Misoprostol Induction of Labour

Dr. Michelle Jacobson MD MHSc FRCSC NCMP
Assistant Professor, Department of OBGYN
University of Toronto

Disclosures

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Objectives

- Review the indications, pharmacokinetics, and physiology of misoprostol
- Analyze the evidence for misoprostol for INDUCTION and ongoing labour management (not cervical ripening)
- Discuss special circumstances: TOLAC, terminations/IUFD versus term labor management
- Present a sample protocol for the use of misoprostol for the induction and management of labor

Misoprostol

- Synthetic prostaglandin E_1 analogue
- Marketed as an oral preparation used to prevent and treat gastroduodenal damage induced by nonsteroidal anti-inflammatory drugs (NSAIDs)
- Off-label use for a variety of OBGYN purposes
  - medication abortion, medical management of miscarriage, induction of labor, cervical ripening before surgical procedures, and the treatment of postpartum hemorrhage
- Although misoprostol is not approved by the FDA for these indications, in 2002, pregnancy was removed from the label as an absolute contraindication to misoprostol use.
- Low cost, long shelf life, lack of need for refrigeration, and worldwide availability

Misoprostol in Canada

Recommendations	Strength of Evidence and Recommendations
SOGC, 2013[1]	
Misoprostol can be considered a safe and effective agent for labour induction for inpatients with intact membranes.	Quality of evidence: I (high) Evidence obtained from at least one properly randomized controlled trial. Recommendation class: A (strong) There is good evidence to recommend the clinical preventive action.
Misoprostol should not be used for vaginal birth in patients with previous Caesarean section due to the increased risk of uterine rupture.	Quality of evidence: II-3 (low) Evidence obtained from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments could also be included in this category Recommendation class: D (moderate) There is good evidence to recommend the clinical preventive action.
Oxytocin should be started no earlier than 4 hours after the last dose of misoprostol.	Quality of evidence: III (low) Expert opinion. Recommendation class: B (weak) There is fair evidence to recommend the clinical preventive action.

- It is approved in Canada for the termination of intrauterine pregnancy with a gestational age of 63 days or less, in combination with mifepristone.

SOGC 2013 IOL Guidelines

MISOPROSTOL

- Is more effective than PGE2 to achieve vaginal delivery
- results in less epidural use
- more uterine tachysystole.
- PGE1 and PGE2 both reduce CS rates in an unfavourable cervix
- The oral and vaginal routes have a similar reduction of CS rates
- The oral route needs more oxytocin stimulation but the vaginal route will have more tachysystole.
- The lower vaginal dose (25 mcg) tends to need more oxytocin stimulation and the higher vaginal dose (≥ 50 mcg) tends to have more uterine tachysystole.

Dosing of misoprotol:

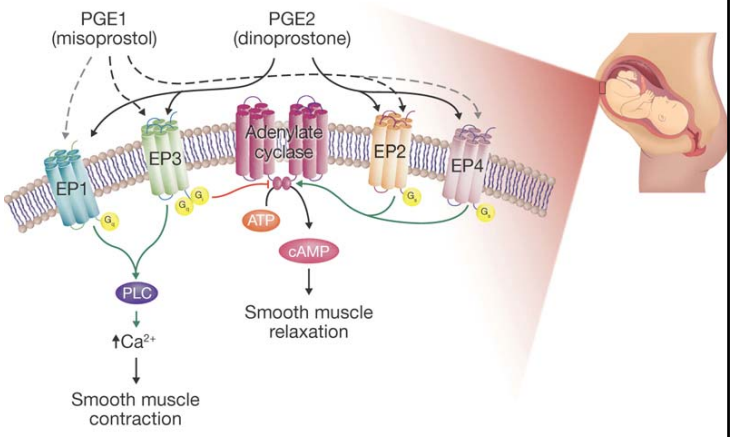
Give 50 mcg orally with a drink of water (ensure that it is swallowed quickly to avoid sublingual absorption) or give 25 mcg vaginally.

