



A STUDY ON EFFECTIVENESS OF PRE OPERATIVE V/S POST OPERATIVE MISOPROSTOL ADMINISTRATION IN CEASEREAN SECTION.

Obstetrics & Gynaecology

Dr Parul Shah	Head of Dept., Obst. & Gynec., Smt.NHLMMC
Dr Harshal Shah*	3rd Yr. Resident, Obst. & Gynec., Smt. NHLMMC *Corresponding Author
Dr Kruti Delivala	Asst. Prof., Obst. & Gynec., Smt. NHLMMC
Dr Devangi Munshi	Asst. Prof., Obst. & Gynec., Smt. NHLMMC
Dr Fiza Saiyed	2nd Yr. Resident, Obst. & Gynec., Smt.NHLMMC

ABSTRACT

Purpose: To compare the effectiveness of the rectally administered misoprostol pre-operative versus post-operative in minimizing intraoperative blood loss and prevention of postpartum hemorrhage in cesarean delivery.

Material and Methods: This study included 180 pregnant women at term (37 - 40 weeks) undergoing Caesarean delivery under regional anesthesia. Group I (n = 84) received 400µg rectal misoprostol preoperatively, and Group II (n = 82) received 400µg rectal misoprostol postoperatively. Hematocrit level was measured and recorded at admission as a preoperative routine investigation and repeated 24 hours following cesarean delivery. The patients were evaluated in terms of operative time, operative blood loss and any side effects of administered drugs.

Results: The demographic characteristics of participants as age, parity and gestational age were comparable between the two groups. As regard the estimated blood loss ($M \pm SD$) during cesarean section in group I (preoperative misoprostol) was 372.33 ± 25.997 ml, in group II (postoperative misoprostol) was 722 ± 34.089 ml ($p = 0.001$). Hematocrit value after cesarean section was significantly lower in group II than in group I ($P = < 0.001$). The 2 groups were not different in terms of side-effects except for abdominal pain (P value 0.02).

Conclusion: Administration of rectal misoprostol prior cases are an appears to be safe, more effective than post operative administration for decreasing the amount of blood loss during cesarean section.

KEYWORDS

Post-partum hemorrhage, Preoperative Misoprost, Postoperative Misoprost, Uterotonics

INTRODUCTION

Postpartum hemorrhage (PPH) continues to be a leading cause of maternal morbidity and mortality worldwide. According to the World Health Organization estimates, more than 585,000 women die every year from pregnancy-related cause, of which 25% were due to severe bleeding

- [1]. In a survey performed at the center of prevention from diseases, hemorrhage was a direct cause of mortality in 18% of maternal deaths
- [2]. Postpartum hemorrhage has many causes, but uterine atony remains the most common cause of PPH representing about 80% of all causes of postpartum hemorrhage
- [3,4]. Active management of the third stage of labor by administration of uterotonic drugs reduces the risk of postpartum hemorrhage, postpartum anemia as well as the need for blood transfusion. The most commonly used uterotonic drugs include oxytocin, methylergonovine, carbetocin, and prostaglandins
- [5]. Misoprostol is a synthetic prostaglandin E1 analogue; it is widely used for management of the third stage of labor and for intractable postpartum hemorrhage as a last resort when other medical interventions failed. It has a potent uterotonic shivering, pyrexia, nausea, vomiting, and diarrhea
- [6]. Rectal effect, cheap, stable at room temperature, easily administered and has few adverse effects. It is well absorbed when administered by oral, vaginal, rectal, and sublingual routes. Side effects of misoprostol include misoprostol is the best route for patient undergoing caesarean delivery due to slower absorption, fewer side effects. The mean T_{max} after rectal administration is 40 - 65 minutes
- [7,8], although a recent study reported a much shorter T_{max} of 20 minutes [9]. This delayed timing of absorption is thought to be beneficial when misoprostol is given prior to surgery as by the end of caesarean section, the maximum effect was obtained
- [8,10]. Many research studies were conducted to evaluate the role of rectal misoprostol as a preventive measure for postpartum hemorrhage. Some of the studies advocate its use for prevention of postpartum hemorrhage
- [11-14], while other studies concluded that misoprostol was not as effective as expected
- [15,16]. Other studies concluded that use of misoprostol must be stopped

[17,18]. For this wide gap of controversy in the results of previous studies about the use of misoprostol for prevention of postpartum hemorrhage with cesarean section. Also the timing of misoprostol administration was not fully studied; this study was conducted to compare preoperative with postoperative rectal misoprostol for decreasing the postpartum hemorrhage.

