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A COMPARATIVE STUDY OF THE EFFICACY OF TAB. MISOPROSTOL 600 MCG (PR) WITH INJ. METHYLERGOMETRINE0.2MG (IM) FOR THE PREVENTION OF POST-PARTUM HAEMORRHAGE.

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ABSTRACT

Background- Maternal Mortality is a major challenge to health care system worldwide. Most common cause of which is post partum haemorrhage. Post-partum haemorrhage is the loss of more than 500 ml of blood within the first 24 hours of delivery or loss of any amount that is enough to cause hemodynamic instability in the mother or the loss of more than 10% of the total blood volume. The common cause of PPH is uterine atony.

Purpose- The aim of this study is to compare the efficacy of the two most frequently used uterotonics, Misoprostol and Methylergometrine. And to assess the incidence of side effects associated with the use of each drug regimen.

Methods- This is s Prospective, Observational study of a total of 100 consecutive registered cases undergoing vaginal deliveries, from which half of the randomly selected patients was given one Misoprostol while other group was given Methylergometrine.

Conclusion- Both drugs i.e. misoprostol and methylergometrine are equally effective in prevention of postpartum haemorrhage and have same efficacy. Misoprostol is an inexpensive drug and easily available. The study intends to provide information for the review and possible revision of the current status on the management of the third stage of labor. It can also help inform policy makers on the feasibility of using Misoprostol in AMTSL (active management of third stage of labour), especially in resource poor settings where other uterotonics are unavailable or wherever AMTSL is not practiced.

- Ethical approval: This article does not contain any studies with animals performed by any of the authors.

KEYWORDS : Misoprostol, Methylergometrine, PPH, uterotonics

INTRODUCTION

Around 830 women die from pregnancy or childbirthrelated complications all over the world every day[1]. According to World Health Organisation, 25% of all maternal deaths are caused by postpartum haemorrhage (PPH) which is a preventable cause of maternal mortality and morbidity[2]. India takes up 17% of the global burden of maternal mortality with the national average of 167[3].

Post-partum haemorrhage is the loss of more than 500 ml of blood within the first 24 hours of delivery or loss of any amount that is enough to cause hemodynamic instability in the mother or the loss of more than 10% of the total blood volume. The common cause of PPH isuterine atony. Active management of third stage of labour (AMTSL) can prevent PPH and thereby prevent maternal death[4-8]. Different uterotonics are available for AMTSL among which oxytocin has been advocated by the WHO[4]. Oxytocin however needs storage at low temperatures and a skilled person to administer the drug by intramuscular (IM) or intravenous (IV) route, which are not feasible in rural areas of resource poor countries like India.

Ergot alkaloids are in use since many decades and are effective in reducing third stage blood loss and preventing PPH, but they cause adverse effects including vomiting, elevation of blood pressure,and pain after birth requiring analgesics[9]. Transient hypertension is induced following intravenous administration.

In recent years, misoprostol (oral or sublingual), a synthetic analogue of prostaglandin E1 (PGE1), is also found to be an effective uterotonic. Pyrexia is more common when the dose exceeds 600μg[10]. Tab Misoprostol has the advantage, that it can be stored at room temperature in peripheral hospitals and can be self-administered.

The aim of this study is to compare the efficacy of the two most frequently used uterotonics, i.e. Inj. Methylergometrine 0.2mg intramuscular (IM) and Tab. Misoprostol 600μg per-rectal (PR) in reducing third and fourth stage blood loss.

AIMS AND OBJECTIVES

1. To compare the efficacy of Tab. Misoprostol 600 mcg (PR) with Inj. Methylergometrine0.2mg (IM) for the prevention of post-partum haemorrhage.
2. To assess the incidence of side effects associated with the use of each drug regimen.

MATERIALS AND METHODS

Study Area:

This Prospective,Observational study was conducted in the Department of Obstetrics & Gynaecology at a tertiary and teaching Hospital, NaviMumbai.

Sampling Technique:

A total of 100 consecutive registered cases undergoing vaginal deliveries with episiotomy, fitting the inclusion criteria

and giving informed consent were included in the study. Selected patients was randomly divided into 2 groups of 50 each using software research randomizer (Geoffrey C. Urbaniak and Scott Plous):

Group A: Patients administered Tab Misoprost (Misoprostol) 600 mcg PR, after the delivery of placenta.
Group B: Patients administered Inj. Methergin (Methylergometrine) 0.2 mg IM, after the delivery of placenta.

