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Original Research Paper

Anesthesiology

MINIMUM EFFECTIVE BOLUS OF OXYTOCIN IN ELECTIVE CAESAREAN SECTION

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ABSTRACT

Objectives To estimate the minimum effective bolus dose of oxytocin required to produce adequate uterine tone at 2min for patients undergoing elective caesarean delivery with spinal anesthesia .

Methodology. 90 healthy term patients undergoing elective CD were randomly allocated into two groups of 45 each.Group A- 45 patients receiving bolus oxytocin 3 IU.Group B- 45 patients receiving bolus oxytocin 5 IU. Uterine tone was assessed by a blinded obstetrician using a verbal numerical scale score .Minimum effective doses of oxytocin were analysed .Oxytocin related side effects were noted.

Results Our results indicate that adequate UT can be achieved with small bolus dose (3 units) of oxytocin in patients undergoing elective CD. The results of this study suggest that the use of 5 units oxytocin as a standard dose to achieve adequate UT during elective CD is excessive and re-evaluation of dosing requirement is necessary. In our study, the incidence of hypotension at 1 min was significantly greater in patients receiving 5 units oxytocin compared with 3 units. Other oxytocin-related side-effects (nausea, vomiting, and flushing) occurred rarely with a bolus dose of 3 units in this study.

Conclusion The routine use of 5 units oxytocin during elective caesarean delivery can be replaced by lower 3 units dose of oxytocin to achieve adequate uterine tone with lesser side effects.

KEYWORDS : Oxytocin Cesarean Delivery Postpartum Hemorrhage Uterine Atony Ergometrine

INTRODUCTION

Oxytocin is the drug of choice both for induction and augmentation of labor, as well as for achieving uterine contraction after delivery, whether spontaneous or operative. Prophylactic oxytocin is commonly administered after delivery of the infant or placenta and has been shown to reduce the incidence of postpartum hemorrhage by up to 40 %.

Oxytocin is routinely administered during elective Caesarean delivery (CD) to initiate and maintain adequate uterine contractility after placental delivery. The uterotonic effect of oxytocin is important in reducing blood loss from the site of placental attachment and decreasing the risk of postpartum haemorrhage. However, adverse haemodynamic effects are known to occur after i.v. oxytocin, notably tachycardia, hypotension, and ECG changes.

METHODOLOGY

The present study was carried out in 90 patients who were attending antenatal clinic and were admitted in obstetric unit of Department of Obstetrics and Gynaecology in Hamidia Hospital and Gandhi.Medical College, Bhopal . They were investigated from October 2016 to September 2017.

After obtaining Institutional Ethics Committee approval and written informed consent, 90 healthy term patients undergoing elective CD were randomly allocated into two groups of 45 each.

Group A- 45 patients receiving bolus oxytocin 3IU.
Group B- 45 patients receiving bolus oxytocin 5IU.

Inclusion criteria were ASA I or II, age between 18 and 40 yr, singleton pregnancies, and elective CD. All enrolled patients received spinal anaesthesia.

Exclusion criteria included active labour, ruptured membranes, known drug allergy to oxytocin, multiple gestation, significant obstetric disease (including pregnancy-induced hypertension or pre-eclampsia), known risk factors for postpartum haemorrhage (including abnor- mal placentation, multiple gestation, uterine fibroids, history of postpartum haemorrhage or uterine atony, and previous classical uterine incision), inherited or acquired coagulation disorder, and thrombocytopenia .

Before spinal anaesthesia, standard monitoring included ECG, NIBP, and pulse oximetry. Measurement of NIBP and HR was taken at 1 min intervals from the time of oxytocin administration. Hypotension was defined as a decrease in mean AP 10% of the baseline value.Tachycardia was defined as a maternal HR 120 beats/min.

Crystalloid solution (lactated Ringer's) was infused during the intraoperative period, with the aim of using a total crystalloid volume of 2 litre. Uterine tone was assessed by a blinded obstetrician as either adequate or inadequate using a verbal numerical scale score (0-10. 0- no uterine tone. 10-optimal uterine tone) at 2,3,6 and 9 minutes after oxytocin administration.Minimum effective doses of oxytocin were analysed .Oxytocin related side effects (tachycardia, hypotention, ecg changes, nausea and vomiting) were noted.

