

# Haemodynamic Effects of Oxytocin as Intravenous Bolus or Infusion on Women Undergoing Caesarean Section

Arshi Taj, Mohamad Ommid

## Abstract

The haemodynamic effects of oxytocin in women undergoing caesarean section include tachycardia, hypotension and decrease in cardiac output. These can be sufficient to cause significant compromise in high risk patients. We aimed to find a simple way to decrease these risks while retaining the benefits of oxytocin for attaining uterine contractions and decrease bleeding after delivery. We recruited 50 patients undergoing elective caesarean section. They were randomly allocated to receive 10 U of oxytocin either as bolus injection over 15 seconds (*Group A*, n=25) or an infusion over 5 minutes (*Group B*, n= 25). Uterine tone was assessed as adequate or inadequate by an obstetrician. Intraoperative heart rate, non-invasive blood pressure, and EKG changes were recorded. The haemodynamic data along with the estimated blood loss were compared between the groups. Marked cardiovascular changes occurred in the bolus group the heart rate increased by the 27(13.9) beats per min compared with 7 ( $\pm 4.7$ ) beats per min in the infusion group. The mean arterial pressure decreased by 27( $\pm 8.4$ )mmhg in the bolus compared with 8 ( $\pm 2.7$ ) mm hg in the infusion group. In elective caesarean cases, oxytocin infusion result in lesser hemodynamic changes than bolus oxytocin with lesser emetic episodes and that oxytocin is equally effective in reducing bleeding when given as an infusion.

## Key Words

Anaesthesia, Obstetric, MAP, Complications, Hypotension, Uterus, Oxytocin, Nausea, Anaesthetic factors

## Introduction

Oxytocin is commonly used in obstetric practice as uterotonic drug for induction and augmentation of labour (1) and remains the drug of choice for facilitating uterine contractions during vaginal and operative delivery (2). Several regimens of oxytocin have been tested during cesarean delivery (CD) with variable wanted (uterotonic) and unwanted (cardiovascular) effects (3-7). When given as a rapid IV bolus it causes hypotension and tachycardia (1). Whilst its cardiovascular effects are widely known there is little agreement as to the mechanism by which they occur. Some studies suggest that the preservative chlorobutanol is the cause of these haemodynamic changes. Oxytocin is an octapeptide secreted by the posterior pituitary along with ADH. oxytocin is inactive orally and is generally administered by intramuscular or intravenous routes. It's rapidly degraded in liver and kidney with a plasma half life of 6 min and is still shortened

at term. oxytocin action on myometrium is independent of innervation.

During pregnancy oxytocin is indicated for the initiation or improvement of uterine contractions. Where this is desirable and considered suitable for a reason of foetal or maternal concern in order to achieve vaginal delivery. It is indicated for induction of labour in patients with an indication for the excitation of labour such as Rh incompatibility, maternal diabetes preeclampsia at or near term when delivery is in the best interest of mother and foetus or when membranes are prematurely ruptured and delivery is indicated (8) stimulation or reinforcement of labour as in selected cases of uterine inertia (9) as adjunctive therapy in the management of incomplete or inevitable abortion. In the first trimester curettage is generally considered primary therapy. In the second trimester oxytocin is successful in emptying the uterus.

From Department of Anaesthesiology & Critical Care, Government Medical college & Associated Hospitals, Srinagar, J&K - India  
Correspondence to : Dr Arshi Taj, Lecturer, Department of Anaesthesiology & Critical Care, GMC Srinagar, J&K-India

Oxytocin is given to women during caesarean section to decrease blood loss. When given as a rapid i.e. bolus it causes hypotension and tachycardia (1). Pinder and colleagues (8) studied the haemodynamic effects of i.e. boluses of oxytocin (5,10) units in women having caesarean section under spinal anaesthesia. Weis and colleagues (7) showed that patients receiving an infusion were more haemodynamically stable; these workers used 10 U of oxytocin.

