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**Original Research Article**

# A comparative study of efficacy of oxytocin, methylergometrine and misoprostol in prevention of post-partum haemorrhage

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## ABSTRACT

**Background:** To compare the efficacy of oxytocin, methylergometrine and misoprostol in active management of third stage of labour (AMTSL).
**Methods:** A clinical study was conducted on 330 low risk pregnant women with a healthy singleton pregnancy and spontaneous onset of labour at term; allocated into three groups where active management of third stage of labour was done with either Oxytocin 10 IU intramuscular, or Methylergometrine 0.2 mg intramuscular, or tab Misoprostol 600µg sublingual on 110 women each group. Primary parameter was blood loss during labour. Secondary parameters were the duration of third stage of labour and changes in haemoglobin level.
**Results:** Blood loss during labour in Oxytocin group was 145.86±11.53 ml, which was significantly less than that in Methylergometrine (164.02±9.36 ml) and Misoprostol groups (183.18±9.70 ml), but no patient in any of the groups had blood loss more than 200ml. Duration of third stage of labour was significantly less in Oxytocin group (5.13±1.91 mins) than in. Methylergometrine (6.16±1.85 mins), and Misoprostol groups (6.47±1.51 mins). No patient had prolonged third stage in any of the groups. There was no significant change in pre-and post-delivery haemoglobin levels in all the groups.
**Conclusions:** Though injectable uterotonics are effective for active management of third stage of labour (AMTSL), misoprostol can also be effectively used, especially in settings where there is no adequate trained personnel and drug storage facility.

**Keywords:** Active management of third stage of labour, Postpartum haemorrhage, Uterotonics

## INTRODUCTION

Around 830 women die from pregnancy or childbirth-related complications all over the world every day.[1] Between 1990 and 2015, maternal mortality worldwide dropped by about 44%.[1,2] According to World Health Organisation, 25% of all maternal deaths are caused by post- partum haemorrhage (PPH) which is a preventable cause of maternal mortality and morbidity.[3] India takes up 17% of the global burden of maternal mortality with the national average of 167 while in Assam it is still high with 300 per lakh live births.[4] Post-partum haemorrhage is the loss of more than 500 ml of blood within the first 24 hours of delivery or loss of any amount that is enough to cause hemodynamic instability in the mother or the loss of more than 10% of the total blood volume. A review of literature in 2006 by WHO highlighted the common cause of PPH as uterine atony and majority of women with PPH have no identifiable risk factor.[5] Active management of third stage of labour (AMTSL) can prevent PPH and thereby prevent maternal death.[6-9]

Different uterotonics are available for AMTSL among which oxytocin is found to be effective in reducing the risk of PPH by 50%.[10,11] It has also been advocated by the WHO during the active management of third stage of

labour[5]. Administration of Oxytocin has been found to be associated with lesser blood loss in the third stage than expectant management.[12,13] But oxytocin need storage at low temperatures and a skilled person to administer the drug by intramuscular (IM) or intravenous (IV) route, which are not feasible in rural areas of resource poor countries like India.

Ergot alkaloids are in use since many decades and are effective in reducing third stage blood loss and preventing PPH, but they cause adverse effects including vomiting, elevation of blood pressure, pain after birth requiring analgesics.[10] Transient hypertension is induced following intravenous administration.

In recent years, misoprostol, a synthetic analogue of prostaglandin E1 ($PGE_1$), is also found to be an effective uterotonic. As per Cochrane review, misoprostol oral or sublingual (S/L) at a dose of 600µg shows promising results when compared to placebo in reducing blood loss after delivery.[14] Highest peak concentrations are achieved with oral and sublingual administrations than in vaginal or rectal administrations.[15] Pyrexia is more common when the dose exceeds 600µg.[16] Tab Misoprostol has also the advantage of storing at room temperature in peripheral hospitals and can be self-administered.

The aim of the study is to compare the efficacy of these most frequently used uterotonics, which are oxytocin 10 IU intramuscular (I/M), methylergometrine 0.2mg I/M, and misoprostol 600µg sublingual (S/L) in reducing third and fourth stage blood loss.

## METHODS

We conducted a clinical study in the Department of Obstetrics and Gynaecology, Assam Medical College Hospital, Dibrugarh to compare the efficacy of injection oxytocin 10 IU IM, injection methylergometrine 0.2 mg IM, and tablet misoprostol 600 µg S/L during the third stage of labour between the period from May 2015 to April 2016. Cases were selected as per the inclusion and exclusion criteria.

### *Inclusion criteria*

Primi, second and third para without any risk factors, and singleton pregnancy with spontaneous onset of labour at term.

### *Exclusion criteria*

Cases with hypertensive disorders, previous uterine surgery, heart disease, respiratory disease, severe anaemia (Hb <7 g), ante partum haemorrhage, asthma, hypersensitivity or contraindication to prostaglandin use, multiple pregnancy, diabetes, mal-presentations, intrauterine fetal death (IUFD), instrumental delivery etc.

