EFFICACY OF SUBLINGUAL MISOPROSTOL VERSUS INTRAMUSCULAR METHYLERGOMETRINE IN PREVENTION OF PRIMARY POSTPARTUM HEMORRHAGE

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ABSTRACT

Introduction: Post partum hemorrhage still remains a major cause of maternal morbidity and mortality in developing countries. Most of oxytocics like methylergometrine require parenteral administration, which requires special storage. Misoprostol is thermo stable, has a long shelf life and is widely recommended for prevention of postpartum hemorrhage. This can be a choice of oxytocic in developing countries like ours, where storage facilities and resources are limited.

Objectives: To compare efficacy of sublingual Misoprostol versus intramuscular Methylergometrine in prevention of primary postpartum hemorrhage after delivery.

Study Design: Quasi experimental study

Place and Duration of Study: Department of Gynae/Obs, Military Hospital and Combined Military Hospital Rawalpindi cantt. December 2007 to July 2008.

Material and Methods: One hundred and thirty six pregnant ladies were selected. On arrival each patient was examined thoroughly along with baseline investigations. Therapeutic option was allocated to the patients simply by using a table of random numbers and dividing them in two equal groups. Informed written consent was taken. Each patient was observed for blood loss estimation and hematocrit drop. All the data was analyzed using SPSS version 10.0. Mean ± SD for age, pre-delivery and post-delivery hematocrit, percentage of drop in hematocrit and blood loss during labour was calculated.

Results: Mean drop of hematocrit and blood loss were compared among two groups. At the end, it was revealed that there was no significant difference among two groups in blood loss (p=0.49) and hematocrit drop (p=0.14).

Conclusion: There is no significant better effect in preventing post partum hemorrhage among the two drugs.

Keywords: Post partum hemorrage, Misoprostol, Methylergometrine.

INTRODUCTION

Post partum hemorrhage (PPH) still remains a major cause of maternal morbidity and mortality in developing countries and accounts for 25% of maternal deaths with a prevalence of 34% in Pakistan[1,2]. The incidence of PPH varies widely, depending upon the criteria used to define the disorder. A reasonable estimate is 1 to 5% of deliveries in the developed countries[3].

PPH is diagnosed clinically as excessive bleeding that makes the patient symptomatic (eg, lightheadedness, vertigo, syncope) and/or results in signs of hypovolemia (e.g, hypotension, tachycardia, or oliguria).

The most common definition of PPH is estimated blood loss ≥ 500 ml after vaginal birth or ≥ 1000 ml after cesarean delivery, or drop in harmatocrit of ≥ 10%.

PPH is also defined as primary or secondary. Primary PPH occurs within 24 hours and secondary PPH occurs 24 hours to 12 weeks after delivery[4].

Most postpartum hemorrhages are caused by uterine atony and occur in immediate postpartum period. Active management involves administration of uterotonic medication after delivery of baby, early cord clamping and cutting and controlled traction of umbilical cord during placental separation and delivery. Active versus expectant management of third stage of labor shows that for all women, including those who

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seemed to be at low risk for post partum hemorrhage, active management decreases the risk of post partum hemorrhage[5].

Most of uterotonics require parenteral administration and methylergometrine is one of them. However, administration and storage of it may not always be possible in some hospitals or rural communities due to non availability of sterile syringes or refrigeration equipment. The efficacy of methylergometrine significantly reduces when it is stored at suboptimal environment[6].

Misoprostol is a synthetic analogue of natural prostaglandin E1. It is uterotonic, thermo stable, has a long shelf life and is widely recommended for prevention of postpartum hemorrhage when other methods are not available[7].

Most of the deliveries in developing countries like ours take place either at home without supervision or are supervised by traditional birth attendants. Unfortunately, even in the health centers with a skilled attendant, storage facilities are either not available or are out of use due to frequent power load shedding problem. The results of many studies have questioned the potency of some routine uterotonic in hot climate[8]. This study was therefore done to identify an alternative uterotonic agent that is effective, cheap and stable at high temperature with an easy route of administration.

