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Research Article

A comparative longitudinal study between sublingual Misoprostol 600 µg and conventionally used Oxytocin 20 IU infusion in active management of third stage of labour from North India.

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Abstract

Background: PPH is the most important cause of maternal mortality and morbidity worldwide with an estimated maternal death of 1,40,000 per year or 1 maternal death every 4 mins. At least one quarter (25%) of these deaths is due to PPH. The majority of deaths occur within 4 hours of delivery which indicates that they are a consequence of the third stage of labour.In various studies, misoprostol was used in different routes and doses (400-800 µg per oral, sublingual or rectal) to control PPH and different results have been reported. We aimed to show the comparative benefit and safety of Sublingual Misoprostol at the WHO recommended dose of 600 mcg versus conventionally used Oxytocin 20 IU infusion for prevention of PPH during active management of third stage of labour. **Objective:**We aimed to show the comparative benefit and safety of Sublingual Misoprostol at the WHO recommended dose of 600 mcg versus conventionally used Oxytocin 20 IU infusion for prevention of PPH during active management of third stage of labour**Methodology:** The present Longitudinal Observational Study was undertaken in the Department of Obstetrics & Gynaecology at Sri Balaji Action Medical Institute, Paschim Vihar, New Delhi from June 2018 to May 2019 involving 84 pregnant women in our study; 42 in each group depending upon the uterotonic drug they will receive.**Results:** In our study majority of women i.e. 50% were 2nd Gravida in Misoprostol group as compared to 57.14% who were Primigravida in Oxytocin group.In our study, 30.95% women from Misoprostol group had blood loss between 500 to 1000 ml as compared to 42.85% from Oxytocin group. The difference in the proportion was found to be statistically not significant ($p>0.05$) though we found that there were more number of cases from Oxytocin group having the blood loss of 501-1000 ml. When we compared the mean blood loss, the difference in the mean values of blood loss was found to be statistically not significant ($p>0.05$) though in Misoprostol group the mean blood loss was found to be clinically significant. When we compared the mean pre-delivery mean Haemoglobin between two groups, the difference in the mean values was found to be statistically not significant ($p>0.05$). When we compared the Post-delivery mean Haemoglobin between two groups, the difference in the mean values was found to be statistically not significant ($p>0.05$) but clinically the Post-delivery mean Haemoglobin was found to be higher Oxytocin group. **Conclusion:**The difference in the mean values of blood loss was found to be statistically not significant ($p>0.05$) though in Misoprostol group the mean blood loss was found to be clinically significant. When we compared the Post-

delivery mean Haemoglobin between two groups, the difference in the mean values was found to be statistically not significant (p>0.05) but clinically the Post-delivery mean Haemoglobin was found to be higher in Oxytocin group.

Key words: blood loss, haemoglobin, sublingual Misoprostol, Oxytocin, active management of third stage of labour.

Introduction

Primary Post Partum Haemorrhage (PPH) is defined as blood loss of 500 ml or more from the genital tract within 24 hours following a normal vaginal delivery, 1000 ml or more following a Caesarean Section and 1500 ml or more following a Caesarean Hysterectomy. Approximately 70% of primary PPH cases are due to uterine atony.[1] Atony of the uterus is defined as the failure of the uterus to contract adequately after the delivery of baby. If such blood loss occurs after 24 hours and within first 6 weeks of delivery, then it is called as Secondary (late) PPH. Most of the times late PPH is due to retained products of conception, infection or both.[2]

The American College of Obstetricians and Gynaecologists (ACOG) defined PPH as decrease in haematocrit value more than 10% following birth.[3] For clinical purposes, any amount of blood loss which has potential to produce haemodynamic instability should be considered as PPH. Clinical estimates of blood loss are often inaccurate.[2] Blood loss greater than 1500 ml is called as massive PPH.[4] Laboratory parameters include a drop in haemoglobin of 4 gm% and acute transfusion of more than 4 units of blood. Early and accurate assessment of blood loss is important to prevent delay in management and prevention of morbidity.[5]

PPH is the most important cause of maternal mortality and morbidity worldwide with an estimated maternal deaths of 1,40,000 per year or 1 maternal death every 4 mins. At least one quarter (25%) of these deaths is due to PPH. The majority of deaths occur within 4 hours of delivery which indicates that they are a consequence of the third stage of labour.[6,7]

Active Management of Third Stage of Labour (AMTSL) is evidence based feasible and low-cost intervention to prevent PPH and when practiced routinely can reduce atonic PPH upto 60-70% and it should be offered to all pregnant women in labour as the presence of risk factors cannot predict all cases of PPH. It is considered to be 'gold standard' to reduce the incidence of PPH.[8]

