

Prophylactic Oxytocin before Versus after Placental Delivery to Reduce Blood Loss in Vaginal Delivery: A Randomized Controlled Trial

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Abstract

Background: PPH has been a leading cause of maternal death around the globe. Prophylactic oxytocin is one of the main components of the active management of the third stage of labor to reduce blood loss. The timing of administration of prophylactic oxytocin varies considerably worldwide and it may have significant impact on the maternal and neonatal well-being.

Objectives: To assess the efficacy and safety of the timing of administration of prophylactic oxytocin via intramuscular route (before compared to after placental delivery) on blood loss in vaginal delivery.

Methods: It is a double blinded study in which 403 patients were randomized in two groups to receive oxytocin 10 IU IM either before or after placental delivery. Primiparous patients, patients with high risk for PPH and those with multiple vaginal or cervical tears were excluded from the study. All patients underwent controlled cord traction, immediate cord clamping. Results: Our results have shown that there were no statistically significant differences between the two study groups regarding the estimated blood loss ($P=0.39$), incidence of PPH ($P=0.78$), length of third stage of labor in minutes ($P=0.29$), the rates of retained placenta ($P=0.77$) and the need for additional uterotonic ($P=0.96$).

Conclusion: The administration of prophylactic intramuscular oxytocin after placental expulsion in vaginal delivery has the same efficacy and safety as when it is used before placental delivery and it is considered an easier alternative especially if there is only a single birth attendant.

Keywords: Prophylactic oxytocin; Vaginal delivery; Placental delivery

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Introduction

Postpartum hemorrhage is the leading cause of maternal mortality in low-income countries and the primary cause of about a quarter of all maternal deaths worldwide [1]. The majority of these deaths occur within 4 hours of delivery, which indicates that they are a consequence of the third stage of labor [2]. Most of the cases of postpartum hemorrhage can be avoided through the adequate use of prophylactic uterotonics during the third stage of labor and by timely and appropriate management [1].

Offering prophylactic uterotonics is recommended to be a

routine element in the active management of the third stage of labor in all women, as their use reduces the incidence of PPH. Oxytocin (10 IU by intramuscular injection) is the uterotonic of choice for prophylaxis in the third stage of labor for women delivering vaginally with no risk factors for PPH. Using a higher dose of oxytocin is unlikely to be of benefit [3].

There is debate among medical practitioners about the timing of administration of prophylactic oxytocic drugs. The main recommended approach in the active management is to administer relevant drugs at the delivery of the anterior shoulder. This, however, can make the process complicated in many busy

maternity units and increases the demand for having more than one healthcare professional present at the time of birth [4].

Aim of the Work

The aim of the study is to assess the efficacy and safety of the timing of administration of prophylactic oxytocin via intramuscular route (before compared to after placental delivery) on blood loss in vaginal delivery.

Patients and Methods

The current study is a double blinded randomized controlled study that allocated 403 patients randomly in two groups; Group I patients who received 10 IU of oxytocin (syntocinon®, NOVARTIS, Egypt) intramuscularly at delivery of anterior shoulder of the fetus and an identical placebo injection (normal saline, NAACL 0.9%) intramuscularly following delivery of the placenta. Group II opposite medication sequence to group I.

The study was presented has been approved from the Ethical Committee of the department of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University. Patients were recruited in the second stage of labor; only multiparous patients with singleton term pregnancy undergoing vaginal delivery were included, with their age ranging between 18 and 35 years old. Primiparous patients, patients with multiple vaginal or cervical tears that may affect estimation of blood loss and any patient with a risk factor for PPH; grand multiparous, previous cesarean section or uterine surgery, maternal illness, history of antepartum or postpartum hemorrhage, abnormal placental site, macrosomic baby, polyhydraminos, multiple gestation, chorioamnionitis, and suspected fetal problem was excluded from the study.

Informed consent was obtained from all patients following the research criteria once they had been admitted in active labor, but they were enrolled and randomized only when they had reached the second stage of labor (fully dilated cervix) as it was difficult in this stage to counsel the patients.

The recruited patients were subjected to history taking with particular emphasis on past medical history (especially for bleeding tendency), past obstetric history, checking vital signs, general and abdominal examination, complete blood count was collected, findings of the initial obstetric evaluation, follow up, labor duration and the need for oxytocin augmentation were recorded through a partogram.

