



Comparing the Effectiveness of Transrectal Misoprostol with Intravenous Oxytocin in Active Management of Third Stage of Labour in Preventing Post-partum Hemorrhage

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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ABSTRACT

Background: PPH which is 500 ml or more blood loss in 24 hours of birth . Uterine atony has been the commonest cause of PPH. To prevent PPH uterotonics like oxytocin and misoprostol should be given. Intravenous route of oxytocin has rapid effect, but is associated with cardiovascular side effects like rise in heart rate and decrease in blood pressure. Slower rate of absorption, lower peak levels and reduced adverse effects is seen with misoprostol given rectally when compared to sublingual and oral routes. This study aims to compare the effectiveness of transrectal misoprostol and intravenous oxytocin in preventing post-partum haemorrhage.

Objectives: To compare the effectiveness of 600mcg transrectal misoprostol with 10IU intravenous oxytocin in active management of third stage of labour in preventing PPH and recommend technique for active management of third stage of labour in preventing PPH.

Methodology: Women randomized into two groups for prevention of PPH and are given 600ug of misoprostol per rectally and 10IU oxytocin intravenously. Duration of third stage, the blood volume

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in kidney tray and additional blood loss in sterile surgical pads for 24hrs will be noted. The blood loss due to episiotomy will be taken as 50ml. Need of additional uterotonics (oxytocin or misoprostol), blood transfusion, removal of placenta manually, haemoglobin before and after delivery will be noted. Monitoring of patients for vital signs, uterine tone, fundal height and vaginal bleeding for 2 hour will be done.

Result: The expected outcome of the study will be a significant difference in the blood loss during third stage of labour and 24 hours in post-partum period when uterotonics like oxytocin or misoprostol are used in managing third stage of labour actively.

Conclusion: Our study will show the effect of intravenous oxytocin and transrectal misoprostol in managing third stage of labour actively to prevent post-partum hemorrhage.

Keywords: Active management; third stage of labour; post-partum hemorrhage; oxytocin; misoprostol.

1. INTRODUCTION

PPH affects 2% of all women giving birth. Within 24 hours of giving birth, if there is blood loss of 500ml or more then it is defined as Post-partum haemorrhage. It can lead to cardiovascular compromise, renal insufficiency and shock in body. Severe PPH is when 1000ml or more blood is lost within 24 hours of giving birth [1].

Among all maternal deaths all over the world one third of them are due to haemorrhage that occur in post-partum period [2].

The etiology can be described by 4Ts:

- Tone – due to atony of uterus and distention of bladder
- Tissue- due to retention of placenta and clots.
- Trauma-due to injury to vagina, cervix or uterus.
- Thrombin formation- due to coagulation problem that may be existing since before or acquired later.

Uterine atony has been the most popular and significant cause of PPH all around the world [3].

PPH prevention can be done by various interventions performed during third stage of labour. This is referred as active management of third stage of labour.

The following is included in managing third stage of labour actively:

1. Just after the baby is delivered prophylactic uterotonic is administered.
2. Cord is clamped and cut early.
3. umbilical cord should be given traction in a controlled manner.

In the managing third stage of labour, massaging the uterus may also be actively practised [4]. It is possible to administer uterotonics to avoid PPH during third stage of labour. Uterotonic suggested is IM/IV oxytocin (10IU). Other alternatives include uterotonic injectables such as ergometrine /ergometrine-methylegometrine, or a mixture of drugs like oxytocin, ergometrine and misoprostol can be used [2].

Frequent and prolonged uterine contractions can be obtained with oxytocin by binding to receptors of myometrium. It is associated with half-life of two to four minutes which is short. There may be symptoms of anti-diuresis that contribute to low sodium levels, headache, vomiting, sleeping and convulsions when oxytocin is given in high volume. Oxytocin can be stored for longer period in the dark at four to eight degrees Celsius. However at room temperature it can be stored for limited period of time, this is its main drawback. Intravenously or intramuscularly is the route of administration [5]. The time taken by oxytocin to work and its effects on pressure of blood and rate of heart are the differences seen with IM and IV route [6]. Uterotonic effect in 3-7 minutes is seen with intramuscular route, it will show its effect for 30-60 minutes. Intravenous route shows an instantaneous response, and plateau concentration is reached at 30 minutes. Venous route lowers the risk of PPH through its rapid effect, but it is also associated with side effects of cardiovascular system like rise in heart rate and decrease in blood pressure [7].