India accounts for 17% of global burden of maternal deaths. Maternal Mortality refers to the "death of a woman while pregnant or within 42 days of termination of pregnancy, irrespective of the site and duration of pregnancy, from any cause related to or aggravated by the pregnancy or its management but not by accidental or incidental cause" (WHO 1994). It is used as proxy indicator to assess the country's maternal and reproductive health status.[9]

The major causes of maternal mortality according to the 2001-2003 Sample Registration System (SRS) survey are haemorrhage (38%), sepsis (11%), hypertension (5%), obstructed labour (5%), abortion (8%), anaemia (19%) and other causes(34%).[10]

Research studies are therefore needed to establish a standard, safe and effective dose of misoprostol for preventing and treating PPH. In various studies, misoprostol was used in different routes and doses (400-800 µg per oral, sublingual or rectal) to control PPH and different results have been reported. We aimed to show the comparative benefit and safety of Sublingual Misoprostol at the WHO recommended dose of 600 mcg versus conventionally used Oxytocin 20 IU infusion for prevention of PPH during active management of third stage of labour.[11]

So increasing acceptance of misoprostol use in rural settings for preventing PPH will definitely reduce the incidence of PPH and resultant mortality and morbidity in near future.

Hence the present study was carried out with the objective to show the comparative benefit and safety of Sublingual Misoprostol at the WHO recommended dose of 600 mcg versus

conventionally used Oxytocin 20 IU infusion for prevention of PPH during active management of third stage of labour.

Objective: We aimed to show the comparative benefit and safety of Sublingual Misoprostol at the WHO recommended dose of 600 mcg versus conventionally used Oxytocin 20 IU infusion for prevention of PPH during active management of third stage of labour.

Materials and methods

Study Area: The present study was undertaken in the Department of Obstetrics & Gynaecology at Sri Balaji Action Medical Institute, Paschim Vihar, New Delhi.

Study Design: Longitudinal Observational Study

Study Period: one year from June 2018 to May 2019

Study Population: The cases under study were selected from pregnant women with labour pains in third stage of labour who received the uterotonic drug treatment after delivery of the baby at Sri Balaji Action Medical Institute, Paschim Vihar, New Delhi.

Sample Size: 84 pregnant women in our study; 42 in each group depending upon the uterotonic drug they received.

Inclusion Criteria:

- Singleton pregnancy of gestational age 37 weeks or more in third stage of labour who received any of the uterotonic drugs

Exclusion Criteria:

- Previous scarred uterus- LSCS, Hysterotomy, Myomectomy
- Placenta Praevia
- Preterm Labour
- Contraindications to use prostaglandins- Hypersensitivity
- Traumatic PPH

Methods of data collection:

A pregnant woman in third stage of labour fulfilling the inclusion and exclusion criteria was enrolled in our study with her consent. Such women were classified as follows depending upon which uterotonic drug they received during the active management of third stage of labour as decided by treating obstetrician.

- Group A – in this we enrolled such women who received Misoprostol 600 µg sublingually immediately after the delivery of baby.
- Group B – in this we enrolled such women who received 20 IU Oxytocin infusion immediately after the delivery of baby.

We collected the data with respect to the detailed history and examination findings from the in-patient case record of these women in third stage of labour. Pre-delivery haemoglobin was also noted.

After cord clamping, amniotic fluid was allowed to drain away and a new sterile pre-weighed absorbent sheet was placed under the woman.Placenta was delivered by controlled cord traction and duration of third stage was recorded. Additional uterotonic drugs were administered if uterus failed to contract after 5 minutes of delivery of placenta or if there was excessive vaginal bleeding in spite of administration of initial uterotonic agent.

A sterile pre-weighed pad was given to the woman for next two hours. All soaked absorbent sheet, sponges and pads were weighed.The amount of blood loss was measured by subtracting their weight from initial dry weight.The specific gravity of blood being 1.08 gm/ml, the amount of blood loss in millilitres was approximately equal to the increase in weight in grams.

The primary outcome measure was estimated blood loss after vaginal delivery of the baby in the first 2 hours observation period. Any amount of bleeding ≥ 500 ml in vaginal delivery was considered as PPH.

The secondary outcome measure was the level of haemoglobin measured after 24 hours of vaginal delivery. Since≥500 ml blood loss signifies a drop of 1 gm % of haemoglobin, so in our study difference in pre and post-delivery haemoglobin was estimated to calculate blood loss in millilitres.

Statistical analysis: All primary data was collected by using a standard proforma.Data was entered in MS Excel sheet and analysed by using SPSS 23.0 version IBM USA. Qualitative data was expressed in terms of proportions.Quantitative data was expressed in terms of Mean and Standard deviation.Comparison of Mean and SD between two groups was done by using Unpaired t test to assess whether the mean difference between groups is significant or not.Descriptive statistics of each variable was presented in terms of Mean, standard deviation, standard error of the mean. A 'P' value of <0.05 was considered as statistically significant whereas a 'P' value < 0.001 was considered as highly significant.

