

Policy

Clinical Guideline

Prostaglandin Analogues for Major Postpartum Haemorrhage

Policy developed by: SA Maternal & Neonatal Community of Practice
Approved SA Health Safety & Quality Strategic Governance Committee on:
19 April 2016
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Summary Clinical practice guideline on the use of prostaglandin analogues for major postpartum haemorrhage

Keywords clinical guideline, prostaglandin analogues for major postpartum haemorrhage, Prostaglandin agonists, misoprostol, cytotec, uterotonic, PPH, postpartum haemorrhage, prostaglandin analogues, Carboprost, hemabate, dinoprost, prostaglandin F2 α

Policy history Is this a new policy? **N**
Does this policy amend or update an existing policy? **Y v2.0**
Does this policy replace an existing policy? **N**
If so, which policies?

Applies to All SA Health Portfolio

Staff impact All Staff, Management, Admin, Students, Volunteers
All Clinical, Medical, Nursing, Allied Health, Emergency, Dental, Mental Health, Pathology

PDS reference CG241

Version control and change history

Version	Date from	Date to	Amendment
1.0	03 Sep 2007	17 Jul 2012	Original version
2.0	17 Jul 2012	19 April 2016	Reviewed
3.0	19 April 2016	Current	

Note

This guideline provides advice of a general nature. This statewide guideline has been prepared to promote and facilitate standardisation and consistency of practice, using a multidisciplinary approach. The guideline is based on a review of published evidence and expert opinion.

Information in this statewide guideline is current at the time of publication.

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Health practitioners in the South Australian public health sector are expected to review specific details of each patient and professionally assess the applicability of the relevant guideline to that clinical situation.

If for good clinical reasons, a decision is made to depart from the guideline, the responsible clinician must document in the patient's medical record, the decision made, by whom, and detailed reasons for the departure from the guideline.

This statewide guideline does not address all the elements of clinical practice and assumes that the individual clinicians are responsible for discussing care with consumers in an environment that is culturally appropriate and which enables respectful confidential discussion. This includes:

- The use of interpreter services where necessary,
- Advising consumers of their choice and ensuring informed consent is obtained,
- Providing care within scope of practice, meeting all legislative requirements and maintaining standards of professional conduct, and
- Documenting all care in accordance with mandatory and local requirements

Explanation of the aboriginal artwork:

The aboriginal artwork used symbolises the connection to country and the circle shape shows the strong relationships amongst families and the aboriginal culture. The horse shoe shape design shown in front of the generic statement symbolises a woman and those enclosing a smaller horse shoe shape depicts a pregnant women. The smaller horse shoe shape in this instance represents the unborn child. The artwork shown before the specific statements within the document symbolises a footprint and demonstrates the need to move forward together in unison.



Australian Aboriginal Culture is the oldest living culture in the world yet Aboriginal people continue to experience the poorest health outcomes when compared to non-Aboriginal Australians. In South Australia, Aboriginal women are 2-5 times more likely to die in childbirth and their babies are 2-3 times more likely to be of low birth weight. The accumulative effects of stress, low socio economic status, exposure to violence, historical trauma, culturally unsafe and discriminatory health services and health systems are all major contributors to the disparities in Aboriginal maternal and birthing outcomes. Despite these unacceptable statistics the birth of an Aboriginal baby is a celebration of life and an important cultural event bringing family together in celebration, obligation and responsibility. The diversity between Aboriginal cultures, language and practices differ greatly and so it is imperative that Perinatal services prepare to respectively manage Aboriginal protocol and provide a culturally positive health care experience for Aboriginal people to ensure the best maternal, neonatal and child health outcomes.



Prostaglandin analogues for major postpartum haemorrhage

Prostaglandin agonists

- > At term pregnancy, prostaglandin activity increases until the placenta is delivered
- > Administration of exogenous prostaglandin agonists produces intense, sustained contraction of the myometrium and provide a very effective **second line** treatment for postpartum haemorrhage due to uterine atony **and unresponsive to uterine massage, oxytocin / ergometrine**
- > **Two classes of prostaglandin analogues are available:** oral (misoprostol) and parenteral agents (carboprost and dinoprost)

Misoprostol (Prostaglandin E₁ analogue)

Introduction

- > Misoprostol differs only slightly from endogenous prostaglandin, with an increased duration of action. It is inexpensive, stable at room temperature (if kept dry) and a very effective uterotonic agent, increasing both the frequency and amplitude of contractions¹
- > Misoprostol for postpartum haemorrhage has been administered orally, rectally or vaginally, and is rapidly absorbed from mucous membranes
- > 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^{3,4}
- > 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 PPH⁵

Dosage and route of administration

- > The most common misoprostol regimens reported for the treatment of PPH are 600, 800 or 1,000 micrograms **rectally**^{4,6}
- > However, doses reported in recent published clinical trials range from 400 micrograms to 1,000 micrograms and have been provided sublingually, rectally and orally^{7,8}
- > 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

Misoprostol	
<p>Dosage</p> <ul style="list-style-type: none"> > 800 to 1,000 micrograms rectally or sublingually 	<p>Contraindications:</p> <ul style="list-style-type: none"> > Known sensitivity to prostaglandins (use with caution in women with asthma) <p>Side effects:</p> <ul style="list-style-type: none"> > Shivering and fever up to 40° C are common (especially via oral and sublingual routes) > Diarrhoea, headache and vomiting <p>Onset of action:</p> <ul style="list-style-type: none"> > Buccal or sublingual 11 minutes, and lasts 3 hours > Per rectum has slow uptake (100 minutes) but prolonged duration (4 hours) > Off label use

