Tool Kit for LARCS in Teens: Clinical Update & Tips and Tricks

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Disclosure slide

• I have no relevant financial relationships with commercial or industry organizations.
Objectives

1. Review counseling for adolescent patient (and parents) about LARC
2. Discuss strategies for IUD insertion in the adolescent and/or nulliparous female
3. Discuss extended efficacy of LARC
3. Review management strategies for common side effects of LARC
<table>
<thead>
<tr>
<th>Product</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nexplanon®</td>
<td>Subdermal Implant</td>
</tr>
<tr>
<td></td>
<td>Single rod containing etonogestrel</td>
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<tr>
<td></td>
<td>(Same product as Implanon except radio-opaque)</td>
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<tr>
<td>ParaGard®</td>
<td>Copper IUD</td>
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<tr>
<td>Mirena®</td>
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<tr>
<td>Skyla®</td>
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<tr>
<td>Kyleena®</td>
<td>Levonorgestrel-Releasing IUDs</td>
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<tr>
<td>Liletta®</td>
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</tbody>
</table>
LARC Counseling Tips for Teens & Young Adults

- Highly effective
- Low-maintenance
- Minimal side effects
- Easily reversible
- Easy to place/Partner does not feel
- Positive experiences
Counseling

• Emphasize “Low Maintenance” NOT “LARC”
• Emphasize beyond effectiveness
• Dispel common myths about LARC methods (such as fears that the IUD causes infertility, weight gain, and infection).
• Engage teens and young adults by talking about how the insertion of an IUD and/or Implant will feel. Help them understand what the IUD will feel like to their partners during sexual intercourse.
Counseling

• While maintaining confidentiality, share other young women’s experiences with the IUD and Implant.
• Let the teen or young adult feel free to make her own decision.
• Research indicates that teens and young adults appreciate the opportunity to see and touch sample IUDs and implant models
• LARC does not protect against STIs.

• It can be effective to practice reflective listening
  • "After hearing this new information about IUDs and the implant, how do you feel about using either method?"
  • "What do you want to know more about?"
Common misconceptions

MYTH #1:

• Adolescents will not tolerate an exam for an IUD
IUD Insertion

- IUD insertion can be painful
- Numerous studies evaluating adjunctive measures to reduce IUD insertion related pain
- Nullips rate pain 6/10 & Multips 3/10
- Components:
  - Speculum placement
  - Tenaculum placement
  - Cervical manipulation
  - Uterine sound
  - Actual IUD placement
there was a presentation at SFP last year that showed that toradol 30 minutes prior to insertion does help with pain in Nulips. Do you want the reference and data to add it?? I will add a slide about it and you can cut if you want...maybe bullet 2 needs to be changed...

NZite, 9/28/2015
Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) & Misoprostol

• Cochrane Review (2009)

• NSAIDs and misoprostol taken together for cervical ripening were NOT effective for reducing pain associated with insertion in nulliparous women
  • Ibuprofen 400 mg & 800 mg, 45-60 min prior to insertion

• NSAIDs may reduce the post insertion pain

Misoprostol

Randomized controlled trials → randomized to:
- misoprostol compared to placebo
  - Buccal & vaginal; 4 hours prior to insertion
- Nulliparous women
- NO difference in:
  - ease of insertion OR
  - insertion pain

Misoprostol After IUD Insertion Failure

• 104 women who requested an insertion of an IUD and the insertion failed at the first attempt.

• After insertion failure, the women received a single tablet of 200 mcg misoprostol or placebo
  • Misoprostol vaginally 14 and 10 hours prior to second attempt

• 88% success rate in misoprostol group, 62% in placebo group

• Initially over 2500 women with 96% success insertion at first attempt

Disadvantages of Misoprostol

- Misoprostol can cause GI symptoms
  - Nausea
  - Abdominal cramping
- Use of misoprostol is a barrier to access
  - Limits same day/single visit insertions
Misoprostol and IUD Insertion

• Routine misoprostol prior to IUD insertion in nulliparous women is not recommended

• Consider using in a patient referred for failed first attempt or difficulties with prior insertion
Lidocaine Gel

- Topical 2% lidocaine gel
  - 1996 British study showed promising results
  - Methodological flaws
  - UK uses lidocaine widely

