Rwanda Medical Journal RMJ

ORIGINAL ARTICLE Open Access

Early Versus Late Administration of Intravenous Oxytocin Infusion in The Prevention of Blood Loss during Elective Cesarean Section - A Randomized-Controlled Trial

Authors: O.P. Aduloju[1,2,*]; A.A. Akintayo[1,2]; I.P. Ade-Ojo[1,2]; T. Aduloju[2]

Affiliations: *[1]Ekiti State University, Ado-Ekiti, Nigeria; [2]Ekiti State University Teaching Hospital, Ado-Ekiti, Nigeria*

ABSTRACT

BACKGROUND: Oxytocin has been shown to be an effective uterotonic agent in the prevention of postpartum hemorrhage.
This study's objective was to evaluate whether administering oxytocin infusion just before uterine incision (group 1) is more effective than administering oxytocin infusion after cord clamping (group 2) in preventing blood loss in elective cesarean sections in Ekiti State University Teaching Hospital, Ado-Ekiti.
METHODS: Women who were scheduled for elective caesarean section at term (> 37 weeks) and were eligible were randomized into group 1 or group 2. The outcome measures were intra- and postoperative blood loss and the need for additional uterotonics, blood transfusion or surgeries. Data were compared using chi-square and student t-tests.
RESULTS: A total of 250 women were randomized into the study. The mean intra-operative and total blood loss was significantly lower in group 1 compared to group 2 [(339.98 ± 84.9ml versus 363.69 ± 48.69ml, p = 0.007); (682.06 ± 74.64ml versus 711.26 ± 62.54ml, p = 0.001) respectively]. Significantly more women in group 2 required additional uterotonics than women in group 1; p = 0.023. The need for blood transfusion and additional surgery were similar in both groups; p > 0.05. There was no difference in Apgar scores at 1 or 5 minutes or in neonatal intensive care unit among the groups; p > 0.05. No maternal or perinatal deaths were recorded in both groups.
CONCLUSION: Early administration of oxytocin infusion is associated with a reduction in blood loss and the need for additional uterotonics or surgeries during elective Cesarian Section.

Keywords: Oxytocin Infusion, Blood Loss, Uterotonics, Postpartum Hemorrhage, Cesarean Section

INTRODUCTION

Cesarean section (CS) remains one of the most commonly performed obstetric procedures, and its rate continues to rise globally [1]. Postpartum hemorrhage (PPH) is one of the leading causes of maternal morbidity and mortality worldwide and accounts for nearly a quarter of all maternal deaths [2,3]. Maternal mortality due to PPH is most prevalent in the first 24 hours after delivery [3].

***Corresponding author:** Dr Olusola Peter Aduloju, Department of Obstetrics and Gynecology, Ekiti State University, Ado-Ekiti, Nigeria, Email: peter.aduloju@yahoo.com; olusola.aduloju@eksu.edu.ng; **Potential Conflicts of Interest (CoI):** All authors: no potential conflicts of interest disclosed; **Funding:** All authors: Partial funding was provided by the University of Maryland Center for Global Engagement, but the funder had no role in the study's design; **Academic Integrity.** All authors confirm that they have made substantial academic contributions to this manuscript as defined by the ICMJE; **Ethics of human subject participation:** The study was approved by the local Institutional Review Board. Informed consent was sought and gained where applicable; **Originality:** All authors: this manuscript is original has not been published elsewhere; **Review:** This manuscript was peer-reviewed by three reviewers in a double-blind review process; **Type-editor:** King (USA).

Received: 07th January 2021; **Initial decision given:** 24th March 2021; **Revised manuscript received:** 07th May 2021; **Accepted:** 30th July 2021.
 Publisher: Rwanda Biomedical Centre (RBC)/Rwanda Health Communication Center, P. O. Box 4586, Kigali. ISSN: 2079-097X (print); 2410-8626 (online)

Citation for this article: O.P. Aduloju; A.A. Akintayo; I.P. Ade-Ojo et al. Early Versus Late Administration of Intravenous Oxytocin Infusion in the Prevention of Blood Loss during Elective Cesarean Section- A Randomized-Controlled Trial. Rwanda Medical Journal, Vol. 78, no. 3, pp. 11-19, 2021.