### Material and Methods

We recruited 50 patients undergoing elective caesarean section. They were randomly allocated into the bolus group (*Group A*) and infusion groups (*Group B*) and each group having 25 patients each. Exclusion criteria included patients with placenta praevia, ruptured membranes, active labour pain hypertension preeclampsia or diabetes mellitus as these could lead to instability during caesarean section. The monitoring and anaesthetic technique was same for all the women. They received ranitidine 150mg on the morning of surgery. On arrival at the theatre ECG and pulse oximetry monitoring were commenced and non-invasive blood pressure recorded. A large bore i.v. cannulae was placed and ringer lactate 500ml infused and thereafter spinal anaesthesia was established in the sitting position at L3-L4 interspace using a 25 gauge spinal Quincke needle. Hyperbaric bupivacaine 0.5% (3ml) was injected intrathecally. Block height was measured by temperature and fine touch bilaterally. Surgery was commenced once the block was reached T4 to cold sensation and T6 to fine touch. Hypotension was treated with ephedrine 3mg boluses aiming to restore mean arterial pressure to within 20% of preoperative values. Oxytocin was administered at delivery either as an IV bolus of 10 u diluted to 5 ml with normal saline was given over 15 seconds or 10 u diluted to 15-20ml of saline and given over 5 minutes. Intraoperative HR, MAP, and electrokardiogram (EKG) changes were recorded. HR was measured at 30-second interval up to 2.5 minutes, then at 5 and 10 minutes. MAP was measured at 1-minute interval up to 5 minutes, then

**Table 1. Demographic Data**

	BOLUS GROUP	INFUSION GROUP
Age (Yr)	29.4 ± 3.2	28 ± 3.5
Indication For C Section		
1.Previous c section	12	10
2.Breech	3	6
3.Oligohydramnios	4	2
4.Others	4	5
5.Parity (median)	1	2
Ephedrine Used	12mg	10 mg
Estimated Blood Loss	500 ml	500 ml

at 7 and 10 minutes. Any EKG changes were monitored.. The last measurement of NIBP and HR before giving oxytocin was recorded as a baseline for subsequent changes. The placenta was delivered by controlled cord traction. Uterine tone was assessed by the obstetrician at 5, 10, 15, and 20 min on a five-point scale, where 1-atonic; 2-partial but inadequate contraction; 3-adequate contraction;4-well contracted; and 5 -very well contracted

The study `period started before giving oxytocin and continued for a further 10 minutes after oxytocin was given. The period allowed us to compare the hemodynamic changes between the 2 methods of administration of oxytocin. Any adverse events like chest pain, flushing, and vomiting was also observed. The occurrence of nausea or vomiting, both before and after the oxytocin bolus, was assessed by patient report and frequent direct questioning until the patient left the operating theatre. Emetic symptoms were treated by correction of any hypotension, then if necessary with rescue antiemetics (one or more of i.v. metoclopramide 10 mg and ondansetron 4 mg).

If uterus was not adequately contracted after 3 minutes, oxytocin 2 IU IV was given as rescue dose. A maximum of 2 rescue doses were given. If still the uterus was not contracted, ergometrine 0.25 mg (i.v.), then intramyometrial prostaglandin carboprost tromethamine 0.25 mg was given. The estimated blood loss during caesarean section was recorded. Blood loss was estimated by visual assessment of suction bottles and drapes. From previous studies (8,9) it was predicted that changes in HR would be more reliable than changes in MAP when using non-invasive monitoring, so the primary outcome was the maximum change in HR after oxytocin A difference in MAP of 10mmhg or above, between the two groups was considered to be clinically significant.

