Management of First Trimester Pregnancy Complications

Presented by Panna Lossy, MD

Thanks to Larry Leeman, MD and Linda Prine, MD

Objectives
• Understand the differential and the work-up needed for the patient with first trimester bleeding
• Compare the risks and benefits of expectant management vs. medical or surgical intervention for miscarriage
• Understand how to use vaginal misoprostol for medical management of miscarriage
• Understand the use of methotrexate for treatment of ectopic pregnancy

Epidemiology of Early Pregnancy Loss
• One in four women will have a miscarriage during her lifetime
• 15-20% of diagnosed pregnancies result in abnormal pregnancies
• May only form a gestational sac (blighted ovum or anembryonic pregnancy) or demise may occur after embryo forms. Usually under 10 weeks gestational age

Marquita: six weeks from LMP, bleeding

What additional history?
What do we look for on physical?

Clinical Presentations of First Trimester Losses
• Vaginal bleeding
• No fetal heart beat on Doppler
• Report from radiology - non-viable pregnancy on ultrasound
• Pelvic pain with positive pregnancy test

Key Counseling Issues
• Woman needs to know that miscarriage is not her fault
• Nothing she did caused this to happen
• Very important to give this information to her partner, too.
• Remember – Half of pregnancies are unintended – not everyone is sad to lose a pregnancy
**Ultrasound Findings/bHcg:**

- Anembryonic pregnancy: Gestational sac of >18 mm
- Without pole or yolk sac OR if < 18 mm with no change on rescan 7 days later
- Embryonic Demise: Fetal pole of >6mm by CRL without heart beat or if ≤6 mm no change in rescan 7 days later
- A gestational sac should be visible in the uterus on vaginal sono if the HCG > 2000

**“Surgical” Options**

- Vacuum aspiration includes Manual Vacuum Aspiration (MVA) vs. Electrical Vacuum Aspiration (EVA)
- Sharp curettage (D and C) no longer an acceptable option due to higher complication rates (Cochrane review 1993)

**MVA Instruments and Supplies**

**Uterine aspiration**

- Manual Vacuum Aspirator
- Electric Vacuum Aspirator

**MVA in ED/Labor Ward vs. Suction D & C (EVA) in OR**

- Waiting time reduced by 52%
- Mean procedure time reduced from 33 to 19 minutes
- Costs reduced by 41% ($1404 to $827, P < .01)
- Better yet - MVA in family medicine office

Marquita

What are the options for how to manage her miscarriage?
Moving Abortion to an Outpatient Setting: Bellevue Hospital

Methods
- Compared costs, staff, complications: OR vs. outpatient
- N = 967; Patients undergoing first-trimester pregnancy termination in outpatient procedure room (2000-2003)

Results

<table>
<thead>
<tr>
<th></th>
<th>Outpatient MVA</th>
<th>Operating Room</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost per procedure</td>
<td>$167</td>
<td>$1,435</td>
</tr>
<tr>
<td>No. of staff</td>
<td>2</td>
<td>5</td>
</tr>
</tbody>
</table>

$1268 savings

No reported complications with outpatient MVA
Bellevue Hospital Improvement Reports, March 2002

Potential Risks of Expectant Management - All Rare

- Infection
- Need for emergent uterine aspiration
- Hemorrhage/blood transfusion

Worth noting: these risks also exist for surgical or medical management and are not statistically different...

Potential Benefits of Expectant Management

- Avoid risks (albeit uncommon) of uterine aspiration including perforation
- Decrease risk of excess curettage (Asherman's syndrome)
- Patient preference
- Cost

Contraindications to Expectant Management

- Excess blood loss
- Infection
- Inability to access an emergent uterine aspiration
- Patient choice

Success of Expectant Management

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Complete day 7</th>
<th>Complete day 14</th>
<th>Success day 49</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incomplete</td>
<td>221</td>
<td>117 (53%)</td>
<td>185 (84%)</td>
<td>201 (91%)</td>
</tr>
<tr>
<td>Missed</td>
<td>138</td>
<td>41 (30%)</td>
<td>81 (59%)</td>
<td>105 (76%)</td>
</tr>
<tr>
<td>Anembryonic</td>
<td>92</td>
<td>23 (25%)</td>
<td>48 (52%)</td>
<td>61 (66%)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>451</td>
<td>181 (40%)</td>
<td>314 (70%)</td>
<td>367 (81%)</td>
</tr>
</tbody>
</table>


Numbers to remember

- Half of incomplete abortions pass by 1 week.
- For Missed Abortions (Anembryonic or Demise)
  - ¼ - 1/3 pass spontaneously at 1 week
  - ½ pass spontaneously at 2 weeks
  - ¼ - 1/3 are still pregnant a 7 weeks
- Anembryonic gestations are the most difficult to pass.
Misoprostol for Early Pregnancy Loss

- Many small studies with varying doses and routes of administration
- Vaginal misoprostol appears to have success rates between 80-90%
- The reason women choose it - still feels somewhat natural yet the expulsion timing is more predictable

