World Journal of Pharmaceutical and Life Sciences
WJPLS
www.wjpls.org
SJIF Impact Factor: 5.008

ORAL MISOPROSTOL VERSUS OXYTOCIN IN THE MANAGEMENT OF THIRD STAGE OF LABOUR

Rashi Rashi[1]*, Sipra Singh[2] and Soma Bandopadhyaya[3]

[1]Senior Resident, Department of Obstetrics & Gynecology, Katihar Medical College and hospital, Katihar, Bihar.
[2]Proffessor, Department of Obstetrics & Gynecology, Katihar Medical College and hospital, Katihar, Bihar.
[3]HOD, Department of Obstetrics & Gynecology, Katihar Medical College and hospital, Katihar, Bihar.

***Corresponding Author: Rashi Rashi**
Senior Resident, Department of Obstetrics & Gynecology, Katihar Medical College and hospital, Katihar, Bihar.

Article Received on 18/12/2018 **Article Revised on 09/01/2019** **Article Accepted on 30/01/2019**

ABSTRACT

Objectives: To compare oral misoprostol versus intramuscular oxytocin in the management of third stage of labour. **Methods:** The quasi-experimental study was conducted at the Department of Obstetrics & Gynecology, Katihar Medical College and hospital, Katihar, Bihar from Januaary 2017 to June 2017, after approval of the study by institute ethical committee. One hundred women attending the labor ward were included after taking informed consent. A total of 100 patients diagnosed in active phase of labour who fulfilled the inclusion criteria were selected by non-probability convenience sampling. These patients were divided into 2 groups of 50 patients each, for Oxytocin (Group 1) and misoprostol (Group 2). Main and secondary outcome measures were analysed. SPSS 10 was used for statistical analysis. **Results:** Average amount of blood loss(ml) was 267.14±140.35 with Oxytocin versus 302.86±160.4, with Misoprostol, this difference was statistically insignificant (p=0.236). Average drop in haemoglobin concentration (g/dl) with Oxytocin was 1.55±0.38 vs 1.66±0.61 with Misoprostol (p=0.684). Drop in haematocrit (%) was 4.18±0.64 with Oxytocin vs. 4.50±0.92 with Misoprostol (p=0.133). There was also insignificant difference in duration of third stage of labour, between oxytocin and Misoprostol groups (5.37±2.20 vs. 5.23±2.46, p=0.451) Shivering, in Misoprostol group occured in n=11 (31.4%) vs n=3 (8.6%) with Oxytocin (p=0.017) and pyrexia in n=6 (17.1%) with misoprostol vs n=0, with oxytocin (p=0.025) thus significantly higher in misoprostol group. **Conclusion:** There were no major differences in oral misoprostol and intramuscular oxytocin in the management of third stage of labour.

KEYWORDS: Postpartum haemorrhage, Third stage of labour, Active management of third stage, Misoprostol, Oxytocic drugs.

INTRODUCTION

Pregnancy and child birth involves significant health risks even to women with no pre-existing health problem. PPH is the most common cause of obstetrical haemorrhage. Atonic post partum haemorrhage(PPH) accounts for a mortality rate of 1,40,000 per year or one maternal death for every four minutes world wide and is the most common preventable cause.[1] As per SRS 2010-12 reports, Indian MMR is 178per one lakh live births while that of Andhra Pradesh is 110 per one lakh live births.[2] Uterine atony accounts for 80% of cases of PPH(3-4).Majority of these deaths are due to problems of third stage of labour and occur within 4hrs of delivery.[5,6] 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 into genital tract following birth of baby within 24hrs of delivery that deteriorates - the maternal condition 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% in comparison to expectant management.[7] These uerotonic 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 side effects. FIGO recommends AMTSL for all parturients to reduce the post partum haemorrhage and its related consequences.[8] Hence current oxytocic drugs are far from ideal, particularly for routine use in developing countries, where 76% of deliveries takes place at home, far from the 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 post partum haemorrhage can improve maternal and fetal survival. Thus there is a need for effective uterotonic drug that can be administered orally and which does not require special storage condition. Misoprostol, a synthetic prostaglandin E1analogue, which causes the uterus to contract and thus can reduce the post partum bleeding. Misoprostol has a range of potential benefits including ease of administration(oral, rectal or sublingual),rapidly absorbable, low cost and doesnot require any specific condition for storage, transport, has a shelf-life of several years and thus is a suitable uterotonic agent for use in the prophylactic management of third stage of labour especially in developing countries like ours. Present study is an attempt to assess the effect of sublingual Misoprostol on third stage of labour in comparison with standard oxytocin regimen.

