

Three Unique Case Scenarios: When & How to Use Misoprostol for Induction of Labor

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28 yo G1 39w6d GA

Indication for IOL: GDM diet control

Bishop score <7

Unable to tolerate speculum examination

Social Hx: Developmental delay
Sexual trauma & assault

28 yo G1 34w1d GA

Indication for IOL: Severe PET
Elevated BP
Pulmonary edema/CHF/AKI
SGA fetus

Preterm GA

Need for fluid restriction in labor

Bishop score <3

32 yo G2P1

39w2d GA

Indication for IOL: Term ROM
GBS+

Morbid obesity

Unable to visualize or palpate cervix on exam

PMHx: BMI 54

Cervical Ripening

A. Pharmacologic

- a. PGE2 vaginal gel
- b. PGE2 vaginal insert
- c. **PGE1 oral, vaginal**

B. Mechanical

- a. Balloon
- b. Osmotic dilators

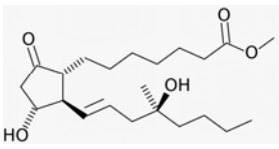
Uterine Activity

A. Oxytocin infusion

- a. low dose
- b. accelerate/high dose

B. **PGE1 oral, vaginal**

PGE1 “Misoprostol”



- Extensive absorption across mucosal surfaces
- ½ life 20-40 min
- Metabolized by liver, excreted in urine
- Binds to membrane EP 2,3,4 receptors (cx, uterus)
- Side effects: GI, fever
- No toxic effect: exaggerated side effects
- WHO Essential Medication
- Available on Black Market

Uses

1. Ulcer prevention
2. Management of PPH
3. Early pregnancy loss
4. TOP (+/- mifepristone) across all trimesters
5. Facilitate cervical dilation
6. **Induction of labor**

↓


Vaginal Birth

? Why Use Misoprostol for Cervical Ripening

ORAL Misoprostol compared with PGE2 gel

		Cervix Bishop score		
		≤3		
Variable	OMS (n = 1724)	Dinoprostone (n = 1769)	P value	
Vaginal delivery	1456 (84.5)	1286 (72.7)	0.006 ^b	<p style="color: red; font-weight: bold;">Higher rate of vaginal birth</p> <p style="color: red; font-weight: bold;">Lower rate of fetal distress, C/S</p> <p style="font-weight: bold;">No difference if Bishop score >4</p>
Cesarean delivery	268 (15.5)	403 (27.3)	<0.001 ^b	
Fetal distress	97 (5.6)	188 (10.6)	0.008 ^b	
Labor process block	151 (8.8)	196 (11.1)	0.183 ^b	
Failed induction	20 (1.2)	19 (1.1)	0.729 ^c	

Wang et al, In J OB Gyn, 2021



Trusted evidence. Informed decisions. Better health.

Cochrane Database of Systematic Reviews | Review - Intervention

Vaginal misoprostol for cervical ripening and induction of labour

G Justus Hofmeyr, A Metin Gülmezoglu, Cynthia Pileggi Authors' declarations of interest
 Version published: 06 October 2010 Version history
<https://doi.org/10.1002/14651858.CD000941.pub2>

121 trials

VAGINAL Misoprostol (25mcg q4h)

Compared with PGE2, Oxytocin

Higher rate of vaginal birth

Greater uterine hyperstimulation

USE ORAL Misoprostol for ripening

? Why Use Misoprostol for Cervical Ripening

Foley™ compared with ORAL misoprostol (n= 2815 participants)

Outcome	RCT's (n)	Women (n)	Risk ratio (95% CI)	
Cesarean section	4	2815	1.22 (1.08–1.38)	Higher rate of C/S Due to FTP
Cesarean section for failure to progress	4	2815	1.50 (1.25–1.79)	
Cesarean section for fetal distress	4	2815	0.97 (0.72–1.30)	
Spontaneous vaginal birth	4	2815	0.94 (0.86–1.03)	
Instrumental vaginal birth	4	2815	0.73 (0.57–0.92)	
Maternal temperature ≥ 38°C	2	2447	1.04 (0.78–1.38)	[
Maternal antibiotics given	2	2033	1.00 (0.97–1.03)	
Clinically diagnosed maternal infection	3	2635	0.85 (0.54–1.33)	
Change in induction method from that allocated	3	2627	1.87 (1.11–3.16)	Higher rate of changing IOL method Higher rate of using oxytocin
Use of oxytocin	4	2815	1.27 (1.06–1.53)	
Uterine hyperstimulation	4	2815	1.03 (0.67–1.58)	
Maternal use of analgesia during labor	3	2635	1.03 (0.97–1.09)	
5-min Apgar score < 7	3	2627	0.79 (0.24–2.63)]

