Original Research Article

Comparative study of 600 mcg sublingual misoprostol and oxytocin 10 iu i. min active management of third stage of labour

Inampudi Anupama[1], P.Vineela[2], P.Viplava[3], Siddula Shireesha[4*]

[1]Assistant Professor, Modern Government Maternity Hospital, Petlaburj/Osmania Medical College, Hyderabad, Telangana, India
[2]Assistant Professor, Modern Government Maternity Hospital, Petlaburj/Osmania Medical College, Hyderabad, Telangana, India
[3]Assistant Professor, Modern Government Maternity Hospital, Petlaburj/Osmania Medical College, Hyderabad, Telangana, India
[4]Assistant Professor, Modern Government Maternity Hospital, Petlaburj/Osmania Medical College, Hyderabad, Telangana, India

Received: 07-11-2021 / Revised: 27-12-2021 / Accepted: 12-01-2022

Abstract

Aims: This study was done to assess the efficacy of oral misoprostol in the active management of the 3rd stage of labour in comparison with intramuscular oxytocin and to assess the side effects of the drugs. **Materials and methods**: 200 women of low risk category were selected randomly with 100 women in each group. After delivery of the baby, the cord was clamped and cut. Misoprostol group was given 3 tablets of misoprostol 200µg each sublingually and oxytocin group was given 10 IU of oxytocin in the intramuscularly. Placenta was delivered by controlled cord traction. Blood loss was measured in both the groups for 1st hour after delivery. The hemoglobin concentration before and 24 hours after delivery was noted. The side effects of the drugs up to 24 hours after delivery were noted. **Results**: The results of the misoprostol group (100 patients) were compared with oxytocin group (100 patients). The average blood loss was 217.9 ml in misoprostol group compared to 233.45 ml in oxytocin group. The fall in hemoglobin percentage was 0.9g/dl in misoprostol group compared to 0.8g/dL in oxytocin group. The difference in observation of both groups was statistically not significant ($p>0.05$). The incidence of postpartum hemorrhage was 2% in both the groups. There was no case of retained placenta in either of the groups. The need for additional oxytocics was also 2% in both the groups as they were given only when the blood loss is more than 500 ml. Shivering and pyrexia were the commonest side effects noted in misoprostol group. **Conclusion**: We found that both sublingual misoprostol and intramuscular oxytocin were equally effective in the management of 3rd stage of labour.

Keywords: Sublingual Misoprostol, Intramuscular Oxytocin, haemoglobin.

Introduction

Pregnancy and childbirth involves significant health risks, even to women with no pre-existing health problem.PPH is the most common cause of obstetrical haemorrhage. Atonic postpartum hemorrhage (PPH) accounts for a mortality rate of 140,000 per year, or one maternal death for every four minutes worldwide and is the most common preventable cause[1]. As per SRS 2010-12 reports, Indian MMR is 178 per one lakh live births while that of Andhra Pradesh is 110 per one lakh live births. Uterine atony accounts for 80% of cases of PPH[2]. Majority of these deaths are due to problems of third stage of labour and occur within four hours of delivery[3]. Catastrophic nature of PPH accounts for the higher maternal morbidity and mortality rates in developing countries like India. PPH is defined as any amount of bleeding from or in to genital tract following birth of baby with in 24 hrs of delivery. Most of these deaths occur in developing countries, often because women lack access of life saving care. Active management of the third stage of labour (AMTSL) which includes early cord clamping, controlled cord traction for placental delivery and intramuscular uterotonic therapy is an effective measure to prevent PPH Active management of third stage of labour has shown to reduce the blood loss by as much as 66 percent in comparison to expectant management. These uterotonic agents stimulate uterine contractions which cause compression of the maternal blood vessels at the placental site after delivery of the placenta and controls bleeding. Oxytocin is unstable at high ambient temperature, need refrigeration for storage and transport, need clean syringe and trained person for administration. It is expensive, has certain limitations and unpleasant sideeffects. FIGO recommends AMTSL for all parturients to reduce the post partumhemorrhage and its related consequences[4].

