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Original Research Article.

A Comparative Study Between Prostaglandin F2α and Methylergometrine In the Active Management of Third Stage of Labor

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ABSTRACT

Introduction: The most serious complication in obstetric practice is post-partum haemorrhage (PPH) The greatest number of maternal deaths from haemorrhage is due to PPH, which is almost entirely a preventable condition Postpartum haemorrhage (PPH) is one of the most common causes of maternal mortality. The study aimed at comparing the efficacy safety and tolerability of intramuscular Prostaglandin 2α versus intravenous Methyl Ergometrine in the active management of the third stage of labor and to compare the efficacy of the above two drugs.

Material and Methods: A total of 100 women in labor were included in the study. Women were randomized to one of the two groups. Active management of the 3rd stage of labor was done in Group II with intravenous methylergometrine (0.2microgram) and in Group I with intramuscular Prostaglandin 2α (125 micrograms).

Results: There was no significant difference if blood loss in 1st hour of third stage of labor for both the groups. Nevertheless, blood loss was significantly lesser at 4th hour and total 3rd stage of labor in group II prostaglandin F2 α group compare to methylergometrine group. None of the woman developed PPH in either group.

Conclusion: Results of the present study suggest that both methylergonovine and 15-methyl PGF2α have great viability when utilized as a prophylactic measure for PPH. 15-methyl PGF2α was observed to be more useful in protecting the blood loss during first four hours of third stage labor when contrasted with methylergonovine in the examination. However, the unfavourable medication responses related with 15-methyl PGF2α are more when contrasted with that of methylergonovine. Likewise, the cost required with 15-methyl PGF2α is considerably higher. In this manner 15-methyl PGF2α can be suggested in situations where methylergonovine is contraindicated, and in cases refractory to other uterotonic operators. Findings of the present study suggest that 15-methyl PGF2α doesn't have all the capabilities to replace the methylergonovine which the medicine of first choice in the management of third stage of labor.

Key words: Prostaglandin F2α, Methylergometrine, Management of Labor, PPH.

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INTRODUCTION

The most serious complication in obstetric practice is post-partum haemorrhage (PPH) The greatest number of maternal deaths from haemorrhage is due to PPH, which is almost entirely a preventable condition Postpartum haemorrhage (PPH) is one of the most common causes of maternal mortality.[1] In the developing world, it accounts for thirty per cent of such deaths in areas where maternal mortality is high, and less than ten per cent where it is low, e.g., in developed countries.[2] Post-partum haemorrhage (PPH) which occurs in up to eighteen per cent of the births carries with it a three per cent risk of death and is a largely preventable event.[2] PPH occurs in approximately four per cent of vaginal deliveries, and approximate that it causes significant morbidity and twenty-five per cent of all the maternal childbirth-related deaths.[3]

The WHO defines PPH as blood loss of 500 ml or more in the first twenty-four hour postpartum.[4] Two types have been described, i.e., primary PPH or early PPH occurring within first 24 hours and secondary PPH or late PPH that occur more than 24 hours after delivery. The most common cause of PPH is uterine atony and it accounts for 80% to 85% of cases. In many women, its subsequent occurrence can be suspected before delivery. Over distended uterus is more prone to hypotony such as women with the large fetus, multiple fetuses and hydramnios. Labor with strong activity or with barely effective contractions increases the risk of uterine atony. In the same way, labor is more likely to be followed by atony and haemorrhage when it is initiated or augmented with oxytocin.[3]

Myometrial contractility is integral to the delivery of the placenta and the arrest of the potential subsequent haemorrhage. For this physiological process, there is a significant contribution of the hormones.[4] Postpartum blood loss is hard to assess particularly in developing country like India where most of the women are anaemic with poor reserve and these conditions are additionally aggravated by increased demand during pregnancy and blood loss during the 3rd stage of labor.[5] In an examination of serious consequences of PPH the days of expectant management, the so-called ''hands off'' approach seems to be over, active management of labor is associated with two to three-fold decreases in the risk of Postpartum haemorrhage PPH. It comprises use of oxytocics with the delivery of the anterior shoulder of the baby, early cord clamping and delivery of placenta by restricted cord traction. Commonly used uterotonics for prevention of postpartum haemorrhage PPH are Oxytocin and methylergometrine.