Repeat every 4 hours as long as contractions are absent or non-painful.

Oxytocin can only be used 4 hours after the last dose

Physiology of Misoprostol

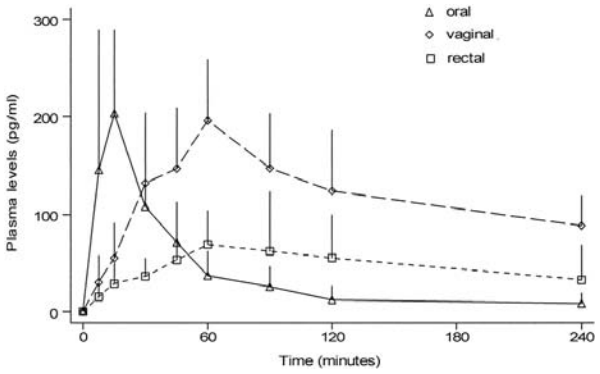
- There are four subtypes of the E prostanoid (EP1–EP4) receptor; in general, EP1 and EP3 mediate contractility, and EP2 and EP4 mediate relaxation of the myometrium
- Prostaglandins may bind to multiple EP receptors, and with different affinities, resulting in effects that reflect a combination of the EP receptor activities.
- The presence of prostaglandin receptors EP1 through EP4 on uterine smooth muscle cells has been confirmed, and their role in labor has been well documented



Pierce 2018

Pharmacokinetics

- Vaginal misoprostol is associated with slower absorption, lower peak plasma levels, and slower clearance, similar to an extended-release preparation
- Vaginal misoprostol is also associated with a greater overall exposure to the drug and greater effects on the cervix and uterus.
- There is no clinically significant difference between vaginal misoprostol that is administered dry and vaginal misoprostol moistened with water, saline, or acetic
- Oral dose had a significantly lower time interval to reach peak concentration levels acid



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Pharmacokinetics of Dosing for Induction

Table 1. *Prostaglandins Used for Cervical Ripening and Induction of Labor*

Drug Name Generic (Brand)	Dose	Route	Onset of Action (min)	Peak Plasma Level (min)	Plasma half-life (min)	Duration of Action (h)	Mean Time To Sustained UA min	Clinical Considerations
Prostaglandin E_1								
Misoprostol (Cytotec)	25-50 mcg	Oral tablet	12 ± 3	20-30	20-40	2	90	Lower doses associated with less uterine tachysystole but longer time to vaginal birth. EFM and UA monitoring 20-30 min prior to placement and continuously after recommended.
Misoprostol (Cytotec)	25-50 mcg	Vaginal posterior fornix tablet	20.9 ± 5.3	60-80	60	4.5 to 5	106	EFM and UA monitoring 30 min prior to placement and after for 2-4 h. Repeat every 3-6 h for maximum of 8 doses. Contraindicated with uterine scar.

Yount 2018

Oral Misoprostol (Cytotec)

- Low cost
- Noninvasive
- Stable at room temperature
- Short time to effectiveness—peaks rapidly then declines by 2 hours
- Bioavailability equivalent to vaginal misoprostol (when oral dose is double the vaginal dose)
- Bioavailability reduced by high-fat meal
- More accurate dosing than vaginal administration
- Less uterine hyperstimulation with FHR changes compared with vaginal misoprostol
- 25 to 50 mcg safe for IOL and cervical ripening in term pregnancies
- Similar in effectiveness and outcomes to vaginal route and better than other induction methods
- Better 5-minute Apgar scores than other methods/routes
- Lower cesarean rates than other methods/routes
- Cochrane Collaboration states oral route is preferable to vaginal route
- Future research needed to determine proper dose for safety

Vaginal Misoprostol (Cytotec)

