

Prophylactic Intramuscular $\text{PGF}_2\alpha$ Versus Intravenous Methylergometrine For Prevention Of Atonic PPH In High Risk Pregnant Women

Shazia Qayoom, Reema Khajuria, Sudhaa Mahajan

Abstract

To assess, evaluate and compare the safety and efficacy of i/m $\text{PGF}_2\alpha$ 125 mcg and i/v methylergometrine 0.2 mg during active management of third stage of labor in high risk pregnant women who are prone to develop atonic postpartum hemorrhage. The study was conducted on two hundred women prone to develop PPH with vertex presentation and spontaneous onset of labor at term. Selected cases were divided into two groups: *Group I* – Comprised of 100 women who were given 125 microgram of intramuscular 15 methyl $\text{PGF}_2\alpha$ (Carboprost) at the time of delivery of anterior shoulder prophylactically. *Group II* – Comprised of 100 women who were given 0.2 milligrams of intravenous methylergometrine, at the time of delivery of anterior shoulder prophylactically. Tools of statistical analysis used were paired 't' test, 'Z' test and mean \pm SD. The mean duration of the third stage of labor after giving uterotonic drug was significantly shorter in Group I (3.50 ± 1.10 mins) as compared to Group II (5.15 ± 1.30 min) ($p < 0.001$). The mean blood loss was significantly less in Group I (85 ± 30 ml) versus Group II (185 ± 40 ml) ($p < 0.0001$). There was no statistical difference in mean haemoglobin concentration observed before and 48 hrs after delivery. The only significant side effect was diarrhoea in Group I. Prophylactic intramuscular $\text{PGF}_2\alpha$ 125 mcg is a better alternative to prophylactic intravenous methylergometrine 0.2 mg in high risk pregnant women who are prone to develop atonic PPH.

Key Words

Prophylactic $\text{PGF}_2\alpha$, Prophylactic Methylergometrine, High Risk Women, Atonic PPH

Introduction

Postpartum hemorrhage is the major cause of material morbidity and mortality in developing as well as developed countries. It is estimated that every year about 600,000 to 800,000 women die during child birth around the world¹. In the developing world, postpartum hemorrhage accounts for half of all maternal deaths. Postpartum hemorrhage occurs in 18% of all births². Even in developed countries, life threatening post partum hemorrhage occurs in about 1 in 1000 deliveries³. In India, maternal mortality rate is 3.9/1000 live births, as many as, 25% of maternal deaths are due to postpartum hemorrhage⁴. The incidence of postpartum is higher in operative deliveries especially when conducted under general anesthesia. The incidence is about 3.9% in vaginal deliveries and 6.4% in caesarean deliveries². Incidence of postpartum hemorrhage is estimated as 2-11% of all deliveries, but if objective assessment of blood loss is made, the incidence may rise upto 20%⁵.

High prevalence of anemia and multiparity add to this morbidity in developing countries like India. Hence, active management of third stage of labor is the most important step towards reduction of maternal morbidity and mortality.

The prophylactic use of oxytocics in third stage of labour significantly reduce the risk of postpartum haemorrhage from 10% to 6%⁴. The safety of labour is increased by administering oxytocics. Methylergometrine is most widely used oxytocic for prevention atonic PPH. Prostaglandins are natural stimulants of myometrial contraction and have proven to be effective in induction of labour and abortion. Most obstetricians are using 250 mcg of 15-methyl $\text{PGF}_2\alpha$ as a therapeutic measure for atonic PPH. It is used when atonic PPH has already taken place and fails to respond to conventional measures like uterine massage, i/v methylergometrine and oxytocin. Use of prostaglandins in the active management

From the Department of Obstetrics and Gynaecology, Govt Medical College, Jammu (J&K)- India

Correspondence to : Dr Sudhaa Mahajan, Professor, Department of Obst & Gyne, Govt. Medical College Jammu (J&K)- India

of third stage of labour is an extension of their use in obstetrics 15- methyl 1 PGF₂ (carboprost) , a synthetic derivative of prostaglandin, has as advantage that it can be given intramuscularly ,is more potent and is longer acting than natural prostaglandin . The present study is undertaken to analyze the efficacy of prophylactic 125 mcg PGF₂ versus intravenous methylergometrine for prevention of atonic post partum haemorrhage in high risk pregnant women.

Material and Methods

The study was conducted on 200 womens with vertex presentation and spontaneous onset of labor at term and prone to develop atonic PPH. The patients were selected on the basis of inclusion and exclusion criteria as shown below.

