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A Comparative Study between Oxytocin Intravenous Bolus versus Oxytocin Intravenous Bolus and Infusion for Control of Blood Loss at Elective Cesarean Section

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ABSTRACT

Background: One of the most crucial steps taken to stop postpartum hemorrhage (PPH) is to take a uterotonic medication as soon after delivery.

Objective: Our main objective was to determine which method was better for controlling intraoperative and early postoperative bleeding after an elective Cesarean section (CS) whether intravenous (IV) oxytocin bolus or oxytocin bolus with infusion.

Patients and methods: Randomized controlled study that included 214 women who were scheduled for an elective Cesarean section after 38 weeks were divided into two equal groups and given an IV slow bolus oxytocin 5 IU and a placebo infusion (500 ml of normal saline over 4 hours) (Control group) or an IV slow bolus oxytocin 5 IU and an oxytocin infusion (40 IU in 500 ml of normal saline over 4 hours) (Study group). Following fetal delivery, all patients were administered the study medication.

Results: The need for additional uterotonics was statistically higher in group A than in group B 26 (24.3%) versus 14 (13.1%). While the estimated blood loss was statistically insignificant between both groups (691.9 ± 233.6 ml in group A versus 543.1 ±179.4 ml in group B

Conclusion: Following IV oxytocin slow bolus during an elective Cesarean section, an additional oxytocin infusion was not superior to IV oxytocin slowbolus alone in reducing the operative blood loss but it may reduce the postoperative need for additional uterotonics

Keywords: Postpartum hemorrhage, Oxytocin, Cesarean section, Third stage.

INTRODUCTION

The loss of 500 ml. of blood or more, through the vaginal tract, in the 1st 24 hours after a baby is born, is the conventional definition of primary PPH. PPH can range from 500–1000 ml to more than 1000 ml. Majors could be classified as severe (more than 2000 ml) or moderate (1000–2000 ml) [(1)]. Definitions differ around the world and are sometimes predicated on imprecise assessments of blood loss. It is also known as a decrease in hematocrit greater than 10% [(2)].

The rate of Cesarean sections has consistently climbed in both industrialized and developing nations, above the WHO's suggested range of 10% to 15% [(3)]. Excessively high rates of Cesarean birth have sparked concerns about the health and financial implications of this practice, even if Cesarean section delivery significantly improves obstetric outcomes when clinically needed. In obstetric practice, major obstetric hemorrhage remained one of the leading causes of maternal death directly [(4)].

Obstetricians and anesthetists share responsibilities for managing bleeding during Cesarean sections. It has been projected that a Cesarean section will result in blood loss ranging from less than 500 ml to more than 1000 ml. The methods used to order blood for this surgery also differ greatly. A number of factors, including training, habit, and medico-legality, may be involved as well as the challenge of assessing blood loss after a Cesarean section [(5)].

One of the most crucial steps taken to stop PPH is to take a uterotonic medication as soon as the fetus is born. The goal when utilizing uterotonic drugs is to achieve an appropriate uterine tone with the least amount of side effects (e.g., hypotension, nausea and emesis), as well as to shorten the time it takes to create and maintain an adequate uterine tone [(6)].

The most widely used uterotonic medication for managing, preventing, and treating postpartum hemorrhage is oxytocin. It is well accepted that routine oxytocin usage through the 3rd stage of vaginal delivery (VD) has significant benefits, and that this also holds true for Cesarean deliveries. A gradual IV bolus of oxytocin is advised by RCOG after a Cesarean section baby is delivered. Some medical professionals give patients an extra oxytocin infusion for a while after the procedure [(7)].

In order to limit blood loss during an elective CS, this study compared the effects of an intravenous (IV) slow bolus of oxytocin with an oxytocin infusion.

MATERIAL AND METHODS

This prospective randomized controlled study was conducted on 214 pregnant women presenting to Kasr Alainy Obstetrics and Gynecology Hospital for elective CS through the period from June 2022 to November 2022.