Patients and Methods

This study was conducted at obstetric and gynecology department at V.S. Hospital, Ahmedabad, India.

Patients: The study included 180 cases recruited according to inclusion and exclusion criteria. They were randomly allocated into 2 groups of preoperative misoprostol and postoperative misoprostol.

Inclusion criteria were pregnant at term (37 - 40) weeks, and elective planned cesarean section done under regional anesthesia.

Exclusion criteria were any condition that prolong surgery or cause uterine atony such as: cesarean section under general anesthesia as it causes uterine atony necessitating more uterotonics, antepartum hemorrhage, and maternal hypertension, maternal anemia, coagulation disorders, previous 2 or more cesarean section, failed trial patient, multiple gestation, fetal macrosomia, polyhydramnios, and previous rupture uterus.

Patients were allocated by simple randomization and alternate allocation into 2 groups:

Group I (Preoperative Misoprostol): Received 2 tablets of misoprostol (400ug) rectally after regional anesthesia and shortly before skin incision.

Group II (Postoperative Misoprostol): Received 2 tablets of misoprostol (400ug) rectally after the end of Caesarean section. Randomization was done by simple method with numbered container, then allocation by alternate method.

METHODS

All patients received the same regimen of management for example: intra operative oxytocin after delivery of fetus Same antibiotics and

analgesics. The need for additional uterotonics as oxytocin or ergometrine, additional antibleeding drugs or the need for blood transfusion was recorded for all patients. Estimation of blood loss during cesarean section was determined by: (i) measuring the amount of blood collected in suction bottles after delivery of placenta plus weight of soaked towels and (ii) comparing pre and postoperative maternal Hematocrit level with the use of computerized programs using weight, height, pre and postoperative hematocrit to calculate estimated blood loss. Post-delivery care was performed such as monitoring the blood pressure, pulse, temperature, and amount of bleeding during first 24 hours after delivery measured by weight method by the following equation: soaked towel weight - dry to wet weight = difference in grams, then every gram = 1 ml blood loss

[19]. The levels of Hemoglobin and Hematocrit were measured and recorded at hospitalization and 24 hours after cesarean delivery.

At this interval, the patients were evaluated in terms of possible complications and side effects of administered drugs such as abdominal pain, vomiting, diarrhea, shivering and pyrexia. Result were reported as mean $\pm$ SD or number (percentage). The p value <0.05 was considered statistically significant.

RESULTS

Demographic data of studied cases were nearly the same. Mean age in group I was 25.4 ± 5.2 years, in group II was 26.7 ± 5.6 years; with no significant difference was observed between three studied groups ($P=0.28$). Also, Mean gestational age in group I was 38.4 ± 1.10 weeks, in group II was 38.5 ± 1.13 weeks; no significant difference was observed between 2 groups ($P=0.82$). (Table 1)

Table 1: Demographic data of studied groups.

	Groups		Test of significance	(P)
	Group I Preoperative Misoprostol (NO = 84) (M $\pm$ SD)	Group II Postoperative Misoprostol (NO = 82) (M $\pm$ SD)		
Age (years)	25.46 ± 5.20	26.73 ± 5.63	1.28	0.280
Parity	1.3 ± 0.4	1.5 ± 0.7	1.330	0.854
Gestational age (weeks) at delivery	38.46 ± 1.10	38.35 ± 1.13	0.18	0.820
BMI	23.3 ± 2.70	22.98 ± 3.40	1.21	0.540
Preoperative Hematocrit level	35.90 ± 4.5	35.77 ± 2.4	2.34	0.345

As regard operative data, Operative time was nearly equal in the 2 groups with no significant difference ($P=0.154$). The estimated blood loss (M $\pm$ SD) during cesarean section in group I was 372.33 ± 25.997 ml, in group II was 722 ± 34.089 ml ($P=0.001$). There was statistically significant decrease in the estimated blood loss with the group I over group II ($P=0.001$). (Figure 2).

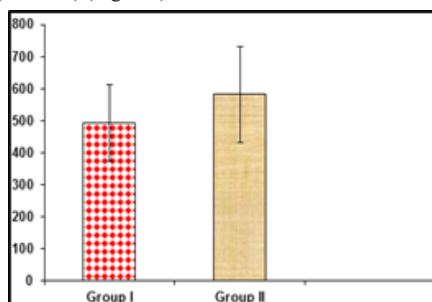


Table 2: Operative data in studied groups.