Uterine atony is the leading cause of postpartum bleeding and is responsible for about 80% of these cases [3,4]. The use of uterotonic agents has been demonstrated to effectively prevent and reduce PPH due to the atonic uterus [5,6].

Oxytocin is the most commonly used uterotonic agent in obstetrics because of its low cost and rapid onset of action. It is routinely administered during normal and operative deliveries to initiate and maintain adequate uterine contractions for minimizing blood loss and preventing PPH [7,8]. In the United Kingdom (UK), the guidelines of the Royal College of Obstetricians and Gynecologists (UK) on caesarean section recommend a slow intravenous bolus dose of 5 IU of oxytocin after delivery of the infant [9]. A survey of obstetricians and anesthetists in the UK revealed that the use of oxytocin bolus was the standard treatment, although the dose varied between 5 IU and 10 IU [10]. However, in the United States, the use of an oxytocin infusion instead of a bolus dose is recommended, a recommendation that reflects the concerns about the physiological effects of an oxytocin bolus [11]. Since intravenous oxytocin has a short half-life (4-10 minutes), an oxytocin infusion at CS has the potential for maintaining uterine contractility throughout the surgical procedure and in the immediate postpartum period [12].

Several studies have evaluated different regimens, routes, and modes of administration of oxytocin in the prevention of PPH [5,8,12,13]. These studies sought to determine doses that would achieve uterine contractility, minimize blood loss, and reduce oxytocin-related side effects. These studies yielded variable effects. Bhattacharya et al. [8] concluded in their study on oxytocin administration during elective CS that intravenous oxytocin infusion produces adequate uterine contractions with the same dose administered as an intravenous bolus and is associated with less adverse hemodynamic changes. Also, in a study conducted by Thomas et al. comparing hemodynamic effects of oxytocin bolus and infusion during CS, they opined the need for caution when using oxytocin bolus in cardiovascularly unstable patients. In contrast, an oxytocin infusion provides reassurances of these effects [14].

Different regimens of oxytocin during CS that have been evaluated include intravenous bolus of oxytocin alone, intravenous oxytocin bolus followed by intravenous oxytocin infusion, intramyometrial oxytocin administration and intravenous infusion of oxytocin [3,4,12,15]. The use of oxytocin infusion only with less hemodynamic changes and effects during CS has not been well studied. Ahmed et al. [12] compared administration of oxytocin infusion before uterine incision (early group) and after umbilical cord clamping (late group) at CS and found a significant reduction in intraoperative blood loss in the early group compared to the late group. However, the need for blood transfusion and additional surgery was similar in both groups, and the researchers suggested that more studies be carried out to confirm their findings. Also, more randomized controlled trials are needed for Cochrane review or meta-analysis before introducing this method into clinical practice [12]. Therefore, this study was carried out to assess and compare the efficacy of different timings of oxytocin infusion administration during CS on blood loss and the need for additional uterotonics, blood transfusion and surgery.

METHODS

This randomised controlled trial was carried out in the Labour ward theatre of the Department of Obstetrics and Gynecology, Ekiti State University Teaching Hospital (EKSUTH), Ado-Ekiti, south-western Nigeria between the 3rd of April and the 2nd of December, 2019. EKSUTH receives referrals from other health facilities in Ekiti State, Ondo, Osun and Kogi States.

This study included all women with a singleton pregnancy scheduled for elective CS at term (37-41 weeks and 6 days of gestation).

Women with 3 or more previous caesarean deliveries, multiple pregnancies, polyhydramnios, placenta praevia, known coagulopathy or medical conditions and those who refused consent were excluded.

Data collection: The sociodemographic characteristics- such as age, parity, gestational age at delivery, and indication for CS- were obtained using a structured questionnaire. Their preoperative packed cell volume (PCV) values were also determined.

