

Evidence-based Changes in Medical Abortion Practice

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Learning Objectives

Eligibility, medicines and pain control

- Recognize the efficacy and outcomes of medical abortion when misoprostol is used at home up to 70 days GA
- Misoprostol- potential degradation
- Pain control with medical abortion

Evidence-based practices immediately after medical abortion

- Identify the recommendations and evidence for provision of DepoProvera or implants on the day of mifepristone.

Evidence-based changes in medical abortion follow-up

WHO recommendation for follow-up

- State the alternatives to in-person follow-up:
 - follow-up by telephone
 - follow-up using the semi-quantitative pregnancy test

Expanding eligibility for medical abortion with home use of misoprostol up to 70 days gestational age

- Mifepristone and home use of misoprostol up to 70 days¹
 - Case series, not randomized
- Randomized clinical trial, US²

1. Boersma, The European Journal of Contraception and Reproductive Health Care, 2011

2. Winikoff. Obstetrics & Gynecology, 2012

Case series in Curaçao

- Regimen: mifepristone 200 mg; 24-36 hrs later, misoprostol 800 mcg buccal route
 - Women were given a second dose of misoprostol to take at home if no bleeding occurred w/in 48 hrs
- 307 women
 - 26 (8%) of women with GA 64-70 days
- Overall efficacy: 97.7%

Results

| GA | # of subjects | Suction curettage |
|------------------|---------------|-------------------|
| <u>≤</u> 49 days | 186 | 2 (1.1%) |
| 50-63 days | 95 | 4 (4.2%) |
| 64-70 days | 26 | 1 (3.8%) |

Limitations:

1. No break-down of ongoing pregnancy by gestational age
2. Very small number of women 64-70 days

Prospective, comparative, open-label trial compared two groups:

57-63 days

64-70 days gestational age¹

Participating sites were:

- FPA, Chicago
- PP League of Massachusetts
- PPNYC
- PP of Waco
- Presidential Women's Center (West Palm Beach)
- PP of Minnesota, North Dakota, South Dakota

Methods:

- Mifepristone 200 mg
- Misoprostol 800 mcg via buccal route taken 24-48 hours later at home
- Return visit 7-14 days after using mifepristone
- A 2nd dose of misoprostol could be given for persistent gestational sac or static size of fetus with no cardiac activity

Results

| GA | # of subjects | Ongoing pregnancy | Suction curettage | Adverse events |
|------------|---------------|-------------------|---------------------------|---|
| 57-63 days | 325 | 10 (3.1%) | 6.5% Success= 93.7% | 12 (3.7%) ER visits 2 (0.6%) blood transfusion 1 non-fatal <i>E-coli</i> sepsis |
| 64-70 days | 304 | 9 (3.0%) | 7.2% Success= 92.8% | 14 (4.6%) ER visits 1 (0.3%) blood transfusion |

Study was not powered to detect a difference in safety outcomes because major adverse events are rare.

Potential degradation of misoprostol

Bérard and Fiala, Fiapac 2012, oral abstracts www.bjog.org



Misoprostol is said to be stable at room temperature– but there are caveats to stability

- Misoprostol stability is susceptible to humidity and high temperature
- If blister is nicked or cut in Cytotec® blister pack and is exposed to normal room air:
 - Active ingredient dosage decreases (-5.1% after 48 hours)
- What this means:
 - Misoprostol can become denatured in hot or humid conditions– be alert to storage conditions

Pain control with medical abortion

Review:
Comparison of
acetaminophen &
ibuprofen:

Ibuprofen was more
effective for pain
relief during medical abortion
than acetaminophen.

The mean pain score was 8;
Reduced by 4.8 points with
ibuprofen



Livshits *Fertility & Sterility* 2009

It's possible that cultural factors impact pain

Study of pain during medical abortion in a clinic in rural India:

- 500 mg acetaminophen was offered at the woman's discretion
- On a 7-point Visual Analogue Scale, women reported a median pain score of 2.4
- 96.9% women reported pain medication was adequate

Mundle et al. *Contraception* 2007

RCT in U.S. 2013

- Randomly assigned to ibuprofen 800 mg q. 4-6 hours as needed (117 women) OR
- 800 mg ibuprofen 1 hour before misoprostol, then q. 4-6 hours (111 women)



Raymond et al. *Obstetrics & Gynecology* 2013

Results

There was no difference in the maximum pain score in the two groups

- No difference in pain severity, duration or acceptability

The mean maximum pain scores were:

Ibuprofen 1 hr before miso = 7.1

Ibuprofen with pain onset = 7.3

- No pain benefit with prophylactic ibuprofen
- Significantly less nausea or vomiting in the prophylactic group

How women assessed pain

| | Group: Ibuprofen 1 hr before miso | Group: ibuprofen taken with pain onset |
|----------|-----------------------------------|--|
| A little | 12% | 9% |
| Some | 35% | 23% |
| A lot | 49% | 58% |

No higher risk of failure with either regimen

Pain compared with what women expected

| | |
|---------------------------|------------|
| More than expected | 25% |
| Same as expected | 31% |
| Less than expected | 45% |

Contraception with medical abortion

Provision of highly effective contraception with medical abortion is a problem

- In some settings, a very high percentage of women don't return for follow-up
- No opportunity to provide LARC
- Quick return to fertility (ovulation as early as 8 days after mifepristone)



World Health Organization Recommendations

World Health Organization. (2012) Safe abortion: Technical and policy guidance for health systems, 2nd edition:

- Women may start hormonal contraception as early as the time of administration of the first pill of a medical abortion regimen.

Strength of recommendation: strong.

Quality of evidence based on randomized controlled trials: very low.

Evidence to determine if contraceptive implants or DepoProvera can be administered on the day of mifepristone

- Some organizations/ systems are already doing this based on WHO recommendations
 - Province of Eastern Cape in South Africa
 - Marie Stopes Mexico

We want to know if implants or DMPA administered on the day of mifepristone:

- Reduces efficacy of medical abortion
- Implants: No direct comparison of the binding affinity to human uterine progesterone receptors of etogestrel implant and mifepristone has been done.
 - However, peak concentration of mifepristone occurs earlier than that of etonorgestrel

We want to know if implants or DMPA administered on the day of mifepristone:

- Reduce efficacy of medical abortion
- Cause other unexpected effects
- DepoProvera: anecdotal evidence

UK prospective observational study:

- mifepristone 200 mg, 48 hours later received misoprostol 600 mcg orally or vaginally in facility; further doses q 4-hr
- Contraceptive implants inserted on day of mife

Gestational age

| | Received implants | No implants |
|-------------|-------------------|-------------|
| < 9 weeks | 29 cases (75%) | 36 (92.3%) |
| 9- 13 weeks | 10 cases (26%) | 3 (7.7%) |

Results

| Success rate of women who received implant | Success rate of women who did not receive implant on day of mifepristone |
|--|--|
| 89.7% | 97.4% |

Difficult to draw conclusions from this study due to major flaws:

1. Higher percentage of subjects who received implants on Day One were > 9 weeks
2. Imprecise definition of “incomplete” abortion
3. Regimen used (oral misoprostol) is known to be less effective after 7 weeks
4. No break-out of ongoing pregnancy

Pilot study of implants on Day One

- 20 patients enrolled; 16 returned for follow-up
- Main purpose of the study was to determine satisfaction and continuation rate of the contraceptive implant placed on initial visit
- Mifepristone 200 mg followed by misoprostol by buccal route 24 hrs later
- GA \leq 63 days LMP

Results

- Of the 20 participants:
 - 16 returned for the follow-up 1 week later
 - 3 who missed the f/u were contacted 1 year later
- 19 patients had follow-up; no ongoing pregnancies

Pilot study of DMPA administered at the time of mifepristone

- The regimen used in U.S.
- 17 participants enrolled so far
- 14 participants have returned for follow-up

Results:

- 1 ongoing pregnancy
- 2 additional women had MVA for incomplete abortion

Studies in progress of DMPA and/or implants at the time of mifepristone

Gynuity Health Projects is conducting a study in multiple countries: “A randomized trial to evaluate the risks and benefits of starting either DMPA or etonogestrel implants on the day of mifepristone”

Boston University: “Same-day long-acting reversible contraception for Medication Abortion (SaLMA)”

Karolinska Institutet: “Quickstart of Nexplanon® at Medical Abortion”

Medical abortion follow-up

World Health Organization recommends:

“There is no medical need for a routine follow-up visit following uncomplicated medical abortion using mifepristone followed by misoprostol. However, women should be advised that additional services are available to them if needed or desired.”