### Statistical Analysis

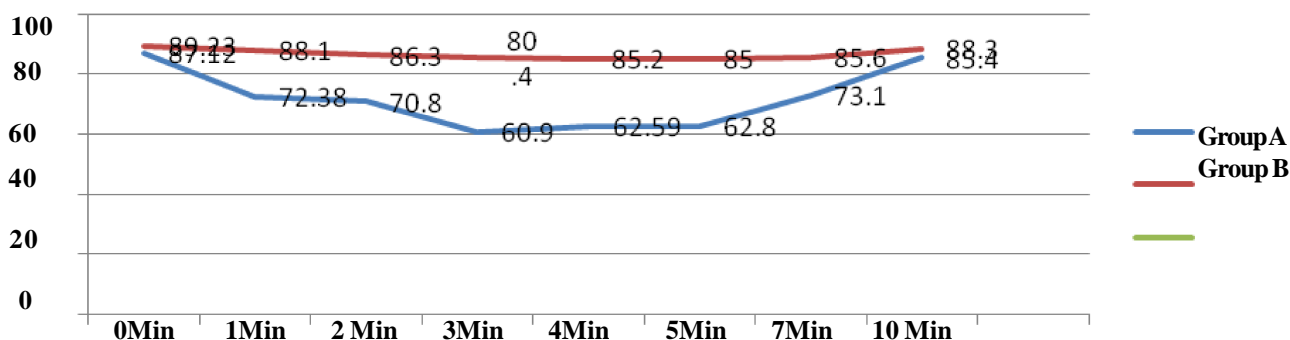
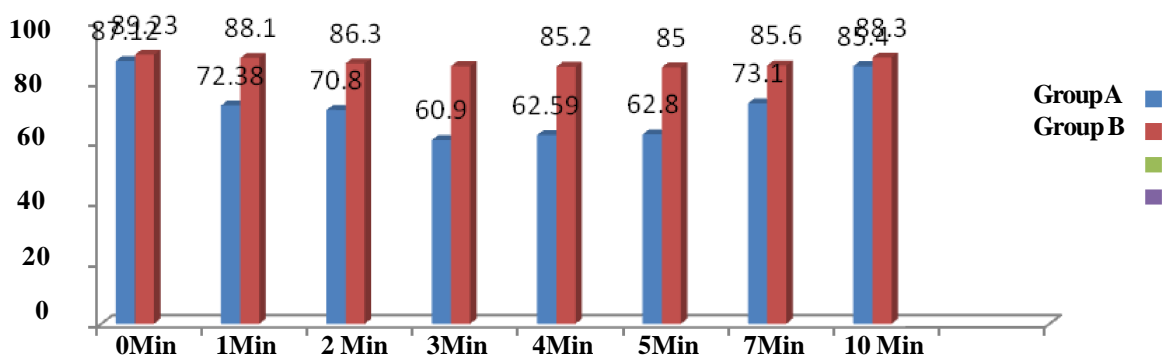
Patient characteristics, obstetric & intraoperative data were presented as mean ± SD. Numerical data were analyzed with Student's t-test and categorical data were analyzed with Chi-square test. AP <0.05 was considered significant. Data was analysed using SPSS version 12.

**Table 2. Changes in MAP between the two Groups over the Study Period**

	0 min	1 min	2 min	3 min	4 min	5 min	7 min	10 min
<b>Group A</b>	87.12 ± 8.7	72.31± 7.8	70.82± 8.2	60.93± 8.4	62.59± 7.9	62.88± 7.2	73.1± 8.2	85.4± 8.8
<b>Group B</b>	89.23± 7.9	88.14± 8.5	86.3± 7.8	80.41± 2.7	86.20± 7.6	85± 7.81	85.6± 7.9	88.3± 7.9
<b>P Value</b>	0.145	0.0001	0.0001	0.001	0.0001	0.0001	0.0001	0.0001