	Groups		Test of significance	(P)
	Group I Preoperative Misoprostol (NO = 84)	Group II Postoperative Misoprostol (NO = 82)		
Operative time (minutes)	40 - 60	39 - 65	1.8854	(0.154)
Min-Max (M $\pm$ SD)	49.25 ± 4.614	50.123 ± 6.956		

Operative blood loss (ml) Min-Max (M $\pm$ SD)	363-388 372.33 ± 25.997	660-845 722 ± 34.089	321.398	(0.001)*
Postoperative blood loss (24 hours)	190.55 ± 30.45	237.65 ± 23.78	10.452	0.001
Postoperative hematocrit (24 hours post-caesarean section) Min-Max (M $\pm$ SD)	33.55 ± 0.7	29.29 ± 0.7	0.22	<0.001

The postoperative blood loss in the first 24 hours was reduced in group I than in group II with mean blood loss of (190.55 ± 30.45 ml and 237.65 ± 23.78 ml) respectively.

There was no significant difference between the level of hematocrit before & after cesarean section in both groups ($P=0.22$). Postoperative hematocrit value after 24 hours of delivery was significantly higher in group I than in group II ($P=<0.001$).

	Group A	Group B	P Value	Remarks
Preop Hb (g/dl)	11.3 ± 0.9	11.4 ± 0.9	0.24	NS
Postop Hb (g/dl)	10.2 ± 0.8	10.1 ± 0.8	0.30	NS
Hb difference (g/dl)	1.10 ± 0.51	1.35 ± 0.49	<0.001	Significant

DISCUSSION

PPH is one of the most common obstetric complications leading to maternal death world wide. Its incidence is increasing and it affects 1-5% of all deliveries. Uterine atony is the most common cause of PPH and is responsible for about 80% of PPHs [20,21].

In the current study, preoperative rectal administration of misoprostol versus postoperative rectal administration was compared in reducing intraoperative blood loss and prevention of postpartum hemorrhage during cesarean delivery. Age, parity and gestational age were not statistically different between the enrolled patients.

The intraoperative blood loss was significantly decreased in preoperative misoprostol group with mean blood loss of 372.33 ± 25.997 ml compared to 722 ± 34.089 ml in the postoperative misoprostol group.

This study also showed that there was a significant hemoglobin difference between the two groups. Mean hemoglobin difference in group A was 1.10 ± 0.51 g/dl where as in group B was 1.35 ± 0.49 g/dl with p value of <0.001 .

The current study, demonstrated that there was a significant decrease in post-delivery hematocrit levels. In postoperative misoprostol group than in preoperative misoprostol group. Reduction of blood loss at cesarean section is beneficial to the patient in term of decreasing postoperative morbidity and decreased the risk associated with blood. In the current study the incidence of side effects of the rectal misoprostol were abdominal pain, hyperthermia, chills, vomiting. Only abdominal pain was significantly lower in preoperative misoprostol group than postoperative misoprostol group. Other complications were not significant in both groups. [26].

Many studies concluded that administration of misoprostol plus oxytocin significantly reduced the amount of blood loss during and after cesarean section compared to oxytocin and misoprostol when given alone, and use of them was not associated with any serious side effects [27,28].

Study Limitations

Non-blinding of this study and the relatively small sample size.

CONCLUSION

Administration of rectal misoprostol in CS prior to incision is safe, more effective, than postoperative administration for decreasing the amount of blood loss during cesarean section and as a prophylactic uterotonic to decrease the incidence of postpartum hemorrhage after cesarean sections.

REFERENCES

- WHO. "Maternal mortality. Factsheet No. 348" (2010).
- Rushwan H. "Misoprostol: an essential for medicine for managing postpartum