Hence current oxytocic drugs are far from ideal, particularly for routine use in developing countries, where 76% of deliveries take place at home, far from hospitals or medical facilities and are supervised solely by trained birth attendants. Where maternal mortality is high and resources are limited, the introduction of low-cost, evidence based practices to prevent and manage postpartum hemorrhage can improve maternal and infant survival. Thus, there is a need for an effective uterotonic drug that can be administered orally and which does not require special storage condition.

Misoprostol, a synthetic prostaglandin E1 analogue , which causes the uterus to contract and thus can reduce postpartum bleeding. Misoprostol has a range of potential benefits including ease of administration (oral or rectal or sublingual), rapidly absorbed, low cost and does not require any specific condition for the storage and transport, has a shelf-life of seveal years and thus is a suitable

*Correspondence
Dr. Siddula Shireesha
Assistant Professor, Modern Government Maternity Hospital, Petlaburj/Osmania Medical College, Hyderabad, Telangana, India.
E-mail: sirika0303@gmail.com

uterotonic agent for use in the prophylactic management of third stage of labour especially in developing countries like ours. The present study is an attempt to assess the effect of sublingual misoprostol on 3rd stage of labour in comparison with standard oxytocin regimen.

Materials and methodology

This randomized study was done to compare the efficacy of sublingual misoprostol with the intramuscular oxytocin in the management of third stage of labour in low risk vaginal deliveries. This study was conducted in the Department of Obstetrics &Gynecology at Guntur General Hospital, Guntur, during the period March 2014 to September 2015.

Inclusion Criteria

Singleton pregnancy with live fetus with cephalic presentation, pregnancy of more than 28 weeks gestation, Spontaneous onset of labour and delivering vaginally.

Exclusion Criteria

Grand multipara – more than 5 ChorioamnionitisHydramnios, Antepartum haemorrhage, Pre-eclampsia and eclampsia, History of previous postpartum hemorrhage Previous cesarean section, Instrumental deliveries,Coagulation abnormalities Severe anemia in pregnancy with Hb% less than 6 gm% **,** Cardiac diseases and diabetes and Intrauterine death

After a detailed history, general and obstetric examination and routine investigation, patients who fulfilled the selection criteria were assigned randomly to two groups:

Group-I: Misoprostol group (100 cases) 3 tablets of misoprostol 200µg each was given sublingually after cord clamping and cutting

Group-II: Oxytocin group (100 cases)Injection oxytocin 10IU intramuscular after cord clamping and cutting.

A total of 200 cases were studied with 100 cases in each group. In third stage of labour,. 500 ml of isotonic fluid (RL) was started in both the groups, and immediately after the delivery of the baby, the cord was clamped and cut.

The women were asked to keep misoprostol 600µg sublingually or injection oxytocin 10 IU was given intramuscularly. The placenta was delivered by controlled cord traction. The duration of third stage of labour was noted in both the groups. Theblood loss was measured in both the groups for the 1st hour after delivery. Blood loss was measured by graduated jar after direct collection in the pan and by gravimetric method. Postpartum hemorrhage in the present study is defined as blood loss >500 ml in 1st hour after delivery. Once the diagnosis of postpartum hemorrhage was made, the patients were managed as per the needs by giving additional oxytocics drugs (injection methyl ergometrine or injection prostadin). The maternal hemoglobin was measured on admission and 24 hours after delivery by Sahil's hemoglobinometer and the change in haemoglobin percentage was taken as an objective measure of postpartum hemorrhage. Patients were observed for 1 hour following delivery for vital signs and bleeding per vagina.

The occurrence of side effects like nausea, vomiting, shivering, fever, diarrhoea, hypotension, etc. within first 24 hours of delivery were recorded. This study was computed by using parametric and non-parametric tests like impaired 't'-test and chi-square test.

