Very early medication abortion (<6 weeks gestation)

Alisa B. Goldberg, MD, MPH

Associate Professor of Obstetrics & Gynecology

Harvard Medical School

Director, Division of Family Planning & Family Planning Fellowship

Brigham and Women's Hospital

Vice President, Research and Clinical Training,

Planned Parenthood League of MA

FIAPAC, Nantes

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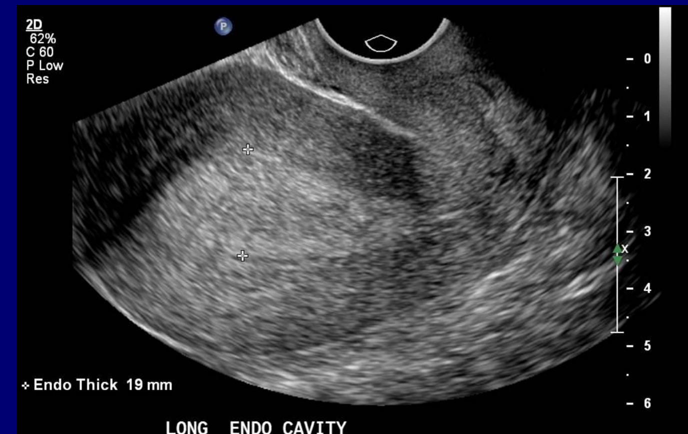
Case

- 30 y.o. G2P1 with regular cycles, 3 days late for menses
- Two home urine pregnancy tests, both positive
- Calls clinic to schedule a medication abortion ASAP
- Appointment booked for 3 days later
  - 4 weeks 6 days LMP (= 34 days amenorrhea)
- Upon presentation she is asymptomatic and pelvic ultrasound reveals no gestational sac
- Urine pregnancy test is positive



OBJECTIVES

- Understand risks and benefits of offering medication abortion very early in pregnancy (<6 wks)
  - Including with pregnancy of unknown location (PUL)
- Gain familiarity with protocols for offering medication abortion for women with PUL
- Review data for follow-up with serial hcg testing

Abortion shifting earlier in gestation

- U.S. 2006[1]
  - 27% of all first trimester abortions ≤ 6 weeks
- U.S. 2014[2]
  - 41% of all first trimester abortions ≤ 6 weeks

1 Pazol et.al., CDC MMWR 2009 (2006 data)
2 Jatlaoui et.al., CDC MMWR 2017 (2014 data)

Medication abortion is increasing

The percentage of abortions completed with mifepristone and misoprostol has increased steadily over time

	Percentage of early abortions (≤ 8-10wks) by medication abortion	
	2006-2008	2014-2017
U.S.	17% (2008)	43% (2014)
U.K.	43% (2007)	80% (2017)
France	48% (2006)	64% (2016)
Sweden	83% (2008)	95% (2017)

US: Jones and Jerman 2017, Guttmacher Institute (2014 data)
UK: Dept of Health and Social Care; abortion statistics 2017
France: http://drees.solidarites-sante.gouv.fr/IMG/pdf/er_1013.pdf
Sweden: Socialstyrelsen.se, through 2017

Medical abortion protocol in U.S.
March 2016 FDA updated label

- ≤ 70 days gestation
- Mifepristone 200 mg PO dispensed in-person
- Misoprostol 800 mcg buccally 24- 48h later at home
- Follow-up with healthcare provider in 7-14 days
  - To ensure pregnancy has passed and patient is well

Efficacy of medication abortion with mifepristone + buccal misoprostol

Systematic review: 20 studies, N=33,846 women

Mifepristone: 200 mg, Misoprostol: mostly 800 mcg

Gestational duration	Efficacy	Ongoing pregnancy
49 days or less (N=12,555)	98.1 (97.9-98.3)	0.4 (0.3-0.5)
50-56 days (N=4161)	96.7 (96.1-97.2)	0.8 (0.6-1.2)
57-63 days (N=2202)	95.2 (94.2-96.0)	1.8 (1.3-2.5)
64-70 days (N=332)	93.1 (89.6-95.5)	2.9 (1.4-5.7)

