

To Study the Effect of Two Different Regimes of Oxytocin on Haemodynamic Parameters in Patients Undergoing Elective Caesarean Section

Himanshu Kumar¹, Ajeet Kumar²

¹Senior Resident, Department of Anaesthesia, NMCH, Jamuhar Sasaram

²Assistant Professor, Department of Anaesthesia, NMCH, Jamuhar Sasaram

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Corresponding Author: Dr. Himanshu Kumar

Conflict of interest: Nil

Abstract:

Introduction: Uncertainty exists over the ideal oxytocin dosage during elective caesarean sections. An insufficient amount of oxytocin might lead to insufficient uterine tone and increased uterine haemorrhage, whilst an excessive dose can have negative cardiovascular consequences including tachycardia and hypotension. To gauge the haemodynamic alterations and uterine contraction in patients undergoing elective caesarean sections, we examined two different oxytocin regimens.

Aims/ Objective: To compare the heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure after giving oxytocin 2U bolus + 20U in RL infusion in combination and 20U in RL infusion alone and to record the need of additional uterotonic (methylergometrine 0.2mg) in elective caesarean section.

Materials and Method: It was a Prospective randomised double-blind study 90 patients were randomised into two groups after elective caesarean section with 45 patients in each group. Patients of group A were given oxytocin at dose of 2U bolus + 20U in 500 ml RL infusion and patients in group B were given oxytocin at dose of no bolus + 20U in 500 ml RL infusion immediately after cord clamping. In both groups haemodynamic parameters (Heart rate, Systolic blood pressure, Diastolic blood pressure, mean arterial pressure) were recorded per minute for first 5 minute and then per 2.5 minutes for 25 minutes and then per 5 minutes for next 30 minutes.

Results: There was increase in heart rate in one and the other groups. But it was more marked in Group A which was statistically highly significant at various pre-specified time intervals as mentioned above. A fall in systolic, diastolic and mean arterial blood pressure was noted in both the groups. The maximum fall was in Group A which is statistically significant at various pre-specified time intervals as mentioned above. Lesser number of subjects in Group A required administration of additional uterotonic agents.

Conclusion: On comparing two regimes of oxytocin viz, 2U bolus + 20U in ringer lactate infusion in combination and 20U in ringer lactate infusion alone, the study concludes that greater hemodynamic changes in heart rate, systolic, diastolic, and mean arterial blood pressures were observed in bolus-infusion combination regimen as compared to the infusion alone regimen.

Keywords: Oxytocin, Haemodynamic Parameters, Heart Rate, Blood Pressure, Dose, Regimen.

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Introduction

Among the most frequently performed surgical procedures in contemporary obstetrics is the caesarean section (CS). Worldwide, there are around 18.5 million CSs each year, with middle- and high-income nations performing between 21 and 33 percent of the excess CSs. Medically speaking, caesarean birth is helpful in avoiding maternal and foetal death and morbidity; nevertheless, there is little evidence to support the advantage of caesarean section for the woman or the new-born child who does not need CS. Similar to other surgeries, CS carries both immediate and long-term hazards that may have an impact on the mother's and her child's physical and reproductive health. Women who have less access to extensive obstetric care are at

increased risk. [1,2] Numerous variables have been taken into account as potential implications on the increased caesarean rate in recent years. The growth in caesarean births is frequently attributed to the altering risk profiles of primiparae who are becoming older. Another factor is the rise in maternal requests for caesarean sections. However, societal changes should not be seen in isolation from the growth in caesarean section rates.

The surgical technique known as CS carries a number of risks for both child and mother. There are several adverse effects that might develop after delivery in addition to the intraoperative dangers (such as infection, organ damage, or the requirement for blood transfusions): thromboembolic

complication, as an illustration. Particular attention should be paid to the problems associated with subsequent pregnancies, including uterine rupture, infertility, and even placental malformations including placenta previa, increta, or accrete. [3,4]

Obstetricians and anaesthetists who treat women having caesarean sections continue to debate the usage of oxytocin, a drug frequently used to avoid postpartum atony and haemorrhage. To begin and sustain appropriate uterine contractility following placental delivery following elective Caesarean Delivery (CD), oxytocin is regularly provided. [5]

The uterotonic action of oxytocin is crucial in lowering postpartum haemorrhage risk and loss of blood from the area of placental attachment. Unfavorable hemodynamic effects, including tachycardia, hypotension, and ECG abnormalities, are known to follow intravenous oxytocin administration.

