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ORIGINAL ARTICLE

Sublingual 400 µg Misoprostol *vs* Intravenous 0.2 mg Methylergometrine for Active Management of Third Stage of Labor

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ABSTRACT

Objectives: To compare the efficacy and side effects of sublingual 400 µg misoprostol with 0.2 mg intravenous methylergometrine in active management of third stage of labor.

Materials and methods: In a prospective, randomized comparative study conduted in Department of Obstetrics and Gynecology, AVBRH, Wardha, 200 women at full-term gestation, without any high risk factors were studied in two groups of 100 each, for safety and efficacy of 400 µg sublingual misoprostol in comparison to 0.2 mg intravenous methylergometrine at the delivery of anterior shoulder from December 2010 to November 2011. Main parameters used were duration of 3rd stage, amount of blood loss, need of aditional uterotonic, complications of third stage, drop in hemoglobin and side effects. Results were analyzed by Student's t-test.

Results: Mean duration of third stage in misoprostol group was 9.67 ± 1.98 min, amount of blood loss was 203 ± 24 ml, need of additional uterotonics was 13%, drop in hemoglobin 0.59 ± 0.79 which were almost comparable with other group and side effects were mainly shivering and pyrexia in misoprostol group and vomiting and giddiness in methergine group.

Conclusion: Sublingual 400 µg misoprostol is almost equally effective as intravenous methergine for active management of third stage of labor with advantage of simplicity of storage of drug, route of administration and no risk of injection associated infections, which make it very much relevant in rural scenario.

Keywords: Third stage, Sublingual misoprostol, Postpartum hemorrhage.

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INTRODUCTION

Postpartum hemorrhage (PPH) is a leading cause of maternal mortality, i.e. approximately 25% in rural areas,[1,2] as these women are more vulnerable for even normal amount of blood loss because of being anemic and malnourished.[1] Although prophylactic use of uterotonics in third stage of labor are routine, the preparations used vary from center to center; oxytocin, ergometrine or a mixture of oxytocin and ergometrine are used, alongwith early suckling of breast.[3] In our hospital, we use methylergometrine 200 µg intravenously as a routine with the delivery of anterior shoulder. Methylergometrine/ oxytocin need maintenance of cold chain as well as syringes, needles, training and licencing.[1,4,5] Furthermore ergometrine is known to induce hypertension, vomiting and contraindicated in pregnancy-induced hypertension and heart disease.[3,5]

Use of prostaglandins in postpartum period was first described in 1976.[3] El-Raphey et al first reported use of misoprostol in third stage of labor,[1,5] since then so many reports revealed that misoprostol is effective in active management of third stage of labor by various routes like sublingual, oral, rectal and vaginal. It is stable at room temperature has very long shelf life and easy to administer, hence it could be a ideal alternative for active management of third stage for rural and peripheral areas.[1,2,4-7]

The aim of our study was to compare safety and efficacy of 400 µg misoprostol with 0.2 mg methylergometrine in active management of third stage of labor.

MATERIALS AND METHODS

This prospective study was conducted in the Department of Obstetrics and Gynecology, Acharya Vinoba Bhave Rural Hospital, JNMC, Sawangi, Wardha, from December 2010 to November 2011.

In a comparative study, 200 women at full-term gestation, without any high-risk factors were observed in two groups of 100 each, for safety and efficacy of 400 µg sublingual Misoprostol in comparison to 0.2 mg intravenous methylergometrine at the delivery of anterior shoulder.

After taking detailed history of present pregnancy, obstetric history, previous pregnancy outcome and any complications, family and medical history was taken to rule out any high-risk factors. General, systemic and obstetric examination was conducted for confirming gestational age, singleton pregnancy, vertex presenting part, dilatation of cervix, effacement and adequacy of pelvis. Pregnancy-induced hypertension, cardiac disease, bronchial asthma, epilepsy, antepartum hemorrhage, induction by misoprostol and instrumental deliveries were excluded from the study.

