

# IM versus IV Oxytocin in the Third Stage of Labour

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Eastern  
Health

# Background

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- Postpartum hemorrhage remains a significant complication of pregnancy and childbirth
- At least one quarter of maternal deaths in the developing world result from **postpartum hemorrhage** (PPH)
- Incidence of PPH in the developed world is approximately 5 – 15%
  - Significant contribution to maternal morbidity

# Definition of PPH (SOGC)

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## **Based on Estimated Blood Loss:**

- Mean blood loss of greater than 500 mL following vaginal delivery
- Mean blood loss of greater than 1000 mL at the time of Cesarean section

## **Based on Maternal Hematocrit:**

- 10% change in hematocrit from pre-delivery to postpartum

# Blood Loss at Delivery

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- Shown to be largely related to the course of the third stage of labour
  - Time from delivery of infant to delivery of placenta
- *Active management* of the third stage of labour is well established as standard of care in the developed world
  - Traditionally has included early cord clamping, controlled cord traction, and administration of a uterotonic agent

# Current SOGC Recommendations

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- Oxytocin: drug of choice for PPH prevention

## **Effective Protocols:**

- Oxytocin 10 units IM
- Oxytocin 5 units IV
- Oxytocin 10 – 20 units/L crystalloid solution IV at 100 – 150 mL/hour

*“There is no evidence that any particular protocol of administration, in terms of dosage or route, is superior to any other”*

# Literature Search

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## Resources:

- PubMed
- CINAHL
- Cochrane Database of Systematic Reviews
- References from related scientific papers
- Up to date
- Obstetrical Textbooks

## Results:

No studies located comparing IM with IV oxytocin for use in the third stage of labour

# Research Question

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During active management of the 3<sup>rd</sup> stage of labour in low–risk women undergoing vaginal delivery of singleton gestations at term, is IV administration of oxytocin better than IM injection for PPH prophylaxis?

# Study Design

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- Non-blinded, randomized controlled trial
- Randomization via computer-generated random numbers table using opaque envelopes opened just prior to delivery
- Patients divided into three study groups:
  - Oxytocin 10 units IM – current standard of care
  - Oxytocin 5 units IM
  - Oxytocin 5 units IV
- Further management of the 3<sup>rd</sup> stage of labour at the discretion of the attending physician

# Study Outcomes

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## **Primary Outcome:**

- ❑ Change in maternal hematocrit (HCT) from pre-delivery to postpartum

## **Secondary Outcomes:**

- ❑ Estimated blood loss (EBL)
- ❑ Incidence of PPH
- ❑ Incidence of hypotension
- ❑ Incidence of retained placenta
- ❑ Need for additional uterotonics
- ❑ Need for blood transfusion
- ❑ Need for hysterectomy

# Sample Size Calculation

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- Based on primary outcome – change in HCT

*Bajzak et al., 2001*

- Chart review of 50 vaginal deliveries at Grace General Hospital
- Mean decrease in HCT:
  - 0.03 +/- 0.03 % PCV
- Mean drop in HCT of 0.042 % PCV or greater felt to be clinically significant

# Sample Size Calculation

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*Using:*

$$\alpha = 0.05, \beta = 0.20, \sigma = 0.03, \Delta = 0.012$$

*Formula for continuous variables:*

$$2N = 4\sigma^2(Z\alpha + Z\beta)^2/\Delta^2$$

**N ~ 100 per group**

**300 patients in total to be recruited**

# Study Subjects: Inclusion Criteria

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- ❑ Pregnant women beyond 32 weeks gestation presenting to the Case Room in active labor
- ❑ Singleton gestations
- ❑ Expectation of vaginal delivery

# Study Subjects: Exclusion Criteria

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- Patients at high risk for PPH
  - Previous PPH
  - Placenta previa
  - Grand multiparity
  - Anticoagulant therapy or known coagulopathy
  - Delivery prior to 32 weeks
  - Operative vaginal delivery
- Antepartum hemorrhage > 20W gestation
- Pre – delivery hemoglobin < 10 g/dL
- Multiple Gestation
- Intrauterine fetal death

# Outcome Assessment

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- Primary outcome – HCT
  - Blood work obtained pre – delivery and approximately 24 hours postpartum
- Blood pressure
  - Serial measurements q15 minutes as per standard protocol in labour and delivery
  - Recorded as usual in L&D record
- Other outcomes assessed through documentation in chart records