Patients randomization and procedure: Eligible women admitted for CS were randomized into two groups by block randomization using random table computer-generated numbers by a statistician and

allocation concealment was ensured using serially labelled sealed opaque envelopes. The envelopes were opened after the order of delivery and once opened, they were not changed. Women in group 1 (early administration of oxytocin infusion group) received 30 IU of oxytocin (Syntocinon, Novartis Pharma, Berne, Switzerland) in 500mL of 0.9% Normal Saline solution at a rate of 125mL/hour [16] which was started just before the incision on the lower segment of the uterus was made. Women in group 2 (late administration of oxytocin infusion group) were given 30 IU of oxytocin (Syntocinon, Novartis Pharma, Berne, Switzerland) in 500mL of 0.9% Normal Saline solution at a rate of 125mL/hour [16] which was started immediately after clamping of the umbilical cord, following the delivery of the baby.

The CS surgical and anesthetic techniques followed the standard procedures. All the women had a transverse lower segment caesarean section under spinal anesthesia with a Pfannenstiel skin incision. They received an intravenous infusion of 500 mL of 0.9% Normal saline solution before administering spinal anesthesia using heavy Marcaine (Bupivacaine). Anesthetists maintained the fluid infusion during the procedure and continued at 1L every 8 hours until the morning after surgery, unless unable to tolerate oral fluids. Women in group 1 had their oxytocin infusion commenced just before the incision was made on the uterine lower segment, while women in group 2 were initiated on oxytocin infusion immediately after the clamping of the umbilical cord. The placenta was delivered by gentle cord traction rather than by forced manual removal in all the women. The fundus and anterior wall of the uterus were palpated to check for its tone after delivery of the placenta, and a contracted uterus was adjudged to be firm and hard. In contrast, the diagnosis of the atonic uterus was made by the presence of a flabby uterus with accompanied by excessive bleeding from the vagina and increasing size of the uterus. The use of additional uterotonic agents (such as intravenous ergometrine, 0.25 milligram or 800 micrograms of misoprostol per rectum etc) or surgical procedures (such as bilateral uterine artery ligation etc) for the management of the uterine atony according to the departmental protocol was recorded. The post-CS management of the women viz-a-viz catheter management, antibiotics and analgesics administration followed the departmental protocol. The vital signs (pulse rate, respiratory rate and blood pressure) were measured continuously pre-, intra-, and post-operatively.

The primary outcome measure was the total volume of blood loss during CS, while the secondary outcomes included the volume of postoperative blood loss, the decrease in pre-and post-operative PCV values and the need for blood transfusion (based on the post-operative PCV of ≤ 24%, additional use of uterotonic agents and additional surgical procedures.

Blood loss during the CS and four hours postoperatively was assessed in a standard manner. The intra-operative blood loss was assessed by measuring the total volume of blood collected in the calibrated suction jar and blood-soaked pre-weighed underlays, drapes, gauze and abdominal mops by deducting their known dry weights. The volume of amniotic fluid collected in the suction jar was noted and excluded in the blood volume estimation. The postoperative blood loss was measured from the blood-soaked pre-weighed underlays placed underneath the women immediately after the CS and blood-soaked pre-weighed pad placed over the introitus to monitor bleeding from the vagina up to four hours after the CS after deducting the known dry weights of the underlays and the pads. The underlays, drapes, gauze and pads were weighed before surgery and 4 hours after surgery using a digital weighing scale (Seca GmbH and co, Hamburg, Germany) which was calibrated before and between use. The difference in weight between the dry and soaked underlay, drapes, and pads were used to estimate the blood loss because a 1-gram difference is equivalent to 1 mL of blood [17]. The PCV values of the women were checked 24 hours after the CS to determine the differences in their pre-and post-operative PCV values. Blood loss was also determined by the differences in the pre-CS and 24-hour post-CS PCV values using this formula [5]: Calculated blood loss = estimated blood volume × (preoperative PCV − postoperative PCV)/preoperative PCV (where estimated blood volume (mL) = booking weight (kg) × 85)

Sample size: The sample size calculation was done based on the reports from a recent study [12]. The mean intraoperative blood loss during elective CS with the administration of oxytocin infusion after cord clamping was 588ml with a standard deviation of 96ml. Assuming that early administration of

oxytocin infusion before uterine incision would further reduce the blood loss by 200ml, a sample size of 250 women (125 women in each group) was calculated to achieve a power of 80% and detect a significance of less than 5%.