- Low cost
- Stable at room temperature
- More sustained plasma levels than oral route (bypasses first-pass effect) with longer exposure
- Longer onset of action then oral route
- More effective for cervical ripening and IOL than oxytocin or dinoprostone
- Fewer failures of birth within 24 hours of administration, less epidural use, and less oxytocin use than dinoprostone or oxytocin
- More uterine hyperstimulation and meconium-stained fluid compared with other vaginal induction methods
- Slow or erratic absorption can occur
- May result in inaccurate dosing
- American College of Obstetricians and Gynecologists recommends 25 mcg every 3 to 6 hours, ideally every 4 hours

Yount 2018

2014 Cochrane Review - Oral misoprostol for induction of labour

- When comparing oral misoprostol with placebo (1109 women)
  - Oral misoprostol were more likely to give birth vaginally within 24 hours (risk ratio (RR) 0.16, 95% confidence interval (CI) 0.05 to 0.49)
  - Less likely to undergo caesarean birth (RR 0.72, 95% CI 0.54 to 0.95)
  - Differences in 'uterine hyperstimulation with fetal heart rate changes' were compatible with no effect (RR 2.71, 95% CI 0.84 to 8.68)
- When comparing oral misoprostol with intravenous oxytocin (1282 women)
  - No differences in the frequency of vaginal birth within 24 hours (RR 0.79, 95% CI 0.59 to 1.05)
  - No difference in uterine hyperstimulation with fetal heart rate changes (RR 1.30, 95% CI 0.43 to 3.91).
  - Fewer caesarean births with oral misoprostol (RR 0.77, 95% CI 0.60 to 0.98)
- When comparing oral misoprostol with vaginal misoprostol (6417 women)
  - No difference in the frequency of vaginal birth within 24 hours (RR 1.08, 95% CI 0.86 to 1.36)
  - No difference in uterine hyperstimulation with fetal heart rate changes (RR 0.71, 95% CI 0.47 to 1.08)
  - No difference in caesarean birth (RR 0.93, 95% CI 0.81 to 1.07)
- The incidence of serious neonatal or maternal morbidity or death was rare and no meaningful results were available for any of the comparisons

Cochrane Review Conclusions

- **Authors' conclusions**
  - Oral misoprostol as an induction agent is effective at achieving vaginal birth. It is more effective than placebo, as effective as vaginal misoprostol and vaginal dinoprostone, and results in fewer caesarean sections than oxytocin alone.
- If using oral misoprostol, the evidence suggests that the dose should be 20 to 25 mcg in solution.

Should misoprostol be used orally or vaginally?

Cochrane review –

- The only consistent findings between oral and vaginal miso were:
  - a reduction in low Apgar score at five minutes in those given oral misoprostol
  - lower rates of postpartum haemorrhage
  - an increase in meconium-stained liquor
  - increased satisfaction with the oral route
- oral route may result in improved clinical outcomes over the vaginal route.
- oral route should be preferred over the vaginal route

