Original Article

Safety and efficacy of 600ug sublingual Misoprostol versus 10 U intramuscular Oxytocin for management of third stage of labor

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Objective: To compare the safety and efficacy of Misoprostol with Oxytocin for management of third stage of labor.

Methodology: This randomized control trial was conducted at Department of Gynecology and Obstetrics, Cantonment General Hospital, Rawalpindi, Pakistan from May to Oct 2015. A total of 212 singleton pregnant women were selected. Women were allocated to either group using simple computer generated randomization table. Group I received 10 U intramuscular Oxytocin while group II received 600ug sublingual Misoprostol. Primary outcome measures were severity of primary postpartum hemorrhage, amount of blood loss and side effects of drugs.

Results: The mean blood loss was 303.50±225.35 in group I and 271.30±206.205 in group II (p=0.035). The average drop in hemoglobin was 0.84±0.78 in group I and 0.81±0.79 in group II (p=0.980). There is no association in two groups with regard to PPH, repeat dose, complications and blood transfusion (p=0.86).

Conclusion: Misoprostol was better than Oxytocin regarding average blood loss for the management of third stage of labor. (Rawal Med J 201;44:137-140).

Keywords: Misoprostol, oxytocin, prevention, postpartum hemorrhage.

INTRODUCTION

Postpartum hemorrhage (PPH) is one of the leading causes of maternal mortality worldwide. Its incidence has been reported as 1-5%.[1] Majority of these deaths are preventable (75-80% occur because of uterine atony) and occur in low resource settings. Active management of third stage of labor has been shown to effectively reduce PPH.[2,3]

Misoprostol reduces the risk of moderate PPH (around 500ml) by 50%,[4] reduces the risk of major PPH (>1 liter) by 80%.[4] It is particularly suitable at the community level due to its ease of administration and storage.[5,6] Only in retained placenta, it has not found to be effective.[7] Several routes and doses of Misoprostol have been explored.[8-15] Sublingual route has the added advantage of earlier absorption, rapid peak concentration and avoidance of 1st pass effect. These features are typically useful for prevention of PPH.

METHODOLOGY

This randomized control trial was conducted at Department of Gynecology and Obstetrics, Cantonment General Hospital, Rawalpindi, Pakistan from May to Oct 2015. An approval of the study was obtained from the hospital ethical committee. A written informed consent was obtained from all women participating in the study. Sample size was calculated using mean blood loss as the test variable.[15] Average blood loss in Oxytocin group: 114.28±26.75, Average blood loss in Misoprostol group: 149.5±30.78 level of significance: 5% and power of test: 99%; sample size came to be at least 40 in each group. Drop in hemoglobin of 0.31±0.16 in group I and 0.49±0.21 in group II. And 8% prevalence of PPH were considered.

All women with singleton pregnancy, in cephalic presentation in spontaneous or induced labor were included in the study. Cases of placenta previa, placental abruption, previous LSCS, macrosomia (defined as estimated fetal weight >4 kg) and polyhydramnios (defined as amniotic fluid index >24) were excluded. Women diagnosed with asthma were also excluded.

A simple two drug randomization table was generated from website www.randomization.com. The drugs were placed in numbered envelops according to the generated table. These were placed in ascending numerical order in the labor room. Once a woman fulfilled the eligibility criteria, the envelope with the smallest number was opened and drug administered accordingly at the time of delivery of anterior shoulder. Women receiving Oxytocin were put in group I while those receiving Misoprostol were put in group II.

PPH was diagnosed by visual assessment of blood loss (>500 ml in vaginal delivery). A pictoral visual assessment chart described by Boss et al.[16] was used to aid accurate assessment. 500-1000 ml blood loss was defined as mild and >1000 ml was defined as moderate to severe PPH. Adverse reactions to drugs including shivering, fever and gastrointestinal upset were also documented. Hemoglobin was measured after 24 hours. Need for transfusion of blood products was noted.

Primary outcome measures were efficacy and safety. Efficacy was assessed by observing primary PPH using pictoral visual assessment chart. This was described by two variables. One was severity of PPH (mild, moderate and severe), which was categorical, and the other was amount of blood loss in ml, which was numeric. Other outcome measures included fall in hemoglobin and need for transfusion of blood products.

Data was analyzed on SPSS version 22. T test was applied for comparison of means (age, gravidity, parity, gestational age) between the two groups. Difference in mode of delivery between the two groups was evaluated by chi square test. Fisher's exact test was used to determine contingency of severity of blood loss between the two groups. Amount of blood loss and fall in hemoglobin was compared using T test. Pearson's chi square test was used to compare frequency distribution of side effects between the two groups. $P<0.05$ was considered significant.

