Our love affair with Misoprostol over the last 20 years

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Introduction

- The Pregnancy Advisory Centre is a government-funded clinic in South Australia established in 1992.
- The services are free at the point of delivery.

- We perform over 2500 surgical Terminations of Pregnancy (TOPs) each year, up to a gestation of 22 completed weeks.

- I will be presenting results from 4 papers published over the last 20 years documenting our implementation of misoprostol use.

- These papers demonstrate significant reduction in operative difficulty, complication rates and improvements in service delivery.

Uterine Perforation during Surgical Abortion: A review of Diagnosis, Management and Prevention (Pridmore et al. 1999 Aust NZ J Obstet Gynaecol)

- Our first study, was a retrospective and prospective analysis of 13,907 abortions over a 6 year period.

Our finding

- The overall perforation rate was 12/13907 procedures (0.086%)
  - 6 in 1st trimester
  - 6 in 2nd trimester (13-20 weeks)
- Previous gynaecological surgery (TOP, LLETZ, LSCS) had been performed in 11 of the 12 women who sustained perforation.

Major risk factor identified

- We hypothesised that previous gynaecological surgery caused scarring of the internal os.
- Misoprostol was added to osmotic dilators in second trimester procedures to increase *passive* dilation of the cervix.
- The perforation rate in the 2 years following this fell to 1/5711 procedures (0.02%, p=0.022)

Comparison of four perioperative misoprostol regimens for surgical termination of first-trimester pregnancy (Chambers et al. 2009 Int J Gynaecol Obstet)

- In 2004, we extended the use of misoprostol into 1st trimester procedures.
- The second study was of 4 cohorts of 1000 women receiving different misoprostol regimens.

- The cohorts were:

1) **No** pre-operative misoprostol
2) 200mcg of *oral* misoprostol 30 mins pre-op
3) 200mcg of *sublingual* misoprostol 30 mins pre-op
4) **200mcg of *oral* misoprostol 3 hours pre-op at home plus 200mcg of *vaginal* misoprostol post-operatively**

We found that the 4th regimen was **most** effective.

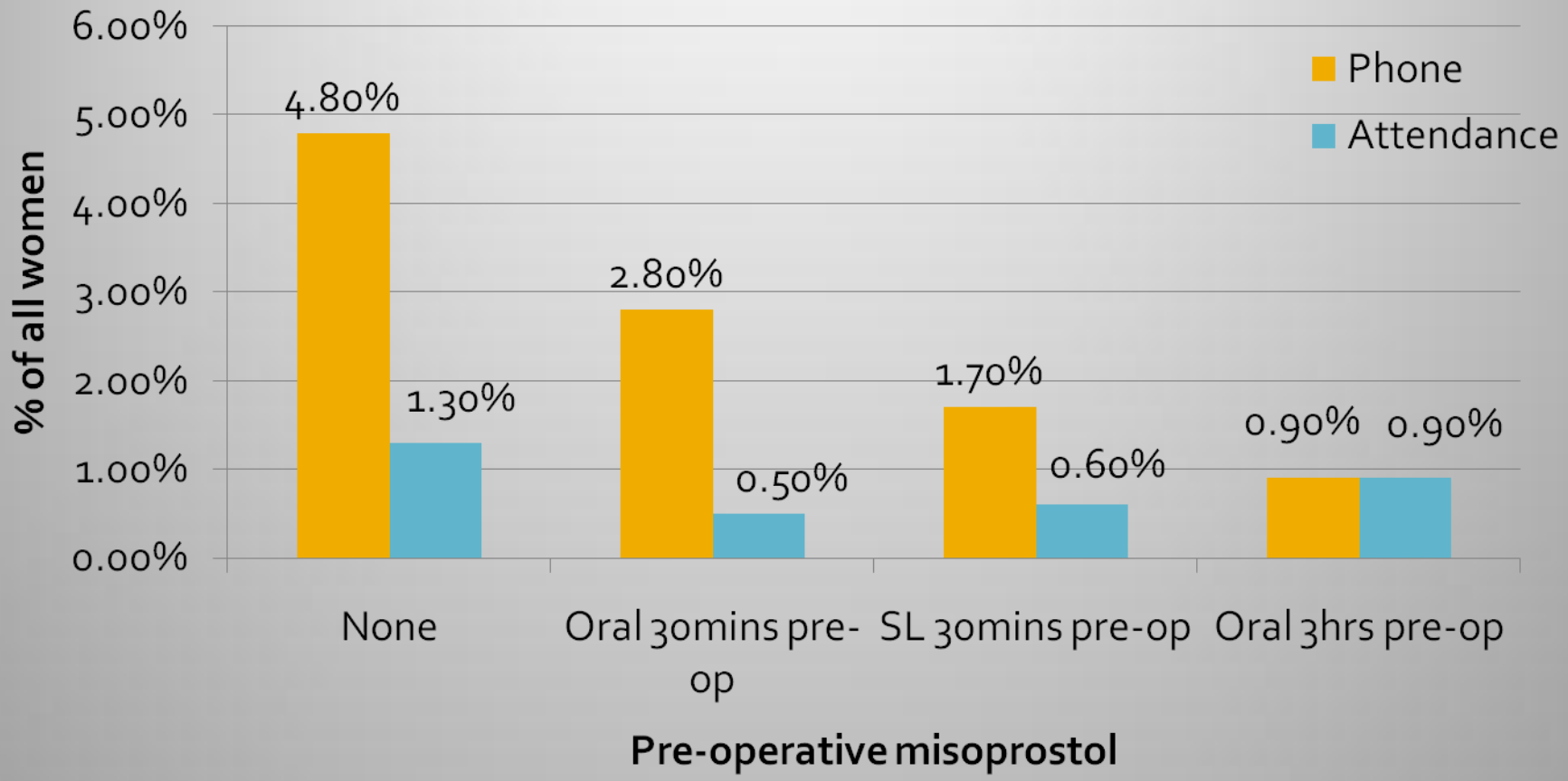
Post-op vaginal misoprostol is to counteract any tendency for post-operative atony