Chen, Creinin, Obstet Gynecol 2015

Efficacy of medical abortion at <6 weeks gestation

- Systematic review comparing efficacy of medical abortion <42 days to 42-49 days
  - <42 days (N=5938, collectively)
- No difference in efficacy between groups
  - 6 RCTs: OR 0.51 (0.21-1.27)
  - 9 prospective observational: OR 0.90 (0.60-1.33)
- Unable to separately evaluate <35 days, or no gestational sac

Kapp, Baldwin, Rodriguez, Contraception 2018

What is different at < 6 weeks?

Difficulty with diagnosis

Often cannot definitively diagnose intrauterine pregnancy (IUP), early pregnancy loss (EPL) or ectopic pregnancy

Close follow-up required

Potential benefits of offering medication abortion without definitive dx of IUP

- Eliminate delays in treatment
  - Reduce repeat visits to clinic
- Increase patient satisfaction
  - Get their desired abortion upon presentation
- Facilitate earlier diagnosis
  - Intrauterine pregnancy vs. ectopic

Potential risks of offering medication abortion without definitive dx of IUP

- Missed or delayed diagnosis of ectopic**
  - If patient does not adhere to follow-up
- Over-treatment
  - Chemical pregnancies and some early pregnancy loss (EPL)
- Expense
  - For women
    - Abortion often out-of-pocket expense

Diagnosing intrauterine pregnancy

Earlier presentation for abortion, increased likelihood of not visualizing IUP on sono

Gestational age	Expected markers of intrauterine pregnancy on transvaginal ultrasound
4.5-5.0 wks	Gestational sac (GS), 2-3 mm Intradecidual sign - eccentrically located GS Double decidua
5.0-5.5 wks	GS, yolk sac (YS) -YS initially seen as 2 parallel lines -YS seen by 8-10 mm GS
6.0 wks	GS, YS, fetal pole (CRL)
6.0-6.5 wks	GS, YS, CRL, fetal heart tones (FHT), FHT early as 1-4 mm CRL

Rodgers et.al. Radiographics 2015

Medical abortion without a yolk sac

- Retrospective study (N=1155)
  - After protocol change in 2011
- Women presenting for MAB at <6 wks
- Allowed to proceed with MAB without yolk sac if
  - LMP < 6 wks
  - Eccentrically placed GS $\geq$ 3 mm with decidual reaction
  - No signs or sx of ectopic (bleeding, pain)
  - No ectopic risk factors (sterilization, tubal surgery, prior ectopic)

Results

- 1030 (89%) had yolk sac (IUP)

Heller and Cameron. J Fam Plann Reprod Health Care 2015

Medical abortion without a yolk sac

Results for women without definitive IUP

- 87 (7.5%) met criteria for MAB w/o YS
  - 76% same-day MAB, 24% had additional testing first
  - No ectopics, all had successful MAB
- 16 (1.4%) had empty uterus (1 ectopic, 0.08%)
  - Not eligible for same-day MAB
  - 15 with PUL had additional testing, IUP and eventual MAB
- 17 (1.5%) had sac, but did not meet criteria (no ectopics)
  - 9 (53%) had immediate MAB
  - 8 (47%) had additional testing, IUP and eventual MAB
- 5 (0.4%) definitive EPL→ treated medically

Heller and Cameron. J Fam Plann Reprod Health Care 2015

Medical abortion in the setting of PUL (no gestational sac)

Li study #1

- RCT to evaluate lower dose mifepristone
- 2500 women (LMP≤35 days)
  - Baseline serum hcg and vaginal ultrasound
    - Thickened stripe or small GS
  - 5 arms, doses from 50-150 mg mifepristone
  - 24 h later 200 mcg oral misoprostol, in hospital
  - Observed 6h in hospital, expelled tissue→pathology
    - If tissue confirmed: weekly hcg + sono (50% drop + ut. empty)
    - If no tissue confirmed, return in 3 days for hcg + sono
    - If no decline by 50%, repeat hcg and sono Q3 days
    - All followed until next menses