Data Analysis: Data collected were analyzed using Statistical Package for Social Sciences (SPSS) version 20 (Chicago, IL, USA). Continuous variables were analyzed using mean and standard deviation, while categorical variables were presented in frequency and percentages. Tests of significance were done for continuous variables using student's t-test or ANOVA, while Chi-square or Fischer's exact tests were done for categorical variables. A p-value of less than 0.05 was statistically significant.

Ethical clearance: The study was approved by the Institution's Ethics and Research Committee (EKSUTH/A245/2019/02/04). All the procedures performed were done following the ethical standards of our Institution's Ethics and Research Committee and with the 1964 Declaration of Helsinki and its later amendments. The trial was also registered in the Pan African Clinical Trial Registry (www.pactr.org) with trial no PACTR201909775190644. The women who participated in the study were adequately informed about the study and the possible complications that could occur from the procedure, including hemorrhage. They were also counselled on the possibility of having a blood transfusion and the complications that could result from it. Written informed consents were obtained from them before enrollment, and they were at liberty to withdraw from the study without the withdrawal affecting their care.

RESULTS

A total of 287 women were counselled to participate in the study, 27 of them were excluded for not meeting the criteria and 10 women declined participation in the study. Two hundred and fifty women were randomized into the study. There were 125 women in the early group, who received an oxytocin infusion before uterine incision (group 1). There were 125 women in the late group who received an oxytocin infusion after cord clamping (group 2). This is shown in the study flow chart (Figure 1).

There were no significant differences in the baseline characteristics of the women involved

