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…

NOT SO FUNNY

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

Finer et al. Contraception 2011; 84:478–485
Grindlay et al. Contraception 2013; 87:162-169

Conditions that may make unintended pregnancy an unacceptable health risk

- 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

Peipert JF et al. Obs Gynecol Oct 2012
Winner B, et al. NEJM May 2012
Secura GM et al. NEJM Oct 2 2014

Etonorgestrel 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
  - 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

What's new with Depot medroxyprogesterone acetate

- Failure rate "0.0-~~0.7%" 6%~~
- Side Effects:
  - Weight gain (1-3 kg)
  - Hypoestrogenic
  - Higher insulin and FBS
  - ↓ HDL
- Uncontrolled HTN/Vascular Dz
  - Progestin only pill and Implant: category 2
  - Depo: category 3

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)

Lanza L, et al. Obs Gynecol March 2013; 121 (3), 593

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 (the pill, COC)	vaginal ring (NuvaRing)	skin patch (Ortho Evra)

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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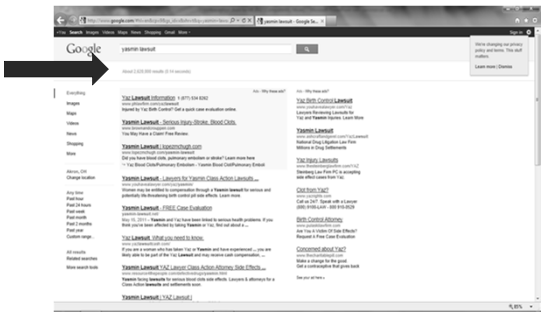
Why are they so mean to drospirenone?



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

[1] **Bayer HealthCare stockholder newsletter, financial report as of September 30, 2013. Page 65 product related litigations**. http://www.stockholders-newsletter-q3-2013.bayer.com/en/bayer-stockholders-newsletter-3q-2013.pdfx

Summary of VTE: absolute risks

Condition	Rate of VTE (per 10,000 women per year)
Reproductive Aged (baseline-no pill)	1-5
Pill users	3-10 (*rates vary by progestins)
Pregnancy	5-20
Postpartum	40-65

ACOG Committee Opinion No 540: Risk of venous thromboembolism among users of DRSP-containing oral contraceptive pills. Obstet Gynecol. 2012 Nov;120(5):1239-42

What's new with CHC Risks?

- **Breast cancer**
- Stroke
- Coronary artery disease
- VTE

No ↑ risk
•Contraception 2012; 85: p342
•Contraception 2009; 80:p 372
•NEJM 1986; 315:p405
•NEJM 2002; 346: p2025

•JAMA 2000;284: p1791
•Br J Cancer 2003;88: p50
•Can Epid Biomark 2010; 19: p2496
•Mayo Clin Proc 2006;81: p1287

What's new with CHC ***BENEFITS***?

- **Breast cancer**

BRCA carriers:
•↓ovarian cancer RR 0.50 (CI 0.33-0.75)
•No association with breast cancer
- Only old formulations used before 1975↑risk: RR 1.47 (1.06-2.04)

Eur J Cancer 2010;46(12): 2275

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

Obstet Gynecol July 2013; 122(1):139

What's new with CHC Risks?

- Breast cancer
- **Stroke**
- Coronary artery disease
- VTE

Obstet 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 ↑ 1.5-2.2
20 mcg EE RR ↑ 0.9-1.7
Patch ?↑ 3.2 [CI 0.8-2.6]
Vaginal ring ↑ 2.5 [CI 1.4-4.4]

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

Does the type of progestin used affect the arterial risk ? ***No***

	CVA		MI	
Type of Progestin/ Hormonal Contraception	# of events/ 100,000 person-years	Adjusted RR (30 mcg EE dose)	# of events/ 100,000 person-years	Adjusted RR (30 mcg EE dose)
Norethindrone	22.1	1.17 (1.49-3.15)	11.0	2.28 (1.34-3.87)
Levonorgestrel	31.3	1.65 (1.39-1.95)	19.8	2.02 (1.63-2.50)
Norgestimate	17.2	1.52 (1.21-1.91)	6.2	1.33(0.91-1.94)
Desogestrel*	31.6	2.20 (1.79-2.69)	13.7	2.09 (1.54-2.84)
Gestodene*	21.6	1.80 (1.58-2.04)	10.1	1.94 (1.03-2.63)
Drosperinone*	18.1	1.64 (1.24-2.18)	6.3	1.65 (1.03-2.63)
Patch	42.1	3.15 (0.79-12.60)	0	0
Vaginal ring	31.4	2.49 (1.41-4.41)	3	7.8 (0.67-6.48)

Lidegaard et al. *N Engl J Med* 2012; 366:2257-66.

What's new with COC Risks?

- Breast cancer
- Stroke
- Coronary artery disease
- **VTE**

Does the VTE risk vary based on the progestin formulation? ***Probably yes*** risk vary based on the progestin formulation? ***No***

	Relative Risk of VTE According to Generation of Progestin			
	Non-use	First	Second	Third
Non-use	1			
First generation	3.2 (2.0-5.1)	1		
Second generation	2.8 (2.0-4.1)	0.9 (0.6-1.4)	1	
Third generation	3.8 (2.7-5.4)	1.2 (0.8-1.9)	1.3 (1.0-1.8)	1

Stegemen BH et al. **Different combined oral contraceptives and the risk of venous thrombosis: systematic review and network meta-analysis.** *BMJ 2013;347.*

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 hepato- renal 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

Medical Considerations:
Rheumatoid arthritis

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

Ann Rheum Dis. 1996 February; 55(2): 94–98.
J of Rheumatology. Vol 31: Supplement 69, March 2004

Emergency Contraception

Method	Dose	Efficacy
high dose estrogen	5 mg EE qd x 5	75-80%
estrogen + progestin	100 ug EE + 0.5 mg levonorgestrel po q12 hr x 2	56-89 %
levonorgestrel	*(Plan B)* 0.75 mg q12 x 2 *(Plan B One-Step)* 1.5 mg x1	60-94 %
ulipristal *(ella™)*	30 mg	85-98.6%
copper IUD	Insert within 5 days	99%

Cleland K, et al. Hum Reprod. 2012 Jul;27(7):1994-2000.

Emergency Contraception

Method	Dose	Efficacy
levonorgestrel	*(Plan B)* 0.75 mg q12 x 2 *(Plan B One-Step)* 1.5 mg x1	60-94 %
ulipristal *(ella™)*	30 mg	85-98.6%

Cleland K, et al. Hum Reprod. 2012 Jul;27(7):1994-2000.

Emergency Contraception

Method	Dose	Efficacy
	EC Hotline: **1-888-NOT-2-LATE**	

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