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Active Management of the Third Stage of Labour: A Prospective Cohort Study to Compare the Role of Oxytocin, Prostaglandin F2 Alpha and Methyl Ergometrine

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Abstract
Aim: *The aim of this study was to analyse the comparative role of Oxytocin, Prostaglandin F2 alpha and Methyl Ergometrine in the active management of the third stage of labour (AMTSL).*
Material and Methods: *A prospective cohort study was conducted in a zonal hospital setting with six hundred selected cases which were divided into three groups of two hundred each. In Group I Oxytocin 10 IU IM, Group II Methyl ergometrine 0.2mg IV & Group III Prostaglandin F2 alpha 125 mcg IM were given at the time of delivery of the anterior shoulder of the baby.*
Results: *Mean blood loss in the third stage of labour was 160 ml in group I (oxytocin), 140 ml in group II (methyl ergometrine) & 130 ml in group III (PGF2 alpha). Mean duration of the third stage of labour were 6.25 min in group I (oxytocin), 5.20 min in group II (methyl ergometrine) & 4.56 min in group III(PGF2 alpha). No incidence of post partum haemorrhage or retained placenta was noted in any of the group.*
Conclusion: *Prostaglandin F2 alpha 125 mcg IM at the delivery of anterior shoulder is safe and efficacious in the active management of the third stage of labour as compared to oxytocin 10 IU IM & methyl ergometrine 0.2mg IV, as well as in preventing post partum haemorrhage, reducing the duration & blood loss in third stage of labour.*
Keywords*: Active management; Third stage of labour (AMTSL); Oxytocin; Prostaglandin F2 Alpha; Methyl ergometrine*

I. Introduction

Postpartum haemorrhage is one of the leading causes of maternal death worldwide; it occurs in about 10.5% of births and accounts for over 130000 maternal deaths annually [1]. Active management of the third stage of labour is highly effective at preventing postpartum haemorrhage among facility-based deliveries. In a systematic review of randomized controlled trials, active management of the third stage of labour was more effective than physiological management in preventing blood loss, severe postpartum haemorrhage (> 500 ml) and prolonged third stage of labour [2]. Routine use of active management of the third stage of labour for all vaginal singleton births in health facilities is recommended by the International Federation of Gynecologists and Obstetricians (FIGO) and the International Confederation of Midwives (ICM) as well as by WHO [3,4].

Active management of the third stage of labour is the most important step towards prevention of postpartum hemorrhage and thereby reducing the maternal morbidity & mortality [5,6,16]. Use of an oxytocic has been recommended since long time. Oxytocin, methyl ergometrine and prostaglandin F2 alpha used as prophylactic uterotonic on delivery of anterior shoulder with early cord clamping and cutting followed by controlled cord traction to deliver the placenta has been associated with decreased blood loss and reduced third stage duration [7].

In view of availability of the three different groups of drugs for management of the third stage of labour, this study was planned to evaluate the comparative efficacy, side effects and complications associated with the use of oxytocin, prostaglandin F2 alpha & methyl ergometrine in the active management of the third stage of labour.

II. Methods

Six hundred patients with singleton pregnancy, cephalic presentation at term gestation were included in the study. Those having hypertension, heart disease, coagulation disorders, renal disease, chronic lung & liver disorders and Anaemia (< 7 gm/dl) were excluded from the study.

They were randomly divided using random number tables in three groups of 200 patients each. Group I received oxytocin 10 U IM, Group II methyl ergometrine 0.2 mg IV & Group III prostaglandin F2 alpha 125 mcg IM at the time of the delivery of the anterior shoulder. The interval between injection and expulsion of the placenta, amount of blood loss in third stage and fourth stage, third stage complications, side effects, and need for second injection of additional drug were noted. Blood loss was estimated by blood and blood clots collected in the kidney tray and adding the difference in the weight of the drapes before and after delivery. Episiotomy site was packed with gauze swab and sutured as soon as placental delivery was accomplished so as to minimize the mixing of blood from episiotomy site with the third stage blood loss.