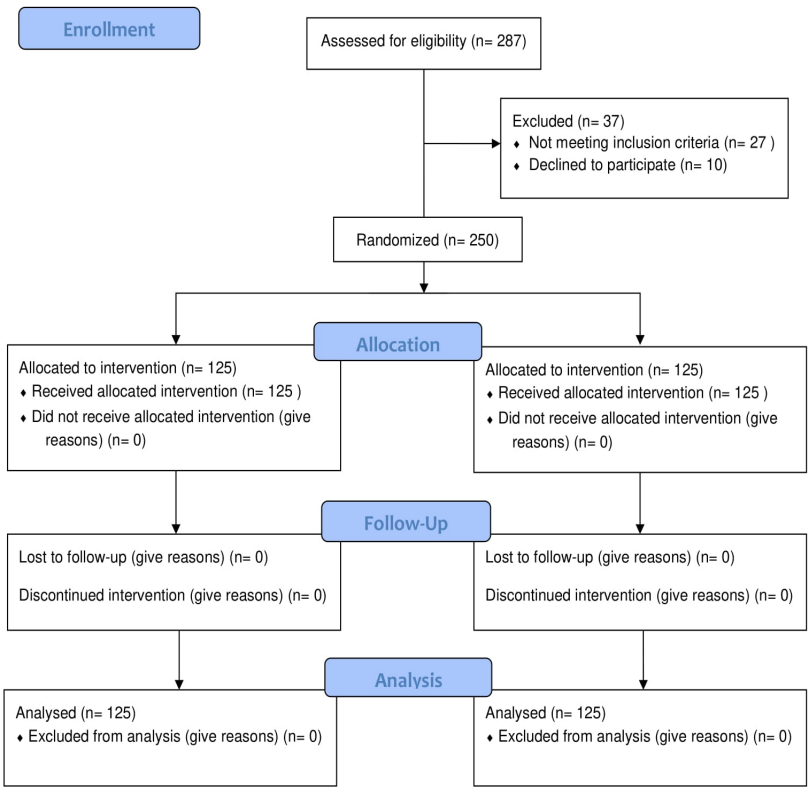

Figure 1: The study flow diagram

Table 1: Sociodemographic characteristics of the participants

Variables	Time of Oxytocin infusion		p-value
	Group 1	Group 2	
Age (years)	28.82 ± 5.29	29.64 ± 5.43	0.226
Parity	2.27 ± 0.97	2.12 ± 0.88	0.195
Maternal weight (kg)	63.47 ± 5.49	64.60 ± 4.87	0.087
Gestation at induction (weeks)	38.24 ± 0.56	38.10 ± 0.73	0.099
Pre-operative vital signs			
Heart rate (bpm)	76.83 ± 3.33	77.63 ± 2.68	0.501
Respiratory rate (cpm)	13.63 ± 1.10	13.79 ± 1.16	0.265
Systolic Blood Pressure (mmHg)	109.52 ± 11.19	110.24 ± 10.86	0.657
Diastolic Blood Pressure (mmHg)	71.07 ± 6.02	70.38 ± 7.87	0.433
Post-operative Packed Cell Volume (%)	35.58 ± 1.69	35.53 ± 4.14	0.889
Parity of women[a]			
0	45 (60.0%)	43 (57.3%)	0.432
≥ 1	30 (40.0%)	32 (42.7%)	
Indication for caesarean section (CS)[a]			
Repeat CS	59 (47.2%)	49 (39.2%)	0.200
Malpresentation/Abnormal lie	46 (36.8%)	60 (48.0%)	
Maternal request	20 (18.0%)	18 (12.8%)	

Group 1: Oxytocin infusion before uterine incision
Group 2: Oxytocin infusion after cord clamping
[a]Variables are presented in frequency and percentages and analyzed using Chi-square test

in the study with respect to their mean age, parity, maternal weight and gestational age at delivery; p > 0.05. The median parity was 2 and the interquartile range was 1. The indications for CS were also similar in the two groups; p > 0.05 and these are shown in Table 1.

Table 2 shows that the mean intraoperative blood loss was significantly lower among women in group 1 compared to women in group 2; (339.98 ± 84.9ml versus 363.69 ± 48.69ml; p = 0.007 respectively). The mean postoperative blood loss was not statistically different among the women in group 1 compared to the women in group 2; (341.14 ± 58.23ml versus 345.89 ± 62.78ml; p = 0.536 respectively). However, women in the late administration of oxytocin infusion group had a higher mean total blood loss and mean a drop in PCV values than women in the early administration of oxytocin infusion group and these results were statistically significant, [(711.26 ± 62.54ml versus 682.06 ± 74.64ml; p = 0.001 respectively); (3.17 ± 0.69% versus 2.85 ± 0.79%; p = 0.001 respectively)]. The duration of the CS and uterine incision-delivery interval were not significantly different among the women in group 1 and those in group 2; p = 0.648 and 0.544, respectively. More women in the late group (22/125) required additional uterotonic agents than in the early group (10/125) and this was statistically significant; p = 0.023. However, there was no difference regarding the need for blood transfusion or additional surgical procedures between both groups, p = 0.154 and 0.500, respectively (Table 2).

Table 3 shows that the preoperative and post-operative vital signs taken just before the commencement of the CS and immediately after the completion of the CS were not significantly different between both groups; p > 0.05. Also, there were no significant changes in the preoperative and post-operative vital signs among the women in each group; p > 0.05. The preoperative and post-operative PCV values did not differ significantly between the two groups; p = 0.889 and 0.266, respectively (Table 3).

The neonatal outcomes of both groups in terms of birth weight, Apgar score, need for admission

Table 2: Outcomes of the study

Variables	Time of Oxytocin infusion		p-value
	Group 1	Group 2	
Intra-operative blood loss (ml)	339.98 ± 84.91	63.69 ± 48.19	0.007*
Post-operative blood loss (ml)	341.14 ± 56.23	345.89 ± 62.78	0.536
Total blood loss (ml)	682.06 ± 74.64	711.26 ± 62.54	0.001*
Calculated blood loss (ml)	772.82 ± 104.22	870,50 ± 65.22	0.001*
Difference in pre- and post-operative PCV (%)	2.85 ± 0.79	3.17 ± 0.69	0.001*
Duration of caesarean section (minutes)	52.06 ± 6.53	51.71 ± 5.38	0.648
Incision delivery interval (minutes)	1.84 ± 0.73	1.78 ± 0.72	0.544
Post-operative vital signs			
Heart rate (bpm)	77.37 ± 3.76	79.84 ± 2.29	0.375
Respiratory rate (cpm)	14.21 ± 0.63	14.37 ± 1.02	0.136
Systolic Blood Pressure (mmHg)	110.87 ±10.17	115.98 ± 9.65	0.192
Diastolic Blood Pressure (mmHg)	69.46 ± 5.90	69.42 ± 0.42	0.172
Post-operative Packed Cell Volume (%)	32.73 ± 1.67	31.37 ± 2.17	0.266
Need for additional uterotonics†	10 (8.0%)	22 (17.5%)	0.023*
Need for blood transfusion†	4 (3.2%)	9 (7.2%)	0.254
Additional surgical procedures†	6 (4.8%)	5 (4.0%)	0.758