Finding 1 – Reduction in difficulty of dilatation

Cohort	Degree of difficulty of cervical dilatation (%)		
	Not Difficult	Moderately Difficult	Very/Extremely Difficult
No pre-operative misoprostol	74.1%	17.9%	**8.0%**
Oral pre-op misoprostol 30mins prior	86.0%	11.1%	2.9%
SL pre-op misoprostol 30 mins prior	84.3%	12.8%	2.9%
Oral pre-op misoprostol 3hrs prior *plus* vaginal miso post-op	95.4%	3.8%	**0.8%**

- Compared to no misoprostol, misoprostol 3 hours pre-op + misoprostol post-op showed a **90%** improvement in ease of dilatation of the cervix.

Finding 2 – Reduction in contact from women for post-operative concerns



Compared to no misoprostol, misoprostol 3 hours pre-op + misoprostol post-op afforded **71%** reduction in incidence of women requiring post-op contact for concerns.

Finding 3 – Reduction in rate of Retained Products treated by surgical Dilatation and Curettage (D+C)

Cohort	Complications (%)	
	Retained products treated with misoprostol	Retained products treated by repeat D+C
No pre-op misoprostol	0.8%	**0.5%**
Oral pre-op misoprostol 30mins prior	0.2%	0.3%
SL pre-op misoprostol 30mins prior	0.4%	0.2%
Oral pre-op misoprostol 3hours prior *plus* vaginal miso post-op	0.7%	**0.2%**

Compared to no misoprostol , the most marked effect was a **60%** reduction in repeat D+C rate.

Comparison of two misoprostol regimens for cervical priming before surgical pregnancy termination at 13 to 16 weeks gestations (Chambers et al. 2011 Open J Obstet Gynaecol)

- The next study was a retrospective analysis performed on the medical records of 2 cohorts of 334 women each.

  1) 3 sublingual doses of 400mcg misoprostol 30mins apart on admission

  2) same dosage *preceded* by 200mcg oral misoprostol 3 hours before admission

Finding 1 – Increased rate of one-day completion of Dilatation and Evacuation (D+E)

- In cohort 1 (no home misoprostol), 7 out of 334 procedures could *not* be completed in a single stage in one day.
  - These women required further cervical priming and D+E the next day.
- In cohort 2 where home misoprostol was given 3 hours prior to admission, **all** 334 procedures were completed in a single stage.
- This is an improvement from 97.3% to 100%, p=0.04

Finding 2 – Reduction in overall theatre time (corresponds to reduction in difficulty of operation)

Cohort	Mean theatre time
No home misoprostol	15.6 minutes n=186
With home misoprostol 3 hrs prior	14.6 minutes n=175

Nulliparous women.
6.4% reduction in theatre time. p=0.003

Cohort	Mean theatre time
No home misoprostol	15.5 minutes n=148
With home misoprostol 3 hrs prior	13.6 minutes n=159