Results

Table-1: Distribution of cases according to patient details

Age (in years)	Misoprostol group	Oxytocin group
< 20	25	34
21-25	57	49
26-30	14	15
> 30	04	02
Total	100	100
Parity		
Primi	49	51
Multi	51	49
Duration (min)		
<4	58	44
4-5	20	38
5–7	13	13
>8	09	05

Maximum of women were between 21-25 years in both the groups. The distribution of patients according to parity was similar in both groups. Almost equal number of cases of primi and multi gravidas were included in the study. Duration of 3rd stage of labour was less than 5minutes in maximum number of patients in both the groups. There were only few cases with 3rd stage of labour more than 8 mts.

Table-2: Distribution of Blood loss in both groups (ml)

Blood loss (ml)	Misoprostol group	Oxytocin group
< 100	10	11
101-200	53	46
201-300	26	27
301-400	08	12
401-500	01	02
> 500	02	02
Total	100	100

In the present study 53% women belonging to misoprostol group and 46% women belonging to oxytocin had blood loss between 100-200ml.26% in misoprostol group and 27% in oxytocin group had blood loss between 200-300 ml. 2% of cases in each group had blood loss more than 500 ml and required additional oxytocics. In both the group blood loss in most of the cases was up to 200 ml. Both the groups have equal number of cases with blood loss more than 500 ml.

Table-3: Distribution of hemoglobin levels before and after delivery in both groups.

Predelivery haemoglobin (g/dl)	Misoprostol group (n=100)	Oxytocin group (n=100)
8.1- 9	10	12
9.1-10	59	42
10.1-11	19	29
11.1-12	05	11
>12	07	06
Maean	10.20	10.30
Postdelivery hemoglobin (g/dl)		
8-9	47	38
9.1-10	40	45
10.1-11	12	13
11.1-13	01	04
Mean	9.3	9.5

In both study groups most of the cases pre delivery haemoglobin levels are in between 9-11 g/dl. In both groups most of the cases post delivery levels in between 8-10g/dl. There was a mean difference of 0.9 and 0.8 between the pre delivery and post deliveryhemoglobin levels noted in the Misoprostol and Oxytocin groups respectively. These particular differences were not statistically significant [Chi square value= 0.001, P value=0.48].

Table-4: Postpartum Complications in both groups

Complications	Misoprostol group (n=100)	Oxytocin group (n=100)
Postpartum Hemorrhage	2	2
Injmethergin and prostaglandin	2	2

There were equal number of cases of postpartum hemorrhage in both the groups. There was no case of retained placenta noted in either of group. There are only 2 cases in each group with occurrence of PPH with blood loss more than 500 ml which required additional oxytocics like methyl ergometrine and prostadin to control blood loss.Number of cases who received additional oxytocics were 2 in each group.

Table-5: Side Effects in both groups

Side effects	Misoprostol group	Oxytocin group
shivering	12	2
Pyrexia	4	2
vomitings	1	1
Pain abdomen	0	0
diarrhea	0	0

In the present study shivering is observed in 12% of cases in misoprostol group and 2% of cases in oxytocin group,4% of cases in misoprostol and 2% of cases in oxytocin group had pyrexia,1% of cases in each group had vomiting.no parturients had pain abdomen or diarrhea. Shivering and pyrexia were the most common side effects noted in the misoprostol group.

Discussion

In developing countries, the risk of dying from PPH is 1 in 1000 deliveries. The incidence of PPH varies from 4 to 6% of all deliveries 75 to 90% of cases PPH is due to atonicity of uterus. More than half of deaths from postpartum hemorrhage occur within the first 24 hours of delivery, of these 88% occur within 4 hours of delivery. Active managementof 3 rd stage of labour by routine use of oxytocic drugs has been estimated to reduce PPH by 40%. Current oxytocic drugs are far from ideal particularly for routine use in developing countries, where simple route of administration, stable and inexpensive drugs are needed because many deliveries take place far from hospitals or medical facilities and are supervised solely by birth attendants. Misoprostol is a PGE1 analogue, which has been shown to have myometrial stimulating property. It can be administered orally and is rapidly absorbed, stable at room temperature, has low cost and can be used by birthattendants. Its use in 3 stage of labour was suggested by many studies.

