

# Comparison of Different Dosages of Oxytocin Required After Elective Caesarean Delivery for Adequate Uterine Contraction

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## ABSTRACT

**Background:** Following the delivery of the baby during a cesarean delivery, a uterotonic drug is administered as a standard procedure. The primary purpose of this is to prevent and treat uterine atony, which is the leading cause of obstetric hemorrhage. Oxytocin is typically the first-line uterotonic drug used for this purpose. **Objective:** Oxytocin was compared with 5 IU given IV 15 seconds after the delivery of baby and clamping of umbilical cord in women undergoing elective caesarean delivery, uterine tone was assessed at 3, 6 and 9 minutes and MAP was measured at 5 and 10 minutes. **Study Design:** A randomized control trial. **Settings:** Study was conducted at maternal and child health center (MCH) Department of Anesthesia PIMS Islamabad Pakistan. **Duration:** From June 2020 to November 2020. **Methods:** A total of 170 patients were included. Patients were randomly divided into two groups: Group A: Patients who received 3 IU oxytocin IV, Group B: Patients who received 5 IU oxytocin IV Adequate uterine tone and fall in mean arterial pressure was compared between both groups. Uterine tone was assessed by obstetrician at 3, 6 and 9 minutes and fall in MAP was recorded at 5 and 10 minutes after administration of bolus dose. All of the information was recorded via study proforma and SPSS version 20 was used for the data analysis. **Results:** A total of 170 patients were enrolled, their overall mean age was  $29.55 \pm 4.94$  years. 96.5 % patients in group A had adequate uterine tone at 3 minutes compared with 98.8 % patients in group B ( $p = 0.312$ ), 90.6 % patients in group A had adequate uterine tone at 6 minutes compared with 95.3 % patients in group B ( $p = 0.231$ ) and 83.5 % patients in group A had adequate uterine tone at 9 minutes compared with 87.1 % patients in group B ( $p = 0.516$ ). 9.4% of patients in group A had hypotension at 5 minutes compared with 31.8% patients in group B ( $p = 0.000$ ) whereas 18.8% of patients in group A had hypotension at 10 minutes compared with 28.2% patients in group B ( $p = 0.148$ ). **Conclusion:** Adequate uterine contraction can be achieved with 3 IU of oxytocin. 3 IU of oxytocin observed to be an appropriate dose to use during elective caesarean deliveries to achieve adequate uterine tone without causing significant hypotension.

**Keywords:** Uterotonic, Oxytocin, Uterine atony, Obstetric haemorrhage, Bolus, Hypotension, Elective caesarean.

## INTRODUCTION

Uterotonic drug is given routinely after the delivery of the baby during caesarean delivery.<sup>1</sup> Oxytocin, first line Uterotonic drug is used to prevent and treat uterine atony, which is the most common reason of obstetric hemorrhage.<sup>2,3</sup> Postpartum haemorrhage can result in

maternal morbidity and mortality. Oxytocin used in mothers is a synthetic analogue of posterior pituitary hormone. Oxytocin receptors are not only located in uterus but also in heart and blood vessels.<sup>4</sup> As compared to other classes of uterotonics oxytocin is the safest uterotonic agent.<sup>5</sup> But when given as large bolus dose rapidly oxytocin has effects on cardiovascular system i.e.