We included 110 cases in each group, where Group A received inj. oxytocin 10 IU intramuscularly (IM), Group B received inj. methylergometrine 0.2 mg intramuscularly (IM), and Group C received Tab misoprostol 600 µg sublingually (S/L) after delivery of the baby. Though routine oxytocin is used as a part of AMTSL, methylergometrine and misoprostol were also used during Basic Emergency Obstetrics Care (BEmOC) and Skilled Birth Attendant (SBA) trainings which are being regularly imparted at our Institute.

In all cases, AMTSL was done routinely in our hospital as per WHO guidelines. After delivery of the baby, linens soiled with amniotic fluid were removed and Kelly's pad was placed under patient's buttock for estimation of blood loss. It is a disposable pre-weighed pad having good absorbent capacity on one side which is in contact with the patient, and the reverse polythene side facing the delivery table. Another polythene bag is also attached to the lower part of the pad overhanging the edge of the table for collection of blood. Duration of the third stage of labour was noted. Placenta and membranes were examined for completeness. At the end of the third stage, with a well contracted uterus and no active bleeding seen, vagina was inspected for blood clots, and if present were removed and put into the polythene bag A fresh pre-weighed sanitary napkin was applied in the perineum for another one hour.

During repair of episiotomy wound, a small pre-weighed gauze pack was placed in the vagina just below and touching the cervical os to soak any blood coming out of the uterine cavity and the pack was changed if it was completely soaked and a new pack was given. These packs were also included in the final calculation of amount of blood loss. Separate gauze pieces used to soak blood from the episiotomy wound were not included in the final calculation.

One hour after the delivery, pre-weighed Kelly's pad with polythene bag containing blood clots, gauze pack and sanitary pads used were weighed for final measurement of blood loss. The specific gravity of blood being 1.06, the amount of blood loss in grams is converted to ml.

Maternal and fetal conditions were monitored all throughout labour up to fourth stage as per standard procedures. Any adverse effects of drugs and complications were noted along with the need for additional uterotonics. Haemoglobin level of all mothers are estimated before and 24 hours after delivery which is a routine procedure in our hospital.

### *Statistical Analysis*

The SPSS version-16 was used for the analysis of data obtained in the study. ANOVA, t-test, chi-square test were applied. Data were presented in terms of percentage and mean ± SD.

## RESULTS

Table 1 shows the differences in maternal age, mean duration of pregnancy, parity and baby's birth weight among three groups, where Group A received inj. oxytocin 10 IU IM, Group B received inj. methylergometrine 0.2 mg IM and Group C received Tab misoprostol 600 µg S/L after delivery of the baby. Values of all the parameters were comparable (ANOVA p-value >0.05) among the three groups.

**Table 1: The differences in maternal age, mean duration of pregnancy, parity and baby's birth weight among three A, B, C groups.**

| Characteristic | Group A oxytocin 10 IU I/M (n = 110) | Group B methylergometrine 0.2mg I/M (n = 110) | Group C misoprostol 600µg S/L (n = 110) |
|---|---|---|---|
| Maternal Age (in years) | 25.81±2.31 | 25.2±2.46 | 24.47±2.42 |
| Duration of Pregnancy (in weeks) | 38.25±1.71 | 38.1±1.08 | 38.3±1.12 |
| **Parity** | | | |
| Primipara | 47 (42.7%) | 59 (53.6 %) | 47 (42.7%) |
| Multipara | 63 (57.2 %) | 51 (46.3 %) | 63 (57.2 %) |
| Birth Weight (in kg) | 2.69±0.16 | 2.69±0.16 | 2.70±0.17 |

There was significant difference in the amount of blood loss among groups A, B and C (ANOVA p-value < 0.05). Mean blood loss in Group A was 145.86±11.53 ml. It was 164.02±9.36 ml in Group B and 183.18±9.70 ml in Group C. The differences among the values were statistically significant from each other between group A and B, group A and C and group B and C. Though blood loss in group C was comparatively high, there was no value more than 200 ml. There was no statistical difference of blood loss between primipara and multipara in all the three groups.

**Table 2: The amount of blood loss, duration of third stage of labour among groups A, B and C.**

| Characteristics | Group A oxytocin 10 IU I/M (n = 110) | Group B methylergometrine 0.2mg I/M (n = 110) | Group C Misoprostol 600 µg S/L (n = 110) | Significance |
|---|---|---|---|---|
| Third stage duration (minutes) | 5.13±1.91 | 6.16±1.85 | 6.47±1.51 | Significant |
| Blood loss in third stage (ml) | 145.86±11.53 | 164.02±9.36 | 183.18±9.70 | Significant |
| Need for additional uterotonic | 2 (1.8 %) | None | 4 (3.6 %) | Not significant |
| Side effects | - | V- 5 (4.5%)<br>HTN- 2 (1.8%) | S - 6 (5.4%)<br>F-2 (1.8%) | – |

V- vomiting, HTN - hypertension, S- shivering, F- fever

We observed that duration of third stage of labour was shortest with oxytocin and results were significant (ANOVA p-value < 0.05).). Mean duration of third stage of labour was 5.13 ± 1.91 minutes in Group A. It was 6.16 ± 1.85 minutes in Group B and 6.47 ± 1.51 minutes in Group C.

