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ORIGINAL ARTICLE

Randomized controlled trial of three oxytocic regimens to prevent primary postpartum haemorrhage at caesarean section

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Abstract

The objective of this present study was to compare the efficacy of three oxytocic regimens to prevent primary postpartum haemorrhage (PPH) at caesarean section. A randomized controlled trial including 90 patients who underwent caesarean section were selected according to inclusion and exclusion criteria assigned randomly into three groups (30 patients in each group) was conducted. Group 1 and group 2 were exposure groups and group 3 was control group. All patients were given 10 units intravenous (IV) bolus oxytocin immediately after delivery of baby. Group 1 was given additional 20 units oxytocin in each 1000 ml fluid for 24 hours. Group 2 received additional 1000 microgram misoprostol per rectal. Group 3 did not receive any additional oxytocic drug. Background characteristics of all the three groups were similar. It was observed that 501-1000 ml blood loss was found among 25 (83.3%) cases in group 1, 27 (90.0%) in group 2 and 27 (90.0%) in group 3. The mean (SD) amount of blood loss was found 733 (190) ml in group 1792 (187) ml in group 2 and 818 (14) ml in group 3. Occurrence of PPH and blood transfusion needed among 1 (3.3%) in group 1, 2 (6.7%) in group 2 and 3 (10.0%) in group 3. Side effects occurred in 7 (23.3%) patients of group 1, 18 (60.0%) in group 2, and 6 (20.0%) in group 3. Shivering was found among 4 (13.3%) in group 1, 10 (33.3%) in group 2 and 3 (10%) in group 3. Vomiting was found among 2 (6.7%) in group 1, 4 (13.3%) in group 2, and 2 (6.7%) in group 3. Pyrexia was 1 (3.3%) in group 1, 4 (13.3%) in group 2 and 1 (3.3%) in group 3. Side effects were more in the group where misoprostol was used. Except side effects there was no statistical difference of occurrence of different events among the three groups. Only bolus IV oxytocin appears to be as effective as oxytocin infusion in addition to bolus IV oxytocin or per rectal misoprostol in addition to bolus IV oxytocin to prevent primary PPH at caesarean section. But occurrence of transient side effects such as shivering, pyrexia and vomiting were noted more frequently with the use of misoprostol.

Key wards: Primary postpartum haemorrhage, caesarean section, oxytocic drugs.

Introduction

Any amount of bleeding from or into the genital tract following birth of the baby up to the end of the puerperium which adversely affects the general condition of the patient evidenced by rise of pulse rate and falling of blood pressure is called postpartum hemorrhage (PPH).[1] Primary PPH occurs within 24 hours of delivery. According to others, at caesarean section if the blood loss is more than 1000 ml then it is called PPH at caesarean section.[2] The prevalence of PPH in

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caesarean deliveries is 0.6%.[3] It is one of the leading causes of maternal mortality and morbidity but a significant disparity exists between developed and developing countries.[4] PPH is the leading cause of maternal mortality in low-income countries and the primary cause of nearly one quarter of all maternal deaths globally.[5] Thirty one percent of maternal death in Bangladesh is due to haemorrhage.[6] The lower maternal mortality rate attributed to PPH in developed countries suggests that medical interventions utilized for prevention and treatment of PPH contributes significantly to survival of this obstetrical emergency.[7]

Atonic uterus is responsible for 75-90% of PPH. So prevention of uterine atony can reduce a large number of primary PPH. Oxytocin remains the first line agent in the prevention of uterine atony. Oxytocin is a hormone released from the posterior pituitary that stimulates contraction of smooth muscle of the uterus. Recent studies suggest that the effective dose of oxytocin for prophylaxis against uterine atony during caesarean section is significantly lower than the 5-10 IU used by anesthesiologists previously. Slow administration of small bolus dose of oxytocin minimizes maternal hemodynamic disturbances. Continuous oxytocin infusion is recommended for maintaining uterine tone after bolus administration, although ideal infusion rate is still to be established.[8] In a Canadian study it was shown that intravenous infusion of oxytocin (20-40 IU in 1000 ml fluid, 150 ml per hour) is an acceptable alternative for active management of third stage of labour.[9]

