

Practice Patterns in the Management of First Trimester Miscarriage

Cook CL, Crane JM, Hutchens D

Introduction



- Spontaneous abortion or miscarriage is the most common early pregnancy complication
 - ❖ 10 – 20% of clinically recognized pregnancies
 - ❖ 80% occur in first 12 weeks
- The Early Pregnancy Assessment Clinic (EPAC) was established at the Health Sciences Center in St. John's in 2003 to allow convenient and timely access to assessment and management for patients with symptoms of possible first trimester miscarriage

Treatment Options

Expectant Management

Surgical Management

- Dilatation and suction curettage

Medical Management

- Misoprostol (Cytotec[®]) most common drug of choice

Misoprostol (Cytotec[®])



- Various opinions on the most appropriate regimen for misoprostol administration
- Available studies entirely inconsistent
 - ❖ Efficacy rates 13 – 96%
- Factors influencing success:
 - ❖ Type of miscarriage
 - ❖ Dosage and duration of use
 - ❖ Time to follow – up
 - ❖ Route of administration

Pharmacodynamics: Misoprostol

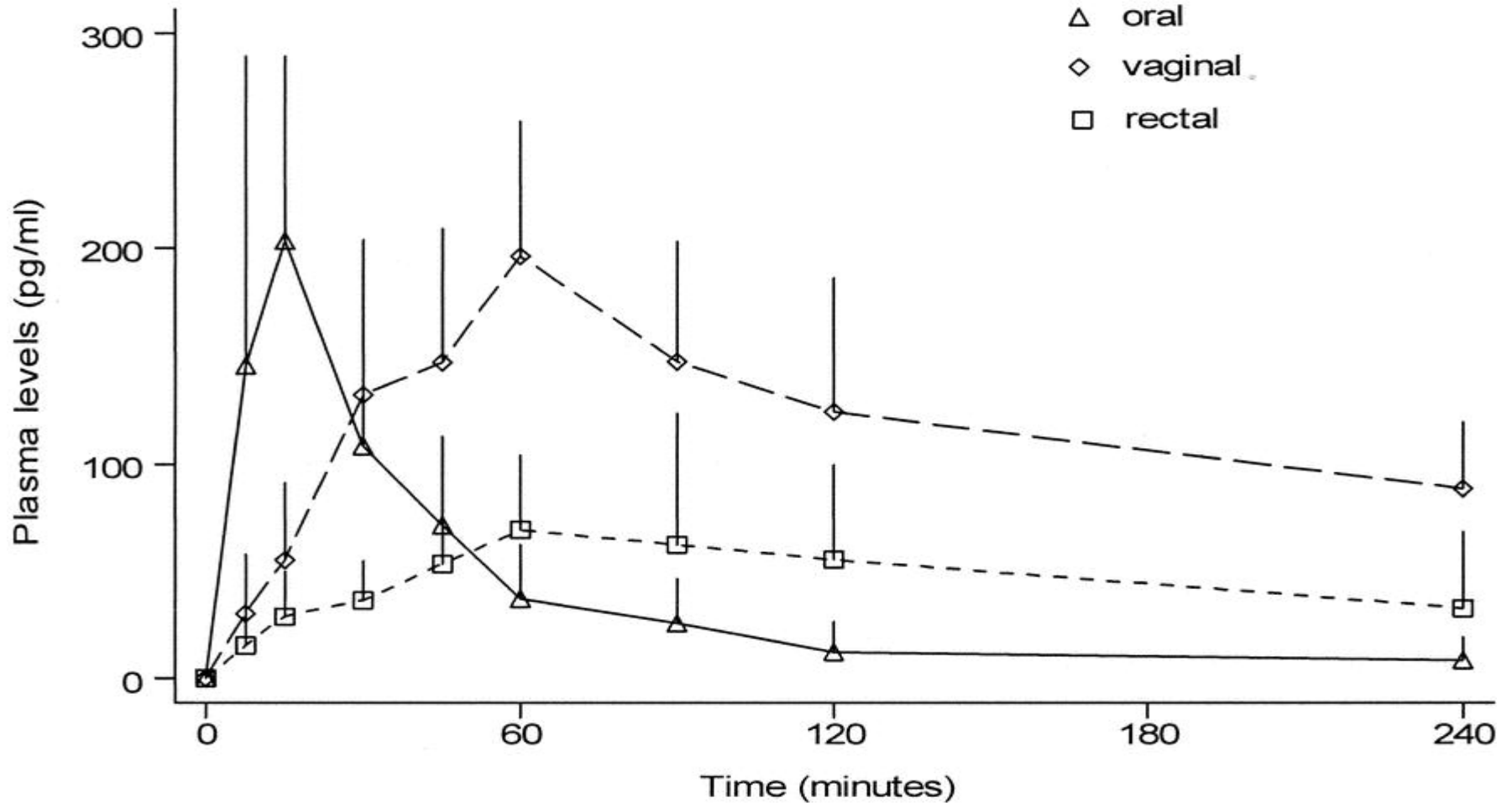


Khan et al.

- 30 patients randomized
- 7 – 14 weeks GA, singleton pregnancies for elective termination
- Given 400 μg misoprostol followed in 3 hours by surgical evacuation
- Examined AUC for vaginal, rectal and oral administration

Khan et al., *Obstet Gynecol.* 2004 May; 103(5Pt1):866–70.

Pharmacodynamics: Misoprostol



Khan et al., *Obstet Gynecol.* 2004 May; 103(5Pt1):866–70.

Misoprostol (Cytotec[®])



Oral Administration:

- Significant variation in study regimens
- Various success rates quoted
- Single dose, 400 μg
 - ❖ 10 – 15% success
- Multiple doses
 - ❖ 50 – 70% success