Vaginal delivery within 24h

Main Study Findings			Authors' Conclusion
Alfirevic et al., 2016[12]			
Failure to achieve VD within 24 hours compared to placebo (n = 28,845) An OR less than 1 favors the intervention.			*"The active interventions most likely to achieve VD* [vaginal delivery] *within 24 hours were i.v. oxytocin with amniotomy, misoprosotol (vaginal tablets – high and low dose; pessary – sustained release; low-dose oral solution; and buccal/sublingual misoprotol) closely followed by vaginal administration of PGE2 (pessary – normal release). It should be stressed that the rankings have wide CrIs for all of the above methods, indicating considerable uncertainty." p.105*
Intervention vs. Placebo	**NMA OR**	**NMA 95% CrI**	
Oxytocin IV with amniotomy	0.05	0.07 to 0.32	
Misoprostol vaginal 50 mcg or more	0.09	0.06 to 0.24	
Misoprostol oral, titrated low-dose	0.1	0.07 to 0.29	
Misoprostol vaginal less than 50 mcg	0.11	0.09 to 0.32	
Misoprostol SR vaginal pessary	0.11	0.05 to 0.22	
Misoprostol buccal/ sublingual	0.11	0.05 to 0.19	
Dinoprostone vaginal NR pessary	0.11	0.05 to 0.19	
Dinoprostone vaginal gel	0.13	0.08 to 0.5	
Dinoprostone vaginal SR pessary	0.15	0.08 to 0.29	
Misoprostol oral 50 mcg or more	0.16	0.05 to 0.2	
Dinoprostone vaginal tablet	0.16	0.03 to 0.26	
Dinoprostone intracervical	0.18	0.09 to 0.38	
Double-balloon or Cook's catheter	0.18	0.01 to 0.16	
Foley catheter	0.19	0.09 to 0.46	
Oxytocin IV	0.2	0.21 to 1.97	
Oral misoprostol less than 50 mcg	0.22	0.07 to 0.39	
Dinoprostone extra-amniotic	0.41	0.07 to 1.33	

The authors concluded that all interventions, even with high heterogeneity between trials, increased the probability of vaginal birth within 24 hours, except for extra-amniotic dinoprostone.

Cesarean Section

Cesarean section compared to placebo (n = 96,771)
An OR less than 1 favors the intervention.

Intervention vs. Placebo	NMA OR	NMA 95% CrI
Misoprostol oral, titrated low-dose	0.62	0.47 to 0.80
Misoprostol buccal/ sublingual	0.68	0.51 to 0.89
Misoprostol vaginal less than 50 mcg	0.7	0.57 to 0.85
Misoprostol oral 50 mcg or more	0.72	0.58 to 0.88
Misoprostol vaginal 50 mcg or more	0.73	0.08 to 2.59
Membrane sweeping	0.74	0.08 to 2.59
Foley catheter	0.76	0.61 to 0.95
Dinoprostone vaginal gel	0.79	0.61 to 0.95
Laminaria	0.8	0.61 to 0.95
Dinoprostone vaginal SR pessary	0.82	0.61 to 0.95
Dinoprostone intracervical	0.83	0.61 to 0.95
Oxytocin IV with amniotomy	0.89	0.61 to 0.95
Oxytocin IV	0.93	0.61 to 0.95
Dinoprostone vaginal NR pessary	0.89	0.61 to 0.95
Misoprostol SR vaginal pessary	0.98	0.61 to 0.95
Dinoprostone extra-amniotic	0.98	0.61 to 0.95
Dinoprostone vaginal tablet	1.04	0.61 to 0.95
Amniotomy	1.06	0.61 to 0.95
Double-balloon or Cook's catheter	1.11	0.61 to 0.95
Oral misoprostol less than 50 mcg	1.11	0.61 to 0.95

"Compared with placebo, several treatments showed a statistically significant reduction in the odds of CS [cesarean section]: titrated low-dose misoprostol, vaginal misoprostol at both≥ 50 µg and <50 µg, vaginal PGE2 [dinoprostone] gel, intracervical PGE2, oral misoprostol tablet (≥ 50 µg), Foley catheter, membrane sweeping and buccal/ sublingual misoprostol. In this group, titrated oral misoprostol achieved the lowest odds of an eventual CS but there was still considerable uncertainty in this finding, as observed by the posterior mean rank of 6th (out of 33) and 95% CrI from 2nd to 13th (out of 33) for oral misoprostol solution." p. 105

Uterine Hyperstimulation

Uterine hyperstimulation compared to placebo (n=43,612)
An OR less than 1 favors the intervention.