- Intracervical lidocaine gel 2%
  - Neither was found to reduce pain at tenaculum site or with IUD insertion
  - Maguire (no placebo) & McNicholas (placebo)

Mills, A. 13545. CDC Public Health Image Library (PHIL).
Paracervical Block & IUD Insertions

10 ml of 1% lidocaine paracervical block

<table>
<thead>
<tr>
<th>American study</th>
<th>Turkish study</th>
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<tbody>
<tr>
<td>• Copper T380 a &amp; Levonorgestrel-releasing IUD</td>
<td>• Copper T380</td>
</tr>
<tr>
<td>• Reduction of pain with injection of local anesthetic at site of tenaculum placement</td>
<td>• Reduction of pain with injection of local anesthetic at site of tenaculum placement (7 → 4)</td>
</tr>
<tr>
<td>• No differences in IUD insertion pain between no treatment and lidocaine</td>
<td>• Reduction in pain scores with insertion with lidocaine paracervical block (6 → 2)</td>
</tr>
</tbody>
</table>

Paracervical Block & IUD Insertion

• Meta-analysis (1973-2013) of various measures concluded:
  • Lidocaine paracervical block reduces pain scores associated with tenaculum placement and IUD insertion
  • Small # of studies (only 2)

• May be more effective at a 20 mg dose
• Paracervical block itself is painful

Ketorolac and Insertion Pain

- Randomized double blinded trial of 30 mg IM Ketorolac v. placebo 30 minutes before insertion
- Data analyzed for all subjects (67) and nullips (16)
- Post procedure pain significantly reduced for all subjects
- Uterine sounding and IUD placement pain significantly reduced in nullips

this is the slide I added about pain, hope it is ok
NZite, 9/28/2015

Perfect!
Nichole Tyson, 9/28/2015
Pain Summary

• No adjuvant measures are universally recommended first line as they may or may not be helpful and may evoke pain/side effects
• Can individualize and consider other methods for second attempts or difficult prior insertions
• Goal is to minimize barriers for IUD insertions
• Counseling
  • “It is going to hurt”
  • “It is quick”
  • The benefit is you get 3-12 years of birth control
• Dr. Zite’s “verbacaine”
Myth #2: A woman should be on her period to get an IUD

- Patient wants IUD
  - Check for contraindications
    - On menses
      - Using Birth Control
      - No IC since LMP, SAB, TAB
      - <4 wks Postpartum
      - <= 7 d after SAB, TAB
      - >85% breastfeeding & <6 mo PP
      - *See footnote below
    - Not on menses
      - IC since LMP, SAB, TAB
      - <= 7 days
      - >7 days
        - Prescribe BC, check UPT, & return in at least 2 weeks for repeat UPT OR
        - Insert with next menses
- Patient Counseling
  - Age <26, check GC/CT
- Place IUD
- Post-insertion Counseling
- Next office visit
Nexplanon® and Mirena®
Extended Efficacy
Nexplanon®

- 68 mg of Etonogestrel (ENG)
- Mean serum concentrations of the hormone
  - Maximum (at 2 weeks): 1200 (±604) pg/ml
  - End of 3 years: 138 (±43) pg/ml.
- FDA approved for 3 years
- Extended efficacy data for up to 5 years
Mechanism of Action

• Suppression of ovulation
• Alterations in the Endometrium
• Changes the amount and viscosity of cervical mucus
Rationale for Extended Use Beyond Year 3

• Few pregnancies reported for Implanon during 3 years of use
• PK data indicated ENG implant likely to be effective for contraception beyond 3 years of use.