Inclusion Criteria:
1. Parity of 1 or more.
2. Longitudinal lie & cephalic presentation.
3. Length of active labor greater than 2 hours but not exceeding 14 hours.
4. Patients giving informed consent.

Exclusion Criteria:
1. Patients undergoing or have a past history of LSCS.
2. H/o manual removal of placenta.
3. H/o asthma or allergy to misoprostol.
4. Past or current H/o hypertension, either chronic or PIH.
5. Presence of polyhydramnios.
6. Presence of multiple gestation.
7. Malpresentation.
8. Traumatic PPH.
9. Abnormal bleeding time.
10. Prolonged rupture of membrane greater than 12 hours prior to the onset of labour.
11. Women who are unable to, or do not want to give consent.

METHODOLOGY:

After the approval by ethical committee and written informed consent100 eligible women who were anticipated to have vaginal delivery,were admitted in labour and their Hemoglobin & Haematocrit was measured on admission. These 100 selected patients were randomly divided into 2 groups of 50 eachas per randomization chart.

Group A: Patients administered Tab Misoprost 600 mcg PR, after the delivery of placenta and;
Group B: Patients administered Inj. Methergin 0.2 mg IM, after the delivery of placenta.

After administering the selected drug (as mentioned above), patient were monitored for vitals, P/V bleeding. The two groups were also compared on the basis of side effects like shivering, headache, nausea, vomiting, need of secondary uterotonics (these cases were labeled as failure of procedure). On post natal day 3rd Hemoglobin & Haematocrit levels were repeated. The difference in the Hemoglobin & Haematocrit levels of the two groups was compared to each other.

Statistical Analysis:

The quantitative data will be represented as their mean ± SD. Categorical and nominal data will be expressed in percentage. The t-test will be used for analysing quantitative data, or else non parametric data will be analysed by Mann Whitney test and categorical data will be analysed by using chi-square test. The significance threshold of p value will be set at <0.05. All analysis will be carried out by using SPSS software version 21.

RESULTS

Table 1. Comparison of Age distribution among study groups

Age Group	Group		Total
	Group A	Group B	
< 20	7	9	16
	14.0%	18.0%	16.0%
21-25	19	21	40
	38.0%	42.0%	40.0%
26-30	19	16	35
	38.0%	32.0%	35.0%
> 30	5	4	9
	10.0%	8.0%	9.0%
Total	50	50	100
	100.0%	100.0%	100.0%
p- value - 0.86			

75% of the females in both groups were between 21-30 years of age with no difference between study groups (p-0.86).

Table 2. Comparison of Obstetric history among study groups

Parity	Group		Total
	Group A	Group B	
Primi	23	24	47
	46.0%	48.0%	47.0%
Multi	27	26	53
	54.0%	52.0%	53.0%
Total	50	50	100
	100.0%	100.0%	100.0%
p- value - 1.0			

Out of the total 100 subjects, 53% were multi-para and 47% were primi-para with no difference between the study groups (p-1.0).

Table 3. Comparison of study groups based on patients who required Induction of Labour

Induction of Labour	Group		Total
	Group A	Group B	
Yes	3	4	7
	6.0%	8.0%	7.0%
No	47	46	93
	94.0%	92.0%	93.0%
Total	50	50	100
	100.0%	100.0%	100.0%
p- value - 1.0			

Induction of labour was required in 6%and 8% cases of Group A and Group B respectively (p-1.0).

Table 4. Comparison of study groups based on mean duration of first & second stage of labour

Variables	Group	N	Mean	SD	p- value
Duration of First stage of labor (hrs)	Group A	50	6.80	1.56	0.221
	Group B	50	7.10	1.62	
Duration of Second stage of labor (mins)	Group A	50	27.01	11.53	0.979
	Group B	50	27.31	11.58	

Mean duration of first and second stage of labor was 6.8 hours and 27.01 minutes in Group A while it was 7.1 hours and 27.31 minutes in Group B (p>0.05).

Table 5. Comparison of study groups based on Mean Birth weight

Variables	Group	N	Mean	SD	p- value
Birth Weight (gm)	Group A	50	2895.70	409.40	0.91
	Group B	50	2892.20	448.10	

Mean birth weight was 2.895 Kg and 2.892 Kg in babies of Group A and Group B respectively (p-0.91).

