Journal of Biology and Today's World
ISSN 2322-3308
Journal home page: http://journals.lexispublisher.com/jbtw

Received: 26 August 2015 • Accepted: 19 November 2015

Research

doi:10.15412/J.JBTW.01041203

Effect of three different doses of oxytocin infusion on hemodynamic changes in cesarean delivery

Shekoufeh Behdad[1], Zohreh Morshedizad[2], Leila Sekhavat[3], Najmeh Heiranizadeh[1*], Sedighe Vaziribozorg[4]

[1] Department of Anesthesiology, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

[2] Shahid Sadoughi University of Medical Sciences, Yazd, Iran

[3] Department of Obstetrics & Gynecology, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

[4] Department of Pain Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

*Correspondence should be addressed to Najmeh Heiranizadeh, Department of Anesthesiology, Shahid Sadoughi University of Medical Sciences, Yazd, Iran; Tell: +989133546657; Fax: +983538224100; Email: n_heiranizadeh@gmail.com.

ABSTRACT

In this study, we compared the effects of three doses of oxytocin infusion on hemodynamice changes at cesarean delivery. This study was double blind randomized clinical trial conducted on 120 patients who underwent cesarean delivery. Patients were randomly divided into 3 groups on the basis of dose of oxytocin to be given after delivery (group 1:10, group 2: 40; group 3: 80 units). Mean arterial blood pressure, heart rate, blood loss and received serum, uterine tone, nausea and vomiting were noted. There was a significant difference in vomiting (p=0.024), uterine tone (p=0.01), and requests for additional uterogenic drug (0.033). However, no significant difference was observed in hemodynamic changes (mean arterial blood pressure, heart rate), blood loss (0.264) and received serum (0.332) among three groups. According to the present study, higher doses of oxytocin are not recommended.

Key words: Cesarean delivery, Hemodynamic, Oxytocin, Uterine tone, Vomiting

1. INTRODUCTION

Cesarean section is a major surgical procedure that promotes the possibility of many types of complications for mothers such as blood loss and uterine atonia (1). Twenty-five percents of maternal mortality is due to bleeding after delivery. Oxytocin is a neurohypophysial hormone that primarily acts as a neuromodulator in the brain. It is released after distension of the cervix and uterus during labor, facilitating birth and breastfeeding. Oxytocin, secreted from the pituitary gland, decreases blood pressure, increases the HR, and induces uterine contraction (2, 3). Moreover, oxytocin causes contractions during labor, assists the uterus in clotting the placental attachment point, and prevents severe blood loss (4). Therefore, it is routinely administered by intravenous bolus and infusion at cesarean delivery after delivery of the fetus; however, the optimal dose is not determined yet (5). Since larger doses and as a rapid bolus are associated with various adverse effects including hypotension, nausea, vomiting, chest pain, headache, flushing, and myocardial ischemia especially in women who are cardiovasculary unstable, bolus is not administered permanently . Different doses for administration of oxytocin (bolus or infusion) have been explored previously, but further studies are needed to establish the effective dose of oxytocin (6). In this study, we compared the effects of three doses of oxytocin infusion on hemodynamic changes, uterine tone, blood loss, and requests for additional uterogenic drug in 120 women during spinal anesthesia for cesarean delivery.

2. MATERIALS AND METHODS

This double-blind clinical trial study obtained ethics approval by Ethics Committee of Medical Sciences University of Yazd (IRCT: 201407082963n18). Obtaining written informed consent, 120 patients were selected randomly for the current study from April to September 2012. The chosen patients were females who underwent cesarean delivery under spinal anesthesia. Exclusion criteria included patients with BMI>35, chronic hypertension, placenta previa, placenta precrata, placenta abruption, placental collaps, gestational age <28 weeks, polyhydroamnious, thrombocytopenia (plt<70000), risk

factors of bleeding and history of tocolytic drugs, and aspirin use. All the patients received 1000 ml of ringer solution and 10 mg metoclopramide before spinal anesthesia. Spinal anesthesia induced with bupivacaine 12.5 mg in vertebral space L3-L4. All patients received 5 units oxytocin bolus immediately after child delivery and cord clamping too. According to random –number table, patients were assigned into three groups of 40. Over 30 minutes, 10, 40, and 80 units of oxytocin were infused in 1000 ml of ringer solution for the first, second, and third groups, respectively. 0.2 mg Metergin IM was administrated given that these doses of oxytocin were insufficient for uterine contraction. Electrocardiograms, pulse oximetry, and non-invasive blood pressure were monitored during spinal anesthesia procedure and surgery. Hemodynamic changes were recorded 30 seconds before oxytocin infusion and were measured at 5-second interval up to 30 after the spinal procedure. Uterine tone was assessed by gynecologist (same gynecologist for all cases) 5 and 15 minutes after placental removal. Patients were asked about nausea and vomiting directly. The collected data were analyzed using Statistical Product for the Social Sciences (SPSS) for Windows, version 15. A *P* value of <0.05 was considered to be statistically significant. The obtained data were analyzed with ANOVA and Chi-square test.

