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Research Article

Efficacy of Early Intravenous Infusion of Oxytocin at Induction of Anesthesia in Decreasing Blood Loss during Elective Caesarean Section: A Randomized Controlled Trial

Ahmed A Tharwat[1], Walaa E Ahmed[2], Mortada E Abdulrahman[1], Ahmed A El Shorbagy[3], Mohamed S Elshorbagy[4] and Ramy Mahrose[4]*

[1]*Department of Obstetrics & Gynecology, Ain Shams University, Cairo, Egypt*

[2]*Department of Obstetrics & Gynecology, Helwan University, Egypt*

[3]*Department of Obstetrics & Gynecology, Ashmoun General Hospital, Egypt*

[4]*Department of Anesthesiology, Ain Shams University, Cairo, Egypt*

Abstract

Aim: To evaluate the efficacy of early administration of intravenous infusion of oxytocin 10 U in 200 ml lactated Ringer over 15 minutes (at the time of induction of anesthesia before skin incision) in decreasing blood loss during cesarean section compared to the usual trend of giving oxytocin after delivery of the fetus.

Methods: Three hundred patients planned for elective caesarean section were randomized into 2 groups. In group A (n=150), patients were given intravenous infusion of oxytocin 10 units in 200 ml of lactated Ringer's over 15 minutes starting before skin incision during induction of anesthesia and in group B (n=150) oxytocin was given after delivery of the fetus. Main outcome was the amount of blood loss. Other outcomes included vital signs, incidence of postpartum hemorrhage, uterine tone, additional uterotonic, duration of the operation, changes in hemoglobin & haematocrit levels, side effects caused by oxytocin and Apgar score.

Results: The mean total blood loss was 340.3 ml ± 199.6 ml in group A and 484.3 ± 243.9 in group B (P<0.001). The mean blood loss in group A was 144 ml ± 25.7 ml (95%CI 93.4-194.6) less than group B and the main difference was intraoperatively 126 ml ± 22.7 ml (95%CI81.2-170.8). Oxytocin infusion before skin incision causes reduction of hemoglobin, haematocrit and blood pressure at a lower rates compared to oxytocin given after fetus delivery (P<0.001). Increase in the heart rate in group A was less than group B (P<0.001). Uterine tone in group A was 4.1 ± 1.1 (=well contracted) versus 3 ± 1 in group B (=adequate contracted) (P<0.001). Postpartum hemorrhage was less frequent among Group A (2%) compared to Group B (3.7%), (P=0.507). Operative time, Apgar score and additional uterotonic values were not statistically different. No oxytocin complications except for nausea and vomiting.

Conclusion: Oxytocin given during CS as an intravenous infusion of oxytocin at the time of induction of anesthesia before skin incision had a priority over giving oxytocin after delivery of the fetus regarding decreasing blood loss and gives a better chance in prevention of PPH with lower changes in haemodaynmic status and no adverse fetal outcome.

Keywords: Oxytocin; Bloodloss; Postpartumhemorrhage; Infusion; Elective cesarean section

Introduction

Caesarean Section (CS) is one of the most commonly performed major operations in women throughout the world [1]. Caesarean section rates have increased to as high as 25% to 30% in many areas of the world [2].

Blood loss during cesarean is twice that of vaginal delivery (1000 ml *vs.* 500 ml)). Postpartum Hemorrhage (PPH) remains a leading cause of maternal mortality, especially in developing countries [3]. In order to reduce maternal mortality and morbidity caused by bleeding, it is important to reduce the amount of bleeding during and after CS [4].

Oxytocin routinely administered after delivery by bolus and infusion to initiate and maintain adequate uterine contractility after placental delivery, to minimize blood loss and prevent PPH. Prophylactic routine use of oxytocin has been shown to reduce the incidence of PPH by up to 40% [5]. Despite being a common practice, oxytocin is used in CS empirically. Surprisingly, to date there is no consensus about the ideal regime of its administration, even after 60 years of its synthesis and routine use in obstetric centers. An example at least 38 different regimens of oxytocin infusion in the UK [6]. An IV bolus of 10 IU oxytocin was traditionally given after delivery. Randomized controlled trials have shown that lower IV bolus doses have same efficacy with fewer side effects and many countries now recommend a 5 IU maximum dose [7]. Intravenous oxytocin has a very short half-life (4-10 minutes) [8]. In elective CS, administration of oxytocin intravenous infusion is better than the same dose administered as an intravenous bolus, to produce adequate uterine contraction and is associated with less adverse hemodynamic changes [9]. This study aimed to evaluate the efficacy of early administration of intravenous infusion of oxytocin at the time of induction of anesthesia before skin incision in decreasing blood loss during cesarean section

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***Corresponding author:** Ramy Mahrose, Department of Anesthesiology, Faculty of Medicine, Ain Shams University, Cairo, Egypt; E-mail: ramymahrose2@gmail.com

compared to the usual trend of giving oxytocin after delivery of the fetus, and if the regimen of a dose 10 U in 200 ml lactated Ringer and duration of infusion in 15 minutes had a priority over other used regimens.