Misoprostol is a synthetic prostaglandin E1 analogue that stimulates contraction of the myometrium. In an Egyptian study it was shown that routine use of 800 microgram of rectal misoprostol was effective in reducing blood loss after delivery.[10] The major advantages of utilizing rectal misoprostol include its ease of administration, low side effect profile and its ability to be administered in patients experiencing vomiting during intrapartum period.[11]

In our country, the rate of caesarean delivery is increasing, so reduction of blood loss at caesarean section is beneficial to the patients in terms of decreased postoperative morbidity and a decrease in risks associated with blood transfusion. In many instances rectal misoprostol and oxytocin infusion along with intravenous oxytocin are used without any evidence with the idea that addition of oxytocic will result in further decrease in blood loss and occurrence of primary PPH but there is no study in our country about the effectiveness of this oxytocin infusion or additional misoprostol for prevention of PPH.

Therefore, the purpose of this study was to compare the effectiveness of oxytocin infusion in addition to oxytocin intravenous bolus, per rectal misoprostol in addition to oxytocin intravenous bolus and only oxytocin intravenous bolus dose at caesarean section to prevent primary PPH by preventing uterine atony.

Materials and Method

This study is a randomized controlled clinical trial study. The study was carried out in the inpatient Department of Obstetrics & Gynecology, Sir Salimullah Medical College & Mitford Hospital (SSMC&MH), Dhaka. Study period was July 2013 to December 2013. Study population was the admitted cases who underwent either elective or emergency caesarean section in SSMC&MH during the study period. Sample size with simple random sampling was 90 patients (30 in each group). The inclusion criteria were: a) admitted patients scheduled for either elective or emergency caesarean section, b) patients with term pregnancy (37-42 weeks), c) singleton pregnancy, and d) caesarean section that was done under spinal anesthesia. The exclusion criteria were: a) patients with any risk factors of PPH such as grand multipara, multiple pregnancies, antepartum haemorrhage, hydromnios, prolonged labour, obstructed labour, suspected ruptured uterus, caesarean wound dehiscence, severe anemia, etc, and b) caesarean section that was done under general anesthesia. Group 1 and group 2 were exposure groups and group 3 was control group. Three

colored cards were drawn by the patients for simple randomization- red cards for group 1, blue cards for group 2 and yellow cards for group 3. Patients randomly drew the cards and were selected into three groups according to the color of the cards drawn.

The patients of group 1 received 10 units intravenous (IV) bolus oxytocin and continuous IV infusion of 20 units oxytocin in each 1000 ml fluid at 30 drops/min for 24 hours while group 2 received 10 units IV bolus oxytocin and 1000 microgram misoprostol per rectal, and group 3 received only 10 units IV bolus oxytocin. A questionnaire was prepared for data collection. After collection, data were checked, verified for consistency and were entered into the computer by using the SPSS software for analysis. The results were presented in tables in mean, standard deviation and percentage. ANOVA, paired *t*-test and chi-square test were used as appropriate, *p* value to <0.05 was taken as significant.

Results

The distribution of the study patients by patients profile is shown in Table 1. It was observed that majority patients belonged to 21-30 years of age in three groups. The mean (SD) age was found 23.4 (3.8) years in group 1, 24.5 (4.8) years in group 2 and 22.9 (4.2) years in group 3. Majority patients came from lower middle class group in three groups. The difference of age (by ANOVA) and socioeconomic condition (by chi-square) between the groups were not statistically significant ($p > 0.05$).

The indications of caesarean section are shown in Table 2. Majority of the patients had previous caesarean section in three groups, which was 9 (30.0%) in group 1, 7 (23.3%) in group 2 and 9 (30.0%) in group 3. Distribution of indications of caesarean section was even among the three groups.

The difference in obstetrical history of the patients, average blood loss at caesarean section, mean blood loss, need for additional oxytocic, incidence of PPH, and need for blood transfusion in the groups and between the groups was not statistically significant (data not shown). It was observed that 501-1000 ml blood loss was found among 25 (83.3%) cases in group 1, 27 (90.0%) in group 2 and 27 (90.0%) in group 3. The mean (SD) amount of blood loss was found 733 (190) ml in group 1, 792 (187) ml in group 2 and 818 (14) ml in group 3. Occurrence of PPH and blood transfusion needed among 1 (3.3%) in group 1, 2 (6.7%) in group 2 and 3 (10.0%) in group 3.