PATIENTS AND METHODS

The quasi-experimental study was conducted in the department of Obstetrics and Gynaecology Katihar Medical College and hospital, Katihar, Bihar from Januaary 2017 to June 2017, after approval of the study by institute ethical committee. A total number of 100 patients who were admitted through outpatient department (OPD) or were admitted in delivery suite with anticipated vaginal delivery were selected. Half of the patients were allocated to receive oral misoprostol 600µg (3tablets of 200µg) and 50 patients were allocated to receive 10 units intramuscular oxytocin for the management of third stage of labour. The technique used for sampling was non-probability convenience sampling. The inclusion criteria for the study entailed: pregnant nulliparous and multiparous women, in active labour and expecting to have vaginal delivery. The exclusion criteria comprised history of previous caesarean section, history of asthma, deranged liver function in severe pregnancy-induced hypertension, and history of viral hepatitis. After informed consent, data was collected on a proforma containing information on maternal demographic characteristics such as age, weight, parity, gestational age at delivery, obstetrical history, including parity, history of PPH, essential or pregnancy-induced hypertension. Labour details were also recorded concerning induction, augmentation of labour, mode of delivery, episiotomy, vaginal or cervical tears. Haemoglobin and haematocrit was performed at the time of admission and repeated 24 hours after delivery. Delivery was conducted by resident R-1 or above. Third stage of labour was managed by early cord clamping and cutting, controlled cord traction and uterine massage. Blood loss was subjectively estimated by visual estimation of blood in a steel bedpan connected to the delivery table. Blood was collected with the help of a plastic sheet. Patients were observed in the labour room for side effects such as shivering, fever (temperature >100°F), nausea, vomiting and diarrhoea and were followed in the ward upto a period of 24 hours after delivery. Data was analysed on SPSS version 10. Continuous variables such as age, parity, weight, gestational age, duration of third stage of labour, amount of blood loss, drop in haemoglobin and haematocrit were presented as mean ± standard deviation. Independent sample t test was applied after checking for normal distribution, by Kolmogorov Smirnov test ($p>0.05$) to compare weight between the two groups. Similarly, independent sample t test was applied for drop in haematocrit and haemoglobin. Main outcocme measures i.e duration of third stage(minutes) and amount of blood loss (ml) were checked for normal distribution by applying Kolomogorov smirnov test and were found non-normally distributed($p<0.001$) so Mann Whitney U test was applied to compare these variables between Oxytocin and Misoprostol groups. Level of significance was <0.05 for all statistical tests. Percentages were calculated for qualitative variables i.e mode of delivery, fever, shivering, nausea and vomiting, blood loss >500ml, need for blood transfusion and additional oxytocic drugs. Chi square test was applied to compare shivering, augmented labour, episiotomy, and also collectively for all adverse effects and those labour variables which could influence amount of blood loss i.e augmented labour, episiotomy, forceps delivery, vaginal and cervical tears.. As the cell count was <5 in certain qualitative outcome variables i.e blood loss >500ml, use of additional oxytocic drugs, blood transfusion, fever, nausea, vomiting, forceps, and vaginal/cervical tears, Fischer exact test was applied to compare these variables. Level of significance was taken as <0.05.

A total of 100 women were enrolled in the study and were divided into 2 equal groups: 50 (50%) in the oxytocin group (Group 1); and 50 (50%) in the Misoprostol group (Group 2). The commonest age group was 21-25 years in both the groups. Mean age of patients in group 1was 26.6±6.11 years and 25.26±4.93 in group 2. Mean weight of patients in group 1 was 60±8.09kg and 61.42±7.03kg in group 2 ($p=0.754$). Mean gestational age (weeks) of patients in group 1 was 39.97±1.74 and that of group 2 was 39.71±2.16 ($p=0.586$). In group 1, (98%) were delivered by spontaneous vaginal delivery and (2%) by forceps delivery.

Table 1: Comparison of labour variables influencing amount of blood loss.

Variable	Group 1 (Oxytocin)	Group 2 (Misoprostol)	p value
Augmented Labour**	06 (12)	04 (8)	0.495
Forceps delivery	01(2)	0	1.000
Episiotomy***	10(2)	17(34)	0.086
Vaginal/cervical tear	1(2)	0	1.000

Values given in parentheses are percentages.
Overall insignificant difference between variables influencing blood loss (p=0.630).
* Labour which progressed normally with adequate uterine contractions without the use of drugs till delivery.
** Labour in which drug (Oxytocin infusion) was used to achieve adequate uterine contractions before delivery.
*** Incision given at perineum to increase the diameter of vulval outlet at delivery.