During caesarean delivery (CD), a number of oxytocin regimens have been explored with varying desired (uterotonic) and undesirable (cardiovascular) consequences. For a sufficient uterine contraction, oxytocin is frequently given as an intravenous (IV) bolus and then as an IV infusion. [6,7] There is not much data to support this approach. Few studies have examined the daily dosage effects of an oxytocin bolus for attaining appropriate uterine tone (UT) during elective CD, despite the fact that smaller oxytocin bolus doses are linked with a decreased incidence of adverse effects.

The goal of the current study was to determine the effectiveness of various oxytocin regimens on haemodynamic parameters during elective CSs. The objectives of the study were to compare the heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure after giving oxytocin 2U bolus + 20U in RL infusion in combination and 20U in RL infusion alone and to record the need of additional uterotonic (methylergometrine 0.2mg) in elective caesarean section.

Materials & Methods

This was a prospective randomised double-blind study conducted at department of anaesthesiology of a tertiary care teaching hospital of eastern India over a duration of two years. The study was done after approval from institutional ethics committee and under principles of declaration of Helsinki and good clinical practice.

Inclusion Criteria: Patients posted for elective caesarean section under spinal anaesthesia, patients

who were willing to give informed and written consent, patients with ASA I and II, and pregnant females between age 21-35 years.

Exclusion Criteria: Patients at risk of excessive bleeding or uterine atony, patients with cardiovascular instability including preeclampsia and essential hypertension, patients with history of more than two previous caesarean sections, patients with history of postpartum haemorrhage, patients with known case of placenta previa and accreta, patients with twin pregnancy and polyhydramnios or patients with systolic blood pressure less than 100 mmHg or MAP less than 60 mmHg just before oxytocin bolus.

90 patients who agreed were fit as per our inclusion and exclusion criteria and agreed to give written informed consent were recruited in the study. These 90 patients were randomised into two groups after elective caesarean section with 45 patients in each group. Patients of group A were given oxytocin at dose of 2U bolus + 20U in 500 ml RL infusion and patients in group B were given oxytocin at dose of no bolus + 20U in 500 ml RL infusion immediately after cord clamping. In both groups haemodynamic parameters (Heart rate, Systolic blood pressure, Diastolic blood pressure, mean arterial pressure) were recorded per minute for first 5 minute and then per 2.5 minutes for 25 minutes and then per 5 minutes for next 30 minutes.

Need of additional uterotonic (Methylergometrine 0.2 mg) was also recorded.

Statistical Analysis: Data were presented in tabular form using Microsoft Excel 365 and then transferred to SPSS (version 25) for further statistical analysis. Unpaired t test was used to test statistical significance of difference between two groups with respect to parameters represented in mean and standard deviations such as age, heart rate and blood pressure. Chi-Square test was used to test statistical significance of difference between two groups with respect to data presented as proportion such as proportion of patients requiring additional uterotonic drugs. A p-value of less than 0.05 was estimated as confirmation of statistical significance between two groups.

Results

Both the groups were similar with respect to age and other baseline demographic and clinical characteristics. Mean age in group A was 26.82 ± 3.16 as compared to 26.49 ± 3.25 in group B.

Table 1: Comparison of heart rate at different time intervals

TIME	Group	Mean	Std. Deviation	Mean diff	P value (Unpaired t test)
1 MIN	AB	81.56 79.76	5.782 6.763	1.800	0.178
2 MIN	AB	85.62 82.78	5.994 6.512	2.844	0.034*
3 MIN	AB	88.38 85.60	6.746 7.063	2.778	0.060
4 MIN	AB	91.18 87.24	7.539 6.726	3.933	0.011*
5 MIN	AB	91.93 88.02	7.485 6.391	3.911	0.009**
7.5 MIN	AB	93.60 89.78	5.813 6.677	3.822	0.005**
10 MIN	AB	93.67 89.69	5.745 6.281	3.978	0.002**
12.5 MIN	AB	93.27 89.56	6.500 6.319	3.711	0.007**
15 MIN	AB	92.71 89.98	5.857 6.348	2.733	0.037**
17.5 MIN	AB	92.29 89.16	5.290 5.958	3.133	0.010**
20 MIN	AB	91.11 88.87	4.682 5.857	2.244	0.048*
22.5 MIN	AB	89.60 88.42	4.769 6.032	1.178	0.307
25 MIN	AB	90.40 87.33	4.859 6.049	3.067	0.010*
27.5 MIN	AB	89.22 86.93	4.587 5.483	2.289	0.034*
30 MIN	AB	88.07 85.78	3.621 6.212	2.289	0.035*
35 MIN	AB	90.09 84.89	6.609 5.662	5.200	<0.001**
40 MIN	AB	89.84 83.56	6.826 5.554	6.289	<0.001**
45 MIN	AB	89.22 82.89	7.298 5.280	6.333	<0.001**
50 MIN	AB	87.24 80.47	7.544 5.695	6.778	<0.001**
55 MIN	AB	86.09 79.78	7.940 5.252	6.311	<0.001**
60 MIN	AB	84.91 79.18	8.777 5.288	5.733	<0.001**