Huber J. Contraception 1998
Nexplanon® Extended Efficacy Data

- WHO study of 390 women age 18-44 with extended use from 3 to 5 years
  - 25 (6.4%) of initial cohort were BMI ≥ 30
- 311 completed 4 years of use (4,606 woman-months)
- 204 completed 5 years of use* (2,454 woman-months)
- 4.8% discontinued for bleeding problems (in years 4-5; 16.7% in years 1-3)
- No pregnancies in the 2 year extension period (3 in 1st 3 years)
- 5-year cumulative pregnancy rate 0.6 per 100 woman-years (95%CI = 0.2-1.8) for full study cohort n = 995

* 1-2% (of initial 390) loss to follow-up; other loss dropout for personal reasons
Nexplanon® Summary

• Extended use for 5 years is effective
• Limited data in women with BMI ≥ 30
  • Biologically plausible differences in pharmacokinetics in obese women
• Need additional data for “off-label” extended use in obese women.
• Bleeding patterns similar in extended use
Mirena®

- 52 mg of Levonorgestrel (LNG 52)
- Initial release rate 20mcg/day
- FDA approved for 5 years
- Extended efficacy data for up to 7 years
Mechanism of Action

• Inhibition of sperm migration
• Change in transport and speed of the ovum
• Damage or destruction of ovum
• Endometrial suppression
• Changes the amount and viscosity of cervical mucus
Mirena Compared to “Low-Dose” Progestin IUDs

<table>
<thead>
<tr>
<th></th>
<th>Mirena</th>
<th>Kyleena</th>
<th>Skyla</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total LNG</td>
<td>52 mg</td>
<td>19.5 mg</td>
<td>13.5 mg</td>
</tr>
<tr>
<td>Effective (FDA approved)</td>
<td>5 years*</td>
<td>5 years</td>
<td>3 years</td>
</tr>
<tr>
<td>Cumulative failure rate</td>
<td>0.7%</td>
<td>1.4%</td>
<td>0.9%</td>
</tr>
<tr>
<td>Size (WxH)</td>
<td>32 x 32 mm</td>
<td>28 x 32 mm</td>
<td>28 x 32 mm</td>
</tr>
<tr>
<td>Insertion tube</td>
<td>4.4 mm</td>
<td>3.8 mm</td>
<td>3.8 mm</td>
</tr>
<tr>
<td>Formulary</td>
<td>YES</td>
<td>NOT YET</td>
<td>NO</td>
</tr>
</tbody>
</table>

*FDA approved for 5 years – extended use 7 years
Mirena®
Extended Efficacy Data

- UNDP/UNFPA/SHO study of 1,884 parous women age 16-40 with use from 0 to 7 years
- 398 women completed 7 years of use* (7,903 woman-years)
- 7 pregnancies in the entire 7 years
- No pregnancies in years 5-7
- 7-year cumulative pregnancy rate 0.5 (SE=0.2) per 100
  - 7-year cumulative pregnancy rate for Copper T380A (ParaGard) studied in the same trial was 2.5 (SE=0.4) per 100

* 6% (of initial 1884) loss to follow-up; other loss dropout for personal reasons
Mirena® Summary

• Mirena is effective for 7 years
• Similar bleeding pattern in years 5 to 7
• 7-year failure rate of Mirena® similar to 5-year failure rates of Mirena and “low-dose” progestin IUD.
LARC Extended Efficacy

<table>
<thead>
<tr>
<th></th>
<th>FDA approved (yrs)</th>
<th>Recent Studies (yrs)</th>
<th>Failure Rate (per 100 woman-yrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PARAGARD</td>
<td>10</td>
<td>12</td>
<td>2.2</td>
</tr>
<tr>
<td>MIRENA</td>
<td>5</td>
<td>7</td>
<td>0.5</td>
</tr>
<tr>
<td>NEXPLANON</td>
<td>3</td>
<td>5*</td>
<td>0.6</td>
</tr>
<tr>
<td>STERILIZATION</td>
<td></td>
<td></td>
<td>1.9</td>
</tr>
</tbody>
</table>

*BMI <30

Failure rate does not change
Summary and Patient Counseling

- Mirena® use can be extended to 7 years with similar failure rates as 5-year use.
- Nexplanon® use can be extended to 5 years with similar failure rates as 3-year use.
  - Limited data in women with BMI ≥ 30
- Extended use is “off-label” (Not FDA approved)
Summary and Patient Counseling

• Benefits:
  • Extends time for removal
    • Fewer re-insertions – avoids pain and infection risk
    • Some women can avoid a re-insertion procedure all together
    • More convenient
  • Reduces cost (if co-pays and deductibles apply)

• Risks:
  • Method failure (same as FDA approved time frame)
  • Slight chance of increased bleeding
Abnormal Uterine Bleeding & LARCs
Progestin Only Methods