Materials and Methods

This pilot randomized controlled clinical study was conducted in Ain-Shams University Maternity Hospital, Cairo-Egypt, from March 2016 to September 2016 on patients planned for elective caesarean section.

Women were recruited to the trial during the initial arrangements being made for elective caesarean section in the antenatal ward prior to surgery. Information on demographic characteristics, medical and reproductive histories was recorded. Vital signs (heart rate and blood pressure) were checked and laboratory examinations (complete blood count, coagulation profile, blood grouping, random blood sugar, kidney functions and liver functions) were made.

Patients with the following criteria: 20-35 years old, BMI 20 kg/m^2 - 35 kg/m^2, HGB ≥ 10 g/dl and Gestational age ≥ 37 weeks were included. Those who were excluded had any of the following: bleeding disorders, intake of steroids, anticoagulant and anti platelets drugs, multiple pregnancy, pregnancy induced hypertension, macrosomia, polyhydramnios, antepartum hemorrhage, placenta previa, any complication during the surgery, history of postpartum hemorrhage, medical disorders (e.g., hypertension, diabetes, heart diseases) and contraindication to oxytocin infusion (e.g., hypersensitivity).

We approach eligible women and offer information about the study. Informed consent was obtained from all participants. All procedures performed in the study were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Candidates were allocated in two groups, experimental arm (Group A) and control arm (Group B), according to a sequence of random numbers generated by computer with ratio 1:1. The assignment was done through opaque, sealed opened at the moment the mother enters the operative theatre. Participants in the experimental arm were given intravenous infusion of oxytocin 10 units in 200 ml of lactated Ringer's over 15 minutes (250 drop/minute) starting before skin incision during induction of anesthesia. Women in the control group were given intravenous infusion of oxytocin 10 units in 200 ml of lactated Ringer's over 15 minutes (250 drop/minute) after delivery of the fetus.

In both arms of the study, surgical and anesthetic techniques were standardized, with all patients undergoing spinal anesthesia. Surgeons were asked to operate to a standard procedure that specifies controlled cord traction for delivery of the placenta, two layer closure of the uterine incision, and to avoid delivering the uterus for suturing unless clinically indicated. Deviations from the standard procedure were recorded.

All towels, swabs and vulval pads were weighted before and after its usage to measure blood loss. The amount of blood lost (ml)=(weight of used towels + unused towels) - weight of all towels /1.05 [10], plus the volume of blood collected in suction containers. In addition, uterine tone assessed by the obstetrician at 5,10,15 and 20 minutes, was scored according to a five-point scale, where 1=atonic; 2=partial but inadequate contraction; 3=adequate contraction; 4=well contracted and 5=very well contracted [11].

The primary outcome was the amount of blood loss during CS. The secondary outcomes included vital signs (immediately post-operative, one and six hours after birth), incidence of postpartum hemorrhage, uterine tone score, the need for other uterotonic (further dose of oxytocin 10 units or a dose of misopristol 800 mcg rectally), duration of the operation, changes in hemoglobin &haematocrit levels (performed before delivery & 24 hours after CS), side effects caused by oxytocin and Apgar score of the fetus at 1 and 5 minutes.

Statistical analysis was performed using SPSS (v16; SPSS, Chicago, IL, USA).Numeric parametric variables were described as mean and standard deviation. Numbers and percentages were used to describe categorical variables. Difference between 2 independent groups was analyzed using independent Student t-test (for numeric parametric variables). Chi-square test was used for comparing the qualitative variables. In parametric data (SD <50% mean), significant level was set at 0.05.

Results

Three hundred women were recruited after consenting and meeting the inclusion criteria and were randomly allocated to each arm (150 in the experimental arm and 150 in the control arm).