Inclusion Criteria: Previous caesarean delivery; Past history of PPH;Grand multiparty;Hydramnios;Placenta Pravias (type-1);Multiple pregnancy;Preexisting anaemia (mild & moderate);Prolonged labour.

Exclusion Criteria: Bronchial asthma;Hypertension; Renal disease;Cardiac disease;Endocrinal problem;EpilepsyCoagulation disorder;Sensitivity to Prostaglandins or methylergometrine

They were randomly divided in two groups of 100 each. Group I received 125 mcg PGF₂ intramuscularly and Group II received methylergometrine 0.2 mg intravenously at the time of delivery of anterior shoulder. In twins it was given during delivery of anterior shoulder of second baby. Before undertaking the procedure, a detailed history was recorded. Complete general, physical, Systemic and local examination was done and written informed consent was obtained from the patients. All the patients underwent routine antenatal investigations including hemoglobin estimation, blood grouping, urinalysis and blood sugar screening. All the women were monitored in the third-stage of labor and during postpartum period. Records were kept about:-

- (i) Duration of third stage, by noting the time interval between delivery of baby and complete delivery of placenta.
- (ii) Amount of blood loss was estimated by using a specially designed low cost calibrated plastic blood collection drape, PPH BAG (Debdass), that objectively measures the amount of blood loss in the immediate postpartum period, in a calibrated corner of bag. Calibrated PPH Bags (Debdass) were obtained from Raj Kumari Foundation Jamshedpur, India. [HM LDPE virgin 60 microns (patented)] PPH Bag has a plastic sheet that is placed under the

buttocks of the patient immediately after the delivery of baby and blood is collected in a marked measuring corner of bag (loss scale) without any wastage. This low cost simple tool has the potential for more accurate measurement of postpartum blood loss, the use of this calibrated PPH Bag (Debdass), diagnoses postpartum hemorrhage four times accurately as compared to visual or gravimetric methods of estimation. The PPH Bag apart from being an objective tool for measurement of postpartum blood loss also provides hygienic delivery surface.

- (iii) Blood pressure was recorded before onset of labour and thirty minutes of after delivery.
- (iv) Hemoglobin was estimated at the time of admission and two days after delivery.
- (v) Both groups were also monitored for side effects like hypertension, diarrhea , nausea and vomiting.

The difference was noted and data was analyzed. The statistical analysis was done using paired 't' test and mean \pm standard deviation

Results

The mean interval between injection and placental expulsion was 3.5 ± 1.10 mins in Group I as compared to 5.15 ± 1.30 mins ($p < 0.001$) in Group II. Hence duration of third stage of labor was significantly less in Group I (*Table 1*). The mean amount of blood loss was significantly less in Group I (85 ± 30 ml) as compared to that in Group II (185 ± 40 ml) ($p < 0.0001$) (*Table 2*). The mean fall in Hb % before and 48 hrs postpartum showed no statistically significant difference (*Table 3*). No statistical difference was observed with respect to mean blood pressure change before and after delivery between two groups as shown in *Table 4*. No patient in both groups had PPH. There were no cases of retained placenta and hemorrhagic shock in either group. Additional drug was not required in both groups. However side effects were more in Group I as compared to Group II as shown in *Table 5*.

Discussion

A joint statement issued by the International Federation of Gynecologists and Obstetricians (FIGO) and International Confederations of Midwives (ICM) identifies the reduction of postpartum hemorrhage as key component of safe motherhood (Midwifery women's Health ,2004)6

Active Management of the third stage of labor (AMTSL) is a collection of therapies and treatments (Uterotonic drugs, controlled umbilical cord traction and fundal massage) thought to be effective in reducing maternal blood loss and morbidity. (Mercer JS ,2001)7

The various - Uterotonics, used are: Ergot and its derivatives, oxytocin and prostaglandins. Uterotonics, primarily oxytocin, in hospital setting are safe and effective for prophylaxis and treatment of atonic postpartum haemorrhage, and their use has been associated with relatively minor side effects (Elbopurne DR, 2005)8. Similar is the case with methylergometrine. However these oxytocics have various problems. These drugs have to be administered parenterally, are not stable at room temperature, and must be protected from light. PGF2_α also has its uterotonic effect and is administered parenterally for prophylaxis and treatment of postpartum haemorrhage. Prostaglandins are the natural stimulant of myometrial activity and have proven to be effective in induction of labour.

