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Comparison of three different regimes of oxytocin in patients undergoing elective caesarean section – to estimate the haemodynamic changes and uterine contraction

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Abstract

Background: In spite of repeated use of oxytocin, the minimum effective dose oxytocin is not clear. Oxytocin when administered in excess dose may cause unwanted cardiovascular effects like tachycardia and hypotension and when the dose is inadequate it can result in uterine atony and increased uterine bleeding. We compared three different regimes of oxytocin in patients undergoing elective caesarean delivery, to compare haemodynamic changes and uterine contraction.

Methods: Ninety patients undergoing elective caesarean delivery were administered an i.v bolus of either 3U or 5U and without bolus of oxytocin after delivery, followed by an oxytocin infusion of 20 U/h. Spinal anaesthesia was administered to all patients and with MAP more than 60 mmHg received respective oxytocin doses. We compared changes in MAP, heart rate, uterine tone, blood loss, the need for additional uterotonic and antiemetic drugs.

Results: In our study maximum hypotension was in 5U oxytocin bolus with infusion group i.e. twenty three patients (76%) when compared with three patients (10%) in 3U bolus with infusion group and five patients (16%) in only infusion group. The pulse rate was increased to a greater extent in 5U bolus group than 3U and without bolus groups. Uterine tone was very good in patients who received 5U, good in 3U and inadequate to adequate in without bolus. Eleven patients (37%) in 20U infusion group were required additional uterotonic drugs when compared to two patients (7%) in 5U and 3U with infusion groups. The antiemetics used were highest after 5U (63%) than 3U (10%) and without bolus (3%).

Conclusion: Lower dose of oxytocin bolus is better than higher bolus dose and without bolus dose based on the oxytocin effect on haemodynamic changes and uterine contraction.

Introduction

Oxytocin is the most widely used uterotonic harmone in obstetrics after caesarian section to maintain adequate uterine tone which is essential in preventing blood loss and postpartum hemorrhage.(1) Oxytocin when administered in excess dose may cause +unwanted cardiovascular effects like tachycardia and hypotension, ischemia, ST-T segment changes, pulmonary edema, chest pain and other side effects like nausea, vomiting, headache, flushing, severe water intoxication and convulsion and when the dose is inadequate it can result in uterine atony and increased uterine bleeding.(2-8) In spite of repeated use of oxytocin, the minimum effective dose of oxytocin and its proper regimen of administration is not clear.

We aimed to estimate the haemodynamic and uterine contraction effects of three different regimes of oxytocin in patients undergoing elective caesarean section.

Materials and Methods

Ninety healthy term pregnant women posted for elective caesarean section were selected in this dose-ranging, randomized, double-blind study after obtaining written informed consent from the patient and the clearance from the Ethical Committee of the institute. The parturient of age group 18-35years, ASA physical status I and II, with uncomplicated pregnancies posted for elective caesarean section under spinal anaesthesia were included in the study. The parturient with active labour, foetal distress, multiple gestation, with complicated pregnancies like preeclampsia and eclampsia, diabetes mellitus, cardiac diseases, uterine fibroids, previous classical uterine incision, abnormal placental presentation and patients with coagulopathy were excluded from the study.

The patients were advised not to take any solid food for 6 hours and allowed to drink only plain water up to 2 hours before the operation. After arriving in the operating room an IV line was secured 18G cannula and parturient was preloaded with Ringer's lactate solution at the rate of 15 ml/kg. Thirty minutes before administering spinal anesthesia, premedication was given to all parturient with intravenous metaclopromide 10 mg and ranitidine 50 mg. Before administering anaesthesia baseline blood pressure (MAP) and heart rate (HR) were recorded. The parturients were allocated to following groups, Group 1: 3 U i.v. oxytocin bolus + 20 U in 500ml RL @ 20 U/h Group 2: 5 U i.v. oxytocin bolus + 20 U in 500ml RL @ 20 U/h Group 3: No i.v. oxytocin bolus, only 20 U in 500ml RL @ 20 U/h.

Randomization was done following a computer-generated random numbers and sealed opaque envelope in order to make patients concerned as well as data collector were unaware of the mode of oxytocin administration. Spinal anesthesia was administered with 12 mg hyperbaric bupivacaine 0.5% with a 26G Quincke spinal needle through the L3-L4 intervertebral space with the patients in the sitting position. Surgery was allowed to proceed after making the patient supine with

left lateral tilt and when the sensory block was up to T4. As per the group allocated, oxytocin was administered to parturients after child birth. Before giving the injection oxytocin, the MAP and HR were recorded. The cardiovascular changes like MAP, HR and electrocardiogram (ECG) were recorded throughout the operative period. After administration of oxytocin the heart rate and NIBP was recorded every minute for 5 min, followed by every 2.5 min for 25 min and every 5 min for 30 min. Any ECG changes were monitored. Side effects of oxytocin like nausea, vomiting, chest pain and flushing were recorded. Patients having hypotension with a fall in MAP less than 60mmHg were excluded from the study and were treated with IV bolus of ephedrine.

