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Original Research Article

LOW DOSE ORAL MISOPROSTOL VERSUS 10 IU INTRAMUSCULAR OXYTOCIN IN THE MANAGEMENT OF THIRD STAGE OF LABOUR

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ABSTRACT

Background: Postpartum hemorrhage (PPH) is a significant cause of maternal morbidity and mortality, especially in resource-constrained settings. The study compares the effectiveness of two doses of oral misoprostol (400µg and 600µg) with intramuscular oxytocin (10 IU) in managing the third stage of labor. The objective is to determine the efficacy, safety, and side effects of each intervention, aiming to identify a suitable alternative in environments where oxytocin's storage requirements pose challenges.

Material and Methods: A prospective, randomized case-control study was conducted on 300 pregnant women in labor, divided into three groups. Group A1 received 400µg of misoprostol, Group A2 received 600µg, and Group B received 10 IU of intramuscular oxytocin. Blood loss was measured using a calibrated drape, and maternal and fetal parameters were closely monitored. Primary outcomes included PPH incidence and drug side effects, while secondary outcomes covered total blood loss, hemoglobin drop, and third-stage labor duration.

Results: The average blood loss was lowest in the oxytocin group (208.25 ml), with slightly higher values in the misoprostol groups (218.25 ml for 600µg and 235.75 ml for 400µg). PPH incidence did not significantly differ among groups. Notably, adverse effects, particularly pyrexia and shivering, were more common in the misoprostol groups, with higher frequencies observed in the 600µg group.

Conclusion: Oral misoprostol presents a viable option for managing the third stage of labor, particularly where oxytocin storage is problematic. However, its increased side effects, especially at higher doses, suggest a careful balance in dose selection. Oxytocin remains preferable where available and feasible for storage.

Keywords: Postpartum hemorrhage, misoprostol, oxytocin, third stage of labor, maternal mortality.

INTRODUCTION

The period following the delivery of a baby is a time of relief and joy for all involved. It is a period when both the parturient and the accoucher may be relieved with the safe delivery of a healthy baby and hence be lured into a false sense of security that all is safe and well. However, potential danger lurks for the mother during this period.[1-2] Although the third stage of labour is usually uneventful, several significant complications may be encountered that may lead to maternal morbidity and mortality. The most common and the most fatal of these complications is primary postpartum haemorrhage (PPH).[2-4]

Postpartum hemorrhage (PPH) is the most serious complication in obstetrics. The greatest number of maternal deaths from hemorrhage is due to PPH, which is almost entirely a preventable condition. It occurs in approximately 4% of vaginal deliveries,

and estimates are that it causes significant morbidity and 25% of all the maternal child birth related death.[5] WHO defines PPH as blood loss of 500 ml or more in first 24 hours postpartum.[6]

Since uterine atony is an important cause of this condition, uterotonic agents to control bleeding are the standard of care worldwide. Yet the risk of dying from the post-partum haemorrhage remains higher in developing countries. To reduce the MMR and achieve MDG5, WHO and professional bodies recommend active management of the third stage of labour (AMTSL) for all vaginal births in order to prevent PPH and when practiced routinely it can reduce hemorrhage by up to 60%.[7,8] This involves prophylactic administration of uterotonic medicines i.e. oxytocin 10 IU intramuscular immediately after the birth of baby, controlled cord traction of the umbilical cord (in settings where skilled birth attendants are available) and uterine massage. Although AMTSL reduces postpartum blood loss, about 3% to 16.5% of women will still go on to experience PPH and will require treatment. Oxytocin injection is the recommended first line uterotonic medicine for preventing and treating PPH. However, oxytocin is unstable at high temperature and requires special temperature storage conditions to remain effective.[9] The cold chain storage required to transport and store oxytocin is unreliable in resource-constrained countries. Oxytocin must be administered parenterally, requires the involvement of skilled health personnel.

A potential benefit of ergot preparations is a longer duration of action. Ergometrine also has to be given parenterally, requires a sterile needle and syringe as well as skilled attendant. It is not stable at high temperature and requires special storage conditions (2- 8ºC). It is contraindicated in diseases like heart disease, severe anaemia and hypertension, hence it is not a drug of choice.