Misoprostol (Cytotec®)



Vaginal Administration

- RCT; 652 women
- 3:1 misoprostol to suction curettage
- Misoprostol 800 μg pv x 1
 - ❖ Repeated day 3 if not completed
- Overall 16% failure rate for medical management vs. 3% for surgical therapy

Zhang et al. NEJM. 2005;353(8): 761 – 9.

Misoprostol (Cytotec[®])



Vaginal Administration

- Misoprostol group
 - ❖ 71% completed by day 3
 - ❖ 84% completed by day 8
 - ❖ Overall 81% for anembryonic pregnancies
 - ❖ Overall 93% for incomplete abortions

Zhang et al. NEJM. 2005;353(8): 761 – 9.

Consensus Statement



- ‘Expert meeting on Misoprostol’
 - ❖ New York, 2004
 - ❖ Sponsored by Reproductive Health Technologies Project/Gynuity Health Projects
- Instructions for Use – Misoprostol for Treatment of Incomplete Abortion and Miscarriage
 - ❖ Available on SOGC Members Website
 - ❖ Also statement on induced T1 abortion

Consensus Statement



Dosage and Administration:

- *Incomplete abortion*
 - ❖ Misoprostol 600 μg po x 1
- *Missed abortion*
 - ❖ Misoprostol 800 μg pv x 1
- *Induced abortion*
 - ❖ Misoprostol 800 μg pv x 1
 - ❖ May repeat after 24 hours x 1

Study Design



- Retrospective chart review using EPAC records dating from February 2003 to August 2006
- Memorial University Human Investigation Committee approval obtained in February, 2007
- Research funding provided through a grant from the Health Care Foundation

Study Outcomes



- Initial management choice
 - ❖ Expectant, medical, surgical
 - ❖ Influence of β hCG and HGB level
 - ❖ Influence of miscarriage type
- Patients managed with misoprostol
 - ❖ Dosing regimens prescribed
 - ❖ Rates of subsequent D&C
 - ie. failed medical management