The obstetrician selected for study with an experience of 4 years or more assessed the uterine tone 3 minutes after the start of injection oxytocin and reassessed at 5, 10, 15 and 20 minutes after the delivery of placenta, gave the comment as adequate or inadequate. A 5 – point scale was used for this assessment. The scale used was as follows: 1. Atonic 2. Partial but inadequate contraction 3. Adequate contraction 4. Well contracted 5. Very well contracted.

A rescue dose of 3U oxytocin as a bolus was given if the uterine tone was not satisfactory. After two rescue doses of oxytocin if the uterine tone was inadequate, other uterotonic agents like methylergonovine maleate 0.2 mg i.m;. carboprost tromethamine 0.25 mg i.m; misoprostol 800– 1000 mg rectal was administered as per the advice of obstetrician.

Mean(SD) was used to represent patient characteristics and obstetric and intraoperative data. Student's *t*-test and Chi-square test were used to analyze numerical data and categorical data respectively (%). For all the tests $p<0.05$ was considered as statistically significant, $p<0.005$ as highly significant and $p<0.001$ considered as very highly significant. Data entry was done using MS Excel 2007 computer software and analyzed using SPSS version 20.0. Significance of study parameters between three groups of patients was checked by utilizing Analysis of variance (ANOVA) test. Numerical variables were presented as mean and standard deviation (SD). Chi-square test has been used to find the significance of study parameters and categorical variables were presented as frequency (%). For all the tests $p<0.05$ was considered as statistically significant, $p<0.005$ as highly significant and $p<0.001$ considered as very highly significant.

Results

In our study maximum hypotension was in 5U oxytocin bolus with infusion group i.e. twenty three patients(76%) when compared with three patients (10%) in 3U bolus with infusion group and five patients)(16%) in only infusion group. The findings in our study show that there was the maximum reduction in MAP in 5U oxytocin bolus with infusion group after 1 min which is statistically significant with a p=0.015. The fall in MAP continued to be statistically significant in 5U oxytocin bolus with infusion group from 2 min to 5 min and very highly significant up to 10 min.

Table 1: Comparison of MAP (mm Hg) among three Groups from baseline to the changes at the time interval from (1-10) min

BP diff. Time(min)	Groups	N	Mean	SD	F score and p
Baseline MAP (mmHg)	1	30	75.53	1.805	2.928 P=0.074 ns
	2	30	72.27	1.302	
	3	30	77.93	1.603	
1	1	30	72.43	9.008	0.069 P=0.069 ns
	2	30	69.33	6.764	
	3	30	73.63	5.846	
2	1	30	71.77	8.439	4.424 P=0.015 s
	2	30	67.83	7.887	
	3	30	73.30	5.325	
3	1	30	71.00	7.483	4.754 P=0.011 s
	2	29	67.07	8.606	
	3	30	72.87	5.501	
4	1	30	71.07	7.492	3.868 P=0.025 s
	2	29	66.97	7.646	
	3	30	71.77	6.224	
5	1	30	71.60	7.609	5.045 P=0.009 s
	2	28	66.64	7.680	
	3	30	72.27	6.659	
10	1	29	73.21	8.274	10.176 P<0.001 vhs
	2	24	64.88	9.607	
	3	28	75.07	7.902	

ns: not significant, **s**: significant, **hs**: highly significant, **vhs**: very highly significant

The maximum pulse rate of each patient in all the groups in 60 min after oxytocin administration was taken. The Mean and Standard deviation of maximum pulse rate in Group 1 (88.87±11.03), in Group 2 (99.87±8.28) and Group 3 (95.43±14.56). There was rise in pulse rate in all the groups(Graphs 1, 2, 3), but it was more marked in 5U oxytocin bolus with infusion group as shown in the Graph(2) which is statistically highly significant $p<0.005$.

Table 2: Changes in pulse rate

	Group	N	Mean	SD	F score
Baseline pulse rate	1	30	83.67	10.76	2.24 P=0.11 ns
	2	30	89.53	8.82	
	3	30	88.47	14.06	
Max.pulse rate	1	30	88.87	11.03	6.93 p<0.005 hs
	2	30	99.87	8.23	
	3	30	95.43	14.56	

ns: not significant, **hs**: highly significant

The comparison of uterine tone in all three groups are shown in Table 3.