The first drug to be used for the active management of the third stage of labor is a semi-synthetic ergot alkaloid derivative, Methylergonovine (methylergometrine), It acts as a fractional agonist at α-adrenergic (α1) and serotonergic (5-HT2) receptors. Constriction of uterine vascular smooth muscle is caused by it. With progress in pregnancy, the sensitivity of the uterus raised to the α1 receptor. At term, the pregnant uterus is most sensitive to the drug. It generates alternate contraction and relaxation at low doses but at high doses, it induces powerful and prolonged contracture, which is the basis of its use in PPH.[6]

Even after the failure of conventional treatment the importance of prostaglandin use, for the treatment of PPH is well established. At the time of delivery 15 methyl Prostaglandin 2α is well used, complement physiological process during labor by causing simulation of uterine contractions and results in the duration of the third stage of labor and thus reduction in blood loss.[7]

The study aimed at comparing the efficacy safety and tolerability of intramuscular Prostaglandin 2α versus intravenous Methyl Ergometrine in the active management of the third stage of labor and to compare the efficacy of the above two drugs.

MATERIALS AND METHODS

Study Design

A prospective study was carried out in the Teerthanker Mahaveer Medical College and Hospital, Moradabad from May 2017 to April 2018.

A total of 100 women in labor were included in the study after obtaining informed consent. It was an open-label randomized parallel comparative study, approved by the institutional ethics committee of medical college and hospital. The study was conducted in the labor room of the Department of Obstetrics and Gynaecology. All of the women had routine antenatal investigations including haemoglobin estimation, urine analysis.

Women were randomized to one of the two groups once they fulfilled all the criteria of the study. Active management of the 3rd stage of labor was done in Group II with intravenous methylergometrine (0.2microgram) and in Group I with intramuscular Prostaglandin 2α (125 micrograms).

Women with singleton pregnancy, between 37 and 42 weeks of gestation, anticipated vaginal delivery, vertical lie, no high-risk factors were included in the study and the women with hemoglobin 6 gm% and above, pregnancy-induced hypertension, abruption placentae/marginal placenta previa/low lying, placenta, multiple pregnancies, grand multipara, malpresentation, polyhydramnios, previous uterine scar, chorioamnionitis, prolonged labor, intrauterine fetal death, coagulation abnormalities, history of medical disorder asthma/epilepsy/heart or renal disease were excluded from the study.

Haemoglobin levels were determined on admission to the labor room. All the women were followed and monitored through the 1st and 2nd stage of labor. The time interval between the delivery of the baby and the placenta was noted. Duration of the 3rd stage was thus calculated. Pulse rate, temperature and blood pressure were recorded 1 hour after delivery. Patient was kept in labor room under observation for a period of 2 hours any complaint such as nausea, vomiting, fever, headache, chills, diarrhoea and shivering was noted The blood loss during the first four hours of delivery was measured objectively, amount of blood loss was assessed at the time of delivery, at one hour and four hours post-delivery It was estimated by weighing the blood clots and used pads During delivery the blood was collected in kidney tray (350 mL) and measured whereas the blood loss at 1 hour and 4 hours was assessed by weighing the used pads during that period. These were previously autoclaved pads which were weighed on a digital pediatric weighing machine. After use, these were put in an air-tight polybag and weighed again. The weight of the polybag was subtracted.

Loss of blood was calculated as blood loss (in gm) in the first four hours postpartum = weight of used pads (g) – the weight of unused pads (g) (1 g = 1 mL). Total blood loss (mL) = blood loss during delivery (mL) + blood loss in first four hours postpartum (mL). On third day postpartum the blood sample was again taken for haemoglobin and hematocrit measurement. The sample was sent to the pathology department for objective measurement. The percentage change of haemoglobin and hematocrit levels predelivery and postpartum third-day levels was measured.