III. Results

The profile of the three groups were similar as regards age, parity, gestational age, haemoglobin and requirement of episiotomy

Table No. 1 Age wise distribution in the three groups

Age (years)	Group I	%	Group II	%	Group III	%
18 - 25	120	60	128	64	112	56
26 - 30	60	30	56	28	68	34
>31	20	10	16	08	20	10
Total	200		200		200	

It was observed that in all the three groups the most common age group was 18 – 25 years. Very few patients were in the age group >31 years. Age differences in the three groups were not significant (Chart no. 1).

Chart no 1. Age distribution of patients

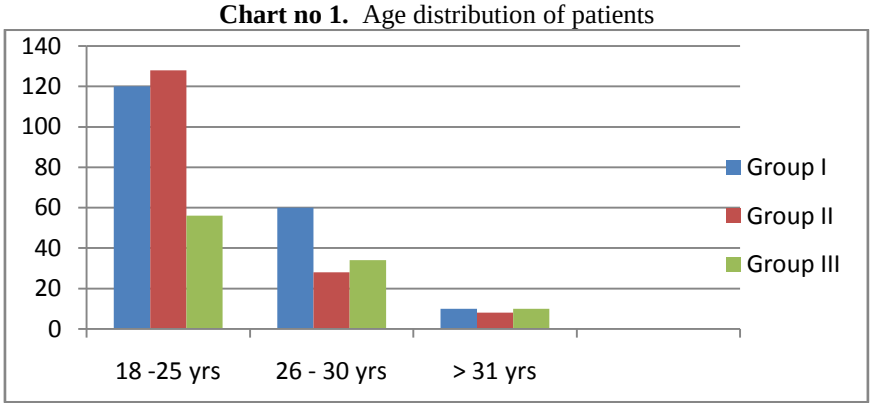

Table No. 2 Parity wise distribution in the three groups

Parity	Group I	%	Group II	%	Group III	%
1	112	56	110	55	116	58
2	70	35	73	36.5	71	35.5
>3	18	09	17	8.5	13	7.5
Total	200		200		200	

In all the three groups the majority of patients were primipara. In group I 56%, group II 55% & group III 58% (Table no 2). Differences in parity among the three groups were statistically not significant (Chart no. 2).

Chart no 2. Parity distribution of patients

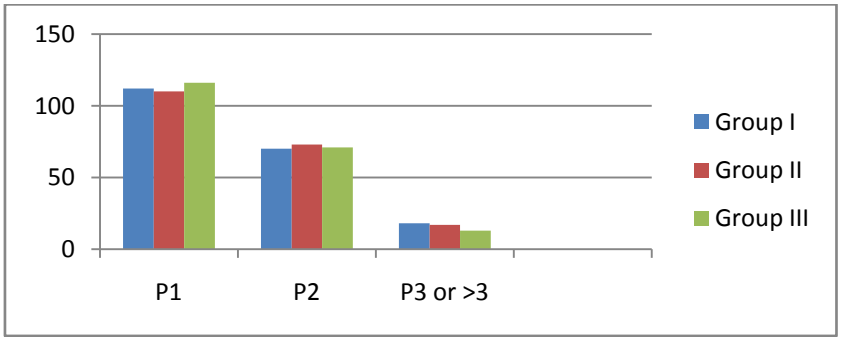

Table No. 3 Gestational age wise distribution in the three groups

Gestational Age (Wks)	Group I	%	Group II	%	Group III	%
37 – 38	40	20	37	18.5	42	21
38w1d- 39w	48	24	50	25	49	24.5
39w1d- 40w	64	32	61	30.5	66	33
40w1d- 41w	48	24	52	26	43	21.5
Total	200		200		200	

Majority of patients in all the three groups were in the gestational age of 39w1d – 41w. 56% in group I, 56.5% in group II & 54.5% in group III were in the gestational age of 39w1d – 41w (Table no. 3). Differences in gestational age in the three groups were statistically not significant (Chart no. 3).