Inclusion criteria: Healthy pregnant females aged >18 years with singleton gestation and gestational age between 38-40 weeks calculated from first day of

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LMPor first trimesteric US.

Exclusion criteria: Women with previous instances of major obstetric hemorrhage in the past, those who are risky for PPH [prior PPH, placenta previa/accreta and those with an oversized uterus (twin pregnancy, polyhydramnios & uterine fibroid)], more than three Cesarean sections and patients who experience trial of labor or preterm labor were not included in the trial.

METHODS

1- Informed consent: All participants gave their informed consent after being made mindful of the reason for and nature of the study.

2- All participants underwent the following:

- Detailed history taking: Including personal, present, past, family, surgical, medical, menstrual, obstetric history regarding number of previous CS, previous pregnancy outcome and complications.

- General examination: Including vital signs measurements and BMI.

- Abdominal and vaginal examination: Obstetric abdominal examination "Leopold maneuvers". The gravid uterus is methodically palpated using the Leopold procedures. It is employed to ascertain the fetus's engagement, presentation, and position in pregnancy. Vaginal examination to assess cervical dilatation, cervical consistency, presenting part and stage of head descend.

- Abdominal ultrasound: When the patient was admitted, an abdominal ultrasound was performed to assess the volume of amniotic fluid, grade, placental site, gestational age, fetal viability, and wellbeing. Identification of any obstetric issues, such as multiple gestations, placenta previa, and congenital defects.

- Routine pre-operative investigations: Including RH, CBC, coagulation profile, liver function tests and kidney function tests.

- Intra operative: Spinal anesthesia was administered using a standardized anesthetic approach. Prior to spinal anesthesia, patients underwent an intravenous 500 mL crystalloid bolus. The CS surgical technique was standardized. Surgeons were instructed to follow standard operating protocol, which calls for a continuous two-layer suturing of the uterine incision following a transverse lower segment CS and not to deliver the uterus for closure unless clinically necessary.

The following are prime instances of active labor stage three management [8]:

- Cutting and clamping the umbilical cord shortly after delivery.
- After cord clamping, either a placebo infusion (0.9% saline solution, 500 ml) or an oxytocin infusion (40 IU in 500 ml of 0.9% saline) is administered as a gradual IV bolus over a period of 4 hours.
- Providing regulated stress on the umbilical cord and concurrently providing counter-pressure through the abdomen to the uterus.

- Post operative: Following delivery, cases were monitored in the recovery area and operating theater to guarantee infusion ongoing continuity and detect uterine atony, early lochial discharge development, postpartum bleeding, and any oxytocin adverse effects. Serial clinical examinations, blood pressure, pulse, and UOP measures were also performed. Hemoglobin and hematocrit were measured 24 hours after delivery with a full blood count (a drop of more than 20% in hemoglobin is considered severe anemia) [9].

Ethical consideration: Ethical Committee of Faculty of Medicine, Cairo University provided its approval to the work. All participants gave informed consents after receiving a brief but comprehensive description of the study's goals, potential benefits, and assurances that there would be no costs to their health. Participants were not required to stay, and they might leave at any moment. For the duration of the research, the Helsinki Declaration was followed.

Statistical analysis

Using IBM SPSS (Statistical package for social research) version 24 for Windows (Chicago, USA), data were coded, calculated, and then analyzed. Frequency tables were used to display qualitative data as numbers and percentages. Standard deviation (SD) was used to portray quantitative data as mean ± SD. To examine the relationship between categorical variables, Chi-square test was used. In four-cell tables, if the expected cell count was fewer than five, the Fisher Exact Test was used.
The Mann-Whitney U test (z) was used for analyzing of two independent non-normally distributed continuous variables, and the Paired samples t-test was used to compare two dependent groups of parametric data. The independent sample t-test was used to test the association between normally distributed continuous variables in two independent groups. A statistically significant P-value ≤ 0.05 and a highly significant P-value ≤ 0.01.