Results:

In our study, we compared the characteristics of the pregnant women between Misoprostol and Oxytocin group.

Table No.1: Age wise Distribution

		Misoprostol		Oxytocin	
		Frequency	Percent	Frequency	Percent
Age in years	20 to 25	15	35.71	9	21.42
	26 to 30	21	50.00	22	52.39
	31 to 35	5	11.90	9	21.42
	≥36	1	2.39	2	4.77
	Total	42	100.0	42	100.0

In our study, half of the women belonged from 26 to 30 years age group in both groups i.e. 50% and 52.39% from Misoprostol and Oxytocin group respectively. This is followed by the common age group of 20 to 25 years (35.75% from Misoprostol and 21.42% each from oxytocin group).

Table No.2 : Gravida wise Distribution

		Misoprostol		Oxytocin	
		Frequency	Percent	Frequency	Percent
Gravida	1	17	40.47	24	57.14
	2	21	50	11	26.19
	3	4	9.53	4	9.52
	≥ 4	0	.0	3	7.15
	Total	42	100.0	42	100.0

In our study majority of women i.e. 50% were 2nd Gravida in Misoprostol group as compared to 57.14% who were Primigravida in Oxytocin group.

Table No 3: Parity wise Distribution

		Misoprostol		Oxytocin	
		Frequency	Percent	Frequency	Percent
Para	Nullipara	17	40.47	25	59.53
	1	22	52.38	13	30.95
	2	3	7.15	4	9.52
	Total	42	100.0	42	100.0

In our study, majority of women i.e. 52.38% were Para 1 in Misoprostol group as compared to 59.53% who were Nullipara in Oxytocin group.

Table No 4: Estimated Blood Loss wise Distribution

Blood Loss	Misoprostol	Oxytocin

(ml)	Frequency	Percent	Frequency	Percent
< 500	29	69.05	24	57.15
501-1000	13	30.95	18	42.85
Total	42	100	42	100

The chi-square statistic is 1.27. The p-value is .25. This result is not significant at p< .05.
In our study, 30.95% women from Misoprostol group had blood loss between 500 to 1000 ml as compared to 42.85% from Oxytocin group. The difference in the proportion was found to be statistically not significant (p>0.05) though we found that there were more number of cases from Oxytocin group having the blood loss of 501-1000 ml.

Table No. 5: Comparison of Estimated Mean Blood Loss in Labour

	Group	N	Mean	SD	T	p	Inference
Estimated Blood loss in labour	Misoprostol	42	485.43	210.35	1.03	0.21 (>0.05)	Not significant
	Oxytocin	42	445.24	139.18			

Mean blood loss in Misoprostol group was 485.43 ± 210.35 ml compared to 445.24 ± 139.18 ml in Oxytocin group during labour. When we compared the mean blood loss, the difference in the mean values of blood loss was found to be statistically not significant (p>0.05)though in Misoprostol group the mean blood loss was found to be clinically significant.

Table No. 6: Comparison of Pre-delivery Mean Haemoglobin

	Group	N	Mean	SD	t	p	Inference
Pre-delivery Mean Haemoglobin (gm%)	Misoprostol	42	10.27	1.01	-1.75	0.42 (>0.05)	Not significant
	Oxytocin	42	10.70	1.27			

In our study, Pre-delivery mean Haemoglobin in Misoprostol group was 10.27± 1.01 gm % as compared to 10.7 ± 1.27 gm % in Oxytocin group. When we compared the mean pre-delivery mean Haemoglobin between two groups, the difference in the mean values was found to be statistically not significant (p>0.05)

Table No. 7: Comparison of Post-delivery Mean Haemoglobin

	Group	N	Mean	SD	T	P	Inference
Post-delivery Mean Haemoglobin (gm%)	Misoprostol	42	10.16	1.86	-1.64	0.051 (> 0.05)	Not significant
	Oxytocin	42	10.26	0.69			

In our study, Post-delivery mean Haemoglobin in Misoprostol group was 10.16± 1.86 gm % as compared to 10.26 ± 0.69 gm % in Oxytocin group. When we compared the Post-delivery mean Haemoglobin between two groups, the difference in the mean values was found to be statistically not significant (p>0.05)but clinically the Post-delivery mean Haemoglobin was found to be higher Oxytocin group.

