Original Article

Hemodynamic Effects of Oxytocin when Given as Bolus or Slow Intravenous Infusion During Cesarean Section

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Abstract

Background*: Oxytocin is a uterotonic drug with profound haemodynamic effects. The effects of oxytocin on women undergoing cesarean section include tachycardia, hypotension and decreased cardiac output. These can be sufficient to cause significant compromise in high risk patients.* ***Objective****: This study aims to find out a simple way to decrease these risks without compromising the therapeutic benefits such as decreasing bleeding after delivery and uterine contraction.* ***Materials and Methods****: We recruited 60 women undergoing cesarean section. The subjects were randomly divided into two groups, 30 subjects per group, randomly selected by blind envelope method. Group A: parturient received 5 IU bolus (approximately over 2 seconds). Group B: parturient received 5 IU oxytocin IV slow infusion (diluted with 10 mL distilled water) over 2 minutes.* ***Results****: A significant increase in heart rate and fall in blood pressure in the group where oxytocin was given IV bolus compared to the slow IV infusion group. There were no differences in the estimated blood loss and uterine contraction between the two groups.* ***Conclusion****: The haemodynamic changes are more marked in the IV bolus than the slow IV infusion of oxytocin. Slower injection of oxytocin can effectively minimize the cardiovascular side effects without compromising the therapeutic benefits.*

Key words*: Obstetric anaesthesia; Anaesthetic techniques; Regional; Spinal; Complications; Haemodynamic; Oxytocin*

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Introduction

The hemodynamic changes in parturient women after cesarean delivery may be caused by the elimination of the aorta-caval compression, autotransfusion of blood immediately after delivery, haemorrhage, and vasoconstriction and excitation, but some studies have reported that uterotonic drug is the main factor.[1,2] Uterotonic drug, which is most frequently used for cesarean section, is oxytocin which induces uterine contraction during cesarean section and peripheral vasodilation along with a decrease in arterial pressure after delivery and thus reduces hemorrhage.[3,4] However, intravenous injection of oxytocin during cesarean section may cause cardiovascular side effects such as tachycardia or hypotension[1,2] and is reported to cause even cardiovascular collapse and death in the most severe cases.[5,6] Moreover, various

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other side effects have been reported including fluid pooling or pulmonary edema by the antidiuretic effect of oxytocin.[7–9]

Hence, determining the oxytocin concentration for cesarean section is important. However, since the activity of oxytocin varies from individual to individual[10] and an appropriate dose has not been established, 5−20 IU is intravenously injected based on experience.[11,12] There is recent assertion that bolus intravenous injection or bolus-continuous parallel intravenous injection of oxytocin is more effective than continuous intravenous injection in cesarean section.[13,14] There is also report that a great quantity of bolus intravenous injection requires caution because it causes hemodynamic changes related to hypotension.[1,2] Therefore, research is necessary on the method of oxytocin injection and the effective minimum concentration for cesarean section to induce uterine contraction without side effects.

In this study, we tried to find out the effects of hemodynamic changes such as changes in heart rate, blood pressure and uterine contraction of the recommended dose (i.e., 5 IU) of oxytocin when given as IV bolus or slow IV infusion (diluted in 10 mL of distilled water) over 2 minutes during cesarean section under spinal anesthesia.

Materials and Methods

This study was approved by the Hospital Ethics Committee. We recruited women undergoing cesarean section under spinal anesthesia who were 38 weeks or more into their pregnancy, and were classified as Class 1 or 2 according to the American Society of Anesthesiologist (ASA) physical status classification. The study was conducted in Obstetrics and Gynecology department in Dhaka Medical College Hospital (DMCH), Dhaka from 1 January 2009 to 30 August 2009. Pregnant women who had contraindication for spinal anesthesia, those whose weight was 100 kg or higher, those who had fetal abnormalities, diabetes, gestational hypertension, cardiovascular disease, or cerebral hemorrhage, and those whose labor pain had already started, were excluded from the study. The subjects were visited before the operation and written consent was given by the subjects. The age, height and weight of the patients were recorded.