vasodilatation, reflex tachycardia and increase in cardiac output which results in increased myocardial oxygen requirement.<sup>6,7</sup> Initially bolus dose of 3- 5 IU slow IV is recommended which is followed by infusion titrated to effect.<sup>1</sup> As half-life of oxytocin is short, therefore at elective delivery slow bolus IV dose of oxytocin should be followed by an infusion to decrease the risk of primary PPH thus improving outcomes.<sup>8</sup> Infusion for maintenance is usually given at the rate of 10 IU per hour i.e. 40 IU over 4 hours to maintain myometrial contraction and to reduce blood loss.<sup>9</sup> Bolus dose as low as 1 IU can produce adequate effect on uterine tone.<sup>10</sup> Oxytocin when given in low dose and slowly, CVS effects are minimal.<sup>2,7</sup> Increasing the dose more than 5 IU during elective c-section has no additional advantage on uterine tone.<sup>11</sup> Use of high bolus dose has serious CVS effects especially in hypovolemic patients and mothers with myocardial dysfunction.<sup>12</sup> Therefore, oxytocin has a narrow therapeutic index as it has dose dependent adverse effects.<sup>7</sup> Butwick et al found that adequate tone of uterine smooth muscles after delivery of fetus can be achieved with dose 0.5 to 3 IU of oxytocin given slowly.<sup>11,12,13,14</sup> Another study concludes estimated effective dose in 90% of patients undergoing elective caesarean section for adequate tone of uterine smooth muscles was 0.35 IU of bolus dose of oxytocin which is far less than 5 to 10 IU dose used in clinical practice.<sup>15</sup> Previous study showed that adequate uterine contraction at 3 minutes was observed in 100% of patients who were given 3 IU oxytocin and 93% of patients who were given 5 IU oxytocin whereas fall in mean arterial pressure at 1 minute occurred in 25% of obstetric patients with 3 IU and 45% of patients with 5 IU oxytocin.<sup>16</sup> Thus, when oxytocin is given in low dose slowly after elective caesarean delivery blood pressure remains stable and effect on uterine tone is adequate as with 5 IU.<sup>17</sup> In this study, bolus dose of 3 IU of oxytocin was compared with 5 IU given 15 seconds after delivery of baby and clamping of umbilical cord in women undergoing elective caesarean delivery, uterine tone was assessed at 3, 6 and 9 minutes and MAP was measured at 5 and 10 minutes. In practice, higher dosage of oxytocin i.e., 5 to 10 IU is given intravenously to achieve adequate uterine contraction but it causes hypotension in patients. So, with lower dosage of oxytocin IV bolus given slowly, adequate uterine contraction can be achieved as well as there is minimal risk of hypotension.

## METHODS

This randomized control trial was done at the Department of Anesthesiology and Critical Care SZABMU, Pakistan Institute of Medical Sciences, Islamabad. Duration of study was six months (1st Jun 2020 to 30th Nov 2020). The study was carried out following the authorization of the hospital's ethical

committee. Consecutive non-probability sampling technique was used. All the woman who is undergoing an elective caesarean section using spinal anesthesia, age between 18- 40 years, ASA class 2 and 3 and having history of 2 or more than 2 caesarean sections were included. Women with active labour, premature rupture of membranes, multiple pregnancy, hypersensitivity to injection oxytocin, pregnancy induced hypertension or preeclampsia, patients at risk of bleeding greater than 800 ml, history of inherited or acquired coagulation abnormalities, thrombocytopenia, pregnant women who are having an elective Caesarean section performed while under general anesthesia and previous history of cardiac disease were excluded. Preoperative assessment was done one day before surgery and patients were kept nil per month for 6 hours for solid food and 2 hours for clear fluids. Written informed consent was taken from all the patients and patients were counselled. In the preoperative period, two peripheral IV lines of 18G were inserted and all patients received 500 ml of Ringer's lactate within 30 minutes before spinal anesthesia. All the patients were pre-medicated with Injection Omeprazole 40mg and Injection Dimenhydrinate 50mg intravenously. Upon arrival in operation theatre, noninvasive blood pressure cuff, pulse oximeter and electrocardiograph leads were attached to the patients. Monitoring for blood pressure, heart rate, oxygen saturation and electrocardiograph was done. Mean arterial pressure and heart rate were documented. The patients were randomly divided into two groups using computer generated random table. Group A: Patients who received 3 IU of bolus dose of oxytocin intravenously. Group B: Patients who received 5 IU of bolus dose of oxytocin intravenously. Subarachnoid block was given to the patients with 25-gauge spinal needle in sitting position at L3-L4 space under aseptic measures and 12.5 mg of 0.5% hyperbaric bupivacaine was given intrathecal. Patients were then placed in supine position along with left lateral tilt. In patients with failure of subarachnoid block, general anesthesia was given and patients were excluded from the study. Monitoring of mean arterial pressure, heart rate, oxygen saturation and electrocardiograph were continued. Mean arterial pressure was recorded before giving the bolus dose of oxytocin intravenously. Adequate uterine contractions were evaluated at 3 minutes 6 minutes and 9 minutes after the administration of bolus dose of oxytocin 15 seconds after the delivery of baby and clamping of umbilical cord. When uterine tone was said to be inadequate at 3, 6 or 9 minutes after the administration of bolus dose of 3IU or 5IU oxytocin intravenously then oxytocin infusion was started, 40 IU of oxytocin in 500ml normal saline at 125ml/h. Mean arterial pressure was recorded again. Any fall in mean arterial pressure as compared to the mean arterial pressure before the administration of oxytocin was recorded at 5 minutes and