No difference in maternal or neonatal adverse effect

ORAL misoprostol was more effective than Foley™

Kemper et al, Ultrasound Obstet Gynecol, 2021

? Can ORAL Misoprostol be used with Foley™ for cervical ripening

Labor induction with combined low-dose oral misoprostol and Foley catheter vs oral misoprostol alone at term gestation—a randomized study

ORAL PGE1 25µg q 4h

VS

ORAL PGE1 25µg q4h + Foley™ catheter

	Foley + PGE1	PGE1	
Successful outcome (delivery within 24 h)	76 (87.4%)	57 (75.0%)	.02 ← Higher rates of vaginal birth within 24h
Vaginal delivery after 24 h of induction	11 (12.6%)	19 (25.0%)	.49
Total vaginal delivery	87	76	.16
LSCD	13	24	.04 ← Lower rates of C/S
Fetal distress	3 (23%)	9 (37.5%)	
Failed progress of labor	10 (77%)	15 (62.5%)	
Instrumental delivery	3	2	.56

LSCD, lower-segment cesarean delivery.

* No difference in the rates of adverse maternal & neonatal events

Combination of Foley™ and ORAL misoprostol is safe & effective

Anjali et al, AJOG, 2022

? Why use Misoprostol for Labor Induction



Cochrane Database of Systematic Reviews | Review - Intervention

Low-dose oral misoprostol for induction of labour

Robbie S Kerr, Nimisha Kumar, Myfanwy J Williams, Anna Cuthbert, Nasreen Aflaifel, David M Haas, Andrew D Weeks
 Authors' declarations of interest

Version published: 22 June 2021 | Version history

- 61 Trials**
20 026 Participants
- Viable fetus
 - Third trimester
 - ORAL PGE1 $\leq 50 \mu\text{g}$

ORAL PGE1	Rate of C/S	Uterine Hyperstimulation With FHR change	Maternal Adverse Effect	Neonatal Adverse Effect
Vaginal PGE2	Lower	Lower	No difference	No difference
Vaginal PGE1	No difference	Lower	No difference	No difference
IV oxytocin	Lower	No difference	No difference	No difference
Mechanical Methods	Lower	No difference	No difference	No difference

ORAL Misoprostol is safe and effective for labor induction

More studies to determine optimal dosing regime

Oral Misoprostol for Induction of Labour in Term PROM: A Systematic Review

Padayachee L et al, JOGC 2020

Goal: to assess the safety and efficacy of ORAL misoprostol in cases of term PROM

12 RCT
1489 participants

Compared Oral PGE1 with Vaginal PGE2, Oxytocin IV infusion, Foley™ } **No differences:**
Mode of delivery
Uterine Hyperstimulation

No induction method has demonstrated superiority over any another method for:

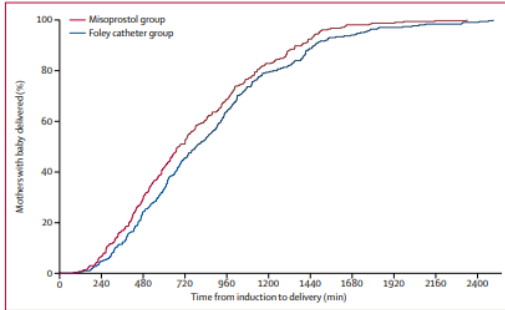
- reducing rates of intrauterine or neonatal infection
- cesarean delivery
- shortening the rupture-to-delivery intervals

* regardless of parity or the Bishop score.

Foley catheterisation versus oral misoprostol for induction of labour in hypertensive women in India (INFORM): a multicentre, open-label, randomised controlled trial

Shuchita Mundie, Hillary Bracken, Vaishali Khedekar, Jayashree Mulik, Brian Faragher, Thomas Easterling, Simon Leigh, Paul Granby, Alan Haycox, Mark A Turner, Zarko Alfrevic, Beverly Winikoff, Andrew D Weeks

India
 RCT
 602 participant
 Dx hypertension/PET needing delivery



- PGE1 25-50 µg q 2h x 12 doses, then oxytocin if not delivered
- Foley x12h then ARM + oxytocin

