

Role of misoprostol for the management of post partum hemorrhage due to uterine atony

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Objective: To determine the effectiveness and adverse effects of misoprostol in management of primary PPH.

Methodology: It was an interventional quasi-experimental study conducted in Allied hospital, Faisalabad, Pakistan from March 2008 to August 2008. All patients with PPH due to uterine atony, delivered in the hospital were included in the study. Their demographic profile (age, parity, booking status), mode of delivery and success rate of misoprostol were checked in terms of hemodynamic status, uterine contractility, reduction in blood loss and side effect profile.

Results: The study included 100 patients with mean age of 28 ± 5.83 year (range 18-40). 60

patients [60%] were unbooked, 80 [80%] were delivered by vaginal route. Out of 100 patients, 72 cases (72%) responded well to misoprostol ($P=0.002$).

Conclusion: Misoprostol was an effective drug to be used in treatment of primary PPH due to uterine atony. It is inexpensive, stable at room temperature, easy to administer, can be handled by untrained person with minimum side effects. These qualities can be extrapolated for its use in community by mid wives and traditional birth attendants. (Rawal Med J 2014;39: 182-185).

Key words: Post partum hemorrhage, misoprostol, uterine atony, utero-tonic agent.

INTRODUCTION

Postpartum hemorrhage (PPH) is a leading cause of maternal mortality and morbidity in low income countries and accounts for 25% of maternal deaths globally.¹ According to the Pakistan Demographic and Health Survey from 2006-2007, the maternal mortality ratio in rural areas is 319 per 100,000 live births.² Primary PPH is defined as blood loss greater than 500ml in 24hours after delivery, While secondary PPH is blood loss after 24 hours of delivery till completion of puerperium.³ Most important cause of PPH is uterine atony occurring in 90% of cases. Others include genital tract trauma, uterine inversion, retained placental tissue, and disseminated intravascular coagulation.⁴ In developed countries, the incidence and mortality from PPH is much lower and PPH contributes 4-11% of maternal mortality, suggesting that PPH related mortality is preventable.⁵

Prostaglandins are effective in controlling hemorrhage but most have the disadvantages of high cost, needing cold chain maintenance and have side effects like diarrhea, vomiting and abdominal pain. One notable exception is misoprostol, a

prostaglandin E1 analogue currently being investigated as a potential utero-tonic drug for use in active management of the third stage of labor.^{6,7} It is relatively inexpensive, stable at room temperature and can be given by different routes, all of which are tremendous advantages over currently available drugs.⁸ These features make misoprostol suitable for its use particularly in developing countries.⁹ The rationale of this study was to determine the effectiveness and adverse effects of misoprostol in management of primary PPH due to uterine atony.

METHODOLOGY

It was interventional quasi-experimental study carried out at Allied Hospital, Faisalabad, Pakistan over a period of 6 months from March 2008 to August 2008. One hundred patients with primary PPH due to uterine atony were included by non-probability purposive sampling technique. Patients who were hemodynamically unstable, with retained placenta, genital tract trauma and disorders of coagulation system were excluded from the study. An informed written consent was taken from all patients. Age, parity, booking status, and mode of

delivery were noted. In case of vaginal deliveries, status of uterus was checked by abdominal examination. On vaginal examination, amount of bleeding was noted by visual assessment. After C section, uterine tone and per operative bleeding were assessed by visual analogue. Complete blood count, Prothrombin Time (PT), activated partial Prothrombin time (aPTT) and cross matching were done.

We used 800ug of misoprostol rectally in all patients. Hemodynamic status and uterine status of patient were monitored at 10minutes interval for 30 minutes. Reduction in vaginal bleeding was assessed after every 10 minutes for 30 minutes as follows: 1. No bleeding, 2. Trickle 3. Passage of clots. No. 1 and 2 were considered responders and No. 3 was considered non-responders. Side effects like shivering, pyrexia, nausea and vomiting were noted. In case of deterioration of vital signs and increase in amount of vaginal bleeding, further medical and surgical intervention was opted even after 10 minutes of misoprostol placement. Effectiveness of misoprostol was described as reduction in postpartum blood loss to less than 500ml, with in 30 minutes after administration, improvement in the hemodynamic status of patient and improvement in uterine contractility. Data analysis was done by SPSS version 11. Chi-square test of significance was applied. P value < 0.05 was taken as significant.