In our study, the effects of Misoprostol were compared with Methylergometrine. It has really helped in deciding the protocol of our active management of the third stage of labor and prevention of postpartum hemorrhage.

MATERIAL AND METHODS

The study was conducted in the department of Gynae/Obs, Military Hospital Rawalpindi cantt from December 2007 to July 2008. One hundred and thirty six pregnant ladies having a singleton pregnancy and vaginal delivery were randomly divided into two groups with 68 patients in each group by using table of random numbers.

Sample Selection

Inclusion criteria:

- Singleton pregnancy with spontaneous onset of labour.
- Parity 2-4.

Exclusion criteria:

- Pregnancy induced hypertension.
- Chronic hypertension.
- Pregnancy with cardiac disease.
- Pregnancy with anaemia.
- Primipara.
- Grand multiparity (parity>4)
- Presence of uterine fibroids.
- Multi-fetal pregnancy.
- Previously scarred uterus (for cesarean section or myomectomy).
- Instrumental deliveries (forceps delivery/vacuum extraction).

Data Collection Procedure

A total number of 136 pregnant ladies in spontaneous labor in the labor ward of Military Hospital were included.

Confounding variables were controlled by excluding presence of contraindications for use of either Misoprostol or Methylergometrine, such as pregnancy induced hypertension, pre-eclampsia, chronic hypertension, pregnancy with cardiac disease, and presence of conditions requiring prophylactic oxytocin infusion after delivery such as multifetal gestation, polyhydromnios, grand multipara or presence of uterine fibroids.

Informed consent was taken after explaining the risks and benefits of respective medication given to the patients (particularly low grade fever, shivering and diarrhea from Misoprostol and raised blood pressure in case of Methylergometrine).

Approval of ethical committee was also taken by explaining safety of clinical trial.

A detailed history was taken from each patient and relevant clinical examination was done. Her blood sample was sent for hematocrit determination.

Patients were randomly allocated into two groups by using random number table. Group A received sublingual misoprostol (400µg) and group B had intramuscular Methylergometrine (one ampoule of 200µg). Misoprostol was administered after the delivery of baby. Methylergometrine was given at delivery of anterior shoulder of the baby. Placenta was delivered by controlled cord traction.

Each patient had estimation of blood loss by weighing pre-soaked and post-soaked clean plastic lined absorbent drapes placed under woman's buttock (one ml of blood weighs approximate one gram). Hematocrit was also checked for each patient 24 hours after delivery. Blood sample was sent to same laboratory to minimize laboratory error. All data was recorded in a proforma.

Data Analysis Procedure

Data was analyzed using statistical software SPSS version 10.0.

Descriptive statistics were used to calculate Mean ± SD for age, pre-delivery and post-delivery hematocrit, percentage of drop in hematocrit and blood loss during labour.

Frequency (as percentage) for parity and age was calculated, "t" test was used to compare pre-delivery hematocrit, 24 hours post-delivery hematocrit, drop in hematocrit and approximate blood loss in group A (Misoprostol) and group B (Methylergometrine). p value < 0.05 was considered significant.

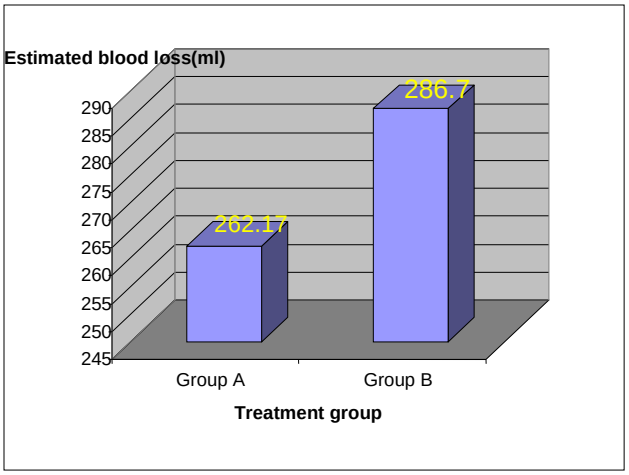

Figure-2: Comparison of estimated blood loss among study group A (Sublingual misoprostol**) and study group B (**Intramuscular methylergometrine**).**