Chart no 3. Gestational age wise distribution

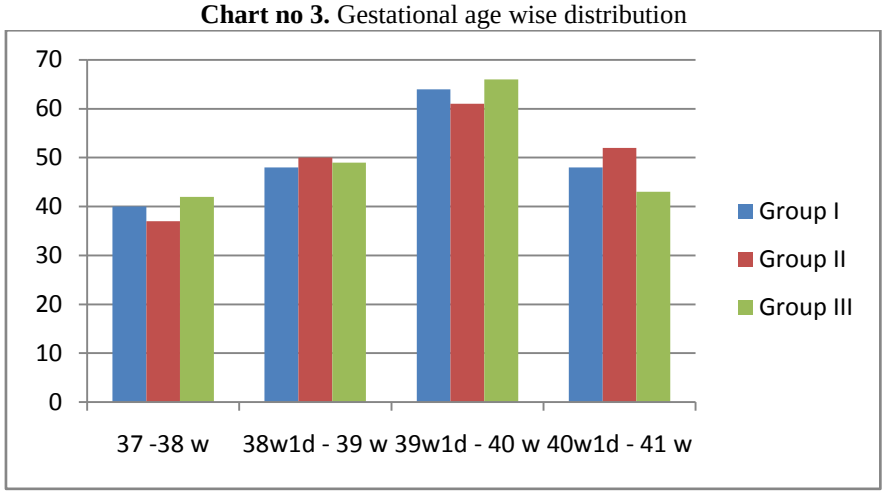

Table No. 4 Episiotomy

	Group I	%	Group II	%	Group III	%
Episiotomy given	121	60.5	125	62.5	129	64.5
Episiotomy not given	79	39.5	75	37.5	71	35.5
Total	200		200		200	

Majority of patients in each group were given episiotomy ie, 60.5% in group I, 62.5% in group II & 64.5% in group III. Difference was not significant (Chart no. 4)

Chart no 4. Episiotomy

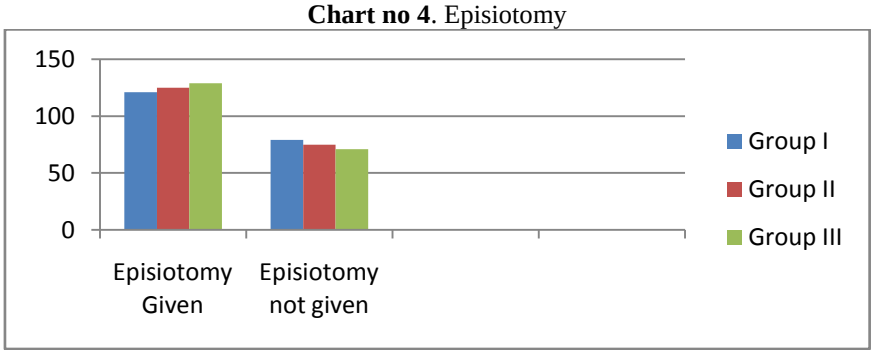

Table No. 5 Hemoglobin wise distribution in the three groups (antepartum)

Hb (gm%)	Group I	%	Group II	%	Group III	%
8 - 10	101	50.5	97	48.5	96	48
10.1 - 12	84	42	87	43.5	91	45.5
> 12	15	7.5	16	08	13	6.5
Total	200		200		200	

Majority of patients in all the three groups were having Hb in the range of 8 – 10 & 10.1 – 12 gm%. In the range of 8 – 10 gm%, group I had 50.5%, group II 48.5% & group III 48% patients. In the range of 10.1 – 12 gm%, group I had 42%, group II 43.5% & group III 45.5% of patients. >12 gm% of Hb was in 7.5% of patients

in group I, 8% in group II & 6.5% in group III (Table no. 5). Hb values in all the three groups were similar. Difference in prepartum Hb values on admission & 24 hours postpartum in all the three groups were not significant (Table no. 5 & 6).