RESULTS

A total of 212 women were included in the study, 106 in each grout. Out of these, 12 women's responses were incomplete so were excluded. Results were calculated for 200 women with 100 in each group. Mean age of women was 26.39±5.23 (Table 1).

Table 1. Descriptive analysis of Quantitative variables.

Variable	Minimum	Maximum	Mean±SD
Age	15	37	26.39±5.23
Gestational age	36	41	38.75±1.39
Blood loss	100	1500	287.40±216.04
Drop in hematocrit	0.0	4.8	0.83±0.78

Table 2. Descriptive analysis of Qualitative variables.

Variables	Categories	Number	%
Gravida	Primi Gravida	70	35.0
	Multi Gravida	106	53.0
	Grand Multi Gravida	24	12.0
Parity	Nulliparous	73	36.5
	Primi parous	53	26.5
	Multi parous	40	20.0
	Grand Multi parous	34	17.0
Mode of delivery	SVD	56	28.0
	SVD with EPI	142	71.0
	VBAC	2	1.0
Primary Post-Partum hemorrhage	Mild	180	90.0
	Moderate	20	10.0
Repeated dose	No	175	87.5
	Yes	25	12.5
Complications	Nil	157	78.5
	Shivering	23	11.5
	Fever	20	10.0
Blood Transfusion	No	197	98.5
	Yes	3	1.5

Table 3. Association of Misoprostol and 10 U intramuscular Oxytocin with different qualitative outcome variables.

Variable	Categories	IM Oxytocin	Misoprostol	P
Primary Post-Partum hemorrhage	Mild	90	10	1.000
	Moderate	90	10	
Repeated dose	No	85	90	0.285
	Yes	15	10	
Complications	Nil	80	77	0.86
	Shivering	11	12	
	Fever	09	11	
Blood Transfusion	No	99	98	0.561
	Yes	1	2	

Maximum women were multi gravida and 142 patients delivered through spontaneous vertex delivery with episiotomy. Two (1%) patients

delivered through Vaginal birth after cesarean (VBAC), one in each group. Overall the incidence of primary PPH was mild in 180 (90%) cases and moderate in 20 (10%) (Table 2). The proportion of complication between two drug groups was not significantly different (p =0.86). Overall blood transfusion was required in only 3 (1.5%) patients. Average blood loss was 287.40±216.04ml. In group one average blood loss was 303.50±225.35ml while in group II it was 271.30±206.21 ml (p=0.035) (Table 3).

DISCUSSION

In our study, 11.5% suffered from PPH. Fourteen percent women in the Oxytocin arm and nine percent in the Misoprostol arm had PPH. This is similar to that reported by Chuadary et al[15] and Aziz et al[17] but were higher than those reported by Bellad et al.[18] Tewetia et al[19] reported that Oxytocin is more efficacious than Misoprostol but there was no significant difference in hemoglobin concentration between the two groups. Bellad et al[18] reported that Misoprostol is more efficacious than Oxytocin.

Mean blood loss in our study was in agreement to those reported by Bellad et al[18] and Aziz et al.[17] However, it was much higher than others.[6,19] These variations range from 100-400 ml. Since estimation of blood loss is subjective, such variation is acceptable. However, the important point is that, in all studies it remained well below the definition of PPH i.e. 500 ml.

Side effects of Misoprostol in PPH are frequently reported as shivering and fever.[1,15,17-21] A meta analysis by Elati and Weeks[22] has shown that the side effects are related to dose and route of administration. We also noted these side effects in the misoprostol group. However, we noted that a significant proportion of women in oxytocin group also suffered from shivering. A possible explanation of this might be vasoconstriction following delivery of fetus.

The incidence of blood transfusion was similar to those reported in other studies.[1,6,18] There was no increase in blood transfusion in Misoprostol group in our study. Kundodyiwa et al[20] also reported similar findings. Minoo et al[1] reported that repeat dose was more frequently needed in the Oxytocin group. This finding was not seen in our cohort.

In PPH, role of misoprostol has been widely explored. However, the first line drug is still Oxytocin because the differences between the groups were small and larger data is needed to recommend it as first line drug for this life threatening complication.[23]

CONCLUSION

Misoprostol and Oxytocin are equally safe and effective with respect of PPH, repetition of dose, complications and blood transfusion but our study showed that Oxytocin is better than Misoprostol regarding average blood loss for the management of third stage of labor.

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