# Statistical Analysis

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- Intention to treat analysis
- Statistical significance set at  $p < 0.05$ 
  - For secondary outcomes, a Bonferroni correction was applied yielding a p value of 0.002 to detect statistical significance
- Continuous variables – ANOVA
  - Change in HCT, EBL, length of 3<sup>rd</sup> stage of labour
- Repeated blood pressure measures:
  - 2–factor repeated measures ANOVA
- Categorical Outcomes – Fisher’s exact test
  - PPH, need for additional uterotonics, need for blood transfusion

# Other Considerations

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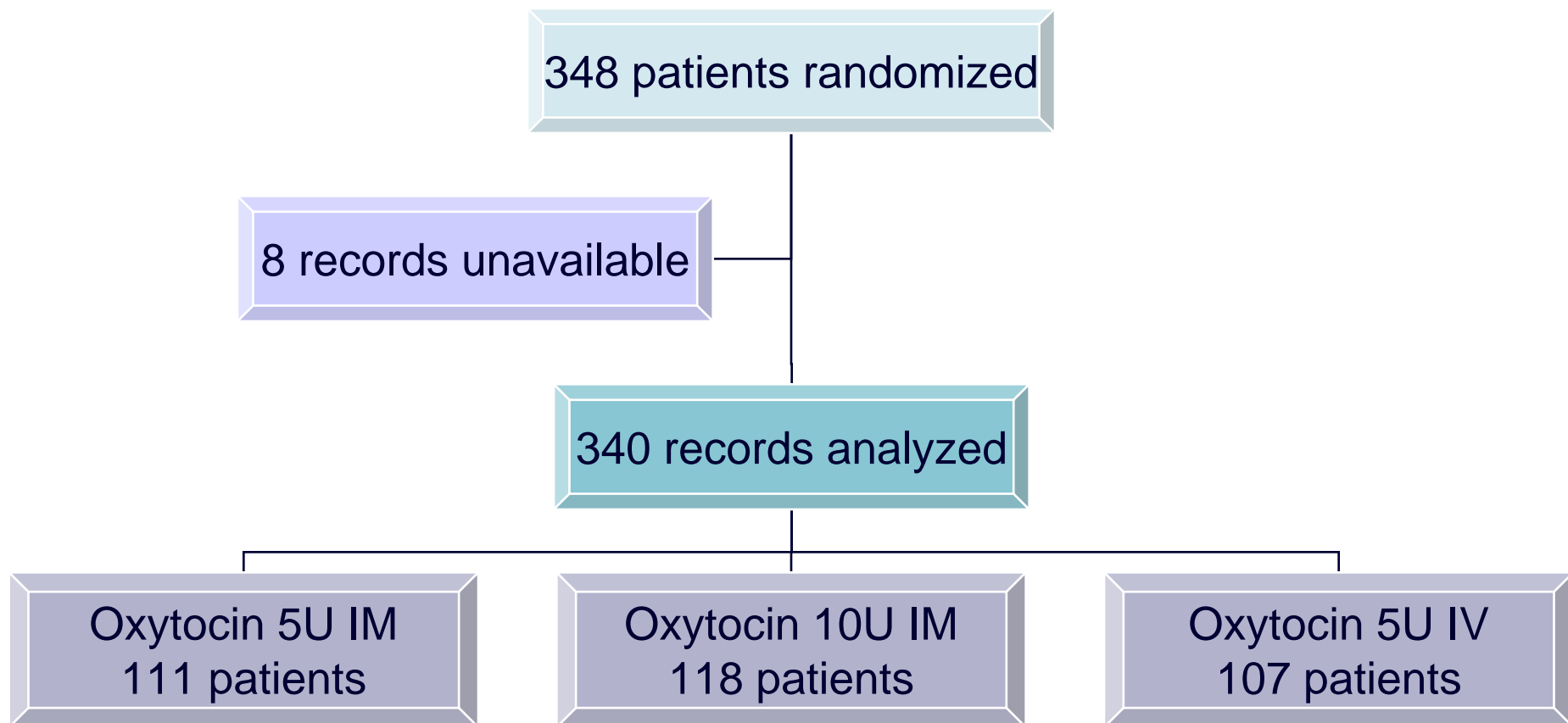
## **HIC Approval:**

