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COMPARISON OF THREE DIFFERENT BOLUS DOSES OF OXYTOCIN FOR UTERINE CONTRACTION IN ELECTIVE CAESAREAN SECTION: A PROSPECTIVE RANDOMIZED DOUBLE BLIND INTERVENTIONAL STUDY

Anaesthesiology

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ABSTRACT

Background: Some amount of blood loss is physiologically normal during childbirth. Oxytocin administration is recommended for routine administration during vaginal birth as well as during Caesarean section. **Aim:** This study aimed at comparing the effect of three different (1-, 2-, and 3 International Units) bolus doses of oxytocin during caesarean section for promoting uterine contraction and reducing the blood loss. **Material and Methods:** This was a hospital based, double-blind, prospective ,randomised, intervention study conducted over a period of 18 months by enrolling 300 participants (100 participants in each group). The data on heart rate, mean blood pressure, uterine contractions, blood loss and side effects were collected and compared. **Results:** The mean blood loss among participants given 1-, 2-, and 3 IU group participants was 267.3, 224.3 and 225.5 ml, respectively (p-value <0.05). A total of 31%, 83% and 100% in the 1-, 2-, and 3 IU group participants had very well contracted uterine tone (p-value< 0.0001). A total of 3% patients in 1 IU group had atonic uterus and 27% had inadequate uterine tone. None of the participants in 3 group had arrhythmia. **Conclusion:** Oxytocin in the dose of 3 IU was most effective in stimulating uterine contraction during C-section without causing any severe side effects.

KEYWORDS

INTRODUCTION

During and immediately after labour, a certain quantity of blood loss is biologically normal(1,2). there are certain circumstances when life-threatening blood loss can occur after birth of the foeto-placental unit, particularly when the uterus is not contracting despite repeated stimulation. Postpartum Haemorrhage (PPH) is one of the main causes of maternal mortality. Postpartum haemorrhage (PPH) can happen following both vaginal and caesarean deliveries (C-section)(3–5). Yet, compared to vaginal birth, the risk of PPH is often greater following a C-section. This is because more blood is lost after a C-section since the uterus is physically not massaged and may not contract as well as it would following a vaginal birth(6–8). Multiple prior C-sections, emergency C-sections, or the use of specific medications like anticoagulants are some C-section-related factors that increase the risk of PPH(6–8). Preventing significant problems and improving outcomes for both mother and child can be accomplished with early detection and management of PPH.

WHO) advised in 2018 that all women should get 10 (IU) of oxytocin during birth (vaginal or caesarean delivery)(3).According to WHO 10 IU of oxytocin should be provided as a split dosage utilising a smaller first intravenous (IV) bolus followed by an infusion when used for PPH prophylaxis after caesarean birth(3). Recent research has shown that dosages considerably lower than 5 IU with significantly less side effects. To maintain uterine contraction during and after caesarean section, it is advised to continue oxytocin infusion after using low bolus doses of the hormone(9,12). The recommendations for infusion rates, however, are based on a scant amount of research. has concentrated on determining the dosages for starting uterine contractions. The use of large dosages, whether by bolus or continuous infusion, is still common in obstetric practise, despite the fact that it is unneeded and may even be harmful to patients due to the risk of adverse effects, particularly cardiovascular. This is because side effects of OT include hypotension, tachycardia, chest discomfort, ECG abnormalities, myocardial ischaemia, flushing headaches, nausea, vomiting, and even convulsions when given rapidly and in high dosages(13,14). However, after elective caesarean delivery, there is no established optimal dose and infusion rate of OT for the prevention of PPH. Consequently, it is imperative to do new research to determine the lowest dose range that can effectively contract the uterus, limit blood loss, and cause the fewest adverse effects. We thus undertook this study to determine the effectiveness of three different oxytocin bolus dosages during caesarean sections performed under spinal anaesthesia for stimulating uterine contraction and minimising blood loss. We specifically determined how three different oxytocin dosages affected uterine tone, blood pressure and heart rate fluctuations, intraoperative blood loss, and side effects.

MATERIAL AND METHODS

Study Design : Hospital based double blinded randomized interventional study.

Study Area: Department of Anesthesia, S.M.S Medical College and attached group of Hospitals, Jaipur.

Ethical consideration: study was approved by the Institutional Ethics Committee – BioMedical Research of SMS, Medical College, Jaipur.

