CHOOSING A CONTRACEPTIVE FOR WOMEN WITH COMMON MEDICAL DISORDERS

Stephanie Teal, MD, MPH
Associate Professor of Obstetrics and Gynecology
Director, Program in Family Planning
University of Colorado School of Medicine

LEARNING OBJECTIVES
Following this presentation the learner will:

 Provide evidence-based counseling on the risks and benefits of various contraceptive options for obese women
 Utilize the appropriate options for contraception in women with headache syndromes
 Effectively use the WHO Medical Eligibility Criteria for Contraceptive Use

DISCLOSURES

 Scientific Advisory Board
  • Bayer Healthcare
  • Implanon Trainer
  • Merck

IS UNPLANNED PREGNANCY A PROBLEM?

 Pregnancy may worsen medical issues
  • Increased demand on compromised systems
 Medical conditions may threaten fetus
  • Hostile intrauterine environment
 Therapies may threaten fetus
  • Teratogenic medications

CONSIDERATIONS FOR CONTRACEPTION

 Safety with baseline disease
 Drug interactions
  • Toxicity
  • Efficacy
 Sufficient efficacy
 Ease of use

MEDICAL CONDITIONS THAT IMPACT CONTRACEPTIVE USE

 Hematologic disorders
  • Thrombophilic
  • Hemophilic
 Endocrine
  • Obesity
  • Diabetes
 Neurologic
  • Seizure disorder
  • Migraine
 Psychiatric
  • Depression
  • Bipolar
  • Developmental delay
 Rheumatologic
  • Lupus
  • RA
 Infectious
  • HIV
 Neoplastic
  • Breast cancer
  • Melanoma
 GI
  • Cystic fibrosis
  • Bariatric surgery
**COC MEDICAL ELIGIBILITY CRITERIA FOR UNITED STATES 2010**

- Adapted from WHO MEC
- >60 characteristics or medical conditions
- Each method type rated 1-4 for risk with initiation or continuation
  - 1=no restriction; 4=unacceptable risk
- Modified for the US for certain conditions
- Certain conditions added for the US
  - Bariatric surgery
  - IBS
  - Organ transplantation

**POLICY CONTEXT**

**OBESETY**

- 26 yo G2 P0 TAB2
- “Healthy”
- Has used COCs in the past, would like a new Rx

**OBESETY & CONTRACEPTION**

- Efficacy
- Synergistic health effects
  - Co-morbidities
  - Worsening obesity
- Technical issues
  - Injectables
  - Intrauterine
  - Surgical

**POSSIBLE MECHANISM OF OBESETY EFFECT ON HC EFFICACY**

- Increased basal metabolic rate
- Increased hepatic enzyme metabolism
- Increased drug sequestration
- Blunted central sensitivity
  - Early FSH activation, delayed suppression

**COC EFFICACY: EPIDEMIOLOGY**

<table>
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<th>Study</th>
<th>Year</th>
<th>Type</th>
<th>RR</th>
<th>Significant?</th>
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<td>South Carolina</td>
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<td>Nat’l Survey of Family Growth</td>
<td>2007</td>
<td>retrospective cohort</td>
<td>1.6</td>
<td>no</td>
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**MAYBE SO...**

- "typical use" retrospective studies: overweight and obese women may be at an increased risk of contraceptive failure
- Physiologic factors?
- Behavioral factors?

Brunner Huber LR et al, Matern Child Health J. 2005
WHAT DOES IT MEAN?
- Epidemiologic studies inconclusive
  - Absolute risk is likely to be small; a 60% increase in risk implies an increase from 7% to 11% in the first year of typical use of OCs in the United States
- Need for prospective studies, designed specifically to examine an association between body weight-contraceptive failure

EURAS
- prospective cohort
- active surveillance
  - 59,510 OC users
- effectiveness of OCs overall
  - by BMI, weight, age, duration of use, EE dose, regimen type, starting/switching status, parity
  - unplanned pregnancies during OC use confirmed by interview
- OC effectiveness analysis
  - 112,659 women-years of exposure
  - 545 unplanned pregnancies
  - little variation in effectiveness by BMI/weight.

