Category: Clinical Guidance Statement

Use of prostaglandins for Induction of Labour (C-Obs 22)

This statement has been updated in response to changes to the Therapeutic Good Administration (TGA) approval of an oral prostaglandin for use in Induction of Labour in Australia. The interim update of the statement provides guidance on induction of labour in term women, approved by the Women's Health Committee, RANZCOG Council and Board.

A list of the Women's Health Committee membership can be found in Appendix A.

Conflict of Interest disclosures were received from all members of this Committee (Appendix C)

Disclaimer: This information is intended to provide general advice to practitioners. This information should not be relied on as a substitute for proper assessment with respect to the particular circumstances of each case and the needs of any patient. This document reflects emerging clinical and scientific advances as of the date issued and is subject to change. The document has been prepared having regard to general circumstances (Appendix D)

First developed by RANZCOG: July 2006
Current version: March 2019 (interim update February 2023)
Review due: March 2024

Objectives:	To provide advice on the use of prostaglandins for induction of labour.
Target audience:	This statement was developed primarily for use by registered health practitioners providing care to women[1] in maternity care.
Background:	The statement was first published in July 2006 and reviewed in March 2019. The most recent interim update of this statement is to provide guidance on this new drug options approved by the TGA for use in induction of labour in term women. The statement draws on earlier evidence-based methodology (i.e. not GRADE methodology), for approval by the Women's Health Committee in March 2023 (Appendix C).
Funding:	The development and review of this statement was funded by RANZCOG.

[1] *RANZCOG currently uses the term 'woman' in its documents to include all individuals needing obstetric and gynaecological healthcare, regardless of their gender identity. The College is firmly committed to inclusion of all individuals needing O&G care, as well as all its members providing care, regardless of their gender identity.*

Contents

2. Purpose and scope

The purpose of this statement is to provide guidance to registered health practitioners providing care to women[1] in maternity care. The statement draws on earlier evidence-based methodology (i.e., NHMRC methodology, that preceded the contemporary approaches to evidence synthesis using GRADE).

An interim partial update to the statement was undertaken in February 2023 to reflect recent additional options approved by the Australian Government Therapeutic Good Administration (TGA) for the Induction of Labour, bringing the advice in line with Aotearoa New Zealand Therapeutic indications for prostaglandins for the induction of labour in term or near-term women.

3. Plain language summary

Some pregnant women are advised to have their baby within a specific time frame, rather than waiting for labour to start naturally. Starting the birth process is called "induction of labour".

Different methods are available to start labour, depending on the reasons for the induction, the woman's previous births, and whether the woman's body has already begun to prepare for labour. Prostaglandins are a type of medication used when the cervix has not softened in preparation for birth. The use of prostaglandins to soften the cervix is often called "cervical ripening". It is usually followed by other methods to start labour, including artificial rupture of membranes ('breaking the waters') and oxytocin (a hormone) given by infusion (drip).

4. Executive summary

When cervical ripening is required, clinicians may choose between mechanical methods and prostaglandins.[1,2] The most appropriate method for cervical ripening is influenced by several factors, including patient characteristics, model of obstetric care and patient preference.

This document discusses the use of prostaglandins for the induction of labour in Australia and Aotearoa New Zealand (New Zealand).

5. Table of recommendations

Recommendation 1	Grade
Prostaglandins (*dinoprostone* or low dose oral *misoprostol*) are appropriate methods of induction for many women with a term pregnancy when cervical ripening is required.	Grade A
Recommendation 2	**Grade**
All maternity units that use prostaglandins for cervical ripening prior to induction of labour should have protocols in place that define: • Dose regimen(s), including time between doses; • Fetal surveillance recommendations; • Duration and place of observation; • Management of subsequent labour including oxytocin regimen; and • Diagnosis and management of uterine hyperstimulation	Consensus-based recommendation

Recommendation 3	Grade
The chosen method of induction should take into account : • Favourability of the cervix (cervical or Bishop score); • Parity of the woman; • Indication for induction of labour and likelihood of fetal maternal compromise with the onset of labour; • The woman's preferences • Previous uterine surgery and • Other clinical circumstance	Consensus-based recommendation

6. Introduction

Rationale

There are many different prostaglandin preparations and regimens for induction of labour. *Dinoprostone* has traditionally been the most common prostaglandin used in Australia. Misoprostol is an approved medicine in New Zealand and has been widely used. It is not approved for use in childbirth, however, it can be regarded and used as a supported indication.[3]

The Pharmaceutical Society of New Zealand states that, while it is recognised that cervical ripening, in the setting of IOL in childbirth has not been listed as a registered indication for misoprostol use in New Zealand, the use of misoprostol in childbirth has been widely researched internationally and endorsed by the WHO.

