CLINICAL PRACTICE GUIDELINE

Uterine Tone and Caesarean Birth: pharmacological management of

This document should be read in conjunction with the Disclaimer

Contents
Uterine Tone and Caesarean Birth: pharmacological management of ................................................................. 1

Quick Reference Guide .................................................................................................................................................. 2
Aims ........................................................................................................................................................................ 3
Background ............................................................................................................................................................ 3
Risk factors for postpartum haemorrhage at caesarean delivery ................................................................. 3
Oxytocin¹ ................................................................................................................................................................. 4

Infusion Preparation ................................................................................................................................................ 5
Suggested dosing .................................................................................................................................................. 5
Weaning of Oxytocin infusions ................................................................................................................................. 5
Prescribing of additional bags of Oxytocin .............................................................................................................. 5
Carbetocin (Duratocin™) ² ...................................................................................................................................... 6

Precautions and Contraindications ......................................................................................................................... 6
Suggested administration ..................................................................................................................................... 6
Ergometrine ............................................................................................................................................................ 7

Indications ............................................................................................................................................................ 7
Precautions and Contraindications ............................................................................................................................ 7
Side Effects ........................................................................................................................................................... 7
Suggested administration ..................................................................................................................................... 7
Misoprostol ............................................................................................................................................................ 8

Indications ............................................................................................................................................................ 8
Precautions and Contraindications ............................................................................................................................ 8
Side effects ............................................................................................................................................................ 8
Suggested administration ..................................................................................................................................... 8
Prostaglandin F2alpha (CARBOPROST) ..................................................................................................................... 8

Indications ............................................................................................................................................................ 8
Precautions and Contraindications ............................................................................................................................ 9
Side Effects ........................................................................................................................................................... 9
Suggested administration ..................................................................................................................................... 9
Glyceryl Trinitrate (GTN)³ .................................................................................................................................... 9

Indications ............................................................................................................................................................ 9
Precautions and Contraindications ............................................................................................................................ 9
Side Effects ........................................................................................................................................................... 10
Suggested Administration .................................................................................................................................. 10
## Quick Reference Guide

### Oxytocin (Syntocinon®)

- **Bolus Doses**
  - Elective caesarean delivery: 2 IU bolus followed by infusion
  - Non elective caesarean delivery: 3 IU bolus followed by infusion
  - Women considered at higher risk of uterine atony: 3 IU bolus followed by infusion

- **Standard Intravenous Infusion**
  - 40 IU of oxytocin diluted into 500 mL of normal 0.9% sodium chloride
    - Normal starting rate: 125 mL/h (10 IU/h)
    - High starting rate: 250 mL/h (20 IU/h)

- **Low volume Intravenous infusion**
  - Dilute 40 IU of oxytocin into a total volume of 50 mL with normal 0.9% sodium chloride.
    - This requires administration via a dedicated syringe driver.
    - Normal starting rate: 12.5 mL/h (10 IU/h)
    - High starting rate: 25 mL/h (20 IU/h)

### Ergometrine
- 200 to 500 mcg IM or 250 mcg IV

### Misoprostol
- 1000 mcg (5 x 200 mcg tablets) PR

### Carbetocin
- A single intravenous dose of 100 mcg administered slowly post-delivery.
- In patients who do not respond to a single dose of Carbetocin, further bolus dosing is not recommended and alternative uterotonic agents should be utilised.

### Prostaglandin f2 alpha (CARBOPROST)
- First dose may be given outside of the operating theatre; The requirement for additional doses is an indication for a Category 1 transfer to the operating theatre.
- The dose is 250 mcg intra-muscularly. This may be repeated every 15 minutes up to a maximum of 2 mg (8 doses).

### Glyceryl Trinitrate (Uterine Relaxant)
- 1 – 2 sprays (400 - 800 micrograms) administered as spray droplets beneath the tongue (do not inhale). Repeat after 5 minutes if hypertonus sustained
- Intravenous;
  - At KEMH ampoules of 1 mg in 2 mL of GTN are available.
  - Dilute 1 mg into 20 mL of 0.9% sodium chloride to make a GTN concentration of 50 mcg /mL.
    - Alternatively a 50 mg ampoule of GTN may be injected into a labelled bag of 1000 mL 0.9% sodium chloride and 20 mL of 50 mcg /mL GTN withdrawn.
  - Administer 2 mL (100 mcg) intravenously.
  - Titrate to effect repeating dose every minute.
Aims

- To standardise the pharmacological management of uterine tone at caesarean delivery.
- To provide suggested administration protocols for all the commonly available uterotonic and tocolytic agents available at King Edward Memorial Hospital for Women (KEMH).