Values are expressed as mmHg ± SD

**Fig A&B. Comparison of Map Between the Two Groups at Different Time Intervals**



**Table 3. Changes in Heart Rate (HR) between the two Groups Over the Study Period**

	0 sec	30 sec	60 sec	90 sec	120 sec	150 sec	300 sec	600 sec
<b>Group A</b>	83.46 ±9.8	108.56±1 4.7	110.25±1 3.9	107.90±1 3.1	109.26±1 3.6	108.65±12. 87	102.65±11. 78	95.36±3. 8
<b>Group B</b>	82.48 ±11.2	85.31±11. 2	89.11±11. 57	79.53±10. 82	86.42±11. 4	87.14±12.0 2	88.1±12.56 0.0001	84.10±1 1 .5
<b>P value</b>	0.78	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001

Values are expressed as mean heart rate ± SD

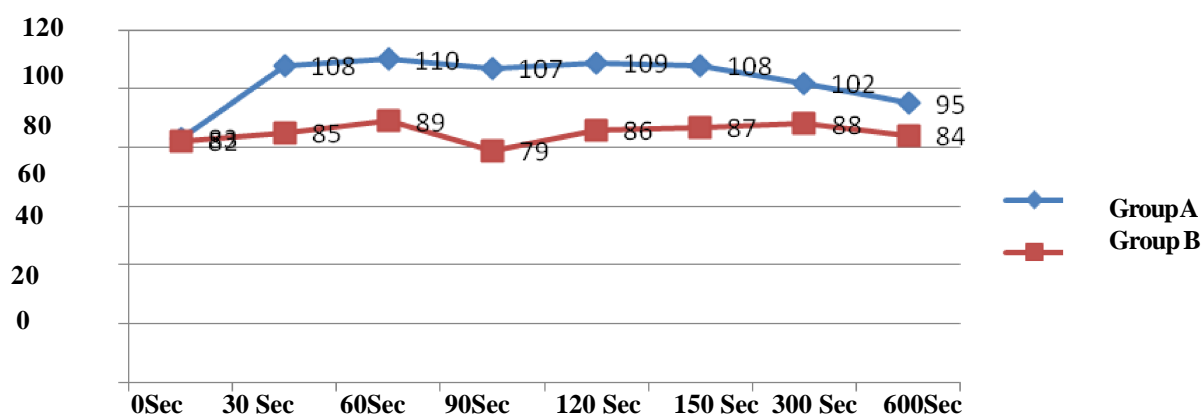
**Results (Table-1-4; Fig A-C)**

Fifty (50) women were successfully recruited. Two women were excluded from the analysis as they had to be converted to general anaesthesia on account of failure of spinal anaesthesia. Patient characteristics are shown in table no.1

A small statistically significant difference was seen in the women age in the two groups. Use of ephedrine, postoperative infusion of oxytocin (40U over 4 hours) and estimated blood loss were similar in the two groups.

Baseline heart rate and MAP were similar in both the groups with a mean MAP in bolus group of 87mmHg; infusion group 89mmHg, mean heart rate in bolus group

**Fig C. Comparison of Heart Rate Changes At Different Study Time Intervals**



**Table 4. Outcomes After Oxytocin Bolus. Data Presented as Number, Mean (SD), or Median (range)**

	Group a (n=25)	Group b (n=25)	P-value
Fluids given (ml)	2000 (1000–3000)	2000 (1000–3500)	0.094
Increase in HR (beats/ min)	27 (±13.9)	7 (±4.7)	0.0001
Decrease in MAP (mm Hg)	27 (±8.4)	8 (±2.7)	0.0001
Nausea	5	2	0.041
Vomiting	3	1	0.026
Antiemetic treatment	5	2	0.078
Blood loss	500 (150–1200)	500 (200–2000)	0.889
Additional uterotonic treatment at 5 min	2	3	1.000
Additional uterotonic treatment overall	6	6	1.000

83 ± 9.8 beats/min, infusion group 82 ± 11.2 beats/min. A rapid increase in heart rate of 27 beats /min was seen at 1 min in the bolus, and remained raised for next 120 seconds. In contrast mean heart rate increased by 7 beats per min in the infusion group which occurred slowly over the duration of infusion. A decrease in MAP of upto 27 (±8.4)mmHg occurred at 1 min in bolus group with recovery to baseline in another 2 min. The infusion group in contrast had a decrease in MAP of upto 8 (±2.7)mmHg during the study period. The cardiovascular changes in the two groups were statistically significant  $p < 0.001$ .