RESULTS

214 singleton pregnant women who had at least 38 full weeks of gestation and an elective CS were divided into two groups: Following an intravenous (IV) slow bolus oxytocin (5 IU) and placebo infusion (0.9% saline solution 500 ml over 4 hours) for group (A) and an oxytocin infusion (40 IU in 500 ml 0.9% saline over 4 hours) for group (B).

Table (1) showed that the mean **age** (30.6 ± 5.4 versus 29 ± 5.6 years), the mean **GA** (38.46 ± 0.64 versus 38.49 ± 0.58 weeks), the mean **gravidity** (3.17 ± 0.995

versus 3.2 ± 1.09), the mean **parity** (1.97 ± 0.916 versus 1.94 ± 0.97), the mean **number of previous CS** (1.66 ± 0.764 versus 1.71 ± 0.75) and the mean **BMI** (34.7 ± 3.12 versus 34.16 ± 3.12).

Table (1): Comparison between study groups according tobase line characteristics (n=214)

Baseline Characteristics	Group A (n=107)	Group B (n=107)
Age (years)	30.6 ± 5.4	29.00 ± 5.6
GA (weeks)	38.46 ± 0.64	38.49 ± 0.58
Gravidity	3.17 ± 0.995	3.2 ± 1.09
Parity	1.97 ± 0.916	1.94 ± 0.97
Number Previous CS	1.66 ± 0.764	1.71 ± 0.75
BMI (kg/m^2)	34.7 ± 3.12	34.16 ± 3.12

Major obstetric hemorrhage was statistically significant higher in group (A) than in group (B) [17 (15%) versus 6 (5.7%) with p-value 0.015], while there were no significant differences between studied groups regarding **estimated blood loss** (688.4 ± 229.5 versus 544.45 ± 177.4 with p-value 0.092) and **complications** [2 (1.9%) versus 0 (0%) with p-value 0.999] (Table 2 & figures 1, 2 & 3).

Table (2): Comparison between study groups according to operative data (n=214)

Operative data	Group A (n=107)	Group B (n=107)	P-value
Complications	2 (1.9%)	0 (0%)	0.99
Estimated Blood Loss (ml)	688.4 ±229.5	544.45 ±177.4	0.092
Major Obs. Hge. ≥ 1000 ml	17 (15%)	6 (5.7%)	0.015