Table 6. Comparison of study groups based on Mean duration of third stage of labour

Variables	Group	N	Mean	SD	p- value
Third Stage of Labour (min)	Group A	50	6.19	0.85	0.89
	Group B	50	6.04	0.73	

Mean duration of third stage of labour was also comparable in both group (6.04 vs 6.19 min; p-0.89).

Table 7. Comparison of study groups based on Incidence of PPH

PPH	Group		Total
	Group A	Group B	
Yes	3	1	4
	6.0%	2.0%	4.0%
No	47	49	96
	94.0%	98.0%	96.0%
Total	50	50	100
	100.0%	100.0%	100.0%
p- value - 0.617			

Incidence of PPH was 6% and 2% among GroupA and GroupB respectively (p-0.617).

Table 8. Comparison of study groups based on requirement of additional Oxytocics

Additional Oxytocics	Group		Total
	Group A	Group B	
Yes	3	1	4
	6.0%	2.0%	4.0%
No	47	49	96
	94.0%	98.0%	96.0%
Total	50	50	100
	100.0%	100.0%	100.0%
p- value - 0.617			

Incidence of additional oxytocics i.e. failure of the procedure was seen in 6% and 2% cases of Group A and Group B respectively (p-0.617).

Table 9. Comparison of study groups based on complications

Complications	Group		Total	p- value
	Group A	Group B		
Shivering	14	1	15	<0.05
	28.0%	2.0%	15.0%	
Pyrexia	8	1	9	<0.05
	16.0%	2.0%	9.0%	
Nausea/ Vomiting	2	8	10	0.09
	4.0%	16.0%	10.0%	
Headache	1	6	7	0.11
	2.0%	12.0%	7.0%	

Significant higher incidence of shivering (28% vs 2%) and pyrexia (16% vs 2%) was observed among cases of GroupA(p<0.05). While Complain of nausea/ vomiting and headache was more in Group B (p>0.05).

Table 10. Comparison of study groups based on mean change in haemoglobin levels

Haemoglobin	Group	N	Mean	SD	p- value
Admission	Group A	50	11.91	0.61	**0.87**
	Group B	50	11.98	0.57	
Post Natal day 3	Group A	50	11.25	0.60	**0.81**
	Group B	50	11.30	0.71	

Mean haemoglobin level on admission and 3rd postnatal day was 11.91 and 11.25 gm% in Group A while it is 11.98 and 11.30 mg% in Group B. No difference was observed between mean haemoglobin levels at admission and post-natal day 3 between both the groups (p>0.05).

Table 11. Comparison of study groups based on mean change in haematocrit levels

Haematocrit	Group	N	Mean	SD	p- value
Admission	Group A	50	33.28	1.37	**0.69**
	Group B	50	33.36	1.04	
Post Natal day 3	Group A	50	32.58	1.36	**0.79**
	Group B	50	32.64	1.06	

Mean haematocrit level on admission and 3rd post natal day was 33.28 and 32.58 in Group A while it was 33.36 and 32.64 in Group B. No difference was observed between mean haematocrit at admission and post-natal day 3 between both the groups (p>0.05).

DISCUSSION

This study was intended to provide information for the review and possible revision of the current status on the management of the third stage of labor. It can also help inform policy makers on the feasibility of using misoprostol in AMTSL, especially in resource poor settings where other uterotonics are unavailable or wherever AMTSL is not practiced.

In present study, we aimed to compare the efficacy of tab. misoprostol 600 mcg (PR) with inj. methylergometrine 0.2 mg (IM) for the prevention of post-partum haemorrhage.

All the baseline parameters i.e. age, parity, ANC registration, gestational age, pre-delivery Hb/ PCV, induction and augmentation of labor, duration of first, second and third stage of labor, were comparable among both study groups (p>0.05).

NEED OF ADDITIONAL OXYTOCICS:

In present study, oxytosics were required in 6% and 2% cases of GROUP A and Group B respectively (p-0.617).

Nasr et al. [13] in their study, observed need for additional uterotonics in 2.3% cases of misoprostol group. Parsons et al.[11] in their study too observed a lower need for additional uterotonic in the misoprostol group (4%). Vimala et al. [14], in their study observed need for additional uterotonics as in 8.3% cases of misoprostol group and 5.0% cases of methergin group (p>0.05). Gohil JT et al. [19] also observed a slight higher requirement of oxytocics in their study in misoprost group. The difference was however statistically insignificant. Singh G et al. [17] and Fawzy et al. [18] in their studies observed low additional uterotonics with both groups (p>0.05).