- hemorrhage in low-resource settings?" *International Journal of Gynecology and Obstetrics* 114(2011):209-210.
3. Dildy GA. "Postpartum hemorrhage: new management options". *Clinical Obstetrics and Gynecology* 45.2(2002):330-344.
4. FazelMR.,etal."Acomparisonofrectalmisoprostolandintravenousoxytocinonhemorrhageandhomeostaticchangesduringcesareansection". *Middle East Journal of Anesthesiology* 22.1(2013):41-46.
5. AllenRandO'BrienBM."Usesofmisoprostol inobstetricsandgynecology". *Reviewsin ObstetricsandGynecology* 2.3(2009):159-168.
6. Cunningham FG., et al. "Williams obstetrics. 24th ed". New York: Medical publishing division, McGRAW-Hill; (2014):780-822.
7. Meckstroth KR., et al. "Misoprostol administered by epithelial routes". *Obstetrics and Gynaecology* 108(2006):582-590.
8. Ragab A., et al. "A randomized clinical trial of preoperative versus postoperative misoprostol in elective cesarean delivery". *International Journal of Gynecology and Obstetrics* 132.1(2016):82-84.
9. TangOS.,etal."Misoprostol:pharmacokineticprofiles,effectsontheuterusandside-effects". *InternationalJournalofGynecologyandObstetrics* 99.2(2007):S160-S167.
10. MasoumehMirteimouri.,etal."EfficacyofRectalMisoprostolforPreventionofPostpartumHemorrhage". *IranianJournalofPharmaceutical Research* 12.2(2013):469-474.
11. Owonikoko KM., et al. "Effect of sublingual misoprostol versus intravenous oxytocin on reducing blood loss at caesarean section in Nigeria: a randomized controlled trial". *Journal of Obstetrics and Gynaecology Research* 37.7(2011):715-721.
12. MinooRajaei., et al. "Safety and Efficacy of Misoprostol versus Oxytocin for the Prevention of Postpartum Hemorrhage". *Journal of Pregnancy*(2014).
13. HofmeyrGJ.,etal."Postpartummisoprostolforpreventingmaternalmortalityandmorbidity". *CochraneDatabaseSystematicReviews*
14. Soon CH., et al. "Additional rectal misoprostol plus intravenous oxytocin versus intravenous oxytocin for prevention of postpartum hemorrhage after cesarean section". *American Journal of Obstetrics and Gynecology* 197.6(2007):S99.
15. Quibel T Ghout L., et al. "Active Management of the Third Stage of Labor With a Combination of Oxytocin and Misoprostol to Prevent Postpartum Hemorrhage: A Randomized Controlled Trial". *Obstetrics and Gynecology* 128.4(2016):805-811.
16. Robert L Barbieri. "Stop using rectal misoprostol for the treatment of postpartum hemorrhage caused by uterine atony". *OBG Management* 28.7(2016):8-10,12.
17. Mousa HA and Alfirevic Z. "Treatment for primary postpartum hemorrhage". *Cochrane Database of Systematic Reviews* 1(2007):CD003249.
18. Gibbins KJ., et al. "Postpartum hemorrhage in the developed world: whither misoprostol?" *American Journal of Obstetrics and Gynecology* 208.3(2013):181-183.
19. Stafford L., et al. "Visually estimated and calculated blood loss in vaginal and cesarean delivery". *American Journal of Obstetrics and Gynecology* 199.5(2008): 519.e1-519.e7.
20. LuMC.,etal."Variations in the incidence of postpartum hemorrhage across hospitals in California". *MaternalandChildHealthJournal*.
21. CallaghanWM.,etal."Trends in postpartum hemorrhage: the United States, 1994-2006". *American Journal of Obstetrics and Gynecology* 202.4(2010):353.e1-6.
22. Abd-ElilahA., et al. "Is the Time of Administration of Misoprostol of a value? The uterine effect of misoprostol given pre- and post-operative after elective caesarean section". *Middle East Fertility Society Journal* 19.1(2014):8-12.
23. Haque N., et al. "Comparative study between rectally administered misoprostol as a prophylaxis versus conventional intramuscular oxytocin in postpartum hemorrhage". *Mymensingh Medical Journal* 18.1(2009):S40-S44.
24. Conde-AgudeloA.,etal. "Misoprostol to reduce intra operative and postoperative hemorrhage during cesarean delivery: a systematic review and meta-analysis". *American Journal of Obstetrics and Gynecology* 209.1(2013): 40.e1-40.e17.
25. Mervat ElSadeeq. "Impact of preoperative rectal Misoprostol on blood loss during and after elective Caesarean section". *International Journal of Obstetrics and Gynecology* 18.2(2012):149-152.
26. Chaudhuri P., et al. "Rectally administered misoprostol versus intravenous oxytocin infusion during cesarean delivery to reduce intra-operative and postoperative blood loss". *International Journal of Gynecology and Obstetrics* 109.1(2010):25-29.
27. Pakniat H and Khezri MB. "The Effect of Combined Oxytocin-Misoprostol Versus Oxytocin and Misoprostol Alone in Reducing Blood Loss at Cesarean Delivery: A Prospective Randomized Double-Blind Study". *Journal of Obstetrics and Gynecology of India* 65.6(2015): 376-381.
28. Badejoko OO., et al. "Adjunctive rectal misoprostol versus oxytocin infusion for prevention of postpartum hemorrhage in women at risk: a randomized controlled trial". *Journal of Obstetrics and Gynaecology Research* 38.11(2012):1294-301.