Results were found to be significant at 2min, 4min, 5min, 7.5 min, 10min,12.5min, 15min, 17.5 min, 20 min, 25min, 27.5 min, 30 min, 35 min, 40 min, 45 min, 50 min, 55 min and 60 min on comparing heart rate of group A and group B.

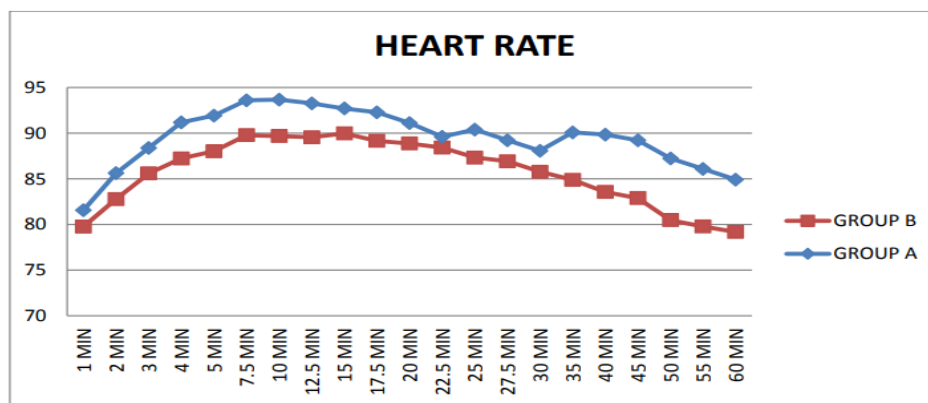


Figure 1: Comparison of heart rate at different time intervals

Table 2: Comparison of MAP at different time intervals

TIME	Group	Mean	Std. Deviation	Mean diff	p-value
1 MIN	A	95.00	4.661	7.578	<0.001**
	B	87.42	3.823		
2 MIN	A	89.13	4.037	2.844	<0.001**
	B	86.29	2.928		
3 MIN	A	88.76	4.129	2.556	0.001**
	B	86.20	3.159		
4 MIN	A	88.02	4.003	1.511	0.066
	B	86.51	3.703		
5 MIN	A	86.60	4.092	0.622	0.440
	B	85.98	3.500		
7.5 MIN	A	87.13	4.546	0.978	0.239
	B	86.16	3.155		
10 MIN	A	85.82	3.898	-0.933	0.225
	B	86.76	3.325		
12.5 MIN	A	85.98	4.025	-0.733	0.380
	B	86.71	3.853		
15 MIN	A	85.80	4.003	-1.489	0.060
	B	87.29	3.382		
17.5 MIN	A	86.24	4.381	-0.867	0.290
	B	87.11	3.256		
20 MIN	A	86.91	4.616	-0.600	0.472
	B	87.51	3.131		
22.5 MIN	A	87.40	3.810	-1.178	0.138
	B	88.58	3.652		
25 MIN	A	87.78	3.444	-1.422	0.053
	B	89.20	3.442		
27.5 MIN	A	88.13	4.020	1.711	0.025*
	B	86.42	3.034		
30 MIN	A	86.56	3.665	0.00	1
	B	86.56	4.104		
35 MIN	A	86.64	3.663	-0.911	0.243
	B	87.56	3.696		
40 MIN	A	87.00	3.303	0.156	0.820
	B	86.84	3.162		
45 MIN	A	87.22	3.022	-0.156	0.825
	B	87.38	3.601		
50 MIN	A	87.91	3.734	0.867	0.227
	B	87.04	2.984		
55 MIN	A	88.22	3.357	1.867	0.009**
	B	86.36	3.241		
60 MIN	A	88.33	2.876	1.378	0.041*
	B	86.96	3.411		

Results were found to be significant at 1 min, 2min, 3 min, 27.5 min, 55 min and 60 min on comparing mean arterial pressure of group A and group B.