Statistical Analysis



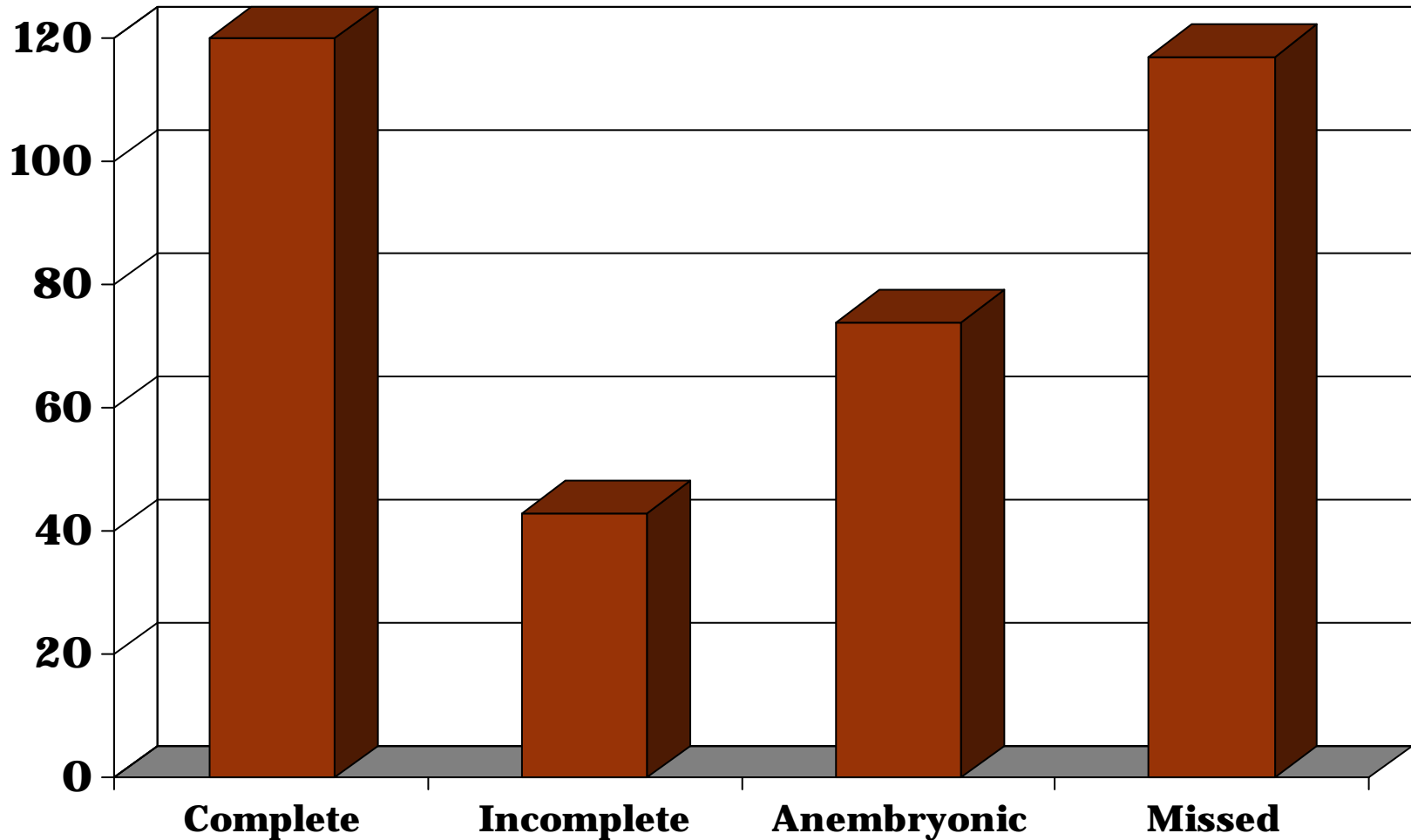
- Convenient sample size
 - ❖ Using all patients records available since the establishment of EPAC in 2003
- Descriptive statistics for initial diagnosis, initial management choice and dosing regimens with the use of misoprostol
- Fisher exact, Chi square and one way ANOVA analyses were performed for other research questions as appropriate
 - ❖ Significance level $p = 0.05$