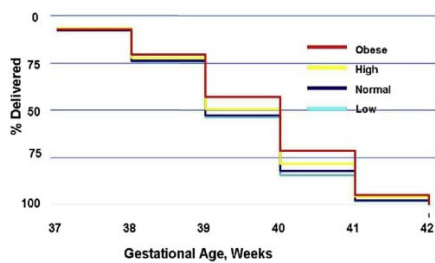
- **More deliveries within 24h**
- **Lower rate of C/S: 41.1% v 50.3%**
- **Less exposure to oxytocin**
- **No difference in maternal & neonatal outcomes**

PGE1 more effective than Foley+ Oxytocin

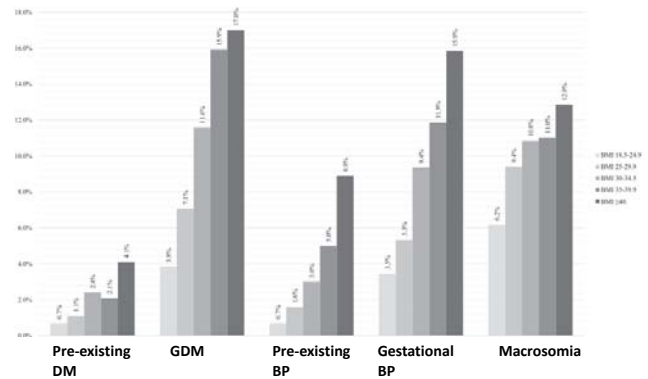
ADV: less exposure to IV fluid
 less exposure to oxytocin
 resource poor country: no IV pumps

Lancet 2017

Increased rate of prolonged pregnancy



Increased rate of indications for IOL



? What is the optimal mode of labor induction in patients with obesity

? Role for Misoprostol with Labor Induction & Obesity

** very little data: small sample sizes,

Foley™ + Vaginal PGE1 v Vaginal PGE1 alone

No difference in C/S rates

Vaginal PGE1 v Oral PGE1

Faster time to Bishop score >3 and to delivery

Foley™ followed by Oral PGE1 v Oral PGE1

Lower rate of C/S

Kehl et al, Eur J OB GYN Repro Bio 2019
Viteri et al, Am J Perinatol, 2020
Soni et, J Mat Fet Neonat Med, 2020

** Focus cervical ripening & NOT labor induction

** Misoprostol total dose increases with BMI

** Oxytocin total dose requires increases with BMI (less responsiveness)

Hypothesis:

Combined cervical ripening decreases C/S rates in all comers inc. increased BMI

Oral PGE1 lower C/S for labor induction in all comers

Oral PGE1 avoids prolonged oxytocin exposure, IV fluids, use of IUPC

Oral PGE1 + Foley™ may be an optimized mode of labor induction in patients with obesity

? How to Use Misoprostol for Labor Induction: Practice Guidelines



1. Suitable for all GA & all indications for IOL
2. Contra-indications: full thickness uterine scar
grand multiparity
3. Based on dosing, not suitable for ambulatory IOL
4. Once regular uterine activity established: CEFM and 1:1 nursing
5. Limits: 8h after vaginal PGE2 gel or after PGE2 insert removed
Wait 2h after last dose before starting oxytocin
6. Vaginal exams based on uterine activity and duration of treatment
7. Reassess after 24h with no delivery and/or progress: no indication change method of IOL sooner

? How to Use Misoprostol for Labor Induction: Protocol



1. Prior to each dose, initiate 20 min NST & maternal vital signs
2. Before the dose: complete **misoprostol safety checklist** with all **YES** answers to proceed with dose
 - Is the 20 minute fetal heart rate strip normal prior to the dose?*
 - Is the patient experiencing less than or equal to 5 contractions in 10 minutes averaged over 30 minutes?*
 - Is there an ABSENCE of continuous pain?*
 - Are the maternal vital signs within normal range?*

3. **Dosing:** 25-50 µg PO (start with 50 µg)
q 2h-4h-6h
based on MD discretion, uterine activity
continue until delivery (including second stage)

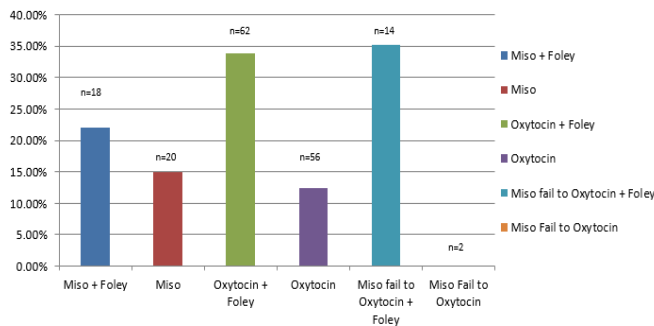
PGE1	Onset of action	Duration of Action
Oral	8 min	2h * <small>first pass metabolism</small>
Vaginal	20 min	4h
Rectal	100 min	4h