10 minutes. Decrease in mean arterial pressure below 60 mmHg along with increase in heart rate was treated with 50µg Phenylephrine intravenously. Monitoring of mean arterial pressure was continued. The collected data was entered and analyzed using SPSS version 20.0.

**RESULTS**

A total of 170 patients were enrolled in this study, their overall mean age was 29.55 ± 4.94 years. Particularly the mean age in group A was 30.14 ± 5.01 years and in group B was 28.95 ± 4.83 years. Table.1

The percentage of patients with adequate uterine tone at 3, 6 and 9 minutes after bolus administration was 166 (97.6%), 158 (92.9%) and 145 (85.3%) as shown in Table 2. Similarly, percentage of patients with fall in mean arterial pressure at 5 and 10 minutes was 35 (20.6%) and 40 (23.5%). Table 2.

In accordance to compare outcomes of 3 IU and 5 IU of oxytocin required after elective caesarean delivery for adequate uterine contraction, the (96.5%) of the patients in group A and (98.8%) cases of group B had adequate uterine tone at 3 minutes (p = 0.312). Although the (90.6%) of the patients in group A and (95.3 %) cases of group B had adequate uterine tone at 6 minutes (p = 0.231), while (83.5%) of the patients in group A and 87.1 %) cases of group B had adequate uterine tone at 9 minutes (p = 0.516). According to the comparison of mean arterial pressure decline in groups A and B at 5 and 10 minutes following a bolus dose of oxytocin. 8 of 85 patients in group A, showed a reduction in mean arterial pressure at 5 minutes, but 27 of 85 patients in group B, who received 5 IU, (p = 0.000). At 10 minutes, mean arterial pressure dropped in 16 patients in group A and 24 of group B (p=0.148). Table.2 Furthermore, adequate uterine contractions were statistically insignificant at 3, 6 and 9 minutes in the both groups according to age (p->0.05). The mean arterial pressure decline was statistically insignificant in both groups according to age (p= >0.05), while it was statistically significant at 5 minutes with age group of 31-40 years (p=0.000). Table.3

**Table 1: Demographic and clinical characteristics of patients n=170.**

Variables	Statistics	
Mean age	Group 1(Oxytocin 3 IU) n= 85	30.14±5.01
	Group 2 (Oxytocin 5IU) n= 85	28.95±4.83
	Overall n= 170	29.55±4.947
Number of previous c-sections	Group 1(Oxytocin 3 IU) n= 85	2.26±0.51
	Group 2 (Oxytocin 5IU) n= 85	2.34±0.60
Frequency of ASA class	Class II	140   82.4%
	Class III	30   17.6%
Fall in Mean Arterial Pressure	Fall in Mean Arterial Pressure at 5 min	35   20.6%
	Fall in Mean Arterial Pressure at 10 min	40   23.5%

**Table 2. Prevalence of adequate uterine tone and fall in mean arterial pressure after bolus administration of 3 IU & 5 IU of oxytocin**

Variables			Oxytocin Dose		Total	P-value	
			3 IU	5 IU			
Adequate uterine contraction	At 3 minutes	Yes	82 96.5 %	84 98.8 %	166 97.6 %	0.312	
		No	3 3.5 %	1 1.2 %	4 2.4 %		
	At 6 minutes	Yes	77 90.6 %	81 95.3 %	158 92.9 %	0.231	
		No	8 9.4 %	4 4.7 %	12 7.1 %		
	At 9 minutes	Yes	71 83.5 %	74 87.1 %	145 85.3 %	0.516	
		No	14 16.5 %	11 12.9 %	25 14.7 %		
	Fall in mean arterial pressure	At 5 minutes	Yes	8 9.4 %	27 31.8 %	35 20.6 %	0.000
			No	77 90.6 %	58 68.2 %	135 79.4 %	
		At 10 minutes	Yes	16 18.8 %	24 28.2 %	40 23.5 %	0.148
			No	69 81.2 %	61 71.8 %	130 76.5 %	

