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TO STUDY ROLE OF MISOPROSTOL BY VARIOUS ROUTES IN MANAGEMENT OF THIRD STAGE OF LABOUR

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ABSTRACT
The most common cause of maternal mortality is postpartum haemorrhage, accounting for one third of maternal deaths. Recently misoprostol, a PGE1 analogue, has been reported to be effective in prevention of PPH. **Aim:** Was to study and analyse the role of misoprostol by various routes in management of third stage of labour. **Material & methods:** This hospital based randomized comparative study was conducted on 200 patients admitted for delivery. Misoprostol was given by oral, rectal and vaginal routes and compared with methyl ergotmetrine. In all the patients time and nature of placental delivery, amount of blood loss, need of other uterotonic agent, change in Hb after 48 hrs of delivery and any side effect of the drugs were noted. **Results and Discussion-** Mean duration of third stage of labour was minimum in ME (4.0 ± 3.2) group and maximum in vaginal misoprostol group (7.8 ± 3.6). Mean blood loss during third stage of labour was minimum in misoprostol rectal group (120 ± 10).Rectal route is best in terms of ease to administer, extremely rapid absorption effectiveness stability and safety profile regarding prevention of PPH.

KEYWORDS: PPH, Misoprostol, Third stage of labour.

To Study the Role of Misoprostol by various routes in management of third stage of Labour

INTRODUTION
The immediate postpartum period (24 hrs of delivery) is the most critical time; almost 90% of deaths occur within 4 hrs after delivery.[1]

99% of these deaths occur in developing countries in women who rarely receive prophylaxis is because they give birth outside hospital setting.

Active management of third stage of labour is strongly recommended. Routine administration of oxytocics reduces the risk of PPH by 40%.

Misoprostol, aPGE1 analogue has been reported to be effective in prevention of PPH.

AIM & OBJECTIVES
- To investigate the use of prostaglandins E1 analogue misoprostol in prevention of PPH.
- To compare misoprostol with standard dose of 600µg by various routes (Oral, Vaginal, Rectal) with methyl ergometrine in active stage of third stage of labour.
- To evaluate the efficacy and side effects of misoprostol after administration in third stage of labour.

MATERIAL AND METHODS
This hospital based randomized comparative study was conducted on 200 patients admitting in department of Obst and gynae, Zenana hospital, SMS Medical College, Jaipur for delivery during a period of nov 2015 till oct 2016.

The standard drug used to prevent PPH at the study hospital is intravenous methyl – ergotmetrine, except in women with PIH and cardiac disease who are given 20 units intravenous syntocinon infusion.

Pregnant women with spontaneous onset of labour were eligible to participate in the study.
Exclusion criteria –
- Oxytocin infusion or augmentation of labour
- Casarean section
- Gestation < 37weeks
- Known Hypersensitivity to prostaglandins

- Pregnancy with hypertension, heart disease, renal disease, asthma

Group A – (50 cases) Tab misoprostol 600µg was given orally at the time of delivery of Anterior shoulder.
Group B – (50 cases) Tab misoprostol 600µg was kept in vagina (posterior fornix) after Delivery of anterior shoulder.
Group C – (50 cases) Tab Misoprostol 600µg was kept rectally after delivery of anterior Shoulder.
Group D – (50 cases) Inj Methyl ergometrine was given at delivery of anterior shoulder.

In all the patients time and nature of placental delivery, amount of blood loss, change in pulse, BP and temperature, need of other uterotonic agent, change in Hb after 48 hrs of delivery and any side effect of the drugs were noted.

RESULTS AND DISCUSSION

Table no. 1: Distribution of cases According to age.

S.no	Age of the patient (in years)	Misoprostol (oral)	Rectal	Vaginal	Methyl Ergotmetrine IV (control)
1.	< 20	10 (20%)	13 (26%)	10 (20%)	11 (22%)
2.	21 – 25	26 (52%)	23 (46%)	27 (54%)	25 (50%)
3.	26 – 30	13 (26%)	13 (26%)	12 (24%)	13 (26%)
4.	31 – 35	1 (2%)	1 (2%)	1 (2%)	1 (2%)

The above table no.1 shows that maximum number of cases were from the age group 21- 25 years and minimum from the age group 31- 35 years.

Table no.2: Distribution of Cases According to Parity.

S.no	Parity	Oral Misoprostol	Rectal	Vaginal	Methyl ergotmetrine IV
1.	Primi	16 (32%)	20 (40%)	18 (36%)	17 (34%)
2.	Para 2 – 4	31 (62%)	28 (56%)	29 (58%)	30 (60%)
3.	Grand multipara ≥P5	3 (6%)	2 (4%)	3 (6%)	3 (6%)

As shown in table no. 2 maximum no of cases were from Para 2 – 4. Cases from the risk group grandmultipara were almost equal in all groups and mainly belonged to rural population. It shows gradual acceptance of concept of small family norms in the population.