About 500 mL of Hartmann solution was rapidly dripped into all the parturient women before inducing anesthesia. An electrocardiograph, automated noninvasive blood pressure device, and a pulse oximeter were attached to the subjects, and oxygen was administered at 5 L/min through a face mask. For the spinal anesthesia, the L3−4 or L4−5 lumbar region was punctured with a 25 G Quincke needle when the parturient women were in the left lateral recumbent position, and a 0.5% hyperbaric bupivacaine solution (10−12 mg) was injected after verifying the cerebrospinal fluid leakage. Immediately after the anesthesia, the parturient women were asked to take the supine position and the maximum sensory block level was set to T4−6. The blood pressure and heart rate (HR) were measured in five-minute intervals from the time just after the anesthesia started to the end of the operation. However, during the 10 minutes after the oxytocin was injected, the blood pressure and HR were recorded in one-minute intervals, and delivery of the newborn was set as the baseline. The parturient women were asked if they felt or experienced nausea or vomiting after oxytocin injection and the results were recorded. When some of the parturient women had severe vomiting or continual nausea, the antiemetic drug, ondansetron 8 mg, was intravenously injected. In the cases where the systolic pressure decreased by more than 20% compared to the blood pressure before coming to the operating room, 10 mg of ephedrine was intravenously injected until the blood pressure was normalized, and these cases were excluded from the study.

The subjects were randomly divided into two groups, 30 subjects per group, randomly selected by blind envelope method. Group A: parturient received 5 IU bolus (approximately over 2 seconds). Group B: parturient received 5 IU oxytocin IV slow infusion (diluted with 10 mL distilled water) over 2 minutes.

After delivery of the fetus, group A was given 5 IU oxytocin bolus (approximately over 2 seconds) and group B was given 5 IU oxytocin IV infusion slowly (diluted with 10 mL distilled water) over 2 minutes. Baseline data were taken before oxytocin was given.

After delivery of the fetus, patient was monitored by measuring systolic and diastolic BP, mean arterial pressure (MAP), heart rate, oxygen saturation (SPO_2), uterine contraction, uterine bleeding and any adverse effects was recorded every one minute. The study period was started just before oxytocin was given and it was continued for a further 10 minutes. The study period of 10 minutes was set after a small pilot study. Patient was observed by the surgeon and the state of the uterine contraction was expressed as mild, moderate or satisfactorily contracted. Uterine bleeding was calculated clinically after suctioning amniotic fluid and blood in separate bottles. Visual estimation of the blood loss was done by surgical sponges and laparotomy pads (laps). A fully-soaked sponge (4″ × 4″) on each side holds 10 mL of blood whereas a soaked "lap" holds 100−150 mL. In case of cesarean section 800−1000 mL of blood loss is considerable. Patient can tolerate this amount of blood loss. So, more than 1000 mL blood loss is considered as excessive blood loss.

At the end of surgery 200 microgram misoprostol was given per-rectally for each patient. Postoperatively patients' state of uterine contraction, P/V bleeding and cardiovascular status were also monitored. The results were compiled and analyzed statistically by unpaired 't' test and 'chi-square' test with level of significance at p value <0.05.

Results

A total of 60 subjects were included in the study. Table I shows age, gestational age and weight distribution of the subjects. Table II shows comparison of hemodynamic mean parameters between group A and group B at 0 minute. Table III shows comparison of hemodynamic mean parameters between group A and group B at 3 minutes. Table IV shows comparison of hemodynamic mean parameters between group A and group B at 5 minutes.

Table I: Age, gestational age and weight distribution of the subjects

	Group A n=30 Mean±SD	Group B n=30 Mean±SD	t values	p values
Age in years	24.1±6.0	25.1±4.7	0.70	0.489^{ns}
Gestational age (wks)	39.4±0.7	39.6±0.8	0.921	0.360^{ns}
Weight of the patients (kg)	59.3±3.0	59.9±2.3	0.99	0.327^{ns}

Group A: 5 IU oxytocin bolus, Group B: 5 IU oxytocin IV infusion. p value for age and weight of the patients was reached by unpaired t test and p value for gestational age was reached by Chi squire test. No significant difference was found between group A and group B.

Table II: Comparison of haemodynamic mean parameters between group A and group B at 0 minute (n=60)

0 min	Group A (n=30) Mean±SD	Group B (n=30) Mean±SD	t values	p values
Heart rate (beats/min)	89.5±8.4	86.9±9.5	0.73	0.471
Systolic BP (mm Hg)	116.7±7.5	119.7±6.7	1.63	0.109
Diastolic BP (mm Hg)	75.7±6.8	77.8±4.9	1.42	0.160
SPO_2 (%)	97.7±0.6	98.0±0.6	1.71	0.093
MAP (mm Hg)	88.9±7.0	86.8±4.4	1.93	0.059

Group A: 5 IU oxytocin bolus, Group B: 5 IU oxytocin IV infusion. p value reached from unpaired t-test. The mean difference of all haemodynamic parameters at 0 minute were not statistically significant (p>0.05) in unpaired t-test.

