A COMPARISON OF RECTAL MISOPROSTOL AND INTRAVENOUS OXYTOCIN ON HEMORRHAGE AND HOMEOSTATIC CHANGES DURING CESAREAN SECTION

MOHAMMAD REZA FAZEL*, MANSOURE-SAMIMI**, AND ESMAEIL-FAKHARIAN***

Abstract

**Background:** Post partum bleeding is a major cause of mortality and morbidity in pregnant women. In this study the effects of rectal misoprostol and oxytocin on post-cesarean bleeding are compared.

**Methods:** In this clinical trial 100 pregnant women candidate of elective cesarean section (CS) were randomly allocated in one of two groups of patients receiving either 400 µg of misoprostol, rectally, after spinal anesthesia, or intravenous oxytocin, after delivery of the baby. Intra-operative bleeding, hemoglobin level before and 24 hour after operation, mean arterial blood pressure, heart rate before and after the administration of the drugs, and adverse drug effects.

**Results:** There was no difference between the groups in age, duration and number of pregnancy, and surgery. The amount of the blood lost in misoprostol group was 578±185 cc, and in oxytocin group 620±213 cc (p=0.39). Decrease in hemoglobin level in the two groups was not statistically significant (p=0.55). Changes in mean arterial pressure and heart rate were only significant in oxytocin group. Shivering was significantly more common in the misoprostol group and respiratory distress in the oxytocin group. Other adverse effects were equally seen in both groups.

**Conclusion:** Misoprostol is an appropriate alternative for intravenous oxytocin in patients undergoing cesarean section, with lesser side effects and longer duration of action.

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Introduction

Bleeding is still the major cause of mortality and morbidity in post-partum period. World health organization (WHO) has reported 585000 deaths for pregnancy each year. Twenty five percent of cases die from post-partum bleeding. Mean amount of blood lost is 500 ml during normal vaginal delivery (NVD), 1000 ml in cesarean section (CS), and 3500 ml during CS with emergency hysterectomy. Four per cent of NVD’s and 6% of CS are accompanied with significant bleeding or more than 10% drop in hemoglobin level mandating blood replacement. Control of blood loss during CS will prevent morbidity associated with blood transfusion. Although routine use of oxytocin may result in decreased blood loss, however it is not a safe drug for use in pre-eclampsia, heart diseases, and cesarean section after prolonged labor. It has negative inotropic, anti-platelet, and anti-diuretic effects, and may result in increased heart rate.

Misoprostol is a prostaglandin E1 (PGE1) analogous with stimulating effects on pregnant uterus through prostanoid EP2, and EP3 receptors. The effect of oral, sublingual, and rectal misoprostol on post-partum hemorrhage in comparison with oxytocin has been documented.

Some studies showed that oral or sublingual misoprostol is more effective than oxytocin in preventing hemorrhage during cesarean section. Due to impossibility of oral use of misoprostol during general anesthesia, difficulty in spinal anesthesia for its nausea and vomiting, and based on pharmacological studies proving that misoprostol holds the same blood level while being administrated whether rectally or orally, therefore, rectal misoprostol can be considered as an alternative to oxytocin.

In this study we compared the effects of rectal misoprostol and oxytocin on intra-operative bleeding, hemoglobin level, and hemodynamic changes in parturients undergoing elective cesarean section.

Methods

One hundred pregnant women candidate of elective cesarean section class 1 or 2 of American Society of Anesthesiology (ASA), admitted to Shabilkhany hospital of Kashan University of Medical Sciences (KAUMS), during 2009, were enrolled to this clinical trial. Cases of twin pregnancy, fetal distress, pregnancy induced hypertension, oligo- or polyhydrannious, macrosomy, more than three deliveries, HELP syndrome, sensitivity to prostaglandins, coagulation disorders, asthma, heart, lung, and liver diseases, previous more than one cesarean section, myomectomy, or any other abdominal operations, and patients with febrile diseases were excluded from the study.

After approval by the ethics committee of the university, and obtaining written informed consent, patients were allocated to one of the two study groups using a table of random numbers, receiving either 400 µg rectal misoprostol just before the incision, or infusion of 10 units of oxytocin in 500 ml of normal saline for 30 minutes after delivery of the baby up to the end of the operation. All of the procedures were performed by a surgeon with 10 years experience in this field.

