

# ORIGINAL ARTICLE

## EFFICACY OF 600MCG OF MISOPROSTOL ORALLY VERSUS PER RECTAL IN THE ACTIVE MANAGEMENT OF 3<sup>RD</sup> STAGE OF LABOUR TO PREVENT 3<sup>RD</sup> STAGE PPH & ITS COMPLICATIONS

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**ABSTRACT: AIMS AND OBJECTIVES:** The aim of the study was to define the efficacy of 600mcg of misoprostol orally versus per rectal in the active management of third stage of labour to prevent third stage PPH and other third stage complications; to evaluate the side effects of the drug and to study the incidence of PPH. **MATERIALS AND METHODS:** The present study was conducted at a tertiary referral centre in Government General Hospital, Kakinada during the period October 2011-October 2012. A total number of 200 cases of vaginal deliveries were included in this study. The patients were divided into two groups; in 100 cases misoprostol 600mcg was given orally and in 100 cases misoprostol was kept per rectally and the results compared. **RESULTS:** The mean duration of third stage in oral misoprostol group was  $5.43 \pm 2.15$  minutes and in rectal misoprostol group was  $3.91 \pm 1.63$  minutes. The mean third stage blood loss in oral misoprostol group was 123.5 sec and in rectal misoprostol group was 73.15 sec. P value is  $<0.001$ , which was statistically significant. In the study in both groups pre delivery and post-delivery Hb% levels were in comparable range with mean fall in Hb% being  $0.69 \pm 0.68$  and  $0.59 \pm 0.81$  in oral and rectal misoprostol groups respectively. In both groups pre delivery hematocrit was between 30-30% and after delivery oral misoprostol group had that between 28-30% in 68% cases and in rectal group was 50% of cases between 30-35%. **CONCLUSION:** It was concluded that the rectal misoprostol used in third stage of labour immediately after delivery of the anterior shoulder is simple, safe, effective, non-invasive method requiring no extra effort, cost and assistance. The routine use of misoprostol should be made mandatory for improving women's health in developing countries where most of the women are anemic before conception. **KEYWORDS:** Misoprostol use in post pattern haemorrhage, to prevent 3<sup>rd</sup> stage PPH & other third stage complication.

**INTRODUCTION:** PPH still remains a dreaded complication in modern obstetrics and accounts for about according to WHO maternal mortality was estimated to be 358,300 deaths. PPH is a major cause of morbidity and mortality both in developed and in developing countries.<sup>1</sup> In India maternal mortality ratio 212 per 100,000 live births, global ratio of 260 maternal deaths per 100,000 live births. It is estimated that, worldwide, 140,000 women die due to PPH each year-one every 4 min.<sup>2</sup> Between 11-17% maternal deaths happened during child birth itself and between 50-71% in the post-partum period. About 45% of postpartum maternal deaths occur during the first 24hrs and more than 2/3<sup>rd</sup> during the first week. The incidence is higher in

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operative deliveries especially when conducted under general anaesthesia. The incidence is 4% in vaginal deliveries and 6% in caesarean deliveries

