

COMPARATIVE STUDY BETWEEN INTRAMUSCULAR INJECTION AND INTRAVENOUS INFUSION OF OXYTOCIN IN THE THIRD STAGE OF LABOR FOR PPH PROPHYLAXIS

Mariam Barakat^{*1}, Raja Rajab² and Maisoon Dayoub³

¹M.D., Department of Obs and Gyn Medicine, Tishreen University Hospital, Lattakia, Syria.

²Prof. Dr., Department of Obs and Gyn, Tishreen University Hospital, Lattakia, Syria.

³Prof. Dr., Department of Obs and Gyn, Tishreen University Hospital, Lattakia, Syria.

Received date: 13 June 2023

Revised date: 04 July 2023

Accepted date: 25 July 2023

*Corresponding Author: Dr. Mariam Barakat

M. D, Department of Obs and Gyn Medicine, Tishreen University Hospital, Lattakia, Syria.

ABSTRACT

Background: Postpartum hemorrhage (PPH) is the leading cause of maternal and fetal morbidity. Prophylactic administration of oxytocin reduces the rates of PPH, and various routes are being used but little information is available regarding the best route. **Objective:** The aim of this study was to investigate the effectiveness of oxytocin infusion versus intramuscular route of drug administration in preventing PPH. In addition to, to determine the safety of oxytocin use in each route. **Patients and Methods:** This is comparative study was conducted for the period one year (2022 –2023) at Tishreen University Hospital in Lattakia-Syria. The study included 150 women with term pregnancies who underwent vaginal delivery. They were assigned randomly either to group I (90 cases) who received oxytocin intravenously or to group II (60 cases) who received oxytocin intramuscularly. **Results:** The mean age was 27.11 ± 6.2 years, without significant difference between the two groups regarding demographic and obstetric characteristics ($p > 0.05$). The mean blood loss in group I was (309.8 ± 222.5) vs (345.3 ± 239.2) , $p: 0.1$ in group II. PPH was detected in 6 cases (6.7%) in group I versus 5 cases (8.3%) in group II, $p: 0.8$. Hemoglobin and hematocrit decline didn't have significant difference in group I versus group II (0.91 ± 0.2 vs 0.86 ± 0.5 , $p: 0.2$) and (3.11 ± 0.2 vs 3.48 ± 1.7 , $p: 0.6$) respectively. The need for blood transfusion and uterotonic agents was in group I versus group II (3.3% vs 5%, $p: 0.7$) and (21.1% vs 26.7%, $p: 0.2$) respectively. Regarding of the side effects: hypotension represented the most frequent complication without significant difference between two groups, $p: 0.6$. **Conclusion:** The current study demonstrated favorable results in efficiency and safety with the two routes of oxytocin administration in preventing PPH.

KEYWORDS: Oxytocin, postpartum hemorrhage PPH, intramuscular, intravenous.

INTRODUCTION

Postpartum hemorrhage (PPH) is an obstetric emergency which is considered one of the most common causes of maternal mortality worldwide.^[1] It is defined by an estimated blood loss ≥ 500 ml after vaginal birth or ≥ 1000 ml after cesarean section.^[2] According to the American College of Obstetricians and Gynecologists (ACOG), PPH is defined by cumulative blood loss ≥ 1000 ml or bleeding within 24 hours of birth process that associated with signs or symptoms of hypovolemia.^[3] PPH is classified to early that occurs in the first 24 hours after birth or late which occurs from 24 hours to 12 weeks after birth.^[4]

There are many factors that associated significantly with the risk of PPH such as macrosomia, lacerations, hypertensive disorders, placental abruption, abnormal placentation, previous PPH, and labor induction. PPH can be managed by a variety of medical and surgical interventions.^[5]