Misoprostol, an analog of prostaglandin E1. Inexpensive and absorption by various routes like vaginal, rectal or oral (sublingually or buccally) are the advantages of misoprostol. Low costing, shelf life that is longer, stable when kept at room temperature, route of administration being non parenteral and minimal side-effects

are some advantages [8]. Nausea, vomiting and diarrhoea are the side effects associated with prostaglandins. Shivering and increased body temperature is also seen with the misoprostol usage in third stage of labour [9]. Slower rate of absorption and lower peak levels is seen with rectal route of administration in comparison to sublingual and oral routes, however incidence of adverse effects is reduced with rectal route [10]. The initial onset of action is fast and initial uterotonic effect is also strong with oral solution and sublingual routes. High incidence of shivering and rise in temperature is seen with these routes. Effects that harmful that appear are related to the peak plasma concentrations achieved by misoprostol. Rectal route of misoprostol achieves a plasma level that is increased gradually and in a sustained manner, with onset of action that is slow and uterotonic effect which has lower initial intensity but it is also associated with lesser side effects [11].

To prevent excessive blood loss oxytocin is used routinely by obstetricians however in resource poor settings it is not feasible as it requires equipment which is sterile, storage which is cool and administration parenterally. Misoprostol is a cost effective drug and have several routes of administration like rectal, oral (sublingual or buccal), vaginal. For reduction of PPH incidence it is relatively safe and effective drug [10].

On studying the advantages and disadvantages of oxytocin and misoprostol and its various routes of administration. In this study we aim to study and compare the effectiveness of misoprostol given transrectally and oxytocin given intravenously in managing third stage of labour actively for PPH prevention.

2. AIM AND OBJECTIVES

2.1 Aim

To compare the effectiveness of 600mcg transrectal misoprostol with 10IU intravenous oxytocin in active management of third stage of labour in preventing post-partum haemorrhage and recommend technique for active management of third stage of labour in preventing post-partum haemorrhage.

2.2 Objectives

1. To study the effectiveness of 600mcg transrectal misoprostol in active management of third stage of labour in preventing post-partum haemorrhage.

2. To study the effectiveness of 10IU intravenous oxytocin in active management of third stage of labour in preventing post-partum haemorrhage.
3. To compare the effectiveness of 600 mcg transrectal misoprostol with 10IU intravenous oxytocin in active management of third stage of labour in preventing post-partum haemorrhage.

3. MATERIALS AND METHODS

3.1 Setting

The study will be conducted in the Department of Obstetrics and Gynaecology, at Acharya Vinoba Bhave rural Hospital (AVBRH), a tertiary care teaching hospital situated in the rural area of Wardha District.

3.2 Subjects

Women with who underwent full term spontaneous vaginal delivery will be recruited after taking care of inclusion and exclusion criteria.

3.3 Study Design

Prospective observational study.

3.4 Inclusion Criteria

- Women expecting a fullterm vaginal delivery i.e spontaneous with or without the need of episiotomy.

3.5 Exclusion Criteria

- Any known disorders of blood coagulation, disease of heart, renal disease that is severe, epilepsy, and hypertension
- All women who had excessive bleeding following episiotomy and were excluded later.
- Known hypersensitivity to prostaglandins.
- Women with gestation less than 37 weeks.

4. METHODS

- Demographic details like age, parity and detailed present and past obstetrical history will be noted.
- Blood sample will be sent for pre-delivery hemoglobin estimation on admission.
- Women will be randomized to one of the two groups in stage two of labour.