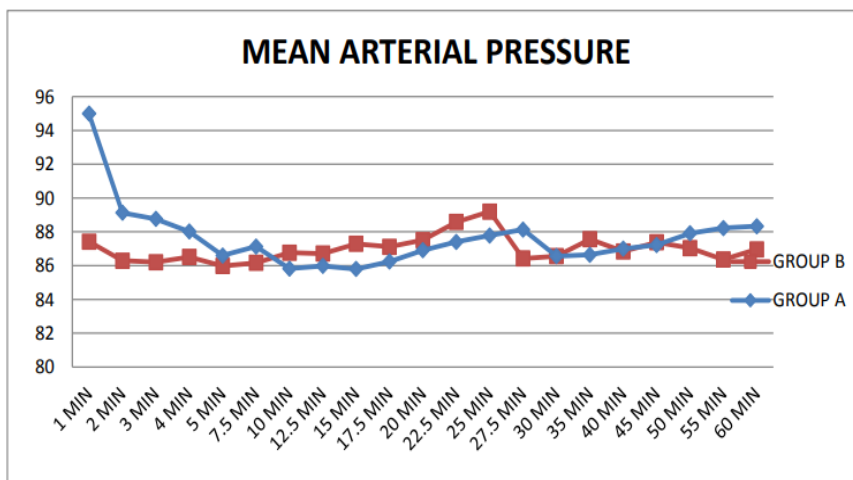


Figure 2: Comparison of MAP at different time intervals

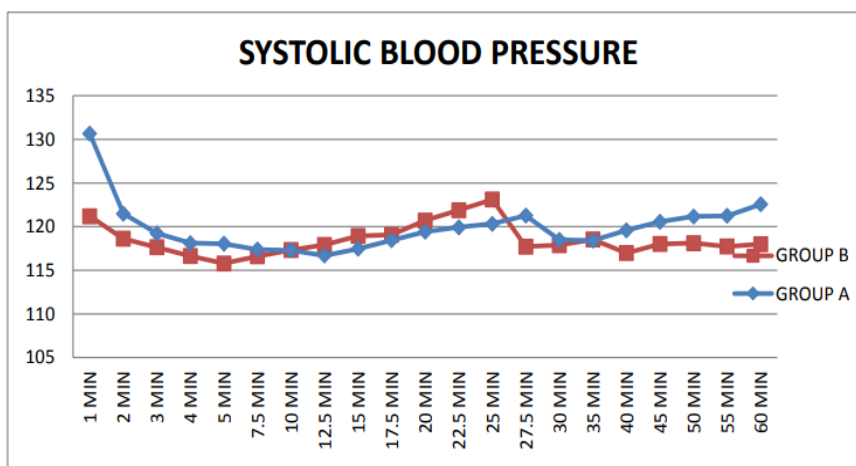


Figure 3: Comparison of MAP at different time intervals

Results were found to be significant at 1 min, 2min, 5min, 22.5 min, 25min, 27.5 min, 40 min, 45 min, 50 min, 55 min and 60 min on comparing systolic blood pressure of group A and group B.

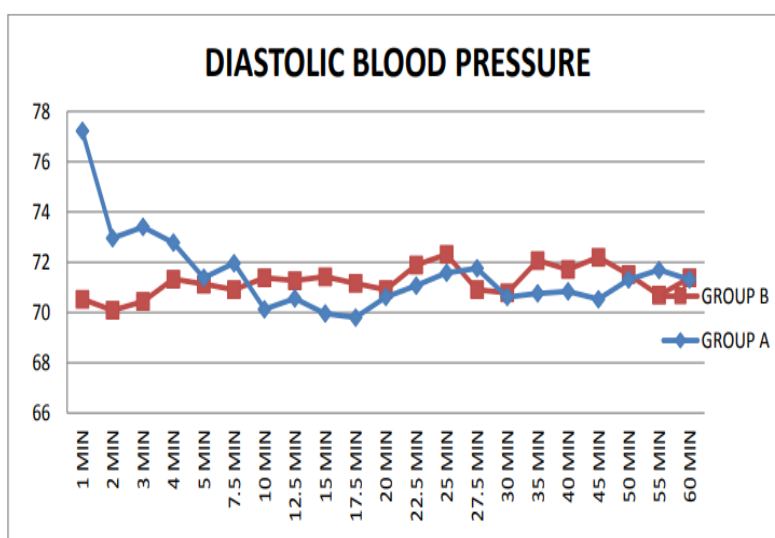


Figure 4: Comparison of DBP at different time intervals

Results were found to be significant at 1 min, 2min, 5min, 22.5 min, 25min, 27.5 min, 40 min, 45 min, 50 min, 55 min and 60 min on comparing systolic blood pressure of group A and group B.