**Table 3. Adequate uterine tone and fall in mean arterial pressure after bolus administration of 3 IU and 5 IU of oxytocin with respect to age n=170**

Variables		Age groups		Oxytocin Dose		Total	P-value
				3 IU	5 IU		
Adequate uterine contraction	At 3 minutes	18 to 30 years	Yes	51	59	110	0.132
			No	02	00	02	
		31 to 40 years	Yes	31	25	56	0.881
			No	01	01	02	
	At 6 minutes	18 to 30 years	Yes	46	57	103	0.056
			No	07	02	09	
		31 to 40 years	Yes	31	24	55	0.435
			No	01	02	03	
	At 9 minutes	18 to 30 years	Yes	44	51	95	0.614
			No	09	08	17	
		31 to 40 years	Yes	27	23	50	0.654
			No	05	03	08	
Fall in mean arterial pressure	At 5 minutes	18 to 30 years	Yes	06	14	20	0.087
			No	47	45	92	
	31 to 40 years	Yes	02	13	15	0.000	
		No	30	13	43		
	At 10 minutes	18 to 30 years	Yes	10	14	24	0.531
			No	43	45	88	
31 to 40 years	Yes	06	10	16	0.095		
	No	26	16	42			

**DISCUSSION**

Postpartum haemorrhage is the leading cause of morbidity and mortality in obstetric patients.<sup>18</sup> The most

common reason of obstetric haemorrhage is inadequate uterine tone. Oxytocin is the uterotonic of choice, causes contraction of uterine smooth muscles thus it reduces postpartum atony and haemorrhage and improves outcomes in parturient.<sup>15</sup> It is routinely given during delivery whether vaginal or caesarean delivery. Recently use of 5 IU of oxytocin is questioned, the particular reason is increasing the dose more than 5 IU has no additional advantage on uterine tone and oxytocin has a narrow therapeutic index and has dose related adverse effects.<sup>7,11</sup> Higher bolus dose  $\geq$  5 IU can lead to hemodynamic instability, has emetic effect, can cause headache and bad metallic taste.<sup>7</sup> Dose more than 5 IU has serious cardiovascular effects in patients who are hypovolemic and have limited cardiac reserve.<sup>12</sup> Most common effect is dose dependent hypotension. Result of a study shows fall in blood pressure occurred in 4% of patients who received 2 IU bolus dose of oxytocin and in 17.33% of patients who received 5 IU bolus dose intravenously.<sup>19</sup> So when oxytocin is given in low dose less than 5 IU slowly after elective caesarean delivery blood pressure remains stable and effect on uterine tone is adequate as with  $\geq$  5 IU dose.<sup>17</sup> This study has been conducted at SZABMU PIMS Islamabad, outcomes of 3 IU and 5 IU bolus dose were compared between two groups of obstetric patients undergoing elective caesarean delivery under subarachnoid block. Outcomes were measured as adequate uterine contraction and fall in mean arterial pressure. Obstetrician, who was blinded to oxytocin dose rate uterine tone as adequate or inadequate after 3, 6 and 9 minutes.

In our study, adequate uterine tone was assessed at 3 minutes (96.5% vs. 98.8%,  $p=0.312$ ), 6 minutes (90.6% vs. 95.3%,  $p=0.231$ ) and 9 minutes (83.5% vs. 87.1%,  $p=0.516$ ). No statistically significant difference found in adequate uterine contraction at 3, 6 and 9 minutes between group A and B. When tone was inadequate at any time, oxytocin infusion was started at the rate of 40 IU per hour. After the study period, patients received maintenance dose of IV oxytocin infusion. Mean arterial pressure was measured before administration of oxytocin. Fall in mean arterial pressure was considered when there was  $\geq$  10% fall in mean arterial pressure. It was measured at 5 and 10 minutes. At 5 minutes after administration of oxytocin fall in MAP occurred in 9.4% patients in group A vs. 31.8% patients in group B, ( $p$  value 0.000). However, at 10 minutes after administration of oxytocin fall in MAP occurred in 18.8% patients in group A vs. 28.2% patients in group B,  $p$  value 0.148. This shows at 5 minutes, there was a significant difference between both groups. Fall in mean arterial pressure was significantly higher ( $p=0.000$ ) in patients who received 5 IU bolus dose of oxytocin IV at 5 minutes. However, there was no significant difference between both groups at 10 minutes after drug administration. In patients with fall in