Prostaglandin analogue, 15 methyl PGF2 is ten times more potent than its natural form and is able to resist enzymatic degradation. It has a longer duration of action. It has advantage that it can be given intramuscularly which is not possible with natural PGF2 because of severe pain at the site of injection as well as

thrombophlebitis. Single intramuscular injection of 15 methyl PGF2 absorbed rapidly and produces increased tone of uterus which is sustained for a period of 5 to 7 hours. Cyclical contractile uterine activity resulted in rapid separation and expulsion of placenta and sustained contraction of uterus resulted in significant control of blood loss.

Thus, the present study was undertaken to compare the safety and efficacy of intramuscular PGF2 versus intravenous methylergometrine in the prophylaxis of atonic postpartum haemorrhage in high risk pregnant women in terms of mean duration of third stage of labour and amount of blood loss.

In the present study we observed a significant reduction in duration of third stage and amount of blood loss in 15 methyl PGF2 group as compared to that in methylergometrine group. Similar observations were made by other authors. (Table-6) Although rescue treatment was required in the form of additional drug other than the test drugs; as well as active intervention in the form of blood transfusion but was not included in the current analysis. Thus remains the limitation of current study.

Table 2. Duration of Third Stage

Duration of Third stage(min)	Group I No. (%)	Group II No. (%)
2-4	79(79)	30(30)
4-6	21(21)	55(55)
6-8	0(0)	15(15)
Total	100	100
Mean ± SD	(3.5 ± 1.10 mins)	(5.15 ± 1.30 mins)

Table 3. Distribution of Blood Loss

t=9.68, p<0.001, Significant

Blood Loss (ml)	Group I No. (%)	Group II No. (%)
50-100 ml	85(85)	0(0)
100-150ml	14(14)	18(18)
150-200 ml	1(1)	70(70)
200-250 ml	0	11(11)
250-300 ml	0	0
>300 ml	100	100
Mean ± SD	(85 ± 30 ml)	(185 ± 40 ml)

Table 4. Mean Haemoglobin Concentration Before and 48 hours After Delivery

t=20.0, p<0.0001, Significant

Haemoglobin	Group I Mean ± SD	Group II Mean ± SD	p-value
Before delivery (gm%)	9.4 ± 0.54	9.42 ± 0.57	0.74* (t=0.150)
After delivery (gm%)	9.39 ± 0.45	9.38 ± 0.49	0.92* (t=0.255)

Table 5. Mean Systolic and Diastolic Blood Pressures

Blood pressure	Group I Mean ± SD	Group II Mean ± SD	p-value
Systolic before delivery (mmHg)	122.27 ± 7.90	122.7 ± 9.40	0.62* (t=0.407)
Systolic after delivery (mmHg)	122.97 ± 7.30	123.14 ± 9.21	0.83* (t=0.204)
Diastolic before delivery (mmHg)	78.38 ± 5.55	78.73 ± 5.78	0.53* (t=0.437)
Diastolic after delivery (mmHg)	79.04 ± 4.54	80.09 ± 6.40	0.71* (t=1.33)

Table 6. Distribution of Side Effects

Side effects	Group I No. (%)	Group II No. (%)
Nausea and vomiting	4 (4)	1 (1)
Diarrhoea	12 (12)	0
Headache	2 (2)	3 (3)

Table 7. Comparison of Various Study with The Current Study

$\chi^2=8.56, p=0.01$, Significant

	Anjaneyulu et al ⁹	Reddy et al ¹⁰	Bhattacharya et al ¹¹	Present study
1. Blood loss (ml)				
Group I	95.2+89.0	127+97	72.0+ 9.4	85+30ml
Group II	154.9+105.6	202+84	145.0+15.1	185+40ml
2. Duration of third stage (min)				
Group I	3.5+1.1	2.33+1.13	4.8+ 0.8	3.5+1.10
Group II	6.1± 2.1	2.44± 0.95	8.06± 0.6	5.15 ± 1.30

Conclusion

The present study concludes that both intravenous methylergometrine and intramuscular carboprost (PGF2) can be used in preventing atonic postpartum hemorrhage in high risk pregnant women but 15 methyl PGF2 is an affective alternative to intravenous methylergometrine as it significantly reduces the duration of third stage of labour and amount of blood loss, which is so important in the anaemic women of our country. PGF2 is more potent, stronger and achieves haemostasis by increasing muscle tone and contractility. Intramuscular injection of carboprost PGF2 could be a life saving drug in atonic postpartum hemorrhage which does not respond to other conventional methods and in women where methylergometrine is contraindicated, especially in remote areas where blood bank and transfusion facilities are not available. This will curtail mortality due to atonic postpartum hemorrhage in high risk pregnant women other than traumatic post partum hemorrhage cases.

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