All deliveries were attended by a senior resident in the hospital. Included patients received the medication according to randomization tables. All patients underwent controlled cord traction (CCT), cord clamping and cutting within 30 seconds of delivery (immediate cord clamping), and uterine massage for 30 seconds after placental delivery. Vital signs (blood pressure and pulse) were checked 15 minutes, 1 hour and 6 hours after placental delivery. CBC was collected 6 hours after delivery (Tables 1-3).

The patients were monitored for estimated blood loss, incidence of PPH, length of third stage of labor, change in vital signs before and one hour after delivery, change in hemoglobin and hematocrit

Table 1 Differences between the two study groups regarding demographic data and initial characteristics.

Variablest	Group I (n=178)	Group II (n=176)	P
Age (years)			
Range	19-35	19-35	0.328 ¹
Mean ± SD	27.74 ± 4.65	28.21 ± 4.35	NS
BMI (kg/m2)			
Range	18.65-42.86	18.34-43.51	0.342 ¹
Mean ± SD	29.69 ± 5.73	30.31 ± 6.43	NS
Parity			
Range	1-4	1-4	0.516 ²
Median (IQR)	2 (1-2)	2 (1-2)	NS
Gestational Age (weeks)			
Range	37-41	37-41	0.082 ¹
Mean ± SD	38.7 ± 1.08	39.06 ± 1.07	NS
Duration (minutes)			
Range	37-41	37-41	0.082 ¹
Mean ± SD	38.7 ± 1.08	39.06 ± 1.07	NS
Use of oxytocin for augmentation of labor	54 (30.3%)	45 (25.6%)	0.318 ³
			NS
Episiotomy	95 (53.4%)	99 (56.3%)	0.586 ³
			NS

SD: Standard Deviation; BMI: Body Mass Index; IQR: Interquartile Range; 1: Analysis using Independent Student's t-Test; 2: Analysis using Mann-Whitney's U-test; 3: Analysis using Chi Square test; NS: Non-Significant

before and 6 hours after delivery, incidence of retained placenta, use of additional uterotonics and neonatal outcomes.

A total of 49 patients were excluded due to multiple vaginal or cervical tears that affected the estimation of blood loss.

Statistical methods

Statistical analysis was performed using Microsoft Excel and SPSS for Windows version 20. Data was described in terms of number (percentage) for categorical variables; range, mean and standard deviation (for numeric parametric variables); or range, median and interquartile range (for numeric non-parametric variables). Difference between two independent groups was analyzed using chi-squared test or Fischer's exact test (for categorical variables; unpaired student's t-test as well as mean difference and its 95% confidence interval (for numeric parametric variables); or Mann-Whitney's U-test (for numeric non-parametric variables). Significance level is set at 0.05.

Results and Discussion

Postpartum hemorrhage is the leading cause of maternal mortality in low-income countries [1]. The majority of these deaths occur within 4 hours of delivery, which indicates that they are a consequence of the third stage of labor [2]. Offering prophylactic uterotonics is recommended to be a routine element in the active management of the third stage of labor in all women, as their use reduces the incidence of PPH. Oxytocin (10 IU by intramuscular injection) is the uterotonic of choice for prophylaxis in the third stage of labor for women delivering vaginally with no risk factors

Table 2 Difference between the two study groups regarding different outcome.

Variables	Group I	Group II	MD	P
	(n=178)	(n=176)	95% CI	
Estimated blood loss (ml)				
Range	70-1100	70-1150	28.7-34.58	0.391 ¹
Median (IQR)	210 (157.5-300)	190 (140-280)	to 36.36 *	NS
Allowable blood loss (ml)				
Range	12.47-605.25	14.08-983.04	23.71*	0.067 ¹
Mean ± SD	204.30 ± 136.16	180.60 ± 150.7	-6.30 to 53.73	NS
Primary PPH	8 (4.5%)	9 (5.1%)	0.88	0.785 ²
			0.35 to 2.23	NS
Retained Placenta	7 (3.9%)	8 (4.5%)	0.87	0.775 ²
			0.32 to 2.33	NS
Duration (minutes)				
Range	4-17.5	4.5-19	0.17*	0.290 ^{3NS}
Mean ± SD	7.57 ± 2.83	7.4 ± 2.96		
Need for additional uterotonics	29 (16.3%)	29 (16.5%)	0.99	0.962 ²
			0.62 to 1.58	NS
Nausea/Vomiting	10 (5.6%)	9 (5.1%)	1.1	0.833 ²
			0.46 to 2.64	NS
Severe Pain (VAS>5)	25 (14%)	19 (10.8%)	1.3	0.354 ²
			0.74 to 2.28	NS