The WHO 2012 guidelines for managing PPH advise the use of misoprostol in situations where the use of oxytocin is not possible.[10] Misoprostol does not require special storage condition and is known to have shelf life of several years. The slightly lower potency of misoprostol is partly offset by these advantages. However, misoprostol is sensitive to moisture and may degrade in areas of high humidity. It also has side-effects which include transient fever, shivering, nausea, vomiting and diarrhea. Misoprostol has been demonstrated to be effective for both the prevention and treatment of PPH.[11-14] With its low cost, pill form, heat stability, ease of administration and rapid oral absorption, there has been increasing evaluation for its doses and routes of administration and promotion of misoprostol in developing countries.[15-18]

Oxytocin, long considered the gold standard of uterotonics, remains an efficient uterotonic, with a slightly more rapid onset of action and more effective in PPH prevention but has a shorter half-life than misoprostol, however, the absolute risk difference is minima.[12,13] A meta-analysis found the incidence of PPH and severe PPH (≥1000 ml) to be similar when limiting the analyses to studies conducted in developing countries.[11] Concern about side effects has been raised, as the incidence of side effects is consistently greater with misoprostol than oxytocin, particularly shivering and pyrexia. As with other side effects, pyrexia associated with misoprostol has been found to be transient and without serious consequence. However, side effects directly related to dose remain a concern.[19] So, we planned to compare the low dose oral misoprostol with 600µg oral misoprostrol and 10IU oxytocin in the management of third stage of labour.

MATERIALS AND METHODS

This study was designed as a prospective case-control study and was conducted in the labour room of the Department of Obstetrics & Gynaecology at J.N. Medical College and Hospital, A.M.U., Aligarh. The study population consisted of pregnant women admitted in labour who were anticipating a vaginal delivery. Inclusion criteria specified that participants had to be carrying a singleton pregnancy at a gestational age of 28 weeks or more, either in spontaneous or induced labour, and were willing to provide informed consent. Women were excluded if they required a caesarean section, instrumental delivery, had multiple pregnancies, a known drug allergy, hemoglobin levels below 8 g/dl, or a history of bleeding disorders or certain pregnancy complications. Additionally, women with grand multipara status, episodes of antepartum hemorrhage during the current pregnancy, or high-risk conditions (such as diabetes, cardiac issues, seizure disorders, or pregnancy-induced hypertension) were also excluded.

The study participants were divided into two main groups based on the intervention received. Group A, the case group, was further divided into subgroups A1 and A2. Participants in Group A1 received 400µg of misoprostol orally, while those in Group A2 received 600µg of oral misoprostol. Both doses were administered immediately after the delivery of the baby and before placental delivery. Group B, the control group, received 10 IU of intramuscular oxytocin at the same point in the delivery process.100 Patients were included in each group.

Upon admission, eligible participants were randomized to receive one of the two oxytocic interventions, with the randomization determining their allocation to Groups A1, A2, or B. Maternal and fetal monitoring followed standard practice throughout the first and second stages of labour. After the delivery of the baby, the umbilical cord was clamped, and blood loss was measured using a calibrated drape placed under the patient's buttocks. This drape collected blood over the first hour post-delivery. The placenta was delivered through controlled cord traction, and both the placenta and

membranes were examined for completeness. If uterine atony was noted, additional uterotonics were administered, and the dosage and route were documented.

The study aimed to assess both primary and secondary outcomes. The primary outcome was the incidence of postpartum hemorrhage (PPH), defined as blood loss of ≥ 500 ml within the first hour following delivery, as well as any side effects of the drugs administered (including shivering, fever, nausea, diarrhea, and vomiting). Secondary outcomes included the total blood loss, the drop in hemoglobin concentration (measured before delivery and again 48 hours after), and the duration of the third stage of labour.

For statistical analysis, data were tabulated and analyzed with results expressed as mean ± standard deviation. The Student's t-test and chi-square test were employed to determine statistical significance, with a significance level set at $p<0.05$.

