

Misoprostol for labour induction

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www.misoprostol.org



Outline

1. The evidence on misoprostol
 - a) Induction of labour
 - b) Intrauterine fetal death
2. Induction in low resource settings
3. The way forward

Vaginal misoprostol

- Systematic review of 10,000 women
“25 mcg 4° ... as effective as other prostaglandins, without increased uterine hyperstimulation”

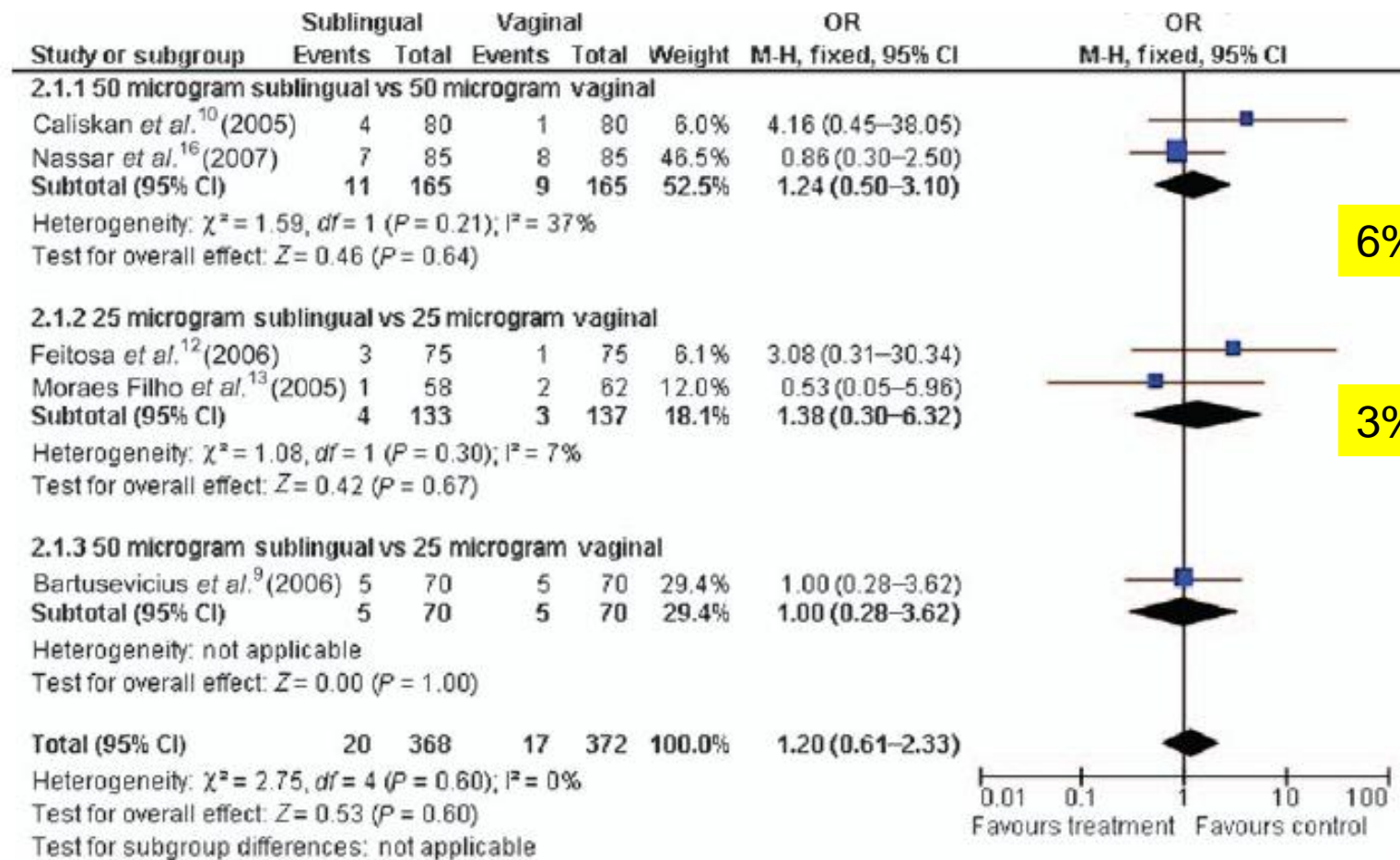
Hofmeyr & Gulmezoglu Cochrane

- WHO, ACOG (but not ‘NICE’)
- 2 UK / US pharma companies attempting to license it – difficulties with proving non-inferiority