Li et.al. Reprod Sciences 2015

Li study #1 (con't)

- Results
  - Mean days of amenorrhea = 31 $\pm$ 2
  - Baseline serum hcg 620-756
  - Endometrial thickness 1.17-1.22 cm
  - Complete abortion rates 97-98%
    - No differnce by mife dose
  - No suspected or confirmed ectopics

Li et.al. Reprod Sciences 2015

Li study #2

- RCT, N=744
  - ≤35 days LMP, elevated serum hcg, thickened stripe
  - 75 mg mife, 24h later 400 oral misoprostol
  - Hospital vs. home misoprostol
    - Hospital follow-up (same as Li #1)
    - Home follow-up, urine hcg testing
      - 24 h, 1 week, 2 weeks (phone calls)
- Results
  - 29% had discernible GS, EM thickness 1.2 cm
  - Complete abortion 98% both groups
  - 99% follow-up both groups
  - All with complete abortions had (-) UPT by week 2
  - 3 suspected ectopics (0.4%) - not confirmed, no treatment reported

Li et.al. Reprod Sciences 2017

Planned Parenthood protocol
(PPLM affiliate protocol, PPFA standards)

Medication abortion in setting of PUL is permitted when patient is low-risk for ectopic and when combined with close follow-up to exclude ectopic pregnancy

Eligibility Criteria

- $\leq$ 35 days LMP
- Positive urine hcg
- Asymptomatic (no bleeding, no pain)
- No ectopic risk factors (tubal surgery, IUD in situ, prior ectopic)
- *Able and willing to comply with close follow-up*

PPLM protocol

- Clinical management
  - Initiate same-day medical abortion
  - Serum hcg sent on day of mifepristone
    - Results return after patient has left clinic
  - Management based on hcg
    - hCG <2000: proceed as planned. Repeat serum hcg 48-72 hours after misoprostol (day 3-5 after mife)
    - hCG 2000-2999: formal diagnostic ultrasound on day hcg results received, or aspirate, or send to ER
    - hCG >3000: or formal ultrasound-no IUP send to ER

Planned Parenthood protocol (con't)

- hCG follow-up
  - If hcg drops $\geq$ 50% 3-5 days after mifepristone, no additional follow-up required
  - If hcg drops $\leq$ 50%, evaluate for continuing pregnancy or ectopic

NAF (National Abortion Federation)

Protocol very similar

Serial hCG follow-up after medical abortion

Ultrasound vs. serum β-hCG

- N=217, <49 days preg
- All had pre and post med ab sono and serum β-hCG
- Follow-up day 6-18
- 2 ongoing pregnancies, 2 retained sacs
- Ongoing pregs: serum β-hCG increased

20% of initial value = 99.5% PPV for expulsion

- This is where 80% drop at 1 week f/u rule came from*

Fiala et.al., Eur J Obstet Gynecol 2003

Ultrasound vs. serum β-hCG

- RCT (N=376)
- Ultrasound vs. serum hCG med ab follow-up
- Primary outcome: additional intervention beyond one scheduled ultrasound or hCG.
  - Suction curettage, additional miso, visits (clinic, ED), testing

Results

- 151 ultrasound, 159 hCG by 2 wks
  - More loss to follow-up with ultrasound (19 vs. 11% $p=0.04$)
- No difference in unplanned interventions:
  - Any: 7% ultrasound vs. 8% β-hCG ($p=0.6$)
  - D&C: 4% ultrasound vs. 1% β-hCG ($p=0.16$)