Strength of recommendation: strong

**Quality of evidence based on randomized controlled trials:
low**

Alternative follow-up

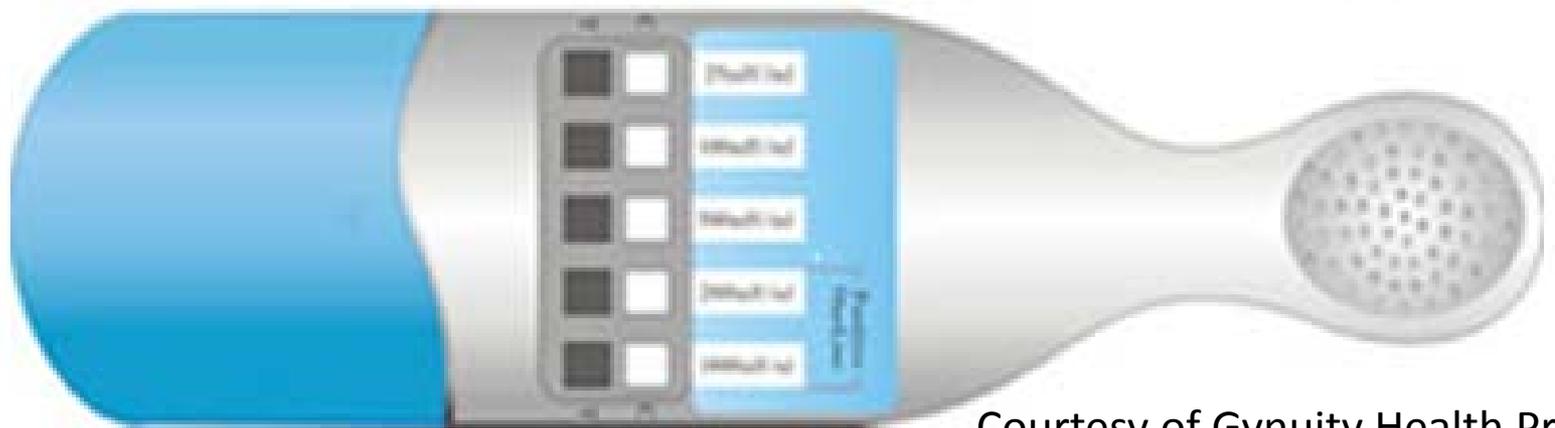
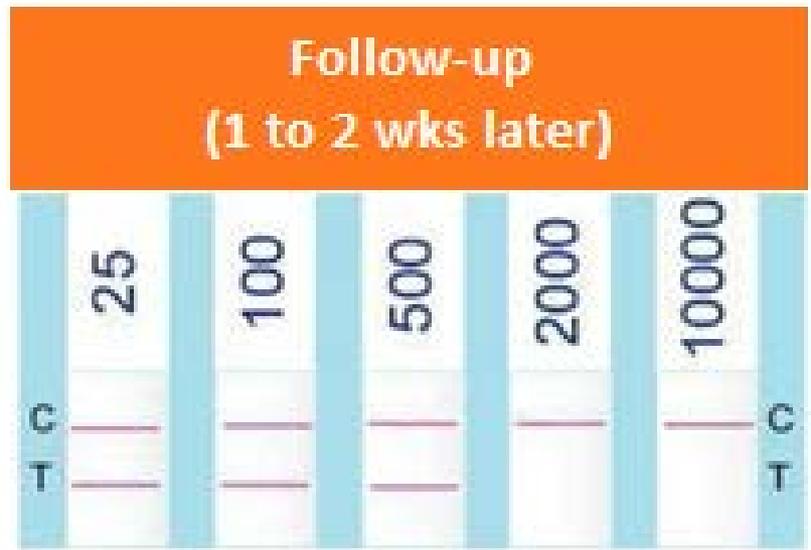
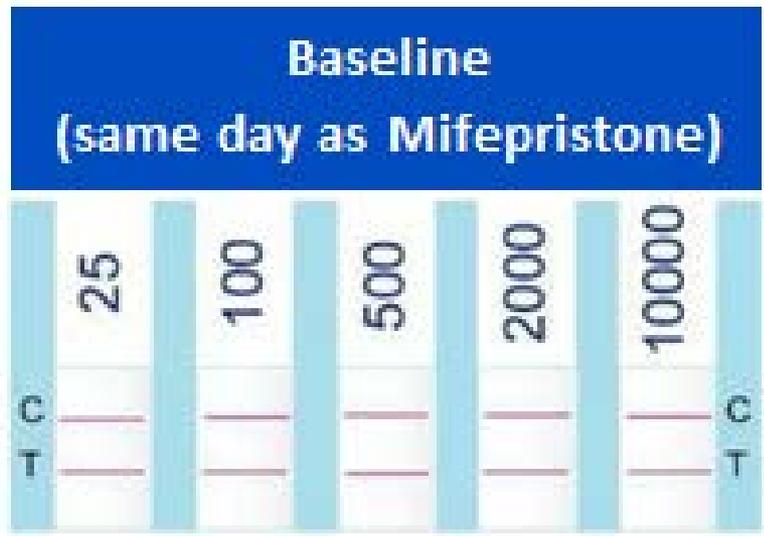
Telephone follow-up has been widely studied and discussed.