Sublingual misoprostol

- rapid onset, prolonged action (use 4-6°)
- non-genital administration
- 5 RCTs (740 women) of vag. miso vs. subling. miso
- Overall no differences

Effect on hyperstimulation synd.



Oral Misoprostol

Advantages:

- accurate dosage and absorption
- use if bleeding / SROM
- non-genital use

Disadvantages:

- unknown long-term stability
- frequent dosaging

Cochrane: “more effective than PGE2”

Systematic review of low dose oral misoprostol

- Cochrane methodology
- 2281 randomised to LDOM or dinoprostone
 - 3 studies used miso to augment also

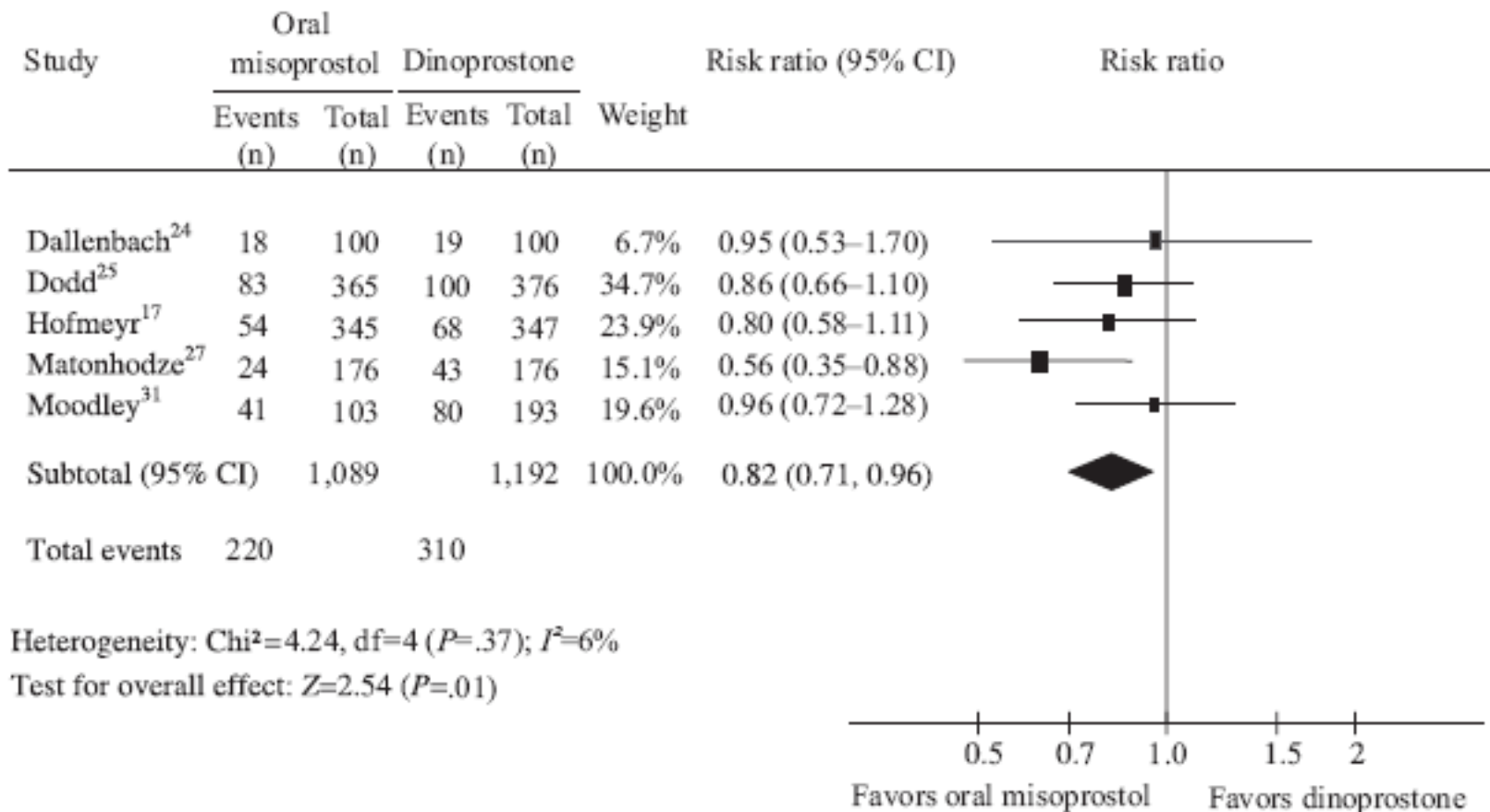
| Study | Oral Misoprostol | | Dinoprostone | |
|------------------------|-----------------------------------|-----------------|--------------|-----------------------------|
| | Dose | Frequency | Dose | Frequency |
| Hofmeyr 2001 | | | | |
| Dallenbach 2003 | | | | |
| Matonhodze 2003 | 20 mcg solⁿ | 2 hourly | 2 mg | 6 hrly x 2 doses |
| Dodd 2006 | | | | |
| Moodley 2003 | | | | |