Table No. 6 Hemoglobin wise distribution in the three groups (postpartum)

Hb (gm%)	Group I	%	Group II	%	Group III	%
8 – 10	106	53.0	103	51.5	99	49.5
10.1 – 12	82	41.0	85	42.5	88	44.0
> 12	12	6.0	12	6.0	13	6.5
Total	200		200		200	

Mean duration of the third stage of labour were 6.08 min in group I (oxytocin), 5.14 min in group II (methyl ergometrine) & 4.5 min in group III(PGF2 alpha). Differences in mean duration of the third stage among three groups were statistically significant, p value 0.045. (Table no.7)

Table No. 7: Duration of third stage of labour in the three groups

Groups	I	II	III	P value
Mean Duration (Min)	6.08 min	5.14 min	4.5 min	0.045

Mean blood loss in the third stage of labour was 160 ml in group I (oxytocin), 140 ml in group II (methyl ergometrine) & 130 ml in group III (PGF2 alpha). Differences in mean blood loss in the three groups were statistically significant with p value of 0.043.

Mean blood loss in the fourth stage was 50.3 ml in group I, 38.9 ml in group II & 36.5 ml in group III. Differences in mean blood loss in three groups were statistically not significant with p value of 0.150. (Table no.8)

Table No. 8: Comparison of blood loss in the third & fourth stage of labour

	Group I	Group II	Group III	P Value
Mean blood loss third stage (ml)	160	140	130	0.043
Mean blood loss fourth stage (ml)	50.3	38.9	36.5	0.150

Among the secondary outcome measures nausea was noted in 05 patients in group I, 08 in group II & 05 in group III, which was similar in all the three groups. There was no episode of vomiting in any of the patients in each group. Incidence of retained placenta was 02 each in group I & group II & nil in group III. There was no change in body temperature of > 0.5º F in any of the groups after administration of the uterotonic agents. (Table No. 9)

Table No. 9: Secondary outcome measures

Uterotonics	Nausea	Vomiting	Change in Temperature (> 0.5º F)	Retained Placenta	Post Partum Hemorrhage	Blood Transfusion
Oxytocin (Group I)	05	Nil	Nil	02	Nil	Nil
Methyl Ergometrine (Group II)	08	Nil	Nil	02	Nil	Nil
Prostaglandin F 2 alpha (Group III)	05	Nil	Nil	Nil	Nil	Nil

There was no incidence of post partum hemorrhage (blood loss of > 500ml) & use of second dose of uterotonic agent in any of the patients in each of the three groups. There was no significant change in pulse rate & blood pressure in each of the three groups after administration of the uterotonic agents. None of the patients in each of the three groups required blood transfusion.

IV. Discussion

In the present study mean duration of the third stage of labour was 6.08 min in group I (Oxytocin), 5.14 min in group II (Methyl ergometrine) & 4.5 min in group III (PGF2 alpha). Difference in the mean duration of the third stage of labour was statistically significant with p Value of 0.045 (Test of homogeneity of variances).

Rani Reddy et al (2001) in their study had mean duration of the third stage of labour as 2.55 min in Carboprost group & 2.73 min in Methergin group, which was statistically not significant. Nisha Singh et al in their study had third stage duration of 6.1 min in Carboprost group & 5.52 min in Methergin group. Girija et al (1994) in their study found that the durations of third stage were 4.79 min in Carboprost group & 4.54 min in Methergin group respectively [9, 10].

Nagaria Tripti et al in their study had mean duration of third stage 3.64 min in Carboprost group & 5.16 min in Methergin group, which was statistically significant [7].

Devi PK et al, Anjaneyulu et al & Bhattacharya et al found that the difference in the third stage duration was less in carboprost group & was statistically significant in their study comparing carboprost & methergin in the active management of the third stage of labour [5, 11, 12].

BJ Purushottam et al in their study noted that the mean duration of the third stage of labour after giving uterotonic agent was significantly shorter in Carboprost group (2.634 min) as compared to Methergin group with p value <0.001 [13].

