Optimal route for administering oxytocin to women in labor to reduce PPH (blood loss)

Introduction

At a hospital in Argentina, 480 women in active labor who did not have a c-section were the study subjects. To test whether intramuscular (IM) administration or intravenous (IV) route is the optimal route of administration of oxytocin to reduce PPH (blood loss) during the third stage of labor, a double-blinded, randomized controlled trial (with convenience sampling) was conducted. Researchers focused on whether there is a difference in average PPH value at 60 minutes after birth between the two groups.

Exploratory data analysis

Table 1. Baseline Characteristics by study groups.

	IV infusion group	IM injection group
Sample size (n)	239	241
Woman's age, mean (SD)	24.13±5.16	24.32±5.72
Gestational age, mean (SD)	38.50±2.12	38.77±1.84
Prepartum Hb, mean (SD)	11.78±1.47	11.73±1.53
Prepartum SBP, mean (SD)	114.77±13.54	114.63±13.73
Prepartum DBP, mean (SD)	75.43±10.78	74.73±11.53
Prepartum HR, mean (SD)	84.43±13.57	84.15±13.59
Preeclampsia, n (%)	1.67	0.83
Diabetes, n (%)	2.51	1.24

From **Table 1**., we can compare can conclude that the IV infusion group and IM injection group had similar sample size, woman's mean age, mean gestational age, mean prepartum Hb value, mean SBP value, mean DBP value, and mean HR value. IV infusion group had higher preeclampsia percentage and diabetes percentage than IM injection group.

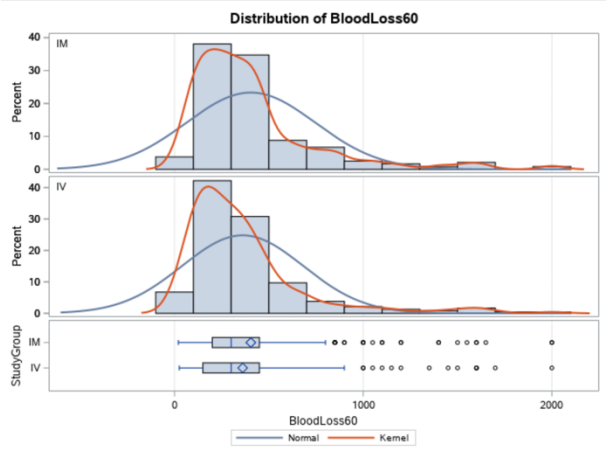

Figure 1. Distribution of blood loss at 60 minutes after birth for IV infusion group and IM injection group.

According to **Figure 1**., the mean blood loss at 60 minutes after birth for IM injection group was 404.3 mL with SD of 342.2. We are 95% confident that the interval from 360.7 mL to 447.9 mL contains the true mean blood loss value at 60 minutes after birth for that group. The distribution is not normal (not Bell-shaped) and positively skewed which it has a long tail to the right. The center of the distribution is around the median (300 mL) which is lower than the mean (404.3 mL). The distribution is unsymmetric. The variability is observed from the population of n=241. The mean blood loss at 60 minutes after birth for IV infusion group was 360.8 mL with SD of 321.6. We are 95% confident that the interval from 319.7 mL to 402.0 mL contains the true mean blood loss value at 60 minutes after birth for that

[1] Durocher, J., Dzuba, I. G., Carroli, G., Morales, E. M., Aguirre, J. D., Martin, R., ... & Winikoff, B. (2019). Does route matter? Impact of route of oxytocin administration on postpartum bleeding: A double-blind, randomized controlled trial. *PLOS ONE*, *14*(10), e0222981.

group. The distribution is not normal (not Bell-shaped) and positively skewed which it has a long tail to the right. The center of the distribution is around the median (300 mL) which is lower than the mean (360.8 mL). The distribution is unsymmetric. The variability is observed from the population of n=239.