The study group received two tablets of 200 µg, put under the tongue after making them wet with sterile normal saline and control group received 0.2 mg of intravenous methylergometrine maleate at the delivery of anterior shoulder and time was noted. Large polythene bags (18 inch width), after making split from midline were kept beneath the buttock of patient before delivery and weighed with or without placenta for assessing blood loss after completion of third stage. Placenta was removed by Brandt's-Andrews technique and extra linen used were weighed separately. Amount of blood loss was calculated by the formula: Weight of blood in polythene bag

and linen (W gm) × 1000/1060, as the density of blood is 1,060. Duration of third stage was recorded with completion of removal of placenta and membranes. Patients with episiotomy were also excluded from the study. Any complication of third stage or excessive bleeding were taken care of promptly and recorded.

Data were analyzed by calculating mean values and Student's t-test.

OBSERVATION

Majority of women in our study were second gravida, from rural locality with mean age of 22.3 ± 3.37 and 22.7 ± 2.15 (Table 1).

The mean duration of first and second stages were comparable but the mean duration of third stage was significantly shorter in methylergometrine group, i.e. 4.87 ± 2.01 min than 9.67 ± 1.98 min in misoprostol group (Table 2). The mean amount of blood loss and change in pre- and postdelivery Hb gm% were comparable.

Additional requirement of uterotonic agents were little more in misoprostol group, i.e. in 13 cases *vs* nine in methylergometrine group which was stastically nonsignificant. Other third stage complications were not seen in any group.

In misoprostol group, main side effects were shivering in 29% and pyrexia in 7% of women but none of them had vomiting or loose motions, while in methylergometrine group side effects were nausea 13%, vomiting 21%, severe epigastric pain 7% and giddiness 5% (Table 3).

DISCUSSION

Third stage of labor is very crucial in the life of parturient. Separation of placenta and membranes along with hemostasis is brought about by violent uterine contractions and retraction.

Methylergometrine maleate when given intravenously acts directly on myometrium, producing tetanic uterine contractions and hasten the separation of placenta and minimizes the blood loss. Misoprost acts by bringing about contractions of uterus and promoting vasoconstriction at the target site (placental bed), produced by a well-contracted and retracted myometrium, ultimately leading to hemostasis, hence minimizing blood loss.

Table 1: Demographic characteristics

S. no	*Profile*	*Misoprostol group (n = 100)*	*Methylergometrine group (n = 100)*	*p-value*
1.	Mean age in years	22.3 ± 3.37	22.7 ± 2.15	>0.05 (NS)
2.	Literate up to middle school	73	67	>0.05 (NS)
3.	Rural background	65	71	>0.05 (NS)
4.	Mean parity	0.81 ± 0.30	0.78 ± 0.51	>0.05 (NS)
5.	Full term, singleton pregnancy with spontaneous onset of labor	100	100	

NS: Not significant

Table 2: Duration of labor and amount of blood loss

S. no.		*Misoprostol group (n = 100)*	*Methylergometrine group (n = 100)*	*p-value*
1.	Duration of first stage of labor	9.69 ± 2.15 hrs	9.81 ± 1.99 hrs	>0.01 (NS)
2.	Duration of second stage of labor	21.90 ± 9.71 mins	22.19 ± 8.79 mins	>0.01 (NS)
3.	Duration of third stage of labor	9.67 ± 1.98 mins	4.87 ± 2.01 mins	<0.01 (S)
4.	Amount of blood loss	203 ± 24 ml *vs*	189 ± 61 ml	>0.01 (NS)
5.	Fall in Hb gm%	0.59 ± 0.79	0.57 ± 0.81	>0.01 (NS)

NS: Not significant; S: Significant

Table 3: Side effects and complications

S. no.		*Misoprostol group (n = 100)*	*Methylergometrine group of mean (n = 100)*	*p-value*
1.	Need of additional uterotonic drugs	13	9	>0.05 (NS)
2.	Nausea	2	13	<0.05 (S)
3.	Vomiting	–	21	<0.05 (S)
4.	Epigastric pain	–	7	<0.05 (S)
5.	Pyrexia	7	5	<0.05 (S)
6.	Giddiness	–		<0.05 (S)
7.	Shivering	29		<0.05 (S)

NS: Not significant; S: Significant

The onset of action of methylergometrine maleate when given by intravenous route is within 30 to 45 seconds, while the action of misoprostol when given orally starts in few minutes, reaches its peak within 12 to 13 minutes and persist for 20 to 40 minutes.