Intervention vs. Placebo	NMA OR	NMA 95% CrI
Double-balloon or Cook's catheter	0.26	0 to 1.18
Laminaria	0.52	0.01 to 2.62
Foley catheter	0.92	0.37 to 1.93
Misoprostol oral less than 50 mcg	1.13	0.28 to 3.15
Dinoprostone vaginal NR pessary	1.4	0.37 to 3.68
Dinoprostone intracervical	1.7	0.37 to 3.68
Misoprostol oral, titrated low-dose	1.93	0.73 to 4.19
Dinoprostone vaginal tablet	1.99	0.73 to 4.19
Oxytocin IV	2.12	0.97 to 4.1
Dinoprostone vaginal gel	2.33	0.97 to 4.1
Misoprostol vaginal less than 50 mcg	2.75	1.36 to 5.04
Misoprostol oral 50 mcg or more	2.85	1.41 to 5.2
Dinoprostone vaginal SR pessary	2.97	1.36 to 5.73
Misoprostol buccal/ sublingual	4.25	1.71 to 9.02
Misoprostol vaginal 50 mcg or more	4.4	2.22 to 7.94
Misoprostol SR vaginal pessary	5.58	1.58 to 14.57
Oxytocin IV with amniotomy	7.44	0.27 to 40.66

Uterine hyperstimulation with FHR [fetal heart rate] changes was one of the key safety outcomes. Here double-balloon catheter, NO [nitric oxide] and laminaria had the highest probability of being among the best three treatments, whereas i.v. oxytocin with amniotomy, slow-release misoprostol pessary and high-dose vaginal misoprostol tablets (which was among the best treatments for efficacy) were most likely to increase

Meta Analysis of 14000 women

- Oral misoprostol is more effective than placebo and equivalent to intravenous oxytocin, vaginal misoprostol and vaginal dinoprostone for the induction of labour in women.
- Oral misoprostol results in fewer caesarean sections than oxytocin alone, similar rates of instrumental delivery, faster time to deliver
- In the comparisons with oxytocin infusions, there seems to be a higher rate of meconium staining at all dosages, but this was not associated with any adverse effect on the fetus. (? A direct effect of the misoprostol on the fetal gut).
- In studies where most women were given low dose oral misoprostol (20-25 mcg two-hourly), the hyperstimulation rates were the same as for vaginal dinoprostone (i.e. around 5% overall and 2.9% with fetal heart rate (FHR) abnormalities).
- No increase in adverse fetal outcomes was seen in these studies