Table 3: Comparative record of other uterotonic agent used

Other Uterotonic Record	Group A	Group B	Total	Chi value	P-value
Needed	1	4	5	1.906	0.167
	2.2%	8.9%	5.6%		
Not Needed	44	41	85		
	97.8%	91.1%	94.4%		
Total	45	45	90		
	100.0%	100.0%	100.0%		

There was no significant difference between two groups with respect to requirement of additional uterotonic agents ($p < 0.05$).

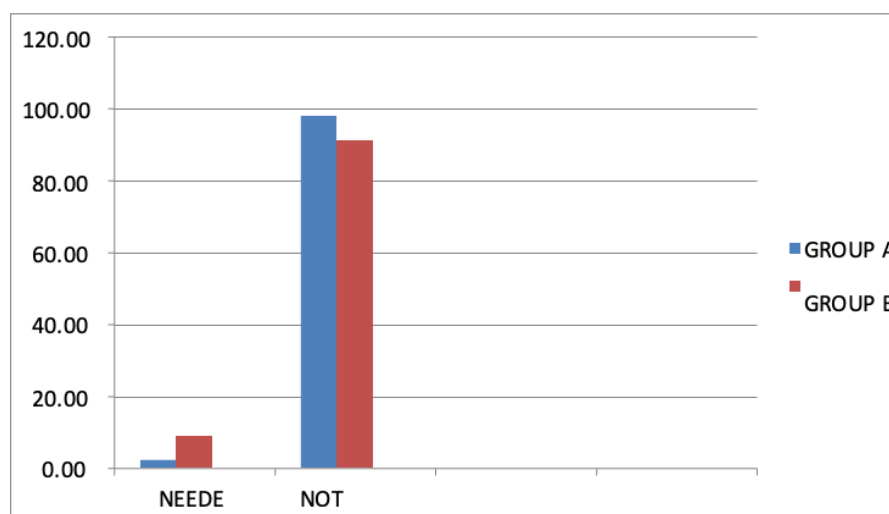


Figure 5: Comparative record of other uterotonic agent used

Discussion

This study was conducted with the objective of comparing various hemodynamic parameters like the heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure after giving either oxytocin 2U bolus + 20U in RL infusion in combination in Group A or 20U in RL infusion alone in Group B. The need of additional uterotonic agent (methylergometrine 0.2mg) in elective caesarean section was also recorded.

Stephens LC and Bruessel T conducted a systematic review in 2012 to ascertain the ideal dose of oxytocin following elective caesarean section. Questions were raised about the use of high dose (10 international units; IU) or moderate dose (5 IU) oxytocin. Evidence was also provided about lower doses of oxytocin which are equally effective but associated with significantly fewer side-effects. Therefore, low dose of oxytocin was used in the present study. [8] In the present study the mean age of mean age of group A and group B was 26.82 and 26.49 years. This shows that the females enrolled in the study were mostly young with no statistically

significant difference between women's ages in the two groups.

The findings in the present study show that at the end of 2 min after the administration, in Group A oxytocin regimen, the HR was 85.62 bpm and 82.78 bpm in Group B. The difference was statistically significant with a $p = 0.034$. Similarly mean heart rate value differences between Group A and Group B were found to be significant at 4min, 5min, 7.5 min, 10min, 12.5min, 15min, 17.5 min, 20 min, 25min, 27.5 min, 30 min, 35 min, 40 min, 45 min, 50 min, 55 min and 60 min. There was increase in heart rate in one and the other groups. But it was more marked in Group A which was statistically highly significant at various pre-specified time intervals as mentioned above.

These findings are similar to studies of Sartain et al and Thomas et al. [9,10] In Sartain et al study, the increase in in HR was significantly greater and more prolonged after 5 u bolus than after 2 u bolus oxytocin.⁹ This shows that greater the bolus intravenous dosing of oxytocin greater are the maternal hemodynamic changes observed.

The findings in the present study show that at the end of 1 min after the administration, in Group A oxytocin regimen, the SBP was 130.67 ± 6.396 in Group A and 121.20 ± 4.561 in Group B. This was statistically significant with a $p < 0.001$. Similarly, results were found to be significant at 2min, 5min, 22.5 min, 25min, 27.5 min, 40 min, 45 min, 50 min, 55 min and 60 min on comparing systolic blood pressure of group A and group B. A fall in SBP was noted in both the groups. The maximum fall was in Group A which was statistically significant at various pre-specified time intervals as mentioned above.