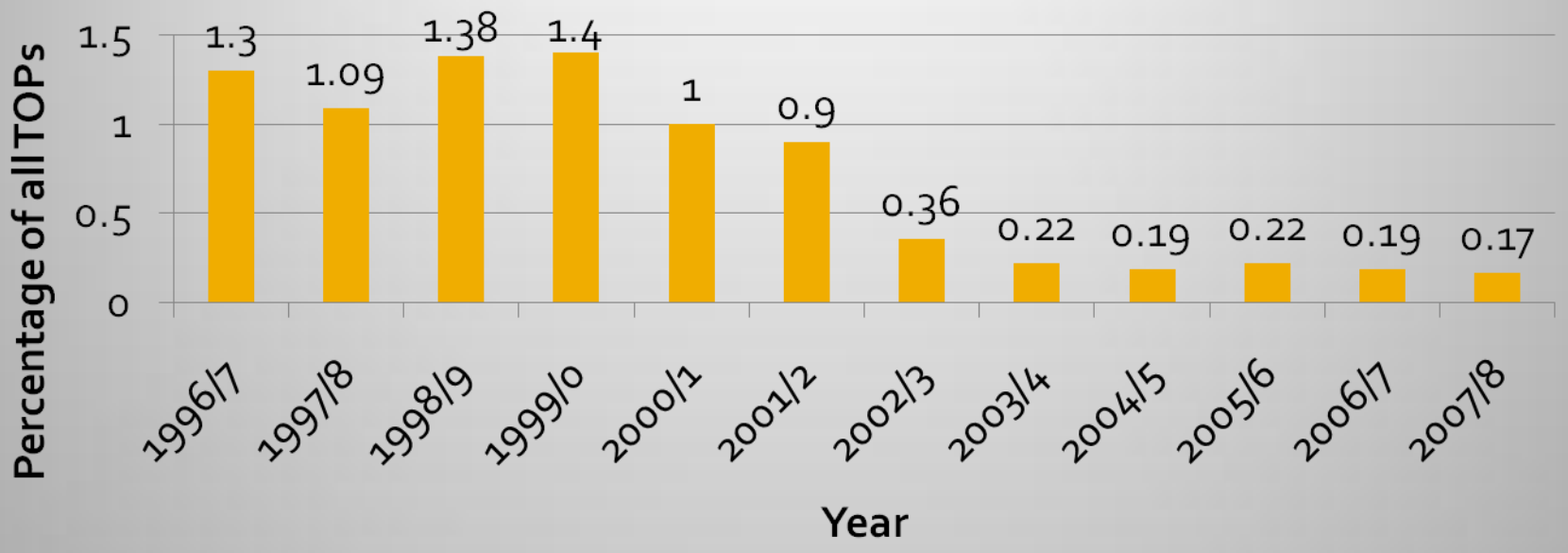
Parous women.
12.3% reduction in theatre time. p=0.001

For both nulliparous and parous women, mean theatre time was significantly reduced in the cohort who had home misoprostol 3 hrs prior, compared to the women who had none.

Treatment of suction termination of pregnancy retained products with misoprostol markedly reduces the repeat operation rate (Chambers et al 2009. Aust NZ J Obstet Gynaecol)

- In 2009, we also published an audit.
- Commencing in 2002, all women returning with cramping and bleeding have been offered a choice between:
  - a repeat D+C or
  - medical treatment with 200mcg misoprostol taken at home orally or sublingually 3 times a day for 2 days.
- In this paper we audited 16,501 TOPs from 6 years *before* 2002, and 17,856 TOPs from 6 years *after* 2002.

Finding - reduction in repeat D+C rate, following routine use of misoprostol for treatment of retained products.



- Repeat D+C rate fell from 1.18% to 0.24% *after* medical management was introduced in 2002.
- This is a 79.6% reduction in D+C rate. $p<0.001$

In summary

- The use of misoprostol at the Pregnancy Advisory Centre over the last 20 years has been instrumental in significantly reducing:
  - Difficulty of operation
  - Complication rates
  - Incidence of women requiring post-operative contact for concerns

Recent publication

- *Complications of first-trimester abortion by vacuum aspiration after cervical preparation with and without misoprostol: a multicentre randomised trial.* (Meirik et al. May 2012 Lancet)

- This trial confirms our findings of a reduction in complications of the same order as we found in our research.

The future

- We continue to explore the uses of misoprostol in increasing surgical safety.
- In particular, we are developing safe methods for conducting procedures beyond 22 weeks.