Initial Diagnosis



- 896 records reviewed
- Initial diagnosis available for 870
 - ❖ Normal IUP – 488 (54.5%)
 - ❖ Complete Abortion – 120 (13.4%)
 - ❖ Incomplete Abortion – 43 (4.8%)
 - ❖ Anembryonic Pregnancy – 74 (8.3%)
 - ❖ Missed Abortion – 117 (13.1%)
 - ❖ Ectopic Pregnancy – 22 (2.5%)
 - ❖ Molar Pregnancy – 6 (0.7%)

Miscarriage Type - Frequencies



Initial Management Choice



	Frequency	Percent
Medical	150	64.4%
Surgical	79	33.9%
Expectant	4	1.7%
<i>Total</i>	233	100%

Management Determinants



Type of Miscarriage:

- No statistically significant difference identified
 - ❖ χ^2 6.489; $p = 0.166$

Initial HGB:

- No statistically significant difference identified
 - ❖ F 0.695; $p = 0.50$
 - ❖ Medical – mean HGB 132.26
 - ❖ Expectant – mean HGB 131.33
 - ❖ Surgical – mean HGB 130.51

β hCG Level:

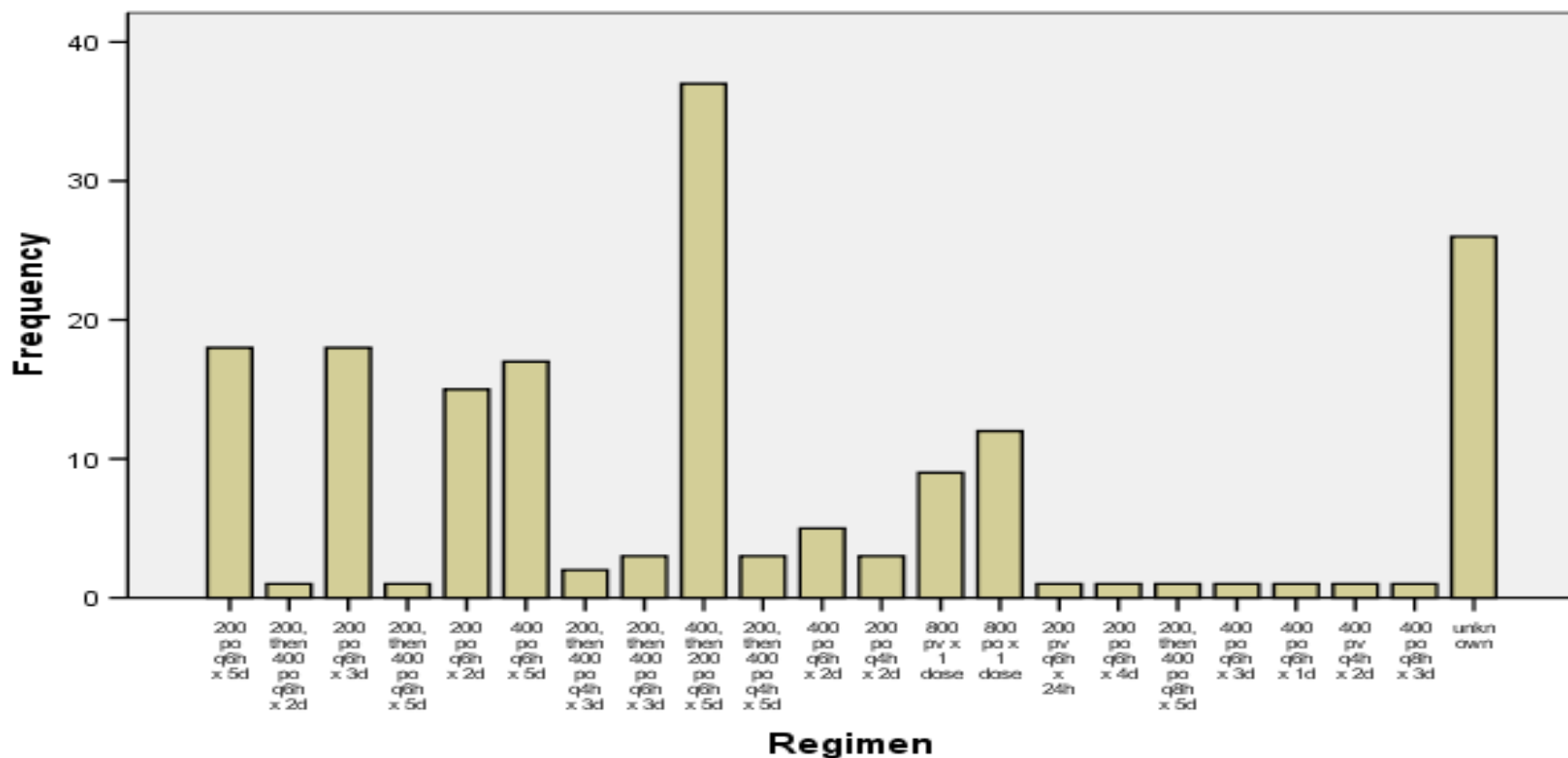
- Statistically significant difference identified between β hCG level and initial management choice (F 4.710; p = 0.01)
 - ❖ Medical – Mean β hCG
 - 10597.51
 - ❖ Expectant – Mean β hCG
 - 13145.00
 - ❖ Surgical – Mean β hCG
 - 19904.83

