours just after the childbirth[2]. Around 4% of vaginal deliveries end in PPH, and then it leads to significant number of mortality cases of about one fourth of entire maternal deaths[3,4]. The most common clinical presentation incudes, an increased breath rate and increased heart rate along with feeling faint upon standing. If situation worsens by more blood loss then the women may feel cold, with sever hypotension and ultimately may become fidgety or unconscious[5].

There is an estimation that 287,000 maternal deaths occur throughout the world in which 85% occur in middle and under developed countries[1]. While 25% of these deaths are due to the postpartum hemorrhage (PPH) during the 24th time of delivery[6].

Hence, in regular practice the use of Oxytocin is for the prevention of PPH. This hormone stimulates uterine contractions and it limits uterine bleeding just after

birth. The use of oxytocin has generally been limited in low-income countries. However, a number of factors are responsible for this. Which includes the cold chain storage, administration by a skilled personnel, and a strict requisite for sterile needles and syringes[6].

Some latest research has begun to challenge these limitations. Misoprostol, a drug of choice as synthetic prostaglandin, which have uterotonic properties. This drug has been suggested as an alternative method for the prevention of PPH. Especially for those setting where oxytocin could not be used. According to some recent studies, it has a number of advantages over oxytocin. Which includes its ability to be administered by oral route along with a long shelf life at even at room temperature. Moreover, the other way of administration of misoprostol is sublingually, which enables this drug to have greater bioavailability because it avoids first-pass metabolism. It also has with more rapid onset of action[7]. Due to These benefits of this drug the civil society organizations in Uganda is using misoprostol as a harmonizing drug to oxytocin in prevention of PPH. In spite of these benefits, most agencies deliberate about the sublingual misoprostol to be a second-line alternative in comparison to the injectable uterotonics Oxytocin. This is due to the lack of evidence about its efficiency in the actively managing the third stage of labor[7,8].

Although some of the studies have compared the use of injectable oxytocin with misoprostol. The relative efficacy of sublingual or per rectal misoprostol contrasted with oxytocin remains mostly unidentified. The reason was that previous studies have only focused on oral administration of misoprostol by less skilled birth attendants. Who evaluated oral as opposed to sublingual per rectal administration of misoprostol, they evaluated it with suboptimal dose[9,10].

One a randomized trial showed that percentage of PPH was 33% with oxytocin and 19% with misoprostol in females after delivery. The difference was significant (p=0.005)[11]. But another study showed that percentage of PPH was 6% with oxytocin and 4% with misoprostol in females after delivery. But the difference was insignificant (p=0.886)[12].

The rationale for conducting this study was to compare the frequency of PPH with sublingual per rectal misoprostol versus intramuscular oxytocin in females undergoing normal vaginal delivery at term. In routine, misoprostol and oxytocin, both are used randomly in local setting for prevention of PPH. According to literature, misoprostol is most effective as compare to the oxytocin in preventing PPH. Furthermore, PPH is a common event in this area, but there is no local research to determine if misoprostol is more effective for preventing excessive blood loss, As a result, this study is being designed to investigate and treat more precisely based on the literature that will be available after this study.

Methods:

This randomized controlled trial was conducted from 1st Jan to 1st December 2019 in the Gynecology and Obstetrics department of Sheikh Zayed Hospital, Lahore. Permission from the Ethical Review Board of the hospital was obtained to conduct this study. Informed written consent was also attained from patients.

The total Sample size was of 306 cases in which 153 cases for each group was calculated. The power of test was kept as 80% along with the 5% level of significance. The expected percentage of PPH was taken as 33% with oxytocin and 19% with misoprostol in females undergoing normal vaginal delivery at term.

Total 306 female patients with age of 18-40 years, parity < 5presenting at gestational age > 37 weeks (on LMP) undergoing normal vaginal delivery (labour pain> 3 contractions in 10 minutes, cervical dilatation > 4cm and Bishop score > 5) patients were included from the study. Those patients were excluded from the study like Females with chronic or gestational hypertension (BP ≥140/90mmHg), preeclampsia (BP≥140/90mmHg plus proteinuria≥+1 on dipstick method), eclampsia (convulsion with BP≥140/90mmHg), chronic or gestational diabetes (BSR>186mg/dl), Anemic (Hb< 10g/l), ALT>40IU, AST>40IU, creatinine>1.2mg/dl and Asthma or cardiac problem females.

All patients were selected randomly and then divided into two equal groups by lottery method. Group A received Misoprostol and group B received Oxytocin. In group A single dose of 400 mcg misoprostol sublingually and 400 per rectal. In group B, 10 units oxytocin intramuscularly followed by 40 units of oxytocin in 1000 ml of ringer lactate was given. Medications were

administered during the time of 1 minute of clamping and cutting the cord. After delivery, females were shifted in post-delivery wards and were followed-up there for 24 hours. During 24 hours, soaked pads were evaluated for blood loss and total blood loss was calculated. If blood loss>500ml, then PPH was labeled (as per operational definition). All the data were entered in a pre-formed proforma.

Data were entered in SPSS 23. Age, gestational age and parity were taken as mean and standard deviation. Categorical data like PPH were presented as frequencies & percentage. Both groups were compared by Chi square test. Different variables like age, gestational age and parity was measured through stratification. Post-stratification along with the Chi square test was applied to see their effect on outcome variables in each groups. P-value≤0.05 was taken as significant.

Results:

In our study, total 306 females included. Group A received Misoprostol and group B received Oxytocin. The mean of women in Group A and in Group B 29.11±6.67 and 29.23±6.70 years. In Group A, the mean gestational age of women was 39.60±1.78 and for Group B it was 39.53±1.72 weeks. The mean blood loss in Group-A women was 458.25±79.34 and in Group-B it was 506.83±96.48.