Table 2: Comparison of adverse effects between two groups n=100.

Adverse Effects	Group 1 (Oxytocin)	Group 2 (Misoprostol)	p value
Shivering	3(6)	11(22)	0.017
Fever *	0	6(12)	0.025
Nausea and Vomiting	1(2)	3(6)	0.614
Total	4	20	<0.001

Values given in parentheses are percentages.
Overall Significant difference in adverse effects between two groups (chi2=16.23, p=<0.001). *Temperature >100.
Average duration of third stage of labour in group 1 was 5.37±2.20 minutes and in group 2 it was 5.23±2.46 minutes (p=0.451).

Average amount of blood loss was higher in group 2 than group 1 (302.86±160.4 vs 267.14±140.35; p=0.236). Amount of blood loss >500ml was found in 3(6%) patients in group 1 as compared to 4(8%) in group 2 (p>0.05). Overall incidence of PPH defined as blood loss >500ml in all the study patients was 10%. None of the patients in the study population had blood loss >1000ml.

In group 1, 8% patients needed additional oxytocic drugs as compared to 10 in group 2 (p>0.05). Blood transfusion was needed postpartum in 1(2%) patient in group 1 as compared to 2(4%) patients in study group 2 (p>0.05). No patient required manual removal of placenta.

The average drop in haemoglobin concentration (g/dl) observed in group 1 was 1.55±0.38 vs 1.66±0.61 in group2 (p=0.684). Average drop in haematocrit (%) level though observed more in group 2 was insignificant between the two groups (4.18±0.64 vs. 4.50±0.92; p=0.133)

DISCUSSION

The risk of maternal death due to PPH is approximately 1 in 1000 deliveries in the developing world.3 Caliskan E et al in a randomised controlled trial compared oral misoprostol 400µg(followed by 2 doses of 100µg 4 hours apart) with intravenous infusion of oxytocin, combination of misoprostol and intravenous oxytocin infusion and combination of methylergonovine and intravenous oxytocin infusion. They also reported insignificant difference in the length of third stage of labour between misoprostol and intravenous oxytocin infusion groups.[9] Pharmacokinetic studies show that absorption times of intramuscular and intravenous oxytocin are similar (1-2min) so their effectiveness is also expected to be similar.[10] Average amount of blood loss was higher in group 2 as compared to group 1 but it was not statistically significant. Overall incidence of PPH (defined as blood loss more than 500ml) in the study group was 10%. Incidence of PPH with blood loss >500ml but < 1000ml in group 2 was slightly higher than group 1 (8% vs 6%) but it was also not statistically significant. None of the patients in the study group had massive PPH defined as blood loss more than 1000ml. World Health Organisation (WHO) multicentre randomised trial which compared 600µg oral misoprostol with 10 IU of intramuscular or intravenous oxytocin showed that blood loss was consistently higher in group 2, with higher rates of blood loss more than 1000ml as compared to group 1, Similarly misoprostol is also associated with increased use of additional oxytocics.[10]

It has been established that prophylactic administration of oxytocic agents in the active management of the third stage of labour could significantly reduce the incidence of primary PPH. In addition, the time for administration of therapeutic oxytocic drugs is reduced from 15 minutes to five minutes.[11] This practice has become a standard of obstetric care, and misoprostol has emerged as a promising treatment alternative.[12]

This prospective randomised comparative clinical trial showed that orally administered misoprostol, with its rapid onset of action, is as effective as intramuscular oxytocin in minimising blood loss in the third stage of labour. No incidence of PPH (blood loss < 500 ml) was recorded in both groups. The average blood loss, drop in haemoglobin concentration levels and the need for additional uterotonics in the two arms of the study were

not statistically significant. This is similar to the findings in previous studies.[12]

Mean duration of third stage with misoprostol was 5.23±2.46 minutes in our study whereas another study on 600 women receiving same dose of misoprostol reported longer duration of 7.9±4.2 minutes.[13] There were slightly greater percentage of patients in group 2 as compared to group 1 who required additional oxytocics in the same proportion as the increased percentage of patients with blood loss >500ml. But the largest ever trial on misoprostol use in third stage of labour involving >9000 women demonstrated higher proportion of women requiring additional oxytocic drugs.[14] Proportion of women requiring blood transfusion postpartum was slightly higher in misoprostol group, but it was not statistically significant.