We'll focus our attention on a test that adds some precision to home follow-up.

Semi-Quantitative Pregnancy Test

- This is a test that in one paddle, has multiple strips which turn positive at different levels of hCG
- One pregnancy test is done before the woman takes mifepristone
- A woman is given a collection cup and another pregnancy test to take home

SEMI-QUANTITATIVE PREGNANCY TESTS AS MEDICAL ABORTION FOLLOW-UP



Multi-center open-label trial in U.S. of alternative f/u of mife/miso

- GA eligibility \leq 63 days
- Results of 394 women were evaluated
- The test could be either first-morning or random urine sample since an earlier study determined no difference in hCG reading
- One week later, women:
 1. Performed the test at home with instructions
 2. Answered a short questionnaire
 3. Returned to clinic for follow-up

Results

| | |
|---|---|
| Success | 97.5% |
| Surgical intervention | 2.5% |
| Ongoing pregnancy | 0.3% |
| At-home test results indicated no need for in-clinic visit | 92.8% |
| Of 10 women whose test showed no change or increase in hCG: | <ul style="list-style-type: none">• 8 were fine-no intervention needed• 1 woman had persistent sac |
| Tests of 6 women showed decrease in hCG– at clinic, ultrasound showed persistent sac | |

Semi-quantitative pregnancy test study in Vietnam

- 292 women completed the study

RESULTS

Test indicated steady or increasing hCG level

100% of women had ongoing pregnancy

Test indicated decreasing hCG level

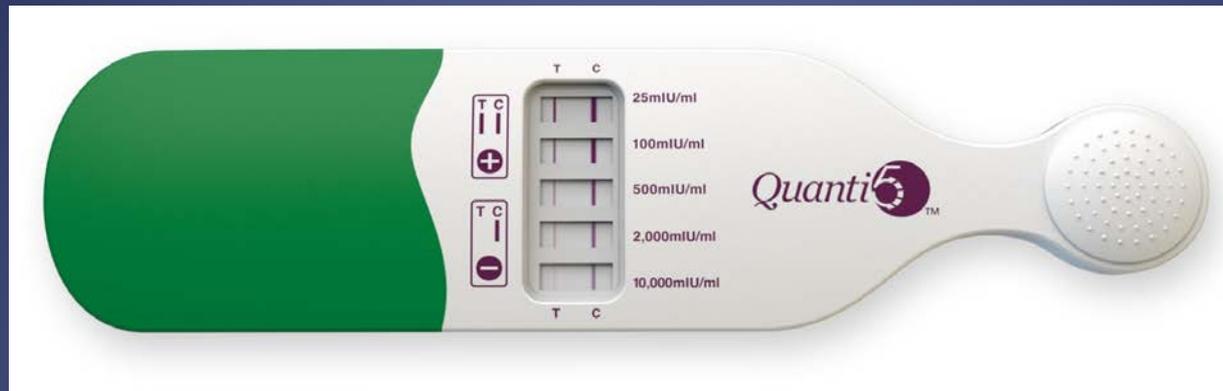
0 women had ongoing pregnancy

Implications of the SQPT studies

- Neither study had a false negative result—a test performed at home that showed decreased hCG but woman was still pregnant.
- Use of this test, combined with a validated questionnaire, could determine with confidence that the medical abortion was successful without necessitating a f/u clinic visit in > 90% of clients

Test will be available in U.S. 1st QTR 2014

Semi-Quantitative Pregnancy Test (SQPT)



Distributed by:



How evidence will make medical abortion more accessible

- Home use of misoprostol through 70 days LMP
- Future studies may identify better pain control medications or combination of medications
- **Quick start of DMPA or implants on Day One!!**
- **Accurate follow-up for most women without routine clinic visit!**