The findings in the present study show that at the end of 1 min after the administration, in Group A oxytocin regimen, the DBP was 77.22 ± 6.157 in Group A and 70.53 ± 5.238 in Group B. This was statistically significant with a $p < 0.001$. Similarly, results were found to be significant at 1 min and 2min on comparing diastolic blood pressure of group A and group B. A fall in DBP was noted in both the groups. The maximum fall was in Group A which is statistically significant at various pre-specified time intervals as mentioned above.

The findings in the present show that at the end of 1 min after the administration, in Group A oxytocin regimen, the MAP was 95 ± 4.661 and in Group 2, it was 87.42 ± 3.823 . This was statistically significant with a $p < 0.001$. Similarly, results were found to be significant at 2min, 3 min, 27.5 min, 55 min and 60 min on comparing mean arterial pressure of group A and group B. A fall in MAP was noted in both the groups. The maximum fall was in Group A which was statistically significant at various pre-specified time intervals as mentioned above.

This is similar to the Thomas et al. study where a decrease in MAP in both the bolus and the infusion groups, however there was a greater decrease in the bolus intravenous administration group. [10] In the Sartain et al. study, there was a significant decrease in MAP in both groups ($P \leq 0.005$), but greater in the 5 U than the 2 U group. [9]

The additional uterotonic drugs needed to be administered to treat inadequate uterine tone were also noted in this study. In the present study they were administered to 5 patients (5.6%). 1 in Group A (2.2%) and 4 in Group 2 (8.9%). The remaining 85 study subjects did not require any additional uterotonic agents. (Table 3) This shows that lesser number of subjects in Group A required administration of additional uterotonic agents. This essentially indicates that the uterotonic effect of 2U bolus + 20U in RL infusion combination of oxytocin produced adequate uterotonic effect.

Recently, Pinder and associates investigated the haemodynamic effects of IV boluses of oxytocin, 5 and 10 U, in females undergoing Caesarean section

under spinal anaesthesia. The dose-dependent effects of oxytocin were further established. [11]

Bhattacharya S et al carried-out research to compare the hemodynamic alterations and uterotonic outcome of same dose of oxytocin administered as an intravenous bolus versus intravenous infusion. The authors concluded that oxytocin administered bolus (at a dose of 3 IU over 15 seconds) or infusion of oxytocin (at a dose of 3 IU over 5 minutes) had comparable uterotonic effect. The bolus regime showed significantly more adverse cardiovascular events. [12]

Guruprasad S et al in 2017 carried out a research to compare three different regimes of oxytocin in patients undergoing elective caesarean delivery. 90 patients following elective caesarean delivery were given an IV bolus of either 3U or 5U and without bolus of oxytocin after cord clamping, pursued by an oxytocin infusion of 20 U/h. The authors concluded that lower dose of oxytocin bolus is better compared to both higher bolus dose and no bolus dose based on the oxytocin effect on haemodynamic changes and uterine contraction. [13]

Another study carried out in 2010 by Butwick et al with the aim to determine the lowest effective bolus dose of oxytocin to produce adequate uterine tone (UT) during elective Caesarean delivery (CD). [14] pregnant patients following elective caesarean section under spinal anaesthesia were randomized to take oxytocin (0.5, 1, 3, 5 units) or no uterotonics. At the end of the study, it was concluded that the routine use of 5 units oxytocin during elective CD can no longer be recommended. This is because, adequate UT can be achieved with lower doses of oxytocin (0.5–3 units). [15]

Thus, the present study re-confirmed all the findings of the previously conducted studies about various dosing regimens of oxytocin used at the time of elective caesarean section.

Conclusion

Even though oxytocin is routinely used as uterotonic during caesarean section, there is a lot of debate about the dosage, regimen, and speed of injection. The maternal hemodynamic changes due to bolus dosages of oxytocin deserve adequate attention. On comparing two regimes of oxytocin viz, 2U bolus + 20U in ringer lactate infusion in combination and 20U in ringer lactate infusion alone, the study concludes that greater hemodynamic changes in heart rate, systolic, diastolic, and mean arterial blood pressures were observed in bolus-infusion combination regimen as compared to the infusion alone regimen. Also, the bolus-infusion combination regimen required lesser requirement of additional uterotonic agent during the course of the study.

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