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RESEARCH ARTICLE

EFFECTIVENESS OF ORAL MISOPROSTOL VERSUS PLACEBO FOR PREVENTION OF POSTPARTUM HAEMORRHAGE

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ABSTRACT

Background and Objective: The clinical definition states "any amount of bleeding from or into the genital tract following birth of the baby up to the end of the puerperium which adversely affects the general condition"3. Postpartum haemorrhage is a leading cause of maternal morbidity and mortality. In India it accounts for 25-30% of maternal deaths1. Uterine atony accounts for 80% cases of primary PPH. Most uterotonics require parental administration, maintenance of cold chain which is necessary for their potency and which is not always possible in some peripheral centre's. Misoprostol a prostaglandin E1 analogue does not need refrigeration, has long shelf life and is stable at high temp. It is very effective for prevention of PPH.

Methodology: Prospective study was conducted in Lalla Ded hospital; associated hospital of Government medical College Srinagar, the only tertiary care hospital for Gynecology and Obstetrics in the Kashmir Valley over a period of 18 months.

Sample size: The number of patients was 200.

Group A: 100 patients (study group) received 600□g of oral misoprostol immediately after delivery of the baby.

Group B: 100 patients (control group) received 3 tabs of placebo similar in appearance.

Our study was primarily designed to study the effectiveness of misoprostol (oral) for prevention of postpartum haemorrhage (PPH). The primary outcomes measured were : amount of blood loss, pre-delivery and post delivery haematocrit, haemoglobin pre delivery and post delivery, duration of third stage of labour, need for manual removal of placenta, need for other oxytocics, need fof blood transfusion and side effects of misoprostol were also recorded

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INTRODUCTION

Postpartum Haemorrhage

Postpartum haemorrhage is a leading cause of maternal morbidity and mortality. In India it accounts for 25-30% of maternal deaths (Derman *et al*., 2006). The clinical definition states "any amount of bleeding from or into the genital tract following birth of the baby up to the end of the puerperium which adversely affects the general condition" (Ambrose A. Repke, 2006). Quantitatively postpartum haemorrhage is defined as estimated blood loss of >500 ml for vaginal delivery and >1000 ml for caesarean delivery. Classical definition of postpartum haemorrhage is 10% change in haematocrit between admission and postpartum period[4]. Postpartum haemorrhage is classified into two types:

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(i) Primary Postpartum Haemorrhage: postpartum haemorrhage which occurs within 24 hours of birth is called primary postpartum haemorrhage and is the most common type (The John Hopkins Manual of Gynaecology and Obstetrics; Holland and Brews). Incidence is 5-8% in places where some form of prophylaxis is given and 18% when physiological approach is norm (Prevendeville and Elbourne, 1989).

(ii) Secondary Postpartum Haemorrhage: postpartum haemorrhage which occurs after 24 hours of birth and up to 6 weeks of puerperium is called a secondary postpartum haemorrhage. (The John Hopkins Manual of Gynaecology and Obstetrics; Prevendeville and Elbourne, 1989) Incidence is <1 to 2% (Ambrose A. Repke, 2006; Carpenter, 2001).

- Uterine atony (poor contraction after delivery) which is most common cause of PPH accounting for about 80%.

Misoprostol

It is a synthetic prostaglandin E1 analogue. Misoprostol can be given orally, vaginally, sublingually, buccally or rectally (Kabelo Monicah Olefile, 2011). Absorption is fast in all routes of administration but most rapid action occurs when given orally, it appears in circulation within 2 minutes with peak concentration after 12 minutes. When taken vaginally or sublingually, it takes longer time to start its action with peak concentration after 60 minutes. Vaginal bleeding and loss of amniotic fluid has negative effect on absorption of misoprostol. Rectal route has slow uptake but prolonged duration of action (Christian Fiala and Andrew Weeker, 2005). Misoprostol is both heat and light stable. It is relatively less expensive as compared to other prostaglandins

MATERIALS AND METHODS

Prospective study was conducted in Lalla Ded hospital; associated hospital of Government medical College Srinagar, the only tertiary care hospital for Gynecology and Obstetrics in the Kashmir Valley over a period of 18 months.

Sample size

The numbers of patients were 200.

Group A

100 patients (study group) received 600µg of oral misoprostol immediately after delivery of the baby.

Group B

100 patients (control group) received 3 tabs of placebo similar in appearance. Permission for the study was taken from the institutional ethical committee. If needed, additional intervention was done in both controls as well as in study groups. Informed verbal consent was taken from the patients before enrolment into the study. Time period was, vigilant monitoring for 2 hours and further observation for 24 hours.

Inclusion criteria

1. Primigravida.
2. At term pregnancy
3. Singleton pregnancy.
4. Women in labour anticipating vaginal delivery.
5. Low risk for postpartum haemorrhage.

Exclusion criteria

1. Multiple pregnancies.
2. Previous caesarean section.
3. Antepartum hemorrhage.
4. Previous history of postpartum hemorrhage.
5. Preeclampsia.
6. Medical conditions like diabetes mellitus, hypertension, anaemia, and cardiac disease.
7. Women with any bleeding disorder or coagulopathy.