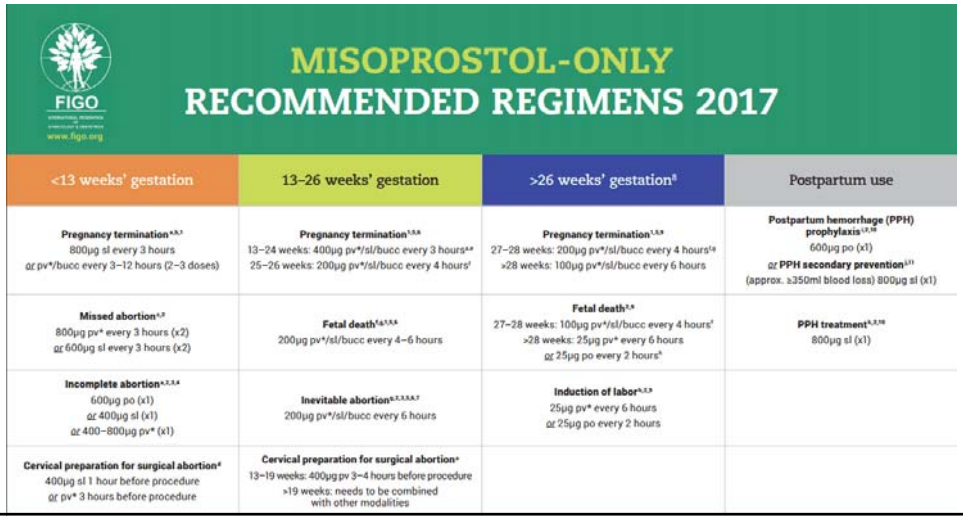
Alfirevic 2016

Misoprostol IOL in TOLAC

- Prostaglandin use for IOL or cervical ripening is contraindicated in women attempting TOLAC
- The rate of uterine rupture with the use of misoprostol on a scarred uterus is unknown
- In a retrospective observational study from Turkey reported a 9.7% rate of uterine rupture in women with a previous cesarean who were administered 50 mcg of misoprostol vaginally
- In 1999, Plaut et al reported a 5.6% rate (5 of 89 case reports) of uterine scar rupture with the use of vaginal misoprostol for IOL in women who had a prior cesarean
- There was no reported incidence of uterine rupture among the women who had a previous cesarean in the Cochrane systematic review that evaluated vaginal versus oral misoprostol

Aslan 2004, Yount 2013, Plautt 1999, Alfirevec 2010

Special Considerations



MISOPROSTOL-ONLY RECOMMENDED REGIMENS 2017

FIGO
www.figo.org

<13 weeks' gestation	13–26 weeks' gestation	>26 weeks' gestation[g]	Postpartum use
Pregnancy termination[a,b,1] 800µg sl every 3 hours *or* pv*/bucc every 3–12 hours (2–3 doses)	**Pregnancy termination**[1,5,6] 13–24 weeks: 400µg pv*/sl/bucc every 3 hours[a,e] 25–26 weeks: 200µg pv*/sl/bucc every 4 hours[f]	**Pregnancy termination**[1,5,6] 27–28 weeks: 200µg pv*/sl/bucc every 4 hours[f,g] >28 weeks: 100µg pv*/sl/bucc every 6 hours	**Postpartum hemorrhage (PPH) prophylaxis**[1,9,10] 600µg po (x1) *or* **PPH secondary prevention**[3,11] (approx. ≥350ml blood loss) 800µg sl (x1)
Missed abortion[c,2] 800µg pv* every 3 hours (x2) *or* 600µg sl every 3 hours (x2)	**Fetal death**[f,g,1,5,6] 200µg pv*/sl/bucc every 4–6 hours	**Fetal death**[2,9] 27–28 weeks: 100µg pv*/sl/bucc every 4 hours[f] >28 weeks: 25µg pv* every 6 hours *or* 25µg po every 2 hours[h]	**PPH treatment**[4,9,10] 800µg sl (x1)
Incomplete abortion[a,2,3,4] 600µg po (x1) *or* 400µg sl (x1) *or* 400–800µg pv* (x1)	**Inevitable abortion**[g,2,3,5,6,7] 200µg pv*/sl/bucc every 6 hours	**Induction of labor**[4,7,9] 25µg pv* every 6 hours *or* 25µg po every 2 hours	
Cervical preparation for surgical abortion[d] 400µg sl 1 hour before procedure *or* pv* 3 hours before procedure	**Cervical preparation for surgical abortion**[a] 13–19 weeks: 400µg pv 3–4 hours before procedure >19 weeks: needs to be combined with other modalities		

Terminations

<13 weeks' gestation	13–26 weeks' gestation
Pregnancy termination[a,b,1] 800µg sl every 3 hours *or* pv*/bucc every 3–12 hours (2–3 doses)	**Pregnancy termination**[1,5,6] 13–24 weeks: 400µg pv*/sl/bucc every 3 hours[a,e] 25–26 weeks: 200µg pv*/sl/bucc every 4 hours[f]
Missed abortion[c,2] 800µg pv* every 3 hours (x2) *or* 600µg sl every 3 hours (x2)	**Fetal death**[f,g,1,5,6] 200µg pv*/sl/bucc every 4–6 hours
Incomplete abortion[a,2,3,4] 600µg po (x1) *or* 400µg sl (x1) *or* 400–800µg pv* (x1)	**Inevitable abortion**[g,2,3,5,6,7] 200µg pv*/sl/bucc every 6 hours
Cervical preparation for surgical abortion[d] 400µg sl 1 hour before procedure *or* pv* 3 hours before procedure	**Cervical preparation for surgical abortion**[a] 13–19 weeks: 400µg pv 3–4 hours before procedure >19 weeks: needs to be combined with other modalities