3. RESULTS AND DISCUSSION

One hundred and twenty patients were recruited for the study who randomly divided into three equal groups. Three groups were compared by age, weight, mean arterial pressure (MAP), and heart rate (HR) prior to oxytocin administration. No significant difference was found in terms of age (P-value=0.570), weight (P-value= 0.757), MAP (P-value=0.368), and HR (P-value=0.32) in three groups (Table 1).

Table 1. Comparison of age, weight, MAP and HR before use of oxytocin between three groups

Group oxytocin / variable	10 unit		40 unit		80 unit		P- value*
	Mean	SD	Mean	SD	Mean	SD	
Age(year)	28.20	6.03	28	5.48	29.25	5.41	0.570
Weight(kg)	70.28	10.53	70.20	12.99	72.13	15.19	0.757
MAP	90.98	16.41	87.05	15.41	91.58	14.54	0.368
HR	99.63	20.67	99.15	24.08	99.18	22.88	0.32

*Analysis of Variance (ANOVA). MAP: mean arterial pressure. HR: heart rate.

Administering oxytocin, no significant difference was observed considering hemodynamic changes (mean arterial blood pressure and heart rate) among three groups at different time points (Table 2, Table 3).

Table 2. Comparison of MAP after use of oxytocin between three groups

MAP / Time**	10 unit		40 unit		80 unit		P- value*
	Mean	SD	Mean	SD	Mean	SD	
5	83.80	15.68	83.65	11.21	83.08	10.79	0.965
10	79.28	15.72	84.48	15.45	82.03	13.66	0.303
15	79.10	12.85	83.18	15.14	85	12.12	0.137
20	81.08	15.12	82.20	14.56	83.98	14.01	0.670
25	81.83	14.49	80.33	12.54	85.58	13.38	0.205
30	79.22	14.18	79.03	11.25	86.18	14.6	0.128

*Analysis of Variance (ANOVA). **Second. MAP: mean arterial pressure.

Table 3.Comparison of HR after use of oxytocin between three groups

HR / Time**	10 unit		40 unit		80 unit		P- value*
	Mean	SD	Mean	SD	Mean	SD	
5	99.98	20.83	107.28	23.36	109.75	17.88	0.097
10	100.83	27.17	102.78	28.36	106.08	15.88	0.626
15	99.08	22.48	105.35	26.74	102.08	17.30	0.462
20	98.9	23.94	108.1	22.97	104.50	17.53	0.139
25	98.23	20.5	103.88	24.32	104.6	17.10	0.341
30	103.28	21.04	103.15	22.16	105	14.21	0.893

*Analysis of Variance (ANOVA). **Second. HR: heart rate.

The comparison of bleeding, received serum, and uterine tone over/at 5 minutes after placental removal showed that mean of uterine tone in group 1 and 2 (10 & 40 unit oxytocin) had minimum level (respectively 4.28 & 4.13) and in group 3 (80 uint oxytocin) had maximum level (4.72). There was significant difference regarding uterine tone among three groups over/ at 5 minutes after placental removal (P =0.01). However, no significant difference was observed considering bleeding and received serum among groups (Table 4).

Table 4. Comparison of Bleeding, received serum and uterin tone between three groups

Group oxytocin / Variable	10 unit		40 unit		80 unit		P- value*
	Mean	SD	Mean	SD	Mean	SD	
Bleeding(cc)	343.38	70.12	376.95	105.25	372.75	117.38	0.264
Received serum(L)	1.64	0.36	1.61	0.29	1.72	0.37	0.334
Uterin tone(T5)	4.28	0.9	4.13	1.18	4.72	0.67	0.01**
Uterin tone (T15)	4.75	0.58	4.65	0.66	4.93	0.26	0.326**

*ANOVA. **Pearson Chi-Square.

Comparing the frequencies of vomiting and uterogenic, significant differences in terms of vomiting (P-value=0.024) and requests for additional uterogenic drug (P-value=.033) were found among all three groups (Table 5).

