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Research Article

MISOPROSTOL VERSUS OXYTOCIN IN PREVENTION OF POSTPARTUM HEMORRHAGE

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ABSTRACT

Post-partum hemorrhage (PPH) is a common cause of maternal mortality in developing countries. Active management of postpartum hemorrhage by an uterotonic drug decreases the rate of postpartum hemorrhage. Studies suggest that the use of misoprostol may be beneficial in clinical settings where oxytocin is unavailable**.** The aim was to compare the safety and efficacy of oxytocin and misoprostol when used in the prevention of PPH. It is a double-blind study with 200 pregnant women who had a vaginal delivery were assigned 100 allocated in each groups of patients receiving either 800µg of misoprostol, rectally, or 5 IU of intravenous oxytocin, after delivery of the baby. Intra-operative bleeding, hemoglobin level before and 24 hour after operation, blood pressure before and after the administration of the drugs, and adverse drug effects were noted. The quantity of blood loss was high in the oxytocin group in comparison to the misoprostol group. There was no significant difference in the decrease in hematocrit and hemoglobin between the two groups. Although there was no significant difference in the need for transfusions and uterotonics between the two groups. Fever and chills are significantly higher among misoprostol patients. Study indicates that misoprostol may be considered as an alternative for oxytocin in low resource clinical settings.

Keywords*: Postpartum Hemorrhage, Misoprostol, Oxytocin, Vaginal Delivery, Low Resources.*

INTRODUCTION

Postpartum hemorrhage (PPH) is a life-threatening obstetric emergency which need at most attention whatever mode delivery may be. World health organization (WHO) has reported 585000 deaths for pregnancy each year. Twenty five percent of cases die from post-partum bleeding (World Health Organization and the World Bank). It is leading cause of maternal mortality due to bleeding (World Health Organization and the World Bank, 1997) which is higher in low-resource countries than the rest of the world (World Health Organization and the World Bank). It is reported that deaths are more in rural area are more than urban.

Misoprostol is a prostaglandin E1 (PGE1) analogous which stimulates pregnant uterus through prostanoid EP2, and EP3 receptors (Kwast *et al.,* 1986). The effect of oral, sublingual, and rectal misoprostol on post-partum hemorrhage in comparison with oxytocin is being studied (Clark *et al.,* 1984; Senior *et al.,* 1993; El-Refaey *et al.,* 1997; Bamigboye *et al.,* 1998; Lam *et al.,* 2004) misoprostol is as much as effective as oxytocin in preventing hemorrhage during vaginal or cesarean section (Vimala *et al.,* 2006; Hamm *et al.,* 2005).

Misoprostol is administered orally or rectally. It also holds good blood level when administrated rectally or orally (Khan *et al.,* 2003; Chaudhuri *et al.,* 2010; Mohammad *et al.,* 2013). But oral use of misoprostol during general anesthesia is impossible, difficulty in spinal anesthesia for its nausea and vomiting, therefore, rectal misoprostol can be considered as an alternative to oxytocin.

The drug's low cost, ease of administration through multiple routes, stability, and safety make it a good option in resource-poor settings (Chong *et al.,* 2004; Derman *et al.,* 2006; Gupta *et al.,* 2006), and in

patients who are vomiting, unable to take medications, or under anaesthesia (World Health Organization and the World Bank, 1997).

In spite of modernization of world still they are cases of mortality recorded due to PPH which is more in low resource areas so here we aim to study in a low-resource setting, the efficacy of 800 µg of rectal misoprostol and 5 IU of oxytocin in intravenous infusion, as prophylaxis against PPH. In this study we compared the effects of rectal misoprostol and oxytocin on intra-operative bleeding, hemoglobin level, and hemodynamic changes in parturients undergoing normal delivery.

MATERIALS AND METHODS

This is a prospective, double-blind study carried out for a period of 8 months from May 2013 to December 2013 at Konaseema institute of medical sciences, Amalapuram. The study was performed at the labor wards of the Department of Obstetrics and Gynecology at our hospital. A complete history and physical examination were undertaken for all possible candidates to determine eligibility for inclusion.

Inclusion Criteria: Were spontaneous normal delivery of a live, singleton neonate, and absence of any contraindications for misoprostol or oxytocin use.

Exclusion Criteria: Women having history of antepartum hemorrhage or bleeding tendency. The diagnosis of hypertensive disorder with pregnancy or the need for anticoagulants.