2nd Trimester Fetal Demise

- No conclusive evidence of superiority of one dose or schedule
- Dickinson and Evans administered vaginal misoprostol either 200 µg every 6 hours, 400 µg every 6 hours, or a 600 µg loading dose followed by 200 µg every 6 hours
  - Both the 400 µg and 600/200 µg regimens were superior to the 200 µg regimen in terms of median time to delivery.
  - The 600/200 µg regimen caused more side effects
- Start with 400 µg vaginally every 6 hours for a 48-hour period
- There is also evidence that the addition of 200 mg of mifepristone to the induction protocol decreases the interval to delivery for termination of pregnancy

Allen 2009

3rd Trimester Fetal Demise

- Although there is some evidence to support a decreasing dose with increasing gestational age, there is little evidence to support the advice given in some international and national clinical guidelines to use lower doses of misoprostol in cases of fetal death
- Insufficient evidence overall of superiority of one dose or schedule of misoprostol over another for use in pregnancies at or over 13 weeks' gestation
- Low doses have been shown to be associated with a longer induction to-delivery interval and lower overall effectiveness, and evidence has supported the safety of the "higher" doses for women.
- Recommendations in FIGO chart were compiled with this in mind, while also acknowledging that it is possible that a range of dosages could be effective and safe

Morris 2017

Fetal Demise in a TOLAC

- Induction of labor with misoprostol in the setting of a previous cesarean delivery scar can be safely performed in the second trimester
- Several randomized studies did include patients with a previous cesarean delivery with no adverse effects
- In a retrospective study, 188 women with a previous cesarean delivery underwent induction of labor between 17 and 24 weeks of gestation with 400 µg orally together with 400 µg vaginally for the first dose followed by 400 µg vaginally every 6 hours for a maximum of 5 doses
  - The main outcomes included hemorrhage requiring transfusion, postabortal infection, retained placenta, and uterine rupture. There was no evidence that a previous cesarean delivery affected the incidence of complications.
- Another retrospective study found 80 women undergoing termination of pregnancy between 13 and 26 weeks of gestation for a variety of reasons with 1 or more cesarean section scars.
  - Misoprostol 400 µg, was administered to women up to 20 weeks of gestation and 200 µg for women greater than 20 weeks of gestation, vaginally or sublingually, every 6 hours up to 24 hours. The mean induction to abortion interval was 16.4 hours and was not statistically different between women with and without a prior cesarean delivery scar. There was no case of uterine rupture or scar dehiscence. No statistically significant differences were found in rates of incomplete abortion, blood loss, or sepsis.
- Misoprostol can be used for women with previous cesarean or other transmural uterine scar throughout 13–26 weeks.

Allen 2009, Daskalakis 2005, Bhattacharjee 2007

SUMMARY

- Misoprostol administered orally and vaginally is used for the induction of labour or cervical ripening, but not currently approved by Health Canada
- The usual dose is 50 mcg orally or 25 mcg vaginally, which may be repeated every 4 hours
- Serious adverse effects with misoprostol for cervical ripening and labour induction are similar to other prostaglandins, and include uterine tachysystole, meconium staining of liquor, and rarely, uterine rupture.
- Other side effects include fever, chills, vomiting, and diarrhea

CADTH Rapid Response Report: Summary with Critical Appraisal
Verla Chatsis and Nina Frey. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2018 Nov 23.