The mean age of participants was 29 ± 3.7 years in the experimental arm and 29.2 ± 3.7 years in the control arm with no statistically significant difference as in Body Mass Index (BMI) with an average of 27.5 kg/m^2 ± 0.9 kg/m^2 and 27.6 kg/m^2 ± 1 kg/m^2, respectively. There is no statistically significant difference regarding parity (1.9 ± 1.5 versus 1.8 ± 1.4) and gestational age (39.1 ± 1weeks versus 39 ± 1weeks) in experimental and control arms respectively (Table 1).

Table 1: Demographic characteristics among the studied groups.

Items	Group A (N=150) Mean ± SD	Group B (N=150) Mean ± SD	P-value
Age (years)	29.0 ± 3.7	29.2 ± 3.7	0.537 (NS)
BMI (kg/m^2)	27.5 ± 0.9	27.6 ± 1.0	0.557 (NS)
Parity	1.9 ± 1.5	1.8 ± 1.4	0.658 (NS)
GA (weeks)	39.1 ± 1.0	39.0 ± 1.0	0.310 (NS)

NS: Non-significant

The indications of caesarean section in the study were previous caesarean section, dystocia, fetal distress and malpresentation .There was no significant difference between the 2 studied groups regarding these indications . Previous caesarean section indication accounted for 39.3% in the study group and 37.3% in the control group. Dystocia as an indication was done in 27.7% of study arm and in 37.3% of the control arm. In the study arm, caesarean section due to fetal distress was 18.7% of cases and in the control arm was 12%. The percentages of caesarean section for malpresentation in the study and control groups were 14.7% and 13.3% respectively (Table 2).

Table 2: Indications of caesarean section among the studied groups.

	Group A (N=150)	Group B (N=150)	P-value
Previous caesarean	59 (39.3%)	56 (37.3%)	0.198 (NS)
Dystocia	41 (27.3%)	56 (37.3%)	
Fetal distress	28 (18.7%)	18 (12%)	
Malpresentation	22 (14.7%)	20 (13.3%)	

NS: Non-significant

In study arm the mean intraoperative blood loss was 315.7 ml ± 175.9 ml and 441.7 ml ± 216 ml in control group. Regarding postoperative blood loss, the mean was 65.3 ml ± 36.2 ml and 76 ml ± 44 ml in study and control groups respectively. The mean total blood

loss was lower in group A (340.3 ml ± 199.6 ml) than group B (484.3 ± 243.9) (Table 3). All these differences were of statistical significance. Table 4 shows the value of oxytocin infusion given before skin incision compared to that given after fetus delivery, the mean total blood loss in group A was 144 ml ± 25.7 ml (95%CI 93.4-194.6) less than group B and the main difference was intraoperatively126 ml ± 22.7 ml (95% CI81.2-170.8).

Table 3: Blood loss (ml) among the studied groups.

	Group A	Group B	P-value
	(N=150) Mean ± SD	(N=150) Mean ± SD	
Intraoperative	315.7 ± 175.9	441.7 ± 216.0	<0.001 (S)
Postoperative(24 hour)	65.3 ± 36.2	76.0 ± 44.0	0.023 (S)
Total	340.3 ± 199.6	484.3 ± 243.9	<0.001 (S)

S: Significant

Table 4: Blood loss differences (ml) between group A and group B.

	Mean ± SD	95% CI
Intraoperative	126.0 ± 22.7	81.2-170.8
Postoperative	10.7 ± 4.7	1.5-19.8
Total	144.0 ± 25.7	93.4-194.6

CI: Confidence Interval

Regarding hemoglobin (gm/dl) and haematocrit (%) levels performed preoperatively, the means were 13.3 gm/dl ± 1 gm/dl and 36.8% ± 3.1% in study arm. In control group, values were 12.3 gm/dl ± 0.8 gm/dl and 36.9% ± 2.6% respectively. In postoperative period, the mean hemoglobin and haematocrit in study arm were 11.1 gm/dl ± 1.1 gm/dl and 34.3% ± 3.3% and control group were 10.6 gm/dl ± 0.9 gm/dl and 33.1% ± 3% respectively. The net reduction of hemoglobin and haematocrit means in group A were 1.2 gm/dl ± 0.9 gm/dl and 2.5% ± 2.4%, while in group B 1.8 gm/dl ± 0.8 gm/dl and 3.9% ± 2.4% respectively. These differences were statistically significance. Administration of oxytocin infusion before skin incision causes reduction of hemoglobin and haematocrit at a lower rate compared to oxytocin infusion given after fetus delivery by 0.6 gm/dl ± 0.1 gm/dl (95% CI:0.4-0.8) and 1.4% ± 0.3% (95% CI:0.8-1.9) respectively (Table 5).