Ultrasound Gestational Age:

- Statistically significant difference identified between U/S gestational age and initial management choice (F 10.836; p = 0.000)
 - ❖ Medical – Mean GA
 - 48.69 days (6w6d)
 - ❖ Expectant – Mean GA
 - 49.50 days (7w0d)
 - ❖ Surgical – Mean GA
 - 57.78 days (8w2d)

Misoprostol Dosing Regimens

Regimen



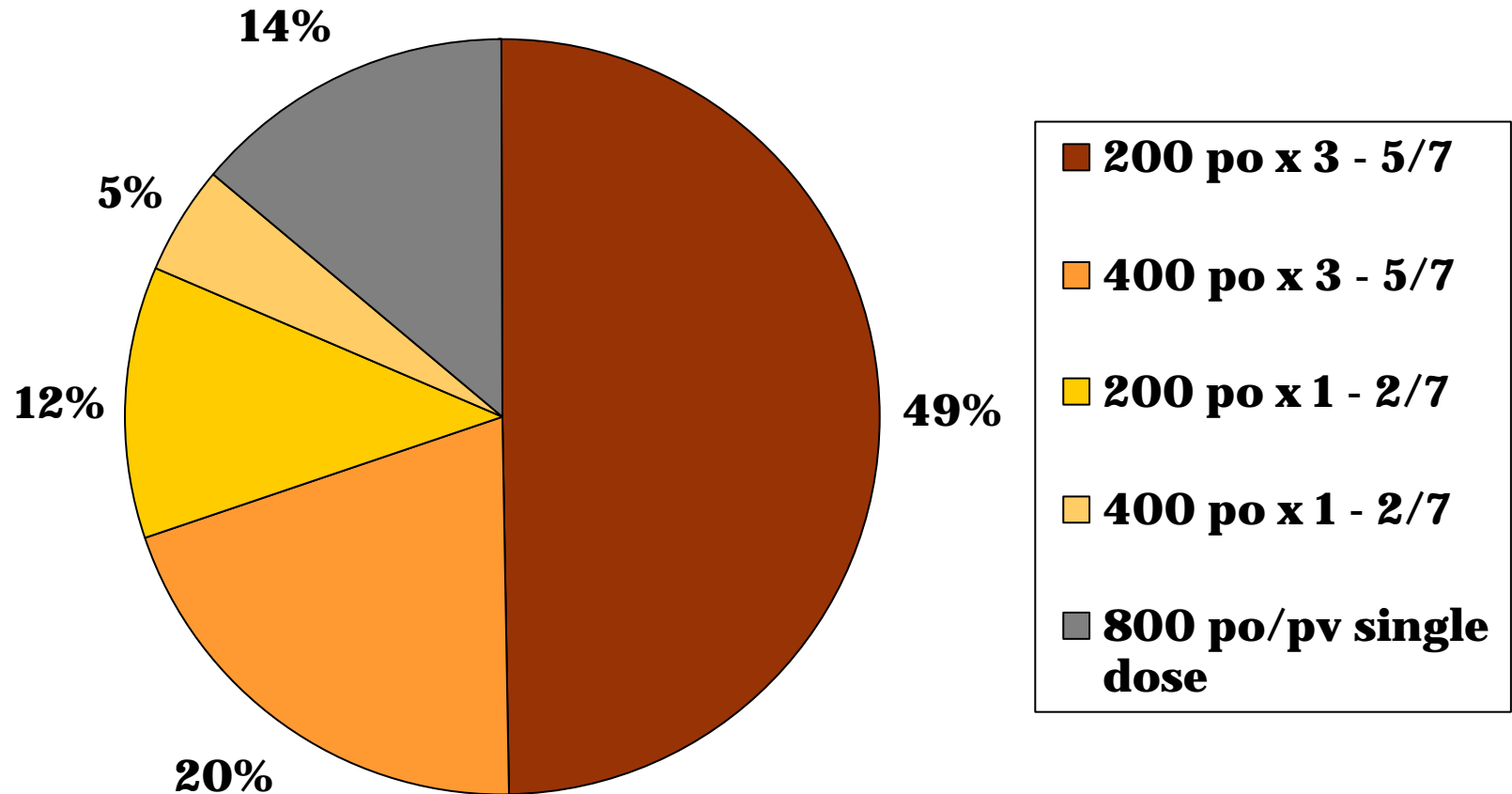
Misoprostol Dosing Regimens



Grouped Regimens:

- Group I – 200 μg po x 3 to 5 days
- Group II – 400 μg po x 3 to 5 days
- Group III – 200 μg po x 1 to 2 days
- Group IV – 400 μg po x 1 to 2 days
- Group V – 800 μg po/pv single dose