Table III: Comparison of haemodynamic mean parameters between group A and group B at 3 minutes (n=60)

3 minutes	Group A (n=30) Mean±SD	Group B (n=30) Mean±SD	t values	p values
Heart rate (beats/min)	101.8±5.1	90.4±4.4	2.23	0.026[S]
Systolic BP (mm Hg)	95.5±5.4	108.7±4.3	2.16	0.006[s]
Diastolic BP (mm Hg)	60.0±9.9	73.7±8.1	2.39	0.022[s]
SPO_2 (%)	98.7±0.5	98.8±0.5	0.25	0.802[ns]
MAP (mm Hg)	64.2±6.2	74.7±7.3	2.07	0.034[s]

Group A: 5 IU oxytocin bolus, Group B: 5 IU oxytocin IV infusion. p value reached from unpaired t-test. The mean difference of all hemodynamic parameters at 3 minute were statistically significant ($p<0.05$) in unpaired t-test except SPO_2, which was not statistically significant ($p>0.05$).

Table IV: Comparison of hemodynamic mean parameters between group A and group B at 5 minutes (n=60)

5 minutes	Group A (n=30) Mean±SD	Group B (n=30) Mean±SD	t values	p values
Heart rate (beats/min)	105.8±5.2	90.1±2.1	2.27	0.029[S]
Systolic BP (mmHg)	97.3±4.5	106.9±3.6	2.21	0.032[s]
Diastolic BP (mmHg)	61.3±3.6	72.6±4.9	2.21	0.032[s]
SPO_2 (%)	98.9±0.3	98.8±0.4	1.20	0.235[ns]
MAP (mmHg)	64.7±4.2	74.3±5.3	2.55	0.016[s]

Group A: 5 IU oxytocin bolus, Group B: 5 IU oxytocin IV infusion. P value reached from unpaired t-test. The mean difference of all hemodynamic parameters at 5 minute were statistically significant ($p<0.05$) in unpaired t-test except SPO_2, which was not statistically significant ($p>0.05$).

Table V shows amount of blood loss and occurance of postpartum haemorrhage in two groups. In case of cesarean section 800−1000 mL of blood loss is considerable. Patient can tolerate this amount of blood loss. So, more than 1000 mL blood loss is considered as excessive blood loss.

Uterus was found mildly contracted in 27 (90%) cases in group A and in 26 (86.7%) cases in group B at 1 minute. However, at 2 minutes uterus was found moderately contracted in 29 (96.7%) in group A, and 28 (93.3%) in group B. Uterus was found fully contracted at 3 minutes and onwards in all patients in both groups. Regarding uterine contraction, no statistical significant ($p>0.05$) difference was found between two groups in chi square test (Table VI).

Table V: Amount of blood loss and occurance of postpartum haemorrhage in two groups

Complications	Group A		Group B	
	Number	Percentage	Number	Percentage
Ignored bleeding up to 1000 mL	30	100.0	30	100.0
Postpartum hemorrhage	0	0	0	0

Group A: 5 IU oxytocin bolus, Group B: 5 IU oxytocin IV infusion. p value reached from chi square test.

Table VI: States of uterine contraction in both groups

Uterine Contraction	Group A (n=30)		Group B (n=30)		p values
	Number	Percentage	Number	Percentage	
1 minute					
Mildly contracted	27	90.0	26	86.7	
Moderately contracted	3	10.0	4	13.3	0.500
2 minute					
Mildly contracted	1	3.3	2	6.7	
Moderately contracted	29	96.7	28	93.3	0.500
3 minute					
Fully contracted	30	100.0	30	100.0	

Group A: 5 IU oxytocin bolus, Group B: 5 IU oxytocin IV infusion. p value reached from chi square test.

