South Australian Perinatal Practice Guidelines

Prostaglandin analogues for postpartum haemorrhage

Misoprostol (Prostaglandin E1 analogue)

Introduction

- Misoprostol (Cytotec®) a prostaglandin E_1 analogue is an inexpensive tablet and is stable at room temperature if kept dry
- Systematic reviews of randomized controlled trials show that misoprostol is less effective than oxytocin and other injectable uterotonics in preventing postpartum haemorrhage and has side-effects, such as high temperature and shivering (Gülmezoglu 2007; WHO 2009)
- The most recent Cochrane systematic review states that there is insufficient evidence to show that the addition of misoprostol is superior to the combination of oxytocin and ergometrine alone for the treatment of primary PPH (Mousa & Alfirevic 2007)

Dosage and route of administration

- The most common misoprostol regimens reported for the treatment of PPH are 600, 800 or 1,000 micrograms rectally (Hofmeyr et al. 2004; Gülmezoglu et al. 2007)
- However, doses reported in recent published clinical trials range from 400 micrograms to 1,000 micrograms and have been provided sublingually, rectally and orally (Derman 2006; Hemmerling 2006)
- The buccal or sublingual route has rapid uptake, prolonged duration and greatest total bioavailability. The rectal route has slow uptake but prolonged duration. The oral route has the most rapid uptake, but the shortest duration
- In order to improve the rapidity of onset of action and overall bioavailability misoprostol regimens may be modified by administering 200 micrograms orally, 400 micrograms sublingually and 400 micrograms rectally or similar (Hofmeyr et al. 2004)

Side effects

- Shivering and fever up to 40° C are common (especially via oral and sublingual routes)
- Diarrhoea, headache and vomiting

Prostaglandin F2α (Dinoprost)

Introduction

- Intramyometrial prostaglandin F2α is an established 2nd line treatment for postpartum haemorrhage unresponsive to oxytocic agents along with ongoing bimanual compression and uterine massage (Belfort & Dildy in James et al. 2011)
- Case series show prostaglandin F2α is effective in 88 % of cases refractory to oxytocics (Oleen & Mariano 1990)
- **This preparation is not suitable for intramuscular injection**

Pharmacology

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Contact: South Australian Perinatal Practice Guidelines workgroup at: cywhs.perinatalprotocol@health.sa.gov.au

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Prostaglandin analogues for postpartum haemorrhage

- Prostaglandin $F_{2}\alpha$ ($PGF_{2}\alpha$) is a potent smooth muscle contractor which is 90 % metabolised on first passage through the lungs
- A large bolus of $PGF_{2}\alpha$ can overload the lung metabolic pathways and allow unmetabolised $PGF_{2}\alpha$ into the systemic arterial system, with resultant cardiovascular effects

Indications

- To control severe PPH caused by uterine atony that is not responsive to oxytocin, ergometrine or uterine massage
- Note - Management of severe postpartum haemorrhage requiring PGF2α requires senior obstetrician involvement

Contraindications

- Prostaglandin $F_{2}\alpha$ ($PGF_{2}\alpha$) is a potent smooth muscle contractor which is 90 % metabolised on first passage through the lungs
- A large bolus of $PGF_{2}\alpha$ can overload the lung metabolic pathways and allow unmetabolised $PGF_{2}\alpha$ into the systemic arterial system, with resultant cardiovascular effects

Relative contra-indications

- Severe asthma, lung disease and cardiovascular disease

Side Effects

The following adverse side effects have been reported:

- Respiratory: bronchospasm, pulmonary oedema due to raised pulmonary artery pressures, hypoxia due to pulmonary shunting
- Cardiovascular: acute hypertension- usually transient. Hypotension secondary to myocardial failure, cardiac arrhythmia including ventricular tachycardia
- Gastrointestinal: abdominal cramps, diarrhoea and vomiting
- Other: convulsions (rarely), flushing, shivering, uterine rupture, headache – usually mild and transient

Prerequisites

- Experienced anaesthetist on standby
- Intravenous access x 2 using 16 gauge cannulas
- Pulse oximetry and oxygen administration
- Resuscitation equipment on hand
- Usually used in a controlled environment (e.g. in theatre at caesarean section) where misoprostol is unable to be administered

Prostaglandin F2α (Dinoprost) preparation and administration

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Presentation:

- $PGF_{2\alpha}$ 5 mg in one mL ampoule

Preparation of Solution

- Dilute (5 mg) 1 mL of $PGF_{2\alpha}$ to 10 mL with sodium chloride 0.9 % to give 0.5 mg $PGF_{2\alpha}$ per mL (NSW Health 2010)
- Discard 4 mL from 10 mL to leave the maximum dose of 3 mg (6 mL). This procedure decreases the chance of overdose

Administration

At laparotomy / LSCS:	After vaginal delivery:
> Infiltrate 2 mL of prepared solution (1 mg) directly into myometrium using a 21 gauge spinal needle, aspirating intermittently to avoid direct systemic injection. > Repeat 10-15 minutes later if necessary. Avoid cervical injection because of increased risk of direct systemic uptake	> Using 22 gauge spinal needle, the medical officer injects 1 mL (0.5 mg) of diluted PGF2α through the anterior abdominal wall into the myometrium on each side of the uterine fundus, or 2 mL (1 mg) into the uterine fundus, aspirating to avoid direct systemic injection > Repeat if required to a maximum dose of 3 mg > Ultrasound guidance may be useful
Last reviewed: 17/07/12	

Unsuccessful response

- Proceed to alternative surgical management e.g. balloon tamponade, uterine packing, B-Lynch suture, uterine artery and internal iliac artery ligation, pelvic arterial embolization and hysterectomy

References

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Useful references

RANZCOG College statements. Available from URL: http://www.ranzcog.edu.au/womens-health/statements-a-guidelines/college-statements.html?start=1

- C-Obs 12: The use of misoprostol in obstetrics and gynaecology
- C-Obs 43: Management of postpartum haemorrhage

Abbreviations

C	Celsius
e.g.	For example
et al.	And others
IV	Intravenous
LSCS	Lower segment caesarean section

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mg	Milligram(s)
mL	Millilitre(s)
NSW	New South Wales
%	Percent
PPH	Postpartum haemorrhage
PG	Prostaglandin
®	Registered trademark

Version control and change history

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Version	Date from	Date to	Amendment
1.0	03 Sept 07	17 July 12	Original version
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