Group 1: Oxytocin infusion before uterine incision
Group 2: Oxytocin infusion after cord clamping
PCV: Packed cell volume
* Statistically significant
† Variables are presented in frequency and percentages and analyzed using Chi-square test

into neonatal intensive care unit and its indications were not significantly different in both groups, $p > 0.05$, as shown in Table 4. No maternal and perinatal deaths were recorded in either study group.

DISCUSSION

A reduction in blood loss during and after CS is beneficial to the patients in decreased postoperative morbidity and mortality and a decrease in risks associated with blood transfusions. The atonic uterus is the leading cause of both intra- and postpartum bleeding, accounting for about 80% of these cases [3,4]. The use of uterotonic agents has been demonstrated to effectively prevent and reduce PPH due to the atonic uterus [5,6]. Oxytocin is the uterotonic of choice and is most commonly used in obstetrics to prevent and treat uterine atony because of its low cost, rapid onset of action, and effectiveness3. There has been no consensus on the optimum dose and rate of administration of oxytocin during caesarean sections. Oxytocin administration by continuous infusion in caesarean section reduces the need for using other uterotonic agents. Sheehan et al. demonstrated in their study that there was a significant reduction in the need for other uterotonic agents when intravenous oxytocin bolus was followed by oxytocin infusion compared with an intravenous oxytocin bolus alone [18]. The use of intravenous oxytocin bolus has been associated with hemodynamic changes accompanied by abnormal electrocardiogram (ECG) findings resulting in hypotension and tachycardia. These changes are of short duration and reversible; hence the use of oxytocin bolus should be avoided, particularly in hypovolemic patients or those with low cardiovascular reserves [18,19]. Also, the preference for oxytocin infusion over intravenous oxytocin bolus during CS due to reduced incidences of adverse hemodynamic changes and effects associated with the bolus injection has been demonstrated in some recent studies [8,12].

Table 3: Neonatal outcomes of the study

Variables	Time of Oxytocin infusion		p-value
	Group 1	Group 2	
Birth weight (kg) †	3.26 ± 0.34	3.28 ± 0.43	0.583
Apgar score†			
1 minute	8.34 ± 0.950	8.19 ± 0.759	0.187
5 minutes	9.82 ± 0.382	9.76 ± 0.429	0.214
Apgar score < 7			
1 minute	4 (3.2%)	3 (2.4%)	0.701
5 minutes	2 (1.6%)	2 (1.6%)	1.000
SCBU admission	5 (4.0%)	6 (4.8%)	0.758
Indication for NICU admission			
Severe birth asphyxia	1 (5.3%)	2 (4.0%)	0.953
Moderate birth asphyxia	1 (2.7%)	1 (2.7%)	
Macrosomia	3 (1.3%)	3 (2.7%)	

† Mean ± standard deviation
NICU: Neonatal Intensive Care Unit

Estimation of both intra-operative and post-operative blood loss is one of the ways of assessing the effectiveness of uterotonic agents. The intra-operative and total blood loss was significantly lower in women commenced on oxytocin infusion before uterine incision than in women who were given oxytocin infusion after cord clamping in this study. Also, the post-operative blood loss was lower among the women in the early group compared to the late group, though not statistically significant. These findings were similar to results reported by Ahmed et al. [12] in their study on the effect of initiating oxytocin infusion before uterine incision during elective CS. They opined that early administration of the oxytocin infusion would lead to a rapid onset of strong uterine contractions that would cause placental separation, thereby minimizing blood loss [12].