Table 5: Hemoglobin (Hb) (gm/dl) and Hematocrit (Hct) (%) in the studied groups.

	Group A (N=150) (Mean ± SD)		Group (N=150) (Mean ± SD)		P-value
	Hb*	Hct**	Hb*	Hct**	
Pre-operative	12.3 ± 1.0	36.8 ± 3.1	12.3 ± 0.8	36.9 ± 2.6	0.586* (NS) 0.652** (NS)
Post-operative	11.1 ± 1.1	34.3 ± 3.3	10.6 ± 0.9	33.1 ± 3.0	<0.001 (S)
Reduction	1.2 ± 0.9	2.5 ± 2.4	1.8 ± 0.8	3.9 ± 2.4	<0.001 (S)

NS: Non-Significant, S: Significant

Regarding pulse rates, no significant difference between groups A and B was observed in preoperative stage. In postoperative stage, pulse rates in group A were significantly lower than group B. In both arms of the study, there is an increase in pulse rate in post operative period to pulse rates in preoperative period (Table 6). However, the increase in the heart rate in the study group was less than the heart rate increase in the control group with P<0.001 (Table 7). Oxytocin infusion reduces the blood pressure in all patients postoperatively. The rate of reduction of blood pressure in study group was lower than the control group with P<0.001 (Tables 8 and 9).

Uterine tone score was statistically significant higher among group A than group B. The mean uterine tone score in group A was 4.1 ± 1.1 (=well contracted) versus 3 ± 1 in group B (=adequate contracted). In addition, postpartum hemorrhage was less frequent among Group A (2%) compared to Group B (3.7%), however, this difference was not statistically significant. No reported complications from the use of oxytocin except for nausea and vomiting, where the incidence was 15.3% in the study arm and 12.7% in the control side. In the study arm, operative duration, Apgar-1 minute, Apgar-5 minutes and the incidence of additional uterotonic usage were [(32.9 ± 7.3), (8.4 ± 0.8), (9.6 ± 0.5) and (8%) respectively]. These values were merely equal to and not statistically different from values in the control arm [(33 ± 7.2), (8.5 ± 0.7), (9.7 ± 0.5) and (8.6%) respectively] (Tables 10 and 11).

Table 6: Pulse rate (Beat/minute) among the studied groups.

Time	Group A (N=150) Mean ± SD	Group B (N=150) Mean ± SD	P-value
Preoperative	83.8 ± 5.7	83.7 ± 5.1	0.923 (NS)
Immediately PO	89.2 ± 6.4	91.5 ± 6.3	0.002 (S)
1-hour PO	91.0 ± 6.9	94.0 ± 6.7	<0.001 (S)
6-hours PO	92.7 ± 7.4	97.2 ± 7.3	<0.001 (S)

NS: Non-Significant; S: Significant; PO: Post Operative

Table 7: Post-Operative pulse rate differences (Beat/minute) from preoperative pulse rate among the studied groups.

	Group A (N=150) Mean ± SD	Group B (N=150) Mean ± SD	P-value
Immediately PO	5.4 ± 2.3	7.8 ± 3.4	<0.001(S)
1-hourPO	7.2 ± 3.1	10.3 ± 4.2	<0.001(S)
6-hoursPO	8.9 ± 3.9	13.5 ± 5.2	<0.001(S)

S: Significant; PO: Post Operative

Table 8: Systolic and diastolic blood pressures (SBP/DBP) (mmHg) among the studied groups.

	Group A (N=150) Mean ± SD		Group B (N=150) Mean ± SD		P-value
	SBP*	DBP**	SBP*	DBP**	
Preoperative	118.4 ± 4.4	75.6 ± 2.2	118.2 ± 4.3	75.4 ± 2.1	0.499**NS) 0.791*(NS)
Immediately PO	112.3 ± 5.2	66.2 ± 4.9	108.9 ± 5.5	64.2 ± 4.5	<0.001(S)
1-hourPO	110.3 ± 5.9	65.9 ± 5.3	105.5 ± 6.3	62.7 ± 5.5	<0.001(S)
6-hoursPO	107.7 ± 7.4	65.2 ± 5.6	101.9 ± 7.5	61.2 ± 7.1	<0.001(S)

NS: Non-Significant, S: Significant, PO: Post Operative

Table 9: Reduction of Systolic and diastolic blood pressure (SBP/DBP) (mmHg) from preoperative values among the studied groups.