Background

- Postpartum haemorrhage (PPH) occurs in approximately 5% of elective caesarean births and in upwards of 7% of non-elective caesarean births (Magann 2005 KEMH data).
- The management of uterine tone at caesarean delivery requires close communication between the obstetric and anaesthetic personnel in conjunction with the nursing and midwifery staff.
- The primary responsibility for the ordering of uterotonic agents lies with the obstetrician. The responsibility for the administration of these agents lies with either the anaesthetist or the obstetrician, depending on the agent concerned and the route of administration.
- Ideally the proposed plan for uterotonic agents as well as the potential risks of medication side effects should be discussed prior to the commencement of surgery (for example at “team time out”).
- In addition to pharmacological techniques, non-pharmacological strategies may also need to be employed, including uterine massage, uterine compression sutures, the placement of intra-uterine tamponade balloons, pelvic artery ligation, aortic compression, embolisation and hysterectomy.

Risk factors for postpartum haemorrhage at caesarean delivery

A large number of risk factors for PPH with caesarean delivery have been identified. These include, but are not limited to:

- Previous history of PPH
- Non elective caesarean delivery
- Prolonged labour
- Use of oxytocin to augment labour
- Multiple gestation
- Pre-eclampsia (PE)
- Obesity
- Polyhydramnios
- Macrosomia
- Classical caesarean delivery
- Placenta praevia (and its variations)
- Pre term delivery
Oxytocin¹

**Background**
Synthetic oxytocin is a nonapeptide that promotes rhythmic uterine smooth muscle contraction. When administered intravenously it has a rapid onset of action (<1 minute) and a short half-life (between 3-20 minutes), thus making administration via an infusion necessary.

Prior exposure to oxytocin (such as may occur with labour augmentation) may result in oxytocin receptor desensitisation and consequently inadequate response to standard doses of oxytocin. Second line uterotonic agents may need to be considered earlier.

Side effects associated with bolus administration of oxytocin are higher with increasing doses. Recent evidence suggests that adequate uterine tone is able to be achieved with lower doses than that previously recommended, although because of receptor desensitisation, higher doses may be required in certain situations.

**Indications**
An oxytocin infusion should be considered routine in all women undergoing a caesarean delivery at KEMH, unless Carbetocin is used as the primary agent. The main caveat is that in women undergoing a planned caesarean hysterectomy for placental abnormalities in which the placenta will be left in situ, the obstetrician may not want a uterotonic administered to avoid placental separation.

**Precautions and Contraindications**
- As even small amounts of oxytocin may cause significant uterine contraction, the bolus dose of oxytocin should not be drawn up until after the delivery of the neonate(s). Infusions must not be connected until after the birth of the neonate (or the final neonate in the case of multiple gestations).
- Oxytocin, particularly when administered as a bolus, may cause significant peripheral vasodilatation and tachycardia. This may not be well tolerated in women with significant cardiac disease/fixed cardiac output lesions.

**Side Effects**
- Hypotension
- Tachycardia and myocardial ischemia
- Arrhythmias
- Nausea and vomiting
- Headache and flushing.
- Hyponatraemia
- Seizures and coma.
Infusion Preparation

- **Standard Intravenous Infusion**
  40 IU of oxytocin diluted into 500 mL of 0.9% sodium chloride
  - Normal starting rate: 125 mL/h (10 IU/h)
  - High starting rate: 250 mL/h (20 IU/h)

- **Low volume Intravenous infusion**
  When excessive fluid administration is of concern (e.g. severe pre-eclampsia) consideration may be given to diluting 40 IU of oxytocin into a total volume of 50 mL with 0.9% sodium chloride. This requires administration via a dedicated syringe driver.
  - Normal starting rate: 12.5 mL/h (10 IU/h)
  - High starting rate: 25 mL/h (20 IU/h)

Suggested dosing

It is recommended that the oxytocin bolus solution is not prepared prior to delivery of the neonate, to avoid accidental administration prior to delivery. Oxytocin bolus doses should be given slowly IV (preferably over 1 minute). If there is an inadequate response to the initial dose this may be repeated after 3-5 minutes.