Sample Size: A sample size of 100 patients in each group is required at 95% confidence level and power 80% to verify the expected minimum difference of 17.3% in proportion of cases with adequate uterine contractions in all study groups (66.3% Vs 83% Vs 100%).

Study group: The study had three groups having 100 patients in each group:

- GROUP A (n=100): patients received 1 IU Oxytocin diluted to 10ml using NS
- GROUP B (n=100): patients received2 IU Oxytocin diluted to 10ml using NS.
- GROUP C(n=100): patients received 3 IU Oxytocin diluted to 10ml using NS.

Inclusion Criteria:
Age group between 18 to 40years, Singleton pregnancy ,Gravida G1, G2 ,Patients undergoing elective caesarean section of duration 1-2hours ,Patients consenting to participate in the study.

Exclusion Criteria:
ASA III, IV ,Twin pregnancy ,Allergy to study drug, A patient refused to take part in the study. ,Obstetrics abnormalities

Randomization: Using the statistical software Stata version 17.0 random numbers were generated using the permuted block design (n=5), and the participants were randomly allocated to the three study groups.

Allocation Concealment: study team using opaque, sealed and impregnated tapes envelopes containing random numbers.

Blinding: double-blind study,

Plan And Procedure:
Pre-anaesthetic evaluation was completed one day before the surgery Vital monitors were attached for measurement of pulse rate, non-invasive blood pressure, pulse oximetry, cardiac rhythm, and body temperature during the peri-operative period.

The patients were placed in sitting position and dural puncture were

performed in L3-L4 interspace taking all aseptic measures. Hyperbaric bupivacaine (0.5%) 2ml were injected intrathecally and patient were made to lie down with adequate lowering of head end.

After delivery of foetus and umbilical cord clamped. The study dose of oxytocin prepared in 10ml NS syringe and were administered over a time period of 15 sec. After removal of placenta by controlled traction and completion of 2min from the administration of the drug, Obstetrician were asked to check the tone of the uterus by manual palpation without exteriorising the uterus.

Then 10 Units of oxytocin infusion in 500ml normal saline was commenced at 125 ml/Hr. A five-point Likert scale (A Likert scale is a unidimensional scale that researchers use to collect respondents' attitudes and opinions) were used to assess the uterine tone by palpation. If contraction was inadequate, then intramuscular methergine 0.2mg was administered as alternative uterotonic therapy. The heart rate, mean blood pressure were recorded for next 40 minutes. Intraoperative bleeding was assessed by checking: After delivery of foetus and placenta uterine tone was assessed by surgeon by manual palpation of uterus using the 5-point scale at 2,3,6,10 minutes.

Five Point Scale For Uterine Tone Assessment

i. Atonic
ii. Partial but inadequate contraction
iii. Adequate contraction
iv. Well contracted
v. Very well contracted

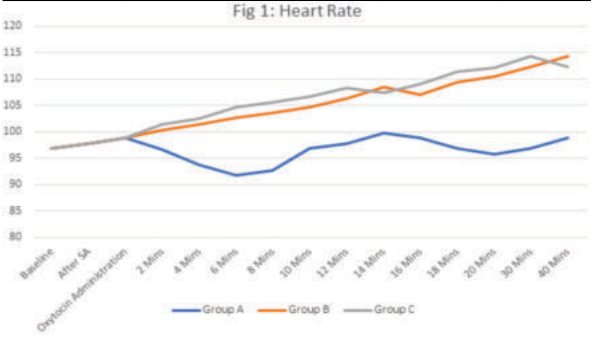
RESULTS:

All 300 enrolled participants completed the study, there were no dropouts, losses to follow up, or withdrawal from study. The mean age of the participants in the group A was 24.28 years, group B was 23.94 years and group C was 23.93 years (p value= 0.84) (Table 1). The mean weight was 64kg, 63.85kg and 63.85kg in group A, group B and group C respectively. The mean height was 160.51cm, 160.52cm and 160.31cm in group A, group B and group C respectively. All three group were comparable in terms of weight and height.