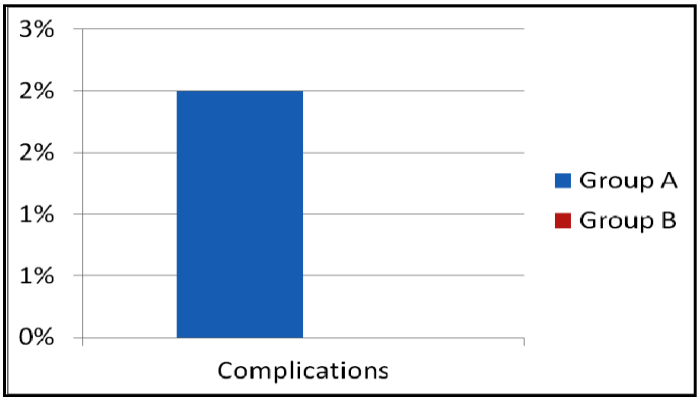

Figure (1): Bar chart between study groups according to operative complications

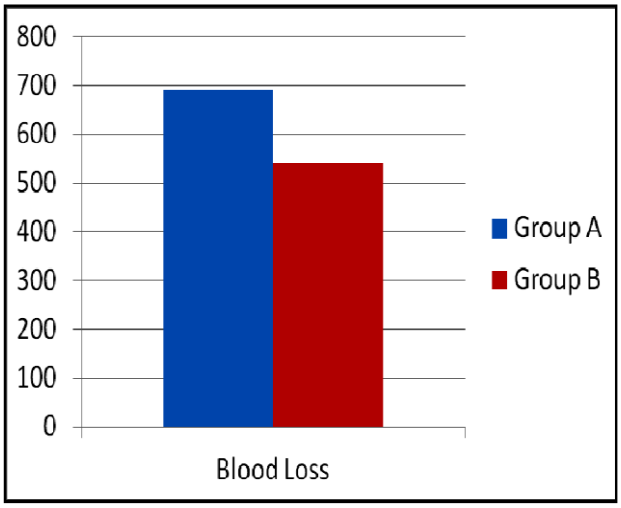

Figure (2): Bar chart between study groups according to estimated blood loss.

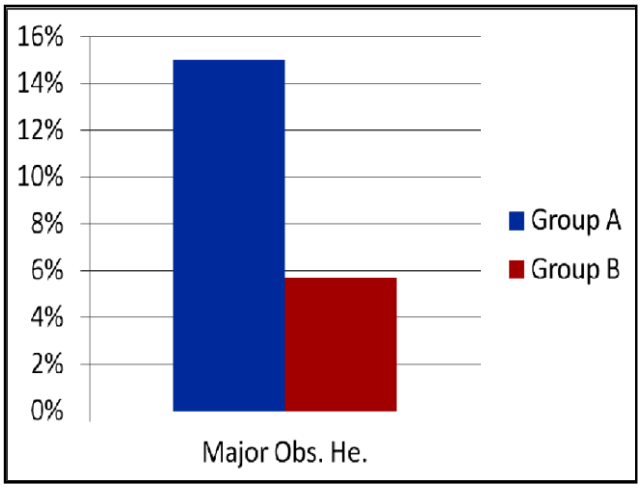

Figure (3): Bar chart between study groups according to major obstetric hemorrhage.

The use of additional uterotonics was statistically significant higher in group (A) than in group (B) [26 (24.3%) versus14 (12.1%) with p-value 0.035]. There were no significant differences between studied groups regarding **PPH** [13 (12.1%) versus 5 (4.7%) with p-value 0.111], **conservative management of PPH** [5 (4.7%) versus 2 (1.9%) with p-value 0.908]**, BL. Transfusion** [5 (4.7%) versus1 (0.9%) with p-value 0.953], **ICU admission**, [3 (2.8%) versus1(0.9%) with p-value 0.972], **side effects** [**6** (5.6%) versus 8 (7.5%) with p-value 0.38] and **hospital stay** [1.24 ± 0.638 versus 1.065 ± 0.315 with p-value 0.235]. Also, there were no significant differences between studied groups regarding **re-exploration**, **hysterectomy, DIC** and **maternal mortality** there (No reported cases) (Table 3 & figures 4 & 5).

Table (3): comparison between study groups according to treatment outcome (n=214)

Treatment Outcomes	Group A (n=107)	Group B (n=107)	P-value
PPH	13 (12.1%)	5 (4.7%)	0.111
Conservative	5 (4.7%)	2 (1.9%)	0.908
Add uterotonics	26 (24.3%)	14 (13.1%)	0.035
BL. Transfusion	5 (4.7%)	1 (0.9%)	0.953
Exploration	0 (0%)	0 (0%)	
Hysterectomy	0 (0%)	0 (0%)	
ICU admission	3 (2.8%)	1 (0.9%)	0.972
DIC	0 (0%)	0 (0%)	
Maternal Mortality	0 (0%)	0 (0%)	
Hospital stay (Days)	1.24 ± 0.638	1.065 ± 0.315	0.235
Side effects	6 (5.6%)	8 (7.5%)	0.38