Table no.3 – Distribution of cases according to mode of delivery.

S.no	Mode of Delivery	Misoprstol (oral)	Rectal	Vaginal	Methyl ergotmetrine IV
1.	Spontaneous vaginal delivery	48 (96%)	48 (96%)	47 (94%)	48 (96%)
2.	With aid of episotomy	32 (64%)	31 (62%)	31 (62%)	30 (60%)
3.	Perineal tear (1 & 2 degree)	10 (20%)	11 (22%)	11 (22%)	11 (22%)wsfswqeebc

Table no 3 shows that mode of delivery in majority of cases was spontaneous vaginal delivery with or without episiotomy.

Table no.4 - Distribution of cases according to Associated Risk factor for PPH

S.no	Risk factors for PPH	Oral Misoprostol	Rectal	Vaginal	Methyl ergometrine IV
1.	Grand – multi	6 (17.14%)	5 (15.62%)	6 (20%)	6 (16.66%)
2.	Hydramnios	1 (2.86%)	0	0	1 (2.77%)
3.	Multiple pregnancy	1 (2.86%)	1 (3.12%)	1 (3.33%)	2 (5.55%)
4.	Macrosomia>4 kg	1 (2.86%)	1 (3.12%)	0	1 (2.77%)
5.	Placenta previa	4 (11.43%)	5 (15.62%)	4 (13.33%)	5 (13.88%)
6.	Abruptio Placentae	1 (2.86%)	1 (3.12%)	0	1 (2.77%)
7.	Prolonged II stage of labour	4 (11.43%)	5 (15.62%)	4 (13.33%)	5 (13.88%)
8.	Instrumental delivery	5 (14.28%)	4 (12.5%)	5 (16.66%)	4 (11.11%)
9.	Anaemia	12 (34.28%)	10 (31.25%)	10 (33.33%)	10 (27.77%)

As shown in table no. 4 shows that cases with associated risk factor for PPH were similar in all four groups Oral – 35%, Rectal – 32%, Vaginal – 30% and methyl ergotmetrine 35% (control group).

The table also shows that among the cases with associated risk factors for PPH, majority were from anaemia group In misoprostol oral group 34.28%, rectal – 31.25%, Vaginal – 33.33% and methyl ergotmetrine – 27.77%.

These people are at risk for PPH as small amount of blood loss may cause PPH in these patients (qualitatively).

Second largest group consists of grand multipara group. PPH is more common in this group as associated anaemia, APH and fibrosis of musculature may be responsible for this.

This study reveals that among the risk factors anaemia and grandmultiparity are still very common in are setup, these two factors are often inter – related to each other and explained their lack of awareness, illiteracy and poverty. PPH also occurred in this group mainly, suggesting these people at high risk for PPH.

Similar results were seen by N Vimla et al[2], Garg et al [3] in their study.

Table no. 5 Distribution of cases according to duration of Third stage of labour.

S.no	Duration (minutes)	Misoprostol (Oral)	Rectal	Vaginal	Methyl ergotmetrine IV
1.	Mean	5.2 ± 3.6	6.1 ± 3.4	7.8 ± 3.6	4.0 ± 3.2
2.	Range	2 – 15	3 – 20	4 – 30	2 – 15
	P < 0.001 (HS)				

As shown in table no.5 that mean duration of third stage of labour was minimum in ME (4.0 ± 3.2) group and maximum in vaginal misoprostol group (7.8 ± 3.6). Active management of third stage of labour reduces the duration of third stage and also amount of blood loss.

Similar results were seen by PS Ng et al[4], Surbeck et al[5], Lumbignanon P et al [6] in their studies.

Table no 6: Distribution of Cases According to Method of Placental Delivery.

S.no	Placental delivery	Misoprostol Oral	Rectal	Vaginal	Methyl ergotmetrine IV
1.	Spontaneous	50 (100%)	50 (100%)	49 (98%)	50 (100%)
2.	MRP	0	0	1 (2%)	0

Above table no. 6 shows that in majority of cases placenta delivered spontaneously. MRP was done only in 2% cases of misoprostol by vaginal route.

Similar results shown in study of Surbeck et al [5].

Table no 7: Distribution of cases According to Blood loss during third stage of Labour.

S.no	Blood loss (ml)	Misoprostol Oral	Rectal	vaginal	Methyl ergotmetrine IV
1.	Mean	130 ± 10	120 ± 10	130 ± 10	130 ± 10
2.	Range	100 – 550	120 – 580	120 – 600	120 – 500
	P = ns				

Table no. 7 shows that mean blood loss during third stage of labour was minimum in misoprostol rectal group (120 ± 10). Active management of third stage of labour reduces the duration of third stage and also amount of blood loss. Minimizing blood loss is an important consideration in our country as anaemia is a prevalent condition here.