Discussion

In our study, half of the women belonged from 26 to 30 years age group in both groups i.e. 50% and 52.39% from Misoprostol and Oxytocin group respectively. This is followed by the common age group of 20 to 25 years (35.75% from Misoprostol and 21.42% each from oxytocin group). Mean age group were 28.6 $\pm$ 4.14 years and 27.33 $\pm$ 4.02 years in Misoprostol and Oxytocin group respectively. **(Table 1)**

Bellad MB et al[12]in his study observed mean age as 23.0 ± 3.1 years and 22.8 ±3.0 years in Misoprostol and Oxytocin group respectively. **Chaudhuri P et al**[13]alsoobserved mean age as 22.07±3.6 years and 22.35±2.97 years in Misoprostol and Oxytocin group respectively.**Gohil JT et al**[14]also observed mean age as 25.7 years and 24.1 years in Misoprostol and Oxytocin group respectively. **Gupta Pratiksha et al**[15]also observed mean age as 22.8 years and 22.02 years in Misoprostol and Oxytocin group respectively.

Majority of women i.e. 50% were 2nd Gravida in Misoprostol group as compared to 57.14% who were Primigravida in Oxytocin group.Majority of women i.e. 52.38% were Para 1 in Misoprostol group as compared to 59.53% who were Nullipara in Oxytocin group.**(Table 2 and 3)**

Bellad MB et al[12]in his study observed similar results and very few were having G4 status in Misoprostol and Oxytocin group respectively. **Chaudhuri P et al**[13]also observed 32.1 % and 37.2% women having parity between 1 to 4 in Misoprostol and Oxytocin group respectively.**Mani Mukta et al**[1]**observed** 42 women each in Primigravida status.Our findings are almost similar with the findings of other authors.

In our study, 30.95% women from Misoprostol group had blood loss between 500 to 1000 ml as compared to 42.85% from Oxytocin group.The difference in the proportion was found to be statistically not significant (p>0.05)**(Table 4)**though in Oxytocin group clinically we observed comparatively more blood loss**.** Mean blood loss in Misoprostol group was 485.43 ± 210.35 ml compared to 445.24 ± 139.18 ml in Oxytocin group during labour. When we compared the mean blood loss, the difference in the mean values of blood loss was found to be statistically not significant (p>0.05) **(Table 5)**) though in Oxytocin group clinically we observed comparatively more blood loss.

Diallo Moussa et al[16] observed average volume of blood loss 196.55 ml in the Misoprostol group and 208.39 ml in the Oxytocin group (p=0.63).**Singhal Savita Rani et al**[17]found the

mean blood loss was 260.35 ± 97.45 ml in the Misoprostol group and 264.20 ± 103.68 ml in Oxytocin group and the difference was not statistically significant. **Mani Mukta et al[1]**in the Misoprostol group, mean blood loss is 145 ml and in the Oxytocin group, mean blood loss in 125.6 ml. **Tewatia Renu et al[18]**found that mean blood loss was significantly lower in Oxytocin group (114.28 ± 26.75 versus 149.50 ± 30.78 ml; p = 0.00) than in Misoprostol group.

In our study, Pre-delivery mean Haemoglobin in Misoprostol group was 10.27± 1.01 gm % as compared to 10.7 ± 1.27 gm % in Oxytocin group.When we compared the pre-delivery mean Haemoglobin between two groups, the difference in the mean values was found to be statistically not significant (p>0.05)**(Table 6).** As well as Post-delivery mean Haemoglobin in Misoprostol group was 10.16± 1.86 gm % as compared to 10.26 ± 0.69 gm % in Oxytocin group.When we compared the post-delivery mean Haemoglobin between two groups, the difference in the mean values was found to be statistically not significant (p>0.05)but clinically the Post-delivery mean Haemoglobin was found to be higher oxytocin group**(Table 7).**

Our findings are consistent with the findings of other authors as follows:**Rajaei M. et al[19]**concluded in his study that there was no significant difference in the decrease in haematocrit and haemoglobin between the two groups.**Diallo M. et al[16]**stated that the average rate of haemoglobin decline was 0.38 g/dl in the misoprostol group and 0.29 g/dl in the oxytocin group (p=0.99). Post-delivery mean haemoglobin in Misoprostol group was 10.1± 1.3 gm % as compared to 9.6 ± 1.1 gm % in Oxytocin group.**Bellad MB et al[12]** observed that 9.7% and 45.6% of women experienced a haemoglobin decline of >10% after receiving misoprostol and oxytocin, respectively (P ≤ 0.001).

Conclusion:

The difference in the mean values of blood loss was found to be statistically not significant (p>0.05) though in Misoprostol group the mean blood loss was found to be clinically significant. When we compared the Post-delivery mean Haemoglobin between two groups, the difference in the mean values was found to be statistically not significant (p>0.05) but clinically the Post-delivery mean Haemoglobin was found to be higher in Oxytocin group.

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