The demographic characteristics of both the groups were comparable in relation to age, parity and period of gestation. Therefore, the present study was undertaken to evaluate the efficacy of sublingual misoprostol in the active management of 3rd stage of labour and compare it with injection oxytocin used intramuscularly in low risk women. Prophylactic administration of uterotonics to reduce blood loss from atonic PPH in the active management of third stage of labour is rising significantly day by day universally. Misoprostol use in AMTSL is increasing enormously, especially in poor resource settings with limited facilities for Oxytocin storage and minimal skilled health care personnel for administration of medication.

In the present study, in both the groups majority of the women belonged to the age group of 21-25 years i.e., 57% in misoprostol group and 49% in oxytocin group. This reflects the peak reproductive period. The mean age of the study participants was 22.5 years ranging from 18 to 35 years.

Table-6: Comparison of variable between both groups

Authors (Years)	Amount of Blood Loss (ml)	
	Misoprostol group	Oxytocin group
Rojaria et al (2013)[5]	210	223
Chaudhuri et al (2012)[6]	153	146
Present study	217.9	233.45
Additional oxytocics(%)		

Mukta mani et al (2013)[7]	22	16
Chaudhuri et al (2012)[6]	6	5
Present study	2	2
Change in haemoglobin value after delivery(gm/dl)		
Mukta mani et al (2013)[7]	0.55	0.48
Rojarialata et al (2013)[5]	0.45	0.48
Present study	0.9	0.8

In the present study average blood loss in the Misoprostol group was approximately 217.9 ml whereas Oxytocin group parturients had a blood loss of 233.45 ml. In the present study, in both the groups majority of women had blood loss up to 200 ml i.e., 70% and 76% in misoprostol group and oxytocin group respectively. Both the groups had equal number of cases with blood loss more than 500 ml i.e, 2% in each group.

The mean blood loss in misoprostol group was more compared to oxytocin group. But the difference between two group was not statistically significant. The result of the present study was in accordance with the above studies. In Rojaria et al[5] study the mean blood losss in misoprostol group is 210 ml and 223 ml in oxytocin group.In Chaudhuri et al[6] the mean blood loss in misoprostol group is 153 ml and 146 ml in oxytocin group respectively.

In the present study additional oxytocics were used in 2% of cases in each group. Addition oxytocics were administered only when blood loss was more than 500 ml or PPH was diagnosed. There are only 2 cases in each group with occurrence of PPH which required additional oxytocics like methyl ergometrine and prostadin to control blood loss.

Number of cases who received additional oxytocics were 2 in each group. The mean blood loss in misoprostol group was more compared to oxytocin group. But the difference between two group was not statistically significant. In Mukta mani et al[7] study 22%of cases in misoprostol group and 16% of cases in oxytocin group developed PPH and given additional oxytocics, in Chaudhuri et al[6] 6% of cases in misoprostol and 5% of cases n oxytocin group developed PPH and received additional oxytocics like methyl ergometrine and prostaglandin.

Both the groups showed postpartum reduction of hemoglobin value. The mean hemoglobin value before delivery in misoprostol group and oxytocin group was 10.2gm/dl and 10.3 gm/dl respectively. The postpartum hemoglobin value (after 24 hours of delivery) in misoprostol group and oxytocin group was 9.3gm/dl and 9.5 gm/dl respectively. The reduction of hemoglobin value in misoprostol group and oxytocin group was 0.9and 0.8g/dl respectively. In Mukta mani study also the mean change in haemoglobin levels were 0.55 and 0.48g/dl in misoprostol and oxytocin group respectively.so the present study was comparable with other studies

Table-7: Side effects of drugs

Author (Year)	Shivering (%)		Pyrexia (%)		Vomiting (%)	
	Misoprostol group	Oxytocin group	Misoprostol group	Oxytocin group	Misoprostol group	Oxytocin group
Atukunda et al (2014)[8]	56	26	9.3	2.1	24	15
Mukta mani et al(2013)[7]	50	8	6	2	4	2
Rojaria et al (2012)[5]	12	3	5	2	2	.1
Present study	12	2	4	.2	1	1

In the present study shivering was observed in 12% cases in misoprostol group compared to 2% cases in oxytocin group. Pyrexia was observed in 4% in misoprostol group compared to 2% cases in oxytocin group. In misoprostol group, 1 case had vomiting in both oxytocin group and misoprostol group.