The Hb% before and after caesarean section are shown in Table 3. Post caesarean section Hb% significantly decreased within the groups after 24 hours ($p < 0.01$, paired *t*-test). However, there was no significant difference in Hb% between groups.

Table 1. Distribution of the study patients by patients profile, (n = 90)

	Group 1 (n = 30)		Group 2 (n = 30)		Group 3 (n = 30)		*p* value
	n	%	n	%	n	%	
Age (years)							
≤20	9	30.0	9	30.0	12	40.0	
21-30	20	66.7	18	60.0	16	53.3	
>30	1	3.3	2	6.7	2	6.7	
Mean ± SD	23.4 ± 3.8		24.5 ± 4.8		22.9 ± 4.2		> 0.05
Range (min - max)	(18 - 32)		(18 - 33)		(18 - 32)		
Socioeconomic condition							
Lower class	2	6.7	2	6.7	1	3.3	
Lower middle class	22	73.3	24	80.0	23	76.7	> 0.05
Higher class	6	20.0	4	13.3	6	20.0	

Table 2. Distribution of the study patients by indications of caesarean section, (n = 90)

Indication	Group 1 (n = 30)		Group 2 (n = 30)		Group 3 (n = 30)	
	n	%	n	%	n	%
Fetal distress	4	13.3	6	20.0	5	16.7
Cephalopelvic disproportion	5	16.7	4	13.3	5	16.7
Previous caesarean section	9	30.0	7	23.3	9	30.0
Premature rupture of membranes with fetal distress	4	13.3	3	10.0	4	13.3
Breech presentation	2	6.7	4	13.3	2	6.7
Oligohydromnios with fetal distress	3	10.0	2	6.7	2	6.7
Postterm pregnancy with fetal distress	3	10.0	4	13.3	3	10.0

Table 3. Hb% of the patients before and after caesarean section, (n = 90)

	Group 1 (n = 30)	Group 2 (n = 30)	Group 3 (n = 30)	*p* value
Hb% before caesarean section (gm/dl)				
Mean ± SD	11.2 ± 0.6	11.1 ± 0.3	11.2 ± 0.4	> 0.05
Range (min - max)	9.5 - 11.8	10.5 - 11.7	10.0 - 11.6	
Hb% after 24 hours caesarean section (gm/dl)				
Mean ± SD	10.4 ± 0.4	10.4 ± 0.3	10.2 ± 0.3	> 0.05
Range (min - max)	10.8 - 11.1	10.0 - 11.0	9.5 - 10.8	
***p* value**	< 0.01	< 0.01	< 0.01	

Table 4. Distribution of the study patients by side effects of drugs, (n = 90)

Side effects of drugs	Group 1 (n = 30)		Group 2 (n = 30)		Group 3 (n = 30)		*p* value
	n	%	n	%	n	%	
No side effect	23	76.7	12	40.0	24	80.0	< 0.01
Side effects	7	23.3	18	60.0	6	20.0	
Shivering	4	13.3	10	33.3	3	10.0	< 0.05
Vomiting	2	6.7	4	13.3	2	6.7	< 0.05
Pyrexia	1	3.3	4	13.3	1	3.3	< 0.05

The side effects of drugs are shown in Table 4. Occurrence of side effects were 7 (23.3%) in group 1, 18 (60.0%) in group 2 and 6 (20.0%) in group 3. The difference among the groups was statistically significant ($p < 0.01$). Majority of the patients had shivering among three groups. Shivering was observed 4 (13.3%) in group 1, 10 (33.3%) in group 2 and 3 (10%) in group 3. Vomiting was observed 2 (6.7%) in group 1, 4 (13.3%) in group 2, 2 (6.7%) in group 3. Pyrexia was observed 1 (3.3%) in group 1, 4 (13.3%) in group 2 and 1 (3.3%) in group 3. All the side effects specially shivering were significantly more in the group where misoprostol was used. The difference was statistically significant ($p < 0.05$).

