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

AJ Peea1, F Begum2, E Saha3

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). 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. The prevalence of PPH in

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caesarean deliveries is 0.6%. It is one of the
leading causes of maternal mortality and
morbidity but a significant disparity exists
between developed and developing
countries. 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. Thirty one
percent of maternal death in Bangladesh is
due to haemorrhage. 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.

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 pitu-
itary that stimulates contraction of smooth
muscle of the uterus. Recent studies sug-
gest that the effective dose of oxytocin for
prophylaxis against uterine atony during
caesarean section is significantly lower
than the 5-10 IU used by anesthesiolo-
gists previously. Slow administration of
small bolus dose of oxytocin minimizes
maternal hemodynamic disturbances. Continuous oxytocin infusion is recom-
manded for maintaining uterine tone after
bolus administration, although ideal infu-
sion rate is still to be established. In a
Canadian study it was shown that intrave-
nous infusion of oxytocin (20-40 IU in
1000 ml fluid, 150 ml per hour) is an
acceptable alternative for active manage-
ment of third stage of labour.

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. The major advan-
tages of utilizing rectal misoprostol include
its ease of administration, low side effect
profile and its ability to be administered in
patients experiencing vomiting during intra-
partum period. 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 addi-
tion of oxytocin 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
come up 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 & Gyne-
cology, 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 elec-
tive or emergency caesarean section, b)
patients with term pregnancy (37-42 weeks),
c) singleton pregnancy, and d) caesarean
section that was done under spinal anesthe-
 sia. 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 anes-
thesia. 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)

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n = 30)</th>
<th>Group 2 (n = 30)</th>
<th>Group 3 (n = 30)</th>
<th>$p$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤20</td>
<td>9 30.0</td>
<td>9 30.0</td>
<td>12 40.0</td>
<td></td>
</tr>
<tr>
<td>21-30</td>
<td>20 66.7</td>
<td>18 60.0</td>
<td>16 53.3</td>
<td></td>
</tr>
<tr>
<td>&gt;30</td>
<td>1 3.3</td>
<td>2 6.7</td>
<td>2 6.7</td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>23.4 ± 3.8</td>
<td>24.5 ± 4.8</td>
<td>22.9 ± 4.2</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Range (min - max)</td>
<td>(18 - 32)</td>
<td>(18 - 33)</td>
<td>(18 - 32)</td>
<td></td>
</tr>
<tr>
<td>Socioeconomic condition</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lower class</td>
<td>2 6.7</td>
<td>2 6.7</td>
<td>1 3.3</td>
<td></td>
</tr>
<tr>
<td>Lower middle class</td>
<td>22 73.3</td>
<td>24 80.0</td>
<td>23 76.7</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Higher class</td>
<td>6 20.0</td>
<td>4 13.3</td>
<td>6 20.0</td>
<td></td>
</tr>
</tbody>
</table>
Table 2. Distribution of the study patients by indications of caesarean section, (n = 90)

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

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

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

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

<table>
<thead>
<tr>
<th>Side effects of drugs</th>
<th>Group 1 (n = 30)</th>
<th>Group 2 (n = 30)</th>
<th>Group 3 (n = 30)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n %</td>
<td>n %</td>
<td>n %</td>
<td></td>
</tr>
<tr>
<td>No side effect</td>
<td>23 76.7</td>
<td>12 40.0</td>
<td>24 80.0</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Side effects</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shivering</td>
<td>4 13.3</td>
<td>10 33.3</td>
<td>3 10.0</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Vomiting</td>
<td>2 6.7</td>
<td>4 13.3</td>
<td>2 6.7</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>1 3.3</td>
<td>4 13.3</td>
<td>1 3.3</td>
<td>&lt; 0.05</td>
</tr>
</tbody>
</table>

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. Vimala et al showed that mean blood loss estimated in misoprostol group was 819 ml which is comparable with this study.

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.

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.

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. Mojibian et al found that there was no difference in major obstetric haemorrhage between the groups (bolus and infusion). Güngördük et al showed a reduction of major obstetric haemorrhage in oxytocin bolus and 30 IU oxytocin infusion than oxytocin bolus only. 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.

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. Vimala et al showed in a study that
the incidence of side effects such as pyrexia, shivering were significantly higher in mifeprogestrol group compared to oxytocin group. In a study, it was shown that shivering and pyrexia were higher in mifeprogestrol group than oxytocin group. The findings of the present study correspond to the findings of other studies.

**Conclusion**

This study was undertaken to compare effectiveness of oxytocin infusion in addition to bolus IV oxytocin, per rectal mifeprogestrol 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 mifeprogestrol 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 mifeprogestrol.

**References**


Suggestion for citation of the above: