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Comparison of Oxytocin 3IU Bolus + I.V. Infusion 0f 30IU at the Rate of 125 ml/Hr.(0.125 IU/Min.) and oxytocin I.V. infusion at 0.125 IU/Min only, in maintaining uterine tone and hemodynamic stability in parturient undergoing caesarean delivery

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Abstract

Oxytocin is routinely administered during caesarean delivery to initiate uterine contraction and thus decrease the blood loss from the site of placental attachment. Adverse effects are known to occur after I.V. oxytocin administration, depending on the dose and rate of administration.

The aim of our study was to compare the effect of oxytocin intravenous bolus +I.V. infusion with oxytocin I.V. infusion alone in maintaining adequate Uterine Tone and Hemodynamic stability in women undergoing elective caesarean delivery.

Sixty parturients undergoing caesarean delivery under spinal anesthesia were recruited for our study. They were randomly allocated to receive 3IU of oxytocin as bolus intravenous injection over 15 seconds followed by I.V. infusion of oxytocin at 0.125 IU/min (group B) or placebo followed by I.V. infusion of oxytocin at 0.125 IU/min over 4 hours (group I). Uterine tone was assessed as adequate or inadequate by the attending obstetrician. Intraoperative heart rate, non-invasive blood pressure, amount of blood loss, and any complications were recorded. Postoperatively they were followed for 24 hours for any complications.

Results: There was significant rise in heart rate and significant decrease in mean arterial pressure in bolus group compared to infusion group. There was no significant change in the amount of blood loss between the groups. Only one incidence of vomiting occurred in the infusion group. There was a gradual and adequate rise in Uterine tone in both the groups by 15th minute post oxytocin.

Conclusion: Infusion of oxytocin raises the uterine tone gradually compared to bolus group. Bolus group shows significantly more adverse cardiovascular events.

Keywords: Caesarean section, Oxytocin bolus, Oxytocin infusion, Uterine tone, Hemodynamic stability.

Introduction

Caesarean section is the most commonly performed operation in women all over the world. It's incidence varies from 20% to 40% from developed to developing countries. These patients are always at increased risk of uterine atony, obstetric hemorrhage, post partum hemorrhage, and it's related morbidities like, anemia, blood transfusion, hysterectomy, major supplying artery ligation and maternal death. Etc.[1,2]

Oxytocin is routinely administered during both vaginal as well as caesarean delivery to initiate and maintain adequate uterine contractility and decrease the risk of post-partum hemorrhage after the placental delivery.[1-5] Oxytocin is used as intramuscular (I.M.), intravenous (I.V.) bolus, infusion and sometimes I.V. infusion following I.V. bolus. But there is no universal conclusion as to how much of oxytocin should be given. The dose varies from 0.5, to 10 IU (International Unit) given over a period of 5 seconds to 1 minute, followed by I.V. infusion of 0.08 IU/min, 0.1 IU /Min, 0.125 IU/min, 0.250 IU/min. However the total dose of oxytocin needs to be adjusted in response to adequate recovery of uterine tone and control of postpartum hemorrhage.[4-12]

In our study we are comparing Oxytocin I.V. bolus versus I.V. infusion in maintaining Uterine Tone, Hemodynamic stability, amount of blood loss, along with any perioperative and postoperative complications.

Materials and Method

After obtaining Institutional Ethical committee approval and written informed consent from the participants, 60 ASA I or ASAII grade, term pregnant women satisfying the inclusion criteria, undergoing elective caesarean delivery were enrolled for our randomized double blind, controlled study. They were divided into two groups of 30 each. Group B received 3 IU of oxytocin bolus over a period of 15 seconds immediately after the extraction of the baby followed by I.V. infusion at 0.125 IU/min over a period of 4 hours. Group I received 1 cc of normal saline as placebo over a period of 15 seconds followed by I.V. infusion of oxytocin at 0.125 IU/min over a period of 4 hours. All the parturients were assessed for Uterine Tone (UT), Hemodynamic stability, amount of blood loss and any perioperative and postoperative complications.

Inclusion and exclusion Criteria: Women aged between 20 to 40 years belonging to ASA I and ASA II with single live intra-uterine gestation undergoing

elective caesarean delivery willing to participate in the study were included in our study.

Women who were in active labor, with premature rupture of membrane, those with risk of uterine atony (abnormal presentation, multiple gestation, fibroid uterus complicating pregnancy, H/O diabetes, women with PIH/ eclampsia, abnormal placental attachment, coagulation disorders, cardiovascular instabilities, severe anemia) were excluded from the study.