THE RCT
- BMI 19-25 vs. 30-40
- 2 pill formulations
- Compliance
  - Serum LNG levels
  - Highly significant difference between BMI arms
- Ovarian suppression
  - twice weekly ultrasound
  - Progesterone
  - Rare ovulations
  - no difference among consistent users

CHC EFFICACY SUMMARY
- Conflicting evidence whether obese women have a higher risk of OC failure during reported perfect use
  - Possible that OCs are less forgiving of imperfect use among obese women
- Level 1 evidence that obese women are less compliant with COCs

VTE RISK
Mild synergistic effect between COC and BMI category

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<td>6.5</td>
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DMPA EFFICACY
- Both 150 mg IM and 104 mg SC produce progestin levels far above that necessary for ovulation suppression
- Small PK study: time to ovulation return did not differ by obesity index
- NO evidence for decreased efficacy
- NO evidence for more frequent dosing
OTHER PROGESTIN-ONLY METHODS: EFFICACY
- POPs
  - Reduced efficacy
- Implanon
  - Small PK study: lower serum levels of etonogestrel in obese subjects
  - Analysis of small number of Implanon failures: no evidence of obesity effect

OTHER HEALTH RISKS
- Do OCs cause DM?
  - No, but not examined in obese women
- Do CHCs cause weight gain?
  - No, but not examined in obese women
- Does DMPA cause weight gain?
  - Maybe, definitely in obese adolescents

INTRAUTERINE CONTRACEPTION
- IUD benefits
  - Minimal systemic interactions
  - Long-term prevention of complicated pregnancy
  - Reduction in endometrial CA risk
- Creative placement techniques
  - Limited bimanual exam
  - Visualization of cervix

OBESITY AND CONTRACEPTION
1. In obese women, combined hormonal contraception
   - May have slight decreased efficacy
   - Confers higher risk of VTE
   - Probably does not cause DM
2. Progestin-only contraception
   - Increased risk of weight gain with DMPA
   - Possible decreased efficacy with Implanon?
   - Decreased efficacy with POPs

OPTIONS BEYOND COCS
3. Progestin-only contraception
   - Increased risk of weight gain with DMPA
   - Possible decreased efficacy with Implanon?
   - Decreased efficacy with POPs
4. Intruterine contraception has
   - Excellent efficacy (both)
   - Health benefits (LNG-IUS)
   - Minimal risk
5. Pregnancy has greater health risks than any contraceptive

FAMILY HISTORY OF BREAST CANCER
- 23 yo G0
- Mother recently dx’d with breast CA at age 50
**COCs and Breast Cancer**
- **Oxford pooled analysis** (Lancet 1996)
  - 54 epidemiologic studies
  - 50,000 breast cancer, 100,000 controls
- **US historical cohort** (JAMA 2000)
  - breast CA 1944-1952
  - F/U 40-50 yrs later with 1st and 2nd degree relatives
- **Women’s CARE study** (NEJM 2002)
  - 4575 cases, 4682 controls

**Increased Risk of Breast Cancer with COCST Family HD?**
- **Oxford**
  - RR 1.24 with current use, less with recent use, no increase with use > 10 yrs prior
  - Extremely small increased absolute risk
  - No difference by family history
- **US cohort**
  - Incr risk only for OCs pre-1975
- **Women’s CARE**
  - No increased risk among current or former users, by length of use, age of initiation, or dose
  - No difference by family history

**BRCA Mutations and COCs**
- Risk of primary breast CA
- Risk of asynchronous second breast CA
- No change for
  - BRCA1
  - BRCA2

**Breast Cancer and LNG-IUS**
- **LNG-IUS vs all population** (Finland)
- **LNG-IUS vs Cu-IUD** (Finland, Germany)
  - Retrospective, population-based, case-control cancer registries
  - No increased risk of breast CA with LNG-IUS
  - No increased risk of recurrence
  - Controlled cohort, Belgium

**Seizure Disorder**
- 22 yo G3 P1 TAB2
- Seizure disorder since childhood
- On dilantin, lamictal, and trileptal

**Anti-Convulsants**
- Induce p450 enzymes
- Decrease EE and P AUC and Cmax
- Increase EE clearance
- Increase SHBG
- Includes parenteral hormones
- COCs may also affect drug levels by changing bioavailability
Most evidence is very poor quality
Surrogate endpoints, few assessments of breakthrough ovulation
No studies with pregnancy as outcome
Correlation of BTB and ovulation unclear
No evidence to support 50 mcg EE pill