**PROS**
- Safe in women with co-morbidities
- Easy to use
- Long-term protection
- Non-contraceptive benefits
- Few contraindications

**CONS**
- Unscheduled bleeding and spotting
- Dissatisfaction
- Discontinuation
Bleeding as a side effect

- Unscheduled bleeding and spotting is subjective.
- Defined in the literature as any bleeding requiring the use of a sanitary product.
- Bothersome or intolerable bleeding patterns is subjective.
- Some women may find daily spotting or long periods a problem, while others may not.
- Amenorrhea does not require any treatment; if a woman finds it unacceptable despite reassurance, she may prefer alternative methods.
- Irregular & frequent bleeding was reported as reason for early discontinuation (within 6 months of initiation):
  - LNG IUD- 9%-19%
  - ENG implant-46-53%

Grunloh DS, 2013
Diedrich JT, 2015
What is causing all this bleeding?

• Poorly understood
• Over the past 35 years, 5 different World Health Organization workshops have attempted to investigate the pathogenesis
• Multiple contributors to the problem
• Influenced by many factors:
  • type/dose of progestin, how the progestin is delivered, duration of use, effects on the endometrium due to the mechanism of action
Irregular Bleeding & LARC

- It is important to provide anticipatory counseling and advise women about the potential of their changing menstrual bleeding.
- Irregular bleeding and amenorrhea do not indicate that the method is less effective.
- It is important to rule out pregnancy, particularly after mid-cycle insertions of LARC, or in patients who also have pregnancy symptoms.
- The other causes of irregular bleeding that should be considered
  - STI
  - Anatomical uterine conditions (e.g. fibroids or polyps)
  - Non-fundal location of IUD
**Implant Bleeding Patterns**

- Recent data suggest that women who initially reported unfavorable bleeding patterns ultimately had an approximately 50% chance of improvement with continued use.

- **11 clinical trials, 942 Implant users, 90 day cycles**
  - Infrequent bleeding 33%
  - Prolonged bleeding 16.9%
  - Frequent bleeding 6.1%

- 30% of users will be amenorrheic by 1 year of use

- 750 patients aged 12-22 followed with implant and only 10% had device removed within a year of insertion

Mansour D, 2008.
Mansour D 2011
Hohmann H & Creinin MD. 2007
Darney 2009
Berlan 2016
LNG IUD Bleeding Patterns

<table>
<thead>
<tr>
<th></th>
<th>Amenorrhea @ 1 year</th>
<th>Amenorrhea @ 2 years</th>
<th>Amenorrhea @ 5 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mirena</td>
<td>20%</td>
<td>50%</td>
<td></td>
</tr>
<tr>
<td>Liletta</td>
<td>20%</td>
<td>50%</td>
<td></td>
</tr>
<tr>
<td>Kyleena</td>
<td>12%</td>
<td>unknown</td>
<td>23%</td>
</tr>
<tr>
<td>Skyla</td>
<td>6%</td>
<td>12%</td>
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</tbody>
</table>

- Up to 52% of women using any form of LNG IUD have some form of unscheduled bleeding.
- Bleeding patterns experienced with the LNG IUD improve with continued use and for most within 3 months of insertion.

Hildago 2002
Bleeding & Newer IUDs

• Mirena is the only IUD that has an FDA indication to treat heavy menstrual bleeding and causes amenorrhea or lighter periods in most women.

• Women typically have more bleeding and spotting days with Skyla and Kyleena.
Treatments for management of irregular bleeding

• Some of the treatments were studied in other progesterone-only methods
  • Such as Norplant (Levonorgestrel Implant)
  • Depomedroxyprogesterone Acetate (DMPA injection)

• While many studies showed short term benefits
  • Bleeding resumed after treatment was stopped
  • Few were evaluated long term after discontinuation of the treatment
## Treatment Options - NSAIDS