Materials and Method

Randomization was done using envelop method. Study person prepared the drug as per the note in the envelop and the other anesthetist administered the drug blindfolded. Concerned Obstetrician performed the surgery and estimated the Uterine Tone (UT) at 2, 3, 6, 10 and 15 minutes and graded 0-10 (0= No UT, 10= Optimal UT) using verbal numerical scale. Other parameters like hemodynamic stability, amount of blood loss, preoperative and postoperative complications, rescue uterotonics used and the doses of vasopressors used were noted by the attending anesthetist. Postoperative complications were treated accordingly.

All the participating parturients were evaluated a day before the surgery, by the anesthetist. They were kept nil orally for 6 hours before surgery. On the day of surgery they were cannulated with 18 G I.V. cannula. All received 500 ml of Ringer's saline within 30 mins. before Spinal anesthesia was given. Baseline Heart rate (HR), Hemoglobin concentration (Hb%) Non-invasive blood pressure (NIBP) values were recorded.

All of them were pre-medicated with inj. Ondansetron 4mg and inj. Ranitidine 50mg slow I.V.

Standard monitoring like, ECG, Pulse-oxymeter, NIBP, were connected. Spinal anesthesia was performed at L3-L4 vertebral space using 27 G Quinke's spinal needle and 10 mg. of 0.5% bupivacaine by an anesthetist who is not involved in randomization. When satisfactory sensory blockade was achieved at T8 level, surgery was allowed.

Pre-oxytocin Mean Arterial Pressure (MAP), Heart Rate (HR) were recorded. After the baby was extracted, oxytocin was administered as per the group allocated. After the extraction of the placenta, Uterine tone(UT) was assessed by the operating obstetrician as said earlier and the data was compared between the two groups. Post-oxytocin MAP, HR, were recorded. Any fall in the MAP >20% pre-oxytocin level was treated with inj. Mephentermine 6 mg/dose at 3 min. interval till MAP was restored. Any fall in heart rate below 50 beats/min. was treated with 0.002 mg/kg of atropine slow I.V. Any other adverse events like, hypotension, tachy/ bradyarrhythmias, nausea, vomiting, chest pain, both in the pre-oxytocin as well as post-oxytocin period was recorded and treated accordingly.

If uterus was not adequately contracted after 3 min. post-oxytocin, additional uterotonic (Inj. Mesoprost 250 µg/125 µg) was given as per the request of the obstetrician.

Post-operatively patient was monitored at 1, 2, 6, 12, 24 hours and any complications treated accordingly.

Results on continuous measurements are presented on mean ± SD and results on categorical measurements are presented as numbers(%). Significance is assured at 5% level ($p<0.05$) of significance. Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between the groups on metric parameters. Chi-square/Fischer Exact test has been used to find the significance of study parameters on categorical scale between the groups.

Statistical software SAS 9.2, SPSS 15.0, Stata 10.1, Systat 12.0 and R environment Ver.2.11.1 were used for the analysis.

Results

Both the groups were comparable with age distribution (group I: 25.87± 3.44 and group B: 25.33±4.19) with P value of 0.592 and ASA grading (group I with 7 patients (23.3%) in ASA I, 21(70%) in ASA II, and 2 (6.7) in ASAII(E), while in group B: 6 patients(20%) in ASA I, 20(66.7%) in ASA II, and 4(13.3%) in ASA II(E)) with P value of 0.844.(Table 1)

Table 1: Age distribution of patients studied

Age in years	Infusion Group	Bolus Group	Total
<20	0(0%)	3(10%)	3(5%)
20-30	28(93.3%)	24(80%)	52(86.7%)
31-40	2(6.7%)	3(10%)	5(8.3%)
Total	30(100%)	30(100%)	60(100%)
Mean ± SD	25.87±3.44	25.33±4.19	25.60±3.91

Samples are age matched with P=0.592

Though both the groups had fall in MAP compared to baseline, fall in MAP was maximum in bolus group at 6 minutes (group B: -8.28±12.76, group I: -6.07± 9.40) with P value of <0.001 and remained significantly same at 10 min(P 0.001), and at 15 min.(P<0.001) which is statistically significant compared to group I.(Table 2)

Table 2: Comparison of MAP (mm Hg) in two groups of patients studied Student t test

MAP levels (mm. of Hg.)	Infusion Group	Bolus Group	Total	P value
0	89.10±8.05	88.60±10.08	88.85±9.05	0.833
1	82.34±7.47	81.56±8.68	81.95±8.04	0.707
2	78.67±7.18	80.89±9.34	79.78±8.33	0.306
3	81.28±6.22	82.36±7.73	81.82±6.98	0.554
4	80.38±9.20	80.60±10.00	80.49±9.53	0.929
5	83.03±5.18	80.32±9.43	81.68±7.67	0.173
6	85.39±3.95	79.44±7.49	82.42±6.65	<0.001**
7	86.04±5.63	80.71±5.99	83.38±6.36	0.001**
8	86.24±3.84	80.98±5.47	83.61±5.39	<0.001**

15 patients in group B had significant hypotension compared to group I (8 patients) who needed vasopressors with a P value 0.007 (Table 3).