- Elective caesarean delivery: 2 IU bolus followed by infusion
- Non elective caesarean delivery: 3 IU bolus followed by infusion
- Women considered at higher risk of uterine atony (see page 3): 3 IU bolus followed by infusion
- Omission of bolus doses should be considered in patients at increased risk of cardiovascular compromise- e.g. severe ongoing haemorrhage or underlying cardiac disease
- Management of Oxytocin infusion is to be discussed with the Obstetric Surgeon at the sign out step at the end of surgery.

Weaning of Oxytocin infusions

- Weaning should be as per Clinical Guideline Therapeutic and Prophylactic oxytocin Infusion regimes

Prescribing of additional bags of Oxytocin

Some women may require additional bags of oxytocin to be prescribed. These women are generally women who have a PPH or are at increased risk of PPH.

*The requirement for an additional bag to be charted should serve as a prompt for clinical obstetric review. The anaesthetic team are not to take responsibility for charting additional bags of oxytocin.*
Carbetocin (Duratocin™)²

**Background**
Carbetocin is a synthetic octapeptide analogue of oxytocin. Compared with oxytocin it has a prolonged duration of action. It has an onset time of less than 2 minutes after intravenous administration with a total duration of action of approximately 1 hour.

**Indications**
Currently Carbetocin is licensed for use in elective caesarean births conducted under regional anaesthesia. Use outside of these circumstances requires a discussion between the anaesthetist and the obstetrician.

**Precautions and Contraindications**
Carbetocin should be used with extreme caution in patients with a history of coronary artery disease.

**Side Effects**
The side effect profile is similar to oxytocin and includes:
- Tachycardia
- Hypotension
- Nausea
- Vomiting
- Flushing
- Pruritus
- Abdominal pain
- Headache
- Tremor
- Hyponatraemia
- Water intoxication

**Suggested administration**
A single intravenous dose of 100 mcg administered slowly after delivery.

In patients who do not respond to a single dose of Carbetocin, further bolus dosing is not recommended and alternative uterotonic agents should be utilised.
Ergometrine

Background
Ergometrine is an ergot alkaloid that has a rapid onset of action (<1 min if given IV and 3-5 minutes if given IM). It has a duration of action of approximately 45 minutes if given IV and of up to 3 hours if given IM.

Indications
• Prophylaxis in high risk postpartum haemorrhage cases.
• Emergency management of postpartum haemorrhage.

Precautions and Contraindications
Ergometrine can produce intense vasoconstriction which can cause an elevated blood pressure and central venous pressure. It is relatively contra-indicated in pre-eclampsia as exaggerated hypertensive effects may be seen. In addition, it is also relatively contra-indicated in patients with hypertension, sepsis and in patients with peripheral vascular disease. It has been associated with clinical exacerbations of porphyria.

Some patients may not respond to Ergometrine if they are hypocalcaemic. Cautious IV calcium replacement may be required for optimal efficacy.

Side Effects
There are a large number of potential side effects and adverse effects with Ergometrine. These include:
• Hypertension
• Nausea, vomiting and diarrhoea
• Headache
• Abdominal pain
• Coronary artery and peripheral vasospasm with chest pain and palpitations
• Dyspnoea

Suggested administration
• Prophylaxis for PPH:
  ➢ 200 to 500 mcg IM after complete delivery of the placenta

• Emergency management of PPH:
  ➢ 250 mcg may be given slowly IV over at least 1 minute (note this route is more likely to cause hypertension and nausea and vomiting)
Misoprostol

Background
Misoprostol is a prostaglandin E1 analogue that may be administered by a variety of routes including rectal, vaginal, oral and sublingual.

Indications
- Prophylaxis or management of postpartum haemorrhage.

Precautions and Contraindications
Serious cardiovascular side effects have been reported. Misoprostol should be used with caution in women with significant cardiovascular disease.

Side effects
- Shivering and fever are common particularly with the oral and sublingual routes.
- Diarrhoea
- Headache
- Abdominal pain
- Nausea and vomiting

Suggested administration
1000 mcg (5 x 200 mcg tablets) per rectum (PR)

Prostaglandin F2alpha (CARBOPROST)
Refer to the KEMH Clinical Guideline Carboprost for administration information

Background
It is important to note that there are two major formulations of PGF2a available throughout the world, Dinoprost and Carboprost. Carboprost has replaced Dinoprost for use at King Edward Memorial Hospital. Carboprost is given via the intra-muscular route (Dinoprost is administered directly into the myometrium).