The incidence of PPH was significantly lower in group A as compared to group B with p-value <0.001. The incidence recorded in two groups was 15.7% and 38.6% respectively. (Figure 1)

Women in the age group 18-25 and 26-32, both had

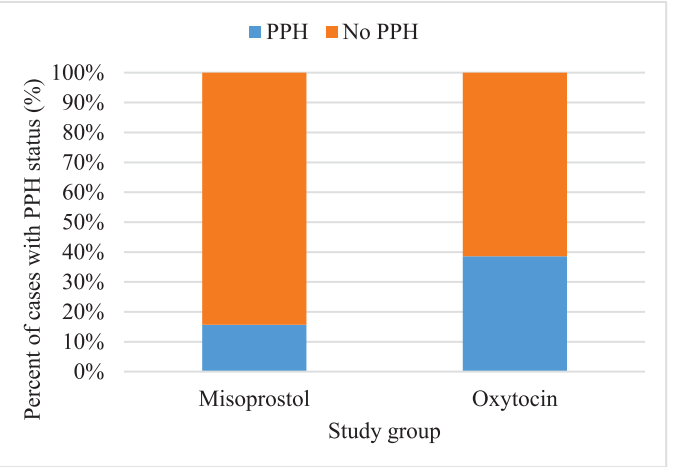

Figure 1: *Incidence of post-partum hemorrhage by treatment groups*

significantly lower incidence of PPH in group A while there was no significant difference for the age group 33–40, the difference was found insignificant with p-value 0.331. With respect to gestational age the group A showed significantly lower incident in both, i.e., the gestational age <39 weeks and > 39 weeks with p-values 0.001 and 0.002 respectively. For each parity the incidence of PPH was lower in group A but the women with parity 2 and 3 had significant difference while other parity groups had insignificant differences. Overall the age, gestational age or parity had no significant association with postpartum hemorrhage as the PPH incidence was always lower in group-A for each stratified group, either significant or insignificant.

Discussion:

In reproductive age, the maternal death is one of the most severe health problems in under developed coun-

Table 1: *Incidence of post-partum hemorrhage and comparison between two treatment groups by age, gestational age and parity*

Variable	Categories	Group A (Misoprostol)		Group B (Oxytocin)		P value
		PPH	No PPH	PPH	No PPH	
Age	18 - 25	5(9.8%)	46 (90.2%)	23(46.9%)	26 (53.1%)	<0.001
	26 - 32	9 (17.3%)	43 (82.7%)	20 42.6%)	27 (57.4%)	0.006
	33 - 40	10 (20%)	40 (80%)	16 (28.1%)	41 (71.9%)	0.331
Gestational Age	37 - 39	9(12.9%)	61 (87.1%)	27 (37.5%)	45 (62.5%)	0.001
	40 - 42	15 (18.1%)	68 (81.9%)	32 (39.5%)	49 (60.5%)	0.002
Parity	Primary	5 (20.8%)	19(79.2%)	14 (41.2%)	20 (58.8%)	0.104
	1	3 (12%)	22 (88%)	11 (31.4%)	24 (68.6%)	0.079
	2	6 (17.1%)	29 (82.9%)	11 (40.7%)	16 (59.3%)	0.039
	3	4 (12.5%)	28 (87.5%)	14 (48.3%)	15 (51.7%)	0.002
	4	6(16.2%)	31(83.8%)	9 (32.1%)	19 (67.9%)	0.131

tries and Post-partum hemorrhage (PPH) is a foremost cause of maternal death. It accounts for about 100 000 women deaths each year[13]. The prevalence of PPH is 34% in Pakistan and home delivery accounts for 27% of these cases. Postpartum hemorrhage (PPH), especially in rural areas of underdeveloped countries is more common, where women are mostly anemic and malnourished[14].

There are many foreign and a very few local studies which have observed different routes of uterotonic drug administration and blood loss pattern with these drugs. A local study from Pakistan showed misoprostol use was as operational as intramuscular oxytocin for management of PPH[14]. Bijoy Kumar Dutta conducted a double blind study which showed misoprostol in 600 microgram rectally is less effective as compare to intramuscular oxytocin in 10 IU dosage. They conducted this study on low risk patients[15]. This study was contradictory to our study, which has observed rectally administered misoprostol more affective.

A systematic review compared the side effects of both drugs that are used to prevent PPH. They found similar blood loss ≥500 mL ($p > 0.05$) but considered misoprostol as more advantageous than oxytocin in preventing PPH. This study was in coherence with our study[16].

In another study, about 800μg rectal misoprostol plus I ampoule of saline was given to A group and 5 IU of oxytocin in 5ml lactated ringer solution was given as along with rectal placebo to group B. They observed that there is not significant differences in the intraoperative bleeding and post partum hemorrhage cases[17].

According to some studies, Misoprostol has been claimed to be effective for preventing PPH when given sublingually[18]. It is an easily available medicine in the form of tablet that is also stable at room temperature. Moreover, it is inexpensive, and does not necessitate any exceptional equipment, skills and facilities to use. Hence according to WHO, Misoprostol is effective in treating PPH, where standard uterotonics are unfeasible to use.

Conclusion:

This study concluded that the frequency of postpartum hemorrhage with the use of per rectal Misoprostol is less as compared to intramuscular oxytocin in females undergoing normal vaginal delivery at term.

Ethical Approval: Given

Conflict of Interest: The authors declare no conflict of interest.

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