## 2. INTRA-OPERATIVE MANAGEMENT

### 2.2 Pharmacological Management of Uterine Tone at Caesarean Birth

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#### 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 Infusion**
  - 30 IU of oxytocin diluted into 500 ml of normal saline
  - Normal starting rate: 125 ml/h (7.5 IU/h)
  - High starting rate: 250 ml/h (15 IU/h)

- **Low volume infusion**
  - Dilute 30 IU of oxytocin into a total volume of 50 ml with normal saline.
  - This requires administration via a dedicated syringe driver.
  - Normal starting rate: 12.5 ml/h (7.5 IU/h)
  - High starting rate: 25 ml/h (15 IU/h)

#### ERGOMETRINE

- 250 to 500 mcg IM or 250 mcg IV

#### MISOPROSTOL

- 1000 mcg (5 x 200 mcg tablets) per rectum

#### CARBETOCIN

- A single intravenous dose of 100 mcg administered slowly over 1 minute after delivery. This should be followed by an oxytocin infusion.
- 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

- One ampoule (5 mg in 1 ml) diluted to 20 ml in 0.9% saline = 250 mcg/ml solution.
- Discard 8 ml to leave a total of 3 mg in 12 ml (this avoids inadvertent overdose).
- The surgeon is to inject this into the myometrium under either direct vision or through the anterior abdominal wall.

**Dose:** Initial recommendation is for 5 X 1 ml injections over one minute (a dose of 1.25 mg in

#### 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 saline 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Alternatively a 50 mg ampoule of GTN may be injected into a labelled bag of 1000 ml saline and 20 ml of 50 mcg /ml GTN withdrawn.
  - Administer 2 ml (100 mcg) intravenously.
  - Titrate to effect repeating dose every minute.
AIM

- 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 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 drug 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 and the placement of intra-uterine tamponade balloons.

RISK FACTORS FOR POST PARTUM HAEMORRHAGE AT CAESAREAN DELIVERY

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

- Previous history of post partum haemorrhage
- Non elective caesarean delivery
- Prolonged labour
- Use of oxytocin to augment labour
- Multiple gestation
- Pre-eclampsia
- Obesity
- Polyhydramnios
- Macrosomia
- Classical caesarean delivery
- Placenta praevia (and its variations)
- Pre term delivery
- General anaesthesia
- Maternal clotting abnormalities

OXYTOCIN

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. The only 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 an uterotonic administered to avoid placental separation.

**Precautions and Contraindications**

- As even small amounts of oxytocin may cause significant uterine contraction, 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.
- Large doses of oxytocin may cause water retention leading to hyponatraemia, seizures and coma.

**Side Effects**

- Side effects of oxytocin include hypotension, tachycardia and myocardial ischemia, arrhythmias, nausea, vomiting, headache and flushing.

**INFUSION PREPARATION**

- **Standard Infusion**
  - 30 IU of oxytocin diluted into 500 ml of normal saline
    - Normal starting rate: 125 ml/h (7.5 IU/h)
    - High starting rate: 250 ml/h (15 IU/h)

- **Low volume infusion**
  - When excessive fluid administration is of concern (e.g. severe pre eclampsia) consideration may be given to diluting 30 IU of oxytocin into a total volume of 50 ml with normal saline. This requires administration via a dedicated syringe driver.
    - Normal starting rate: 12.5 ml/h (7.5 IU/h)
    - High starting rate: 25 ml/h (15 IU/h)

**Suggested dosing**

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: 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

**WEANING OF OXYTOCIN INFUSIONS**

- Weaning should be as per Clinical Guideline B.9.1.3 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 post partum haemorrhage or are at increased risk of post partum haemorrhage. **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™)

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. As carbetocin has similar a similar structure to oxytocin, hyponatraemia and water intoxication may occur in rare circumstances.

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

Suggested administration
A single intravenous dose of 100 mcg administered slowly over 1 minute after delivery. This should be followed by an oxytocin infusion.

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 min if given IM). It has a duration of action of approximately 45 min if given IV and of up to 3 hours if given IM.

Indications
- Prophylaxis in high risk post partum haemorrhage cases.
- Emergency management of post partum 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 post partum haemorrhage:
  - 250 to 500 mcg IM after complete delivery of the placenta

- Emergency management of post partum haemorrhage:
  - 250 mcg may be given slowly IV over at least 1 minute (note this route is more likely to cause hypertension)

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 post partum 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 may occur.

Suggested administration

1000 mcg (5 x 200 mcg tablets) PR
PROSTAGLANDIN F2ALPHA (DINOPROST)

Background
It is important to note that there are two major formulations of PGF2a available throughout the world, Dinoprost and Carboprost-Dinoprost is the formulation used at King Edward Memorial Hospital and this formulation is for INTRA-MYOMETRIAL administration only (compared to Carboprost which is given via the intra-muscular route).

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 postpartum haemorrhage.

Precautions and Contraindications
PGF2a must be administered in the operating theatre. This ensures a controlled environment with intravenous access, resuscitation equipment and respiratory and cardiac monitoring in place.

Side Effects
- Acute hypertension, arrhythmias
- Bronchospasm, pulmonary edema and hypoxia
- Abdominal cramps, diarrhea and vomiting
- Flushing, shivering and headache

Suggested administration
One ampoule (5 mg in 1 ml) diluted to 20 ml in 0.9% saline = 250 mcg/ml solution.
Discard 8 ml to leave a total of 3 mg in 12 ml (this avoids inadvertent overdose).
The surgeon is to inject this into the myometrium under either direct vision or through the anterior abdominal wall.
Dose: Initial recommendation is for 5 X 1 ml injections over one minute (a dose of 1.25 mg in total)

GLYCERYL TRINITRATE (GTN)

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:
- breech birth: obstructed after-coming head or shoulders
- multiple pregnancy: second twin in transverse-lie
- 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 saline 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 saline and 20 ml of 50 mcg /ml GTN withdrawn.
  - **DISCARD bag of saline after use.**
  - Administer 2 ml (100 mcg) intravenously.
  - Titrate to effect repeating dose every minute.

**REFERENCES**