Active Management of Third Stage of Labor: A Comparison of Various Uterotonic

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ABSTRACT

Aims and objectives: This study was aimed at comparing the various uterotonics in active management of third stage of labor and reducing blood loss.

Materials and methods: A prospective study was conducted in the Department of Obstetrics and Gynecology of SRMSIMS, Bareilly, in 100 women. Patients were randomized into four groups of 25 each and were given oxytocin within 1 minute of delivery of the baby. Oxytocics used were 10 IU intramuscular oxytocin, 0.2 mg intravenous methylergometrine, 125 µg intramuscular 15-methyl PGF2-alpha and 600 µg tablet misoprostol per rectally in groups A, B, C and D respectively.

Results: Duration of third stage of labor recorded was minimum with mephermine with mean duration of 3.84 ± 0.99 minutes and was maximum with prostodin with mean duration of 5.04 ± 1.02 minutes. Amount of blood loss observed was minimum with mephermine (mean 131 ± 72.037 ml) and maximum with Prostodin (mean 435 ± 147.578 ml). Hemoglobin drop was also seen maximally with prostodin with mean drop of 0.872 ± 0.458 gm% and minimally with mephermine with mean drop of 0.236 ± 0.221 gm%. Change in the general condition of the patients in the form of tachycardia, fall in systolic and diastolic blood pressure was observed maximum with prostodin group whereas, in other groups, there was no significant change.

Conclusion: It is concluded from this study that mephermine is the uterotonic of choice followed by oxytocin for active management of third stage of labor.

Keywords: Third stage, Postpartum hemorrhage, Uterotonics, Active management.


Source of support: Nil

Conflict of interest: None

INTRODUCTION

The third stage of labor refers to the period from delivery of the newborn to the delivery of placenta which has significant complications that may arise immediately following delivery. An uneventful and uncomplicated labor can suddenly become catastrophic within no time.

Postpartum hemorrhage is the most dreadful complication of third stage of labor and is the leading cause of maternal mortality worldwide. Twenty-five percent of all maternal deaths are caused by hemorrhage in particular postpartum hemorrhage. Postpartum hemorrhage is defined as any amount of bleeding following delivery which can lead to deterioration in the condition of woman. It is difficult to delineate the risk factors for postpartum hemorrhage. So, all woman are considered at risk.

Active management of third stage of labor has been universally recommended as not an option but a rule. This includes administration of uterotonics, controlled cord traction and fundal massage the placenta will be delivered safely after the delivery of fetus and can prevent postpartum hemorrhage and maternal deaths.

Objective of the study was to evaluate and compare the efficacy of various uterotonic drugs in the active management of third stage of labor and thereby reducing the blood loss.

MATERIALS AND METHODS

The present prospective study was conducted in the Department of Obstetrics and Gynecology, Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly, Uttar Pradesh, over the period from 2012 to 2013, after taking approval from Institutional Ethical Committee. Hundred patients were enrolled and these patients were distributed in four different groups randomly.

Informed consent and counseling of the patients was done. A detailed history of all the patients was taken including name, age, parity, socioeconomic status, and menstrual history, period of gestation (in weeks), obstetrical history including postpartum hemorrhage and history of any medical disorder.

Complete general and systemic examination was done which included the recording of weight, height, pulse, blood pressure, temperature, respiratory rate, pallor, edema, jaundice.
Detailed systemic and obstetrical examination was done. Vaginal examination was done to know the effacement, dilatation of cervix, station of presenting part, membrane status and adequacy of pelvis.

After detailed history and examination, patients were randomized into four groups of 25 each as follows:

- **Group A** — these patients received 10 IU intramuscular oxytocin.
- **Group B** — these patients received 0.2 mg intravenous methylergometrine.
- **Group C** — these patients received 125 µg intramuscular 15-methyl PGF2-alpha.
- **Group D** — these patients received 600 µg tablet misoprostol per rectally.

Placebo control is not possible in this study because we can’t deny a uterotonic to a patient after delivery.

**Inclusion Criteria**

Women with singleton pregnancy, between 37 and 42 weeks of gestation, Vertex presentation, with no high risk factors, induced/spontaneous labor, between gravida 1 and 3.