Nearly, half of the cases had separation of placenta in 10 to 20 minutes after the delivery of fetus in misoprostol group, while in methylergometrine maleate group all had expelled the placenta within 9 minutes.[4]

Sublingual misoprostol is effective in reducing the incidence of severe PPH. This study shows only 13% of cases required additional uterotonic agent. In our study, none of the women who were given misoprostol had a loss of ≥500 ml similar to some other studies.[1,4] PPH was not seen in any group although it was higher in misoprost group in some other studies.[3] Amount of blood loss in misoprostol group was observed by us as 203 ± 24 ml *vs* 189 ± 61 ml relatively higher amount of blood loss noted in some other studies (Table 4).

In WHO multicentric randomized trial,[8] 4% of misoprostol group had PPH against 3% in oxytocin group. American College of OB/GY suggests that definition of PPH may be based on change in Hb concentration, the change in Hb gm% before and after delivery is a better method to assess the amount of blood loss and further management regarding blood transfusion or iron replacement therapy.[6] Reduction in Hb gm% in our study was 0.59 ± 0.79 and 0.57 ± 0.81 in misoprostol and methylergometrine group respectively. Hemoglobin reduction was similar in both the groups, similarily found by few others.[1,6]

Side effects of misoprostol are shivering, nausea, vomiting, pyrexia and diarrhea.

Shivering and pyrexia, the main side effects observed in misoprostol group may be due to its effect on thermoregulatory centers but self limiting and responded very well to paracetamol or diclofenac rectal suppository. In methylergometrine group, giddiness, epigastric pain, nausea and frank vomiting were the important side effects, similarly observed in other studies[4] (see Table 4).

Table 4: Comparison with other studies

Sl. no.	*Author and study*	*Years*	*Drug and dosage*	*Duration of 3rd stage*	*Amount of blood loss*	*Need of additional oxytocic agent*	*Change in hemoglobin*	*Side effects*
1	Nagariya T et al Obst and Gynecol, India	2009	Oral 400 µg *vs* 0.2 mg intravenous methergine	10.17 ± 6.87 mins *vs* 5.68 ± 1.91 mins	None had >500 ml blood loss			Shivering in 37 *vs* 9% pyrexia in 14% *vs* 1%
2	Chhabra et al J Obst & Gynaecol Research	2008	100 µg SLM and vs 200 mg SML methergine	9.1 ± 5 9.1 ± 5 8.6 ± 5	None had >500 ml blood loss	5% 4% 3%		
3	G Walraven et al Rural Gambia BJOG	2005	600 µg oral misoprostol *vs* 100 µg tablets of 0.5 mg ergometrine		11% *vs* 12% had >500 ml 1.4% *vs* 2.2% had >1000 ml		>2 gm% in 16.4% *vs* 21.2%	a. 32.7% had shivering *vs* 11.7% b. 5.7% of methergin had vomiting *vs* 2.9% of miso
4	WHO multicenter trial Lancet	2001	600 µg oral misoprostol *vs* 10 U intravenous or intramuscular oxytocin	Similar	4% *vs* 3% had >1000 ml			
5	Frederi Anant et al Belgium BJOG	1999	600 µg moral misoprostol *vs* 200 mg IV methergine	Similar (p = 0.88)	Similar (p = 0.57)	12.8% *vs* 4.4%		Shivering and fever significantly more in misoprostol (p < 0.001)
6	G Hofmayr et al Johannesburg BJOG	1998	Sublingual 400 µg *vs* placebo	3.2% had >30 mins *vs* 5% in placebo	6% had >1000 ml *vs* 9.2% in placebo	8.4% *vs* 13%		19% shivering *vs* 5.2% p-value less than 0.01

CONCLUSION

Third stage of labor is life-threatening if not managed promptly, specially in peripheral centers and in rural parts of India, where active management of third stage by drugs requiring parenteral route and maintenance of cold chain is not always feasible and, after hemorrhage, a lot of precious time is wasted in search of transportation and tertiary care help. Misoprostol is a drug to compass all the adversities with almost equal effectiveness.

It is the simplest route desirable in developing countries, especially in rural India, where many deliveries are conducted at home and not attended by medically trained staff.

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