South Australian Perinatal Practice Guidelines

Medical induction for 2nd trimester TOP and miscarriages

Medical induction methods in the second trimester

<table>
<tr><td rowspan="6">Induction – no previous uterine surgery</td><td colspan="2">Misoprostol (misoprostol 200 micrograms Cytotec®)
> Misoprostol may be given sublingual or vaginally</td></tr>
<tr><td>Sublingual
> 400 micrograms (i.e. 2 tablets) misoprostol every three hours for a total of 1600 micrograms of misoprostol or a total of 4 doses in 24 hours</td><td>Vaginal
> 400 micrograms misoprostol tablets per vaginam every six hours for a total of four doses in 24 hours</td></tr>
<tr><td colspan="2">Mifepristone and misoprostol
> Single dose 200 mg mifepristone
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> gemeprost 1 mg vaginally every 3 hours to a maximum of five pessaries in 24 hours</td></tr>
<tr><td colspan="2">Syntocinon®
> The high dose infusion regimen may be considered when other methods of induction have failed
(see in PPG ‘Syntocinon® high dose infusion regimen for IUFD’)</td></tr>
<tr><td>Induction – previous uterine surgery</td><td colspan="2">Discuss the dosage / regimen with the obstetrician / consultant if the woman has had previous uterine surgery</td></tr>
</table>

Introduction

- Many women prefer medical rather than surgical termination of pregnancy when it is available and suitable for them (RANZCOG 2009)
- Second trimester medical termination with mifepristone followed by a prostaglandin is effective and is associated with considerably shorter induction to delivery intervals than methods using prostaglandin alone or supplemented by oxytocin infusion (RCOG 2004)

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Medical methods

- Regimens for medical termination of pregnancy in the second trimester may include a combination of:
  - mifepristone (Mifegyne®) and misoprostol (Cytotec®)
  - mifepristone (Mifegyne®) and gemeprost (Cervagem®)

  OR
  - misoprostol (Cytotec®) OR gemeprost (Cervagem®) alone
- The Syntocinon® high dose infusion regimen may be considered when other methods of induction have failed (refer to the PPG 'Syntocinon® high dose infusion regimen for IUFD')

Care of women with a history of uterine surgery

- The method and / or dose of induction agent/s for second trimester induction of labour should take into account the clinical circumstances, availability of preparations and local guidelines and be determined in consultation with the obstetrician / consultant
- Women with a single lower segment scar should be advised that, in general, induction of labour with prostaglandin is safe but not without risk (RCOG 2010)
- Women with two previous LSCS should be advised that, in general, the absolute risk of induction of labour with prostaglandin is only a little higher than for women with a single previous LSCS (RCOG 2010)
- Women with more than two LSCS deliveries or atypical scars should be advised that the safety of induction of labour is unknown (RCOG 2010)

Mifepristone

- In Australia, mifepristone has not been approved for general use by the Therapeutic Goods Administration (TGA). Practitioners may apply for authorised prescriber status (section 19(5) of the Therapeutic Goods Act 1989) or on a case by case basis through the Special Access Scheme (SAS) (RANZCOG 2009)
- The administration of mifepristone must be carried out by the nominated practitioner to the consented patient as specified on the SAS Category B Form (RANZCOG 2009)
- Mifepristone is a steroid derived from norethisterone that acts by blocking the effects of progesterone, a hormone necessary for the continuation of a pregnancy
- Mifepristone is anti-progesterone, which sensitises the myometrium to prostaglandins, increases uterine contractility, and softens and dilates the cervix. It is not sufficient for medical termination of pregnancy when used on its own, but is effective when used synergistically with prostaglandins

Indications

- Mifepristone, in combination with a prostaglandin may be given for:
  - Second trimester genetic termination of pregnancy
  - Intrauterine fetal death (see PPG)

  And
  - Is generally indicated for late second trimester miscarriage
- Ensure informed consent is signed before commencing treatment

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Contraindications

- Confirmed or suspected ectopic pregnancy
- Renal or hepatic impairment
- Chronic adrenal failure
- Severe uncontrolled asthma
- Hereditary porphyria (disorder of enzymes in the haeme biosynthetic pathway that affects the skin, nervous system or both)

Precautions

The following may interact with the action of mifepristone:

- Erythromycin, rifampicin
- Ketoconazole,
- Carbamazepine, Phenytoin, phenobarbitol
- Corticosteroids
- NSAIDs (backup in Stockley's Drug Interactions)
- St John's Wort
- Grapefruit juice

Side effects

- Uterine bleeding and gastrointestinal (nausea, vomiting, diarrhoea)

Mifepristone and prostaglandin regimens

Mifepristone (Mifegyne®) and misoprostol (Cytotec®)

- Give oral mifepristone 200 mg followed 36 to 48 hours later by sublingual misoprostol 400 micrograms every 3 hours to a maximum of 4 doses in 24 hours (RCOG 2004 p. 12)
- Alternatively give oral mifepristone 200 mg followed 36 to 48 hours later by misoprostol 800 micrograms vaginally

Mifepristone (Mifegyne®) and gemeprost (Cervagem®)

- Give oral mifepristone 200 mg followed 36 to 48 hours later by gemeprost 1 mg vaginally every 3 hours to a maximum of five pessaries in 24 hours (RCOG 2004)

Observations

- Perform the following observations before commencing procedure, then every 4 hours (unless otherwise indicated) until prostaglandin is commenced:
  - Temperature
  - Pulse
  - Respirations
  - Uterine activity
  - Vaginal loss
  - Record an accurate fluid balance chart