**Exclusion Criteria**

Period of gestation <37 weeks and >42 weeks, intrauterine death, intrauterine growth retardation, postmaturity, hypertension—pre-eclampsia/eclampsia/chronic hypertension, abruptio placentae/placenta previa, multiple pregnancies, grand multipara, malpresentations, chorioamnionitis, patient with known blood coagulation disorder, patient with known allergy to prostaglandins, history of medical disorders – cardiac disease/reusal disease, anemia (Hb < 8 gm%), pulse rate of >100 bpm, blood pressure < 90/60 mm Hg).

Active management of third stage of labor was done within one minute after the birth of the baby using one of the four uterotonics as per the group of the patient.

Within a minute of delivery of baby, linen soiled with amniotic fluid was removed, and Brass-V drapes were immediately applied to measure the amount of blood loss.

Placenta was delivered by controlled cord traction as soon as signs of placental separation appeared. Inspection of vulva for perineal tears and per speculum examination for cervical tear was carried out and if present patients were not taken into series. Repeat hemoglobin estimation was done on second postpartum day. The statistical analysis was performed using student’s t-test and paired t-test for continuous variables. p-value of < 0.05 was considered statistically significant. Data were calculated as means, standard deviation (SD), numbers and frequency (%).

The data were evaluated for the following:

- Duration of third stage of labor in all groups.
- Amount of blood loss during third stage of labor.
- Drop in mean hemoglobin levels in various groups.
- Postdelivery change in the general condition of the patient, i.e. pulse and blood pressure of the patient.
- Comparison of the side effects of various uterotonics.

**RESULTS**

Patients in all four groups were comparable with regards to their age, socioeconomic status, parity, booking status, BMI and number of episiotomies given (Table 1).

Mean duration of third stage of labor was 4.72 minutes in group A, 5.04 minutes in group C and 4.93 minutes in group D. It was lowest in group B (3.84 minutes) which is statistically significant with p value of 0.002 (Table 2) (Graph 1).

Mean blood loss in various study groups A, B, C and D was 223.2, 131.8, 435 and 255.8 ml respectively. Maximum blood loss was in patients given PGF2α and minimal in patients given methergin with a p-value of < 0.001 which is statistically significant (Table 2) (Graph 2).

Groups A, B and D showed comparable drop in hemoglobin 0.3, 0.2 and 0.4 gm%. The maximal drop was observed in group C up to 0.8 gm% with a significant p-value of 0.002 (Table 2).

Post delivery tachycardia, i.e. pulse rate more than 100 was observed in only group C and D in those administered PGF2α and misoprostol. However the only statistically significant change was observed in group C where median pulse increased from 86 bpm to 94 bpm. On comparison pre- and postdelivery systolic blood pressure, a significant fall was observed in only group C from 120 to 102 mm Hg. Group B on the contrary showed a rise in blood pressure from 120 to 140 mm Hg in 12% patients.

Median diastolic blood pressure in all groups was 80 mm Hg. Following delivery, the predelivery diastolic blood pressure did not change in any of the groups except in group C which showed a statistically significant fall.

It was observed that no patients in groups A, B or D had postpartum hemorrhage. However 6 patients in group C had postpartum hemorrhage (statistically significant with p-value of 0.004) (Table 2).

Two patients out of six who had postpartum hemorrhage necessitating additional oxytocics and blood transfusion which is statistically significant with a p-value of 0.111 (Table 2).

Nausea and vomiting were found to be the commonest side effects in all groups followed by shivering and fever.

Hypertension was observed in group B in three patients. Whereas tachycardia was observed in group C and D in 9 and 5 patients respectively.
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Table 1: Biosocial characteristics of the study subjects