**Discussion**

Pregnant women undergoing CD are at increased risk of obstetric hemorrhage, mainly due to uterine atony. Oxytocin is the mainstay of treatment of uterine atony (11) Prophylactic routine use of oxytocin has been shown to reduce the incidence of postpartum hemorrhage by up to 40%. (12) Our study shows that infusion of oxytocin can minimize the cardiovascular side effects of a bolus dose without compromising the therapeutic benefits.

Uterine oxytocin receptor population increases progressively during pregnancy and reaches a peak near term reaching almost 80 times higher than non pregnant

uterus. As the non-laboring uterus at term remains more sensitive to oxytocin, low dose of oxytocin might have an optimum efficacy while not inviting the deleterious effects of high dose of oxytocin. (13) In this study, we selected mothers undergoing elective CD not in labour expecting a good response with low dose of oxytocin. (9) It is observed that adequate uterine tone can be achieved with small bolus doses like 0.5-3 IU of oxytocin, (4) Increasing the bolus dose of oxytocin to above 10 IU during elective CD does not offer any advantage. (14) The cardiovascular effects of oxytocin in bolus doses is hypotension and tachycardia. our study demonstrated an average decrease in MAP of 27mmhg (±13.9) in healthy women having an elective caserean section who received 10 u of oxytocin as a rapid bolus. In our study 2 women had a MAP decrease to 31mmhg. It took them 2 min to return to baseline after bolus injection.

During this period of decrease in MAP there were complaints of nausea or vomiting in 5 patients of group A and 3 patients of group B easily treated with antiemetics and correction of fall In MAP It is reassuring for the anaesthetist who prefer to maintain a cardiovascular equilibrium so this physiological insult can be avoided

simply by giving oxytocin over 5 minutes. The small decrease in MAP  $4 (\pm 2.7)$  mmHg and the small increase in heart rate are certainly clinically preferable. A significant fall of MAP 30 seconds after administration of a 10 IU bolus oxytocin, but a significant increase in HR and cardiac output (CO), occurred 1 minute after 5 IU administration has been reported earlier. (8) In our study patients were randomly allocated into bolus and infusion groups. Low dose (5u) is recommended, this is even supported by the work of Pinder & colleagues (8) who showed dose related haemodynamic effects. Other work has been done by J.S. Thomas and colleagues (9) in which they have used invasive haemodynamic monitoring to look for haemodynamic changes during bolus and infusion and found that infusion group is better than bolus.

Although decreasing (or omitting) the oxytocin bolus minimizes haemodynamic changes, (8,9) many doctors may be cautious about doing so because of concerns about poor uterine contraction and resultant increased bleeding & CVS effects. (16-19) We found no differences between the groups in blood loss, uterine tone, or the need for further uterotonics. Rapidly injected large doses of oxytocin are known to produce various adverse effects such as hypotension, nausea, vomiting, chest pain, headache, flushing, myocardial ischemia, ST-T segment changes, pulmonary edema, and severe water intoxication with convulsions. (13). ED 90 of oxytocin reported to prevent uterine atony and PPH after an elective CD is 0.29 IU/minute, or approximately 15 IU of oxytocin in one liter of IV fluid administered over one hour period. (15) This dose of oxytocin infusion is 30% less than the infusion dose currently in use.

An important limitation of our study is that we only studied elective patients at low risk of postoperative bleeding. The situation at emergency Caesarean section is quite different: as uterine responsiveness may be greatly decreased in this situation, higher doses of oxytocin are often required, and the early use of alternative uterotonics (e.g. ergometrine) may be preferable (5,20).

### Conclusion

The observation that infusion of oxytocin results in less haemodynamic change than bolus oxytocin, with less nausea supports the need for caution using oxytocin as bolus doses.

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