Journal of Saidu Medical College 2016; 6(2)

PROPHYLACTIC USE OF MISOPROSTOL FOR THE PREVENTION OF POSTPARTUM HAEMORRHAGE AND ATONIC UTERUS IN CESARION SECTION DELIVERIES.

NUZHAT AMIN
Gynae B Ward Mardan Medical Complex Hospital Mardan.

ABSTRACT

BACK GROUND: Post partum hemorrhage still remains a major cause of maternal death. Syntocinon is the first line protective measure in this regard. However this is heat sensitive and losses its efficacy after storage for some time. On the other hand misoprostol do not losses its efficacy for long time after storage, is cheap, can be stored at room temperature and give the same result as syntocinon in preventing postpartum hemorrhage and atonic uterus.

OBJECTIVE: To assess the prophylactic use of misoprostol in preventing PPH and management of atonic uterus, and compare it with conventional i/v syntocinon routinely used in hospitals for cesarion deliveries.

MATERIAL AND METHODS: This is a semi experimental study, which was conducted in Mardan medical complex Hospital Mardan, department of obstetrics and gynecology unit A, between May 2014 to May 2015. 200 women have give birth to their babies by C-section were included in the study and divided into 2 groups, a control group (100 women who received syntocinon) and a study group (100 women who received rectal misoprostol). Syntocinon 10u i/v injection and misoprostol 800ug (4tablets) per rectum were given to women in control and study group respectively, immediately after delivery of the baby. Blood loss after delivery and frequency of atonic PPH were recorded and compared between the two groups. Side effects of both drugs were also noted.

RESULTS: There was no significant difference in blood loss after delivery. Control group 250ml, study group 300ml, P value -0.18). The frequency of atonic PPH in study and control groups was similar ranging between 3% and 4%.Side effects of misoprostol (shivering 25% , fever 15% , vomiting 12% and diarrhea 5%) were significant (P value <0.05) but all were temporary and not life threatening.

CONCLUSION: Misoprostol can be used for the prevention of PPH and to reduce atonic uterus after C-section deliveries, especially in poor countries where facilities for storage of oxytocin are not available. Benefits of misoprostol outweigh its side effects.

Key Words: prophylaxis, atonic postpartum hemorrhage, rectal, misoprostol, syntocinon, underdeveloped countries.

INTRODUCTION:

Obstetric hemorrhage especial the postpartum hemorrhage is the large single medical cause of maternal mortality accounting for about 25% of all maternal deaths. Majority of these deaths occur in poor countries[2].

Postpartum hemorrhage is excessive bleeding (> 500ml in vaginal delivery and >1000ml in cesarean section) from the genital tract after birth. The condition can result uterine atony, retained placenta, genital tract trauma and coagulation disorders. It is said to be primary if it occurs within 24h of delivery and secondary if it occurs 24h after delivery. It complicates 4-5% of deliveries[3].

Uterine contraction and retraction is the first line followed by platelet plug formation as second and clot formation as third line mechanism to control bleeding from placental site after delivery. Different types of drugs (methergine, syntocinone, syntometrine) which are uterotonic drugs are used to cause contraction and retraction of uterus after delivery. Ergot alkaloids have been used for decades for this purpose but they are associated with risk of hypertension and are there for,

contraindicated in patients with hypertension and heart diseases[10].

The drug of first choice in third stage of labor in modernpractice is syntocinon due to its excellent efficacy as well as few side effects as compared toergometrine.[5,7] But syntocinon as well as syntometrine are available as injections only and their use need sterilized needles and trained staff.[8,9]

Another problem associated with the use of injectable drugs is that they need refrigeration to remain effective. Facilities like trained staff and refrigeration might not be available in poor countries especially at primary health care level. Moreover some of the studies have shown syntocinon to have cardio toxic effect due to the presence of chemical chlorobutanol as preservative in syntocinon ampoules.[8,9]

Prostaglandins are other groups of drugs that have strong uterotonic property. They are not associated with the effect like hypertension. These qualities make prostaglandins a good alternative to syntocinone and methergine that can be routinely used in the management of third stage of labor.[10]

Misoprostol is an E1 prostaglandin analogue that has been used for decades for management of gastric ulcers. It is also used in gynecology and obstetrics for various indications i.e. cervical priming, medical termination of pregnancy and induction of labor. Recent research shows that misoprostol can also be used for prophylaxis and treatment of postpartum hemorrhage.