INCIDENCE OF POST-PARTUM HAEMORRHAGE:

In present study, incidence of PPH was 6% (3 cases) and 2% (1 case) among misoprostol and methylergometrine group respectively (p-0.617).

Similar findings by Nasr et al. [13] in their study, who observed the incidence ofPPH as 6.6%. Vimala et al. [14], in their study, observed that misoprostol group (400mcg) demonstrated a slightly increased incidence of PPH than methylergometrine [2/60(3.3%) vs. 0/60(0%), P>0.05], but these results were not statistically significant.Amant et al. [15] evaluated higher dose of misoprostol, 600 mcg, administered orally in comparison to 200 mcg methylergometrine. The frequency of PPH was 7.3% vs. 4.3% among misoprost and methergin group respectively (p>0.05). Patil NB et al.[16] observed the incidence of PPH as 9% in misoprostol group & 6% in methylergometrine group (p >0.05). Similarly Singh G et al. [17] and Fawzy et al. [18] in their studies also observed no difference in duration of PPH with both groups (p>0.05).

MEAN HEMOGLOBIN AND HEMATOCRIT:

In present study, mean hemoglobin level on admission and 3rd post op day was 11.91 and 11.25 gm% in misoprost group while it is 11.98 and 11.30 mg% in methergin group. No difference was observed between mean haemoglobin levels at admission and post-natal day 3 between both the groups (p>0.05). Mean hematocrit level on admission and 3rd post op day was 33.28 and 32.58 in misoprost group while it was 33.36 and 32.64 in methergin group. No difference was observed between mean hematocrit at admission and post-natal day 3 between both the groups (p>0.05).

Amant et.al. [15] in their study observed no difference in their primary outcome, defined as the percentage of subjects with a haematocrit drop of >10% at 24hours [10/291 (3.7%) vs.11/294(3.7%), p-0.98]. Singh G et al. [17] in their study also observed that baseline and 24-hour postpartum haemoglobin and haematocrit level was similar among the groups (P>0.05). Similar results, with no difference, was also observed by Gohil JT et al. [19]

COMPLICATIONS:

Studies comparing misoprostol to ergot alkaloids have demonstrated that misoprostol typically experienced a greater frequency of pyrexia and shivering. In present study too, we observed significant higher incidence of shivering (28% vs 2%) and pyrexia (16% vs 2%) was observed among cases of misoprostol group (p<0.05). While complain of nausea/ vomiting and headache was more in methergin group (p>0.05).

In the Canadian group Study [12] subjects receiving misoprostol had a higher rate of shivering (6.8%) and fever (12.5%). Fawzy et al. [18] in their study observed that most common side effects occurred in misoprostol group as fever (8%) and shivering (30%). Amant et al. [15] in their study observed that shivering was nearly four times more common in the subjects in the misoprostol Group as compared to methylergometrine group (36/86(41.9%) vs. 8/94(8.5%). Patil NB et al. [16] in a similar study observed that shivering was significantly more common in misoprostol group (36% Vs 2% p< 0.05). Gohil JT et al. [19] observed that as regards to side effects, misoprostol was associated with shivering and pyrexia in significantly high number of patients while nausea, vomiting and headache were more associated with methylergometrine and methylergometrine–oxytocin.

CONCLUSION

Both drugs i.e. misoprostol and methylergometrineare equally effective in prevention of postpartum haemorrhage and have same efficacy. Both drugs are equally safe, though shivering and pyrexia is more with misoprostol.

Misoprostol is an inexpensive drug and easily available. It is easy to use and does not require special storage conditions (i.e., can be stored easily at room temperature; is thermostable and light stable; does not require specific conditions for transfer) and has a shelf life of several years. It can be administered orally, sublingually, or rectally, not requiring infusion pump or syringe or drip set. These advantages make it a good alternative to methylergometrine for prevention of postpartum haemorrhage.The study intends to provide information for the review and possible revision of the current status on the management of the third stage of labor. It can also help inform policy makers on the feasibility of using misoprostol in AMTSL, especially in resource poor settings where other uterotonics are unavailable or wherever AMTSL is not practiced.

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