Guidelines for Misoprostol Use for Early Pregnancy Loss

- Non-viable pregnancy is diagnosed by ultrasound and/or subnormally rising quantitative hCG levels
- 10 weeks or under by ultrasound
- Rule out ectopic pregnancy because medical treatment for ectopic pregnancy differs from that for a missed abortion
- Testing: Ultrasound, Rh screen, hematocrit, quantitative serum hCG (quant not always needed if ultrasound diagnosis is definitive)

Dosage for Misoprostol Use
Based on Gynuity Consensus Guidelines

- For incomplete abortions
  - 600mcg PO
- For missed abortions (anembryonic or demise)
  - 800 mcg PV
- Repeat dose at 48 hours if no significant bleeding has occurred (i.e. as much as a period)

Effectiveness of Misoprostol vs. Expectant Management

<table>
<thead>
<tr>
<th></th>
<th>Effectiveness of Expectant</th>
<th>Effectiveness of Misoprostol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incomplete Abortion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>At 1 week</td>
<td>53%</td>
<td>93%</td>
</tr>
<tr>
<td>At 7 weeks</td>
<td>91%</td>
<td></td>
</tr>
<tr>
<td>Embryonic Demise</td>
<td></td>
<td></td>
</tr>
<tr>
<td>At 1 week</td>
<td>30%</td>
<td>88%</td>
</tr>
<tr>
<td>At 7 weeks</td>
<td>76%</td>
<td></td>
</tr>
<tr>
<td>Anembryonic Preg.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>At 1 week</td>
<td>25%</td>
<td>81%</td>
</tr>
<tr>
<td>At 7 weeks</td>
<td>66%</td>
<td></td>
</tr>
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</table>

Numbers to remember

- Misoprostol makes the miscarriage 2 -3 times faster.
- With Missed abortion 80 – 90% complete the miscarriage at 1 week (compared with 25-30%with expectant management)
- With incomplete abortion >90% complete at one week (compared with about 50% with expectant management)

Side Effects of Misoprostol
(same as for medication abortion)

- Bleeding – typically lasts up to 2 weeks with spotting until next period
- Cramping – usually starts within the first few hours, NSAIDs can be used
- Fevers and/or chills – common side effect. If lasts >24 hours, evaluate for infection
- Nausea and vomiting – more common after oral misoprostol. Should resolve in 6 hours
- Diarrhea – also more common after oral misoprostol and should resolve in 24 hours
Patient Instructions (same as for expectant management)

- Call for “heavy bleeding” defined as soaking two pads per hour for more than 2 hours
- Patient does NOT need to bring products of conception back to the provider
- Contact information for quickly reaching provider must be supplied
- Pain medications prescribed

Failure to Pass Tissue

- If no passage of tissue occurs (the patient has not bled as much as a period) within 12-24 hours, the patient may use the second vaginal dose of 800 mcg misoprostol
- If no passage of tissue occurs by 1-2 weeks consider MVA, patient may continue expectant management if desired

Follow-up in One to Two Weeks to Ensure Completion

Diagnose completion by either:

1) Follow-up quantitative serum hCG after passage of tissue (a drop of 50% expected 48-72 hours after passage of tissue)
2) A transvaginal ultrasound with absence of sac

Note: if one of these criteria has been met, no further follow-up of serum hCGs is warranted.

Stephanie: 6 weeks from LMP

Came to you for unintended pregnancy, sure of her dates
No pregnancy on ultrasound
Quantitative HCG = 2100

What about Ectopics?

- bHcg rising but not increasing by >66% in 48 hours may be nonviable Intrauterine Pregnancy (IUP)
- Date of LMP not consistent with no IUP on ultrasound
- No IUP on transvaginal ultrasound (beware of “pseudosac”) with bHcg > 2000
- If woman has symptoms – bring to Emergency Room STAT!
Role for Expectant Management

Criteria include:

- Minimal pain or bleeding
- Reliable follow-up
- No evidence of tubal rupture
- $\beta$hCG <1000 and falling
- Adnexal mass <3cm, or not detected
- No embryonic heart beat

Medical Treatment: Methotrexate (MTX)

- Safe, effective, less costly than surgery
- Equal or better fertility preservation

Criteria for use:

- Stable vital signs, few symptoms
- No contraindication to drug
- Access to emergent care and reliable for follow-up
- Unruptured ectopic
- Absence of embryonic cardiac activity
- Ectopic mass <3-4cm or not visible
- $\beta$hCG levels <5000 mIU/ml (relative)

- Single vs. Multidose regimens

HCG Level and MTX Success

<table>
<thead>
<tr>
<th>Initial Beta HCG Rate</th>
<th>Success</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1000</td>
<td>98%</td>
</tr>
<tr>
<td>2000-4999</td>
<td>92%</td>
</tr>
<tr>
<td>5000-9999</td>
<td>87%</td>
</tr>
<tr>
<td>&gt;10000</td>
<td>68%</td>
</tr>
</tbody>
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Lipscomb NEJM 1999; 341:1976