In this study, an analysis of the side effects of the two uterotonic agents revealed that nauseaand shivering was mainly seen in the misoprostol group, and this was a statistically significant. This is in tandem with the results of other studies.[15]

However, these undesirable side effects of misoprostol were found to be self-limiting, and shivering could be contained by simply covering the patient with blankets.

Misoprostol has many advantages. It is cheap per treatment compared to oxytocin at 640 Naira), has a long shelf life and is thermostable (storable at tropical temperatures, and hence requiring no refrigeration). No special training is needed to administer it, and it has an acceptable safety profile.

CONCLUSION

In conclusion, this study suggested that oral misoprostol appeared to be as effective and as safe in minimising blood loss in the third stage of labour as intramuscular oxytocin. Further research to determine the least effective dose of misoprostol that will result in the least acceptable side effects is recommended. Meta -analytic studies on this topic are also desirable.

Misoprostol has great potential for use in the active management of the third stage of labour, especially in developing countries. Although this clinical trial was limited to low -risk parturients, misoprostol is also effective in high -risk patients with bronchial asthma, pregnancy -induced hypertension and Rhesus -negative blood groups, where other oxytocics (especially ergometrine) may be contraindicated.

REFERENCES

1. http://nrhm.gov.in/nrhm-components/rmnch-a/maternal. health/jananishishusurakshakaryakram/background. html/tmpl=component&print=1.
2. http://www.censusindia.gov.in/vital_statistics/SRS_ Bulletins/MMR_Bulletin-2010-12.
3. Kane TT,el-kady AA, Saleh S,Hage M,Stanback J,Potter L.Maternal mortality in Giza,Egypt:magnitude, causes and prevention,Stud Fam Planning, 1992; 23: 45-57.
4. G.A.Dildy III," Postpartum haemorrhage: new management options," clinical Obstetrics and Gynaecology, 2002; 45(2): 330-344.
5. Abou Zahr C Global burden of maternal death and disability. Br Med Bull, 2003; 67: 1-11.
6. Ramanathan G, Arulkumaran S. Postpartum haemorrhage. Curr Obstet Gynaecol, 2006; 16(1): 6-13.
7. Begley CM, Gyte GM, Murphy DJ, Devane D, McDonald SJ, McGuire W. Active versus expectant management for women in the third stage of labour.
8. FIGO Safe Motherhood and Newborn Health(SMNH) Committee. FIGO GUIDELINES Prevention and treatment of postpartum haemorrhage in low-resource settings. International Journal of Gynaecology and Obstetrics, 2012; 17: 108-118.
9. Caliskan E, Dilbaz B, Meydanli MM, Ozturk N, Narin MA, Haberal A. Oral misoprostol for the third stage of labor: a randomized controlled trial. Obstet Gynecol, 2003; 101: 921-8.
10. Gulmezoglu AM, Villar J, Ngoc NT, Piaggio G, Carroli G, Adetoro L, et al. WHO multicentre randomised trial of misoprostol in the management of the third stage of labour. Lancet, 2001; 358: 689-95.
11. Amant F. The misoprostol third stage study: a randomised controlled comparison between orally administered misoprostol and standard management: A double-blind placebo controlled randomised trial of misoprostol and oxytocin in the management of the third stage labour. BJOG, 2001; 108: 338-9.
12. Oboro VO, Tabowei TO. A randomised controlled trial of misoprostol versus oxytocin in the active management of third stage of labour. J Obstet Gynaecol, 2003; 23: 13-6.
13. Chandhiok N, Dhillon BS, Datey S, Mathur A, Saxena NC. Oral misoprostol for prevention of postpartum hemorrhage by paramedical workers in India. Int J Gynaecol Obstet, 2006; 92: 170-5.
14. Gulmezoglu AM, Villar J, Ngoc NT, Piaggio G, Carroli G, Adetoro L, et al. WHO multicentre randomised trial of misoprostol in the management of the third stage of labour. Lancet, 2001; 358: 689-95.
15. Amant F, Spitz B, Timmerman D, Corremans A, Van Assche FA. Misoprostol compared with methylergometrine for the prevention of postpartum haemorrhage: a double-blind randomised trial. Br J Obstet Gynaecol, 1999; 106: 1066-70.