8:45 – 9:30 am
Advances and Options in Female Contraception

SPEAKER
Pelin Batur, MD, FACP, NCMP, CCD

Presenter Disclosure Information

The following relationships exist related to this presentation:
► Pelin Batur, MD, FACP, NCMP, CCD: No financial relationships to disclose.

Off-Label/Investigational Discussion
► In accordance with pmiCME policy, faculty have been asked to disclose discussion of unlabeled or unapproved use(s) of drugs or devices during the course of their presentations.

Advances & Options in Female Contraception
Pelin Batur, MD, FACP, NCMP, CCD

Education Director,
Primary Care Women’s Health

Deputy Editor,
Cleveland Clinic Journal of Medicine

Learning objectives

► Become familiar with the newest contraceptive options available
► Understand how a patient’s medical background affects recommended choice of contraceptive

Some fun facts…

50% of pregnancies unintended
4/10 of these lead to abortion
54% of those who had abortions had used a contraceptive that month

Breast cancer
Complicated valvular heart disease
Diabetes with vascular complications
Endometrial or ovarian cancer
Epilepsy
Bariatric surgery within 2 years
HIV/AIDS
Ischemic heart disease
Malignant liver tumors
Peripartum cardiomyopathy
Schistosomiasis with liver fibrosis
Severe cirrhosis
Sickle cell disease
Solid organ transplant within 2 years
Stroke
SLE
Thrombogenic mutations
Tuberculosis

CDC. MMWR. 2010 Jun 18;59(RR-4):1-86.
Long Acting Reversible Contraceptives (LARCs)

- The contraceptive CHOICE project
- Prospective study: what happens if cost is not an issue?
  - LARCs chosen by 75% of women
  - LARCs 20x more effective than combined hormonal contraceptives (pill, patch, ring)
  - 2008-2013 pregnancy and birth rate 1/5 the national rate
  - Abortion rates less than ¼ national rate

Winner B, et al. NEJM May 2012
Secura GM et al. NEJM Oct 2, 2014

Etonogestrel subdermal implant: 
**Implanon Nexplanon**

- Lasts 3 yrs
- 99% effective
- 30-40% amenorrhea at 1 yr
  - ↑ bleeding often occurs in first year

Intrauterine Permanent Contraception: **Essure**

- Local anesthesia, 10 minutes
- Back-up method needed for first 3 months

MRI Safety

- MR Safe (MR)
  - Mirena (5 yr LNG IUD)
  - Nexplanon (3 yr arm implant)
- MR Conditional (⚠️)
  - Safe if scanner <3 T
    - Essure (hysteroscopic coils)
    - ParaGard (copper IUD)
    - Skyla (3 yr LNG IUD)
- MR Unsafe (🚫)
  - No contraceptives

Bone Health: **DMPA**

- Black box warning: Osteopenia
  - Studies on bone mineral density (BMD) mixed
  - BMD ↓ at 5 yrs vs controls
    - -5.38% in LS (-3.13% 2 yrs after dc)
    - -5.16% in TH (-1.34%)
    - -6.12% in FN (-5.38%)
  - Decline is more pronounced in first 2 yrs
- ACOG & WHO: Advantages of DMPA > risks
  - Can continue for decades!

Batur P, Joy S. Clinical Reviews of Bone and Mineral Metabolism; 3(2): 103-113, 2005
Bone Health: DMPA

- Use of DMPA and incidence of bone fracture
  - 312,395 women in UK, retrospectively followed 5 yrs
  - Fx incidence in 1000 women: 9.1 (DMPA) vs 7.3 (non-DMPA)
  - Incidence RR 1.23 (95% CI 1.16-1.130)
- Overall “message”: no significant increase
  - DMPA cohort higher risk of fx at baseline
  - Risk did not increase further after DMPA initiated
  - Longer term users had lower fx risk than short term
  - No excess risk of axial fx (hip, pelvis, vertebral)


Bone Health: Depo-Provera

Take home points

- Use it if patient needs it
- Consider LARC method instead
- Perimenopausal women have less time to recover BMD after discontinuation
- DXA scan not needed to monitor

Progestin only pill
"mini-pill"

- For those who cannot tolerate estrogen
  - CAD, VTE, stroke
  - Migraine w/ aura
  - <6 wks postpartum
  - Uncontrolled hypertension
- Often used in lactating women
  - Higher rates of breakthrough bleeding
  - Back up method for 2 days if > 3hrs late w/ dose
  - Concern re: lower contraceptive efficacy