Atonicity is most common cause for PPH. Active management of labor includes 3 aspects as per WHO guidelines 1. Uterine massage 2. Controlled cord traction, 3. Using uterotonic agents. Among these Uterotonic drugs, Oxytocin & Methergin must be handled & stored properly because they are when exposed to light & high ambient temperature. Furthermore, these drugs must be injectibles. So, not only does this require qualified persons to administer these drugs, but it also requires already available supply of sterile syringes & needles that must be handled & disposed of properly. Even today large amount of deliveries occur with/without trained birth attendants in rural settings in India. Refrigeration facilities and cold chain are not available at all the times hence drugs lose their potency. Many of birth attendants are also not trained for giving parental injections. So, there is a need of a drug which is safe, effective in prevention of PPH (postpartum hemorrhage), cheap, easily available, stable at room temperature not requiring storage facility or skilled person to administer. Misoprostol is a prostaglandin E1 analog and it is one of the cheapest prostaglandins, easily used and stored. Misoprostol is available in tablet form that can be administered by oral, sublingual, rectal or vaginal route. It is stable at room temperature and inexpensive. The use of misoprostol is proliferating around the world. It is a lifesaving treatment for severe postpartum hemorrhage and it is also used to reduce blood loss during labor. It is also used in induction of labor and induction of abortion. Also it has other nonobstetric use as it is used in the treatment of peptic ulcer.<sup>3,4</sup> Govt. of India has included Tab Misoprostol 600mcg for Prevention of PPH & in training of active management of 3 stage of labor after delivery of baby for Auxiliary Nurse, Midwives & staff nurses. WHO and Drug Controller General of India have also included Tab misoprostol for prevention & treatment of PPH in the list of essential drugs. Several studies are available worldwide on use of misoprostol as effective drug for prevention & treatment of PPH in different dosage form & routes. The drug Tab Misoprostol 600mcg is permitted & approved by Drug Controller General of India under rules 122-B of Drugs & Cosmetic Rule 1945 with effect from 14 Jan 2009 for the indication of prevention & treatment of PPH (vide permission letter no.MF-7059/06, file no.04-103/2001/DC dated 10/12/2006 and 14/1/2009)

The present study is an attempt to evaluate the efficacy of misoprostol when used 600mcg orally at the birth of anterior shoulder in comparison with 600mcg per rectal in the active management of third stage of labour.

**MATERIALS AND METHODS:** Total of 200 cases of vaginal deliveries done at Government General Hospital, Kakinada was recruited into the study from October 2011 to October 2012.

The patients are divided into two groups, in 100 cases misoprostol 600mcg was given orally and in 100 cases misoprostol 600mcg was kept per rectally immediately after the delivery of the anterior shoulder and the following parameters will be assessed: 1. Duration of third stage 2. Blood loss will be assessed using a PPH bag 3. Hb% & haematocrit was assessed both antepartum & postpartum on 3<sup>rd</sup> postnatal day 4. Percent of patients that needed additional uterotonic agents 5. Percentage of patients developed atonic PPH 6. Side effect of the drug 7. Maternal complications. 8. Third stage complications.

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**CASE SELECTION:** All patients were randomly selected irrespective of their weight at the time of admission. Patients age, parity, gestational age, booking status & investigations such as haemoglobin level, blood grouping & typing HIV & HbsAg status were noted. Their medical history was properly elicited. Careful obstetric examination was done, pelvic evaluation was done to note the dilatation and effacement of cervix, station of the head and pelvic adequacy. Patients were randomly allocated into two treatment groups misoprostol oral and rectal group.

**MATERIALS:** ®Misoprostol 600mcg tablet, Disposable PPH bag., Stopwatch, Weighing machine, Measuring jar.

**Inclusion Criteria:** Patient with vaginal delivery, Primi and second gravid, Gestational age >37wks, Cephalic presentation, With a live foetus, Spontaneous onset of labour & in active phase.

**Exclusion Criteria:** Grand multipara, Polyhydramnios, Hypertensive disorders, PROM/chorioamnionitis, Medical disorders, Instrumental deliveries, IUD, Bronchial asthma, Multiple gestation, Malpresentation, Patients who had traumatic PPH due to cervical tears are excluded from the study.

**DETAILS OF STUDY:** The patients were recruited at random. Women who had vaginal delivery with or without episiotomy were enrolled. After shifting the patient to labour room table she was put in lithotomy position and cleaning the genitalia, bladder was catheterized and drained. After delivery of the anterior shoulder of the baby for a group of 100 cases misoprostol 600mcg was given orally and for another group misoprostol 600mcg kept per rectally. Duration of first and second stage of labour was noted and details of third stage labour were carefully observed and recorded. The placenta is delivered by Brandt-Andrews technique in both groups and the duration of third stage was calculated. Patients are kept in labour room for one hour following delivery. The third stage blood loss was estimated by collecting the blood and clots in to a PPH bag immediately after the delivery of the baby till delivery of placenta. Blood loss is measured by measuring jar, Blood clots are weighed on weighing machine. Amount of blood in ml=blood amount in grams  $\times 1000 \div 1060$ . As the density of blood is 1060.

