ABNORMAL UTERINE BLEEDING

Update on Medical and Surgical Therapy

Sara Jane Pieper, MD
Chair, Gynecology Development Team
Goals

• Review appropriate medical therapies for abnormal uterine bleeding
• Review appropriate indications for surgical therapy of abnormal uterine bleeding

No conflict of interest to report
Learning Objectives

At the conclusion of this learning activity, participants should be able to:

• Describe appropriate medical therapy of AUB
• Describe the appropriate use of LNG-IUS for AUB
• Describe the appropriate use of endometrial ablation for AUB
• Describe the appropriate use of hysterectomy for AUB
Benign Hysterectomy in the United States

<table>
<thead>
<tr>
<th>Indication</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibroids</td>
<td>37%</td>
</tr>
<tr>
<td>Abnormal Uterine Bleeding</td>
<td>19%</td>
</tr>
<tr>
<td>Prolapse</td>
<td>13%</td>
</tr>
<tr>
<td>Pelvic Pain (inc endometriosis)</td>
<td>12%</td>
</tr>
</tbody>
</table>

SelectHealth Data on AUB Hysterectomy

- 60% of hysterectomies for AUB have no appropriate claim for intervention in the 2 years prior to surgery
- 54% of patients have hysterectomy within 2 months of first AUB diagnosis on a claim
- 25% have first claim for AUB at the time of hysterectomy
- Fewer than 10% of patients tried LNG-IUS prior to hysterectomy

Unpublished data on AUB, N=313, SelectHealth, Jan 2016
Current Intermountain Volumes for AUB Hysterectomy

2017 YTD data from iCentra only
MANAGEMENT OF
Abnormal Uterine Bleeding
2017 Update

Program Goals and Measurements

- Reduce number of hysterectomies performed for AUB by maximizing less-invasive therapies
- Increase number of patients offered and/or attempted therapy with LNG-IUS
- Increase compliance with hysterectomy criteria set
- Increase compliance with EA criteria set
- Reduce number of EAs performed that have high likelihood of failure
- Eliminate EAs performed without prior EMB
- Compliance with the AUB Hysterectomy Checklist

Throughout this CPM, this icon indicates an Intermountain measure
PALM-COEIN Classification of AUB

**Structural**
- P  Polyp
- A  Adenomyosis
- L  Leiomyoma
- M  Malignancy

**Medical**
- C  Coagulopathy
- O  Ovulatory
- E  Endometrial
- I  Iatrogenic
- N  Not otherwise specified

Presume patient has been seen, examined and likely cause is medical; refer to Gyn for likely structural cause.
Medical Therapies for AUB

- Levonorgestrel intrauterine releasing system (LNG-IUS)
- Extended cycle oral progestins
- Combined estrogen-progestin oral contraceptive pills (OCPs), patch or vaginal ring
- Anti-fibrinolytic therapy
- NSAIDs
Comparative Medical Treatments for AUB

• Systematic review comparing effectiveness of nonsurgical AUB treatments for bleeding control
• Diagnoses were endometrial and/or ovulatory dysfunction
• Twenty-six articles met inclusion criteria.

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Reduction in blood loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>LNG-IUS</td>
<td>71-95%</td>
</tr>
<tr>
<td>Oral Progestins</td>
<td>87%</td>
</tr>
<tr>
<td>OCPs</td>
<td>35-69%</td>
</tr>
<tr>
<td>Tranexamic Acid</td>
<td>26-54%</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>10-52%</td>
</tr>
</tbody>
</table>

OCPs for AUB

- Most common rx for AUB
- Non-contraceptive benefits including reduced acne, decreased PMS sx, decreased risk of ovarian, endometrial and colon cancer
- Extended cycle and continuous use for AUB
- Contraindicated in history of VTE or known thrombogenic mutations, *migraine with aura*

Pearl - Use monocyclic pills with 4 day hormone-free interval, extended or continuous cycle
Progestin-Only Therapies for AUB

- Norethindrone acetate (Aygestin) 5mg daily
- Medroxyprogesterone acetate (Provera) 10-40mg daily
- Megestrol (Megace) 40mg daily
- Reduces blood flow 40-87% when used continuously
- Side effects - dysphoria, bloating, increased appetite
- Does not increase risk of VTE (except high dose Megace)

Pearl – Choose daily dosing over cyclic dosing for AUB; excellent choice for older women, control of acute bleeding

Anti-fibrinolytic Therapy for AUB

• Tranexamic acid competitively blocks the conversion of plasminogen to plasmin, thereby reducing fibrinolysis
• Dose - 1300mg po tid x 5 days during menses
• Reduces blood flow by 40% compared to placebo
• Side effects – menstrual cramps, headache, nausea
• Contraindications – history of or high risk for VTE

Takeaway – Use for patients unable to use hormonal therapies or for acute control of bleeding

LNG-IUS for Abnormal Uterine Bleeding

• How does it work?
• Indications - Mirena is the only FDA-approved device for HMB
• Contraindications
  – abnormal uterine cavity (arcuate, bicornuate)
  – distortion of cavity by submucous fibroid
  – active pelvic infection
  – known or suspected pregnancy
LNG-IUS and Serum Progesterone Concentrations

- **How does it work?**
  
  Progesterone (lawnmower) vs Estrogen (fertilizer)

- Endometrial concentration of LNG is 1000 times higher than the levonorgestrel (LNG) subdermal implant

- Serum estradiol levels are not affected

<table>
<thead>
<tr>
<th>Progestin</th>
<th>Serum LNG pg/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mirena, Liletta, Kyleena</td>
<td>100-250</td>
</tr>
<tr>
<td>Nexplanon</td>
<td>350</td>
</tr>
<tr>
<td>Progestin pills</td>
<td>1500-2000</td>
</tr>
</tbody>
</table>