MD (95% CI): Mean Difference and its 95% Confidence Interval; 1: Analysis Using Mann-Whitney's U-test; 2: Analysis Using chi-squared test; NS Non-Significant; 3: Analysis Using Independent Student's t-Test; *: MD (95% CI) Mean Difference and its 95% Confidence Interval; #: RR (95% CI) Risk Ratio and its 95% Confidence Interval

Table 3 Difference between the two study groups regarding hemoglobin concentration.

Variables	Group I	Group II	MD	P
	(n=178)	(n=176)	95% CI	
Difference in Hemoglobin				
Range	0.2-1.4	0.3-1.6	-0.04	0.085 ¹
Mean ± SD	0.57 ± 2.1	0.61 ± 1.9	-0.45 to 0.04	NS
Difference in Hematocrit				
Range	0.62-4.4	0.9-4.6	-0.29	0.112 ¹
Mean ± SD	1.81 ± 1.9	2.1 ± 1.7	-1.02 to 0.13	NS
Difference in Pulse Rate (bpm)				
Mean ± SD	-2.26 ± 4.36	-2.45 ± 4.93	-0.19	0.35 ¹
Difference Sys BP (mm Hg)				
Mean ± SD	6.36 ± 4.79	6.84 ± 5.81	-0.48	0.198 NS
Difference Dias BP (mm Hg)				
Mean ± SD	3.69 ± 5.37	3.26 ± 4.95	0.43	0.233 NS

SD: Standard Deviation; MD: (95% CI) Mean Difference and its 95% Confidence Interval; 1: Analysis using Independent Student's T-Test; NS: Non-Significant.

for PPH. There is debate among medical practitioners about the timing of administration of prophylactic oxytocic drugs [3]. The aim of the current study has been to assess the efficacy and

safety of two different timings of administration of prophylactic oxytocin (before versus after placental delivery) on blood loss in vaginal delivery.

The sample size of the current study, 403 patients, is greater than most of other similar studies. Allocated 55 patients randomly in two groups and administered 10 IU of prophylactic oxytocin intramuscularly at the beginning versus the end of the third stage of labor in vaginal delivery [5]. Conducted a clinical trial that included 110 patients who were randomized in 2 groups to receive 10 IU of intramuscular oxytocin either before or after placental delivery in vaginal delivery [6]. Compared oxytocin administration before and after delivery of the placenta to prevent postpartum hemorrhage in vaginal delivery. The sample size was 1486 patients [7]. In spite of their large sample size, the blood loss was not estimated as part of the study, only incidence of PPH was part of their outcome. In the current study there were no statistically significant differences as regards demographic and initial characteristics between the two study groups (age, BMI, parity and gestational age); only patients with low risk for PPH were involved in the study. The main outcome of the current study was the estimated blood loss in the third stage of labor and for one hour postpartum. The results of the current study have shown that there was no statistically significant difference regarding estimated blood loss between the two study groups (mean 343.6 vs.314.9 mean difference (MD) 28.7, 95% confidence interval (CI) -34.58 to 36.36).

The results of the current study concur with the findings of who found that postpartum blood loss in vaginal delivery did not differ significantly according to the timing of oxytocin administration (MD 55, 95% CI-37.63 to 147.63) [5].

Also, the results of the current study agree with the results of the study of who revealed that there was no statistically significant difference between their two study groups regarding the blood loss estimated from the child birth till the placental delivery (P=0.6) [6].