The primary outcome is the prepartum values of two groups involved no large difference and the distribution of blood loss at 60 minutes after birth of the two groups shown similar shapes (both of them were positively skewed) although IV infusion group had less difference (60.8 mL) between median (300 mL) and mean (360.8 mL) than the value of IM injection group (difference is 104.3 mL between mean 0f 404.3 mL and median 300 mL).

Inference

Since we aim to find whether there is a difference in average blood loss at 60 minutes after birth between two groups, we use two-tailed t test to answer the research question. The alternative hypothesis is the blood loss of both groups is not equal, which involved a two-tailed test. We assume it is random sample, each observation is independent, and sampling distribution of sample means is approximately normal with a large sample size. We assume the mean blood loss of IV infusion group and IM injection group are the same at 60 minutes after birth.

Table 2. t-test results of blood loss at 60 minutes after birth in IV infusion group and IM injection group.

Difference (BloodLoss60 values between IM injection group and IV infusion group)	95% Cl mean		Std dev	95% Cl std dev		T value	Pr>|t|	DF
43.47	-16.35	103.3	332.1	312.2	354.7	1.43	0.15	474

According to **Table 2**., we can say that with 95% confidence that the people who took IM injection at 60 minutes after birth will have a blood loss difference in the range between -16.35 mL to 103.3 mL. The null value fall in the confidence interval, we have evidence to say that the true population value is different from the null value. Since the p value (0.15) is larger than α value of 0.05, we fail to reject the hypothesis. We don't have sufficient evidence to reject the null hypothesis that there is no difference in average blood loss at 60 minutes after birth between two groups. We do not have enough evidence to say that there is no difference in blood loss at 60 minutes after birth between two groups.

Conclusion

To answer the research question, we can conclude that we do not have evidence to prove there is difference in average blood loss at 60 minutes after birth between two groups. We cannot decide which one is the optimal route for administration oxytocin to women in labor to reduce blood loss. I don't think these results can apply to all women who give birth. I think detailed analysis should be made including the factors of prior illness/condition upon arrival to hospital indicator, prior chronic hypertension indicator, and other indicator to help women choose the optimal route for administration oxytocin case-by-case. Further study can be done to explore the influence of those factors on the efficiency of oxytocin administration.

[1] Durocher, J., Dzuba, I. G., Carroli, G., Morales, E. M., Aguirre, J. D., Martin, R., ... & Winikoff, B. (2019). Does route matter? Impact of route of oxytocin administration on postpartum bleeding: A double-blind, randomized controlled trial. *PLOS ONE*, *14*(10), e0222981.

Appendix

```
proc import
DATAFILE = "/home/u59373588/My SAS/project 1/PPH-Oxytocin-RCT.csv"
OUT = PPH
DBMS = csv
REPLACE;
GETNAMES = yes;
run;

PROC CONTENTS DATA=PPH; RUN;
 %web_open_table(PPH);
 proc univariate data=PPH;
 Class StudyGroup;
 VAR Age;
 run;
```

Table 3. Statistics results of age in IV infusion and IM injection groups.

The UNIVARIATE Procedure
Variable: Age
StudyGroup = IM

Moments			
N	241	Sum Weights	241
Mean	24.3153527	Sum Observations	5860
Std Deviation	5.71548817	Variance	32.666805
Skewness	0.84593195	Kurtosis	0.39072957
Uncorrected SS	150328	Corrected SS	7840.0332
Coeff Variation	23.5056766	Std Error Mean	0.36816696

The UNIVARIATE Procedure
Variable: Age
StudyGroup = IV

Moments			
N	239	Sum Weights	239
Mean	24.125523	Sum Observations	5766
Std Deviation	5.16461551	Variance	26.6732534
Skewness	0.75913845	Kurtosis	0.20655265
Uncorrected SS	145456	Corrected SS	6348.23431
Coeff Variation	21.4072686	Std Error Mean	0.33407121

```
PROC CONTENTS DATA=PPH; RUN;
 %web_open_table(PPH);
 proc univariate data=PPH;
 Class StudyGroup;
 VAR GestAge;
 run;
```

Table 4. Statistics results of gestational age in IV infusion and IM injection groups.