Combined Hormonal Contraceptives (CHC)

- Have been used ~ 50 years in the US
- Most popular contraceptive choice along with sterilization

Combined Oral Contraceptives

- vaginal ring
- skin patch

Combined Oral Contraceptives

- the pill, COC

Combined Oral Contraceptives: Progestin Formulations

- 1st Generation: (cycle control problems)
  - norethindrone
  - ethynodiol diacetate
- 2nd Generation: (androgenic problems)
  - norgestrel
  - levonorgestrel
- 3rd Generation: (RR VTE 1.7-6x)
  - desogestrel
  - etonogestrel
  - norgestimate
  - norelgestromin
- 4th Generation: (RR VTE 0.9-3x)
  - drospirenone
  - dienogest

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  - drospirenone
  - dienogest
Why are they so mean to drospirenone?

The aftermath...

- $1.575 billion settlements in the U.S.\(^1\)
  - 7,660 claimants (mostly VTE)
  - average claim per case: $ 212,000
- Bayer agreed to settle ~ 8800 gallbladder injuries = $24 million

Litigation not directed towards providers

Summary of VTE: absolute risks

<table>
<thead>
<tr>
<th>Condition</th>
<th>Rate of VTE (per 10,000 women per year)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reproductive Aged</td>
<td>1-5</td>
</tr>
<tr>
<td>(baseline-no pill)</td>
<td></td>
</tr>
<tr>
<td>Pill users</td>
<td>3-10</td>
</tr>
<tr>
<td>(rates vary by progestins)</td>
<td></td>
</tr>
<tr>
<td>Pregnancy</td>
<td>5-20</td>
</tr>
<tr>
<td>Postpartum</td>
<td>40-65</td>
</tr>
</tbody>
</table>


What’s new with CHC Risks?

- Breast cancer
- Stroke
- Coronary artery disease
- VTE

What’s new with CHC BENEFITS?

- Breast cancer

BRCA carriers:
  - 4-ovarian cancer RR 0.50 (CI 0.33-0.75)
  - No association with breast cancer
  - Only old formulations used before 1975"

Ovarian Cancer Prevention

NNT 185 x 5 yrs
Longer use is better
Protection attenuates after d/c
Consider using in 40s

Oncol Gynecol. Aug 2013; 122(2):380
OR Ischemic stroke = 1.90 (95% CI 1.24-2.91)
Very few with EE 35mcg dose
Insufficient data to stratify by progestin

NEJM 2012; 366:2257
30-40 mcg EE RR 1.6-2.2
20 mcg EE RR 0.9-1.7
Patch 1.2 (CI 0.8-2.6)
Vaginal ring 2.5 (CI 1.4-4.4)

Obstet Gynecol Aug 2013; 122(2):380
Obstet Gynecol Oct 2013; 122(4):800
Vaginal ring not increased compared to oral
**What's new with CHC Risks?**

- Breast cancer
- Stroke
- MI
- VTE

Obstet Gynecol Aug 2013; 122:380

**OR = 1.34 [CI 0.87-2.08]**

Insufficient data to stratify by EE dose

NEJM 2012; 366:2257

30-40 mcg EE RR ↑ 1.3-2.3

20 mcg EE RR ↑ 0.0-1.6

Patch RR 0.0

Vaginal ring ↑ 2.1 [CI 0.7-6.5]