Prostaglandin analogues for major postpartum haemorrhage

Carboprost (15-methyl prostaglandin F_{2α})

Introduction

- > Carboprost acts as a smooth muscle stimulant
- > Carboprost should only be used by medically trained personnel in a hospital with 24 hour medical cover
- > A multicenter surveillance study of 237 cases of postpartum haemorrhage refractory to standard oxytocics reported an efficacy of 88% with carboprost. The majority of women in this study required a single dose only¹⁰
- > Carboprost is available via the Special Access Scheme (SAS). An SAS Category A form must be completed

Pharmacology

- > Carboprost is an analogue of PGF_{2α} (dinoprost) with a more prolonged action than dinoprost, attributed to its resistance to inactivation by oxidation at the 15-position

Indication

- > Treatment of postpartum haemorrhage due to uterine atony not responsive to uterine massage, oxytocic agents and ergometrine (used either alone or in combination)

Administration

- > Carboprost is only licensed for intramuscular injection; however, it has been administered by the intramyometrial route. Direct intramyometrial injection is the responsibility of the administering senior obstetrician
- > **Carboprost must NOT be given intravenously**

Storage

- > It is both light- and heat-sensitive and **must be kept refrigerated at 2-8°C**

Carboprost preparation and administration

Presentation:

- > Carboprost 0.25 mg in one mL ampoule

Caution

- > History of asthma, hypo or hypertension, cardiovascular, renal, or hepatic disease, glaucoma or raised intra-ocular pressure, anaemia, jaundice, diabetes or epilepsy

Contraindications

- > Cardiac and pulmonary disease

Side effects

- > Due to its vasoconstrictive and bronchoconstrictive effects, carboprost can result in **nausea, vomiting, diarrhoea, pyrexia and bronchospasm**
 - > Concomitant administration of anti-emetics and antidiarrhoeal drugs significantly reduces the very high incidence of the gastrointestinal side effects

Onset of action

- > Intramuscular: 20 to 30 minutes, lasting up to 3 hours
- > Intramyometrial: less than 5 minutes

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Prostaglandin analogues for major postpartum haemorrhage

Administration: (Intramuscular)

- > Draw up 250 micrograms (1 mL) in a one mL syringe and administer as a deep intramuscular injection
- > Repeat as required every 15 to 90 minutes
- > **One dose is sufficient in the majority of cases**
- > The total dose of carboprost should not exceed 2 mg (8 doses)

Administration (intramyometrial)

- > **NB: The senior obstetrician who prescribes and administers carboprost via the intramyometrial route is responsible as it is not recommended for intramyometrial use²**

At laparotomy / LSCS:

- > Draw up 250 micrograms in 5 mL of 0.9% sodium chloride¹¹
- > Infiltrate prepared solution (250 micrograms) directly into myometrium using a 21 gauge spinal needle, aspirating intermittently to avoid direct systemic injection
- > Repeat 15 to 90 minutes later if necessary. Avoid cervical injection because of increased risk of direct systemic uptake

Dinoprost (prostaglandin F_{2α})

Introduction

- > Intramyometrial dinoprost is an established **2nd line treatment** for postpartum haemorrhage unresponsive to oxytocic agents along with ongoing bimanual compression and uterine massage⁹
- > Case series show prostaglandin F_{2α} is effective in 88 % of cases refractory to oxytocics¹⁰
- > **This preparation is not suitable for intramuscular injection**
- > Dinoprost has been discontinued worldwide and limited supply may be available via the Special Access Scheme

Pharmacology

- > Prostaglandin F_{2α} (PGF_{2α}) is a potent smooth muscle contractor which is 90 % metabolised on first passage through the lungs
- > A large bolus of PGF_{2α} can overload the lung metabolic pathways and allow unmetabolised PGF_{2α} 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 PGF_{2α} requires senior obstetrician involvement

Contraindications

- > Prostaglandin F_{2α} (PGF_{2α}) is a potent smooth muscle contractor which is 90 % metabolised on first passage through the lungs

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- > A large bolus of $\text{PGF}_{2\alpha}$ can overload the lung metabolic pathways and allow unmetabolised $\text{PGF}_{2\alpha}$ 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 analogues for major postpartum haemorrhage

Prostaglandin F_{2α} (Dinoprost) preparation and administration

Presentation:

- > PGF_{2α} 5 mg in one mL ampoule

Preparation of Solution

- > Dilute (5 mg) 1 mL of PGF_{2α} to 10 mL with sodium chloride 0.9 % to give 0.5 mg PGF_{2α} 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 (Intramyometrial)

At laparotomy / LSCS:

- > 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

After vaginal delivery:

- > Using 22 gauge spinal needle, the medical officer injects 1 mL (0.5 mg) of diluted PGF_{2α} 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

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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

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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

Prostaglandin analogues for major postpartum haemorrhage

Abbreviations

C	Celsius
e.g.	For example
et al.	And others
IV	Intravenous
LSCS	Lower segment caesarean section
mg	Milligram(s)
mL	Millilitre(s)
NSW	New South Wales
%	Percent
PPH	Postpartum haemorrhage
PG	Prostaglandin
®	Registered trademark

Version control and change history

PDS reference: OCE use only

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1.0	03 Sep 2007	17 Jul 2012	Original version
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