Oral Misoprostol vs Dinoprostone

| Outcome | Studies | Oral | | RR | 95% CI | Heterogeneity* (%) |
|---|---------|-------------|--------------|------|-----------|--------------------|
| | | Misoprostol | Dinoprostone | | | |
| Vaginal delivery not achieved within 24 h | 5 | 461/1,090 | 475/1,191 | 1.07 | 0.97-1.18 | 0 |
| Hyperstimulation+FHR changes | 5 | 64/1,147 | 47/1,077 | 1.10 | 0.76-1.60 | 29 |
| Hyperstimulation without FHR changes | 4 | 48/896 | 52/1,003 | 0.90 | 0.31-2.62 | 83 |
| Cesarean delivery | 5 | 220/1,089 | 310/1,192 | 0.82 | 0.71-0.96 | 6 |
| Oxytocin augmentation | 5 | 338/1,089 | 449/1,191 | 0.69 | 0.45-1.08 | 91 |
| Epidural use | 4 | 539/985 | 545/997 | 1.00 | 0.93-1.08 | 34 |
| Meconium-stained liquor | 4 | 103/744 | 99/845 | 1.14 | 0.88-1.48 | 0 |
| Apgar score less than 7 at 5 min | 4 | 20/983 | 31/997 | 0.65 | 0.37-1.13 | 0 |
| NICU admission | 5 | 36/1,087 | 58/1,190 | 0.81 | 0.54-1.21 | 0 |
| Perinatal mortality | 4 | 1/986 | 2/996 | 0.60 | 0.08-4.50 | 0 |
| Maternal adverse effects (all) | 4 | 307/961 | 309/987 | 1.04 | 0.86-1.26 | 51 |
| Uterine rupture | 4 | 0/1,089 | 0/1,191 | - | - | - |
| Postpartum hemorrhage | 4 | 185/985 | 203/997 | 0.92 | 0.77-1.10 | 0 |
| Maternal death | 2 | 0/711 | 0/725 | - | - | - |