The UNIVARIATE Procedure
Variable: GestAge
StudyGroup = IM

Moments			
N	241	Sum Weights	241
Mean	38.7713693	Sum Observations	9343.9
Std Deviation	1.84177501	Variance	3.3921352
Skewness	-3.0372149	Kurtosis	16.7305834
Uncorrected SS	363089.91	Corrected SS	814.112448
Coeff Variation	4.75034812	Std Error Mean	0.11863916

The UNIVARIATE Procedure
Variable: GestAge
StudyGroup = IV

Moments			
N	239	Sum Weights	239
Mean	38.4987448	Sum Observations	9201.2
Std Deviation	2.11635252	Variance	4.478948
Skewness	-1.9825619	Kurtosis	5.04291489
Uncorrected SS	355300.64	Corrected SS	1065.98962
Coeff Variation	5.49719877	Std Error Mean	0.13689546

```
PROC CONTENTS DATA=PPH; RUN;
 %web_open_table(PPH);
 proc univariate data=PPH;
 Class StudyGroup;
```

[1] Durocher, J., Dzuba, I. G., Carroli, G., Morales, E. M., Aguirre, J. D., Martin, R., ... & Winikoff, B. (2019). Does route matter? Impact of route of oxytocin administration on postpartum bleeding: A double-blind, randomized controlled trial. *PLOS ONE*, *14*(10), e0222981.

VAR HbBaseline;
run;

Table 5. Statistics results of HbBaseline in IV infusion and IM injection groups.

The UNIVARIATE Procedure
Variable: HbBaseline
StudyGroup = IM

Moments			
N	241	Sum Weights	241
Mean	11.7290456	Sum Observations	2826.7
Std Deviation	1.52822975	Variance	2.33548617
Skewness	0.04210575	Kurtosis	0.41813547
Uncorrected SS	33715.01	Corrected SS	560.51668
Coeff Variation	13.0294467	Std Error Mean	0.09844193

The UNIVARIATE Procedure
Variable: HbBaseline
StudyGroup = IV

Moments			
N	238	Sum Weights	238
Mean	11.7768908	Sum Observations	2802.9
Std Deviation	1.46610494	Variance	2.14946371
Skewness	-0.4838012	Kurtosis	0.26870445
Uncorrected SS	33518.87	Corrected SS	509.422899
Coeff Variation	12.4489984	Std Error Mean	0.09503347

PROC CONTENTS DATA=PPH; RUN;
%web_open_table(PPH);
proc univariate data=PPH;
Class StudyGroup;
VAR SBPBaseline;
run;

Table 6. Statistics results of SBPBaseline in IV infusion and IM injection groups.

The UNIVARIATE Procedure
Variable: SBPBaseline
StudyGroup = IM

Moments			
N	241	Sum Weights	241
Mean	114.634855	Sum Observations	27627
Std Deviation	13.7289031	Variance	188.48278
Skewness	0.12598572	Kurtosis	0.05114574
Uncorrected SS	3212253	Corrected SS	45235.8672
Coeff Variation	11.9762032	Std Error Mean	0.88435639

The UNIVARIATE Procedure
Variable: SBPBaseline
StudyGroup = IV

Moments			
N	239	Sum Weights	239
Mean	114.769874	Sum Observations	27430
Std Deviation	13.5380483	Variance	183.278753
Skewness	0.43119803	Kurtosis	1.14730491
Uncorrected SS	3191758	Corrected SS	43620.3431
Coeff Variation	11.7958205	Std Error Mean	0.87570355

PROC CONTENTS DATA=PPH; RUN;
%web_open_table(PPH);
proc univariate data=PPH;
Class StudyGroup;
VAR DBPBaseline;
run;

Table 7. Statistics results of DBPBaseline in IV infusion and IM injection groups.

[1] Durocher, J., Dzuba, I. G., Carroli, G., Morales, E. M., Aguirre, J. D., Martin, R., ... & Winikoff, B. (2019). Does route matter? Impact of route of oxytocin administration on postpartum bleeding: A double-blind, randomized controlled trial. *PLOS ONE*, *14*(10), e0222981.