RESULTS

During the study period, total number of deliveries was 2740. Out of these, 288 patients had PPH. Out of these 288 patients, 216 (75%) had uterine atony and 72 (25%) had genital tract trauma, retained placental tissue and coagulation disorders. Out of 216 patients, 100 stable patients were included in the study. Mean age was 28 ± 5.83 year (range 18-40). Out of 100 patients, 30% (n=30) were primigravida, 48% (n=48) were multigravida [2-5 pregnancy] and 22 (22%) were grand multigravida [more than 5 pregnancies]. Most of these were unbooked (n=60; 60%).

Eighty (80%) patients were delivered by vaginal route, while 20 (20%) by C-section. Out of 100 patients, 72 cases (72%) responded well to

misoprostol while rest of 28 cases (28%) did not. Thus success rate of misoprostol in controlling PPH was 72% (p=0.002).

Only 10% developed shivering and 6% developed pyrexia. None of the patient had nausea, vomiting and diarrhea. These side effects were easily treatable.

DISCUSSION

Massive PPH is a leading cause of maternal death globally, accounting for one third of maternal deaths.¹⁰ In our study, the frequency of PPH was found to be 10.66%. Cameron et al reported that PPH is a potentially life-threatening complication of childbirth occurring in up to 10% of births.¹¹ Roohi et al showed frequency of 13% in her study done in Faisalabad.¹² Derman et al showed incidence of 9.9% in a randomized controlled study from India.¹³ In our study, 75% (216 patients) had uterine atony, 15% (43 patients) had genital tract trauma, 8% (23 patients) had retained tissue and 2% (6 patients) had coagulation disorders. These findings were similar to other studies.^{14,15} In our study, mean age of patients was 28 years which is similar to reported studies.^{14,16} Regarding parity, 30% cases were primipara while 70% were multipara. Grand multiparity has been reported to be major risk factor which was present in 50% patients.¹⁷ Total number of booked cases in our study was 40% while rest of 60% was unbooked. Others found 30% booked patients.¹⁷ This ratio is comparable to many other local studies but not to international studies where almost majority of patients are booked cases.

We used 800mcg misoprostol rectally, as used in earlier studies.¹⁸ 1000mcg given rectally was an effective intervention in PPH,¹⁹ so was 800mcg dose.²⁰ Success rate of misoprostol in our study was 72%. In randomized trial by Lokugamage et al, 32 patients were recruited in which 30 patients responded.²⁰ Rectally administered misoprostol was successful in 100% patients of PPH unresponsive to oxytocin.¹⁹ Hemorrhage was controlled in 63% patients within 10 min of the administration of rectal misoprostol,²¹ 75% success was reported from Tanzania.²²

Side effects of misoprostol include high

temperature, sweating, shivering, nausea and vomiting. In Gambia trial, 2.53% females receiving 200mcg had temperature $\geq 39^{\circ}\text{C}$ although none had temperature $\geq 40^{\circ}\text{C}$.²³ In another study, shivering occurred in 36.4% of cases, vomiting in 19.4%, high temperature in 10.4% of cases.²² Walraven et al reported that shivering occurred in 29.1% of cases, nausea 3.8%, headache in 8.9%, temperature in 20.3% of cases.²⁴ In our study, shivering occurred in 10% of cases, high temperature in 6% of cases. No patient had nausea and vomiting.

A systemic review included three trials (n = 2346), which compared misoprostol to a placebo. Shivering (RR 2.75; 95% CI 2.26-3.34) and pyrexia (RR 5.34; 95% CI 2.86-9.96) were significantly more common with misoprostol than with a placebo.²⁵ Hofmeyr et al²⁶ concluded that 54.3% patients had shivering after receiving 1000mcg of oral misoprostol and pyrexia $>38.4^{\circ}\text{C}$ was present in 9.64% of patients. These side effects may be related to rapid absorption of misoprostol given orally and high bioavailability when given sublingually. That's why these side effects were less in our study because misoprostol was given by rectal route.

CONCLUSION

Currently, Misoprostol is the only thermo stable uterotonic agent available which would be economically beneficial for developing countries where refrigeration of drugs poses a problem. We recommend that 800 ug Misoprostol used rectally may be effective in controlling primary PPH due to uterine atony with minimum adverse effects. However, trials should be done on large scale in community settings by Trained Birth Attendants to establish its efficacy in Pakistan.

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