This study showed that the need for additional intraoperative uterotonics, a measure of the effectiveness of any uterotonic agent, was less among women who received an oxytocin infusion before uterine incision compared to those who had an oxytocin infusion after cord clamping [8.0% (10/125) versus 17.5% (22/125); p = 0.023]. This finding was in agreement with the report of the study of Gungorduk et al. [19] that oxytocin infusion after an initial oxytocin bolus decreases both the use of additional uterotonics and major obstetric hemorrhage. This was also corroborated by the finding of Sheehan et al. [16] that continuous oxytocin infusion reduces the need for additional uterotonics after an initial intravenous oxytocin bolus. In both studies, oxytocin infusion was commenced after cord clamping [16,19].

However, in another study by Ahmed et al. [12], it was demonstrated that an oxytocin infusion alone effectively maintained adequate uterine contractility and reduced blood loss and the need for additional uterotonics. The study further showed that early administration of the oxytocin infusion before the uterine incision was significantly associated with a reduced need for additional uterotonics compared to administration after cord clamping. They opined that the use of oxytocin infusion before uterine incision could be superior to both the intravenous oxytocin bolus and infusion after cord clamping to reduce the need for additional uterotonics [12]. This was similar to the finding in this study.

Women in both groups did not experience significant changes in the vital signs like the heart rate, respiratory rate and diastolic and systolic blood pressure recorded before and after the procedure. This was in agreement with the findings of Ahmed et al. [12] also on oxytocin infusion but in contrast to the findings of Bhattacharya et al. [8] and Sheehan et al. [16] that reported significant effects of intravenous oxytocin bolus on the vital signs. The findings of our study also

corroborated the conclusion of Thomas et al. in a study comparing hemodynamic effects of oxytocin bolus and infusion during CS that an oxytocin bolus should be used with caution in patients who are cardiovascularly unstable while oxytocin infusion did not have the same considerations in these cases [14].

The preoperative and post-operative packed cell volume, the need for blood transfusion, additional surgical procedures and the neonatal outcomes did not differ in the two groups. There were no maternal or perinatal deaths recorded in this study.

The strengths of this study lie in the fact that it was a randomized controlled trial, thereby eliminating bias in patients' recruitment while anesthesia and surgery were performed according to standard procedure and the method of blood estimation was objective using the weighing method as opposed to visual estimation.

The study's limitations are an inability to blind the surgeons as to the timing of commencement of oxytocin infusion, exclusion of women at high risk of uterine atony and exclusion of women with multiple pregnancies who could have other fetuses trapped due to contractions arising from early initiation of oxytocin infusion.

CONCLUSION

This study has demonstrated that intravenous oxytocin infusion can be safely used as routine uterotonic during elective CS to reduce blood loss without the adverse hemodynamic changes associated with an intravenous oxytocin bolus. It also showed that early administration of intravenous oxytocin infusion before the uterine incision is superior to administering the oxytocin infusion after cord clamping in reducing blood loss and the need for additional uterotonics and surgeries during elective CS. Therefore, we recommend using intravenous oxytocin infusion before uterine incision during elective CS in obstetric practice.

Acknowledgement

The authors wish to acknowledge all the pregnant women who consented to participate in this study, the residents and the nursing staff involved in the clients' randomization and management.

REFERENCES

[1] A.P. Betran, J. Ye, A.B. Moller, A. Moller, J. Zhang, A.M. Gulmezoglu, M.R. Torloni. The increasing trend in caesarean section rates: Global, Regional and National Estimates: 1990-2014. PLoS One 2016; 11(2): e0148343

[2] N.A. Sathe, F.E. Likis, J.L. Young, A. Morgans, D. Carlson-Bremer, J. Andrew. Procedures and Uterine-Sparing Surgeries for Managing Postpartum Hemorrhage: A Systematic Review. Obstet Gynecol Surv 2016 71(2): 99-113

[3] E.T. Yamaguchi, M.M. Siaulys, M.L.A. Torres. Oxytocin in cesarean-sections. What's new? Rev Bras Anestesiol 2016. http://dx.doi.org/10.1016/j.bjane.2014.11.015.