LNG-IUS for AUB

- Randomized controlled trial comparing LNG-IUS to hysterectomy for AUB, 10 year follow up
- 236 women aged 35-49 with menorrhagia randomized to LNG-IUS or hysterectomy
- **No difference** in QOL or patient satisfaction at 1, 5 and 10 years
- Rate of hysterectomy in LNG-IUS cohort – 46%

10 year cost for LNG-IUS cohort $3423
10 year cost for hysterectomy cohort $4937

LNG-IUS - Cost Effective Therapy for AUB

- Decision analysis of LNG-IUS, endometrial ablation, and hysterectomy
- Costs and quality-adjusted life years over 5 years for premenopausal women with HMB
- LNG-IUS cost-effective compared with hysterectomy in the majority of scenarios (90%)
- Endometrial ablation associated with reduced costs but lower average quality of life than hysterectomy

# Options for LNG-IUS

<table>
<thead>
<tr>
<th>Name</th>
<th>Dose</th>
<th>Duration</th>
<th>Amenorrhea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mirena</td>
<td>52mg</td>
<td>5 years</td>
<td>30-50%</td>
</tr>
<tr>
<td>Liletta*</td>
<td>52mg</td>
<td>4 years</td>
<td>30-50%</td>
</tr>
<tr>
<td>Kyleena</td>
<td>19.5mg</td>
<td>5 years</td>
<td>20%</td>
</tr>
<tr>
<td>Skyla</td>
<td>13.5mg</td>
<td>3 year</td>
<td>12%</td>
</tr>
</tbody>
</table>

*Not on Intermountain Formulary

**Takeaway** – Offer LNG-IUS **early and often** for patients who do not desire conception and have no contraindications
Surgical Therapies for AUB

- Endometrial ablation
- Hysterectomy
Endometrial Ablation for AUB

- 3681 women aged 25-67 with endometrial ablation
- 3-8 year follow up
- Future hysterectomy not influenced by presence of fibroids or type of ablation
- Main risk for future hysterectomy was age
- <35 yo had significantly greater risk for hysterectomy (HR = 3.2; 95% CI, 2.4–4.2) compared with women aged 50 or older

- Hysterectomy rate overall 21%
- Hysterectomy rate age< 40 40%

Takeaway - Endometrial ablation may not be an appropriate option for patients under the age of 40
Criteria for endometrial ablation (ANY below?):

☐ Normal endometrial sampling without hyperplasia/atypia within 3 months or at time of surgery

☐ Finished with childbearing

☐ No submucous fibroids or polyps ≥ 2 cm (CONSIDER hysteroscopic resection prior to EA)

☐ Failure of LNG-IUS or other medical therapy or intolerance to medical therapy

☐ Age ≥ 40 (if age < 40, CONSIDER placement of LNG-IUS at time of EA)

☐ Plan for contraception (CONSIDER placement of LNG-IUS at time of ablation to provide contraception and increase success rate of ablation)

Note:
Factors with a high risk of EA failure and subsequent hysterectomy:

- Age < 40
- Uterus > 12-week size
- Sound > 10 cm
- Submucous fibroids > 2 cm
- Cavity width > 6 cm
- Dysmenorrhea
Criteria for hysterectomy

- Medical therapy with LNG-IUS for a minimum of 3 months within 2 years prior to hysterectomy unless contraindicated or not tolerated

OR

- Medical therapy with oral contraceptive pills/patch/ring, progestins, or other hormonal control or tranexamic acid (Lysteda) for a minimum of 3 months within 2 years prior to hysterectomy unless contraindicated or not tolerated

OR

- EA with/without placement of LNG-IUS unless contraindicated (prefer failure of medical therapies prior to proceeding to EA; see criteria for EA)

AND

- Persistent excessive bleeding during trial of therapy that results in persistent anemia or dramatically altered quality of life

Notes:

- Patients should attempt more than a single therapy prior to hysterectomy, including control of bleeding with LNG-IUS, unless contraindicated.

- Exclusions from criteria include uterus > 12-week size, or estimated size > 250 g; submucous fibroids ≥ 2 cm; and other concurrent indications for hysterectomy including malignancy, bulky fibroids, and symptomatic uterovaginal prolapse.

- A questionnaire to document alternate therapies attempted will be required at the time of surgery scheduling in ICentra (see online questionnaire here).
How Can Primary Care Help?

• Counsel patients about medical therapies, especially LNG-IUS, and encourage use
• Counsel patients about appropriate use of endometrial ablation
• Counsel patients about appropriate use of hysterectomy
Use of Mirena IUD with Novasure ablation

- Retrospective cohort design
- 23 women with heavy menstrual bleeding and dysmenorrhea, Novasure + Mirena IUD
- 65 women in historic reference group with ablation only
- 4 year follow up

<table>
<thead>
<tr>
<th></th>
<th>Mirena + Novasure</th>
<th>Novasure or Thermachoice</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Combined Failure</td>
<td>2/23 (8.7%)</td>
<td>19/65 (29.2%)</td>
<td>0.47</td>
</tr>
<tr>
<td>Hysterectomy</td>
<td>0/23 (0%)</td>
<td>16/65 (24.0%)</td>
<td>0.009</td>
</tr>
<tr>
<td>Persistent Bleeding</td>
<td>1/23 (4.3%)</td>
<td>15/65 (23.1%)</td>
<td>0.59</td>
</tr>
<tr>
<td>Persistent Pain</td>
<td>1/23 (4.3%)</td>
<td>8/65 (12.3%)</td>
<td>0.242</td>
</tr>
</tbody>
</table>

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