Table 5. Frequency distribution of vomiting and requests for additional uterogenic drug between three groups

Group oxytocin / Variable	10 unit		40 unit		80 unit		P- value*
	N	%	N	%	N	%	
Vomiting	34	85	38	95	40	100	0.024
Uterogenic drug	36	90	38	95	39	97.5	0.033

*Chi-square

The purpose of this study was to determine and evaluate the effects of three different doses of oxytocin on hemodynamic changes in women with viable pregnancies undergoing cesarean delivery at 24 weeks of gestation or greater. Comparing 10, 40 and 80 units of oxytocin infused in 1000 ml of ringer solution, no significant difference was observed in terms of hemodynamic changes among the participants. Mcleod et al. compared the effects of oxytocin infusion and placebo on hemodynamic changes. Both groups received bolus dose of oxytocin then group 1 received oxytocin infusion 30 units and group 2 received placebo. No significant difference was reported in hemodynamic changes (heart rate, systolic and diastolic blood pressure, and stroke volume) between two groups. The aforementioned study is somehow in line with this study. However, the number of groups differs and only one group receives oxytocin. This study demonstrates that administration of oxytocin infusion, even at high doses, did not affect the hemodynamic changes (7). In another study, Thomas et al. compared the effects of infusion and bolus doses of oxytocin on hemodynamic changes in 30 pregnant women underwent non-emergency cesarean delivery. Considering hemodynamic changes between two groups, significant difference was found (P-value< 0.01) and heart rate was reported higher in bolus group. There was no significant difference in terms of bleeding between two groups (8). Thomas et al was also consistent with current study; nevertheless, they merely compared the effects of infusion and bolus doses of oxytocin on hemodynamic. Regarding uterine tone, significant differences in uterin tone were revealed at 5 minutes after oxytocin infusion whereas no significant difference was observed at 15 minutes among three groups. Munnet al. evaluated the effects of two different doses of oxytocin on uterine tone. In their study, there were significant differences in uterine tone between two groups (group 1: 2667mu/min and group 2: 333 mu/min); however, no proper evaluation about uterine tone was reported in this study (9). According to the recent study, there was a non-significant difference considering bleeding and received serum among three groups. Justus et al. explored the effect of two different doses of oxytocin infusion (20 units and 80 units) in 80 pregnant women. There were significant differences in uterine tone and requests for additional uterogenic drug among three groups, but not for bleeding. Comparing two studies, the current study was similar to aforementioned study in terms of exploring the effect of three different doses of oxytocin on bleeding; however, this study did not present proper evaluation about uterine tone (10). Unlike our study, Roach et al. compared the dose and duration of oxytocin used, study population, and outcomes (estimated blood loss, need for additional uterotonics, and change in hematocrit after delivery) in studies. The dose of oxytocin administered ranged from 5 to 100 IU and duration of administration ranged from 5 to 30 seconds (intravenous bolus) to 8 hours diluted in crystalloid. According to their study, higher infusion doses (up to 80 IU/500 mL) and bolus doses of oxytocin appear to be more beneficial than lower doses or protracted administration of a fixed dose at reducing outcome measures of postpartum hemorrhage, particularly among cesarean deliveries7. Moreover, vomiting and requests for additional uterogenic drug in 80 unit's oxytocin group was higher than other two groups (10 and 40 units) based on the recent study. Sartain et al. compared two different bolus doses of oxytocin (5 and 2 units) on hemodynamic changes in 80 pregnant women underwent non-emergency cesarean delivery (10, 11). There was significant differences in heart rate (P-value = 0.030) mean arterial blood pressure (P-value = 0.015) nausea and vomiting but not in bleeding, uterine tone, and requests for additional uterogenic drug between two groups (12). Significant differences in hemodynamic changes and adverse effects (such as nausea and vomiting) between groups in their study could be due to bolus doses; therefore, oxytocin was infused to the patients in our study to reduce hemodynamic changes and adverse effects among groups. In both studies, there were no significant differences in uterin tone and bleeding among different groups indicating no different effects of bolus and infusion doses of oxytocin on bleeding and uterine tone. According to the present

study, higher doses of infused oxytocin did not increase cardiovascular adverse effects. Since there was no significant difference in hemodynamic changes and blood loss regarding different doses of oxytocin, high doses of oxytocin infusion is not recommended.

4. CONCLUSION

According to the present study it seems that high doses of oxytocin infusion is not necessary and could not be recommended. Cesarean section is the most common surgeries in the world; even though, it increases the likelihood of many short and long term complications in mothers such as blood loss and uterine atonia. Oxytocin is a neurohypophysial hormone that causes contractions during labor and prevents severe blood loss; therefore, it is routinely administered by intravenous bolus and infusion at cesarean delivery after delivery of the fetus.

ACKNOWLEDGMENT

The authors would like to express their thanks to the Directors Board of Shahid Sadoughi Medical Sciences University.

FUNDING/SUPPORT

Not mentioned any funding/ support by authors.

AUTHORS CONTRIBUTION

This work was carried out in collaboration among all authors.

CONFLICT OF INTEREST

The authors declared no potential conflicts of interests with respect to the authorship and/or publication of this article.

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