The statistical analysis was performed using paired student's t-test. A p value of <0.001 was considered statistically significant. Data were calculated as means, standard deviation (SD), numbers and frequency (%).

RESULTS

Results of the current study showed that most of the women belonged to 23 – 27 years of age group, followed by 28-32 years of age group in both the groups. Antenatal check-ups of most of the women were done in both the groups. There was no significant difference between demography of population according to urban and rural population. The parity and gestational age distribution did not showed any significant difference in both the groups. (Table 1)

Oxytocin was given to most of the nullipara in both groups during the first stage of labor. Four multipara were given oxytocin in group II to induce sustained contractions. Others had a spontaneous labor and normal vaginal delivery. (Table 1)

The mean duration of third stage of labor in methylergonovine was 3.36±0.65 minutes whereas, it was 3.12±0.55 minutes in 15-methyl PGF2α. There was no case of retained placenta and no extra effort was required for placental removal in any of the cases. Comparison between two groups showed no statistically significant difference in the duration of third stage of labor with either drug (p>0.05) (Table 1).

Table 2 shows that there was no significant difference if blood loss in 1st hour of third stage of labor for both the groups. Nevertheless, blood loss was significantly lesser at 4th hour and total 3rd stage of labor in group II prostaglandin F2 α group compare to methylergometrine group. None of the woman developed PPH in either group. (Table 2) It is evident from fig 1 that there was statistically significant difference in the total amount of mean blood loss during first 4 hours (p< 0.01) in group II prostaglandin F2 α group compare to methylergometrine group.

The difference of hemoglobin change (i.e., predilevery and 3rd day postpartum) between group I and group II was insignificant (p<0.05). Similarly the difference in hematocrit between the two groups measured both pre-delivery and post-delivery (p<0.05) was insignificant (Table 3).

Adverse effects noted in methylergonovine group I was a single episode of vomiting (4%) whereas in the 15-methyl PGF2α group II, 1 woman had nausea and vomiting (4%), 2 women (8%) had diarrohea and 1 had fever (4%).

Table 1: Basic characteristics of both groups

Characteristics	Methylergometrine group (n=50)	Prostaglandin F2α group (n=50)	p value
Age groups (Years)			>0.05
18-22	2 (4%)	8 (16%)	
23-27	28 (56%)	26 (52%)	
28-32	18 (36%)	12 (24%)	
≥33	2 (4%)	4 (8%)	
Area			>0.05
Urban	38 (76%)	42 (84%)	
Rural	12 (24%)	8 (16%)	
Parity			>0.05
Primigravida	32 (64%)	24 (48%)	
Multipara	18 (36%)	26 (52%)	
Gestational age			>0.05
34-36	2 (4%)	6 (12%)	
36-38	10 (20%)	14 (28%)	
38-40	36 (72%)	30 (60%)	
≥40	2 (4%)	0	
Oxytocin use during first stage of labor	10 (20%)	4 (8%)	>0.05
Weight of baby			>0.05
<2.5	4 (8%)	0	
2.5-3.5	42 (84%)	44 (88%)	
>3.5	4 (8%)	6 (12%)	
Length of third stage of labor ≤ 5 minutes	50 (100%)	50 (100%)	>0.05
Duration of third stage of labor	3.36± 0.65	3.12± 0.55	>0.05