4. After each dose, NST for 1 hour until regular uterine activity
5. Once established uterine activity (> 2/10min): initiate CEFM, insert IV, maternal vital signs as per labor protocol
6. Uterine tachysystole +/- change in FHR pattern: Rx nitro spray sublingual
7. Rx maternal temp > 38°C with acetaminophen
8. ARM & vaginal exams at discretion of MD/RM

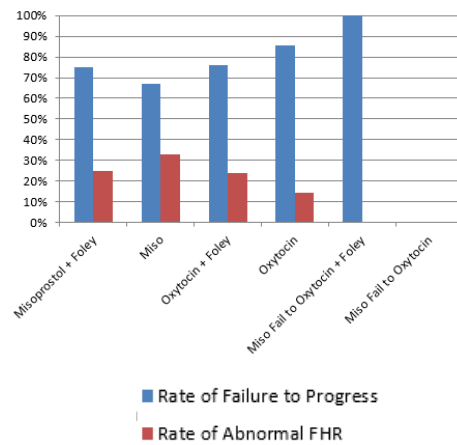
Canadian Setting Quality Assurance Data: First month in use (2019) 172 IOL



Rate of C/S



Indications for C/S



- No unexpected:
 - Admissions to NICU
 - Apgar score <7 at 5min
 - Adverse maternal effect

28 yo G1 39w6d GA

Indication for IOL: GDM diet control
BMI 38

Social Hx: Developmental delay
Sexual trauma & assault

1. Attempt to place Foley- failed to insert, able to perform digital exam with nitrous: Cx fingertip
2. Started PGE1 protocol
 - 50 µg q 2h
 - Uterine activity after 2 doses- placed epidural for pain management & to tolerate vaginal exam
 - ARM at 3cm after 3 doses
 - FD after 6 doses
 - Vaginal birth: 23h post first dose

Cervical Ripening

- A. Pharmacologic
 - a. PGE2 vaginal gel
 - b. PGE2 vaginal insert
 - c. PGE1 oral, vaginal
- B. Mechanical
 - a. Balloon
 - b. Osmotic dilators

Uterine Activity

- A. Oxytocin infusion
 - a. low dose
 - b. accelerate/high dose
- B. PGE1 oral, vaginal

Oral Misoprostol compared with PGs:

Higher rate of vaginal birth
Lower rate of fetal distress, C/S

Oral Misoprostol compared to Foley™

Lower rate of C/S

Oral Misoprostol with Foley™:

Higher rates of vaginal birth in 24h
Lower rates of C/S

Oral Misoprostol compared with oxytocin:

Lower rates of C/S

Oral Misoprostol compared with PGs:

Low rate uterine hyperstimulation
Lower rate of C/S (PGE2)

Vaginal Birth

Advantages of Oral PGE1	Disadvantages of Oral PGE1
<ul style="list-style-type: none"> • Any indication, any gestational age • Any Bishop score/unknown Cx exam • Unripe cx: can be used with Foley™ • No toxic maternal side effect • No risk associated with prolonged exposure • Not a High Alert Medication (ISMP Canada) • No increased risk of uterine hyperstimulation • No increased risk of adverse maternal/neonatal effect • Use with oxytocin allergy • Use with patients on fluid restriction <ul style="list-style-type: none"> - PET, Cardiac Dx, Renal Dx • Low cost (resource restricted settings) • Stable at room temperature • Easy to administer, requires less equipment • CEFM not required until uterine activity • Avoids vaginal / speculum exam • Allows for mobility on labor • Alternative to oxytocin use/failed IOL 	<ul style="list-style-type: none"> • Q2-4h dosing: difficult to use as outpatient • No standardized dosing regime yet established • Long half life • More challenging to reverse uterine hyperstimulation • Can not use with uterine scar (risk of rupture), grand multiparity • Preparing the dose: <ul style="list-style-type: none"> - oral solution (100µg in 20cc H2O, 5µg/ml- drink 10cc) - compound pharmacy <div data-bbox="979 720 1245 846" style="border: 1px solid black; padding: 5px; margin: 10px auto; width: fit-content;"> <p style="text-align: center; margin: 0;"> Easy & Pragmatic to Use Less Resource Utilization Safe & Effective Special Populations </p> </div>

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