Induction of hepatic enzymes, reduction of EE or P level
NO Induction of hepatic enzymes, no reduction of EE or P levels

Carbamazepine (Tegretol) Ethosuximide (Zarontin)
Felbamate (Felbato) Gabapentin (Neurontin)
Oxcarbazapine (Trileptal) Lamotrigine (Lamictal)*
Topiramate (Topamax) Zonisamide (Zonegran)
Primidone (Mysoline) Vigabatrin (Sabril)
Phenobarbital Valproate (Depakote)
Phenytoin (Dilantin) Levetiracetam (Keppra)

Determine drug(s) interactions
Recommend higher dose pill with back-up (e.g. condoms)—Level C
Recommend DMPA, LNG-IUD, Cu-IUD—Level B
Progestin-only pills, subdermal implant not recommended—Level B

21 yo new patient
Severe dysmenorrhea
Desires contraception
History of migraine
Bilateral
“tightening” sensation
Photophobia
No ↑ with activity
Respond to NSAIDs
Mom and sister with migraines
Recommended COCs by her best friend
Is a CHC appropriate for her?

26 yo G1P1, non-smoker
Has used COCs x 2 yrs.
Severe HA 4-5x/year
Unilateral, pulsating, photophobia OR
Nausea/vomiting
Common vs. classic
Tension HA does not increase stroke risk
Should she continue OCs?
**Migraine and Stroke Risk**

- Migraine and stroke
  - RR 2.2-3.5 (general)
  - RR 1.6-3.0 (no aura)
  - RR 2.9-6.2 (with aura)

- COC and stroke
  - RR 1.0-3.5

**Migraine, COC, and Stroke**

- Synergistic effect
  - RR 6.6-13.9
    - Compared to women without migraine or COC use
  - RR 2-4
    - Compared to migraineurs without COC

- How robust are the data?
  - No prospective studies
  - Case-control studies subject to recall, selection, ascertainment, observation bias
  - Not controlled for smoking, gender
  - Probable increased risk, size of risk is in dispute

**Headache 3**

- 32 yo G2P2
  - Migraine without aura
  - Occur ONLY in the 2 days pre-menses, resolve within first few days of bleeding
  - NSAIDS: minor relief
  - Smokes 2-5 cigs/day

- Is COC appropriate?

**Possible Effects of COC on Migraine**

- No change
- Improvement (usually without aura)
- Migraine without aura in pill-free week only
- More severe/more frequent (typically with aura)
- New onset migraine (typically with aura)

**Lupus**

- 27 year old G1P0 with SLE. She has + LA activity and + aCL-abs, and a hx of a brachial DVT for which she is on warfarin. Moderate lupus nephritis, rx MTX and cyclophosphamide, now quiescent x 6 mo. In a new sexual relationship, and wants OCPs.
**ISSUES WITH SLE AND CONTRACEPTION**

- **Thrombophilia**
  - Who is at risk for clots with exogenous hormones? Which hormones?
- **Immunosuppression**
  - Does hormonal contraception worsen? Can she use an IUD?
- **Disease flares**
  - Do OCs promote flares, and in who?
- **Osteopenia**
  - Concomitant use of prednisone and ovulation suppressors?

**SLE AND OC’S: 2 RCTS**

- N=183; COC vs. placebo
- Inactive (76%) or stable (24%) lupus
- Excl: mod/high levels of anticardiolipin abs, LAC, or hx thrombosis
- No diff in mild, mod or severe flares
- No diff complications (thrombosis, infection)

- N=162; COC v IUD v POP
- Mild/mod dz, 134 active
- 30% with ACA
- Global dz activity by SLEDAI score
- No difference in global or max dz activity, clots, infxn

**CLINICAL PEARLS:**

- Progestins do not promote thrombosis.
- Anti-coagulated patients benefit from menstrual reduction
- Patients on teratogenic medications MUST be adequately contracepted.