Table 1: Age, Weight, and Height of the participants (n=300)

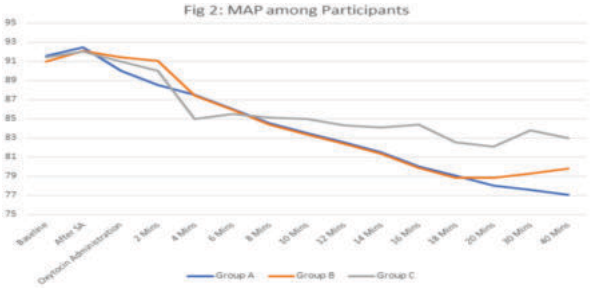
Parameter	Group A	Group B	Group C	P-value
	Mean (SD)	Mean (SD)	Mean (SD)	
Weight (Kg)	64 (7.67)	63.85 (7.97)	63.85 (7.97)	0.98
Height (cm)	160.51 (7.27)	160.52 (7.13)	160.3 (7.1)	0.97
Age	24.28(4.92)	23.94(4.76)	23.93(4.83)	0.84

Fig 1: Heart Rate



There was no significant difference in the Heart Rate, SBP, DBP and MAP among the participants in the three groups at baseline. se group as (p-value >0.05). There was no significant difference at baseline and after spinal anaesthesia between heart rate (p value >0.05), however, as the surgery progressed, the heart rate among the participants in all three groups that was statistically significant (p<0.05).

Fig 2: MAP among Participants



There was a gradual decline in the MAP (including SBP and DBP) as the surgery progressed that was statistically significant.

Table 2: Distribution of cases according to Uterine Tone.

Uterine tone	Group A	Group B	Group C	P-value
	n (%)	n (%)	n (%)	
Atonic	3 (3%)	0 (0%)	0 (0%)	<0.0001
Partial but inadequate	27 (27%)	0 (0%)	0 (0%)	
Adequate contraction	18 (18%)	0 (0%)	0 (0%)	
Well contracted	21 (21%)	17 (17%)	0 (0%)	
Very well contracted	31 (31%)	83 (83%)	100 (100%)	

In the present study, we observed that majority (100% patients in group C, 83% patients in group B and 31% patients in group A) had very well contracted uterine tone. Only 3% patients in group A were atonic and 27% patients in group A were partial but inadequate uterine tone. There was statistically highly significant difference (p-value< 0.0001). The mean blood loss in group A was 267.31ml, in group B it was 224.25ml and in group C it was 225.49. There was significant difference found between these group as p value was <0.05. More blood loss was noted in group A.

Table 3: Distribution of cases according to Side-effects.

Side effects	Group A	Group B	Group C	P-value
	n (%)	n (%)	n (%)	
Nausea	12 (12%)	18 (18%)	18 (18%)	0.75
Vomiting	2 (2%)	4 (4%)	4 (4%)	0.076
Chest pain	1 (1%)	3 (3%)	3 (3%)	0.843
Arrhythmia	0 (0%)	0 (0%)	0 (0%)	0.893
Flushing	3 (3%)	6 (6%)	6(6%)	0.089

In above table we found that 12% patients in group A, 18% patients in group B and 18% patients in group C reported having nausea. Vomiting was seen in 2% patients of group A , 4% patients of group B, 4% patients of group C. Chest pain , flushing were seen in group A, and group B and group C .No arrhythmia reported in any group .We did not find any significant difference between these group as p value was >0.05.

DISCUSSION

Due to uterine atony, pregnant women who have caesarean deliveries are more likely to experience obstetric haemorrhage(2,15). OT receptors (OTRs) are found in the heart and major arteries in addition to the uterus. The main cardiovascular consequence of OT usage is vasodilatation(16–18). As a response to vasodilatation, tachycardia, increased stroke volume, and cardiac output (CO) happen. When OT is administered as a bolus, these effects are more prominent and may be hazardous to individuals with diminished cardiovascular reserve(16–18). From a large dosage to a low bolus dose, oxytocin dosing has steadily changed. Five units of oxytocin are recommended by the UK caesarean section directive as a gradual intravenous bolus dosage following delivery of the newborn(13). This may be explained by the lack of comparability across trials using doses of oxytocin less than five units and the rise in reports of major side effects associated with dosages over five units that have no further benefit for uterine tone or haemorrhage prevention. Tsen and Balki's "Rule of Threes" was a novel method for oxytocin administration during caesarean sections. They suggested administering a three-unit oxytocin bolus over 30 seconds and, if necessary, two more doses of oxytocin following a three-minute break(19). Three units of oxytocin per hour would be the maintenance injection. If the three oxytocin dosages do not result in a sufficient contraction, three more medications might be administered (19).