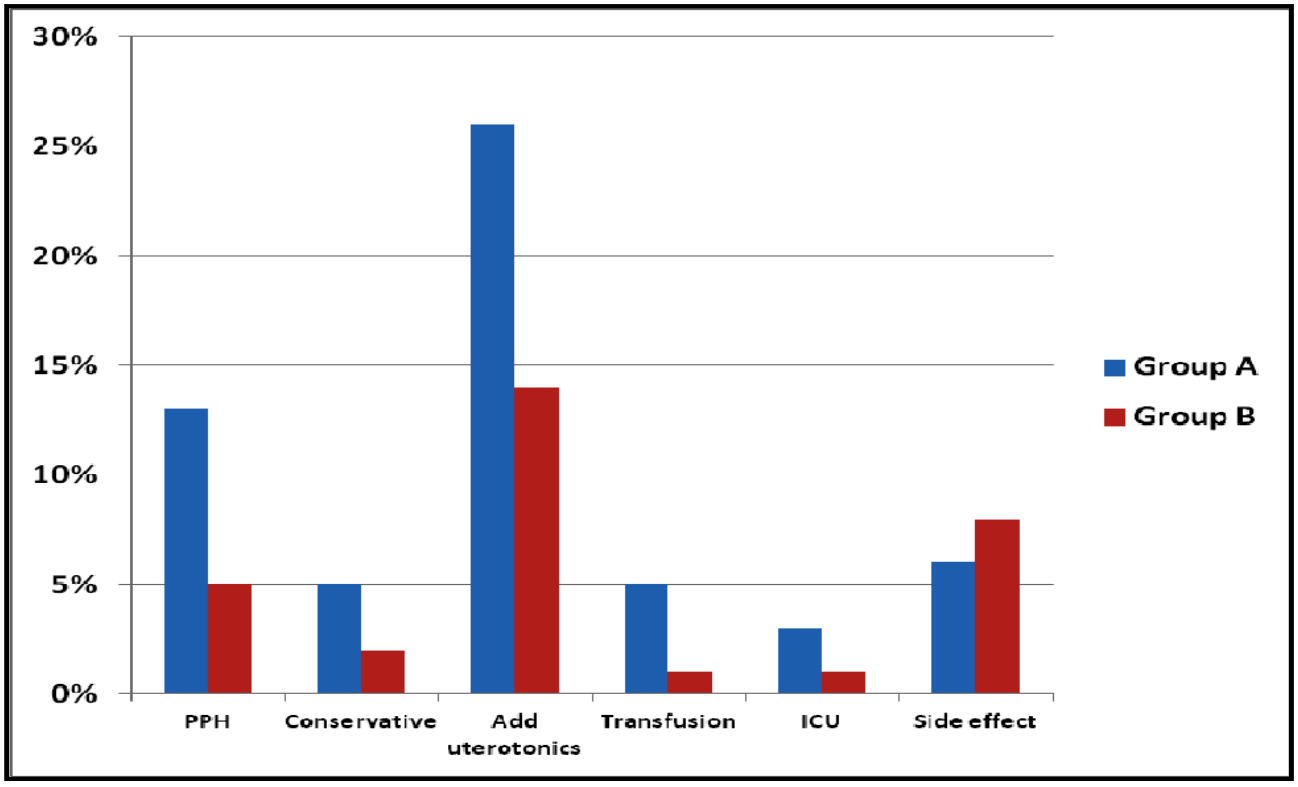

Figure (4): Bar chart between study groups according to operative outcome.