Obstet Gynecol Oct 2013; 122(4): 800

Vaginal ring not increased compared to oral

**What's new with COC Risks?**

- Breast cancer
- Stroke
- Coronary artery disease
- VTE

**CVA**

<table>
<thead>
<tr>
<th>Type of Progestin/Hormonal Contraception</th>
<th># of events/100,000 person-years</th>
<th>Adjusted RR (30 mcg EE dose)</th>
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<th>Adjusted RR (30 mcg EE dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Norethindrone</td>
<td>23.1</td>
<td>1.17 (0.69-1.95)</td>
<td>19.9</td>
<td>2.68 (1.34-5.39)</td>
</tr>
<tr>
<td>Levonorgestrel</td>
<td>19.3</td>
<td>1.65 (0.99-2.76)</td>
<td>19.8</td>
<td>2.02 (1.03-3.94)</td>
</tr>
<tr>
<td>Norgestimate</td>
<td>17.2</td>
<td>1.52 (0.91-2.60)</td>
<td>6.2</td>
<td>1.30 (0.51-3.34)</td>
</tr>
<tr>
<td>Desogestrel*</td>
<td>11.6</td>
<td>2.20 (1.70-2.86)</td>
<td>13.7</td>
<td>2.03 (1.56-2.64)</td>
</tr>
<tr>
<td>Gestodene*</td>
<td>21.6</td>
<td>1.80 (1.58-2.06)</td>
<td>10.1</td>
<td>1.94 (1.03-3.62)</td>
</tr>
<tr>
<td>Drosperinone*</td>
<td>21.1</td>
<td>1.40 (1.09-1.79)</td>
<td>6.3</td>
<td>1.81 (1.34-2.45)</td>
</tr>
<tr>
<td>Patch</td>
<td>42.1</td>
<td>3.15 (0.79-12.60)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Vaginal ring</td>
<td>31.4</td>
<td>2.49 (1.41-4.43)</td>
<td>3</td>
<td>7.8 (2.07-26.48)</td>
</tr>
</tbody>
</table>


**Does the VTE risk vary based on the progestin formulation? **

<table>
<thead>
<tr>
<th>Relative Risk of VTE According to Generation of Progestin</th>
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<tbody>
<tr>
<td>Non-use</td>
</tr>
<tr>
<td>Non-use</td>
</tr>
<tr>
<td>First generation</td>
</tr>
<tr>
<td>Second generation</td>
</tr>
</tbody>
</table>


**Medical Considerations:**

**Bariatric Surgery**

- Gastric bypass
  - Oral pills are category 3
  - All other methods category 1
- Restrictive (lap band)
  - All category 1

**Seizure Disorder**

- Decreased contraceptive efficacy, consider IUD

- Use estrogen doses >50 mcg EE with:
  - Barbiturates, carbamazepine, oxcarbazepine, felbamate, topiramate levels reduced
  - Levetiracetam, valproic acid ok

- Lamotrigine levels ↓ 50% with COC pills
  - May need higher doses of lamotrigine to control seizure
  - Can get toxic levels in placebo week
  - Use continuous regimen if COC must be used
Medical Considerations: Organ Transplant

- Amenorrhea/infertility common with hepatorenal disease
  - Up to 1/20 transplant patients have become pregnant

- Pregnancy risks post transplant:
  - Graft rejection
  - Pregnancy complications
  - Most antirejection agents are pregnancy class D

- IUD, hormonal options are category 2
  - Unless graft failure, rejection, allograft vasculopathy
    - COC category 4
    - IUD category 3
    - Depo, POP category 2

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Medical Considerations: Rheumatoid arthritis

- DMARDs: methotrexate & leflunomide are pregnancy category X
  - Stop MTX 3 months & leflunomide 2 yrs prior to conception

J of Rheumatology. Vol 31: Supplement 69, March 2004

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Emergency Contraception

<table>
<thead>
<tr>
<th>Method</th>
<th>Dose</th>
<th>Efficacy</th>
</tr>
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<tbody>
<tr>
<td>high dose estrogen</td>
<td>5 mg EE qd x 5</td>
<td>75-80%</td>
</tr>
<tr>
<td>estrogen + progestin</td>
<td>100 µg EE + 0.5 mg levonorgestrel po qd x 2</td>
<td>56-89%</td>
</tr>
<tr>
<td>levonorgestrel (Plan B)</td>
<td>0.75 mg qd x 2</td>
<td>60-94%</td>
</tr>
<tr>
<td>levonorgestrel (Plan B One-Step)</td>
<td>1.5 mg x1</td>
<td>60-94%</td>
</tr>
<tr>
<td>ulipristal (ella™)</td>
<td>30 mg</td>
<td>85-98.6%</td>
</tr>
<tr>
<td>copper IUD</td>
<td>Insert within 5 days</td>
<td>99%</td>
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<tr>
<td>1-888-NOT-2-LATE</td>
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Take home points

- Long acting reversible contraceptives (LARCs) are preferred due to better efficacy
- Use CDC 2010 guidelines help to decide which method is appropriate
- Use CDC 2013 guidelines help to decide how to use the method
- Only a BP and PMHx is needed to initiate CHC
- Ulipristal and copper IUD are more effective forms of emergency contraception than the OTC products