Oral misoprostol vs dinoprostone

Effect on caesarean section

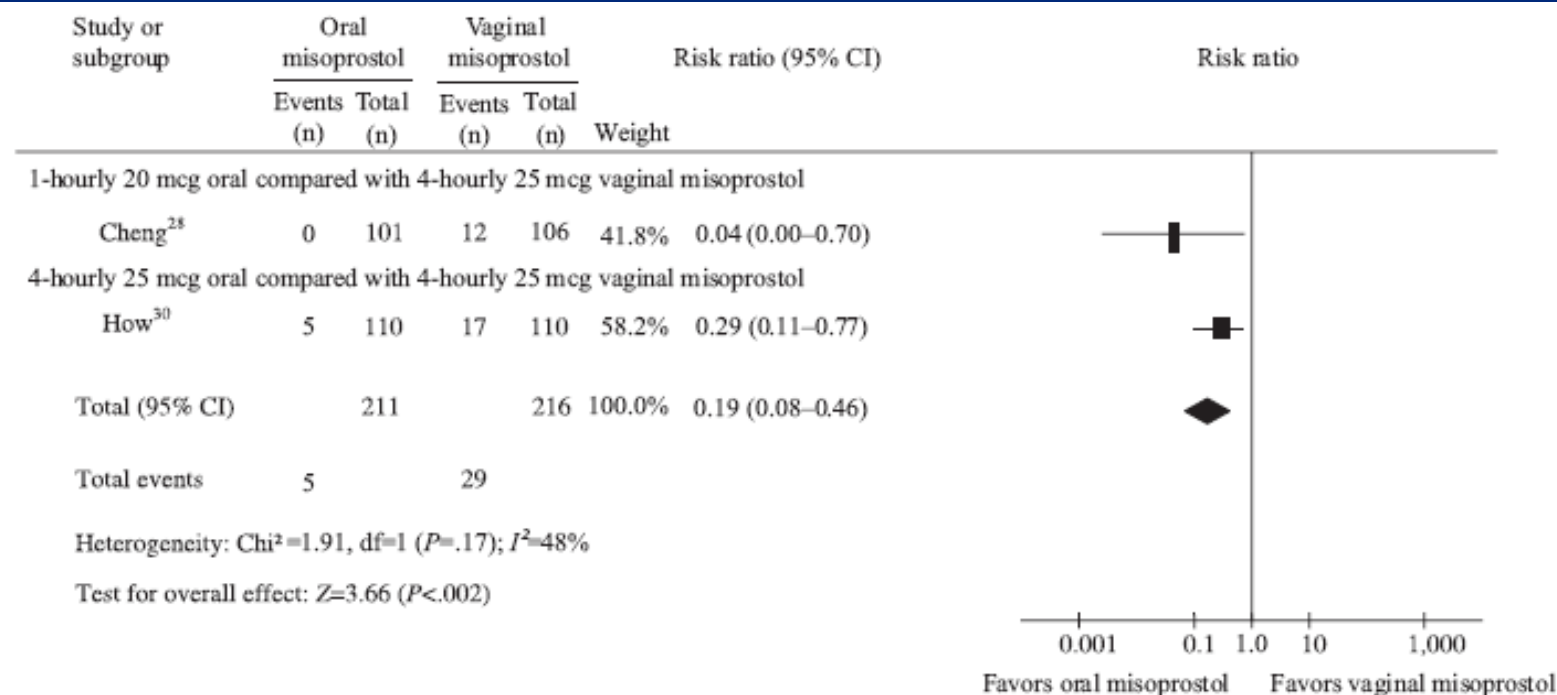


Oral vs vaginal misoprostol

| Study | Oral Misoprostol | | Vaginal Misoprostol | |
|----------------------------------|-------------------------------|-----------------|---------------------|-----------------|
| | Dose | Frequency | Dose | Frequency |
| How 2001 (220 women) | 25 mcg tab | 4 hourly | 25 mcg | 4 hourly |
| Cheng 2008 (208 women) | 20 mcg solⁿ | 1 hourly | 25 mcg | 4 hourly |