Methotrexate Dosing: Single Regimen

- Single dose IM regimen with 1mg/kg or 50mg/m2

- Obtain serum $\beta$hCG on 4th and 7th day post-treatment
  - Follow until level reaches 5mIU/ml (3-4 wks)

- Expect 15% or greater drop between days 4 and 7

- Repeat dose on day #7 (if without appropriate fall) needed in 20%

- Side effects minimal - mild nausea

Surgical Management

Criteria for selecting surgery

- Unstable vital signs or hemoperitoneum
- Uncertain diagnosis
- Advanced ectopic pregnancy
- Unreliable follow-up
- Does not meet criteria for expectant management or methotrexate

Methotrexate Summary

- Can save a woman from surgery and from loss of her fallopian tube

- Need setting with close follow-up and quick phone contact

- $\beta$hCG levels for acceptable candidate varies in different protocols

- Rupture with bleeding can happen at any level – higher levels = higher risk
Alisha • 39 y/o presents to clinic for vag bleeding. LMP 6 weeks ago. Reports spotting X 1 week but no overt bleeding. • Bimanual exam grapefruit size uterus, non tender, min blood in vault • Differential? Next steps?

Tips about sizing • This is a physical exam skill worth practicing! • Is the uterus anterior or posterior? • Can you feel something bulging back/filling the pelvis? • What size fruit? • Lemon = non pregnant – 7 weeks • Orange= 8-10 weeks • Grapefruit = 10-12 weeks

Alisha’s ultrasound

Partial vs Complete Mole

<table>
<thead>
<tr>
<th></th>
<th>Partial Mole</th>
<th>Complete Mole</th>
</tr>
</thead>
<tbody>
<tr>
<td>Embryo Present?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Cardiac Activity</td>
<td>Sometimes</td>
<td>Never</td>
</tr>
<tr>
<td>Amniotic Fluid</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Karyotype</td>
<td>69 XXXYXXXYY</td>
<td>46 XXXXY</td>
</tr>
<tr>
<td>HCG level</td>
<td>Normal</td>
<td>Very High</td>
</tr>
</tbody>
</table>

Molar Pregnancy • 1 in 1000 pregnancies in North America • More common in Asia • Risk Factors: • Extremes of Age – Especially >35 • Hx of Molar Pregnancy

Symptoms of Molar Pregnancy • Vaginal Bleeding • Enlarged Uterus • Pelvic pressure or pain • Anemia • Hyperemesis gravidarum • Preeclampsia before 20 weeks • Vaginal passage of hydropic vessicals
Pearls about Molar Pregnancy

- Commonly diagnosed as incomplete or missed abortion on ultrasound
- POC are thicker and more cystic than normal POC – Looks seaweed bulbs
- 90% are benign and there is not malignant disease but you have to follow quants to zero

Cases for Review: Sonia

- LMP 10 weeks ago
- Started spotting 3 days ago
- Now having heavier cramping with bleeding
- Appears comfortable, normal vital signs

Sonia, Continued

Your exam reveals the following:

- Abdomen: soft, nontender
- Vaginal vault: scant amount of blood, consistent with a menses
- Cervix: os open, tissue at os noted
- Bimanual exam: uterus enlarged, approx. 8 weeks size, nontender
- Hemoglobin: 12.2
- Urine pregnancy test: positive

What is your working diagnosis?
Would you do further testing?
How would you counsel her?

Sonia’s ultrasound - no FH

What are the treatment options available for her?

If she elects medical or expectant management, what would you instruct her about what she might see when she passes the pregnancy?

Blanca

- Blanca comes to you after being seen for a positive pregnancy test two days ago by one of your colleagues, who enrolled her in prenatal care and ordered an ultrasound and quant because of her unsure LMP
- She actually wants a pregnancy termination. Her quant was 3500, and the ultrasound reports no IUP.
- She is asymptomatic.

Diagnosis?
Blanca, continued

• One possibility is inadequate ultrasound, so you can repeat it if you can easily do so.
• Other option - repeat the quant stat.
• Treatment: methotrexate or (if IUP still possible) mifepristone AND methotrexate

Katie

Presents for prenatal care. LMP 8 weeks ago, certain of her dates. The pregnancy has been uncomplicated except for a small amount a bleeding she had about 3 weeks ago. On exam, you find that her uterine size is consistent with a 6 week IUP, os is closed.

Katie, Continued

After 6 days of watchful waiting, Katie returns with further spotting and cramping. You send a STAT serum $\beta$-hCG, and get a repeat ultrasound. The ultrasound shows a large irregular shaped gestational sac. The serum $\beta$-hCG level has dropped.

What is your assessment?

What options do you offer her now?

Katie, Continued

She decides to opt for treatment with medication.

What regimen do you use and how do you advise her?

Summary

• Management of first trimester pregnancy complications can be done in a Family Practice setting.
• Expectant management or medical or surgical intervention (MVA or EVA) are appropriate with EPL based on patient choice.
• Education and close follow-up are essential for medical & expectant management.
• Incomplete abortions are more likely to have successful expectant management than missed abortions/anembryonic pregnancies.
• Misoprostol hastens the completion of the miscarriage.