OBSERVATION TABLES

TABLE 1 – Maternal And Patient Characteristics And Obstetric Data.

	3 IU Oxytocin	5 IU Oxytocin	P Value
N	45	45	Not Significant
Age [years]	31 [26 -35]	31 [26 -35]	Not Significant
Weight [kg]	73.5	71.9	Not Significant
Parity	1 -2	1 -2	Not Significant
Previous C section	1 or primigravida	1 or primigravida	Not Significant
Gestational age [weeks]	38.6	38.6	Not Significant

TABLE 2 - Prevalence Of Adequate Ut At 2, 3, 6, And 9 Min After Oxytocin Administration And Total Number Of Patients Requiring Supplemental Oxytocin During The Study Period.

	3 IU Oxytocin	5 IU Oxytocin	P Value
Time 2 minutes	42/45[93.33%]	43/45 [95.55%]	Not Significant
Time 3 minutes	44/45 97.77%]	43/45[95.55%]	Not Significant
Time 6 minutes	45/45 [100%]	45/45[100%]	Not Significant
Time 9 minutes	45/45[100%]	45/45[100%]	Not Significant
Patients requring supplemental oxytocin	2/45 [4.44%]	2/45 [4.44%]	Not Significant

FIGURE 1 Numerical Scores For Ut According To Assessment By The Obstetrician Using A Numerical Scale Of 0 (absent Ut) To 10 (optimal Ut) For Groups Receiving 3 And 5 Units Oxytocin.

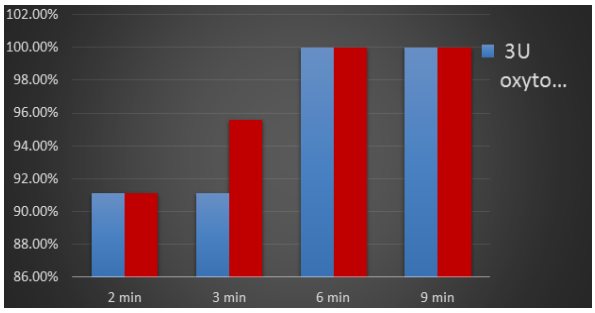
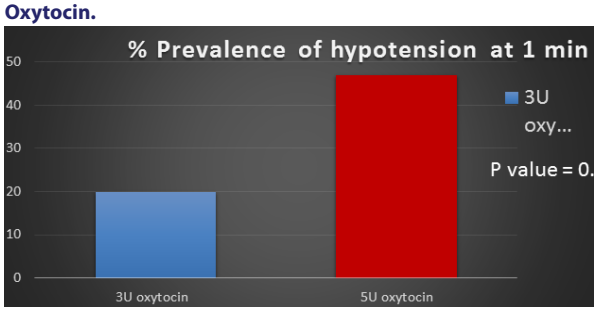


FIGURE 2 Prevalence Of Hypotension At 1 Min After Bolus Administration Of Oxytocin For Groups Receiving 3 And 5 Units Oxytocin.



RESULTS

Minimum effective doses of oxytocin were analysed (ED_{50} and ED_{95}) using logistic regression. The high prevalence of adequate UT after placebo and low-dose oxytocin precluded determination of the ED_{50} and ED_{95}. UT scores were significantly lower in patients receiving 0 unit oxytocin at 2 and 3 min compared with 3 and 5 units oxytocin ($P<0.05$, respectively). The prevalence of hypotension was significantly higher after 5 units oxytocin *vs* 0 unit at 1 min (47% *vs* 7%; $P=0.04$).The routine use of 5 units oxytocin during elective CD can no longer be recommended, as adequate UT can occur with lower doses of oxytocin (0.5–3 units.

Our results indicate that adequate UT can be achieved with small bolus dose (3 units) of oxytocin in patients undergoing elective CD. The results of this study suggest that the use of 5 units oxytocin as a standard dose to achieve adequate UT during elective CD is excessive and re-evaluation of dosing requirement is necessary. In our study, the incidence of hypotension at 1 min was significantly greater in patients receiving 5 units oxytocin compared with 3 units. (P value – 0.012) Other oxytocin-related side-effects (nausea, vomiting, and flushing) occurred rarely with a bolus dose of 3 units in this study.