[4] M.K. Roach, A. Abramovici, A.T.N Tita. Dose and Duration of Oxytocin to Prevent Postpartum Hemorrhage: A Review. Am J Perinatol 2013; 30(7): 523-527

[5] S.R. Sharon, A.A. Montgomery, M. Carey. Oxytocin bolus versus oxytocin bolus and infusion for control of blood loss at elective caesarean section: double blind, placebo controlled, randomized trial. BMJ 2011; 343: d4661. doi: 10.1136/bmj.d4661

[6] C.A. Grotegut, M.J. Paglia, L.N. Johnson, B. Thames, A.H James. Oxytocin exposure during labor among women with postpartum hemorrhage secondary to uterine atony. Am J Obstet Gynecol 2011; 204(1):56.e1–56.e6

[7] R.A. Dyer, D van Dyk, A. Dresner. The use of uterotonic drugs during caesarean section. Int J Obstet Anesth 2010; 19(3): 313–319.

[8] S. Bhattacharya, S. Ghosh, D Ray, S. Mallik, A. Laha. Oxytocin administration during cesarean delivery: Randomized controlled trial to compare intravenous bolus with intravenous infusion regimen. J Anaesthesiol Clin Pharmacol 2013; 29:32-5

[9] Royal College of Obstetricians and Gynaecologists. Postpartum haemorrhage, prevention and management. (Green-top Guideline No. 52) 2016. http://www.rcog.uk>gtp52 Accessed June 20, 2019

[10] S.R. Sheehan, L. Wedisinghe, M. Macleod,

D.J. Murphy. Implementation of guidelines on oxytocin use at caesarean section: a survey of practice in Great Britain and Ireland. Eur J Obstet Gynecol Reprod Biol 2010; 48: 121- 4[11] ACOG. Practice bulletin summary: Clinical management guidelines for obstetrician-gynecologists. Number 183. Postpartum hemorrhage. Obstet Gynecol 2017; 130(4): 923-925

[12] A.A. Abdelaleem, A.M. Abbas, A.L Thabet, E. Badran, I.H El-Nashar. The effect of initiating intravenous oxytocin infusion before uterine incision on the blood loss during elective cesarean section: a randomized clinical trial. J Matern Fetal Neonatal Med 2019; 32 (22): 3723-3728. doi: 10.1080/14767058.2018.1471461

[13] A. Duffield, C. McKenzie, B. Carvalho, B. Ramachandran, V Yin, Y.Y. El-Sayed, E.T. Riley, A.J.Butwick. Effect of a high-rate versus a low-rate oxytocin infusion for maintaining uterine contractility during elective cesarean delivery: A prospective randomized clinical trial. Anesth Analg 2017; 124: 857–62

[14] J.S Thomas, S.H. Koh, G.M. Cooper. Haemodynamic effects of oxytocin given as i.v. bolus or infusion on women undergoing caesarean section. Br J Anesth 2007; 98 (1): 116-119

[15] C. Akinaga, S. Uchizaki, T. Kurita, M. Taniguchi, H. Makino, A. Suzuki, T. Uchida, K. Suzuki, H Itoh, S. Tani, S. Sato, K. Terui. Randomized double-blind comparison of the effects of intramyometrial and intravenous oxytocin during elective cesarean section. J Obstet Gynaecol Res 2016; 42(4): 404-409

[16] S.R. Sheehan, A.A. Montgomery, M. Carey, F.M. McAuliffe, M. Eogan, R. Gleeson, M. Geary, D.J. Murphy. Oxytocin bolus versus oxytocin bolus and infusion for control of blood loss at elective caesarean section: double blind, placebo controlled, randomized trial. BMJ 2011; 343:d4661.

[17] K.A Frass. Postpartum hemorrhage is related to the hemo-globin levels at labour: an observational study. Alex J Med. 2015; 51(4):333-337.

[18] A.J. Butwick, L. Coleman, S.E. Cohen, E.T. Riley, B. Carvalho. Minimum effective bolus dose of oxytocin during elective caesarean delivery. Br J Anaesth 2010; 104(3): 338-343.

[19] K. Gungorduk, O. Asicioglu, O. Celikkol, Y. Olgac, C. Ark. Use of additional oxytocin to reduce blood loss at elective caesarean section: a randomized controlled trial. Aust N Z J Obstet Gynaecol 2010; 50(1):36-39.