**OBSERVATION AND RESULTS:** Total number of 200 cases was randomly recruited into study, 100 for each treatment regimen and the results were compared.

Sl. No.	Duration of third stage in minutes	Oral misoprostol group (n=100)		Rectal misoprostol group (n=100)		P value
		No.	%	No.	%	
1	≤3	15	15	12	12	<0.001
2	3-6	29	29	75	75	
3	6-10	54	54	13	13	
4	>10	2	2	0	0	

Table 1: Duration of Third Stage in Minutes

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The duration of the third stage in oral misoprostol group was between 6-10 minutes in 54% cases. The duration of third stage in rectal misoprostol group was between 3-6 minutes in 75% cases. 15% of patients in oral misoprostol and 12% of patients in rectal misoprostol were below 3 minutes. 2% of patients in oral misoprostol group had duration more than 10 minutes.

The mean duration of third stage in oral misoprostol was  $5.43 \pm 2.15$  minutes and in rectal misoprostol was  $3.91 \pm 1.63$  minutes.

Sl.no	Third stage blood loss (ml)	Oral misoprostol group (n=100)		Rectal misoprostol group (n=100)	
		No.	%	No.	%
1	50	27	27	53	53
2	51-100	25	25	30	30
3	101-200	39	39	16	16
4	201-300	4	4	1	1
5	301-400	3	3	-	-
6	>500	2	2	-	-

Table 2: Third Stage Blood Loss

Majority of patients 53% in rectal misoprostol group had blood loss below 50cc, while 39% of oral misoprostol group had blood loss between 101-200cc. 2% of patients in oral misoprostol group had blood loss more than 500cc when compared to nil in rectal misoprostol group.

The mean third stage blood loss in oral misoprostol group was 123.5cc and in rectal misoprostol group was 73.15cc.

	Oral Misoprostol Group (n=100)	Rectal Misoprostol Group (n=100)
Pre Delivery	10.14±0.24	10.23±0.25
Post delivery	9.44±0.9	9.637±1.07
Fall in Hb%	0.69±0.68	0.593±0.81

Table 3: Comparison Of Changes in Hb% Level Between The Two Groups

Sl. No.	Side effects	Oral Misoprostol Group [n=100]	Rectal Misoprostol group [n=100]
1	Retained Placenta	-	-
2	Nausea and Vomiting	1	-
3	Diarrhea	1	-
4	Pyrexia	5	2
5	Shivering	20	4
6	PPH	2	-

Table 4: Maternal Side Effects

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In the present study, in both groups predelivery and post-delivery Hb% levels were in comparable range with mean fall in Hb% being  $0.69 \pm 0.68$  and  $0.59 \pm 0.81$  in oral and rectal misoprostol groups respectively. In both groups pre delivery haematocrit was between 30-33% and after delivery misoprostol group had that between 28-30% in 68% and in rectal group were 50% of cases between 30-33%. Additional 10 units of Oxytocin drip was needed in 9% of cases in oral misoprostol group and 3% in rectal misoprostol group. 0.2mg of methergin was needed in 9% of cases in oral misoprostol group and 3% in rectal misoprostol group. 250mcg of intramuscular carboprost was needed in 5% of cases in oral misoprostol group and 2% of cases in rectal misoprostol group. Oral misoprostol caused shivering in 20% of cases compared to 4% of cases in rectal misoprostol group. 5% of cases in oral misoprostol group developed pyrexia compared to 2% of cases in rectal misoprostol group. 2% of cases in oral misoprostol group developed PPH.