Table 3: Peri-operative side effects (post oxytocin) in two groups of patients studied

Peri-operative side effects (post oxytocin)	Infusion Group (n=30)	Bolus Group (n=30)	Total (n=60)
Nil	33(110%)	15(50%)	37(61.7%)
Yes	8(26.7%)	15(50%)	23(38.3%)
• Hypotension	8(26.7%)	15(50%)	23(38.3%)

P=0.007**, significant, chi-Square test

There was no significant change in the amount of blood loss between the groups, group B had 24(80%) patients who had estimated blood loss of >500ml compared to 22(73%) patients in group I (P 0.944) (Table 4).

Table 4: Blood Loss distribution in two groups of patients studied

Blood Loss	Infusion Group	Bolus Group	Total
<500	8(26.7%)	6(20%)	14(23.3%)
500-1000	22(73.3%)	24(80%)	46(76.7%)
>1000	0(0%)	0(0%)	0(0%)
Total	30(100%)	30(100%)	60(100%)
Mean ± SD	576.00±170.41	573.33±119.43	574.67±145.90

P=0.944, Not significant, student t test

There was statistically significant fall in post-operative hemoglobin concentration in both the groups after 6 hours compared to pre-operative concentration with P <0.001 (group B 10.90 ± 1.09 to 10.09 ±0.97 and in group I 11.17±1.35 to 10.23±1.25) (Table 5).

Table 5: Comparison on of Hemoglobin (g/dl) in two groups of patients studied

Hemoglobin (g/dl)	Infusion Group	Bolus Group	Total	P value
Pre-Operative	11.17±1.35	10.90±1.09	11.04±1.22	0.385
Post-Operative	10.23±1.25	10.09±0.97	10.16±1.11	0.620
Difference	0.943	0.801	0.88	-
P value	<0.001**	<0.001**	<0.001**	-

Though optimal UT was attained early in few cases of group B compared to gradual and sustained increase in group I, all 30 patients in group I had maximum UT (10/10) by 10^{th} minute while only 16 in group B had 10/10 by 10^{th} min. (P<0.001). Only 2 patients in group I needed additional uterotonic (mesoprost 250 µg and 125 µg) which was not significant.(Table 6)

Table 6: Comparison of Post oxytocin uterine tone in two groups of patients studied

Post oxytocin uterine tone	Infusion Group (n=30)	Bolus Group (n=30)	Total (n=60)	P value
UT1				
• ≤8	30(100%)	29(96.7%)	59(98.3%)	1.000
• >8	0(0%)	1(3.3%)	1(1.7%)	
UT2				
• ≤8	30(100%)	28(93.3%)	58(96.7%)	0.492
• >8	0(0%)	2(6.7%)	2(3.3%)	
UT3				
• ≤8	27(90%)	25(83.3%)	52(86.7%)	0.706
• >8	3(10%)	5(16.7%)	8(13.3%)	
UT4				
• ≤8	0(0%)	14(46.7%)	14(23.3%)	<0.001**
• >8	30(100%)	16(53.3%)	46(76.7%)	
UT5				
• ≤8	0(0%)	0(0%)	0(0%)	1.000
• >8	30(100%)	30(100%)	60(100%)	

Discussion

Parturient women undergoing Caesarean Delivery are at increased risk of obstetric hemorrhage due to Uterine atony.[1,2] Oxytocin is routinely administered in these cases to initiate and maintain contractility and reduce the incidence of postpartum hemorrhage by upto 40%.[1-5] However there is limited data to guide the total dose of oxytocin to be administered. It needs to be adjusted in response to adequate recovery of Uterine tone and control of postpartum hemorrhage.[4-12]

There is progressive increase in oxytocin receptors in pregnant women and attains on an average 12 times higher in early pregnancy and about 80 times higher than non-pregnant uterus in late pregnancy.[5] These receptors behave heterogeneously during onset of labor and the dose of oxytocin required may reach nine times higher in these patients compared to non-laboring women.[5]

Uterine massage and routine use of oxytocin during third stage of labor has been shown to decrease blood loss and lessor requirement of additional uterotonics suggesting both prophylactic oxytocin administration and uterine massage both are important.[3]

In previous studies, bolus doses varying from 0.5-10 IU has been used to achieve adequate uterine tone. But it is observed that the incidence of hypotension increases significantly at 5 IU and more. Use of large doses are known to produce hypotension, nausea, vomiting, headache, chest pain, flushing and even myocardial infarction.[3]

In our study, we have found higher increase in heart rate (20-32 beats/min.) in bolus group at 2 min. which did not return to baseline even after 15 min, compared to infusion group (16-26beats/min.) which returned gradually to near normal by 10th min. Decrease in Mean Arterial Pressure(MAP) was maximum in bolus group at 6 min. and remained significantly same at 10th and 15th min. compared to infusion group (P <0.001).