STASTISTICAL ANALYSIS

Statistical analysis done using student t-test. SPSS 13.0 software was used to calculate p value.P<0.05 was taken as statistically A descriptive analysis was done on all variables to obtain a frequency distribution. The mean + SD and ranges were calculated for quantitative variables. Continuous variables were compared by the Student t test. Proportions were analyzed with the chi-square test.

DISCUSSION

Several empirical regimens have been proposed for oxytocin administration during cesarean delivery, and this has led to many different practices in its administration worldwide.–38 These protocols usually recommend a fixed dose of oxytocin, irrespective of the indication for cesarean delivery. In a previous study we estimated the minimum effective dose (ED_{90}) of oxytocin required to produce adequate uterine contraction after elective cesarean delivery in nonlaboring women, noting that such women required much lower doses than those commonly administered in many centers.

Laboring women requiring cesarean delivery constitute a subset of patients that may exhibit an unpredictable response to oxytocin, because either prolonged labor or use of intravenous oxytocin to augment labor may desensitize the uterus and render it less responsive to the same drug during cesarean delivery. Therefore, the purpose of this study was to estimate the minimum effective dose (ED_{90}) of oxytocin to produce adequate uterine contraction after cesarean delivery for labor arrest in women who had received oxytocin during labor.

Balki, Mrinalini et al did a study to estimate the minimum effective intravenous dose of oxytocin required for adequate uterine contraction after cesarean delivery for labor arrest.

They did a randomized single-blinded study in 30 parturients undergoing cesarean deliveries under epidural anesthesia for labor arrest despite intravenous oxytocin augmentation. Oxytocin was administered as a slow intravenous bolus immediately after delivery of the infant. After assisted spontaneous delivery of the placenta, the obstetrician, blinded to the oxytocin dose, assessed uterine contraction as either satisfactory or unsatisfactory. Additional boluses of oxytocin were administered as required, followed by a maintenance infusion. The minimum effective dose of oxytocin required to produce adequate uterine response in 90% of women (ED90) was estimated to be 2.99 IU (95% confidence interval 2.32–3.67). The estimated blood loss was 1,178 ± 716 mL.Women requiring cesarean delivery for labor arrest after oxytocin augmentation require approximately 3 IU rapid intravenous infusion of oxytocin to achieve effective uterine contraction after delivery. This dose is 9 times more than previously reported after elective cesarean delivery in nonlaboring women at term, suggesting oxytocin receptor desensitization from exogenous oxytocin administration during labor. Therefore, alternative uterotonic agents, rather than additional oxytocin, may achieve superior uterine contraction and control of blood loss during cesarean delivery for labor arrest.[1]

Similar study was done by A. J. Butwick L. Coleman et al .The aim of this study was to determine the lowest effective bolus dose of oxytocin to produce adequate uterine tone (UT) during elective Caesarean delivery (CD).Seventy-five pregnant patients undergoing elective CD under spinal anaesthesia were randomized to receive oxytocin (0.5, 1, 3, 5 units) or placebo. UT was assessed by a blinded obstetrician as either adequate or inadequate, and using a verbal numerical scale score (0–10; 0, no UT; 10, optimal UT) at 2, 3, 6, and 9 min after oxytocin administration. Minimum effective doses of oxytocin were analysed (ED_{50} and ED_{95}) using logistic regression. The high prevalence of adequate UT after placebo and low-dose oxytocin precluded determination of the ED_{50} and ED_{95}. UT scores were significantly lower in patients receiving 0 unit oxytocin at 2 and 3 min compared with 3 and 5 units oxytocin ($P<0.05$, respectively). The prevalence of hypotension was significantly higher after 5 units oxytocin *vs* 0 unit at 1 min (47% *vs* 7%; $P=0.04$).The routine use of 5 units oxytocin during elective CD can no longer be recommended, as adequate UT can occur with lower doses of oxytocin (0.5–3 units.[2]