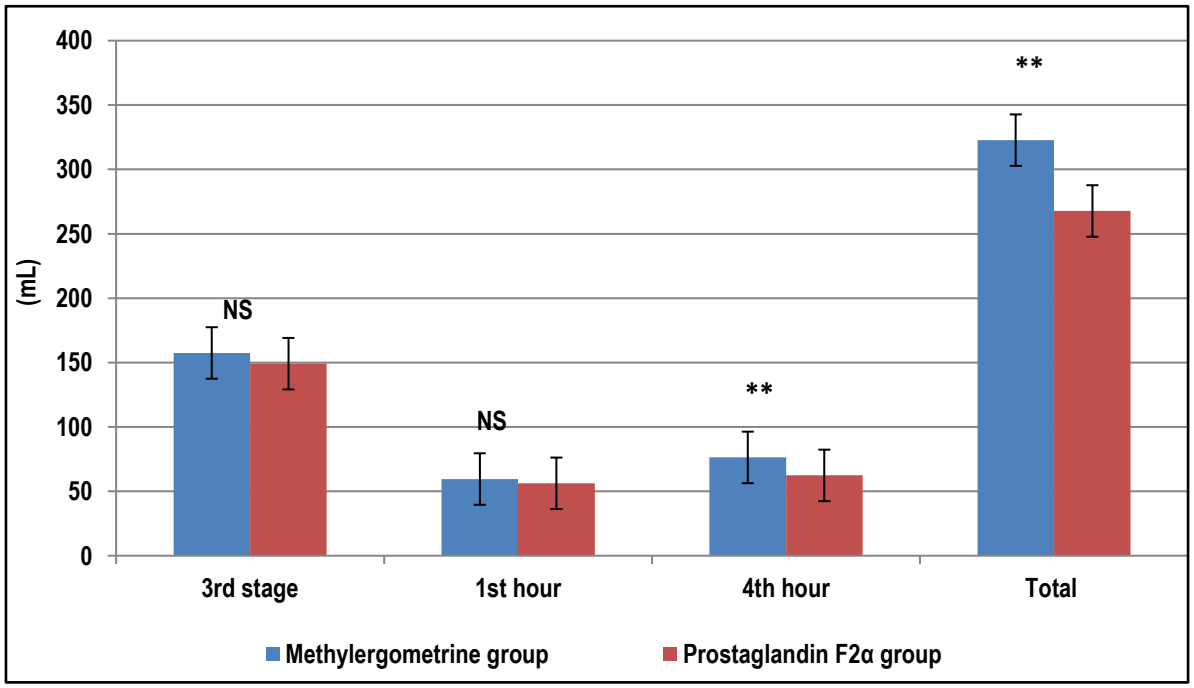
Table 2: Comparison of blood loss between two groups

Blood loss (mL)	Methylergometrine group (n=50)	Prostaglandin F2α group (n=50)	p value
During 3rd stage	157.46± 34.32	149.14± 31.28	>0.05
At 1 hour	59.54± 14.14	56.23± 15.73	>0.05
At 4 hour	76.35± 15.22	62.37± 11.64	<0.01
Total blood loss (3rd stage + postpartum)	322.75±63.28	267.74±58.65	<0.01

Table 3 Comparison of pre and post hemoglobin and hematocrit in both groups

Characteristics	Methylergometrine group (n=50)	Prostaglandin F2α group (n=50)	p value
Hemoglobin (mg/dL)			
Pre-Delivery	11.45 ± 1.8	11.12 ± 1.89	>0.05
Postpartum 3rd day	11.19 ± 1.67	10.79 ± 1.82	>0.05
Hemoglobin change	-0.26 ± 0.13	-0.33 ± 0.13	>0.05
Hematocrit (%)			
Pre-Delivery	34.98 ± 3.89	33.26 ± 4.16	>0.05
Postpartum 3rd day	34.56 ± 3.57	33.03 ± 3.92	>0.05
Hematocrit change	-0.42 ± 0.32	-0.23 ± 0.24	>0.05

Fig. 1: Mean blood loss during 4 hours.