Table 3: Comparison of Uterine Tone

Tone (min)	Group	N	Mean	SD	F
5	1	30	3.87	0.900	48.996 P<0.001 vhs
	2	30	4.10	0.712	
	3	30	2.37	0.556	
10	1	30	4.10	0.960	53.143 P<0.001 vhs
	2	30	4.33	0.661	
	3	30	2.50	0.572	
15	1	30	4.33	0.661	102.808 P<0.001 vhs
	2	30	4.47	0.730	
	3	30	2.37	0.490	
20	1	30	4.37	0.669	81.991 P<0.001 vhs
	2	30	4.43	0.728	
	3	30	2.57	0.504	

vhs: very highly significant

The above table shows very highly significant difference among the three groups. In 3U oxytocin with infusion group there is well contracted uterine tone, in 5U oxytocin with infusion group very well contracted and in 20U infusion group adequate contraction at the end of 20 min.

Eleven patients (37%) in 20U infusion group were required additional uterotonic drugs when compared to two patients (7%) in 5U and 3U with infusion groups.

Table 4: Additional Uterotonic drugs

			Group 1	Group 2	Group 3
Drugs	Nil	Count	28	28	19
		%	93	93	63
	Prostaglandin	Count	2	2	11
		%	7	7	37
Total		Count	30	30	30
		%	100	100	100

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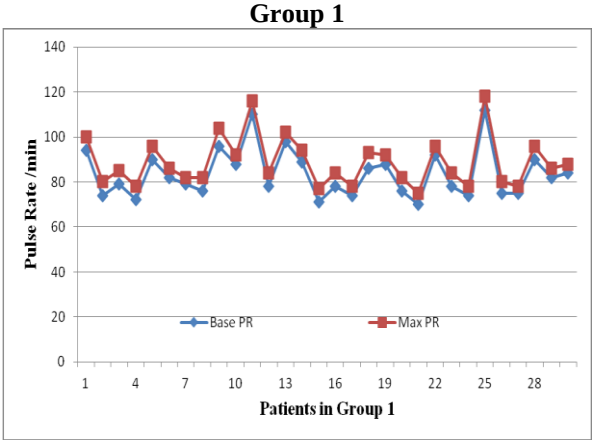
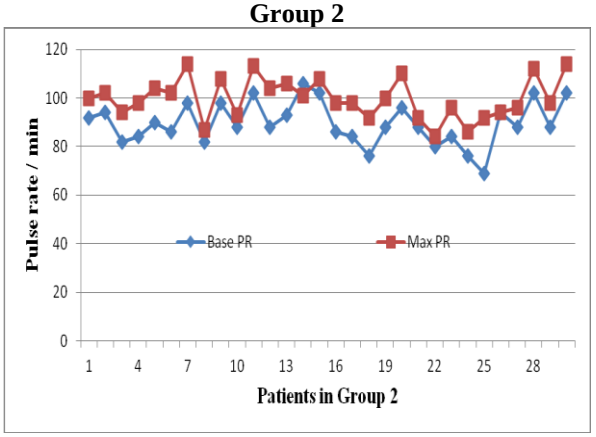
Eleven patients out of 30 (63%) in 5U oxytocin with infusion group had vomiting when compared to three patients(10%) in 3U oxytocin with infusion group and one patient(3%) in only infusion group. So the antiemetic drugs administered for vomiting was comparatively higher in 5U oxytocin with infusion group.

Graph 1: Comparison of increase in pulse rate in Group 1



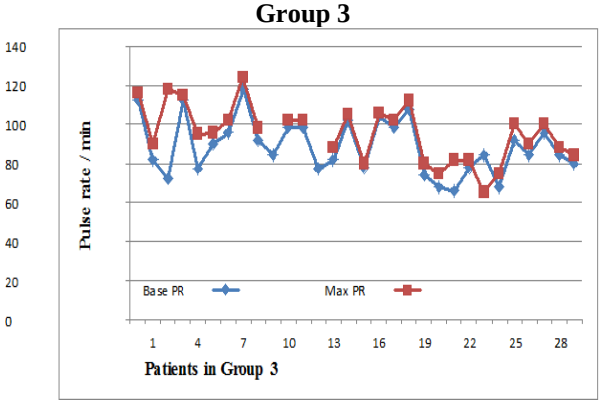
This graph demonstrates rise in pulse rate in Group 1 but the rise is minimal.