Table-1: Mean age of patients (n=136) in study group A (sublingual misoprostol**) and study group B (**Intramuscular methylergometrine**).**

Study group	Mean	Standard deviation
Study group A	23.82	2.99
Study group B	24.25	2.92
Total	24.04	2.95

p=0.4

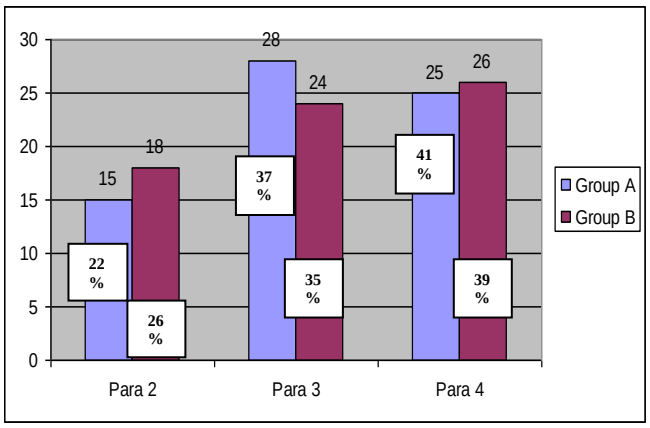

Figure-1: Parity among study group A (sublingual misoprostol**) and study group B (**Intramuscular methylergometrine**).**

RESULTS

In this study, 136 pregnant ladies were selected fulfilling inclusion criteria. They were divided into two equal groups for therapeutic purposes.

Descriptive statistics for age of both groups is shown in table-1. Parity of both groups is

shown in figure-1. Regarding parity, there was no significant difference among the two groups (p=0.8).

In group A and B, the mean pre-delivery hematocrit value was found to be 39.89 ± 2.32 and 39.54 ± 2.41 respectively (p=0.38). Maximum values being 44 in group A and 45 in group B while minimum values being 36 in group A and 36 in group B.

Post-delivery hematocrit was also calculated. In group A and B, the mean post-delivery hematocrit value was found to be 35.75 ± 2.46 and 34.78 ± 3.33 respectively (p=0.056). Maximum values being 41.5 in group A and 42 in group B while minimum values being 31 in group A and 27 in group B.

Hematocrit drop was also calculated by subtracting pre-delivery hematocrit from post delivery value of hematocrit. Mean drop in hematocrit was observed as 3.69 ± 0.64 in group A and 3.89 ± 0.71 in group B. Maximum values being 5.0 in group A and 5.1 in group B while minimum values being 2 in both group A and in group B. When compared to each other, drop in hematocrit was found to be insignificant with a 'p' value of 0.09.

Estimated blood loss is compared among the two treatment groups in figure-2 (p=0.49). This was calculated and showed mean value 262.17 ± 76.40 in group A, with minimum value of 185.77 ml to maximum amount of 338.57 ml. Whereas, in group B, mean blood loss was found to be 286.7 ± 90.19 ml. Minimum and maximum values in this group were 196.51 to 376.89 ml.

DISCUSSION

Postpartum hemorrhage (PPH), an obstetric emergency is a major cause of maternal morbidity, with sequelae such as shock, renal failure, acute respiratory distress syndrome, coagulopathy and Sheehan's syndrome. It is also one of the top five causes of maternal mortality in both high income and low income countries[3]. That demands active management of third stage of labour and prevention of postpartum hemorrhage.

Methylergometrine use in prevention of post partum hemorrhage is long established. However, it is heat labile, requires cold chain, parenteral administration and skilled person. One of the alternatives to Methylergometrine in modern day obstetrics are the prostaglandins. But prostaglandin F2 alpha and E2 are heat labile and too expensive. However, Misoprostol is cheaper, easy to store and well absorbed orally and across mucus membranes. Its absorption is very rapid, being detected within 2 minutes after oral ingestion and peaking between 12 and 30 minutes. Sublingual route may even be faster. Therefore, it may be a promising substitute of other well-established injectable agents if effective in preventing post partum hemorrhage.