In the operation room all of the patients were monitored and received 10 ml/kg Ringer solution before spinal anesthesia with 10-15 mg of Bupivacaine injected to L4/L5 space with a gauge 25 spinal needle. If the block was failed or blood pressure dropped below 90 mmHg the patient was excluded from the study, and replaced with another patient.

During the operation an isolated suction was used for evacuation of amniotic fluid through a small incision over the uterus, and another one used for collection of blood. Every small gauze soaked with blood was considered to contain 20 ml, and every large one 50 ml of blood, and every gram increase in the patient gown weight considered 1 ml of blood. These items added to the amount blood collected in suction and calculated as the total amount of blood loss.

Hemoglobin level was measured before and 24 hour after the operation. Blood pressure and pulse rate was measured before operation, 3 minutes after and every 5 minutes during the procedure. Shivering, number of nausea and vomiting along the operation and up to 2 hours after it, was recorded. Oral temperature was also recorded in 20, 40, and 60 minutes after...
the operation. Temperature above 40 degrees was considered as hyperpyrexia.

On the base of previous studies the mean amount of blood loss with the use of oxytocin during a CS is 600 cc, and misoprostol can reduce it by 200 ml\textsuperscript{17}. So considering 90% power and 5% error the sample size was determined to be 50 cases in each group. Data was analyzed with SPSS software using chi-square and T-tests.

Results

There was no difference between the groups in age, duration of pregnancy, duration of operation, and number of pregnancies (table 1).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Misoprostol group</th>
<th>Oxytocin group</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>26.6±5.4</td>
<td>27.1±5.3</td>
<td>0.64</td>
</tr>
<tr>
<td>Duration of pregnancy (week)</td>
<td>38.65±0.58</td>
<td>38.66±0.85</td>
<td>0.94</td>
</tr>
<tr>
<td>Duration of operation (min)</td>
<td>38.5±5.8</td>
<td>40.42±6.1</td>
<td>0.11</td>
</tr>
<tr>
<td>Number of pregnancies</td>
<td>1.85±0.92</td>
<td>1.91±0.86</td>
<td>0.73</td>
</tr>
</tbody>
</table>

There were no differences in preoperative and postoperative hemoglobin concentration as well as the amount of intraoperative blood loss between the two groups (table 2).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Misoprostol group</th>
<th>Oxytocin group</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HB preoperative (g/dl)</td>
<td>12.35±1.02</td>
<td>12.29±0.62</td>
<td>0.72</td>
</tr>
<tr>
<td>HB postoperative (g/dl)</td>
<td>11.32±0.83</td>
<td>11.19±0.58</td>
<td>0.36</td>
</tr>
<tr>
<td>Intra-operative Bleeding (ml)</td>
<td>578±185</td>
<td>620±213</td>
<td>0.39</td>
</tr>
<tr>
<td>HB=Hemoglobin</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

There was no significant change in the mean arterial pressure before (82.4 ±15.5 mmHg) and after (78.3 ± 14.8 mmHg) (p=0.24) administration of rectal misoprostol while there was a statistically significant drop before (83.3 ±13.3 mmHg) and after (75.1 ±11.5 mmHg) (p=0.003) intravenous administration of oxytocin. The heart rate of patients in oxytocin group significantly increased from 104 ± 17 beats/min to 122 ± 21 beats/min (p=0.005). There was no change in the heart rate in the patients who received rectal misoprostol (96 ± 21 vs. 99 ± 18; p= 0.48).

Comparison of the side effects revealed that shivering in misoprostol and respiratory distress in oxytocin group were significantly different from the other group. The difference of other side effects was not significant (table 3).

Table 3
The comparison of side effects during and after operation in the two study groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>Misoprostol group</th>
<th>Oxytocin group</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transfusion</td>
<td>0</td>
<td>0</td>
<td>N.S</td>
</tr>
<tr>
<td>Nausea</td>
<td>5</td>
<td>7</td>
<td>N.S</td>
</tr>
<tr>
<td>Vomiting</td>
<td>2</td>
<td>3</td>
<td>N.S</td>
</tr>
<tr>
<td>Shivering</td>
<td>8</td>
<td>1</td>
<td>0.03</td>
</tr>
<tr>
<td>Hyperpyrexia (&gt;40 c)</td>
<td>4</td>
<td>1</td>
<td>N.S</td>
</tr>
<tr>
<td>Chest pain</td>
<td>1</td>
<td>7</td>
<td>0.03</td>
</tr>
</tbody>
</table>

N.S = No Significant

The incidence of shivering was statistically higher in the misoprostol group while the incidence of chest pain was statistically higher in the oxytocin group. Other side effects were not statistically different between the two groups (table 3).