Various research work done on misoprostol done by Chandhiok N et al[7], Dermon J et al[8], Singh G et al[9], Patted S et al[10] showed similar results. However the differences in amount of blood loss in comparison between various uterotonics was statistically not significant.

However significant reduction in in the rate of acute PPH was associated with use of misoprostol.

Table no. 8: Depiction of Haemoglobin changes before and after delivery.

S.no	Haemoglobin gm/dl	Misoprostol oral	Rectal	vaginal	Methyl ergotmetrine IV
1.	Before delivery	10.00 ± 1.2	10.56 ± 1.4	10 ± 1.2	10.00 ± 1.83
2.	Postpartum	9.3 ± 0.8	9.9 ± 1.2	9.2 ± 0.8	9.2 ± 1.2
	P = ns				

Table no – 8 shows that there was no significant differences among the four groups with regards to a drop in haemoglobin concentrations. Although change in Hb was minimum in miso rectal group.

Similar results seen in studies conducted by Caliskan et al[11], Walraven et al[12], Walley H et al.[13]

Table no. 9 Distribution of cases according to need for additional uterotonic

S.no	Uterotonic given	Misoprostol oral	Rectal	vaginal	Methyl ergotmetrine IV
1.	Oxytocin IV	8 (16%)	6 (12%)	12(24%)	7 (14%)
2.	Methyl ergotmetrine IV	3 (6%)	3 (6%)	5 (10%)	-
3.	Misoprostol	0	-	-	2 (4%)
	P = ns				

Above table no. 9 shows that need for additional uterotonic agent was minimum in misoprostol rectal group (12%). There were more women in misoprostol who required additional uterotonics but the differences were not statistically significant.

Similar results seen in study done by Joy et al[16], Lam et al.[17]

Table no. 10 Distribution of cases according to complication of third stage of labour

S.no	Complication	Misoprostol oral	Rectal	vaginal	Methyl ergotmetrine IV
1.	Retained placenta	-	-	1 (2%)	-
2.	PPH ≥ 500 ml	8 (16%)	4 (8%)	10 (20%)	6 (12%)
3.	Need for BT	-	-	-	-
4.	Maternal death	-	-	-	-
5.	Inversion uterus	-	-	-	-
6.	Shock	-	-	-	-
	P = ns				

However Obora et al[18] showed that there was no significant difference between misoprostol and oxytocin with regard to incidence of PPH(1% vs 0%).

Karkanis et al[15] concluded that rectal misoprostol is of equivalent efficacy to parenteral oxytocin for the prevention of primary PPH.

Table no. 10: Distribution of cases according to side effects of drug within 24 hours of delivery

S no.	Side effects	Misoprostol oral	Rectal	Vaginal	Methy ergotmetrine IV
1.	Nausea	7 (14%)	4 (8%)	3 (6%)	15 (30%)
2.	Vomiting	4 (8%)	2 (4%)	3 (6%)	10 (20%)
3.	Shivering	19 (38%)	13 (26%)	15 (30%)	-
4.	Fever > 38.0^{0}C	7 (14%)	4 (8%)	2 4%)	-
5.	Diarrhoea	2 (4%)	1 (2%)	1 (2%)	-
6.	Headache	-	-	-	5 (10%)
7.	Giddiness	-	-	-	10 (20%)
8.	Rise in Systolic BP > 10mm of Hg	-	-	-	10 (20%)
9.	Abdominal discomfort	1 (2%)	-	-	-

Distribution of cases according to side effects of drug shows that shivering is the main side effect found in misoprostol group and was minimum in rectal group. Other side effects are nausea, vomiting, fever, diarrhoea and abdominal discomfort. All these side effects were dose related and self - limiting.

Methyl ergotmetrine is contraindicated in hypertensive patients during pregnancy while misoprostol can be safely used.

Similar results were shown in almost all studies. Khan et al [19] reported that rectal use of misoprostol was associated with lower level of side effects both shivering and pyrexia were most common side effect of misoprostol as concluded by Lumbiganon et al.[20]

CONCLUSION

Misoprostol is a potent uterotonic agent, can be safely used for effectively for the active management of third stage of labour. Misoprostol can be given by various routes like oral, rectal and vaginal. But among all the three routes Rectal route is best in terms of ease to administer, extremely rapid absorption effectiveness stability and safety profile regarding prevention of PPH. Overall misoprostol is as effective as methyl-ergotmetrine in active management of third stage.

Misoprostol is stable at room temperature that means does not require special storage condition and known to have shelf life of several years unlike methylergotmetrine (not stable at high temperature) and oxytocin (2–8^{0}C).

It has several advantages over others as it is inexpensive, easily available, does not require refriegeration and has few side effects. It's an effective myometrial stimulant of the pregnant uterus, selectively binding to EP-2 /EP-3 prostanoid receptors.

Ther fore a route which provides a faster and a higher plasma level is preferable Simple interventions can be

easily implemented in rural health care settings to reduce blood loss.

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