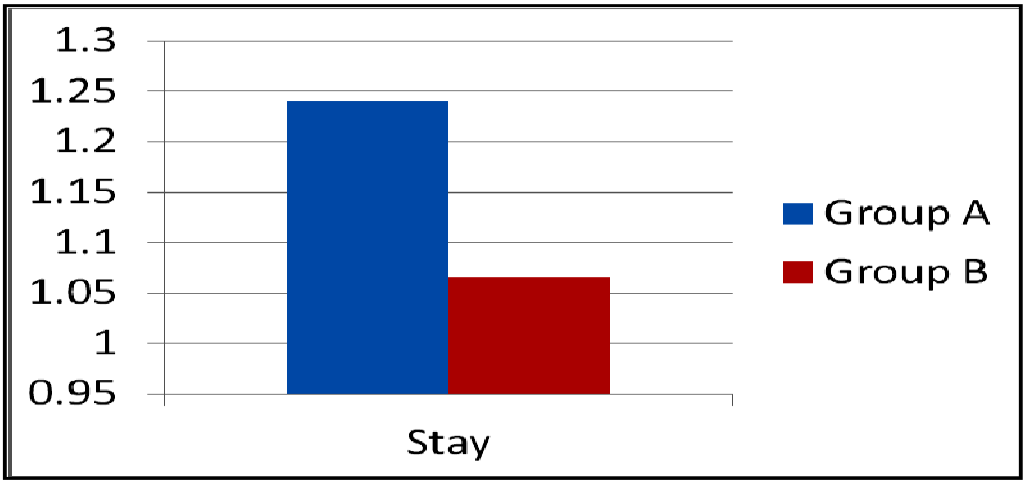

Figure (5): Bar chart between study groups according to post-operative hospital stay

There were no significant differences between studied groups regarding **pre-operative HCT** (36.15 ± 2.99 versus 36.83 ± 2.2 with p-value 0.060) and **Post-operative HCT** (33.86 ± 2.85 versus 34.17±2.30 with p-value 0.378**)**. Also, there was no significant differences between studied groups regarding **pre-operative Hb** (11.24 ± 0.822 versus 11.24 ± 0.67 with p-value 0.17**)** and **post-operative Hb** (10.18 ± 1.21 versus 10.47 ± 0.833 with p-value 0.122**)** (Table 4 and figure 6).

Table (4): Comparison between study groups according to blood indices (n=214)

Blood Indices	Group A(n=107)	Group B(n=107)	P-value
Pre-operative HB (gm/dl)	11.24±0.822	11.24±0.67	0.17
Post-operative HB (gm/dl)	10.18±1.21	10.47±0.833	0.122
Pre-operative HCT (%)	36.15±2.99	36.83±2.2	0.060
Post-operative HCT (%)	33.86±2.85	34.17±2.3	0. 378

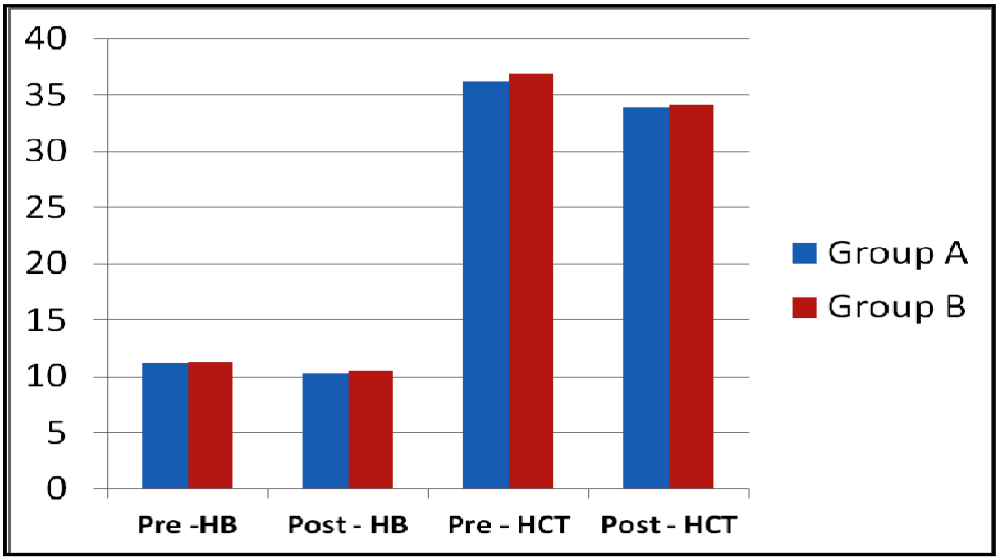

Figure (6): Bar chart between study groups according to blood indices.