Oxytocin is a neurohophysial hormone, naturally synthesized during pregnancy, which plays a central role in contraction uterine during labor.^[6] Oxytocin is a part of active management of the third stage of labor which is defined by the time between fetal expulsion and placental expulsion. It reduces the risk of PPH, and the route of administration varies widely among institutions. Intravenous route is preferable due its effectiveness and

rapid onset of action, whereas intramuscular route is an acceptable alternative, but the onset of action is slower, clinical effects last longer, with low rate of the serious side effects that observed with intravenous administration.^[7] Absence of local studies about the optimal route of oxytocin administration to prevent PPH prompted us to conduct this study. Therefore, the objectives of the study were to: 1- detect the effectiveness of intramuscular route versus intravenous infusion of oxytocin on the following variables: blood loss, characteristics of the third stage of labor, and hematologic parameters. 2- to compare the complications between the two groups.

PATIENTS AND METHODS

This is a comparative study of a group of women who went into spontaneous vaginal delivery attending department of Obstetrics and Gynecology at Tishreen University Hospital in Lattakia-Syria during one-year period (2022-2023). The inclusion criteria were: women with viable singleton intrauterine pregnancy in a cephalic presentation who went into labor spontaneously without labor induction. The exclusion criteria were: preoperative hemoglobin <9 g/dL, presence of coagulopathy or use of anticoagulants during perinatal period, diseases of the heart, liver, or kidney, women with risk factors that associated with increasing the risk of PPH (retained placenta, placenta accreta spectrum, large for gestational age, preeclampsia and eclampsia, previous history of PPH), and occurrence of serious complications during delivery (uterine rupture).

The following workup included: history, physical examination and laboratory investigations including complete blood count to detect hemoglobin(Hb) and hematocrit(Hct) were performed. Patients were randomized into two groups: group I (90 women) who received 10 IU oxytocin in 250 ml of saline at a rate of 125 drop/minute which given after the delivery of the anterior shoulder and group II (60 women) who received 10 IU oxytocin intramuscularly soon after delivery of the anterior shoulder. Baseline vital signs were taken before

initiation the first dose, and reevaluated after administration. The main outcome measures were perioperative blood loss(ml), rate of blood transfusion, decline in Hb and Hct values.

Quantify blood loss was performed by measuring the total weight of bloody materials and subtract the known weight of the same materials when dry, and difference in weight between wet and dry in grams approximates the volume of blood in milliliters.

Ethical consideration: All patients were provided a complete and clear informed consent after discussion about the study. This study was performed following the Declaration of Helsinki.

Statistical Analysis

Statistical analysis was performed by using IBM SPSS version 20. Basic Descriptive statistics included means, standard deviations(SD), median, Frequency and percentages. To examine the relationships and comparisons between the two group, chi-square test was used. Independent t student test was used to compare 2 independent groups. All the tests were considered significant at a 5% type I error rate ($p < 0.05$), β :20%, and power of the study:80%.

RESULTS

The study included 150 women with spontaneous vaginal delivery at term. Ages range from 18 to 43 years, with a mean age 27.11 ± 6.2 years. As table one shows, there was no significant difference between the two groups regarding patients' characteristics included: age (28.74 ± 7.1 vs 27.32 ± 4.6 , $p = 0.8$), gestational age (38.13 ± 1.4 vs 37.86 ± 0.8 , $p = 0.1$), and average duration of the third stage of labor (5.32 ± 0.8 vs 5.47 ± 0.6 , $p = 0.9$). The age group (20-24 year) represented the most frequent group followed by 25-30, >30 and <20 in group I versus group II as follow; (46.7% vs 51.7%), (37.8% vs 33.3%), (10% vs 8.3%) and (5.5% vs 6.7%), $p = 0.2$. Majority of the cases were multiparous (77.8% in group I versus 75% in group II, $p = 0.3$).

Table 1: Demographic characteristics of the study population by comparison of the two group.