Misoprostol Dosing Regimens



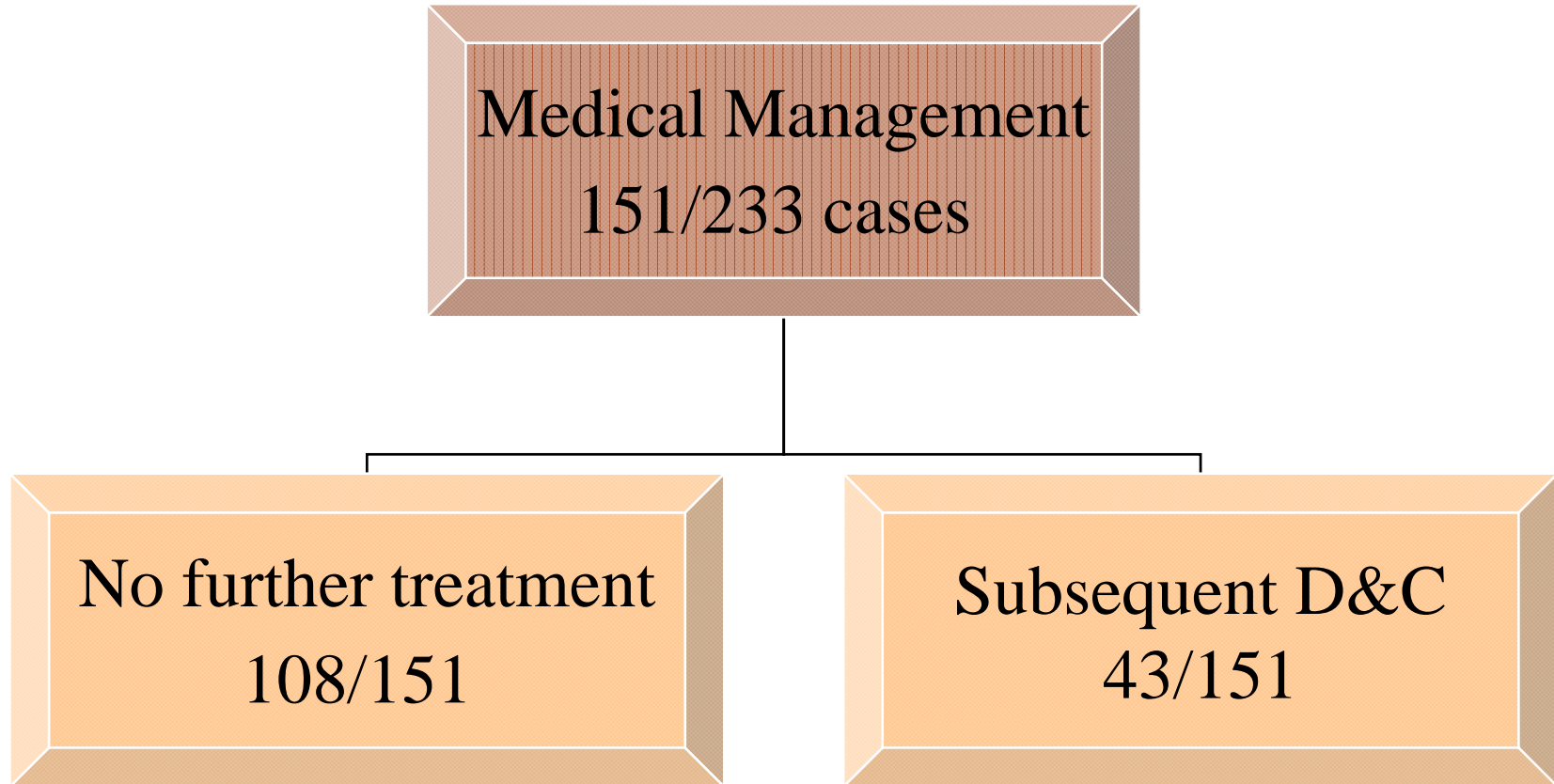
Misoprostol Dosing Regimens



	2003 & 2004	2005 & 2006	Total
Group I	19	56	75
Group II	12	18	30
Group III	10	8	18
Group IV	0	7	7
Group V	0	21	21

χ^2 20.407; $p = 0.000$

Overall Success



28.5% D&C rate for all misoprostol regimens combined

Success of Grouped Regimens



	D&C	No D&C	Total
Group I	25 (33.3%)	50 (66.6%)	75
Group II	6 (20%)	24 (80%)	30
Group III	4 (22.2%)	14 (77.8%)	18
Group IV	2 (28.6%)	5 (71.4%)	7
Group V	6 (28.6%)	15 (71.4%)	21

Fisher exact = 0.7048

Conclusions



- Most patients presenting through EPAC were found to have normal intrauterine gestations
- Medical management of miscarriage was chosen as the initial course of treatment in 64.4% of cases
- Patients with higher GA on U/S and those with higher β hCG levels were more likely to receive surgical management

Conclusions



- In the medical management of miscarriage, there is little consensus among prescribing physicians as to the most appropriate dosing regimen
- The overall D&C rate with medical management of miscarriage at our centre is 28.5%

Study Limitations



- Study design – chart review
 - ❖ Not powered adequately for most outcomes
- EPAC not representative of full spectrum of patients presenting with miscarriage
 - ❖ Patients seen through ER not reviewed
- No information on patient compliance with misoprostol dosing
- Potential loss to follow up in the assessment of D&C rates