<table>
<thead>
<tr>
<th></th>
<th>MIRENA</th>
<th>NEXPLANON</th>
<th>NORPLANT</th>
<th>DMPA</th>
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<tbody>
<tr>
<td><strong>NSAIDS</strong></td>
<td></td>
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<tr>
<td><strong>Mefenamic acid</strong></td>
<td>500mg TID qd prn No benefit</td>
<td>500mg TID X 5d +Benefit</td>
<td>500mg BID X 5d +Benefit</td>
<td>500mg BID X 5d +Benefit</td>
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<tr>
<td>(increase cost and</td>
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<tr>
<td>side effects)</td>
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<tr>
<td><strong>Ibuprofen</strong></td>
<td></td>
<td>800mg TID X 5d +Benefit</td>
<td>800mg BID X 5d No Benefit</td>
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<tr>
<td><strong>Aspirin</strong></td>
<td></td>
<td></td>
<td>80 mg q D X 10 d No Benefit</td>
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<td></td>
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<tr>
<td><strong>Naprosyn</strong></td>
<td>500mg BID X 5d every 4 wks +Benefit</td>
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<tr>
<td><strong>Celecoxib (C)</strong></td>
<td></td>
<td>(C) 200mg qD X 5d +Benefit</td>
<td>(V) 40mg qD X 5d +Benefit</td>
<td></td>
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<tr>
<td><strong>Valdecoxib (V)</strong></td>
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## Treatment Options- Hormonal

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<tr>
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<tr>
<td><strong>HORMONAL TREATMENTS</strong></td>
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<tr>
<td>Levonorgestrel</td>
<td></td>
<td></td>
<td>30mcg BID X 20d +Benefit</td>
<td></td>
</tr>
<tr>
<td>Oral Ethinyl Estradiol</td>
<td></td>
<td></td>
<td>50mcg q D X 20d +Benefit</td>
<td>50mcg q D X14 d +/- benefit</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>20mcg qD X 10d No Benefit</td>
<td></td>
</tr>
<tr>
<td>Estradiol patch</td>
<td>0.1mg/Wk X 12 w -Benefit/harm</td>
<td></td>
<td>0.1mcg/Wk X 6w No Benefit</td>
<td></td>
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<tr>
<td>Combined OBCP</td>
<td>LNG150mcg/EE 30mcg X 14 d +Benefit</td>
<td>LNG 250mcg/EE 50mcg X 20d +Benefit</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>LNG 150mcg/EE30mcg X 4w Study too small</td>
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</table>
## Treatment Options - Other

<table>
<thead>
<tr>
<th></th>
<th>Mirena</th>
<th>Nexplanon</th>
<th>Norplant</th>
<th>DMPA</th>
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<tr>
<td><strong>Other</strong></td>
<td></td>
<td></td>
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<tr>
<td>Doxycycline</td>
<td></td>
<td>100 mg BID X 5 d +Benefit</td>
<td></td>
<td>100 mg BID X 5d No Benefit</td>
</tr>
<tr>
<td>Tranexamic Acid (Lysteda®)</td>
<td>500mg TID prn No Benefit</td>
<td></td>
<td>500 mg BID X 5 d +Benefit</td>
<td>250 mg QID X 5d +Benefit</td>
</tr>
<tr>
<td>Mifepristone (low doses not commercially available – could affect BC efficacy)</td>
<td>25 mg BID X 1d or 25 mg BID X 1 day plus EE 20mcg X 4d +Benefit</td>
<td>100mg qD X 2 d every 30 days for 6 months +Benefit</td>
<td></td>
<td>50mg every 14 days for 24 weeks +Benefit</td>
</tr>
<tr>
<td>Tamoxifen</td>
<td>10 mg BID for 7 days +Benefit</td>
<td>10 mg BID X 10 d +Benefit</td>
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Summary

• Unscheduled spotting and bleeding is a common cause for discontinuing progestin only contraception
• Anticipatory guidance may improve compliance and satisfaction
• It may take up to 3 months to establish bleeding patterns
• Problem bleeding improves over time
• When bleeding occurs:
  • Reassure
  • Evaluate to rule out pregnancy, STI, other pathology
  • With IUD, confirm proper placement
Take Home Points

• A short course of NSAIDs may be helpful for acute episodes of bleeding but may not improve overall bleeding patterns.

• Hormonal treatments, doxycycline and tranexamic acid can improve irregular bleeding with progestin only methods, however symptoms tend to recur once treatment is stopped.

• Future research in this area is needed, so we can help promote LARC retention and alleviate a bothersome side effect for the short and long term.