Dayananda, Goldberg et.al. Obstet Gynecol 2013

Serum hCG decline early days after medical abortion

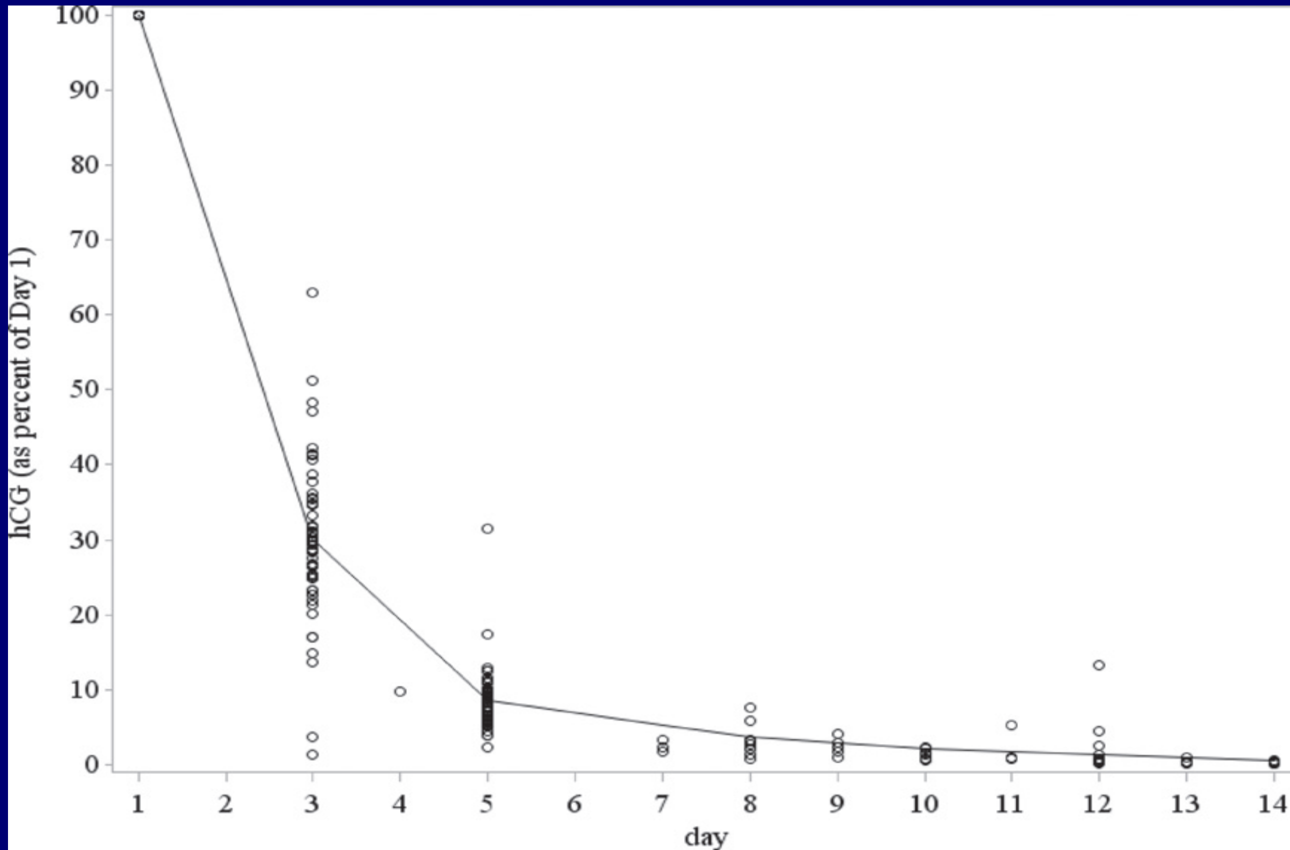


Fig. 2. Decrease in serum hCG from Day 1 among women with complete abortion, n=57.