Contraindications of Misoprostol

1. Drug allergy
2. Bronchial asthma
3. Acute PID

Material used

1. Misoprostol (hospital supply)
2. Placebo tabs → artificial sweetening agent made of protein aspartame.
3. Cotton swabs.
4. Weighing machine.

Method

1. Detailed history, past history, personal, family and drug history was asked.
2. Detailed general physical examination was done.
3. All patients undergo obstetric examination to assess foetal presentation, gestational age, amniotic fluid level and fetal cardiac activity.
4. All patients undergo baseline laboratory investigations:

- Delivery details were noted including
  - Date and time of delivery
  - Pulse and blood pressure during and after delivery
  - Time of drug administration
  - Duration of third stage
  - Time taken for expulsion of placenta
  - Blood transfusion needed
  - Need for manual removal of placenta

Prostaglandin E_1 analogue misoprostol (600µg) was given orally to study group of patients after delivery of the baby and 3 tablets of placebo were given to control group.
Blood loss was measured by

1. In immediate postpartum period i.e. first two hours by weighing cotton swabs before and after use (in fourth stage of labour room) and next up to 24 hours by weighing sanitary pads before and after use (in postnatal ward).
2. Haemoglobin and haematocrit level at the time of admission to labour room and 24 hours after delivery.

Statistical Analysis

The collected data was statistically analyzed by Independent 't' Test and Paired t test for metric data and Chi square test for non-metric data. P value of < 0.05 was considered as significant.

RESULTS

Table 1. Comparison of blood loss

Group	No.	Range	Mean ± SD	P value
Misoprostol (Cases)	100	160 – 550ml	235.20±75.86	< 0.001
Placebo (Control)	100	200 – 610ml	399.60±101.88	

Our study was primarily designed to study the effectiveness of misoprostol (oral) for prevention of postpartum haemorrhage (PPH), amount of blood loss and to reduce the maternal morbidity and mortality. Cases were compared with placebo and following were the observations. The blood loss in patients in whom misoprostol was given was less with mean 235.20ml as compared to placebo with mean 399.6ml. The below graph shows the need for manual removal of placenta in two groups. Manual removal of placenta was less in misoprostol group, 5 patients only (5%) while as it was 18 patients (18%) in placebo group with p value of 0.004 which was statistically significant.

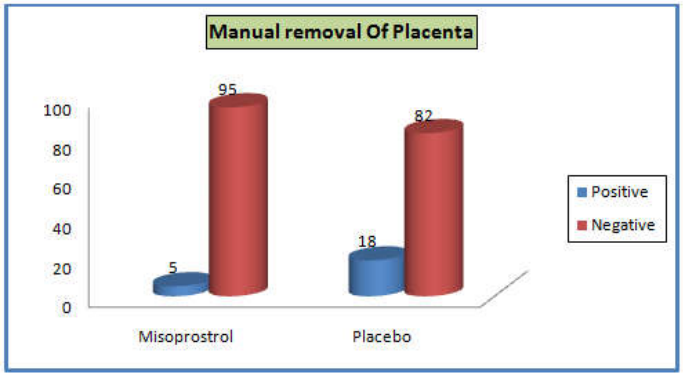


Table 2. Comparison of need for further oxytocics in Group I and Group II

Group	Need for further oxytocics		Total
	Positive	Negative	
Misoprostrol (Cases)	14	86	100
Placebo (Controls)	88	12	100
Total	102	98	200
□2 = 109.6	d.f. = 1	P – value < 0.001	

Table 3. Comparison of need for blood transfusion in Group I and Group II

Group	Need for Blood Transfusion		Total
	Positive	Negative	
Misoprostrol (Cases)	6	94	100
Placebo (Control)	15	85	100
Total	21	179	200
□2 = 4.310	d.f. = 1	P – value = 0.038	

The above table depicts the need for further oxytocics for augmentation of placental delivery and for prevention of PPH and uterine atony. The need was less in misoprostol group (14 out of 100) as compared to placebo (88 out of 100) with p value of < 0.001 which was statistically significant.