The difference was statistically significant between Group A and B and A and C. It was, however, statistically not significant between Group B and C. Though the duration of third stage of labour was comparatively longer (11 minutes in 5.4% of women) in Group C, it was not prolonged. There was no statistical difference among primipara and multipara for the duration of third stage in all the groups.

There was no significant difference in the pre, and post-delivery haemoglobin levels in all the groups (t-test). Additional uterotonics were required in 2 cases in Group A, and 4 cases in Group C. This was statistically not significant (Chi-squire test >0.05).

**Table 3: Comparison of difference in pre, and post-delivery haemoglobin level among three groups.**

| Uterotonic used | Hb (in gram) (Pre-delivery) | Hb (in gram) (post-delivery) | p-value |
|---|---|---|---|
| Group A: Oxytocin 10 IU I/M | 8.98±0.56 | 8.69±0.55 | > 0.05 |
| Group B: Methylergometrine 0.2mg I/M | 8.97±0.57 | 8.62±0.69 | |
| Group C: Misoprostol 600µg S/L | 8.98±0.57 | 8.59±0.56 | |

Blood transfusion was not required in any of the study groups. Adverse effects of drugs were nausea and vomiting in 5 cases and hypertension (systolic blood pressure less than 150 mm of Hg) in 2 cases of Group B. Shivering in 6 cases and fever in 2 cases of Group C. Fever subsided on the same day. There was no case record of PPH, retained placenta or blood transfusion in any of the study groups.

## DISCUSSION

On comparing oxytocin 10 IU I/M, methylergometrine 0.2mg I/M and misoprostol 600µg S/L for active management of third stage of labour, we found that there was significant difference in the amount of blood loss among groups studied, with oxytocin showing the minimum blood loss (145.86±11.53) compared to other uterotonics. Intramuscular Oxytocin 10 IU, given after the delivery of anterior shoulder, has been found to be an ideal uterotonic in various studies.[11] Some authorities consider methylergometrine as second line drug for AMTSL compared to oxytocin.[17] Studies have shown that Misoprostol is not as effective as Oxytocin for the prevention of PPH and that maternal pyrexia is a significant adverse effect.[14,16,18-20] However, misoprostol is a suitable agent for management of the third stage of labour when other agents are not available for reasons of cost, storage, or difficulty of administration.[18,21,22.] Though blood loss in group C was comparatively higher, there were no values found more than 200 ml. It signifies that even Tab Misoprostol 600 µg S/L can be an effective uterotonic in third stage of labour. WHO Guideline Development Group considers use of misoprostol in settings where skilled birth attendants are not available.[1] In other studies, Gohil JT et al also found misoprostol less effective than injectable uterotonics.[23] However, Gunjan Singh et al and Megha Sharma et al found lesser amount of blood loss with misoprostol compared to other uterotonics.[24,25]

When duration of third stage of labour was compared in the groups studied, we observed that it was highest with tablet misoprostol 600µg. Though the duration of third stage of labour was comparatively longer in this group, it was not prolonged. Hence, Tab Misoprostol 600 µg can be an effective uterotonic in AMTSL. Gohil JT et al also noted longer duration with misoprostol while others had found duration of third stage shorter with misoprostol compared to injectable uterotonics.[23-25] There was no significant change of pre, and post-delivery haemoglobin concentration in any of the groups studied which is similar to the other studies.[23,24]

Side effects of drugs in this study included 5 cases of nausea and vomiting and 2 cases of hypertension in Group B. 6 cases of shivering and 2 cases of fever were there in Group C. Rise of blood pressure with methylergometrine, shivering and fever with misoprostol were also noted in other studies.[23,24,25] Though there were no records of retained placenta, post- partum haemorrhage or blood transfusion in any of our study group, other studies noted retained placenta and requirement of blood transfusion with methylergometrine.[24,25] WHO multi-centric trial reported statistically higher rate of PPH and use of additional uterotonics with 600µg of misoprostol compared to other injectable uterotonics.[19] Additional uterotonics were required in 2 cases in group A and 4 cases in group C which is similar to other workers who had also used additional uterotonics following AMTSL with oxytocin and misoprostol.[24,25]

## CONCLUSION

Post-partum haemorrhage (PPH) is the leading cause of maternal deaths (25%) the world over, uterine atony contributing to the bulk of such deaths. Prevention and management of PPH is an ongoing challenge among healthcare providers and the search for a superior uterotonic still continues. Though injection Oxytocin or methylergometrine are effective in reducing third stage blood loss, the problems of drug storage at two to eight-degree temperature and the need for trained medical personnel to administer the drug, make its use difficult in rural settings where considerable number of deliveries occur. Misoprostol was found to have slightly higher blood loss compared to injectable uterotonics, but may be a suitable agent for management of the third stage of labour especially in resource poor rural areas, as it is not expensive and can be stored at room temperature with a feasibility of self-administration. Regarding the dose of misoprostol for AMTSL further studies are required.

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