	Group A (N=150) Mean ± SD		Group B (N=150) Mean ± SD		P-value
	SBP*	DBP**	SBP*	DBP**	
Immediately PO	6.1 ± 2.4	9.3 ± 4.2	9.3 ± 4.6	11.2 ± 4.0	<0.001 (S)
1-hour PO	8.1 ± 3.6	9.7 ± 4.9	12 ± 5.4	12.7 ± 5.1	<0.001(S)
6-hours PO	10.7 ± 5.5	10.4 ± 5.5	16.3 ± 6.8	14.2 ± 6.8	<0.001(S)

S: Significant; PO: Post Operative

Table 10: Operation time, Apgar score and uterine tone score in the studied groups.

	Group A (N=150) Mean ± SD	Group B (N=150) Mean ± SD	P-value
Uterine tone	4.1 ± 1.1	3.0 ± 1.0	0.001 (S)
Operation time (minutes)	32.9 ± 7.3	33.0 ± 7.2	0.886 (NS)
Apgar-1minute	8.4 ± 0.8	8.5 ± 0.7	0.418 (NS)
Apgar-5 minutes	9.6 ± 0.5	9.7 ± 0.5	0.434 (NS)

NS: Non-Significant; S: Significant

Table 11: Incidence of post partum hemorrhage, additional uterotonicand oxytocin side effects in the two studied groups.

	Group A (N=150)	Group B (N=150)	P-value
Postpartum Hemorrhage	3 (2%)	5 (3.7%)	0.507 (NS)
Additional uterotonic	12 (8%)	13 (8.6%)	0.432 (NS)
Nausea & vomiting	23 (15.3%)	19 (12.7%)	0.506 (NS)

NS: Non-Significant

Discussion

There is very limited evidence to guide practice in the third stage at caesarean section. A national survey of practice in the use of oxytocin found general consistency in the use of bolus oxytocin. The perceived risk of side effects with oxytocin was low for infusions [12].

Our study aimed to assess the efficacy of oxytocin in decreasing blood loss and preventing postpartum hemorrhage in patients undergoing cesarean sections when given as an early intravenous

infusion (at the time of induction of anesthesia before skin incision), in low dose (10 U in 200 ml lactated Ringer infusion) over short duration (15 minutes) and assess this regimen's hemodynamic and fetal effects.

Ghulmiyyah et al. [13] studied three different doses of oxytocin on 189 patients equally allocated to 3 groups receiving, immediately after delivery of the infant, 20, 30, and 40 U of oxytocin in 500 ml lactated Ringer solution and infused over 30 minutes respectively. No significant difference in the three groups regarding blood loss (798.6 ml ±298.3 ml, 794.4 ml ±313.5 ml, 820.2 ml ±316.2 ml; p=0.893), Hb drop (1.4 g/dl ± 1.1 g/dl, 1.1 g/dl ± 0.8 g/dl, 1.0 g/dl ± 1.1 g/dl; p=0.097), uterine tone at 5 and at 10 minutes and the incidence of uterine atony [13].

In a randomized double blind study of 115 elective CS, a regimen of 5 IU oxytocin bolus dose plus a placebo infusion (n=54) and 5 IU bolus dose plus oxytocin 30 IU infusion after delivery of the baby over 4 h (n=56) was conducted. Estimated blood loss was lower in the oxytocin infusion group (576 ml) compared to placebo (624 ml). Additional uterotonic agent was given 6 cases in placebo infusion compared to 3 cases in oxytocin infusion [12].

Thomas et al. [14] compared the blood loss after 5 units of oxytocin given as intravenous bolus (bolus group n=15), and 5 units infusion in 5 minutes (infusion group n=15) in patients undergoing elective or emergency caesarean section. Mean blood loss was 820 ml ± 91 ml in the bolus group and 898 ml ± 107 ml in the infusion group and this was not statistically significant [14].

A randomized, double-masked trial of two oxytocin regimens (10 U/500 ml or 80 U/500 ml of lactated Ringer's solution infused over 30 minutes after cord clamping was performed to prevent postpartum uterine atony at cesarean. Women in the low-dose group received additional uterotonic medication significantly more often than those in the high-dose group (39% compared with 19%, P<.001, relative risk 2.1, 95% CI: 1.4-3.0) [15].

