

Effectiveness of Misoprostol in the Prevention of Postpartum Hemorrhage

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ABSTRACT

Aim: To determine the effectiveness of misoprostol through rectal route in the prevention of primary postpartum hemorrhage and determine its therapeutic effect.

Methods: This Randomized Controlled Trial was carried out in the Labour Wards Nishtar Hospital Multan from January 2013 to June 2013. Two hundred women selected as per inclusion and exclusion criteria coming to labour ward with the ascertainment of period of gestation through ultrasonography. Two groups were formed by using random number tables. In the case of group A, 800 µg of Misoprostol P/R was given in addition to oxytocic drugs used routinely while group B was control group.

Results: Out of 200 patients, 82% in group-1 and 93% in group had spontaneous labour while 18% in group-A and 7% in group-B had induced labour. Episiotomy was performed in 22% patients in group-A and 33% patients in group-B. As regards blood loss, in PPH patients 22% in group-A and 18% in group B had blood loss > 500 ml. Out of 100 patients, 93% in group-A and out of 100 patients, 95% in group-B had therapeutic effect of misoprostol. The mean age of the patients was 26.62 ± 0.47 vs. 25.25 ± 0.41 years respectively in group-A and group-B. In group-A 71% and in group-B 75% patients had vaginal delivery.

Conclusion: Misoprostol administration using rectal route, though not statistically significant, is effective as there were fewer side effects.

Keywrds:- Postpartum haemorrhage (PPH), Misoprostol,

INTRODUCTION

The third stage of labour is potentially the most hazardous part of labour having grave implications for the mother. The main risk is that of postpartum haemorrhage (PPH), which is the most common form of major obstetric hemorrhage. The World Health Organization (WHO) estimated that 529,000 women died from obstetric causes in 2000¹. Fourteen million cases of PPH occur each year with a case-fatality rate of 1%. It accounts for one quarter of all maternal deaths worldwide². In developing countries, PPH is most common cause of maternal mortality and accounts for over one-third of all maternal deaths³. Most of these deaths occur in the resource-poor countries of Africa and Asia, particularly in rural areas and are avoidable⁴.

The postpartum hemorrhage is defined as blood loss of more than 500 ml following vaginal delivery and more than 1000 ml in case of caesarean section⁵. This quantity is extremely difficult to identify outside a controlled trial setting. Even trained physicians are reported to typically underestimate blood loss by about half⁶. While there are many

known risk factors⁷, PPH occurrence is random, making it impossible to predict in both low and high risk populations. Furthermore, blood loss can be rapid. In developing countries, where nearly half the women deliver without the aid of a skilled birth attendant there is simply not enough time to seek treatment for PPH. The only way to help women without access to trained attendants is through preventive measures⁸.

To manage PPH effectively a number of medical and surgical interventions are required to control the bleeding⁹. Recently considerable attention has been paid to the choice of uterotonic agent particularly comparing the cheap and orally administered prostaglandin misoprostol with other uterotonics¹⁰. The findings seem to indicate that the rectal misoprostol is a viable (Safe, inexpensive, thermostable and effective) alternative¹¹ to parenteral oxytocin in areas where storage and parenteral administration of drugs are problems¹²; as oxytocin has to be stored at 40 °C to retain its efficacy. Whereas tablets of misoprostol kept dry retain their efficacy even at tropical temperatures for several years or more. Oxytocin (10. i.u) given parenterally is an effective uterotonic agent reaching peak levels within minutes of administration, requires skills and sterile equipment for safe administration. It may be inactivated if exposed to high ambient temperature

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and needs storage at 40°C. It causes water retention, vasodilatation and hypotension when given in high doses.

Misoprostol is a methyl ester, a synthetic prostaglandin E1 analogue registered for the prevention and treatment of gastric ulcers, is well known for its off-label use as a uterotonic agent. There is credible scientific evidence that misoprostol is useful in the active management of third stage of labour¹³. It reaches peak in 30 minutes but detectable in blood plasma immediately. It can be given orally, sublingually¹⁴ or rectally, appears to be as effective as 10. i.u parenteral oxytocin in minimizing blood loss during third stage of labour as determined by change in Hb concentration¹⁵. Side effects of misoprostol include nausea, vomiting, fever, diarrhea and shivering¹⁶. Commonest regimes for treatment of PPH are 1000µg rectally¹⁷. Rectal route is free of gastrointestinal side effects and also reduces the risk of transmitting hepatitis C, AIDS and other blood borne diseases¹⁸. Through this route the uptake is slow but for prolonged duration. Rectal route also has side effects like shivering and pyrexia but are dose dependent¹⁹. Misoprostol is safe inexpensive, thermostable and effective uterotonic and can replace parenteral oxytocin for low risk women in rural and remote areas of underdeveloped countries. Where parenteral oxytocin may be unavaible²⁰. As more than 50% of births occurs at home in Asia misoprostol is suitable for preventing PPH at home births²¹ because it is given orally or rectally, not heart or high sensitive, inexpensive, rapidly acting and side effect, are predictable and self limiting.