Moreover, though both the drugs are effective and available but cost is a problem for Methylergometrine as compared to Misoprostol. In addition to cost of the drug, tolerability is also a problem as shivering and hypertension is common with ergot group.

Our result is consistent with several other trials in different low-income countries such as India[9], Guinea Bissau[10], Nepal[11], and Nigeria[12]. In these studies, they have shown that misoprostol is effective in preventing postpartum hemorrhage in community and hospital settings and unskilled birth attendants are successfully able to use misoprostol for the prevention and treatment of postpartum hemorrhage.

Another study of rectal misoprostol versus intramuscular oxytocin for prevention of postpartum hemorrhage was done in khatmandu Nepal. A total of 200 women were included to receive either 1000 microgram rectal misoprostol tablets or 10 IU oxytocin intramuscularly. The frequency of PPH was 4% in misoprostol subjects and 6% in control subjects (p=0.886) showing rectal misoprostol is as effective as intravenous oxytocin in prevention of post partum hemorrhage[13].

Unlike other studies, a trial in India found misoprostol more effective. For prevention of postpartum hemorrhage, a double blind randomized controlled trial with sublingual misoprostol or intramuscular oxytocin was done in teaching hospital, N.J Medical college, Belgam, India. The incidence of PPH was 3.1% with misoprostol and 9.1% with oxytocin. Here they found sublingual misoprostol more effective in reducing PPH, with only transient side effects being greater in misoprostol group[14].

In a prospective, double-blind, randomized controlled trial conducted in a tertiary maternity hospital Canada, 622 women received either 400 microg of oral misoprostol or 5 IU of oxytocin after delivery of anterior shoulder or within one min of delivery. The primary outcome was hematocript drop of 10% or greater 24h postpartum. Ten percnt or more drop in hematocrit occurred in 3.4% and 3.7% of participants in oxytocin and misoprostol groups, p=0.98 showing misoprostol was no less effective than 5u of oxytocin in reducing blood loss after delivery[15].

Also a study in Kolkata India comparing efficacy of sublingual misoprostol versus intramuscular oxytocin shows that the efficacy of 400 microgram of misoprostol administered sublingually was equivalent to that of 10 units of oxytocin given intramuscularly for prevention of PPH in low risk vaginal delivery[16].

Data from a randomized controlled trial comparing misoprostol to placebo in a home birth setting in rural Pakistan show that 600 mcg oral misoprostol reduces the rate of PPH by 24%, compared with placebo[17] and is effective in preventing postpartum hemorrhage in community and hospital.

Our study showed that Misoprostol is effective in the prevention of post partum hemorrhage in women with low risk pregnancy. Blood loss was less in Misoprostol group as compared to ergot group but the difference was found to be insignificant statistically (p=0.49). Difference of pre and post-delivery hematocrit was also measured among the two treatment groups and it was found that this difference was statistically not significant (p= 0.14).

There were a few cases who had shivering with misoprostol but it was mild and self-limiting only. No significant hyperpyrexia or vomiting was noted with this drug at this dose. However, some ladies had feeling of transient nausea with methylergometrine.

Most of international studies have similar findings regarding blood loss and drop in hematocrit seen in subjects given misoprostol. Also local material regarding role of misoprostol in prevention of primary postpartum have similar results.

This study showed that misoprostol has a place in the prevention of primary post partum hemorrhage during the third stage of labor especially in resource-poor settings where cool storage facilities for other oxytocics are not feasible. The provision of sublingual misoprostol in addition to existing oxytocics to maternity centers in the remote resource-poor settings of developing countries may be the solution to curbing the high maternal mortality rates that result from post partum hemorrhage because it can be effective, cheap, heat stable (requires no refrigeration), has a long shelf life and has fewer deleterious effects.

CONCLUSION

There was no significant difference in prevention of post partum hemorrhage among the two drugs and misoprostol can be used in maternity facilities owing to its easy storage and ease of administration.

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