Randomized double-blind placebo-controlled study Group A (360 women) received oxytocin 5 IU bolus and placebo; group B (360 women) received oxytocin 5 IU bolus and 30 IU infusion. Mean estimated blood loss and the proportion of women with blood loss estimated to be greater than 1000 ml were significantly less for group B than for group A (RR 0.35, 95% CI 0.20-0.63). In addition, more women in the group A required additional uterotonic agents (RR 0.35, 95% CI 0.22-0.56) and blood transfusion (RR 0.12, 95% CI 0.01-0.98) [16].

The fore mentioned studies [12-16] were not identical with our study. In these studies, the differences in protocols used, methods of estimating blood loss, numbers of participants and outcome variables, limit direct comparisons with our study. Despite this, the oxytocin regimen used in our study showed lower values regarding e.g., blood loss, Hb drop and additional uterotonic usage.

We attribute better results in our study to the following two reasons. Firstly, using oxytocin in low dose (10 U) in 200 ml lactated Ringer solution and giving it in short duration (15 minutes) allows higher concentration of oxytocin in blood. This concept was synergized by [5,6]. High doses of oxytocin for prolonged periods may lead to desensitization of oxytocin receptors in myometrium, resulting in clinical inefficiency [6]. The decrease in sensitivity is dependent upon the duration of oxytocin exposure [5], which was avoided in our study.

Secondly, oxytocin was given as an early intravenous infusion at the time of induction of anesthesia before skin incision and not after fetal delivery as in the other studies. This rational was in concordance with [12,17]. When oxytocin is administered by IV infusion, the uterus responds almost immediately to oxytocin with response subsiding in about an hour [17]. It maintains uterine contractility throughout the surgical procedure and immediate postpartum period, when most primary hemorrhages occur [12].

We assume that giving oxytocin in low dose (10 U), high concentration (in 200 ml lactated Ringer infusion), over short duration (15 minutes) , early (at the time of induction of anesthesia before skin incision) in addition to its shown results, has positive economic impact . Oxytocin is an inexpensive drug but infusions require either a 4 hour period of monitoring or the use of a controlled infusion pump. The delay in transferring patients to the postnatal ward affects case throughput [18].

The use of oxytocin at the time of induction of anesthesia before skin incision was not associated with fetal adverse outcome. The Apgar-1 and Apgar-5 minutes values in the study group (8.4 ± 0.8) and (9.6 ± 0.5) were not statistically different from values in the control arm (8.5 ± 0.7) and (9.7 ± 0.5) respectively, where oxytocin was given after fetal delivery.

The most consistent cardiovascular changes observed after oxytocin are a dose-related decrease in arterial pressure due to peripheral vasodilatation, with a compensatory increase in HR and cardiac output .Whereas an inadequate dose can result in increased uterine bleeding [19].

Regarding the relation between oxytocin adverse haemodynamic effects and the does and method of administration the following is stated. Thomas et al. [14] assumed marked cardiovascular changes occurred in the bolus group; the heart rate increased by 17 ± 10.7 beats/min compared with 10 ± 9.7 beats/min in the infusion group. The mean arterial pressure decreased by 27 mmHg ± 7.6 mmHg in the bolus group compared with 8 mmHg ± 8.7 mm Hg in the infusion group. Our study showed less hemodynamic effects [14].

Randomized, double-blind, active controlled trial on 80 parturient undergoing elective cesarean delivery, under spinal anesthesia, were randomly allocated to receive 3 IU of oxytocin either as a bolus intravenous injection over 15 seconds (group B, n=40) or as an intravenous infusion over 5 minutes (group I, n=40). There was significant rise in heart rate and significant decrease in mean arterial pressure in bolus group compared to infusion group [9].

Conclusion

In conclusion, the protocol of oxytocin given during CS as an intravenous infusion of oxytocin at the time of induction of anesthesia before skin incision had a priority over giving oxytocin after delivery of the fetus regarding decreasing blood loss and gives a better chance in prevention of PPH with lower changes in haemodaynmic status and no adverse fetal outcome. In addition, infusion of 10 unit's oxytocin appears to be effective as higher dose of oxytocin. Our study was the first to present this protocol and there are no comparative studies. Consequently, further studies are required. Future work should also address emergency CS and cases at higher risk of PPH to provide more evidence for the efficacy of this regimen in reducing blood loss and PPH incidence.

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