RESULTS

Mean age of misoprostol 600µg, misoprostol400µg and oxytocin group was 25.44 ± 3.49yrs, 24.82 ± 3.02yrs and 26.03 ± 3.57yrs respectively. The age group was almost similar in three groups except that oxytocin group had significantly higher age group ($p < 0.05$) as compared to misoprostol 400µg group. [Table 1]

20% patients were primiparous in misoprostol 600µg and oxytocin group, while 26% in misoprostol 400µg group. Maximum primiparous were in 18-22yrs age group in all 3 groups (65%, 61.53% and 60% respectively). Maximum multiparous were in 23-27yrs age group in all three groups (56.25%, 68.92% and 51.25% respectively). [Table 2]

Difference for gestational age was not significant between groups ($p > 0.05$). [Table 3]

Mean duration of third stage of labour of misoprostol 600µg, misoprostol400µg and oxytocin group was 4.70 ± 1.37min., 5.06 ± 1.10min. and 5.16 ± 1.29min. respectively. In all three groups maximum patients had ≤5 minutes duration of third stage of labour. There was no significant difference between misoprostol 400µg and 600µg groups. [Table 4]

Misoprostol 600µg and oxytocin groups had maximum number of patients (43% and 45%) in which blood loss was in the lowest range(100-199ml) as compared to Misoprostol 400µg group of patients(33%) where blood loss was in higher range (200-299ml). Mean blood loss was lower in oxytocin group as compared to misoprostol groups but it was significant only between oxytocin and misoprostol 400µg group ($p < 0.05$). [Table 5]

Blood loss was more in multiparous patients in comparison to primiparous patients in all three groups but the difference of blood loss between multiparous and primiparous patients was not significant in any group ($p > 0.05$). [Table 6]

There was no significant difference between misoprostol 600µg and misoprostol 400µg group. [Table 7]

Difference for incidence of postpartum hemorrhage was not significant between any groups. [Table 8]

Need of blood transfusion was lower in oxytocin group but the difference for additional oxytocics and blood transfusion was not significant between any groups. [Table 9]

Shivering and pyrexia were significantly high in misoprostol groups as compared to oxytocin group. Misoprostol groups compared together, shivering and pyrexia were more in misoprostol 600µg group but it was not significant ($p > 0.05$). [Table 10]

Table 1: Distribution of age (years)

Age group (years)	Misoprostol 600		Misoprostol 400		Oxytocin	
	N= 100	%	N= 100	%	N= 100	%
18-22	23	23.0	21	21.0	16	16.0
23-27	50	50.0	59	59.0	49	49.0
28-32	24	24.0	20	20.0	31	31.0
33-37	3	3.0	0	0.0	4	4.0
(Mean ± SD)	25.44 ± 3.49		24.82 ±3.02		26.03 ± 3.57	

Table 2: Age distribution of primiparous & Multiparous patients

Age group (years)	Misoprostol 600		Misoprostol 400		Oxytocin	
	n	%	n	%	n	%
Primiparous patients						
18-22	13	65.0	16	61.53	12	60.0
23-27	5	25.0	8	30.77	8	40.0
28-32	2	10.0	2	7.7	0	0.0
33-37	0	0.0	0	0.0	0	0.0
Multiparous patients						
18-22	10	12.5	5	6.75	4	5.0
23-27	45	56.25	51	68.92	41	51.25
28-32	22	27.5	18	24.32	31	38.75
33-37	3	3.75	0	0.0	4	5.0

Table 3: Gestational age (weeks)

Period of gestation (weeks) (mean ± SD)	Misoprostol 600	Misoprostol 400	Oxytocin
	38.84 ± 1.38	39.18 ± 1.36	39.25 ± 1.11

Table 4: Distribution of duration of third stage of labour (minutes)

Third stage of labour duration(minutes)	Misoprostol 600	Misoprostol 400	Oxytocin
≤5 minutes	68	62	53
5.1- 10 minutes	32	38	47
(mean ± SD)	4.70 ± 1.37	5.06 ± 1.10	5.16 ± 1.29

Table 5: Distribution of blood loss (milliliter)