DISCUSSION

Nowadays, worldwide, Cesarean sections are the most common type of surgery conducted. According to a recent study, Egypt has a calculated 51.8% estimated Cesarean section rate, placing it third among all countries in the globe [(10)]. Considering that intravenous (IV) oxytocin has the criterion of a short half-life (4–10 minutes), it may be advantageous to maintain uterine contractions during Caesarean section operation and the first few hours after delivery through which the majority of primary bleeding happens [(7)].

The primary goal of this research was to gauge the influence of two different oxytocin regimens; intravenous slow oxytocin boluses (5 IU) and oxytocin infusions (40 IU in 500 ml 0.9% saline over 4 hours) on the body. After a great deal of debate, we selected two primary outcomes, both of which represented uterine atony. Given that severe obstetrical bleeding is the leading cause of maternal fatalities globally, it is the most relevant clinical outcome. In cases of uterine atony, however, medical professionals step in and give an extra uterotonic medication. This intervention would be a significant result in and of itself.

In the interest of objectivity, we evaluated the total blood loss during Caesarean section and right after surgery; however, we opted to use a calculation-based estimate derived from preoperative and postoperative packed cell volume (PCV). In resource-poor environments where blood tests are not frequently conducted, the measured blood loss would have greater significance.

The findings of our research demonstrated that, while there was no significant difference between the studied groups regarding estimated blood loss (EBL) (688.4 ± 229.5 versus 544.45 ± 177.4. Major obstetric hemorrhage (EBL ≥ 1000 ml) was statistically significantly higher in **group (A)** [17 (15%) versus 6 (5.7%)]. Similar to our trial, **Selim and colleagues** [(11)] looked at 180 women scheduled for elective CS and contrasted the outcomes of a 10-IU oxytocin bolus vs. a 10-IU oxytocin bolus & infusion of 30-IU oxytocin over a 4-hour period. With a p-value of 0.07, they discovered that there is no discernible difference between the two groups' mean blood loss (436.9 ± 51 versus 461.3 ± 50.7).

Conversely, **Kajendran and associates** [12] carried out a study analyzing oxytocin bolus (5 IU) versus oxytocin bolus (5 IU) and infusion of 20 IU oxytocin over 4 hours, they examined 92 pregnant women scheduled for an elective CS. Their findings, in contrast to ours, showed that oxytocin bolus and infusion group (intervention group) had significantly diminished mean computed blood loss and declined surgeon visual evaluation of blood losses (476.9 vs. 552.1) (p=0.01), but there was no significant difference in the incidence of major obstetric hemorrhage (p=0.153) **.**

In terms of the results of the treatment, our research showed that group (A) used more uterotonics than group (B) [(26 (24.3%) versus 14 (12.1%) with a p-value of 0.035]. This aligns with the conclusions of **Gungorduk *et al.*** [13] where statistically significant difference was observed between the oxytocin bolus and infusion groups and the bolus group, with more women in the former group requiring extra uterotonic medications than in the latter [69 (19.2%) vs. 28 (7.8%), P < 0.001]. In contrast, there was no discernible difference in the extra uterotonic agent required or therapies after blood loss when compared to **Kajendran and colleagues** (P= 0.216) [12].

In our study, PPH occurred in 13 (12.1%) versus 5 (4.7%) with p-value 0.111) where cases were conservatively managed in 5 (4.7%) bolus group versus 2 (1.9%) bolus & infusion group with p-value 0.908 using bimanual compression, bilateral uterine artery ligation and B-lynch sutures. Fortunately, therewere no reported cases that underwent re-exploration, Hysterectomy and DIC or maternal mortality.