Women were counselled about their participation in the present study. Written informed consent was taken and they had the right to refuse to participate and/or withdraw from the study at any time without being denied their regular full clinical care. Personal information and medical data collected were confidential and were not made available to a third party.

A total of 200 women were included in the study. 100 Participants in each group were selected and

Group -1 received 800 µg of rectal misoprostol plus 1 ampoule of saline (0.9%) in 5 mL lactated Ringer solution intravenously, and Group-2 received rectal placebo plus 5 IU of oxytocin in 5 mL lactated Ringer solution was given after delivery of the anterior shoulder to each women of normal delivery.

Estimation of blood loss was not done on a quantitative basis; measures to control postpartum blood loss were based on a subjective estimation of blood loss by the obstetrician. Data collection sheets were filled after delivery by the experienced obstetrician managing delivery. Data collection was carried out for 24 hours by the resident physician in charge of the labor wards. Blood pressure, hemoglobin, and hematocrit values were recorded on admission and after 24 hours post partum, together with the obstetrician's decision, served as the criteria to transfuse blood. Changes in blood pressure were noted by measuring the blood pressure 60 minutes after delivery of the placenta. Women remained in the post delivery ward for 24 hours and were then discharged.

Data were statistically calculated as mean ± SD. Comparison of quantitative variables between the study groups was done using‘t’ test for independent sample. $P < 0.05$ was considered statistically significant. Statistical analysis were done using SPSS version 15.0.

Results

Two hundred pregnant women were included in the study. One hundred patients were included in each group. All the data was noted and patients were discharged home after 24 hours post partum.

There were not significant differences in the mean age of pregnant women, weight, BMI, parity, and gestational age at delivery, duration of operation and initial hematocrit concentrations in both groups. There were not significant differences in the intra-operative bleeding number of patients with post partum

hemorrhage, number of patients needing blood transfusions, number of patients needing additional uterotonics and hematocrit concentrations in both groups.

Table 1: Demographic characteristics in groups

Variables	Misopristol (Group-1) (Mean ± SD)	Oxytocin(Group-2) (Mean ± SD)	P- value
Age(in years)	25.1± 4.8	26.1± 5.1	0.57
Weight(in Kgs)	63.4 ± 4.5	64.1 ± 5.3	0.91
BMI (Wt/Ht ^{2})	23.4 ± 1.8	22.1 ± 1.9	0.81
Parity	3.1 ± 0.9	3.3 ± 0.9	0.31
Gestational age (in weeks)	38.73 ± 1.1	38.86 ± 1.3	0.82
Initial hematocrit concentration (%)	37.2 ± 2.4	36.9 ± 2.5	0.23

Table 2: Intra operative bleeding, transfusion and hematocrit concentration in groups

Variable	Misopristol (Group-1) (Mean ± SD)	Oxytocin (Group-2) (Mean ± SD)	P- value
Intra operative bleeding (in ml)	574 ± 173	601± 190	0.46
No of Patients developing PPH	10 ± 3.2	8 ± 2.9	0.56
No of Patient needing transfusion	4 ± 2.2	3 ± 1.9	0.71
No of Patients needing additional uterotonics	5 ± 3.1	6 ± 2.5	0.56
No of patients having ≥ 10% drop in hematocrit	6 ± 2.9	5 ± 2.2	0.71

Table 3: Hemoglobin % and blood pressure before and after delivery

Variables	Misopristol (Group-1) (Mean ± SD)	Oxytocin (Group-2) (Mean ± SD)	P- value
Before Delivery			
Hemoglobin %	10.9 ± 1.4	11.2 ± 1.6	0.87
Systolic B.P	125 ± 21.3	127 ± 23.5	0.77
Diastolic B.P	88 ± 11.2	85 ± 12.1	0.83
After Delivery			
Hemoglobin %	9.8 ± 1.2	10.3 ± 1.4	0.71
Systolic B.P	118 ± 21.1	113 ± 22.3	0.82
Diastolic B.P	77 ± 16.1	79 ± 15.4	0.63

Table 4: Comparison of side effects in both groups

Variable	Misopristol (Group-1) N=100	Oxytocin (Group-2) N=100	P- value
Nausea	5	6	N.S
Vomiting	2	4	N.S
Chills	6	1	0.02
Fever	21	5	<0.001
Chest pain	0	1	0.5
Hypotension	1	0	0.5

Present study does not very much in Hemoglobin % ,systolic BP and Diastolic BP in both groups after and before delivery. Hemoglobin measurements before and after delivery did not differ significantly between both groups, despite being slightly higher among the oxytocin group (P=0.87 and P=0.71). No significant changes were observed in systolic or diastolic blood pressure measurements before and after delivery in both groups.