- Granted in June 2005

## **Research Grant:**

- General Hospital Research Foundation

# Study Flow Chart



# Patient Demographics

	<b>Oxytocin 5U IM (Mean (SD))</b>	<b>Oxytocin 10U IM (Mean (SD))</b>	<b>Oxytocin 5U IV (Mean (SD))</b>
Age	28.3 (4.9)	29.4 (5.1)	29.1 (4.8)
BMI	33.0	32.6	33.1
Parity	0.70 (0.82)	0.58 ((0.71)	0.53 ((0.68)
GA (days)	278.5 (13.2)	276.7 (11.2)	276.8 (11.7)
Length 1 <sup>st</sup> stage (min)	368.9 (249.0)	336.7 (198.9)	378.9 (257.7)
Length 2 <sup>nd</sup> stage (min)	52.1 (49.1)	62.0 (63.3)	64.1 (68.8)
Length 3 <sup>rd</sup> stage (min)	6.2 (5.2)	6.2 (4.4)	8.1 (9.4)

# Patient Demographics

	<b>Oxytocin 5U IM (Mean (SD))</b>	<b>Oxytocin 10U IM (Mean (SD))</b>	<b>Oxytocin 5U IV (Mean (SD))</b>
Pre – delivery HCT	0.356 (0.03)	0.356 (0.029)	0.357 (0.028)
Pre – delivery HGB	122.7 (9.8)	122.5 (10.7)	122.9 ((15.6)
SVD	107	108	101
Vacuum	3	9	4
Forceps	1	1	2
BW (grams)	3522.9 (494.6)	3454.8 (482.6)	3465.3 (540.4)

# Results – Primary Outcome

Oxytocin Dosing	Pre – Delivery HCT [Mean (SD)]	Decrease in HCT [Mean (SD)]
5 units IM	0.356 (0.03)	0.032 (0.03)
10 units IM	0.356 (0.03)	0.037 (0.04)
5 units IV	0.359 (0.03)	0.033 (0.03)

***The difference between groups was not statistically significant  
(F=0.47, p=0.63)***

# Results – Secondary Outcomes

Outcome	5U IM (n=111)	10U IM (n=118)	5U IV (n=107)	p value
Decrease in HGB	12.1 (10.2)	12.0 (10.5)	12.2 (10.8)	0.99*
EBL (mL)	302.9 (133.0)	328.8 (185.3)	343.3 (202.9)	0.24*
Length 3 <sup>rd</sup> stage (min)	6.3 (5.5)	6.1 (4.2)	7.9 (9.9)	0.10*
PPH	1 [0.01]	7 [0.06]	10 [0.09]	0.02**
Severe PPH	0 [0.0]	1 [0.01]	0 [0.0]	1.0**
Additional oxytocin	44 [0.40]	46 [0.39]	40 [0.37]	0.62**
Hemabate use	1 [0.01]	2 [0.02]	4 [0.04]	0.46**
Manual removal placenta	1 [0.01]	1 [0.01]	5 [0.05]	0.23**

Mean (SD), N [%], \*ANOVA, \*\*Fisher exact

# Results – Secondary Outcomes

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## **Hemodynamic Outcomes:**

- Limited records available
  - 5U IM – 49/111
  - 10U IM – 53/118
  - 5U IV – 32/107
- Blood pressure assessments during labour and then postpartum q15 minutes x 2
- Continuous cardiac monitoring not used

# Results – Secondary Outcomes

## Systolic Blood Pressure Readings:

<b>Group</b>	<b>Intrapartum</b>	<b>15 min</b>	<b>30 min</b>
5U IM	119.4 (10.5)	118.6 (13.4)	115.1 (12.5)
10U IM	119.3 (10.7)	121.7 (12.2)	119.5 (12.1)
5 U IV	119.0 (11.0)	120.0 (9.8)	119.5 (10.3)

**$F = 2.56; p = 0.09$**

# Conclusions

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- Change in hematocrit post – delivery is similar with oxytocin administered as 5U IM, 10U IM or 5U IV in the management of the third stage of labour
- The route of delivery of oxytocin in the management of the third stage of labour can be chosen based on physician preference

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