In Australia, the recent introduction of a TGA approved 25mcg oral (tablet) dose of misoprostol allows a wider range of options for clinicians and women.[4]

A number of metanalyses have compared the use of low dose oral misoprostol with mechanical methods of induction and vaginal *dinoprostone*. Each published review has a slightly different emphasis and conclusion, due to different methodology and inclusion criteria, but low dose oral misoprostol is consistently ranked as having similar or better outcomes, in terms of hyperstimulation, time to delivery, rate of vaginal delivery and costs, in comparisons to other methods.[5,6,7,8]

Australian and international data suggests that women prefer oral medication to vaginal medication or mechanical means of induction in the setting of IOL, [9,10] however when given a choice of induction method, satisfaction is the same across methods.[11]

Oral *misoprostol* is used in a more frequent dosing schedule than vaginal prostaglandins, and so may have implications for staffing. Oral administration may have the added benefit of fewer vaginal examinations.

Recommendation 1	Grade
Prostaglandins (*dinoprostone* or low dose oral *misoprostol*) are appropriate methods of induction for many women with a term pregnancy when cervical ripening is required.	Grade A

Indications

Term Induction of labour

Prostaglandins are appropriate for term induction of labour in scenarios in which vaginal delivery is planned. Where there is concern for fetal compromise, mechanical methods of cervical ripening may be preferred, because of the lower rate of uterine hyperstimulation documented in some reviews.

FDIU[2]

Misoprostol is widely used in Australia and New Zealand for management of midtrimester and third trimester fetal death in utero and termination of pregnancy. Dosing for this indication is commonly based on the International Federation of Gynaecology and Obstetrics (FIGO) guidance and should take into account gestation, previous caesarean section and the use of *mifepristone*.[12,13]

PPROM

Please refer to the RANZCOG statement: Term Prelabour Rupture of Membranes (Term PROM) (C Obs 36).

Previous CS or uterine surgery

In women with a history of a prior caesarean section, prostaglandin induction of labour has been associated with rates of uterine rupture ranging from 1.4 to 2.45%.[14,15] Please refer to the RANZCOG Statement: Birth after previous caesarean section (C-Obs 38). Prostaglandins are generally not recommended with previous caesarean section with a live fetus, but may be used in the setting of fetal death or termination of pregnancy.

For women with other uterine surgery, e.g., myomectomy, care should be individualised.

Precautions

Syntocinon (oxytocin) should not be used for 4-6 hours after the last prostaglandin dose. [16]

7. Governance

All units offering prostaglandin induction of labour should inform women about the risks and benefits of this method of induction. Units should have protocols in place including dosing regimens[3], appropriate fetal surveillance following prostaglandin administration and prevention and management of complications including uterine hyperstimulation.[6]

Recommendation 2	Grade
All maternity units that use prostaglandins for cervical ripening prior to induction of labour should have protocols in place that define: • Dose regimen(s), including time between doses; • Fetal surveillance recommendations; • Duration and place of observation; • Management of subsequent labour including oxytocin regimen; and • Diagnosis and management of uterine hyperstimulation	Consensus-based recommendation

[2] Fetal death in utero

[3] Oral misoprostol 25 microgram in solution two-hourly is widely used internationally and is recommended by the World Health Organization (WHO).

Recommendation 3	Grade
The chosen method of induction should take into account : • Favourability of the cervix (cervical or Bishop score); • Parity of the woman; • Indication for induction of labour and likelihood of fetal maternal compromise with the onset of labour; • The woman's preferences • Previous uterine surgery and • Other clinical circumstance	Consensus-based recommendation

An analysis of cost-effectiveness was not undertaken.

8. Legal and ethical implications

9. Recommendations for future research

This Clinical Guidance Statement identified a gap in available, current and accessible research on the following topics:

Association between induction of labour is not associated and an increased risk of caesarean section.

10. References

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16. Australian Commission for Safety and Quality in Health Care: NPS Medicinewise. Consumer Medicine Information (online): Syntocinon. [Available at: https://www.nps.org.au/medicine-finder/syntocinon-solution-for-injection#full-pi]

11. Links to relevant College Statements

The use of misoprostol in obstetrics and gynaecology (C-Obs 12)

RANZCOG statement: Term Prelabour Rupture of Membranes (Term PROM) (C Obs 36).

RANZCOG Statement: Birth after previous caesarean section (C-Obs 38).

Evidence-based Medicine, Obstetrics and Gynaecology (C-Gen 15)

12. Links to relevant Clinical Guidelines

Aotearoa New Zealand College of Midwives. Induction of Labour in Aotearoa New Zealand - A clinical practice guideline (2019). Available at: https://www.midwife.org.nz/wp-content/uploads/2020/02/induction-of-labour-in-Aotearoa-New-Zealand-guideline-2019.pdf

13. Consumer resources

RANZCOG Patient Information Pamphlet: Induction of Labour. Available at: https://ranzcog.edu.au/wp-content/uploads/2022/06/Induction-labour-pamphlet.pdf

14. Links to relevant ATMs and learning modules

FRANZCOG Training Program Handbook. Basic Obstetric Skills Workshop (mandatory workshop). Available at: https://ranzcog.edu.au/wp-content/uploads/2022/05/FRANZCOG-Training-Program-Handbook_After-1st-December-2013.pdf