Blood loss(ml)	Misoprostol 600		Misoprostol 400		Oxytocin	
	N= 100	%	N= 100	%	N= 100	%
100- 199	43	43.0	33	33.0	45	45.0
200-299	38	38.0	40	40.0	43	43.0
300- 399	13	13.0	22	22.0	9	9.0
400-499	3	3.0	1	1.0	1	1.0
500-599	2	2.0	1	1.0	1	1.0
≥ 600	1	1.0	3	3.0	1	1.0
mean ± SD	218.25 ± 95.93		235.75 ± 101.76		208.25 ± 73.68	

Table 6: Comparison of blood loss between primiparous and multiparous patients

Blood loss (ml) (mean ± SD)	Misoprostol 600	Misoprostol 400	Oxytocin
Primiparous	196.25 ± 67.51	224.04 ± 73.30	202.50 ± 86.94
Multiparous	223.75 ± 101.40	239.86 ± 110.17	211.69 ± 70.54
P value	NS	NS	NS

Table 7: Fall in hemoglobin (gm/dl)

Fall in hemoglobin(gm/dl) (mean ± SD)	Misoprostol 600	Misoprostol 400	Oxytocin
	0.800 ± 0.288	0.809 ± 0.265	0.702 ± 0.225

Table 8: Incidence of postpartum hemorrhage

Incidence of postpartum hemorrhage	Misoprostol 600		Misoprostol 400		Oxytocin	
	n	%	n	%	n	%
	3	3.0	4	4.0	2	2.0

Table 9: Need for additional oxytocics & blood transfusion

	Misoprostol 600		Misoprostol 400		Oxytocin	
	n	%	n	%	n	%
Additional oxytocics	11	11.0	15	15.0	9	9.0
Blood transfusion	3	3.0	5	5.0	3	3.0

Table 10: Uterotonic drug related adverse effects

Adverse effects	Misoprostol 600		Misoprostol 400		Oxytocin	
	n	%	n	%	n	%
Pyrexia	16	16.0	9	9.0	0	0.0
Shivering	15	15.0	7	7.0	2	2.0
Nausea	6	6.0	3	3.0	5	5.0
Vomiting	3	3.0	3	3.0	1	1.0
Diarrhea	4	4.0	2	2.0	0	0.0

DISCUSSION

300 pregnant women in labour were recruited for the present study, when vaginal delivery was imminent; 100 in each group. Patients were randomly allocated to receive oral misoprostol 400µg, oral misoprostol 600µg or intramuscular 10 IU oxytocin after delivery of baby and before the delivery of placenta.

In our study demographic variables of the parturients including their mean age, parity and period of gestation in weeks were similar in the three arms of the study. No statistically significant differences were found in any of these variables except for oxytocin group which had significantly higher age. These baseline parameters are comparable in our study as observed in various randomized controlled trials.[15,19]

In this study, the duration of the third stage of labor was lower in both misoprostol groups compared to the oxytocin group, with a statistically significant reduction observed only in the misoprostol 600µg group ($p < 0.05$). This finding is comparable to the results of Robert L. Walley et al,[15] who compared 400µg oral misoprostol with 10 IU intramuscular oxytocin in the routine management of the third

stage of labor and found a similar duration between the two groups (6.2 ± 3.8 minutes for misoprostol vs. 7.3 ± 13.1 minutes for oxytocin). Additionally, Chandhiok N. et al. 20, in a large-scale study involving 1200 women across 30 peripheral health centers in India, reported a significant reduction in the duration of the third stage of labor in the 600µg misoprostol group compared to the oxytocin group (7.9 ± 4.2 minutes vs. 10.9 ± 4.3 minutes; $p < 0.001$), findings that align closely with our results. In contrast, Mukta Mani et al,[21] observed no significant difference between oral misoprostol 600µg and 10 IU intramuscular oxytocin, with mean durations of 3.76 minutes for the misoprostol group and 3.50 minutes for the oxytocin group ($p > 0.05$), which differs from our findings.