Sample Protocol – Sinai Health

- Use of misoprostol for Induction of labor is suitable for all gestational ages and indications for induction of labor.
- Contraindications for use of misoprostol include women attempting a trial of labor after caesarean section (TOLAC). Misoprostol is also contraindicated for a woman who has had any full thickness myometrial surgery: myomectomy, open fetal surgery, multiparity > 4 or any contraindication to vaginal birth.
- Misoprostol use for induction of labor requires an obstetrical consultation for patients under the care of midwifery.
- Prior to initiating the induction process, the physician/registered midwife will explain and document the following: the indication for induction, the induction process and confirmation of consent.
- The woman will be admitted as an inpatient for the use of Misoprostol for labour induction.

Sample Protocol – Sinai Health

- Once regular uterine activity (more than 2 contractions in 10 min) is present, continuous monitoring will be established with a 1:1 nursing assignment.
- Once uterine activity has been established, continue with Misoprostol dosing as ordered; **this is NOT an indication to switch to labor augmentation with oxytocin.**
- The goal of induction by pharmacological method, ie., Misoprostol, is to achieve and maintain contractions every 3-5 minutes of sufficient strength to cause cervical dilatation and/or effacement.
- Induction of labor with misoprostol is suitable regardless of Bishop Score
- If cervical ripening was performed using a Foley catheter, the catheter may be removed before starting Misoprostol. Alternatively the catheter can remain in place if the cervix is not suitably ripe.
- If cervical ripening was performed using dinoprostone (PGE2), there should be an 8 hour interval between the dose of dinoprostone and starting misoprostol.
- If the cervical ripening was performed using cervidil (PGE2), the cervidil should be removed before initiating misoprostol.

Sample Protocol – Sinai Health

- Dosing/Administration of misoprostol will be as follows (nursing/RM administration)
  - First dose of misoprostol 25 to 50 micrograms (mcg) PO as per the physician/RM
  - Subsequent dosing of misoprostol will be at 4h intervals, 25 mcg PO. This will be the dose regardless of maternal BMI.
  - The dose may be increased to 50 mcg at the direction of the physician/midwife in the context of uterine activity and fetal well-being.
  - The dose interval may be increased to 6h by the direction of the physician/midwife in the context of uterine activity.
  - The diagnosis of "failure to progress"(dilate and or descend) will be made by the physician in the context of adequate uterine activity and an absence of change in the vaginal examination. Dosing of misoprostol will stop once this diagnosis has been made.

Sample Protocol – Sinai Health

- The nurse/RM will complete a 20 minute NST prior to beginning Misoprostol induction to be reviewed with the physician.
- After the first and every oral administration of Misoprostol the nurse/RM will complete one hour of continuous fetal monitoring

Sample Protocol – Sinai Health

- Once uterine activity has been achieved at a pattern of palpable contractions every 5 minutes or 2 in 10 minutes (with pain), the nurse/RM will initiate IV access, initiate continuous fetal monitoring, monitor maternal vital signs, perform a vaginal exam prior to each dose of misoprostol to determine labour progress and communicate labour progress findings, fetal monitoring and maternal vital signs to physician.
- If tachysystole is present **without** fetal heart rate change, the nurse will inform the physician; the RM will inform the consulting obstetrician
- If tachysytole **with** fetal heart rate change (as defined by more than 3 late decelerations, more than 2 complicated variable decelerations, prolonged deceleration, bradycardia, tachycardia more than 15 minutes), the nurse/RM will inform the physician. In utero resuscitation and nitroglycerin spray (2 puffs) sublingual (SL) as part of the Misoprostol order set may be given by the physician or nurse
- An increase in maternal temperature can be associated with the use of misoprostol. Acetaminophen 1000mg should be given q 6hourly if maternal temperature is greater than 38C
- If the temperature is greater than 39C on 2 occasions (30 minutes apart) nursing/RM will inform the physician; blood cultures and antibiotics may be initiated at the review of the medical care provider.
- The use of artificial rupture of the membranes, fetal scalp electrode and intrauterine pressure catheter will be at the discretion of the physician/RM.

Thank you

- Questions?