Carvalho, José C, Balki, Mrinalini et al did a study on oxytocin requirements at elective cesarean delivery . Current dosing regimens are arbitrary whereas large doses may pose a serious risk to the mother. The purpose of this study was to estimate the minimum effective intravenous bolus dose of oxytocin (ED_{90}) required for adequate uterine contraction at elective cesarean in nonlaboring women. A randomized study was undertaken in 40 healthy term pregnant women presenting for elective cesarean under spinal anesthesia. Uterine contraction was assessed by the obstetrician, who was blinded to the dose of oxytocin, as either satisfactory or unsatisfactory. After achieving sustained uterine contraction, an infusion of 40 mU/min of oxytocin was started. Oxytocin-induced adverse effects and intraoperative complications were recorded and blood loss was estimated. The bolus dose of oxytocin used at elective cesarean deliveries in nonlaboring women

can be significantly reduced while maintaining effective uterine contraction. Alteration in practice will likely reduce the potential adverse effects of this drug when given in large bolus doses, but may require modification of the techniques to remove the placenta. Oxytocin when given in large doses and as a rapid bolus, it is associated with various adverse effects, including hypotension, nausea, vomiting, chest pain, headache, flushing, and myocardial ischemia. The purpose of study was therefore to estimate the minimum effective dose (ED90) of oxytocin required to produce adequate uterine contraction at elective cesarean delivery in nonlaboring women.[3]

Ronald B., George Dolores, McKeen et al worked on Up-down determination of the ED90 of oxytocin infusions for the prevention of postpartum uterine atony in parturients undergoing Cesarean delivery .Use of the lowest effective dose of oxytocin may reduce side effects. This study was designed to determine the effective dose (ED)90 of oxytocin infusion for an elective Cesarean delivery (CD) to prevent uterine atony.The participants were ASA I and II, non-obese, non-labouring adult women undergoing an elective CD at term with a singleton gestation. The spinal anesthetic technique was standardized, and a blinded infusion of oxytocin was administered after delivery. The obstetrician rated the uterine contraction as either satisfactory or unsatisfactory. The initial dose of oxytocin infusion was 0.4 IU·min−1,In this study, the authors found the ED90 of oxytocin required to prevent uterine atony and postpartum hemorrhage after an elective CD to be 0.29 IU·min−1—approximately 15 IU of oxytocin in 1 L of intravenous fluid administered over a one-hour period—(95% CI 0.15-0.43 IU·min−1). This oxytocin infusion dose is 30% less than the clinical infusions currently in use. [4]

Dyer, Robert A Butwick et al studied oxytocin for labour and caesarean delivery and its implications for the anaesthesiologist. The implications of the obstetric use of oxytocin for obstetric anaesthesia practice are summarized and the review focuses on recent research on the uterotonic effects of oxytocin for prophylaxis and management of uterine atony during caesarean delivery.Oxytocin remains the first-line agent in the prevention and management of uterine atony. In-vitro and in-vivo studies show that prior exposure to oxytocin induces uterine muscle oxytocin receptor desensitization. This may influence oxytocin dosing for adequate uterine tone following delivery. Oxytocin has important cardiovascular side-effects (hypotension, tachycardia and myocardial ischaemia). Recent studies suggest that the effective dose of oxytocin for prophylaxis against uterine atony during caesarean delivery is significantly lower than the 5–10 IU historically used by anaesthesiologists. Slow administration of small bolus doses of oxytocin minimises maternal haemodynamic disturbance. Continuous oxytocin infusions are recommended for maintaining uterine tone after bolus administration.[5]

CONCLUSION

Oxytocin remains the first-line uterotonic after vaginal and caesarean delivery. Recent research elucidates the therapeutic range of oxytocin during caesarean delivery, as well as receptor desensitization. Evidenced-based protocols for the prevention and treatment of uterine atony during caesarean delivery are recommended.

The routine use of 5 units oxytocin during elective caesarean delivery can be replaced by lower 3 units dose of oxytocin to achieve adequate uterine tone with lesser side effects. Further studies should be conducted to assess optimal modes of oxytocin administration to achieve and maintain UT during CD in healthy patients and patients at-risk of developing uterine atony.

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