MATERIAL AND METHOD

This Randomized Controlled Trial was carried out in the Labour Wards Nishtar Hospital Multan from January 2013 to June 2013. Two hundred women selected as per inclusion and exclusion criteria coming to labour ward with the ascertainment of period of gestation through ultrasonography. Two groups were formed by using random number tables. In the case of group A, 800 µg of Misoprostol P/R was given in addition to oxytocic drugs used routinely while group B was control group.

RESULTS

Present study was conducted on 200 patients with primary PPH. Out of 200 patients, 82% in group-1 and 93% in group had spontaneous labour while 18% in group-A and 7% in group-B had induced labour. Episiotomy was performed in 22% patients in group-A and 33% patients in group-B. As regards blood loss, in PPH patients 22% in group-A and 18% in

group had blood loss > 500 ml. Out of 100 patients, 93% in group-A and out of 100 patients, 95% in group-B had therapeutic effect of misoprostol. The mean age of the patients was 26.62 ± 0.47 vs. 25.25± 0.41 years respectively in group-A and group-B (Table 1). In group-A 71% and in group-B 75% patients had vaginal delivery as shown in table 2. Side effect of therapy in patients of PPH are shown in table-3.

Table 1: Descriptive Statistics

Variables	Group A	Group B
Age (years)	26.6±0.47	25.25±0.41
Parity	25.25±0.41	2.10±0.12
Height (cm)	160.52±0.52	160.18±0.48
Weight (kg)	69.07±.18	63.39± 0.72

Table-2: Mode of Delivery

Mode	Group A	Group B
Vaginal	71 (71%)	75 (75%)
Instrumental	03 (03%)	01 (01%)
CS	26 (26%)	24 (24%)

Table 3: Side Effects of Therapy

Side effect	Group A	Group B
Nausea	1 (1%)	5 (5%)
Vomiting	1 (1%)	9 (9%)
Diarrhoea	2 (2%)	1 (1%)
Fever	6 (6%)	-
Fluid retention	-	2 (2%)
Hypertension	-	7 (%)
Shivering	6 (6%)	2 (2%)

DISCUSSION

Postpartum hemorrhage is the most common cause of maternal morbidity and mortality world wide²². Majority of these deaths (88%) occur with first four hours of delivery due to events in the third stage of labour. There are 600,000 maternal deaths reported world wide every year and 99% of these occur in developing countries⁵.

Misoprostol, a new and inexpensive prostaglandin E1 analogue, has been suggested as an alternative for routine management of the third stage of labour²³. The advantages of misoprostol over other uterotonic agents are that it does not require parenteral administration and is associated with serious side effects. It is used in the third stage of labour primarily to prevent maternal death²⁴.

Present study was conducted to determine the effectiveness and therapeutic effect of misoprostol through rectal route in the prevention of primary PPH. Mean age of cases was 26.62±0.47 years and that of controls 25.25±0.41 years. Mean parity was 3.07±0.18 vs 2.10±0.12 in group-A and B respectively. Almost similar results have been reported in other local and international studies. In a

study mean age of the patients was 26.49+5.50 vs 25.60 + 5.60 years in two groups respectively, 50% vs 40% patients were para 1-4 in misoprostol and oxytocin group respectively²⁵.

Operative and instrumental delivery increases the risk for PPH. In our study 71% vs 75% patients delivered vaginally in cases and controls respectively, 3% vs 1% instrumental deliveries and 26% vs 24% cesarean deliveries. In a study, 28.8% were delivered by spontaneous vaginal delivery, 33% by instrumental delivery while 38.1% were delivered by cesarean section¹¹. In another study showed that 90% vs 89% patients had vaginal deliveries and 10.1% vs 11% patients had cesarean deliveries in their patients²⁶.

In present study blood loss was evident in 18% vs 22% cases and controls respectively. While therapeutic effect of rectal misoprostol was 95% vs 93% compared to oxytocin. Fever and shivering was more frequent (6% each) in group-A while vomiting and hypotension was frequent in group-B (4% each). Our study results are in accordance with local and international literature.

Aliya et al used misoprostol 800 microgram per rectally just before the start of cesarean section for the prophylaxis of postpartum hemorrhage, 8% patients had PPH²⁷. Misoprostol administered per rectally had equal efficacy to ergometrine given intravenously for the prophylaxis of postpartum hemorrhage but the side effect profile and patient tolerability was better with misoprostol.

CONCLUSION

This study concluded that misoprostol administered using rectal route, though not statistically significant, is effective as there were fewer side effects with 95% efficacy rate and 18% blood loss.