Low dose oral vs vaginal misoprostol

| Outcome | Studies | Oral Misoprostol | Vaginal Misoprostol | RR | 95% CI | Heterogeneity* (%) |
|---|---------|------------------|---------------------|------|-----------|--------------------|
| Vaginal delivery not achieved within 24 h | 2 | 75/210 | 85/216 | 0.51 | 0.03–9.62 | 98 |
| Hyperstimulation with FHR changes | 2 | 5/211 | 29/216 | 0.19 | 0.08–0.46 | 48 |
| Hyperstimulation without FHR changes | 2 | 18/211 | 51/216 | 0.36 | 0.22–0.59 | 0 |
| Cesarean delivery | 2 | 39/210 | 37/216 | 0.69 | 0.09–5.54 | 92 |
| Oxytocin augmentation | 2 | 92/211 | 98/216 | 0.64 | 0.06–7.03 | 98 |
| Meconium-stained liquor | 1 | 16/109 | 11/110 | 1.47 | 0.71–3.02 | – |
| Apgar score less than 7 at 5 minutes | 2 | 4/210 | 11/216 | 0.35 | 0.04–3.54 | 57 |
| NICU admission | 2 | 7/210 | 11/216 | 0.44 | 0.02–8.50 | 74 |



Low dose oral misoprostol

Low-dose oral misoprostol seems to be at least as effective as the other PGs

... equal efficacy to dinoprostone but with lower CS rates

... equal efficacy to vaginal miso, but with lower hyperstimulation rates

... can use up to time of delivery

Oral misoprostol solution would therefore seem to be the optimal choice for induction of labour.

Transcervical Foley catheter

- Cochrane (2001) 45 small RCTs
 - less hyperstimulation than PGs (PGE2 / miso)
 - no difference in CS rate
- Preger et al (BJOG 2008)
 - 600 women
 - Foley / dinoprostone / vag miso (25mcg 4°)
 - No sig. differences, except Foley quicker
 - Hyperstimulation 1% vs 3% vs 3% (n.s.)

Intrauterine fetal death

- Complex mix of doses, routes indications.
- Bellagio group 2007 (Gomez, Wing, Fiala)

Recommended Dosages

13-17 weeks: vaginal misoprostol 200 μ g 6-hourly (x 4)

18-26 weeks: vaginal misoprostol 100 μ g 6-hourly (x 4)