In this study, the mean blood loss was 218.25 ± 95.93 ml for the misoprostol 600µg group, 235.75 ± 101.76 ml for the misoprostol 400µg group, and 208.25 ± 73.68 ml for the oxytocin group. While mean blood loss was generally lower in the oxytocin group compared to the misoprostol groups, the difference was statistically significant only between the oxytocin and misoprostol 400µg groups ($p < 0.05$). Misoprostol 600µg and oxytocin groups had the highest proportion of patients (43% and 45%, respectively) with blood loss in the lowest range (100-199 ml), compared to 33% in the misoprostol 400µg group, where blood loss was in a higher range (200-299 ml). Among all groups, similar percentages of patients experienced blood loss ≥500 ml (3%, 4%, and 2%, respectively). Differences in blood loss between primiparous and multiparous patients were not statistically significant within any group ($p > 0.05$), although multiparous patients tended to experience slightly higher blood loss. These findings align in part with those of Pisake Lumbiganon et al,[22] who found similar mean blood losses across misoprostol 400µg, misoprostol 600µg, and oxytocin groups (341 ml, 371 ml, and 353 ml, respectively). However, our results contrast with Robert L. Walley et al., 15 who observed comparable blood loss between oral misoprostol 400µg and intramuscular oxytocin (190 ± 78 ml vs. 187 ± 91 ml). Similarly, Afolabi E.O. et al,[23] found no significant difference in blood loss between 400µg misoprostol and oxytocin (153.20 ml vs. 155.60 ml), a finding that does not align with our study. Conversely, our results are consistent with Chandhiok N. et al,[20] who reported a significant reduction in blood loss with 600µg misoprostol compared to oxytocin in a large-scale study (100 ml vs. 200 ml, $p < 0.001$), although our results differed in mean blood loss values. Mukta Mani et al,[21] also reported no significant difference between misoprostol 600µg and oxytocin, with mean blood loss at 145 ml and 125.6 ml, respectively, similar to our findings. Abdulkarim O. Musa et al,[24] compared 600µg misoprostol and 10 IU oxytocin and found no statistically significant difference in mean blood loss (325.85 ± 164.72 ml vs. 303.95 ± 163.33 ml, $p = 0.391$), in line with the trends observed in our study.

In this study, the mean fall in hemoglobin level was 0.800 ± 0.288 g/dl for the misoprostol 600µg group, 0.809 ± 0.265 g/dl for the misoprostol 400µg group, and 0.702 ± 0.225 g/dl for the oxytocin group. The hemoglobin reduction was significantly greater in both misoprostol groups compared to the oxytocin group ($p < 0.05$), with no significant difference between the two misoprostol doses. This finding contrasts with the results of Robert L. Walley et al,[15] who found no significant difference in hemoglobin drop between oral misoprostol 400µg and intramuscular oxytocin in a double-blind placebo-controlled trial. Similarly, Afolabi E.O. et al,[23] reported comparable hemoglobin reductions of 0.4 g/dL in both groups, and Mukta Mani et al,[21] observed non-significant differences in hemoglobin fall between oral misoprostol 600µg (0.55 g/dl) and oxytocin (0.48 g/dl), findings that do not align with our results.

In this study, the incidence of postpartum hemorrhage (PPH) was 3% in the misoprostol 600µg group, 4% in the misoprostol 400µg group, and 2% in the oxytocin group, with no significant differences between groups. These results align with findings from Kundodyiwa T.W. et al,[25] who observed PPH in 15.2% of women receiving 400µg misoprostol and 13.3% of those receiving 10 IU oxytocin ($p = 0.534$), and Afolabi E.O. et al,[23] who reported no cases of PPH in either group. Similarly, Abdulkarim O. Musa et al,[24] recorded a PPH incidence of 15% with misoprostol 600µg and 14% with oxytocin ($p = 0.841$), findings that correspond closely with our study's results.