REFERENCES

1. Maternal Mortality in 2000: estimates developed by WHO, UNICEF and UNFPA. Geneva: The World Health Organization; 2004.
2. Hill K, Thomas K, AbouZahr C, Walker N, Say L, Inoue M et al. Estimates of maternal mortality worldwide between 1990 and 2005: an assessment of available data. *Lancet* 2007; 370: 1311-9.
3. Sheikh L, Zuberi NF, Riaz R, Rizvi JH. Massive primary postpartum hemorrhage: setting up standards of care. *J Pak Med Assoc.* 2006; 56(1): 26-9.
4. WHO recommendations for the prevention of postpartum haemorrhage. Geneva: World Health Organization; 2007.
5. Boumeester FW, Bolte AC, van Geinun HP. Pharmacological and surgical therapy for primary postpartum hemorrhage. *Curr Pharma* 2005; 11: 759-73.

6. Toledo P, McCarthy RJ, Hewlett BJ, Fitzgerald PC, Wong CA. The accuracy of blood loss estimation after simulated vaginal delivery. *Anesth Analg* 2007; 105: 1736-40.
6. Al-Zirqi I, Vangen S, Forsen L, Stray-Pedersen B. Prevalence and risk factors of severe obstetric haemorrhage. *BJOG.* 2008; 115: 1265-72.
7. Pagel C, Lewycka S, Colbourn T. Estimation of potential effects of improved community-based drug provision, to augment health-facility strengthening, on maternal mortality due to post-partum haemorrhage and sepsis in sub-Saharan Africa. *Lancet* 2009; 374: 1441-8.
8. Baskett TF. Uterine compression sutures for postpartum hemorrhage. *Obstet Gynecol* 2007; 110(1): 68-71.
9. Lapairea O, Schneider MC, Stotz M. Oral misoprostol vs. intravenous oxytocin in reducing blood loss after emergency cesarean delivery. *Int J Gynecol Obstet.* 2006; 95(1): 2-7.
10. Nasr A, Shahin AY, Elsamman AM. Rectal misoprostol versus intravenous oxytocin for prevention of postpartum hemorrhage. *Int J Obstet Gynecol* 2009; 105(3): 244-7.
11. Walraven G, Blum J, Dampha Y, Sowe M, Morison L, Winikoff B, et al. Misoprostol in the management of the third stage of labour in the home delivery setting in rural Gambia: a randomised controlled trial. *BJOG.* 2005; 112(9): 1277-83.
12. Burns M. Misoprostol use in obstetrics and gynecology. *Outlook* 2005; 21(4): 1-8.
13. Soltan MH, El-Gendi E, Imam HH, Fathi O. Different doses of sublingual misoprostol versus methylergometrine for the prevention of atonic postpartum haemorrhage. *Int J Health Sci Qassim Univ* 2007; 1(2)- 229-36.
14. Parsons SM, Walley RL, Crane JM, Matthews K, Hutchens D. Oral misoprostol versus oxytocin in the management of the third stage of labour. *J Obstet Gynaecol Can.* 2006; 28(1): 20-6.
15. Lumbiganon P, Villar J, Piaggio G, Gulmezoglu AM, Adetoro L, Carroli G. Side effects of oral misoprostol during the first 24 hours after administration in the third stage of labour. *BJOG.* 2002; 109: 1222-6.
16. Bose P, Regan F, Brown SP. Improving the accuracy of estimated blood loss at obstetric hemorrhage using clinical reconstructions. *Br J Obstet Gynaecol.* 2006; 113: 919-24.
17. Nellore V, Mittal S, Dadhwal V. Rectal misoprostol vs 15-methyl prostaglandinF2α for the prevention of PPH. *Int J Gynaecol Obstet* 2006; 94: 45-6.
18. Alfirovic Z, Blum J, Walraven G, Weeks A, Winikon B. Prevention of postpartum hemorrhage with misoprostol. *Int J Gynaecol Obstet* 2007; 99 Suppl 2: 198-201.
19. Ozkaya O, Sezik M, Kaya H. Placebo-controlled randomized comparison of vaginal with rectal misoprostol in the prevention of PPH. *J Obstet Gynaecol Res.* 2005; 31: 389-93.
20. World Health Organization. Proportion of births attended by a skilled attendant: 2007 updates. Geneva: World Health Organization; 2007.
21. Stainsby D, MacLennan S, Thomas D, Isaac J, Hamilton PJ. Guidelines on the management of massive blood loss. *Br J Haematol* 2006; 135: 634-41.
22. Ojala K, Perala J, Kariniemi J, Ranta P, Raudaskoski T, Tekay A. Arterial embolization and prophylactic catheterization for the treatment of severe obstetric hemorrhage. *Acta Obstet Gynecol Scand.* 2005; 84: 1075-80.
23. Ong S. Guidelines for perinatal care, 6th edition. *Obstet Gynaecol.* 2008; 10:3: 207-50.
24. Vaid A, Dadhwal V, Mittal S, Deka D, Misra R, Sharma JB et al. A randomized controlled trial of prophylactic sublingual misoprostol versus intramuscular methyl-ergometrine versus intramuscular 15-methyl PGF2alpha in active management of third stage of labor. *Arch Gynecol Obstet* 2009; 280(6): 893-7.