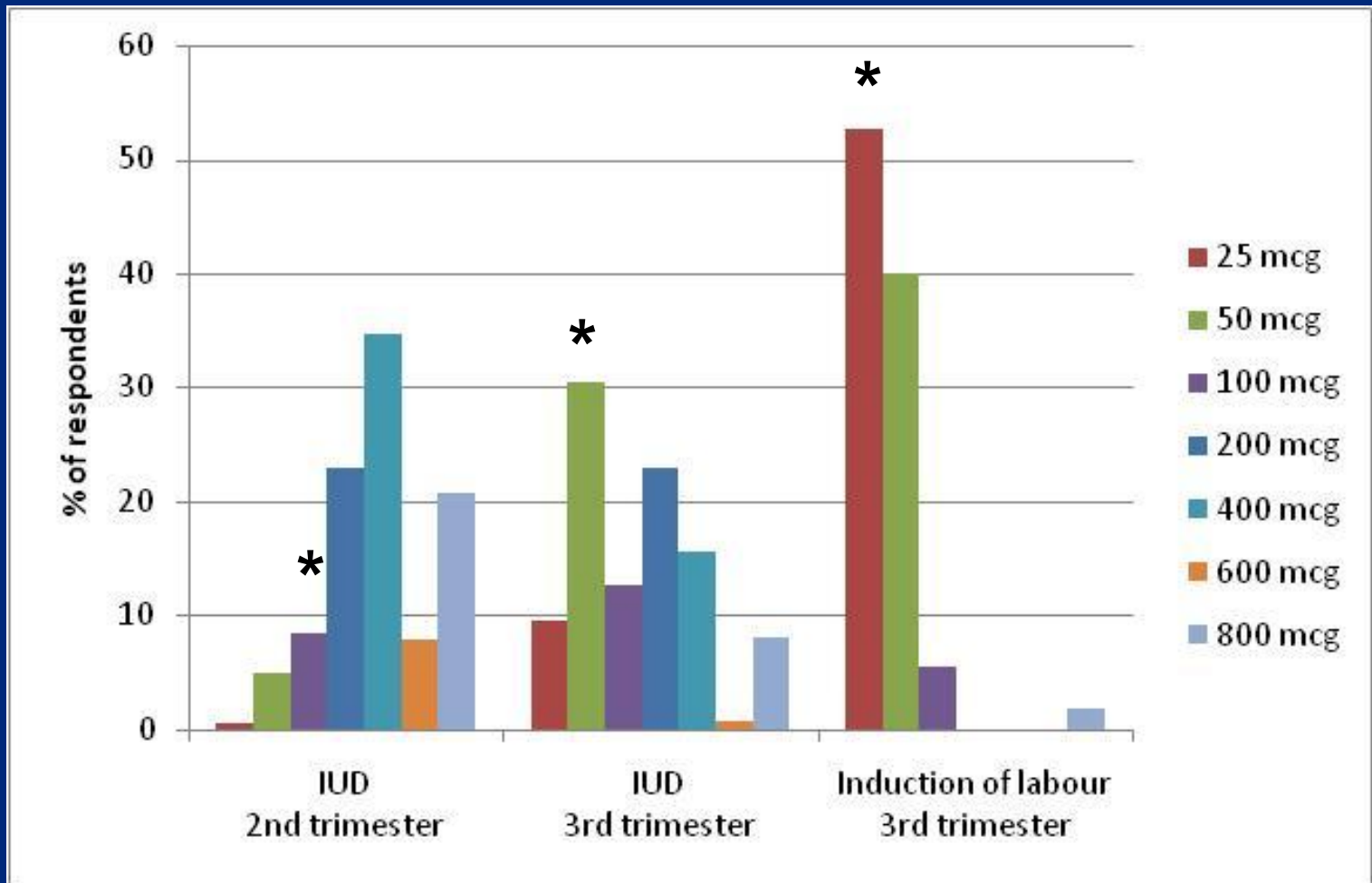
27-43 weeks: vaginal misoprostol 25-50 μ g 4-hourly (x 6)

↓ dose with previous CS

↑ dose with TOP (even if post-fetocide)

Snowball survey of practice

271 respondents (77% Europe / N. America)



Induction in LRS (1)

| Indication | UK Rate |
|------------------------|---------|
| Prolonged pregnancy | 43% |
| Pre-eclampsia | 9% |
| Maternal (eg Diabetes) | 5% |
| Fetal (eg IUGR, APH) | 24% |
| PROM | 7% |
| Multiple pregnancy | 3% |
| Overall rate | 19% |

“Balancing risks and benefits of IOL”

Induction in LRS (2)