Discussion

Oxytocin, a hormone that is secreted from the pituitary posterior lobe, decreases blood pressure by causing peripheral vasodilation and increasing the HR and induces uterine contraction.[3,4] Uterine contraction by oxytocin is enhanced since there are more intrauterine oxytocin receptors.[15] The oxytocin sensitivity of pregnant women reaches the maximum in the full term of the pregnancy because of the increase of intrauterine oxytocin receptors by gestational estrogen.[10] Hence, during normal delivery, the oxytocin discharged from the pituitary posterior lobe by the obstetric canal stimulus of the fetus can induce labor pain and sufficient uterine contraction with an extreme low-dose of 10 mIU/min.[16] In the case of a planned cesarean section, however, a relatively high-dose of oxytocin (5−20 IU) is intravenously injected since the action of the oxytocin is not normal.[11,12] Since hemodynamic changes are proportional to the intravenously injected dose of oxytocin, studies have been done on effective concentrations and intravenous injection methods.

Sarna et al[11] reported that oxytocin infusion at a rate of 1 IU/min did not show any difference in uterine contraction and blood loss with that of 5 IU/min by intravenous injection even though the total dose may have been more than 5 IU. Kim et al[12] published the same assertion. On the contrary, Zarzur[17] recommended an infusion at a rate lower than 1 IU/min because infusion at a rate higher than 0.25 IU/min may cause such symptoms as hemangiectatic hypotension, tachycardia, increased cardiac output, and myocardial ischemia.

According to many recent studies, oxytocin bolus injection was reported to be more effective than infusion by intravenous injection to reduce blood loss by inducing the appropriate uterine contraction[13], and thus, the minimum bolus dose has been discussed.[18−20] A suggested method to reduce hemodynamic changes is the repeated intravenous injections of a small quantity of a bolus dose and bolus-continuous parallel intravenous injection.[14,21] Svanstrom et al[6] stated that attention is required because a bolus injection of 10 IU oxytocin may cause temporary hypotension and tachycardia as well as myocardial ischemia, apart from the operation, pregnancy, and autonomic blocking by spinal anesthesia. Pinder et al[2] recommended 5 IU as the bolus dose since 10 IU of bolus intravenous dose might not be considered as safe, either. On the contrary, Butwick et al[19] asserted that a dose of more than 5 IU might not be necessary because the appropriate uterine contraction occurred even with a bolus dose of 0.5−3 IU. Their results were similar to our results and the hemodynamic changes were always temporary. This study shows that slower infusion of 5 IU oxytocin can effectively minimize the cardiovascular side-effects but rapid bolus oxytocin causes marked cardiovascular instability.

The current study demonstrated that there was an average decrease in MAP of 24 mm Hg ranging from

19 to 32 mm Hg in group A during 2 to 5 minutes who received 5 IU of oxytocin as a rapid bolus. But in group B average decrease in MAP was 12 mm Hg ranging from 8 to 18 mm Hg during 2 to 5 minutes. It was observed that the changes in heart rate were significantly higher in group A compared to group B during 2 to 5 minutes.

Thus, it was found that the hemodynamic changes varied by the bolus injected oxytocin dose and changes were recovered from in about 4−5 minutes after oxytocin injection. It is shown in this study that delivery of the newborn and the following excitement may affect the HR because parturient women are conscious during cesarean section under spinal anesthesia. However, the main factor of the changes may be the effect of oxytocin itself.

The half-life of oxytocin is about 2−5 minutes and a blood steady state is reached in about 30−60 minutes after intravenous injection.[21] Thus, the oxytocin dose and injection method play an important role in the hemodynamic changes before a steady state is reached. These hemodynamic changes by oxytocin are always temporary and the effect on healthy parturient women is small. However, it may be dangerous to parturient women who have hypovolemia or cardiovascular diseases. Hence, continuous intravenous injection of oxytocin at a low concentration is primarily recommended as a safe injection method for parturient women in a high-risk group.[1,2] Nevertheless, repeated bolus intravenous injection with a small quantity of bolus or parallel intravenous injection of a small quantity of bolus plus continuous injection is also used because of rapid desensitization by which the hemodynamic changes are significantly decreased in the repeated oxytocin than in the initial injection.[14,22]

While the cardiovascular results of this study are unequivocal, it was acceptable that <1000 mL bleeding during cesarean section was ignored in this study. Uterine contraction and uterine bleeding were in satisfactory level in both groups. This study supports the need for caution in using oxytocin as a bolus in cardiovascular unstable patients and offers relatively less adverse effects when given as an infusion over two minutes. The hemodynamic changes are more marked in the IV bolus than the slow IV infusion of oxytocin. Slower injection of oxytocin can effectively minimize the cardiovascular side effects without compromising the therapeutic benefits.

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