In this study, the need for additional oxytocics was 11% in the misoprostol 600µg group, 15% in the misoprostol 400µg group, and 9% in the oxytocin group, while the need for blood transfusion was 3% in the misoprostol 600µg and oxytocin groups and 5% in the misoprostol 400µg group, with no significant differences between groups. These results are consistent with findings by Robert L. Walley et al,[15] who observed similar needs for additional oxytocics between groups, with only one transfusion case in the oxytocin group. Similarly, Kundodyiwa T.W. et al,[25] found no significant difference in additional oxytocic or transfusion needs between women given 400µg misoprostol or 10 IU oxytocin. Afolabi E.O. et al,[23] also reported comparable requirements for additional uterotonics (7% overall), and Mukta Mani et al,[21] observed similar trends, with 22% requiring additional oxytocics in the misoprostol group and 16% in the oxytocin group. These findings align with the outcomes observed in our study.

In this study, adverse effects were most frequent in the misoprostol 600µg group, with incidences of pyrexia (16%), shivering (15%), nausea (6%), diarrhea (4%), and vomiting (3%). The misoprostol 400µg group showed lower incidences of pyrexia (9%), shivering (7%), nausea (3%), vomiting (3%),

and diarrhea (2%). The oxytocin group experienced minimal adverse effects, including nausea (5%), shivering (2%), and vomiting (1%), with no reports of pyrexia or diarrhea. Shivering and pyrexia were significantly higher in both misoprostol groups compared to the oxytocin group, and while shivering and pyrexia were more common in the misoprostol 600µg group than in the 400µg group, the difference was not statistically significant ($p > 0.05$). These findings are consistent with results from Pisake Lumbiganon et al,[22] who reported a dose-effect relationship in shivering prevalence across misoprostol 600µg, misoprostol 400µg, and oxytocin groups (56/199, 38/198, and 25/200, respectively). Similarly, Robert L. Walley et al,[15] noted more frequent shivering in the misoprostol group, along with a non-significant trend toward increased temperature. Kundodyiwa T.W. et al. 25 also observed significant shivering [RR=1.32 (95% CI 1.11-1.58); p=0.002] and increased temperature [RR=2.02 (95% CI 1.75-2.33); p<0.001] in the misoprostol group, aligning with our findings. Afolabi E.O. et al,[23] documented comparable shivering rates between groups, while Chandhiok N. et al,[20] and Abdulkarim O. Musa et al,[24] reported significantly higher shivering, pyrexia, and diarrhea incidences in the misoprostol group, further supporting the trends observed in our study.

CONCLUSION

In country like ours, where maternal anemia compounds the problem of PPH, and resources are low, implementation of simple measure of administration of oral misoprostol after delivery of baby can go a long way in reducing the maternal morbidity and mortality. By avoiding intravenous and intramuscular routes, the ease of administration is increased and this could lead to a widespread acceptance of oral misoprostol 400µg in active management of third stage of labor in primary health care setup.