PGF2a is an established second line agent in the management of postpartum haemorrhage. It is a potent contractor of smooth muscle which is metabolised in the lungs. Large bolus administration may cause systemic effects if the metabolic pathways in the lungs are overloaded.

Indications
- Second line agent in the management of PPH.
Precautions and Contraindications
The first dose of PGF2a may be administered outside of the operating theatre, however if a second dose is required this is an indication for a Category 1 transfer to theatre. This ensures a controlled environment with intravenous access, resuscitation equipment and respiratory and cardiac monitoring in place.

Side Effects
- Bronchospasm, pulmonary oedema and hypoxia – use with caution in asthmatics
- Acute hypertension, arrhythmias
- Abdominal cramps, diarrhoea and vomiting
- Flushing, shivering and headache

Suggested administration
The recommended dose is 250 mcg given intra-muscularly. This can be repeated every 15 minutes up to a maximum dose of 2 mg (i.e. 8 doses).

Glyceryl Trinitrate (GTN)³

Background
The principal pharmacological action of glyceryl trinitrate is relaxation of smooth muscle. It causes relaxation of the uterus (tocolysis) as well as producing a vasodilator effect on both peripheral arteries and veins, with more prominent effects on the latter. GTN may be administered by the intravenous or sublingual route. The systematic availability of sublingual GTN is approximately 39%. Therapeutic effect is seen within 1-2 minutes of administration independent of the route and the therapeutic effect lasts 3 to 5 minutes.

Indications
Situations when uterine relaxation may be necessary during caesarean birth include:
- Fetal malpresentation
- Inadvertent oxytocics overdose prior to birth
- Uterine constriction ring

Precautions and Contraindications
GTN may cause hypotension and tachycardia and should be avoided in the following situations:
- Acute circulatory failure (shock, circulatory collapse)
- Cardiac disease
- Pronounced hypotension (systolic BP < 90 mm Hg)

Side effects such as hypotension can be managed by the administration of vasoactive medications such as ephedrine, metaraminol or phenylephrine by the anaesthetist.
Side Effects
Due to the vasodilating effects of GTN the following side effects may occur:

- Headache
- Hypotension
- Reflex tachycardia or bradycardia
- Rarely nausea, vomiting, flushing

Suggested Administration

- **Sublingual via metered pump spray:**
  - Nitro-lingual Pump spray should be primed before using it for the first time by pressing the nozzle five times.
  - 1 – 2 sprays (400 - 800 micrograms) administered as spray droplets beneath the tongue (do not inhale).
  - Repeat after 5 minutes if hyper tonus is sustained.

- **Intravenous:**
  - At KEMH ampoules of 1 mg in 2 mL of GTN are available.
  - Dilute 1 mg into 20 mL of 0.9% sodium chloride to make a GTN concentration of 50 mcg /mL.
  - Alternatively a 50 mg ampoule of GTN may be injected into a labelled bag of 1000 mL 0.9% sodium chloride and 20 mL of 50 mcg /mL GTN withdrawn.
    - **DISCARD bag of 0.9% sodium chloride after use.**
    - Administer 2 mL (100 mcg) intravenously.
    - Titrate to effect repeating dose every minute.

References

Related WNHS policies, procedures and guidelines

- **Primary Postpartum Haemorrhage**

Keywords: Postpartum, haemorrhage, PPH, caesarean, oxytocin, carbetocin, ergometrine, misoprostol, carboprost, GTN,
<table>
<thead>
<tr>
<th>Document owner:</th>
<th>OGID</th>
</tr>
</thead>
<tbody>
<tr>
<td>Author / Reviewer:</td>
<td>Anaesthetics/ Obstetrics</td>
</tr>
<tr>
<td>Date first issued:</td>
<td>March 2013</td>
</tr>
<tr>
<td>Last reviewed:</td>
<td>January 2017</td>
</tr>
<tr>
<td>Endorsed by:</td>
<td>MSMSC</td>
</tr>
<tr>
<td>Standards Applicable:</td>
<td>NSQHS Standards: 1 Clinical Care is Guided by Current Best Practice 4 Medication Safety</td>
</tr>
</tbody>
</table>

Printed or personally saved electronic copies of this document are considered uncontrolled. Access the current version from the WNHS website.