In our clinical trial, there were no significant differences between studied groups regarding post-operative HCT (33.86 ± 2.85 versus 34.17 ± 2.30 with p-value 0.378) and post-operative Hb (10.18 ± 1.21 versus 10.47 ± 0.833 with p-value 0.122**).** This agrees with **Sheehan *et al.*** [14] where about 2000 women assigned for elective CS were evaluated. Comparing oxytocin bolus (5 IU) versus oxytocin bolus (5 IU) & infusion of 40 IU oxytocin over 4 hours. They found no significant difference as regards hemoglobin drop and mean fall in hematocrit.

Similarly, **Kajendran and colleagues** [12] found no significant difference in postoperative haemoglobin drop (1.37 (1.1 – 1.6) vs. 1.40 (1.1 – 1.7) P=0.92) or postoperative packed cell volume (3.28 (2.7 – 3.9) vs. 4.08 (3.4 – 4.7) P=0.07). However, unlike our results **Gungorduk and colleagues** [13] declared that mean estimated loss of blood was statistically significant higher in bolus only group than in bolus & infusion group (686.89 ± 232.28 versus 609.63 ± 208.52 with P < 0.001). Postoperative Hct was statistically significant higher in bolus & infusion group than in bolus only (29.93 ± 1.06 versus 29.38 ± 1.00 with P < 0.001). Also, postoperative Hb was statistically significantly higher in group bolus & infusion group than in bolus only (9.56 ± 0.69 versus 9.46 ± 0.73 with P < 0.001)**.**

Hemodynamic instability, nausea, vomiting, and headaches are among the adverse reactions of oxytocin, according to a number of investigations and observational research [15]. In our study, side effects occurred in 6 (5.6 %) in bolus group versus 8 (7.5%) in bolus & infusion group, with p-value 0.38). This agrees with **Kajendran and colleagues** [12] where occurrence of side effects in bolus & infusion group was 208/1033 (20.1%) compared to185/1025 (18.0%) in bolus only (p=0.21).

Again, **Gungorduk and colleagues** [13] found that there were statistically insignificant differences between both groups regarding side effects [15 (4.2%) vs 21 (5.8%), P = 0.31]**.**

Our study, however, was restricted to women having elective CS; non-elective deliveries should be the focus of future research. From a scientific standpoint, we need to add a third comparison group that represents applying an injection of oxytocin (infusion only) combined with a placebo bolus in contemporary clinical practice. To accommodate this extra group would mean deviation from the hospital policy in accordance with guidelines issued by the Royal College of Gynecologists and Obstetricians. However, we concluded that this strategy may not be permitted in any of our enrollment facilities where oxytocin bolus is the routine standard practice.

Further investigation aimed at minimizing significant maternal hemorrhage and hemorrhagic consequences is crucial, even as the frequency of CS continue to rise. Research from the past has demonstrated that an emergency CS carries a higher risk of serious obstetric hemorrhage than an elective one. Future research should focus on non-elective deliveries as our study was restricted to women awaiting elective CS.

CONCLUSION AND RECOMMENDATIONS

Ultimately, this randomized study revealed that following a 5 ml. IV oxytocin slow bolus during an elective CS, an additional infusion of 40 IU oxytocin in 500 ml. of saline solution over the following four hours reduced the risk of major obstetric hemorrhage and lessens the need for additional uterotonics. One strategy would be to suggest that all women having an elective CS get an oxytocin infusion after a gradual IV bolus. This strategy would lessen the objective clinical judgment on when to administer a further uterotonic drug and decrease maternal hemorrhage during and 24 hours following birth, when most PPH occur.

The manuscript's authors declare that:

1) The work is not being considered by anybody else.

2) None of the material has been previously published.
3) This manuscript has been revised and approved by all writers.

- **Conflict of Interest:** No conflict of interest. **Acknowledgment:** None.
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