Appendices

Appendix A: Women's Health Committee Membership

Name	Position on Committee
Dr Scott White	Chair
Dr Gillian Gibson	Deputy Chair, Gynaecology
Dr Anna Clare	Deputy Chair, Obstetrics
Associate Professor Amanda Henry	Member and Councillor
Dr Samantha Scherman	Member and Councillor
Dr Marilla Druitt	Member and Councillor
Dr Frank O'Keeffe	Member and Councillor
Dr Kasia Siwicki	Member and Councillor
Dr Jessica Caudwell-Hall	Member and Councillor
Dr Sue Belgrave	Member and Councillor
Dr Marilyn Clarke	Aboriginal and Torres Strait Islander Representative
Professor Kirsten Black	SRHSIG Chair
Dr Nisha Khot	Member and SIMG Representative
Dr Judith Gardiner	Diplomate Representative
Dr Angela Brown	Midwifery Representative, Australia
Ms Adrienne Priday	Midwifery Representative, New Zealand
Ms Leigh Toomey	Community Representative
Dr Rania Abdou	Trainee Representative
Dr Philip Suisted	Māori Representative
Prof Caroline De Costa	Co-opted member (ANZJOG member)
Dr Steve Resnick	Co-opted member

RANZCOG wishes to acknowledge the significant contribution of A/Professor Alexis Shub in conducting the interim update of this statement to provide guidance on new drug options approved by the Australian Government Therapeutic Good Administration (TGA) for use in induction of labour.

Appendix C: Overview of the development and review process for this statement

i. Declaration of interest process and management

Declaring interests is essential in order to prevent any potential conflict between the private interests of members, and their duties as part of RANZCOG Women's Health Committee or working groups.

A declaration of interest form specific to guidelines and statements (approved by the RANZCOG Board in September 2012). All members of the Statement Development Panels and Women's Health Committee were required to declare their relevant interests in writing on this form prior to participating in the review of this statement.

Members were required to update their information as soon as they become aware of any changes to their interests and there was also a standing agenda item at each meeting where declarations of interest were called for and recorded as part of the meeting minutes.

There were no significant real or perceived conflicts of interest that required management during the process of updating this statement.

ii. Steps in developing and updating this statement

This statement was developed in July 2006 by the RANZCOG Women's Health Committee, and an update published in March 2019. It was most recently reviewed by the Women's Health Committee in February 2023 in response to changes to TGA recommendations for new drug options approved for use in Induction of Labour. The Women's Health Committee carried out the following steps in reviewing this statement:

- Declarations of interest were sought from all members prior to reviewing this statement.
- An interim review of review of meta-analyses and systematic reviews was undertaken in lieu of a full review of all published evidence.
- At the February 2023 meeting of the Women's Health Committee, the existing recommendations tables were reviewed and updated (where appropriate) based on the available body of evidence and clinical expertise.

RANZCOG statements are developed according to the standards of the Australian National Health and Medical Research Council (NHMRC), Levels of Evidence and Grades of Recommendations for Developers of Guidelines. Where no robust evidence was available but there was sufficient consensus within the Women's Health Committee, consensus-based recommendations were developed or existing ones updated and are identifiable as such. Consensus-based recommendations were agreed to by the entire committee. Good Practice Notes are highlighted throughout and provide practical guidance to facilitate implementation. These were also developed through consensus of the entire committee.

Recommendation category		Description
Evidence-based	A	Body of evidence can be trusted to guide practice
	B	Body of evidence can be trusted to guide practice in most situations
	C	Body of evidence provides some support for recommendation(s) but care should be taken in its application
	D	The body of evidence is weak and the recommendation must be applied with caution
Consensus-based		Recommendation based on clinical opinion and expertise as insufficient evidence available
Good Practice Note		Practical advice and information based on clinical opinion and expertise

Appendix D: Full Disclaimer

Purpose

This Statement has been developed to provide general advice to practitioners about women's health issues concerning Induction of Labour and should not be relied on as a substitute for proper assessment with respect to the particular circumstances of each case and the needs of any person. It is the responsibility of each practitioner to have regard to the particular circumstances of each case. Clinical management should be responsive to the needs of the individual person and the particular circumstances of each case.

Quality of information

The information available in this statement is intended as a guide and provided for information purposes only. The information is based on the Australian/New Zealand context using the best available evidence and information at the time of preparation. While the Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) has endeavoured to ensure that information is accurate and current at the time of preparation, it takes no responsibility for matters arising from changed circumstances or information or material that may have become subsequently available. The use of this information is entirely at your own risk and responsibility.

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Version	Date of Version	Pages revised / Brief Explanation of Revision
v1.0	July / 2006	The statement was first published, approved by the RANZCOG Women's Health Committee/Board.
V2.0	March / 2019	Routine review of the statement, approved by the RANZCOG Women's Health Committee/Board
V2.1	February / 2023	Interim update of the statement in response to new drug options approved by the TGA for use in induction of labour.

Policy Version:	Version 2.1
Policy Owner:	Women's Health Committee
Policy Approved by:	RANZCOG Council/Board
Review of Policy:	February / 2023