The use of misoprostol brought a revolution in obstetrics and gynecology practice. The observation that misoprostol has uterotonic properties was first time documented in literature by E1-Refacy et al in 1993[11]. Later on it was shown to have some side effects like nausea, vomiting and shivering. Misoprostol is a good drug for developing countries because it is a pill easy to use (oral, sublingual, buccal, vaginal and rectal routs), is stable at ambient temperature and does not require special storage facilities, can be easily delivered at the community level, is cheap and widely available.

That's why this study was conducted to evaluate the efficacy and safety of rectal misoprostol and compared them to that of syntocinon for the management of third stage of labor, with special emphasis on PPH prevention.

MATERIAL AND METHODS

This study was conducted in Mardan medical complex Hospital Mardan between May 20114 to May 20125 on 200 patients. An informed consent taken from all women included in the study.

INCLUSION CRITERIA: Women with full term pregnancy who gave birth to their child by c. section were included in the study.

EXCLUSION CRITERIA: Cases with who had extended tears during cesarean section ,who had bleeding disorders, placenta previa and abruption ,multiple gestation, previous history of PPH, fibroid in uterus and women with BMI more than 30 were also excluded.
Cases were admitted through emergency and OPD and they were randomly selected. Thorough history and examination was done on all patients.

INVESTIGATIONS
Baseline investigations were performed on all patients e.g. urine R/E, blood complete picture, blood grouping, clotting profile and screening for hepatitis B and C.

The women in control group were given syntocinon 10iu i/v injection which is routinely used in hospital as part of active management of third stage of labor whereas the study group received 800ug(4 tablets) of misoprostol per rectum. Both drugs were given immediately after delivery of baby.

Postpartum hemorrhage according to WHO criteria is define as bleeding >500ml after vaginal delivery. On clinical grounds, we can define PPH as blood loss after delivery sufficient to cause hemodynamic instability.

Atonic PPH is the one that results from relaxation of uterine muscles. Blood loss after delivery was estimated by special drapes put under the parturient and removed after 1 hour of delivery and blood collected in graduated plastic bags.

OUTCOME MEASURES

1. Estimation of blood loss.
2. Frequency of primary PPH.
3. Side effects of misoprostol and syntocinon.
4. Acceptability of the drug by the women via the rectal route. Women vital signs were noted and any excessive bleeding was managed according to WHO recommendations. Side effects of the drugs were noted and recorded.

Calculations: Data were analyzed using SPSS version 13 for windows using T test. A p-value of < 0.05 was taken as statistically significant.

RESULTS

The age and parity of women in the study and control groups were met statistically different comparison of age and parity between study and control group.

Mean blood loss after delivery was not significantly different in the two groups. It was lower in misoprostol group compared to oxytocin group (300ml verses 250ml, p=0.18)

The frequency of atonic uterus was the same in the control and study groups.

Groups	No of cases with PPH (no)	Percentage	P-Value
Control	3	3%	
Study	4	4%	.2

Frequency of atonic PPH in control and study groups.

In the control group, there were 3 cases of atonic PPH and in study group 4 cases of atonic PPH.

Table 2: SIDE EFFECTS OF DRUGS.

Side Effects	Study Group	Control Group	P-Value
Shivering	25	4	<0.05
Fever	15	3	<0.05
Vomiting	12	2	<0.05
Diarrhea	5	1.6	<0.05

Table 2 shows side effects of drugs in both groups. It can be seen that the most common side effects is shivering followed by fever while vomiting and diarrhea as well.

DISCUSSION

For decades, it was planned to have strategies for reducing the rise of PPH[14].

Misoprostol is cheap, stable at room temperature, is rapidly absorbed after oral, sublingual and rectal routes. It has strong uterotonic activity. It was thought to be ideal for this purpose especially at Primary health care level[15,16]. Literature supports the use of misoprostolin resources poor settings[12,15]. High dose of (800 Mg) misoprostol can bring results comparable to injectable uterotonics.