We studied three different bolus doses of oxytocin in three groups of 100 patients each. Demographic data like mean age, mean weight, mean height were comparable in all the groups. Baseline parameters were also comparable. We recorded pulse rate and MAP at various time points after infusion of oxytocin. We did not find any significant difference at baseline and after spinal anaesthesia as p value was >0.05. But there was statistically significant difference found in pulse at all time interval. A recent study by Badheka J P et al found that the mean heart rate increased at 20–25 beats/min at 3–5 min in group B and 8–10 beats/min at 2–4 min and reached the baseline at nearly 8–9 min in group B as well as in group I(20). Also, a significant fall in the mean blood pressure was observed at 3–5 min in group B. Weis and colleagues used 10 IU of OT and observed that the patients receiving an infusion were haemodynamically stable. Bhattacharya et al. in their study showed an increase in the HR (25–30 beats/min) in the bolus group in 30 s and did not return to the baseline even after 10 min and in

the infusion group, a rise of only 10 beats/min and gradually touched the baseline(21).

We observed that all patients in group C, 83% patients in group B and 31% patients in group A had very well contracted uterine tone. Only 3% patients in group A were atonic and 27% patients in group A were partial but inadequate uterine tone. (P-value <0.0001). Akhtar N et al., found that adequate uterine contraction was seen in 55.6% of participants who received one unit of oxytocin, and in 78.3% of participants who received two units of oxytocin (p=0.03)(22). A similar study by Badheka J P et al., found that no uterotonic agents were required in group I whereas four patients required other uterotonics (injection methylergometrine) in group B(20). Similar observations were found by Bhattacharya et al., in their study(21). Three patients required injection carboprost as rescue uterotonics. Jose CA et al., found that an infusion of 10–40 IU/L is recommended for the prevention of postpartum haemorrhage(14). Other suggested different dosages and routes are OT 10 IU intramuscular, 5–10 IU rapid intravenous bolus, 10–20 IU/L intravenous drip at the rate of 100–150 mL/h. There are various empirical regimens and studies of OT and its dosage, but to date, there is no consensus about the ideal regime of administration for the dosing and routes for effective uterine contraction in patients undergoing elective cesarean delivery.

In our study mean blood loss in group A was 267.31ml, in group B it was 224.25ml and in group C it was 225.49 (p-value <0.05). Thomas et al. also compared the effects of the recommended dose, that is, 5 U of OT, when given as an IV bolus or as an infusion over 5 min and showed that bolus doses should be used with caution and further studies should ascertain if OT is equally effective in reducing blood loss when given in a slower rate(23). Badheka J P et al., found that the estimated blood loss in both groups was not statistically significant(20). Kovacheva et al. observed no difference in significant blood loss(24). Akhtar N et al., found that blood loss was 1038.2 mL in group A and 740.6 mL in group B. A non- significant difference was observed (P> 0.05)(24).

We found that 12% patients in group A, 18% patients in group B and 18% patients in group C felt nauseated. Vomiting was seen in 2% patients of group A and 4% patients of group B. and 4% patients in group C .Chest pain, flushing were seen in group A, and group B and group C .faces chest pain, flushing, non of the group had arrhythmia (p value >0.05). Badekha J P et al., found that eight patients had chest pain, two patients had facial flushing, nausea and headache were there in four patients each in group B, while in group I, only two patients had chest pain(20). No patient had facial flushing, one patient had nausea and vomiting and one had a headache. Sartain et al. observed more nausea and antiemetic use with OT 5 IU (32.5%) versus 2 IU (5%) administered over 5–10 s(25). In contrast to our study, Kovacheva et al., observed no difference in such adverse effects(24). Thus, a low incidence of these adverse effects may be related to the dose, frequency and rate of OT. Carvalho et al., observed nausea (38%), vomiting (13%) and flushing (63%) in their study(26).

CONCLUSION:

In conclusion, in elective cesarean delivery, oxytocin in all three doses viz. 1-, 2-, and 3 IU was effective for contracting uterus during C-section, however, 3 IU of oxytocin was most effective in contracting uterus and preventing blood loss during the C-section. In addition, the 3 IU of oxytocin IV infusion is well tolerated by patients without causing any severe side effects. In elective caesarean sections, a bolus oxytocin dose lower than three units is inadequate for attaining optimum uterine contraction. We recommend the use of three units bolus oxytocin, as it provides adequate uterine contraction, steady haemodynamics, nominal blood loss and lesser side effects. Thus, it is high time we endorse a slow intravenous low bolus dose for oxytocin universally, especially in elective caesarean since the debate has been on for more than three decades.

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