In the first postpartum hour, significantly more women in the misoprostol group had fever (P<0.001) and shivering (P<0.05) compared with the oxytocin group. Postpartum fever did not exceed 38.5 °C and lasted less than 24 hours. Although vomiting and diarrhea were more common but not significant, nausea was reported in only 11 patients all together but not significant when compared.

Discussion

We compared the administration of misoprostol with infusion of oxytocin as part of management of vaginal delivery. The outcomes of both groups were comparable and oxytocin was as effective as misoprostol in reducing the incidence of PPH.

The overall incidence of PPH in the present study was 9 % following all deliveries. Carroli *et al.,* (2008) reported the incidence of PPH to be 10.45% in Africa. Our results were nearly same.

In present study the patients in the oxytocin group had greater need for additional oxytocin than misoprostol. There are studies comparing misoprostol with other uterotonics to control or treat PPH are been done. As studies From low-resource settings (Derman *et al.,* 2006; Vimala *et al.,* 2006) considered the drug to be a low-cost, easy, and comparable option to oxytocin (Gupta *et al.,* 2006), oxytocin and ergot preparations (Bamigboye *et al.,* 1998) or prostaglandin F2-α (Nellore *et al.,* 2006) (Table-2).

In this study there is no significant difference between intra-operative bleeding and post-operative hemoglobin level in patients receiving either rectal misoprostol or intravenous oxytocin. Vimala *et al.,* (2006) study on comparison of 400 µg sublingual misoprostol with oxytocin found that intra-operative bleeding was more significant in oxytocin group, although post-operative hemoglobin level was not different. In another study by Hamm (2005) comparing 200 µg buccal misoprostol with oxytocin, there was no difference between intra-operative bleeding and 24 hour post-operative hemoglobin level in the two groups.. In Chaudhuri *et al.,* (2010) study with 800 µg rectal misoprostol, although post-operative hemoglobin level was not different in the two groups, the intra-operative bleeding was significantly lesser in misoprostol group. The rate of bleeding and the hemoglobin changes found in our study was similar to most others studies (Ahmed *et al.,* 2009).

In our study decrease in systolic and diastolic blood pressure were not significantly in compared with both groups but there is significance between after and before delivery (Table-3). Several studies have been done on hemodynamic changes resulting from the use of oxytocin as Svanström (Svanstrom *et al.,* 2008) and coworkers showed that oxytocin reduces mean arterial blood pressure and peripheral vascular resistance.

The difference of nausea and vomiting in the two groups was not significant. Similar findings were reported in previous studies (Combs *et al.,* 1991; Chaudhuri *et al.,* 2010), despite that for its metallic taste misoprostol when used orally or sublingually was associated with higher frequency of nausea and vomiting (Tang *et al.,* 2003) (Table-4).

Chills is side effect of misoprostol and it independent to the kind of anesthesia, temperature of the operation room, and fluids used during the procedure (Combs *et al.,* 1991; Tang *et al.,* 2003). We used

fluids with 37 ºC (either IV or irrigation) and room temperature was 25ºC in the other hand epidural anesthesia was not used in our study because shivering is more common in epidural anesthesia (Combs *et al.,* 1991). Oral use of misoprostol results in higher blood level of the drug and higher incidence of chills. Vimala *et al.,* (2006) has reported shivering in 26% of patients with 400 µg of sublingual misoprostol, and 4% in oxytocin group (Vimala *et al.,* 2006). In Lapaire study with 800 µg of misoprostol, the incidence of chills was 36% in comparison with 8% in oxytocin group (Prendiville *et al.,* 1989). Chaudhuri reported 8.3% and 1.1% in the misoprostol and oxytocin groups respectively (Chaudhuri *et al.,* 2010). Chills were seen in 6% of our patients in misoprostol group and 1% in oxytocin group which is significant when compared between both groups. These findings are coherent with previous studies.

Hyperpyrexia was seen in 21% of patients who received misoprostol and 5% with oxytocin. The difference was significant. This finding was similarly reported in other trials comparing both drugs through different routes (Combs *et al.,* 1991; Tang *et al.,* 2003).

Conclusion

We conclude that rectal misoprostol is effective against 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.

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