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
<th>Group C</th>
<th>Group D</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years)</td>
<td>22.96</td>
<td>22.16</td>
<td>22.84</td>
<td>23.16</td>
<td>0.051</td>
</tr>
<tr>
<td>Booking (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Booked</td>
<td>52</td>
<td>48</td>
<td>44</td>
<td>52</td>
<td></td>
</tr>
<tr>
<td>Unbooked</td>
<td>48</td>
<td>52</td>
<td>56</td>
<td>48</td>
<td>0.931</td>
</tr>
<tr>
<td>Socioeconomic status (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Upper middle</td>
<td>36</td>
<td>32</td>
<td>36</td>
<td>44</td>
<td>0.921</td>
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<tr>
<td>Lower middle</td>
<td>44</td>
<td>40</td>
<td>40</td>
<td>36</td>
<td></td>
</tr>
<tr>
<td>Upper lower</td>
<td>12</td>
<td>24</td>
<td>20</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Lower</td>
<td>8</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Parity (%)</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>P1</td>
<td>64</td>
<td>72</td>
<td>76</td>
<td>56</td>
<td>0.803</td>
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<tr>
<td>P2</td>
<td>28</td>
<td>20</td>
<td>12</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>P3</td>
<td>8</td>
<td>8</td>
<td>12</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>BMI (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>&lt;18.50</td>
<td>8</td>
<td>8</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>18.50-24.99</td>
<td>84</td>
<td>84</td>
<td>100</td>
<td>96</td>
<td></td>
</tr>
<tr>
<td>25.00-29.99</td>
<td>8</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0.286</td>
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<tr>
<td>30.00-34.99</td>
<td>0</td>
<td>4</td>
<td>0</td>
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<td></td>
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<tr>
<td>35.00-39.99</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>≥40</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Episiotomy (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Given</td>
<td>80</td>
<td>72</td>
<td>84</td>
<td>64</td>
<td>0.369</td>
</tr>
<tr>
<td>Not given</td>
<td>20</td>
<td>28</td>
<td>16</td>
<td>36</td>
<td></td>
</tr>
</tbody>
</table>

Table 2: Post-delivery data in four groups

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
<th>Group C</th>
<th>Group D</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of third stage of labor (minutes)</td>
<td>4.72</td>
<td>3.84</td>
<td>5.04</td>
<td>4.93</td>
<td>0.002</td>
</tr>
<tr>
<td>Amount of blood loss (ml)</td>
<td>223.2</td>
<td>131.8</td>
<td>435</td>
<td>255.8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Drop in hemoglobin (gm%)</td>
<td>0.372</td>
<td>0.236</td>
<td>0.872</td>
<td>0.44</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Number of patients having blood loss &gt; 500 ml</td>
<td>0</td>
<td>0</td>
<td>6</td>
<td>0</td>
<td>0.0004</td>
</tr>
<tr>
<td>Number of patients requiring blood transfusion</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>0.111</td>
</tr>
</tbody>
</table>

DISCUSSION

Patients in all four groups were comparable with regards to their age, socioeconomic status, parity, booking status, BMI and number of episiotomies given.

In our study, duration of third stage of labor was >4 minutes in 48% of the patients in group A and mean duration of third stage was 4.72 ± 1.02 minutes, whereas in the study of Gohil J et al (2011), mean duration of third stage was much higher, i.e. 8.94 ± 4.18 minutes.5
Duration of third stage of labor in group B was < 4 minutes in 68% of the patients, however mean duration of third stage was 3.84 ± 0.99 minutes. Surprisingly, it is much lower in our study than studies of Bhattacharya et al (1988), Nagarla Tripti et al (1988) and Gohil J et al (2011), where mean duration of third stage was 6.1 ± 2.1, 5.16 ± 1.58, 7.18 ± 3.10 minutes respectively.\(^5\)\(^7\)

Duration of third stage of labor in our group D was >4 minutes in equal number of patients as in group C with mean duration of third stage 4.93 ± 1.63 minutes, it is in consistent with the study of El-Rafaey et al (1997) with a duration of third stage of five minutes. Whereas in the study by Gohil J et al (2011) duration of third stage of labor, in this group was much higher, i.e. 7.84 ± 3.19 minutes.\(^5\)\(^8\) However, Gohil J et al in their study used 400 µg misoprostol.\(^5\)

It is observed from above that mean duration of third stage of labor was minimum in group B followed by group A.

In group A, our study is consistent with Gohil J et al (2011) with blood loss of 281 ± 131.27 ml against 223.2 ± 122.53 ml of ours.