REFERENCES

1. Abu MMH. Obstetric haemorrhage. In: Lawson JB, Harrison KA, Bergston S, eds. Maternity Care in Developing Countries. London: Royal college of obstetrics and gynaecology Press, 2001: 160-8.
2. Sarah BH, Poggi MD, Kerperick PS. Postpartum haemorrhage and the abnormal pueperium. In DeCherney AL, ed. Current obstetric and gynaecological diagnosis and treatment. 9th ed. New York: Lange Medicals, 2006: 531-2.
3. Cunningham FG, Gant NF, Leveno KJ. Conduct of normal labor and delivery. In: Cunningham FG, Williams JW, eds. Williams Obstetrics. 21st ed. New York: McGraw-Hill, 2001:320- 5.
4. Adinmma JIB. Aetiology and management of obstetric haemorrhage. In: Okonofua F, Odunsi K, eds. Contemporary obstetrics and gynaecology for developing countries. Benin City: Women's Health and Action Research Center 2003: 630-4.
5. Chien PFW. Third stage of labour and abnormalities. In: Edmonds DK, ed. Dewhurst's Textbook of Obstetrics and Gynaecology for Postgraduates. 6th ed. London: Blackwell Science, 1999:330-4.
6. Fenton JJ, Baumeister LM, Fogarty J. Active management of third stage of labour among American Indian women. Fam Med. 2005; 37(6):410-4.
7. Managing complications of pregnancy and childbirth: a guide for midwives and doctors. Geneva: World Health Organisation, United Nations Population Fund, United Nations Children's Fund and the World Bank; 2003 (WHO/RHR/00.7).
8. PATH. Postpartum hemorrhage prevention and treatment website.2011. Available at: http://www.pphprevention.org/pph. Last accessed 18 September 2024.
9. De Groot AN, Vree TB, Walker GJA. Stability of oral oxytocics in tropical climates: Results of simulation studies on oral ergometrine, oral methylergometrine, buccal oxytocin and buccal desaminooxytocin. Geneva, WHO, 1994. Available at: http:// apps. who.int/ medicinedocs/pdf/s2231e/s2231e.pdf. Last accessed 14 October 2024. Priority medicines for europe and the world 2013.
10. World Health Organisation. World Health Organisation multicountry survey on maternal and newborn health. Geneva: WHO; 2012.
11. Sloan NL, Durocher J, Aldrich T. What measured blood loss tells us about postpartum bleeding: a systematic review. Br J Obstet Gynaecol 2010; 117: 788–800.
12. Gülmezoglu AM, Forna F, Villar J, Hofmeyr GJ. Prostaglandins for preventing postpartum haemorrhage. Cochrane Database Syst Rev 2007; 3: CD000494.
13. Langebach C. Misoprostol in preventing postpartum haemorrhage: a meta-analysis. Int J Gynoecal Obstet 2006; 92:10–8.
14. Winikoff B, Dabash R, Durocher J. Treatment of post-partum haemorrhage with sublingual misoprostol versus oxytocin in women not exposed to oxytocin during labour: a double-blind, randomised, non-inferiority trial. Lancet 2010; 16: 375.
15. 15. Walley RL, Wilson JB, Crane JM. A double-blind placebo controlled randomised trial of misoprostol and oxytocin in the management of the third stage of labour. BJOG 2000; 107: 1111 5.
16. Høj L, Cardoso P, Nielsen BB. Effect of sublingual misoprostol on severe postpartum hemorrhage in a primary health centre in Guinea-Bissau: randomized double blind clinical trial. Br Med J 2005; 331: 723–7.
17. Bugalho A, Daniel A, Faundes A, Cunha M. Misoprostol for prevention of postpartum hemorrhage. Int J Gynecol Obstet 2001; 73: 1–6.
18. Derman RJ, Kodkany BS, Goudar SS, Geller SE, Naik VA, Bellad MB. Oral misoprostol in preventing postpartum haemorrhage in resource-poor communities: a randomised controlled trial. The Lancet 2006; 368: 1248–1253.
19. WHO Department of Reproductive Health Research. WHO statement regarding the use of misoprostol for postpartum haemorrhage prevention and treatment. Geneva, World Health Organization: 2009.
20. 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 Feb; 92(2):170-5.
21. Mani M, Bala SP. Role of misoprostol 600µg oral in active management of third Stage of labor: A comparative study with oxytocin 10IU i.m. The Journal of obstetrics and gynecology of India (September–October 2013) 63(5): 325–327.
22. Lumbiganon P, Hofmeyr J, Giilmezoglu AM, Pinol A, Villar J. For the WHO collaborative trial of misoprostol in the management of the third Stage of labour. Misoprostol doserelated shivering and pyrexia in the third stage of labour. British Journal of Obstetrics and Gynaecology; April 1999, Vol.106, pp. 304-308.
23. Afolabi EO, Kuti O, Orji EO, Ogunniyi SO. Oral misoprostol versus intramuscular oxytocin in the active management of the third stage of labour. Singapore Med J 2010; 51(3): 207-211.
24. Musa AO, Ijaiya MA, Saidu R, Aboyeji AP, Jimoh AA, Adesina KT et al. Double-blind randomized controlled trial comparing misoprostol and oxytocin for management of the third stage of labor in a Nigerian hospital. International Federation of Gynecology and Obstetrics; June 2015 volume 129, Issue 3, Pages 227- 230.
25. Kundodyiwa TW, Majoko F, Rusakaniko S. Misoprostol versus oxytocin in the third stage of labor. Int J Gynaecol Obstet. 2001 Dec; 75(3): 235-41.