In the present study the mean blood loss in the third stage of labour was 160 ml in group I (Oxytocin), 140 ml in group II (Methyl ergometrine) & 130 ml in group III (PGF2 alpha). Difference in mean blood loss in the third stage among three groups was statistically significant with p Value of 0.043 (Test of Homogeneity of Variances).

Girija et al (1994) noted more blood loss in Carboprost group (127.6 ml) compared to Methylergometrine group (110.2 ml) but the difference was statistically not significant [8].

Devi PK et al (1988) in their study found that blood loss in Carboprost group (99.8 ml) was significantly less than in Methylergometrine group (283 ml). The number of patients studied by them was less (120 patients) compared to the present study [12].

Kamalajayaram et al (1994) found that blood loss immediately after delivery in Carboprost group (64 ml) & in Methergin group (63 ml) was statistically not significant but 4 hours after delivery blood loss with Carboprost was less (86 ml) than Methergin (140 ml), which was statistically significant. However, dose of Carboprost used in this study was 250 mcg [14].

Anjaneyulu et al (1988) found that blood loss in Carboprost group (95.2 ml) was significantly less than Methergin group (154.9 ml). Rani Reddy et al found that blood loss in Carboprost group (160 ml) was significantly less than in Methergin group (269 ml) [5, 9].

Sunil Kumar KS and et al in their study had shown that carboprost tromethamine 125 µg had a significant reduction in duration of third stage of labor ($p < 0.05$) and blood loss ($p < 0.01$) when compared to the subjects who received oxytocin 10 units. Likelihood of occurrence of postpartum hemorrhage was reduced without significant side effects except for diarrhea. Additional need for other uterotonics after carboprost was significantly less compared to oxytocin. Intramuscular carboprost 125 µg is a better cost-effective alternative as compared to 10 units intramuscular oxytocin in active management of third stage of labor [17].

Neri-Mejia M and et al found in their study on three different routes of oxytocin administration (IM, IV and IV infusion) in AMTSL equally effective on the obstetrical hemorrhage prevention [18].

Nagaria Tripti et al in their study had mean blood loss in third stage as 74.84 ml in Carboprost group & 93.6 ml in Methergin group, which was statistically significant [7].

Most of the studies have evaluated the mean blood loss in the third stage of labour only. However, in the present study, mean blood loss in the fourth stage of labour is also evaluated. However, the difference in the mean blood loss in fourth stage in the three groups was statistically not significant (p value 0.150).

Retained placenta was noted one each in group I (Oxytocin) & group II (Methyl ergometrine) in the present study. However, there was no incidence of retained placenta in group III (PGF2 alpha) in present study. Devi PK et al (1988) & Nisha Singh et al in their studies did not find any case of retained placenta [12, 10].

Main side effect of the uterotonic agents noted in the present study was nausea which was similar in all the three groups. Singh PD et al in their study observed vomiting as main side effect in the Carboprost group (250mcg). Nagaria Tripti et al in their study had nausea & vomiting in 2 cases in Carboprost group [4, 12]. Anjaneyulu et al & Bhattacharya et al noted diarrhoea as the most common side effect with vomiting in only 2% of the cases receiving Carboprost [5, 11]. BJ Purushottam et al in their study noted the main side effect as nausea in 3 cases & diarrhea in 5 cases in Carboprost group [13].

Cochrane Database on timing of prophylactic uterotonics in the AMTSL showed that the administration of oxytocin before and after the expulsion of placenta did not have any significant influence on many clinically important outcomes such as the incidence of postpartum haemorrhage, rate of placental retention and the length of the third stage of labour [19].

V. Conclusion

To conclude, prostaglandin F 2alpha 125 mcg IM at the delivery of anterior shoulder is safe, efficacious & cost effective measure in the active management of the third stage of labour as compared to

oxytocin 10 U IM and methyl ergometrine 0.2 mg IV and recommended for the prevention of post partum haemorrhage.

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