Multiple controlled trails[17,21] investigating misoprostol for prophylaxis of PPH has been reported. Many trails have suggested that misoprostol is effective and convenient in poor countries. The blood loss after delivery should not exceed 500 ml.

A similar study had been conducted in India in department of obstetrics and gynecology, All India institute of medical sciences new Delhi 2005. Sublingual misoprostol versus oxytocin infusion to reduce blood loss at cesarean section. They found that the mean blood loss

was significantly lower in misoprostol group compared to oxytocin group (819ml versus 974ml p= 0.004)[19].

In a randomized study in international journal of obs and gynae a similar study conducted in 2014 however in this study misoprostol was given rectal like our study and like our study they also found no significant difference in misoprostol and oxytocine[20].

The results of our study show that blood loss and hemoglobin deficit were not significantly different in control and study group. This is accordance with the result of other studies comparing rectal misoprostol wit injectable uterotonics[21,22].

The incidence of PPH in our study is 3-4% which is comparatively less than the reported incidence in general obstetric population.

This may be due to the fact that study was carried out at tertiary care hospital with majority of patient studied were with low risk for PPH. Syntocinon used as uterotonics in the study and misprostol in control group. So rectal misoprostol has an excellent potential for prophylaxis of PPH in C-section deliveries.

PPH is one of the commonest indication for blood transfusion which is associated with complications like transmission of infections, anaphylactic reactions and clotting disturbance in case of massive transfusion.
We did not note a significant difference in frequency of blood transfusion give between the study and control group.

The adverse effects of misoprostol are dose related. One study reported the incidence of shivering and fever decreased to 11% and 4% respectively with 400 mg of misoprosl[29]. One small study showed that if we decrease the dose, the incidence of shivering will decrease but this will also affect the efficacy of the drug for controlling PPH.

Our study had some limitations. The sample included both high and low risk women. The need is to conduct such studies on high risk cases under controlled conditions.

CONCLUSIONS

Overall, this study shows that rectal misoprostol is safe and effective for the prophylaxis 0f postpartum hemorrhage in C-section deliveries. Our study results strongly recommend misoprostol to be included in protocols to manage postpartum hemorrhage in developing world to reduce the risk of postpartum hemorrhage, and maternal mortality and morbidity related with this condition.

REFERENCES

1. Change J, Elam-Evans LD, Berg CJ, et al. Centers for Disease Control and Prevention, Pregnancy related Mortality Surveillance; USA, 1991-1999, In Surveillance Summaries, Feb, 2003, MMRW, 2003; 52, (NO. SS-2).
2. Selo-Ojeme DO. Primary Postpartum Hemorrhage. J, Obstet Gynecol, 2002; 22: 463-469.
3. Prendiville WJ, Elbourne D, McDonald S. Active versus Expectant Management of 3rd Stage of Labor, Cochrane Database Syst Rev 2000;3-7.
4. Sibai, BM. Pre-eclampsia-eclampsia, Curr Probl Obstet Gynecol Fertil 1990; 13: 1-5.
5. Botting JH, Manely DG, The Action of Commercial Preparation of Oxytocin on the smoth muscle of gut Pharma Pharmacol, 1967; 19-66.
6. Maycork EJ, Russell WC, Anaphylactic Reaction to Oxytocin, Anesthesia Intensive care 1993; 21: 211-2.
7. Hofman H, Goerz G. Plewig G. Anaphylactic Shock from chlorobutanol-preserved oxytocin, Contact Dermatitis 1986; 15; 24 (Medline).
8. Rosaeg OP, Cicutti NJ, Labow RS, The Effect of Sytocinon on contractile force of human atrial trabeculae. Anesth Analog 1998; 86: 40-44.
9. Barrigon S, Tejerina T, Delgado C, Tamargo, J. Effect of chlorobutanol on 45ca movement and contractile responses of rat aorta and its relevance to the action of syntocinon. J Pharm Pharmacol 1984; 36; 521-69 Medline.
10. Weis Jr FR, Markello R, MO B, Bochiechio P, Obstet Gynecol 1975; 46: 211-411.