DISCUSSION

It has involved discussion since quite a while with respect to the perfect uterotonic sedate in dynamic administration of third stage of labor. This did not depend on adequacy of the medications alone; yet in addition on numerous different elements like simple accessibility, stockpiling conditions, symptoms and cost factor of the medications.[8] Methylergometrine and prostaglandin F2α are two of the most viable medications accessible in the market. Our endeavor in this examination was to make sense of which among these two medications are more adequate in dynamic administration of third stage of labor. PPH is one of the leading causes of maternal mortality.[9,10]

Excessive loss of blood is considered when it is more than 500 ml in vaginal delivery and in excess of 1,000 ml in caesarean segment. The different inclining factors for PPH incorporates a history of postpartal bleeding in previous pregnancy, delayed, expanded or rapid labor, pre-eclampsia, caesarean, chorioamnionitis, injury to the genital tract, i.e., large episiotomy, an overdistended uterus because of macrosomia, twins, or hydramnios and coagulation defects. A large number of these hazard components can be recognized amid prenatal care or in early labor so that, preferably, women are referred to hospital where prophylaxis and treatment are accessible.[3] During pregnancy there are 48% expansion in plasma volume and 17% expansion in red cell mass of the cardiovascular system via physiological adaptation.[11]

There is defensive hemodilution bringing about fall in hemoglobin, hematocrit, red cell check which sustain normal mean corpuscular volume and mean corpuscular hemoglobin concentration. Circulatory blood volume increases by 37%, which gives satisfactory placental perfusion and a compensatory hold for acute blood loss during delivery. Visual estimation of blood loss at vaginal and stomach may not be accurate to diagnose the exact quantity of blood loss.[7] Most of the time, visual assessment of blood loss is half of the actual blood loss. Blood loss should be measured subjectively. Moreover, standardized way for the assessment of blood loss instead of clinical estimation especially when blood loss is more than 1,000 mL.[12]

As the pregnancy progresses uterus become sensitive to various drugs like prostaglandins, oxytocin, methylergonovine etc.

Various studies have suggested that active management of third stage of labor is better instead of expectant management which leads to diverse complications including increased duration of labor and blood loss.[9,12-14]

Use of prophylactic oxytocics, rapid cord clamping before the delivery of placenta are included in active management of third stage of labor.[15] Numerous studies suggested that ideal management of third stage of labor include significantly preserving the blood loss to minimum quantity.[11,14,15]

Most of the studies incorporated intramuscularly or intravenously single dose (0.2 mg or 0.25 mg) of methylergonovine for the prophylactic management during third stage of labor.[9,11,16] However, all these studies recorded decreased duration of third stage of labor as well as blood loss after using methylergonovine.[17,18] On the other single dose of 15-methyl PGF2α intramuscularly or intravenously during third stage of labor has been also found effective reducing blood loss.[16-18]

Results of the present study showed that 15-methyl PGF2α was significantly effective in reducing blood loss during third stage of labor in comparison of methylergonovine.

However, results of the current study revealed that there was decrease of time duration of third stage for both 15-methyl PGF2α group and methylergonovine group. Further, no complications like PPH, retained placenta etc were recorded in either groups.

As 15-methyl PGF2α has a detriment of staggering expense, in this manner it isn't doable to be utilized in all cases for prophylactic administration of third phase of labor particularly so in developing nations like India. Both methylergonovine and 15-methyl PGF2α have great viability when utilized as a prophylactic measure for PPH. In spite of the fact that the decline in blood loss is altogether more with 15-methyl PGF2α yet the cost and adverse medication response profile is better for methylergonovine.

To finish up both the medications were powerful in hemostasis amid the active management of third stage of labor. None of the women had blood loss more than 500 mL in both groups.

15-methyl PGF2α was observed to be more useful in protecting the blood loss during first four hours of third stage labor when contrasted with methylergonovine in the examination.

However, the unfavorable medication responses related with 15-methyl PGF2α are more when contrasted with that of methylergonovine. Likewise, the cost required with 15-methyl PGF2α is considerably higher. In this manner 15-methyl PGF2α can be suggested in situations where methylergonovine is contraindicated, and in cases refractory to other uterotonic operators. Findings of the present study suggest that 15-methyl PGF2α doesn't have all the capabilities to replace the methylergonovine which the medicine of first choice in the management of third stage of labor.

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