Pocius, Goldberg, et al. Contraception 2017

Serum hCG decline after medical abortion

With complete abortion

Day(s) after mifepristone	N	Decrease in hCG from Day 1 (mean ± SD)	Range
3	55	70.0 ±10.6%	36.9-98.6%
5	49	91.4 ±4.4%	68.4-97.7%
7-9	18	97.1 ±1.7%	92.4-99.2%
10-11	11	98.5 ±1.4%	94.7-99.6%
12-14	23	98.7 ±2.8%	86.7-99.9%

Others:

1. Persistent gestational sac: decline, 41% day 3, 74% day 5, 79% day 7
2. Ectopic: decline, 0.4% day 3, increase 17% day 5

Pocius, Goldberg et al. Contraception 2017

hCG trend in ectopic pregnancy

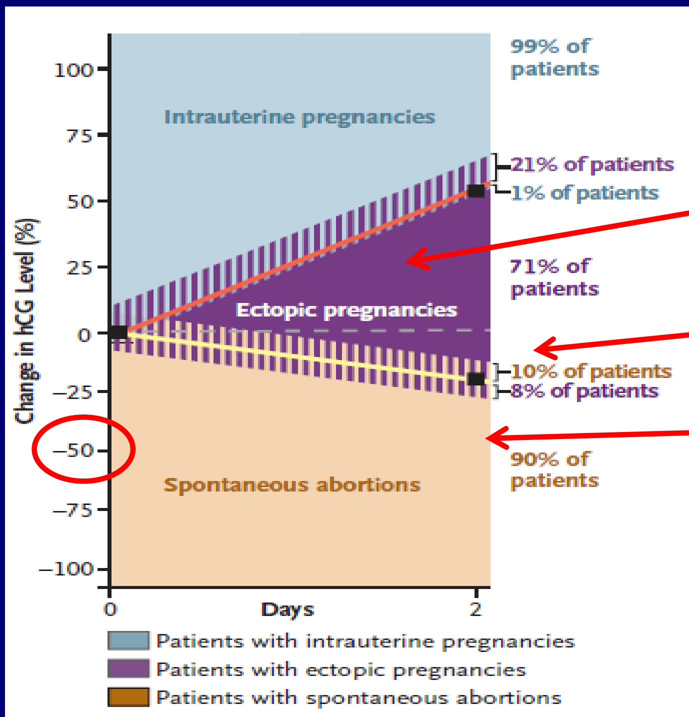


Figure 2. Change in the hCG Level in Intrauterine Pregnancy, Ectopic Pregnancy, and Spontaneous Abortion.
An increase or decrease in the serial human chorionic gonadotropin (hCG) level in a woman with an ectopic pregnancy is outside the range expected for that of a woman with a growing intrauterine pregnancy or a spontaneous abortion 71% of the time. However, the increase in the hCG level in a woman with an ectopic pregnancy can mimic that of a growing intrauterine pregnancy 21% of the time, and the decrease in the hCG level can mimic that of a spontaneous abortion 8% of the time.

Ectopic pregnancies

Most patients have slow rise or flat hcg

Some have slowly declining hcg

When declining, none of the ectopics had $\geq$ 50% decline within 48 hours

Barnhart, NEJM 2009

Summary

Offering same-day start of medication abortion to women with pregnancy of unknown location is a reasonable clinical option:

- Low risk of ectopic pregnancy
- Close follow-up to exclude ectopic pregnancy

More research needed

- Same-day start with simultaneous testing r/o ectopic versus delay-for-diagnosis

Case

- Patient 34 d amenorrhea, thickened stripe, no symptoms
- No history of tubal surgery, no IUD in situ, no prior ectopic
- States she understands risk of ectopic and agrees to close follow-up
- You give patient mifepristone in clinic, misoprostol to take home and draw her blood for serum hcg.
  - Serum hcg = 732 (returns after she leaves)
- She takes misoprostol 24h later
- Thinks she passed the pregnancy and feels well
- Goes to local lab for serum hCG 48h after misoprostol
  - Serum hcg (day 4) = 146 (80% decline)
- Done! ☺

Thank You

Questions?