Shivering and pyrexia were the most common side effect noted in misoprostol group. The result of the present study was in accordance with the above studies. Like other studies, this trial found sublingual misoprostol is equally effective to intramuscular oxytocin in reducing PPH, with side effects being greater in the misoprostol group. The sublingual route may increase the effectiveness of misoprostol, and render it equally efficacious to injectable oxytocin for the prevention of PPH[9,10]. Further research is needed to confirm these results.

Conclusion

Administration of sublingual misoprostol in the active management of third stage of labour in patients is as effective as intramuscular oxytocin in terms of reduction of PPH. Hemoglobin levels 24 hours after delivery were comparable with before delivery levels. Side effects like shivering and pyrexia are more common with misoprostol,but not severe enough to discontinue use of the drug for AMTSL. Misoprostol is safe to use in the third stage of labour for prevention of atonic PPH. Sublingual route of administration of misoprostol offers the advantage of administration by unskilled health personnel and making it an important medication in the underserved regions to prevent atonic PPH.

No requirement of refrigeration for storage of misoprostol when compared to intramuscular Oxytocin adds to its potential use in poor resource settings. Further randomized controlled trials involving larger study populations are needed to assess the safety profile and effectiveness of sublingual misoprostol over intramuscular oxytocin in prevention of atonic postpartum hemorrhage.

References

1. http://nrhm.gov.in/nrhm-components/rmnch-a/maternal-health/janani shishusurakshakaryakram/background.html?tmpl=component&print=1&pag e= (Accessed on 27/09/2014) .
2. http://www.censusindia.gov.in/vital_statistics/SRS_Bulletins/MMR_Bulletin- 2010-12.pdf (Accessed on 19/10/2014) .
3. Ramanathan G, Arulkumaran S. Postpartum haemorrhage. CurrObstetGynaecol 2006;16(1):6–13.
4. FIGO Safe Motherhood and Newborn Health (SMNH) Committee. FIGO GUIDELINES Prevention and treatment of postpartum hemorrhage in low- resource settings. International Journal of Gynecology and Obstetrics. 2012;117: 108–118
5. Rajoria et al : Active management of third stage of labour in low resource setting: sublingual misoprostol or intramuscular oxytocin. Indian Journal of Medical Case Reports: 2013 July-September. Vol.2 (3).
6. Chaudhuri P, Biswas J, Mandal A : Sublingual misoprostol versus intramuscular oxytocin for prevention of postpartum hemorrhage in low-risk women. Int J Gynaecol Obstet:2012: 116: 138–142
7. Mukta, Mani & Sahay, Priti. Role of Misoprostol 600 mcg Oral in Active Management of Third Stage of Labor: A Comparative Study with Oxytocin 10 IU i.m. The Journal of Obstetrics and Gynecology of India.2013: 63. 10.
8. Atukunda EC, Brhlikova P, Agaba AG, Pollock AM: Registration, procurement, distribution, and use of misoprostol

in Uganda: an interview- based observational study. Lancet :2014: 382: 10.
9. Bellad MB, Tara D, Ganachari MS, Mallapur MD, Goudar SS, Kodkany BS, Sloan NL, Derman R. Prevention of postpartum haemorrhage with sublingual misoprostol or oxytocin: a double-blind randomised controlled trial. BJOG. 2012 Jul;119(8):975-82.
10. Anyakora, C., Oni, Y., Ezedinachi, U. et al. Quality medicines in maternal health: results of oxytocin, misoprostol, magnesium sulfate and calcium gluconate quality audits. BMC Pregnancy Childbirth :2018: 18, 44.

Conflict of Interest: Nil Source of support: Nil