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Misoprostol (Cytotec®)

- Misoprostol is a synthetic prostaglandin E1 analogue. Serum misoprostol peak levels occur at 34 and 80 minutes respectively for oral and vaginal routes of administration (Hofmeyr & Gülmezoglu, 2003)
- Misoprostol is not approved for use during pregnancy because it causes miscarriage, vaginal bleeding and in continuing pregnancies, fetal malformations including the Mobius sequence (congenital facial paralysis, with or without limb defects) (Alfirevic, 2003)
- Misoprostol is not approved for use in pregnancy by the Australian Therapeutic Goods Administration (TGA). However, the United States (US) FDA has revised their product information to specify that the contraindication to misoprostol in pregnancy applies to pregnant women who are using misoprostol for peptic ulcer disease (ACOG committee opinion, 2003)
- As an abortifacient in the second trimester, the vaginal regimen of misoprostol has shown a success rate of 90 % with a low recourse to surgical intervention for retained products (Carbonell et al. 2003)
- An Australian prospective randomised controlled trial by Dickinson et al., 1998, comparing intravaginal misoprostol 200 micrograms every 6 hours for 4 doses with gemeprost 1 mg every 3 hours for 5 doses, found no difference in induction to delivery interval or side effects apart from an increase in vomiting with misoprostol
- In view of the significant saving and ease of storage associated with misoprostol, Dickinson et al, 1998 have recommended that misoprostol should be the preferred prostaglandin for second trimester termination of pregnancy
- Sublingual administration has a greater bioavailability than oral administration presumably because of the absence of a hepatic first pass effect, and a similar time to peak levels. Time to peak levels is longer after vaginal administration, but the effect may be more sustained after vaginal administration (Muzonzini & Hofmeyr 2004)

Indications

- Second trimester genetic termination of pregnancy
- Second trimester miscarriage
- Intrauterine fetal death (see PPG)
- Ensure informed consent is signed before commencing treatment

Contraindications

- Known sensitivity to misoprostol or other prostaglandin

Advantages

- Inexpensive
- Stored at room temperature
- Few systemic side effects
- Rapidly absorbed orally or vaginally
- Effective in causing uterine contractions

Side effects

Although there are relatively few side effects, the following may occur:

- Pyrexia
- Vomiting

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- Diarrhoea
- Flushing and shivering
- Headache

Administer antiemetics, antipyretics as indicated with medical order

Seek medical review if:

- Temperature > 38˚ Celsius (may be a prostaglandin E effect or an indication of chorioamnionitis)
  - Chorioamnionitis (rising C-Reactive Protein, offensive / purulent vaginal discharge, maternal pulse > 100 bpm, uterine tenderness) requires antibiotic treatment. Give ampicillin 2 g IV initial dose, then 1g IV every 4 hours, gentamicin 5 mg / kg IV daily, metronidazole 500 mg IV every 12 hours, unless allergic to penicillin
  - If allergic to penicillin, give lincomycin 600 mg IV in 100 mL over 1 hour every 8 hours or clindamycin 450 mg IV in 50 – 100 mL over at least 20 minutes until delivery
  - Antipyretics such as Panadol (1 g rectally) can be administered
- Abnormal abdominal pain or other symptoms of uterine rupture
- Dizziness

Precaution

- Bronchospasm and collapse are rare but may occur when prostaglandins are administered to asthmatics

Dosage and administration

- Ensure that informed verbal consent is obtained and documented
- There are three possible routes of misoprostol administration:
  - Oral
  - Sublingual
  - Vaginal
- The first intravaginal misoprostol dose should be administered by a medical officer

Termination for genetic reasons and mid trimester miscarriage

Sublingual (the route usually preferred by women)

- 400 micrograms (200 micrograms x 2 tablets) misoprostol every three hours for a total of 1600 micrograms of misoprostol or a total of 4 doses in 24 hours

Vaginally

- 400 micrograms misoprostol tablets per vaginam every six hours for a total of four doses in 24 hours

Second trimester intrauterine fetal death

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See PPG 'Misoprostol' – Dosage and administration – Before 34^{+0} weeks of gestation

If no products passed after 24 hours

Sublingual and per vaginam

- Consider repeating the same dose regimen or other method of induction. (e.g. intravaginal Cervagem®, extra-amniotic prostaglandins, intravenous oxytocin)
  - **NB**: Intravenous oxytocin should not commence within 4 hours of the last intravaginal dose of misoprostol

* refer to individual hospital midwifery standard

Observations

- Perform the following observations before commencing procedure and hourly thereafter:
  - Temperature
  - Pulse
  - Respirations
  - Uterine activity
  - Vaginal loss
  - Record an accurate fluid balance chart

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ACOG	American College of Obstetrics and Gynecology
bpm	Beats per minute
et al	And others
FDA	Food and Drug Administration (United States)
g	Gram(s)
Int	International
IV	Intravenous
J	Journal
kg	Kilogram
mg	Milligram(s)
mL	Millilitre(s)
NSAIDs	Non steroidal anti-inflammatory drugs
RANZCOG	The Royal Australian and New Zealand College of Obstetricians and Gynaecologists
RCOG	Royal College of Obstetricians and Gynaecologists
SAS	Special access scheme
TGA	Therapeutic Goods Administration (Australian)
US	United States

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Useful references

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Abbreviations

Version control and change history

PDS reference: OCE use only

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1.0	18 Dec 04	19 Mar 07	Original version
2.0	19 Mar 07	20 Sept 11	Reviewed
3.0	20 Sept 11	current	

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