Even though the fall in postoperative hemoglobin concentration (Hb%) was statistically significant when compared to preoperative level, (P<0.001), the total amount of blood loss in both the groups was not significant (>1000 ml.) with P value of 0.944.

Adequate Uterine Tone(UT) >8 was attained early in few cases of bolus group at 2 min. compared to infusion group, where UT >8 was attained gradually and in sustained manner, and all had UT >8 at 10thmin.

Only 1 patient in infusion group had vomiting post operatively among all the 60 patients studied, which was not statically significant.

Conclusion

In elective caesarean delivery, adequate uterine tone can occur with smaller bolus doses of oxytocin (3 IU) early and can be sustained with additional I.V. infusion at lower doses (0.125 IU/min). But perioperative cardiovascular side effects like hypotension, and tachycardia associated with bolus doses can be minimized by using I.V. infusion of oxytocin at 0.125IU/min. alone.

Using only I.V. infusion of oxytocin at lower doses (0.125 IU/min) along with uterine massage by the operating Obstetrician gives satisfactory Uterine Tone and thus reduces the associated complications.

Limitations of the study

Small sample size in our study may not be sufficient in interpreting the data observed between the groups. Only subjective assessment of uterine tone by the operating Obstetrician may not be reliable. Uterine massage immediately after the placental extraction may give false assumption that the bolus dose /infusion has

helped in attaining optimal UT at 2 min. Further clinical studies are necessary to assess optimal doses and modes of administering oxytocin to achieve optimal uterine tone and reduce perioperative and postoperative complications in parturients undergoing elective caesarean delivery.

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Conflict of interest
Nil.

References
1. Kovacheva, Vesela P., Mieke A. Soens and Lawrence C. Tsen. "A Randomized, Double-blinded Trial of a "Rule of Threes" Algorithm versus Continuous Infusion of Oxytocin during Elective Cesarian Delivery." Anesthesiology 123.1 (2015):92-100.
2. Butwick, A. J., B. Carvalho and Y. Y. El-Sayed. "Risk factors for obstetric morbidity in patients with uterine atony undergoing Caesarean delivery." British Journal of Anaesthesia 113.4(2014):661-668.
3. Butwick, A. J., et al. "Minimum effective bolus dose of Oxytocin during elective Caesarean delivery." British Journal of Anaesthesia 104.3(2010):338-343.
4. Weale, N. and C. Laxton. "Prophylactic use of Oxytocin at Caesarean section: where are the guidelines?" Anaesthesia 68 (2013):995-1009.
5. Bhattacharya, Sushmita, et al. "Oxytocin administration during Caesarean delivery: Randomized controlled trial to compare intravenous bolus with intravenous infusion regimen." Journal of Anaesthesiology Clinical Pharmacology 29.1 (2013): 32-35.
6. Davies, Gregory A. L., et al. "Maternal Hemodynamics after Oxytocin Bolus Compared with infusion in the Third stage of labor: A Randomized Controlled Trial." Journal of Obstetrics and Gynaecology 105.2 (2005): 294-298.
7. Sharon R. Sheehan, et. al. "Oxytocin bolus verson Oxytocin bolus and infusion for control of blood loss at elective caesarean section: double blind, placebo controlled, randomized trial." British Medical Journal 343 (2011): d4661.
8. Yamaguchi, Eduardo Tsuyoshi, Monica Maria Siaulys Capel Cardoso and Marcelo Luis Abramides Torres. "Oxytocin in Cesarean Sections. What is the best way to use it?" Revista Brasileira de Anesthesiologia 57.3 (2007): 324-330.
9. Tsen, Lawrence C. "Oxytocin Use for Cesarean Delivery: Time for a Paradigm Shift." Minnesota Society of Anesthesiologists, Fall Conference 2013. Minnesota: Minnesota Society of Anesthesiologists, 2013. 1-4.
10. Nordstorm I, Fogelstom K, Fridman G, Larsson A, Rhydhstroem H. Routin oxytocin in the third stage of labor: A placebo controlled randomized trial. Br J Obstet Gyanecol 1997;104:781-6.
11. Devikarani D, Harsoor SS. Are we using right dose of oxytocin? Indian J Anaesth 2010; 54; 371-3.
12. Abdel-Aleem H, Hofmeyr GJ. Shokry M, El-Sonoosy E. Uterine massage and postpartum blood loss. Int J GynaecolObstet 2006; 93: 23.