11. Refaey H, O, Brien P, Morafa W, Walder J, Rodeck C, Misoprostol for 3rd satge of labor, Lancet 1996; 347; 1257 (Medline).
12. Derman et al, Oral misoprostol in prevention of post-partum hemorrhage I resource poor countries, Lancet 2006; 368: 1248-53.
13. Maternal and Neonatal Health programme, preventing PPH; A community based approach proves effective in rural Indonesia, Baltimore US; MNH Programme, 2005.
14. Hoj L et al, Effect of sublingual misoprostol on severe PPH in a primary health care center in Guinea-Bissau, RCT, BMJ; 2005; 331-723.
15. Rajabhandari S et al, Prevention of PPH at home delivery with misoprostol in Bank District, Nepal. International Journal of Gynecology and Obstatrics 2006; 94; s143-s144.
16. Hammerling A, The safety of Misoprostol, Inter J. OF Gynecology and Obstetrics; 2006; 94: 149-150.
17. Parson SM, Walley RL, Crane JM, Mattews K. Hutchens. D, Oral misoprostol versus oxytocin in the management of 3rd stage of labor, J. Obstet. Gynecol. Can. 2006; 28: 20-6.
18. Ng PS, Lai CY, Sahota DS, Yuen PM,A double blind RCT of use of oral misoprostol and I/M syntometrine in the management of 3rd stage of labor, Gynecol. Obstet. Invest, 2007; 63; 55-60.
19. Jadesimi A, Okonofua FE. Tackling, The unacceptable; Nigeria approves misoprostol for PPH, J. Fam, Plann, Repord. Health CARE 2006; 32: 213-341.
20. Gupta B, Jain V, Aggrarwal N, Rectal misoprostol versus syntocinon in the prevention of PPH, Int. J. Obstetrics and Gynecology; 2006; 94:139-140.
21. Int j Reporod contracept obs gynaecol 2014;3(3):512-515
22. Lapairo et al. Oral misoprostol versus I/V syntocinon in reducing blood loss after cesarean delivery, International J. Gynecology and Obstetrics, 2006; 95: 02-07.
23. Andeson T. Prostaglandins for prevention of POST-PARTUM HEMORRHAGE, Prect. Midwife. 2005;8: 43-51.
24. El Refaey H et al, The misoprostol in 3rd stage of labor.an RCT comparison between oral misoprostol and standard treatment, British J. Obstetrics and Gynecology 2000; 107: 1104-10.
25. Surbek DV, Fehr PM, Hoslil. Holzgreve W, Oral misoprostol for 3rd stage of labor; A randomized placebo controlled trail, Obstetrics Gynecology 1999; 94; 255-82.
26. Gulmezoglu AM, WHO multicenter RCT of misoprostol in the management of 3rd stage labor, Lancet 2001; 385: 689-695.
27. Chong VS, Postpartum intrauterine pressure studies of the uterotonic effects of oral misoprostol versus I/M syntometrine, British J Obstetrics and Gynecology; 2001; 108; 41-47.
28. Mousa HA, Alfirevic Z, Treatment of primary postpartum hemorrhage. Cochrane Data base System, Revision, 2003; 1; CD003249.
29. O Brain et al. Rectal misoprostol for the treatment of postpartum hemorrhage unresponsive to syntocinon and ergometrine, Obstet Gynecol 1998; 92: 212-214.
30. Caliskan E et al. Is rectal misoprostol really effective in the treatment of 3rd stage of labor? An RCT, American J of Obstetrics and Gynecology, 2002; 187: 1038-45.
31. Diab KM, Ramy AR, Yahia MA. The use of rectal misoprostol as an active pharmacological management of 3rd stage of labor, Journal Obstet Gynecol; Res. 1999; 25: 327-332.

CORRESPONDENCE ADDRESS

Name: Dr. Nuzhat Amin
Address: Flat no 11, Doctors Flats,
Mardan, Medical Complex Hospital, Mardan.
Cell no: 03369848607, 03449166384
Email: nuzhat_amin@yahoo.com