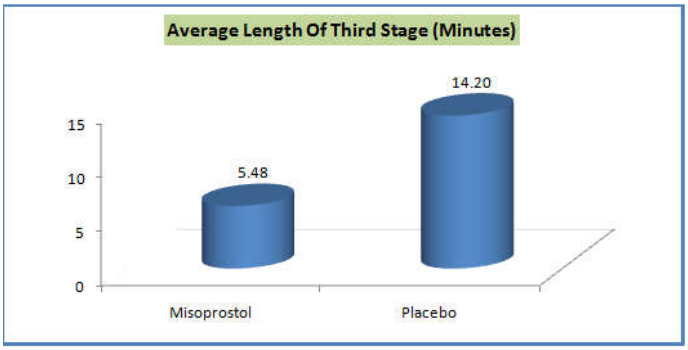


Table 4. Distribution of Group I Patients according to haemoglobin

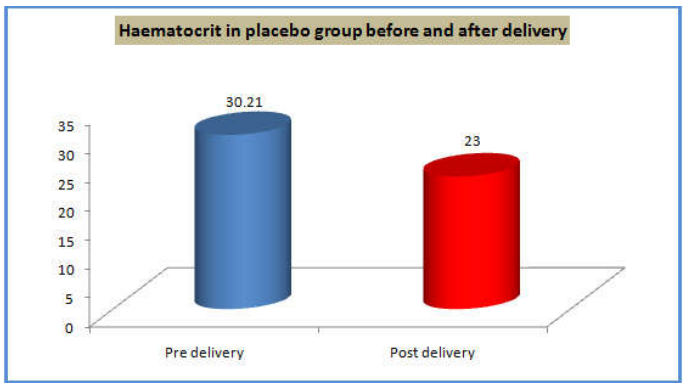
Haemoglobin (HB)	No.	Mean ± SD	P – Value
Pre delivery	100	10.42±1.026	< 0.001
Post delivery	100	9.24±0.906	

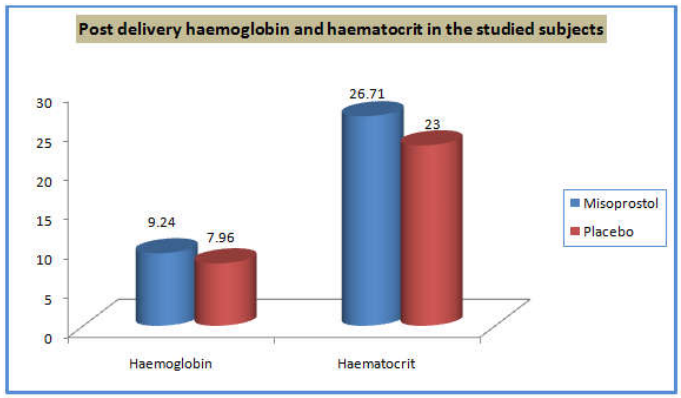
Table 5. Distribution of Group II Patients according to haemoglobin

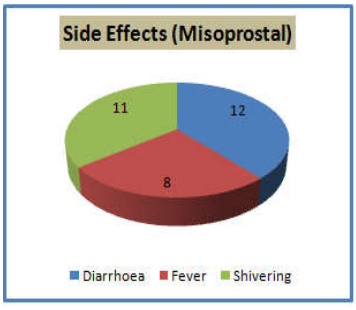
Haemoglobin (HB)	No.	Mean ± SD	P Value
Pre delivery	100	10.45±0.734	< 0.001
Post delivery	100	7.96±0.749	

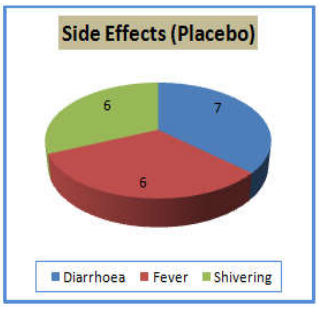
Table 6. Distribution of Group I Patients according to haematocrit

Haematocrit	No.	Mean ± SD	P Value
Pre delivery	100	30.12±2.965	< 0.001
Post delivery	100	26.71±2.618	









The above table compares the need for blood transfusion in misoprostol and placebo groups. As is evident only 6 patients in misoprostol group required transfusion as compared to 15 in

placebo group with p value of 0.038 which was statistically significant. It was found that the duration of third stage was curtailed in the misoprostol group (5 min, 48 sec) as compared to placebo group (14 min and 20 sec) with a p value of < 0.001 which was statistically significant. There was a little decrease in the haemoglobin levels in misoprostol administered patients in our study 10.42 to 9.24gm/dl. The decrease in haemoglobin level in placebo group was more from10.45 to 7.96gm\dl. In our study, in the misoprostol group there was a little decrement in haematocrit from 30.12 to 26.71% post delivery.

Distribution of Group II Patients according to haematocrit

In control group, haematocrit decreased from 30.21 to 23.00% which was marked decrease. Post delivery haemoglobin and haematocrit of studied subjects. Above graph depicts that there is significant difference in post delivery haemoglobin and haematocrit in misoprostol and placebo with p value < 0.001 which was statistically significant. Minimal side effects like diarrhoea, fever and shivering were observed with misoprostol.

Conclusion

Two hundred patients were studied in Lalla Ded Hospital. Among these 100 patients received misoprostol 600µg orally after delivery of baby and 100 patients received three tablets of placebo. On the basis of observations in the study following conclusions were drawn:

1. Uterine atony is the commonest cause of Postpartum haemorrhage.
2. Use of misoprostol reduces the amount of blood loss, shortens the duration of third stage, reduces need for the manual removal of placenta, need for further oxytocics and blood transfusion requirements.
3. Oral misoprostol is a life saving drug for prevention of postpartum haemorrhage especially in situations where facilities of storage and parenteral administration are limited.

To conclude, use of misoprostol can definitely bring down the incidence of maternal morbidity and mortality due to postpartum haemorrhage in developing countries where facilities for storage transport and parenteral administration is limited.

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