MAP less than 60 mmHg along with increase in HR were treated with vasoconstrictor 50 micrograms phenylephrine intravenously. In the comparison of this study, the Butwick et al in a double blind randomized controlled study compared the effects of 0.5 IU, 1 IU, 3 IU and 5 IU oxytocin on uterine tone. Uterine tone was assessed by obstetrician at 2, 3, 6 and 9 minutes, and the concluded that the adequate uterine contraction can be achieved with dose 0.5 to 3 IU oxytocin.<sup>7</sup> In another study, Sartain et al compared bolus dose 2 IU vs. 5 IU at elective caesarean delivery in aspect of uterine tone and hemodynamic effect. They observed that with 5 IU greater decrease in MAP and greater increase in HR and nausea vomiting occurred among parturient.<sup>8</sup> Langesaeter et al enrolled 60 patients in the study and administered 5 IU bolus intravenously rapidly. More than 20% fall in systolic blood pressure was observed in all patients.<sup>14</sup> Thomas et al also compared hemodynamics in parturient who were given 5 IU and 3 IU bolus dose and observed similar findings with 3 IU.<sup>14</sup> So to minimize hypotension and tachycardia, even small doses less than 3 IU should be used. Another study concludes estimated effective dose in 90% of patients undergoing elective caesarean section for adequate uterine tone was 0.35 IU of bolus dose of oxytocin.<sup>15</sup> Previous study concluded that percentage of adequate uterine contraction at 3 minutes after 3 IU oxytocin was 100% and with 5 IU was 93% whereas percentage of fall in MAP at 1 minute was 25% with 3 IU oxytocin and 45% with 5 IU oxytocin given intravenously.<sup>16</sup> In a study by King et al 5 IU bolus was compared with no bolus before prophylactic infusion. It was observed that bolus dose prior to infusion reduces the need of other uterotonic drugs within 24 hours of C-section.<sup>7</sup> In 2012, it was concluded by Stephens and Bruessel that bolus dose of oxytocin should be followed by an infusion.<sup>15</sup> Half-life of oxytocin is 1 to 6 minutes.<sup>5</sup> There are certain limitations to this study, adequate uterine contraction was assessed by obstetrician who was blinded to the dose of oxytocin. Uterine tone in 170 patients was assessed by different obstetricians and different obstetricians might have different assessment of satisfactory uterine tone. Secondly, this was subjective assessment we did not use any objective method to assess uterine tone. Patients who had inadequate uterine tone at 3, 6 and 9 minutes after the bolus dose administration, we did not administer rescue bolus dose instead we started maintenance oxytocin infusion. Obstetric patients who had inadequate uterine tone at 3 or 6 minutes and oxytocin infusion was started, oxytocin response at 9 minutes might be altered but we could not allow inadequate uterine tone to remain untreated. Similarly, the women who had hypotension at 5 minutes received vasoconstrictor, so response at 10 minutes might be altered but we could not leave the patient hypotensive. Changes in blood pressure or mean arterial pressure during caesarean section can have other causes i.e.

sympathetic blockade due to subarachnoid block, compression of aorta and inferior vena cava, bleeding and use of vasoconstrictor agents.

## CONCLUSION

In conclusion, administration of 3 IU of oxytocin slow intravenously during elective caesarean delivery has the same therapeutic effect on uterine tone as 5 IU of oxytocin. However, fall in mean arterial pressure is significantly lower in patients administered with 3 IU bolus dose of oxytocin compared to 5 IU bolus dose at 5 minutes after administration, there is no significant difference at 10 minutes. So, we recommend the use of 3 IU of oxytocin slow intravenously after elective caesarean delivery followed by oxytocin infusion.

## LIMITATIONS

This was a limited sample size and single centre study.

## SUGGESTIONS / RECOMMENDATIONS

Further, larger-scale trials, particularly at the local level, are recommended to prove the findings

## CONFLICT OF INTEREST / DISCLOSURE

None.

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