Studies by Dr Ibrahim Ayyad et al (2004) and Bellad MB et al (2012) are not consistent with our study in group A as 6% of case had blood loss of 500 ml and 2% patients had blood loss of >1000 ml respectively. No case of postpartum hemorrhage was observed in this group in our study.

Sorbe (1978) in his study assessed the blood loss to be 306 ± 271 ml and Gohil J et al (2011) measured the blood loss to be 243 ± 121.22 ml with methyl ergonovine.\(^5\)\(^10\) Our study is not consistent with any of the studies as blood loss in this group in our study is much less amounting to 131.8 ± 72.037 ml. Lower blood loss in our study could be due to significantly decreased duration of third stage of labor.

In group D, also blood loss is not consistent with the studies of Dr Ibrahim Ayyad et al (2004) and Gohil J et al (2011) showing a mean blood loss of 500 ml in 7% of patients and 355 ± 115.72 ml respectively, against mean blood loss of 255.8 ± 102.160 ml in our study.\(^5\)\(^9\) Overall lower parity in our study could also contribute to less blood loss in all groups as compared to other studies.

Groups A, B and D had no case which was complicated by postpartum hemorrhage, whereas in group C postpartum hemorrhage was observed in 24% of the patients.

Our study for hemoglobin drop in group A is consistent with Gohil J et al (2011) who had predelivery hemoglobin 10.04, postdelivery 9.41 and fall of 0.63 ± 0.30 gm% against ours of 10.976, 10.612 and fall of 0.372 ± 0.347 gm% respectively.\(^5\)

Our study in group B is consistent with F Amont et al (1999) and El-Rafaey et al (2000) where there was no significant change in pre- and postdelivery hemoglobin levels.\(^11\)

Our study is in concurrence with the study by Gohil J et al who reported methylergonovine to be the best uterotonic drug.\(^5\)

In group D, the study is consistent with Gohil et al (2011) where average hemoglobin levels were 10.23 and 9.51 and drop of 0.72 ± 0.315 gm% which are similar to our study with levels of 10.16, 9.72 and 0.44 ± 0.396 gm% respectively. Our study in this group is not consistent with Ayyad et al (2004) as there was a drop of 1.4 ± 1.3 gm% in hemoglobin levels.\(^5\)

Mean hemoglobin drop was maximally observed in group C, i.e. 0.8 against 0.4, 0.3 and 0.2 in groups D, A and B respectively. Change in hemoglobin for group C is statistically significant with a p-value of 0.002.

Two patients in group C had blood loss of 750 ml and 800 ml with a hemoglobin drop of 1.1 to 2 gm% respectively, requiring additional oxytocic and blood transfusion.

In group A, minor side effects in the form of shivering, vomiting and headache were observed. Our findings are not consistent with that of Gohil J et al (2011) as the incidence of these minor side effects was much lower in their study.\(^5\)

In group B in addition to shivering and nausea, side effects like hypertension was also observed in 12% of patients, study being consistent with that of Gohil J et al (2011) as patients exhibited hypertension in their study also.\(^5\)

Diarrhea and vomiting were most commonly observed in group C along with chills in 24%. Tachycardia was observed in 36% patients which were attributed to increased blood loss in this group. This is comparable to the study of Chua S et al (1995) where they found a significant increase in the incidence of diarrhea with prostidin.\(^12\)

In group D, minor side effects, like shivering and fever, were present in 48% and 56% of patients. Our study is consistent with the study of El Refaey et al (1997), Hofmeyer GJ et al (1998), F Amant et al (1999), Hazem El-Rafaey et al (2000) in which their patients also exhibited fever and shivering.\(^8\)\(^11\)\(^13\)

**CONCLUSION**

From the study, it is concluded that Methergine is uterotonic of choice in active management of third stage of labor followed by oxytocin.

Oxytocin can be safely recommended where methergine is contraindicated.
Though misoprostol comes next in order, yet was found adequately effective especially in surroundings where storage facilities are unavailable and adequate technical skills are lacking.

Prostodin was found to be least effective in prevention of postpartum hemorrhage in our study. However, larger randomized trials are required with higher doses (250 µg) for establishing its effectiveness and establishing equivalence between standard oxytocin in prevention of postpartum hemorrhage.

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