In the current study there was no statistically significant difference between the two study groups regarding the incidence of primary postpartum hemorrhage (risk ratio (RR) 0.88, 95% CI 0.35 to 2.23), which agree with the results of who showed that administration of oxytocin before and after delivery of the placenta did not significantly affect the incidence of postpartum hemorrhage that requires at least one additional uterotonic agent (RR 0.77, 95% CI 0.55 to 1.08) [7].

The results of our study disagree with who found that there was a significantly higher incidence of postpartum hemorrhage (14.8 vs. 0.0%, p=0.049) when oxytocin was administered at the time of delivery of the anterior shoulder immediately after delivery of the fetal head rather that after placental delivery [5].

The most likely explanation of this discrepancy in result may be due to the small sample size of only 55 patients, and the significant differences between their two study groups regarding the initial confounding factors (the gestational age and the use of epidural analgesia), also explained this result by inability of the uterus to contract fully with the placenta in place [5].

In the current study there was no statistically significant difference between the two study groups regarding the change in hemoglobin concentration before and 6 hours after delivery (MD - 0.04, 95% CI -0.45 to 0.04), also there was statistically significant difference between the two study groups regarding the change in hematocrit concentration before and 6 hours after delivery. (MD-0.29, 95% CI-1.02 to 0.13).

The findings of the current study go with the result of who found that the timing of oxytocin administration did not significantly influence the change in hemoglobin concentration measured at admission and on second postpartum day (MD 0.06, 95% CI-0.60 to 0.72) [5].

In the current study there were no statistically significant differences between the two study groups regarding the changes in pulse, systolic and diastolic blood pressure measured before and one hour after placental delivery (P=0.35, P=0.19, P=0.23 respectively).

The results of the current study support the study that showed that the change in pulse, systolic and diastolic blood pressure measured before and 15 minutes after delivery of the placenta were comparable in patients who received oxytocin at different timings (P=0.22, P=0.82, P=0.14 respectively) [6].

In the current study there was no statistically significant difference between the two study groups regarding the duration of third stage of labor in minutes (MD 0.17, P=0.29). Which is consistent with (MD -0.40, P=0.23) [7], and against who proved that the length of third stage of labor was significantly shorter among the group of patients who received intravenous oxytocin after delivery of the fetal head (P<0.001) [8].

The results of the current study have shown that there was no statistically significant difference between the two study groups regarding the rates of retained placenta (RR 0.87, 95% CI 0.32 to 2.33).

The result of the current study goes with systematic review which included three studies that were conducted on 1671 patients who were randomly allocated to receive different doses of oxytocin via different routes, before versus after placental delivery, and that showed that there were no significant differences between patients who received oxytocin before or after placental delivery regarding the rates of retained placenta (RR 1.54, 95% CI 0.76 to 3.11) [4].

References

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The results of the current study have found that there was no statistically significant difference between the two study groups regarding the rates of administration of additional uterotonics (RR 0.99, 95% CI 0.62 to 1.58).

The findings of the current study concur with the results of that showed no statistically significant difference regarding the rate of use of additional uterotonics whether oxytocin was used as prophylactic measure before or after placental delivery (RR 1.10, 95% CI 0.80 to 1.52) [4].

The results of the current study have shown no statistically significant difference between the two study groups regarding the neonatal outcome (Apgar score, need for NICU admission, rate of neonatal RDS). Meanwhile, none of the relevant studies provided information regarding the neonatal outcome.

However, the main limitations of the current study were that only low risk patients for PPH were included in the study, which limits generalization of results on patients with different risk factors.

Patients with episiotomy were included in the study which affected the amount of blood loss. As a trial to reduce the incidence of episiotomy, primiparous patients were excluded from the study, but still the incidence of episiotomy was high (54.8% of patients)

Delayed cord clamping was not used as an element of active management of third stage of labor, which may affect the results of the influence of timing of oxytocin administration on neonatal outcome. In addition, the study was conducted in a university hospital which is a tertiary care level, thus restricts generalization of results on other health care facilities.

Conclusion

The administration of prophylactic intramuscular oxytocin after placental expulsion in vaginal delivery has the same effect on blood loss as when it is used before placental delivery, and it is considered an easier alternative especially if there is only a single birth attendant. All data demonstrated that oxytocin can be used safely before or after placental delivery to reduce blood loss in vaginal delivery and its use was associated with the same maternal and neonatal outcomes.

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