Discussion

In this study there is no significant difference between intra-operative bleeding and post-operative hemoglobin level in patients receiving either rectal misoprostol or intravenous oxytocin.

Vimala et al\textsuperscript{5} in their study on comparison of 400 µg sublingual misoprostol with oxytocin found
that intra-operative bleeding was more significant in oxytocin group, although post-operative hemoglobin level was not different. In another study by Hamm7 comparing 200 µg buccal misoprostol with oxytocin, there was no difference between intra-operative bleeding and 24 hour post-operative hemoglobin level in the two groups. In Lapaire6 study with 800 µg oral misoprostol, the amount of bleeding and hemoglobin levels 24, and 48 hours post-operative were similar with oxytocin group. In Chaudhuri et al20 study with 800 µg rectal misoprostol, although post-operative hemoglobin level was not different in the two groups, the intra-operative bleeding was significantly lesser in misoprostol group.

Although in different studies intra-operative blood loss was equal between the two groups but intra-operative blood loss with the use of misoprostol has a wide ranged from 500 ml20 to 1000 ml5. This wide range of blood loss may be due to differences in the dose, route, and timing of administration of misoprostol. Chaudhuri20 used 800 µg rectal misoprostol before making incision on the uterus followed by infusion of 6 units of oxytocin in half an hour, but Vimala used 400 µg of sublingual misoprostol and 2 units of oxytocin in half an hour. On the other hand, in these studies, a similar method has not been used to estimate the amount of amniotic fluid and its admixture with blood which may result in inaccurate estimation of blood loss, for example Chaudhuri has used amniotic fluid index (AFI) for estimation of the amount of amniotic fluid, but it has shown that AFI is not a reliable index for this purpose23,24,25.

In measuring hemoglobin level the aforementioned factors are less likely effective and so its changes are almost similar in different studies, e.g. in spite of 500 cc difference in amount of intra-operative blood loss in Chaudhuri and Vimala the difference in hemoglobin changes is only 0.3 mg/dl (0.411 versus 0.1 mg/dl respectively). The rate of bleeding and the hemoglobin changes found in our study was similar to most others studies6,7. The differences between our study and that of Chaudhuri may be due to the lower dose of rectal misoprostol (400 versus 800 µg) and higher dose of oxytocin in our study.

Changes in blood pressure and heart rate are side effects of oxytocin. In our study decrease in mean arterial blood pressure and increase in heart rate were significantly more common in patients receiving oxytocin. Several studies have been done on hemodynamic changes resulting from the use of oxytocin. Langesaeter9, Svanström10 and co-workers showed that oxytocin reduces mean arterial blood pressure and peripheral vascular resistance, increases heart rate and creates ST-segment changes and consequently will lead to chest pain. This study showed that the oxytocin receiving group had significantly more decrease in blood pressure and increase in heart rate than misoprostol group and dyspnea and chest pain were more common in this group as well. These similar changes are reported in many other studies26,27,28.

Shivering is a side effect of misoprostol and is dependent to the kind of anesthesia, temperature of the operation room, and fluids used during the procedure5,6,19,29. We used fluids with 37 degrees of centigrade (either IV or irrigation) and room temperature was 25 centigrade in the other hand epidural anesthesia was not used in our study because shivering is more common in epidural anesthesia19. Oral use of misoprostol results in higher blood level of the drug and higher incidence of shivering. Vimala has reported shivering in 26% of patients with 400 µg of sublingual misoprostol, and 4% in oxytocin group5. In Lapaire study with 800 µg of misoprostol, the incidence of shivering was 36% in comparison with 8% in oxytocin group6. Chaudhuri reported 8.3% and 1.1% in the misoprostol and oxytocin groups respectively20. Shivering was seen in 16% of our patients in misoprostol group and 2% in oxytocin group. These findings are comparable to previous studies.

The difference of nausea and vomiting in the two groups was not significant. Similar findings were reported in previous studies5,20, despite that for its metallic taste misoprostol when used orally or sublingually was associated with higher frequency of nausea and vomiting29.

Hyperpyrexia was seen in 8% of patients who received misoprostol and 2% with oxytocin. The difference was not significant. Previous studies have reported similar findings5,20.
Conclusion

Rectal misoprostol is an appropriate alternative for intravenous oxytocin in patients undergoing cesarean section, with lesser side effects and longer duration of action.

Acknowledgment

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