Misoprostol Protocols

MISOPROSTOL PROTOCOLS (Current October 2012)			
GESTATION	**MISOPROSTOL**	**OTHER MEDICATION**	**NOTES**
5 - 9 weeks	200mcg orally at home 3 hours prior to appointment	2 x 500mg Paracetamol on admission	
5 - 9 weeks same day service	200mcg sublingually on admission	2 x 500mg Paracetamol on admission	
10 weeks	200mcg orally at home 3 hours prior to appointment	2 x 500mg Paracetamol on admission	
	200mcg sublingually on admission		
10 weeks same day service	2 x 200mcg sublingually on admission	2 x 500mg Paracetamol on admission	
11 weeks	200mcg orally at home 3 hours prior to appointment	2 x 500mg Paracetamol on admission	
	2 x 200mcg sublingually on admission	10mg Metoclopromide on admission	
11 weeks same day service	2 x 200mcg sublingually on admission	2 x 500mg Paracetamol on admission	
	1 x 200mcg sublingually after 30 minutes	10mg Metoclopromide on admission	
12 - 13 weeks and 14 weeks non-parous	200mcg orally at home 3 hours prior to appointment	2 x 500mg Paracetamol on admission	
	2 x 200mcg sublingually on admission	10mg Metoclopromide on admission	Theatre 1/2 - 3 hours after last dose
	2 x 200mcg sublingually 30 minutes later	Analgesia/antiemetic as ordered	
14 weeks parous, 15 weeks and 16 weeks same day service	200mcg orally at home 3 hours prior to appointment	2 x 500mg Paracetamol on admission	Theatre 1 - 3 hours after last dose
	2 x 200mcg sublingually on admission	10mg Metoclopromide on admission	at 14 weeks
	2 x 200mcg sublingually 30 minutes later		Theatre 3 hours after last dose
	2 x 200mcg sublingually 30 minutes later	Analgesia/antiemetic as ordered	at 15 - 16 weeks
	2 x 200mcg sublingually 7.00am at home	10mg Metoclopromide 6.30am	
17 - 22 weeks before Dilapan-S	2 x 200mcg sublingually on admission 8.00am	100mg Tramadol 6.30am	**Withhold misoprostol if uterus is contracting strongly.** Theatre 3 hours after last dose
cervical dilator (CD) procedure	2 x 200mcg sublingually 8.30am	Analgesia/antiemetic as ordered	
	2 x 200mcg sublingually 9am if poor responder		
After CD for same day D&E	2 x 200mcg per rectum/vagina at end of CD procedure	Analgesia/antiemetic as ordered	**Withhold misoprostol if uterus is contracting strongly.** Theatre 3 hours after last dose
	1 x 200mcg sublingually at 30 minute intervals x 4		
After STOP procedure 5-12 weeks	1 x 200mcg in posterior vaginal fornix or rectum		
After D&E procedure 13-22 weeks	2 x 200mcg in posterior vaginal fornix or rectum		
Medical Abortion	4 x 200mcg vaginally 2 days after mifepristone tablet		
	1 x 200mcg s-l tds 3 & 4 days after mifepristone tab		
RPOC	4 x 200mcg bucally stat, then 2 buccally QID for 2 days (20 total)		

References

1) Pridmore, BR; & Chambers, DG. (1999**). Uterine perforation during abortion: a review of diagnosis, management and prevention.** *Aust N Z J Obstet Gynaecol.* Vol. 39, No. 3, (Aug 1999), pp.349-353
2) Chambers, DG; Mulligan, EC; Laver, AR; Weller,BK; Baird, JK; & Herbert, WY. (2009).**Comparison of four perioperative misoprostol regimens for surgical termination of first-trimester pregnancy.** *Int J Gynaecol Obstet*. Vol. 107, No. 3, (Dec 2009), pp.211-5
3) Chambers, DG; Willcourt, RJ; Laver, AR; Baird, JK; & Herbert, WY. (2011a). **Comparison of two misoprostol regimens for cervical priming before surgical pregnancy termination at 13 to 16 weeks gestations.** *Open J Obstet Gynecol*, Vol. 1, No. 4 (Dec2011), pp.187-190
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5) Meirik, O; My Huong, NT; Piaggio, G; Bergel, E; von Hertzen, H. (May 2012) **Complications of first-trimester abortion by vacuum aspiration after cervical preparation with and without misoprostol: a multicentre randomised trial.** *Lancet*

- Thank you!

- www.pregnancyadvisorycentre.com.au