Graph 2: Comparison of increase in pulse rate in Group 2



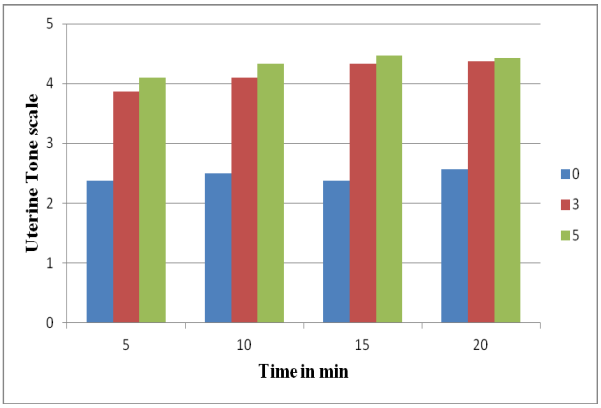
This graph demonstrates rise in pulse rate in Group 2, the rise being significant.

Graph 3: Comparison of increase in pulse rate in Group 3



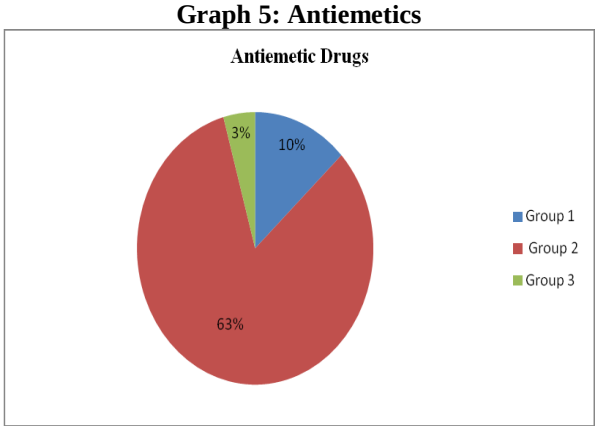
This graph demonstrates the rise in pulse rate in Group 3, but the rise in minimal.

Graph 4: Comparison of uterine tone in Group 1, 2 and 3



The graph showing uterine tone between the three Groups at the interval of 5, 10, 15 and 20 min.

Graph 5: Antiemetics



Graph 6: Additional uterotonic drugs

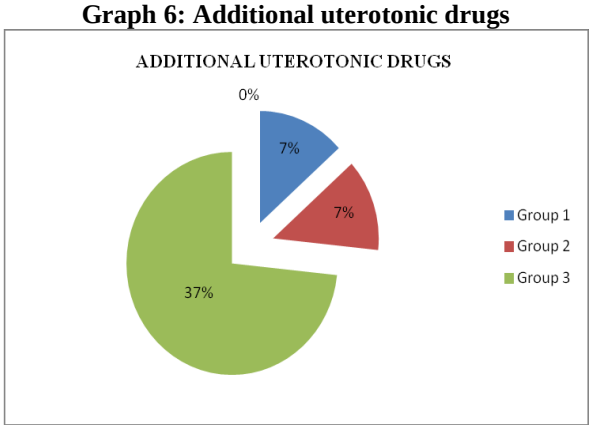


Table 5: Antiemetic drugs

			Group 1	Group 2	Group 3
Drugs	Nil	Count	27	11	29
		%	90	37	97
	Antiemetic	Count	3	19	1
		%	10	63	3
Total		Count	30	30	30
		%	100	100	100

Table 6: Average blood loss

Blood Loss	Group	N	Mean	SD	F
	1	30	528.67	28.616	5.834
	2	30	516.00	17.140	P<0.005hs
	3	30	537.67	26.741	

hs: highly significant

The above table shows statistically highly significant among the three Groups, but clinically insignificant.

Discussion

Obstetric hemorrhage and uterine atony are the two main complications for mothers undergoing caesarean delivery. In uterine atony, uterus does not contract after delivery; it will remain relaxed and open resulting in heavy bleeding.[2] Oxytocin is released from the pituitary gland after distention of the uterus and cervix during labor, decreases blood pressure, increases the HR, and induces uterine contraction.[3-6] Oxytocin induced uterine contractions assists the uterus in clotting the placental attachment point and prevents severe blood loss.[5-7] It is routinely administered by intravenous bolus and infusion after both normal and caesarian delivery to initiate and maintain adequate uterine contractility after placental delivery.[8,9] However, the optimal dose, route and proper regime of oxytocin administration are not yet clear.[10] It is suggested that excessive doses of oxytocin to achieve adequate uterine tone during elective caesarean delivery needs re-evaluation.[11,12] Since larger and rapid bolus doses of oxytocin administration are associated with many unwanted effects like hypotension, nausea, vomiting, chest pain, headache, flushing and myocardial ischemia especially in women with cardiovascular instability, bolus is not administered permanently.[14,15] It is observed that adequate uterine tone can be achieved with small bolus doses like 0.5-3 IU of oxytocin[16,17] but the incidence of hypotension increases significantly after 5 IU. Different doses and routes of administration of oxytocin have been tried previously, but further studies are needed to establish the effective dose of oxytocin.[18-20]