Resource usage

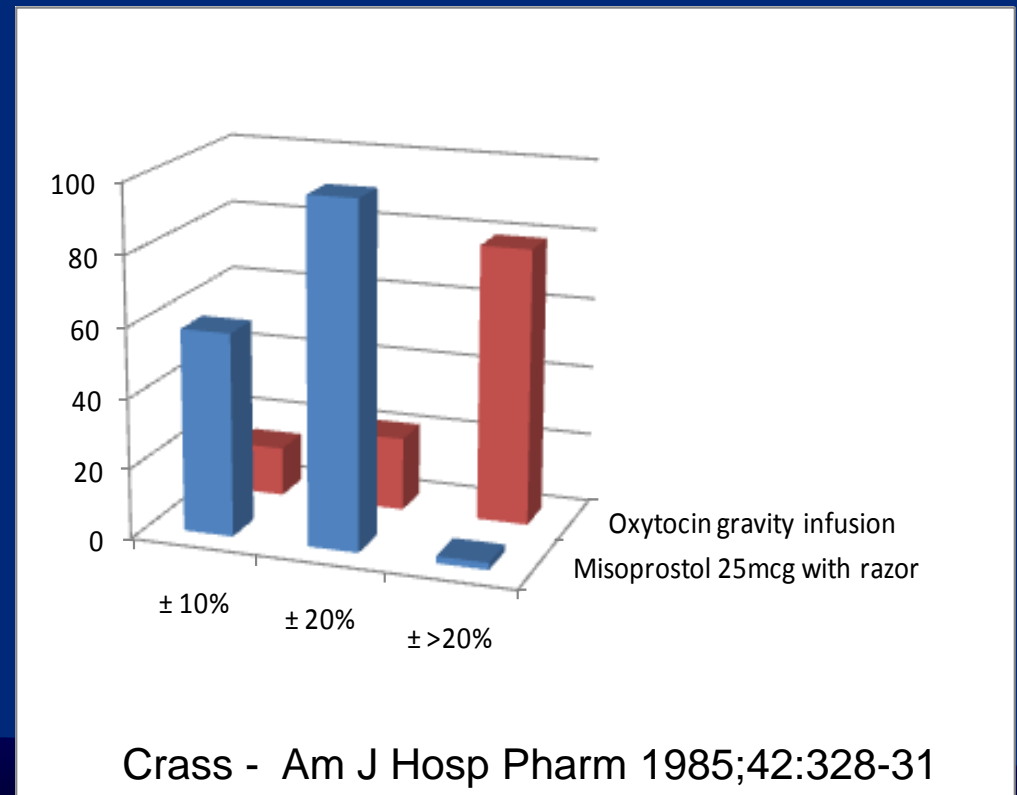
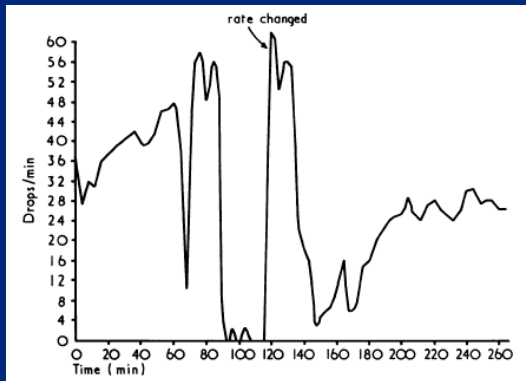
- oxytocin - infusion equipment and monitoring
- oral miso – frequent dosages

| Ripening | Induction / aug | Cost |
|------------------------|------------------|--------|
| Prostaglandin E2 | Oxytocin | \$ 40 |
| Laminaria | Oxytocin | |
| Transcervical catheter | Oxytocin | \$2.5 |
| Oxytocin | Oxytocin | \$ 4 |
| Misoprostol | Oxytocin | \$ 3.5 |
| Misoprostol | Oral misoprostol | \$ 1.5 |
| Transcervical catheter | Oral misoprostol | \$ 2 |

Induction in LRS (3)

Hyperstimulation syndrome – 5%

- monitoring, tocolytics (esp. if long acting)
- much less with mechanical methods



Br Med J 1974;3:439-43

Crass - Am J Hosp Pharm 1985;42:328-31

Williams - Am J O&G 2002;187:615-9

Induction process

RIPENING

x

Speed

x

Supervision

x

Hyperstim'n

Very mobile

Mobility

Foley / laminaria

INDUCTION / AUG.

✓

✓✓

-

**Depends on
monitoring**

Oxytocin (via pump)
Oral misoprostol

Induction options

Oral miso solution

Logistics of making solution

Frequent dosages

Accurate drug dosages

Foley / oxytocin

Logistics of inserting Foley

Need for oxytocin pump

Less research evidence

? Ideal is Foley then oral misoprostol

The Way Forward

1. “Do no harm”

a. prevent misuse

- EB guidelines for IOL in LRS
- information e.g. www.misoprostol.org

b. Reduce hyperstimulation risk

- mechanical ripening methods

The Way Forward

2. Move to oral misoprostol for induction

- suspension in water initially

Pharma companies

- private / public partnership
- produce in syrup / suspension

www.misoprostol.org