Variables	Group I Intravenous oxytocin (n=90)	Group II Intramuscular oxytocin (n=60)	P value
Age (years)	28.74±7.1(18-43)	27.32±4.6(20-39)	0.8
Age groups			0.2
<20	5(5.5%)	4(6.7%)	
20-24	42(46.7%)	31(51.7%)	
25-30	34(37.8%)	20(33.3%)	
>30	9(10%)	5(8.3%)	
Gestational age(week)	38.13±1.4	37.86±0.8	0.1
Obstetric status			0.3
Nulliparous	20(22.2%)	15(25%)	
Multiparous	70(77.8%)	45(75%)	
Duration of the third stage of labor(min)	5.32±0.8(3-8.5)	5.47±0.6(3-9)	0.9

Postpartum hemorrhage (PPH) was developed in 6 cases (6.7%) in group I versus 5 cases (8.3%) in group II, $p:0.8$. The mean of blood loss was 309.8 ± 222.5 ml in the group I versus 345.3 ± 239.2 in group II, $p:0.1$. The mean preoperative Hb in group I was (11.12 ± 0.9) and (11.24 ± 0.8) in group II, $p: 0.8$. The mean preoperative Hct in group I was (35.77 ± 3.4) and (35.68 ± 1.3) in group II, $p: 0.8$. The rates of decline in Hb and Hct were in the group I compared to group II; $(0.91 \pm 0.2$ vs 0.86 ± 0.5 , $p:$

$0.2)$ and $(3.11 \pm 0.2$ vs 3.48 ± 1.7 , $p: 0.6)$, respectively. The rate of blood transfusion was 3.3% in group I versus 5% in group II, $p:0.7$. The volume of blood lost in group I versus group II ranged from 100-250 ml (27.8% vs 31.7%), to 251-499 ml (65.6% vs 60%), 500-1000 ml (3.3% vs 5%) and >1000 ml (3.3% vs 3.3%), $p:0.5$. Uterotonic agents were used in 6 cases (6.7%) in group I versus 5 cases (8.3%) in group II, $P:0.8$.

Table 2: Hematologic diameters of the study population by comparison of the two group.

Variables	Group I Intravenous oxytocin (n=90)	Group II Intramuscular oxytocin (n=60)	P value
Preoperative Hb	11.12±0.9	11.24±0.8	0.8
Postoperative Hb	10.21±1.1	10.38±1.3	0.5
Hb decline	0.91±0.2	0.86±0.5	0.2
Preoperative Hct	35.77±3.4	35.68±1.3	0.8
Postoperative Hct	32.66±3.6	32.20±3.01	0.3
Hct decline	3.11±0.2	3.48±1.7	0.6
Blood loss(ml)	309.8±222.5 100-1000)(345.3±239.2 200-1000)(0.1
Volume of lost blood			
100-250 ml	25(27.8%)	19(31.7%)	0.5
251-499 ml	59(65.6%)	36(60%)	
500-1000 ml	3(3.3%)	3(5%)	
>1000 ml	3(3.3%)	2(3.3%)	
Need for blood transfusion	3(3.3%)	3(5%)	0.7
Need for uterotonic agents	6(6.7%)	5(8.3%)	0.8

Side effects that observed in group I versus group II were as follow; hypotension (22.2% vs 25%, $p:0.6$), emesis(1.1% vs 0%, $p:0.8$), nausea(4.4%vs 3.3%, $p: 0.1$),

dizziness(5.5% vs 11.7%, $p:0.09$), shivering (7.8% vs 16.7%, $p:0.06$) and tachycardia(6.7% vs 16.7%, $p:0.05$).

Table 3: Side effects of the study population by comparison of the two group.

Variables	Group I Intravenous oxytocin (n=90)	Group II Intramuscular oxytocin (n=60)	P value
Side effects			
Hypotension	20(22.2%)	15(25%)	0.6
Emesis	1(1.1%)	0(0%)	0.8
Nausea	4(4.4%)	2(3.3%)	0.1
Dizziness	5(5.5%)	7(11.7%)	0.09
Shivering	7(7.8%)	10(16.7%)	0.06
Tachycardia	6(6.7%)	10(16.7%)	0.05

After excluding the cases who received additional uterotonic agents, there were no significant differences between two groups (I versus II) regarding blood loss

(238.66 ± 31.2 versus 250.92 ± 23.8 , $p: 0.6$), changes in Hb (0.53 ± 0.08 versus 0.56 ± 0.1 , $p:0.5$) and Hct(1.12 ± 1.1 versus 1.38 ± 0.09 , $p:0.5$), table 4.