Discussion

This randomized controlled trial was carried out with an aim to compare the effectiveness of oxytocin infusion, per rectal misoprostol

and only oxytocin IV bolus regimen to prevent primary PPH at caesarean section by preventing uterine atony there by blood loss. A total of 90 pregnant women admitted in the Department of Obstetrics & Gynaecology, SSMC&MH during the study period were included in this study. Thirty cases were included in each group. Group 1 and group 2 were exposure groups and group 3 was control group. All the patients were given 10 units IV bolus oxytocin immediately after delivery of baby. Group 1 was given additional 20 units oxytocin in each 1000 ml fluid for 24 hours. Group 2 received additional 1000 microgram misoprostol per rectal. Group 3 did not receive any additional oxytocic drugs. In this randomized trial of women delivered by caesarean section, it was found that an oxytocin infusion or rectal misoprostol in addition to an oxytocin bolus had no effect on overall occurrence of major obstetric haemorrhage compared with an oxytocin bolus only. However, use of additional misoprostol after an initial bolus increases the occurrence of side effects.

Regarding amount of blood loss in the present study, the difference was not statistically significant among the groups. In a study, Murphy et al compared oxytocin 5 IU and placebo infusion versus oxytocin 5 IU and 30 IU infusion for the control of blood loss at elective caesarean which showed mean estimated blood loss was lower in the oxytocin infusion and fewer women had a major haemorrhage (>1000 ml, 14% versus 17%) which is consistent with this study.[12] Vimala et al showed that mean blood loss estimated in misoprostol group was 819 ml which is comparable with this study.[13]

Additional oxytocic needed among the groups in this study is consistent with the result reported in other similar studies that women in the bolus and infusion group were less likely to require an additional uterotonic agent than those in the bolus only group.[13-15]

In this study, post caesarean section Hb% significantly decreased within the groups after 24 hours; however, there was no significant difference in Hb% between the groups. In other study, it was shown that the difference of preoperative and postoperative Hb% of misoprostol and oxytocin groups was not remarkable which is consistent with this study.[16]

Regarding PPH, there was no difference among the groups in this study. Sheehan et al showed that women were less likely to have a major obstetric haemorrhage in the bolus and infusion group than in the bolus only group.[14] Mojibian et al found that there was no difference in major obstetric haemorrhage between the groups (bolus and infusion).[3] Güngördük et al showed a reduction of major obstetric haemorrhage in oxytocin bolus and 30 IU oxytocin infusion than oxytocin bolus only.[15] Conde-Agudelo et al showed that misoprostol combined with oxytocin appears to be more effective than oxytocin alone in reducing intraoperative and postoperative hemorrhage during cesarean section; however, there was no significant differences in intraoperative and postoperative hemorrhage when misoprostol was compared to oxytocin.[17]

Side effects occurred in 7 (23.3%) patients of group 1, 18 (60.0%) in group 2, and 6 (20.0%) in group 3. Shivering was found among 4 (13.3%) in group 1, 10 (33.3%) in group 2 and 3 (10%) in group 3. Vomiting was found among 2 (6.7%) in group 1, 4 (13.3%) in group 2, and 2 (6.7%) in group 3. Pyrexia was 1 (3.3%) in group 1, 4 (13.3%) in group 2 and 1 (3.3%) in group 3. The side effects were more in the group where misoprostol was used. Except the side effects there was no difference of occurrence of different events among the three groups. Only bolus IV oxytocin appears to be as effective as oxytocin infusion in addition to bolus IV oxytocin or per rectal misoprostol in addition to bolus IV oxytocin to prevent primary PPH at caesarean section. But occurrence of transient side effects such as shivering, pyrexia and vomiting were noted more frequently with the use of misoprostol. Chaudhuri et al found that the incidence of shivering was higher in the misoprostol group.[18] Vimala et al showed in a study that

the incidence of side effects such as pyrexia, shivering were significantly higher in misoprostol group compared to oxytocin group.[13] In a study, it was shown that shivering and pyrexia were higher in misoprostol group than oxytocin group. The findings of the present study correspond to the findings of other studies.[13-18]

Conclusion

This study was undertaken to compare effectiveness of oxytocin infusion in addition to bolus IV oxytocin, per rectal misoprostol in addition to bolus IV oxytocin and only bolus IV oxytocin at caesarean section. Only bolus IV oxytocin appears to be as effective as oxytocin infusion in addition to bolus IV oxytocin and per rectal misoprostol in addition to bolus IV oxytocin to prevent primary PPH at caesarean section. But occurrence of transient side effects such as shivering, pyrexia and vomiting were noted more frequently with the use of misoprostol.

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