The findings in our study show that there was the maximum fall in MAP (mean arterial pressure) in 5U oxytocin bolus with infusion group after 1 min which is statistically significant with a p=0.015. In the studies of Thomas et al[14] and Sartain et al[13] the fall of MAP was before 1 min. The difference is mainly because our monitor recorded BP at 1 min interval, whereas as Thomas et al[14] had an invasive monitoring. The fall in MAP continued to be statistically significant in 5U oxytocin bolus with infusion group from 2 min to 5 min and very highly significant up to 10 min. In the study of Thomas et al[14] the fall in MAP was before 1 min and regained to normal after 2 min. Their mode of injecting oxytocin was different. They diluted 5U of oxytocin in normal saline either in 5ml or 15 ml and the

rate of injection was slower to that of ours. In the study of Sartain et al[13] oxytocin bolus was injected i.v. without dilution. In their study the fall in MAP continued to be over 10 min which is comparable to our study.

The maximum pulse rate of each patient in all the groups in 60 min after oxytocin administration was taken. The Mean and Standard deviation of maximum pulse rate in Group 1 (88.87±11.03), in Group 2 (99.87±8.28) and Group 3 (95.43±14.56). There was rise in pulse rate in all the groups(Graphs 1, 2, 3), but it was more marked in 5U oxytocin bolus with infusion group as shown in the Graph(2) which is statistically highly significant $p<0.005$. The degree of rise in pulse rate decreases with a decrease in bolus dose and without bolus dose of oxytocin. This marked increase in 5U oxytocin bolus with infusion group is similar to studies of Sartain et al[13] and Thomas et al[14] Our results regarding heart rate match with the study of Pinder et al.[12] The degree of rise in pulse rate decreases with a decrease in bolus dose and without bolus dose of oxytocin. This again is in agreement with the studies of Sartain et al[13] who administered 5 U and 2 U boluses.

The percentage of patients with adequate UT at 3U, 5U and infusion group, are shown in Table 3. The above table shows very highly significant difference among the three groups. In 3U oxytocin with infusion group there is well contracted uterine tone, in 5U oxytocin with infusion group very well contracted and in 20U infusion group adequate contraction at the end of 20 min. The total number of patients in each group who required rescue doses of oxytocin (2.5–5 units) to treat uterine atony is shown in Table 5. Eleven patients (37%) in 20U infusion group were required additional uterotonic drugs when compared to two patients (7%) in 5U and 3U with infusion groups. This is in concurrence with studies of Munn et al.[22] In their study the uterine tone was proportional to the bolus dose of oxytocin whereas in other studies there was not much difference in the tone of uterus. However their oxytocin boluses were different from our studies.

As far as blood loss is concerned the comparison between three groups (Table 6) shows $p<0.005$ which is statistically highly significant. But a blood loss of 500-1500 ml (Graph 5) in caesarean section is acceptable. Hence this statistical change is clinically insignificant.

Our study is comparable to study conducted by Roach et al,[23] in their study there was a non-significant difference considering bleeding and received serum among three groups.

Conclusion

Oxytocin is routinely used as uterotonic during caesarean section. There is no agreement about the dosage, regimen and speed of injection. Many workers have tried different boluses and infusion of oxytocin with the expectation of maximum uterotonic effect and minimal haemodynamic changes. In the same quest we tried 3 regimes of oxytocin viz, 3U i.v. oxytocin bolus with 20 U / h, 5U i.v. oxytocin bolus with 20 U / h and only 20 U/ h without bolus. At the end of the study we found that 5U bolus with infusion had the best uterotonic effect. However, it was associated with remarkable hypotension and tachycardia and also side effects like nausea and vomiting. In the other group of 3U bolus with infusion had good uterine contraction with lesser cardiovascular disturbances and lesser side effects like nausea and vomiting, whereas in the last group of only infusion the uterotonic effect was not satisfactory in the majority of the patients which required additional uterotonics, but the haemodynamic and other side effects were minimal.

Considering the uterotonic effect, haemodynamic changes which required treatment and other side effects, we conclude that regimen of 3U i.v. oxytocin bolus with infusion is preferred.

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