Table 4: Hematologic diameters of the study population by comparison of the two group.

Variables	Group I Intravenous oxytocin	Group II Intramuscular oxytocin	P value
Preoperative Hb	11.32±1.14	11.18±0.91	0.6
Postoperative Hb	10.79±1.22	10.62±1.02	0.2
Hb decline	0.53±0.08	0.56±0.1	0.5
Preoperative Hct	34.24±2.18	33.74±1.92	0.8
Postoperative Hct	33.12±2.31	32.36±2.01	0.1
Hct decline	1.12±1.1	1.38±0.09	0.5

Blood loss(ml)	238.66±31.2	250.92±23.8	0.6
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DISCUSSION

This comparative study of 150 pregnant women at full term who went into vaginal delivery spontaneously assessed efficiency of intravenous infusion oxytocin versus intramuscular route in preventing PPH, as well as the safety of each route.

Our clinical trial demonstrated no superiority of oxytocin infusion to intramuscular injection in reducing the volume of blood loss after spontaneous vaginal delivery. The rate of PPH was lower in intravenous route but without significant difference ($p > 0.05$). No statistical difference was observed between two groups in postoperative concentrations of hemoglobin, hematocrit, and without significant difference in requirement for blood transfusion or uterotonic agents. Hypotension represented the most frequent complication in the two groups without presence of significant difference ($p > 0.05$).

Orhan et al (2013) demonstrated in a trial conducted in 600 women at full term who received oxytocin either by intravenous or intramuscular route that blood loss was lower in intravenous compared to intramuscular route (226.6 vs 253.3, $p:0.1$). Reduction in Hb and Hct was significantly lower in intravenous route (2.9 vs 3.1) and (9.1 vs 10), $p < 0.05$ respectively without significant difference in requirement of uterotonic agents.^[8]

Dagdeviren et al (2016) showed in a study performed in 256 pregnant women at full term who assigned to intramuscular oxytocin group (128) and intravenous infusion group (128) to prevent PPH that there were no significant differences between two groups regarding blood loss, need for blood transfusion or the rate of PPH ($p > 0.05$).^[9]

Charles et al (2019) showed in a study performed in Egypt which included pregnant women at full term assigned to intramuscular oxytocin group (2014) and intravenous infusion group (2108) to prevent PPH that blood loss was lower in intravenous route approximately 5.9% compared to other route. There were significant differences between two groups regarding changes in Hb (0.54 vs 0.52, $p:0.8$), need for blood transfusion (0.2% vs 0.5%, $p:0.2$) and uterotonic agents (0.6% vs 1.1%, $p:0.09$).^[10]

Durocher et al (2019) demonstrated in a study performed in Argentina which included pregnant women at full term who went into vaginal delivery spontaneously and assigned to intramuscular oxytocin group (241) and intravenous infusion group (239) that blood loss, PPH, and blood transfusion were lower in intravenous route but without significant difference ($p > 0.05$). The need for uterotonic agents was significantly lower in intravenous group (5% vs 12%, $p:0.007$).^[11]

Oladapo et al (2020) demonstrated in an analytic study included 7817 pregnant women at full term who received oxytocin to prevent PPH either by intravenous infusion route or intramuscularly that intravenous administration reduces the risk of PPH > 500 ml with relative risk RR:0.78 and the need for blood transfusion was lower RR:0.44. The difference between two groups regarding hypotension was absent or low RR:1.01.^[12]

In summary, efficiency that occurred after two methods of oxytocin administration and safety were similar so we can use the two routes of administration efficiently to prevent PPH.

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