The UNIVARIATE Procedure
Variable: DBPBaseline
StudyGroup = IM

Moments			
N	241	Sum Weights	241
Mean	74.7302905	Sum Observations	18010
Std Deviation	11.5321053	Variance	132.989454
Skewness	0.19720251	Kurtosis	0.35899534
Uncorrected SS	1377810	Corrected SS	31917.4689
Coeff Variation	15.4316346	Std Error Mean	0.74284821

The UNIVARIATE Procedure
Variable: DBPBaseline
StudyGroup = IV

Moments			
N	239	Sum Weights	239
Mean	75.4309623	Sum Observations	18028
Std Deviation	10.7778583	Variance	116.162231
Skewness	0.077014	Kurtosis	0.27639092
Uncorrected SS	1387516	Corrected SS	27646.6109
Coeff Variation	14.2883744	Std Error Mean	0.6971617

```
PROC CONTENTS DATA=PPH; RUN;
 %web_open_table(PPH);
 proc univariate data=PPH;
 Class StudyGroup;
 VAR HRBaseline;
 run;
```

Table 8. Statistics results of HBPBaseline in IV infusion and IM injection groups.

The UNIVARIATE Procedure
Variable: HRBaseline
StudyGroup = IM

Moments			
N	241	Sum Weights	241
Mean	84.1452282	Sum Observations	20279
Std Deviation	13.5895053	Variance	184.674654
Skewness	0.44384975	Kurtosis	0.574256
Uncorrected SS	1750703	Corrected SS	44321.917
Coeff Variation	16.1500605	Std Error Mean	0.87537699

The UNIVARIATE Procedure
Variable: HRBaseline
StudyGroup = IV

Moments			
N	239	Sum Weights	239
Mean	84.4267782	Sum Observations	20178
Std Deviation	13.5659715	Variance	184.035582
Skewness	0.81881003	Kurtosis	1.43700177
Uncorrected SS	1747364	Corrected SS	43800.4686
Coeff Variation	16.0683278	Std Error Mean	0.87750975

```
proc freq data = PPH;
tables StudyGroup * PreeclampsiaStatus;
run;
```

Table 9. Frequency statistics results of prior pre eclampsia indicator in IV infusion and IM injection groups.

[1] Durocher, J., Dzuba, I. G., Carroli, G., Morales, E. M., Aguirre, J. D., Martin, R., ... & Winikoff, B. (2019). Does route matter? Impact of route of oxytocin administration on postpartum bleeding: A double-blind, randomized controlled trial. *PLOS ONE*, *14*(10), e0222981.

The FREQ Procedure

Frequency Percent Row Pct Col Pct	Table of StudyGroup by PreeclampsiaStatus		
	PreeclampsiaStatus		
StudyGroup	0	1	Total
IM	239 49.79 99.17 50.42	2 0.42 0.83 33.33	241 50.21
IV	235 48.96 98.33 49.58	4 0.83 1.67 66.67	239 49.79
Total	474 98.75	6 1.25	480 100.00

```
proc freq data = PPH;
tables StudyGroup * DiabetesStatus;
run;
```

Table 10. Frequency statistics results of prior diabetes indicator in IV infusion and IM injection groups.

The FREQ Procedure

Frequency Percent Row Pct Col Pct	Table of StudyGroup by DiabetesStatus		
	DiabetesStatus		
StudyGroup	0	1	Total
IM	238 49.58 98.76 50.53	3 0.63 1.24 33.33	241 50.21
IV	233 48.54 97.49 49.47	6 1.25 2.51 66.67	239 49.79
Total	471 98.13	9 1.88	480 100.00

```
proc ttest data = PPH alpha=0.05;
Class StudyGroup;
VAR BloodLoss60;
run;
```

[1] Durocher, J., Dzuba, I. G., Carroli, G., Morales, E. M., Aguirre, J. D., Martin, R., ... & Winikoff, B. (2019). Does route matter? Impact of route of oxytocin administration on postpartum bleeding: A double-blind, randomized controlled trial. *PLOS ONE*, *14*(10), e0222981.