- Drug to which the patient will be randomized will be given.
- Misoprostol group :3 tablets 200ug of misoprostol will be placed in the rectum after the delivery of the baby
- Oxytocin group: 10IU oxytocin will be given intravenously following the anterior shoulder delivery.
- The cord of umbilicus will be clamped and cut, following the delivery of baby after the cord pulsations have stopped.
- Linen that will be soiled with amniotic fluid will removed in order to collect the blood from uterine cavity and a kidney tray will be placed under the patients vulval region with the beginning of third stage which will be further facilitated by pad.
- Delivery of placenta is done by controlled traction given to cord, and the duration of stage three of labour will be noted.
- Examination for completeness of removal is done for placenta and membranes.
- Blood clots are expressed out if any from the vagina.
- Blood volume in kidney tray will be measured in a measuring jar and noted.
- Additional blood loss in sterile surgical pads for 24hrs will be calculated by the subtraction of pre-weighed dry pads weight from the blood soaked surgical pads weight.
- The average immeasurable blood loss due to episiotomy was taken as 50ml.
- Need of additional uterotonics (oxytocin or misoprostol), blood transfusion and manual removal of placenta will be noted.
- Monitoring of patients is done for the vital signs, uterine tone, fundal height and vaginal bleeding for 2 hour post-partum.
- Blood for hemoglobin will be again sent 24 hours after delivery.

5. FORMULA FOR CALCULATION OF BLOOD LOSS

- Amount of blood(ml)=Amount of blood in measuring jar(ml) + Amount of blood(grams) x 1000/1060

5.1 Sample Size

Sample size = In this study, 200 participants from each group (i.e.100 from each group) will be taken. Before enrolling the patient into the study, every woman will be given explanation about the type.

5.2 Outcome

5.2.1 Primary outcome

- Postpartum hemorrhage (500ml or more loss of blood)
- Postpartum hemorrhage severe in nature. (that is 1000 ml or more loss of blood)
- Usage of additional uterotonics. (oxytocin /misoprostol).

5.2.2 Secondary outcome

- haemoglobin concentration chang.
- Stage three duration.
- Transfusion of blood if needed.
- Manual removal of placenta.

We shall be applying for funding from intramural grant/icmr grant/concession for synopsis.

5.2.3 Statistical methods

Chi-square test and Student's unpaired t test

5.2.4 Statistical Analysis

Descriptive statistics parameters like minimum, maximum, range, mean and standard deviation in each group will be computed separately. The statistical significance within each group will be carried out by utilizing chi square test for all the categorial variables and Z test for all the discrete variables. Less than 0.05 value of P will be taken as statistically to be significant.

5.2.5 Software's Used in study

SPSS 24.0 version, EPI-INFO 7.0 version and GraphPad Prism7.0 version.

6. RESULTS

The study will include 200 women with full term normal vaginal delivery. The effect of both the uterotonics i.e oxytocin given intravenously and misoprostol given transrectally as a part of actively managing stage three of labour in PPH prevention will be studied which in this case will be blood lost during the stage three of labour and 24hrs post-partum and secondary outcomes will include haemoglobin concentration change, third stage duration, need for blood transfusion and removal of placenta manually. The outcome desired in the following study is the reduction in the blood loss i.e prevention of post-partum

hemorrhage. When uterotonics like oxytocin (given intravenously) or misoprostol (given transrectally) are used in stage three of labour for management of labour actively, difference in the loss of blood during stage three of labour that is significant and twenty four hours post-partum is seen.

7. DISCUSSION

In Obafemi Awolowo University Teaching Hospitals, Nigeria carried a randomized controlled trial that was double blinded and concluded in the study that rectal misoprostol and oxytocin given intravenously effective in same way in post-partum haemorrhage prevention in women having the risks of uterine atony. Many such other studies have been done which develop conspiracy in the use of transrectal misoprostol or intravenous oxytocin in actively managing the stage three of labour. To bring a conclusion to these controversies this study will help study and compare the effectiveness of 600mcg misoprostol with 10IU oxytocin given transrectally or intravenous respectively in managing the third stage of labour actively [10]. Studies related to labour and postpartum hemorrhage was reviewed [11-14]. Penumadu et. al. studied role of condom balloon tamponade for postpartum hemorrhage [15]. Key issues around pregnancy and delivery were addressed in Global burden of disease studies [16-18]. A number of related studies from this region were reviewed [19-22].

8. CONCLUSION

By using this study, a valuable data can be developed which will help obstetricians know whether transrectal misoprostol or intravenous oxytocin should be used as a part of stage three of labour's active management for the prevention of PPH.

CONSENT

Patients will be recruited after informed verbal and written consent and all eligible women giving informed written consent to be a part of study.

ETHICAL APPROVAL

The study will be undertaken after approval from institute ethical committee.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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