**DISCUSSION:** PPH is the leading cause of maternal deaths in India causing 25.7% of maternal deaths. Postpartum hemorrhage is the most common cause of maternal mortality and accounts for one-quarter of the maternal deaths worldwide. The optimal solution for the vast majority, if not all, of these tragedies is prevention, both before the birth, by assuring that women are sufficiently healthy to withstand postpartum hemorrhage should it occur, and at the time of the birth, by the use of physiological or active management of labor, a management strategy that unfortunately is dependent on circumstances and the availability of uterotonics.<sup>5</sup> Active management of third stage of normal labor includes administration of uterotonic medications after delivery of the baby, early clamping and cutting the umbilical cord and controlled traction of umbilical cord while separation and delivery of the placenta. Uterotonic medications are oxytocin, ergot alkaloids, syntometrine and misoprostol.<sup>6</sup> and the ability of the uterine muscle to contract. It is a critical stage in the management and prevention of post-partum hemorrhage.<sup>7,8</sup> Therefore, minimising the blood loss with active management of third stage of labour by utilizing oxytocin, ergometrine and PGs. Misoprostol can be administered orally, sublingually and rectally. The present study was undertaken to compare the efficacy of misoprostol when given orally and rectally in the active management of third stage of labour. Analysing all the parameters there is significant difference in duration of third stage, average blood loss during third stage of labour, incidence of PPH. There is reduced incidence of additional oxytocic usage. Pre delivery and post-delivery Hb levels were in comparable range in both groups. Side effects like pyrexia and shivering were 5% and 20% in oral misoprostol group compared to 2% and 4% in rectal misoprostol group. From this comparative study of the methods of management of third stage of labour it is clear that rectal misoprostol is superior to oral misoprostol in terms of blood loss, PPH, other serious complications, post-partum anemia and need for blood transfusion. The side effect of the drug is also less with rectal misoprostol group. Singh et al.<sup>9</sup> have suggested that administration of sublingual misoprostol was more effective than intravenous oxytocin, and intravenous methylergometrine for active management of the third stage of labor in a double-blind randomized trial of 300 women with a healthy singleton pregnancy allocated into groups to receive either: 400 mcg or of sublingual misoprostol, 5 IU of intravenous oxytocin, or 200 mcg of intravenous methylergometrine. This is matching with our results. Winikoff et al.<sup>10</sup> have

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suggested that in settings in which use of oxytocin is not feasible, sublingual misoprostol might be a suitable first-line treatment alternative for post-partum hemorrhage. As Chhabra et al.<sup>11</sup> Have suggested that a low dose of sublingual misoprostol appears to be as effective as a low dose of IV methyl ergometrine in the prevention of post-partum hemorrhage in low-risk cases. So given the advantages of its stability at room temperature, low cost and easy route of administration, misoprostol appears to be a better choice. Shivering and hyperpyrexia were the most common side effects of misoprostol. Patted et al.<sup>12</sup> mentioned in their study that misoprostol is associated with a significant increase in postpartum maternal shivering and fever.

**CONCLUSION:** Our premise that the rural birth attendants who do not have skill to administer injectable at delivery and a suitable heat stable drug in absence of cold chain facilities was the start point of the study. Since Misoprostol, prostaglandin E1 analogue, does not lose efficacy in absence of cold chain various administration routes were available to us. Here in this study we have successfully compared sublingual and rectal route for ease of administration considering rural settings. Our randomized placebo controlled double blind study has concluded that Misoprostol 600mcg would play essential role and can be used as a safe agent in prevention of PPH with AMTSL. Amount of blood loss is lower in sublingual group as compared to rectal group, but since side effects are more with sublingual route, rectal route should be preferred for routine use in AMTSL for prevention of PPH though both routes are effective for prevention of PPH. We recommend that following method may be employed for prevention of Post-Partum Hemorrhage as tested in our study and also prescribed by WHO for active management of 3 and 4 stage of labor, 1. Controlled cord traction 2. Optimum uterine massages 3. Tab Misoprostol (600mcg) to be placed rectal at the delivery of anterior shoulder after ruling out contraindication of prostaglandin like asthma, liver disease.

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