Table 11. t-test results of blood loss at 60 minutes of birth in IV infusion group and IM injection group.

The TTEST Procedure

Variable: BloodLoss60

StudyGroup	Method	N	Mean	Std Dev	Std Err	Minimum	Maximum
IM		239	404.3	342.2	22.1347	20.0000	2000.0
IV		237	360.8	321.6	20.8898	25.0000	2000.0
Diff (1-2)	Pooled		43.4657	332.1	30.4436		
Diff (1-2)	Satterthwaite		43.4657		30.4356		

StudyGroup	Method	Mean	95% CL Mean		Std Dev	95% CL Std Dev	
IM		404.3	360.7	447.9	342.2	314.0	376.0
IV		360.8	319.7	402.0	321.6	295.0	353.5
Diff (1-2)	Pooled	43.4657	-16.3553	103.3	332.1	312.2	354.7
Diff (1-2)	Satterthwaite	43.4657	-16.3401	103.3			

Method	Variances	DF	t Value	Pr > |t|
Pooled	Equal	474	1.43	0.1540
Satterthwaite	Unequal	472.64	1.43	0.1539

Equality of Variances				
Method	Num DF	Den DF	F Value	Pr > F
Folded F	238	236	1.13	0.3400

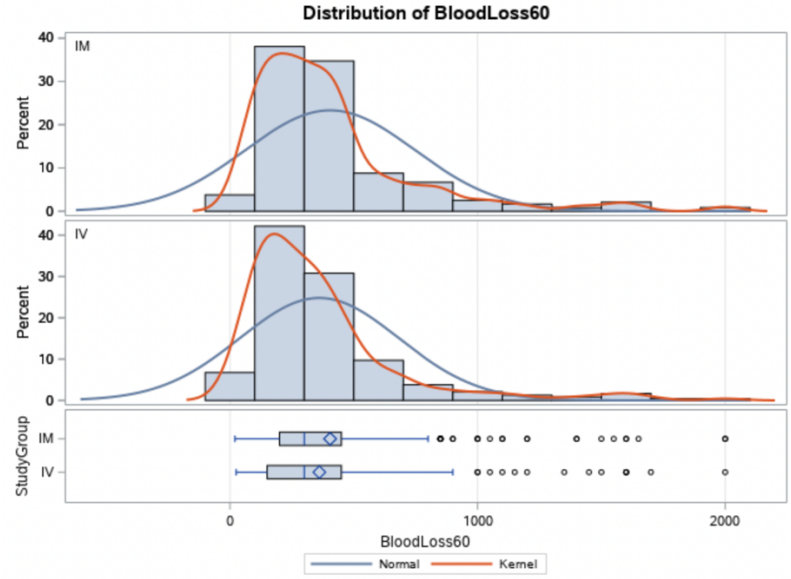

Figure 1. Distribution of blood loss at 60 minutes after birth for IV infusion group and IM injection group.

```
proc means data=PPH chartype MEAN MEDIAN Q1 Q3 QRANGE RANGE MIN MAX
STD maxdec=2;
Class StudyGroup;
VAR BloodLoss60;
RUN;
```

Table 12. Statistics results of mean blood loss at 60 minutes after birth in IV infusion group and IM injection group.

The MEANS Procedure

Analysis Variable : BloodLoss60										
StudyGroup	N Obs	Mean	Median	Lower Quartile	Upper Quartile	Quartile Range	Range	Minimum	Maximum	Std Dev
IM	241	404.31	300.00	200.00	450.00	250.00	1980.00	20.00	2000.00	342.19
IV	239	360.84	300.00	150.00	450.00	300.00	1975.00	25.00	2000.00	321.59

[1] Durocher, J., Dzuba, I. G., Carroli, G., Morales, E. M., Aguirre, J. D., Martin, R., ... & Winikoff, B. (2019). Does route matter? Impact of route of oxytocin administration on postpartum bleeding: A double-blind, randomized controlled trial. *PLOS ONE*, *14*(10), e0222981.