Update on Emergency Contraception

Association of Reproductive Health Professionals

www.arhp.org
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Advisory Committee

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Learning Objectives

• Describe emergency contraceptive (EC) options available in the U.S.
• Provide evidence-based information about the safety and effectiveness of EC.
• Discuss mechanism of action of ECPs.
Question 1:
Which emergency contraception pill regimen is most effective 3 days after unprotected sex?

C. Ulipristal acetate (ella)
Question 2:

Is there a limit to how many times a woman can safely use emergency contraceptive pills?

B. No
Question 3:

Women who weigh more than 150lbs should consider alternatives to levonorgestrel EC pills?

A. True
Emergency Contraception Methods
ParaGard® (Copper-T IUD)

- Studied since 1976
- Off label use
- Placed within 5 days after intercourse
- Effectiveness does not decline with
  - Delay, obesity, repeated sex
- Requires prompt access to trained clinician
- Cost: may be $500
  should be free without copay thanks to ACA
EC Pills Available in the US:

Dedicated products
• One 30mg ulipristal acetate pill
• Label: Take within 120 hrs after intercourse
• Rx: available by prescription
• Cost: has been coming down

online prescription + shipping now = $42
http://www.ella-kwikmed.com/

June 20, 2013

- FDA approved *PlanB® One-Step* (levonorgestrel) pills as nonprescription product in the US
  - Available on shelf without age restrictions
  - Women and men

Dr. Susan Wood
ECPs “Over-the-Counter” in the US

Plan B® One-Step
- Over the counter for all ages

Next Choice One Dose™
- Behind counter for ≥ 17 years
- Rx needed if < 17 years

My Way™

Levonorgestrel

ECPs to be “Over-the-Counter”

Plan B® One-Step
- Over the counter for all ages

Next Choice One Dose™
- Behind counter for ≥ 17 years
- Rx needed if < 17 years

My Way™

Levonorgestrel

Plan B® One-Step

- One 1.5mg levonorgestrel pill
- **Label:** Take within 72 hrs after intercourse
- Effective up to 120 hrs after intercourse
  - Most effective as soon as possible
- Cost: OTC: $35-$60
  - Rx: $30+

Next Chose One Dose™ My Way™ (generic)

- One 1.5mg levonorgestrel pill
- Label: Take within 72 hours after intercourse
- Recommended: up to 120 hrs after sex if needed

- Cost: $35 ($24-$42)
  - 10-20% cheaper than Plan B One-Step

Levonorgestrel (generic)

- Two 0.75mg levonorgestrel pills
- **Label:** Take 1 pill immediately, 2\textsuperscript{nd} pill 12 hrs later
- **Recommended:** Both pills immediately
- **Label:** Take within 72 hours after intercourse
- **Recommended:** up to 120 hrs after sex if needed

- **Cost:** as low as $19, generally about $30
  - 10-20\% cheaper than Plan B One-Step

Do it yourself EC: Combined Pills

Yuzpe method

Less effective, more nausea

EC dosing chart for combined pills available at http://ec.princeton.edu/questions/dose.html#dose

<table>
<thead>
<tr>
<th></th>
<th>First Dose&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Second Dose&lt;sup&gt;b&lt;/sup&gt; (12 hours later)</th>
<th>Ethinyl Estradiol per Dose (μg)</th>
<th>Levonorgestrel per Dose (mg)&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alesse</td>
<td>5 pink pills</td>
<td>5 pink pills</td>
<td>100</td>
<td>0.50</td>
</tr>
<tr>
<td>Aviane</td>
<td>5 orange pills</td>
<td>5 orange pills</td>
<td>100</td>
<td>0.50</td>
</tr>
<tr>
<td>Cryselle</td>
<td>4 white pills</td>
<td>4 white pills</td>
<td>120</td>
<td>0.60</td>
</tr>
<tr>
<td>Enpresse</td>
<td>4 orange pills</td>
<td>4 orange pills</td>
<td>120</td>
<td>0.50</td>
</tr>
</tbody>
</table>
Emergency Contraception Effectiveness
<table>
<thead>
<tr>
<th>ParaGard</th>
<th>ella</th>
<th>Plan B/Next Choice</th>
<th>Yuzpe</th>
<th>Nothing</th>
</tr>
</thead>
</table>

Pregnancies per 1000 Women after Unprotected Intercourse
Relative effectiveness of EC options

Pregnancies expected per 1000 women who had unprotected sex in last 3 days

- Paragard IUD
- Ella pills
- Levonorgestrel
- Yuzpe
### Efficacy of IUDs as EC

<table>
<thead>
<tr>
<th>Country</th>
<th>Population</th>
<th>Pregnancies</th>
<th>Rate</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>China*</td>
<td>5629</td>
<td>6</td>
<td>0.11%</td>
<td>(0.05%- 0.23%)</td>
</tr>
<tr>
<td>UK</td>
<td>496</td>
<td>0</td>
<td>0.00%</td>
<td>(0.00%- 0.70%)</td>
</tr>
<tr>
<td>US</td>
<td>401</td>
<td>0</td>
<td>0.00%</td>
<td>(0.00%- 0.85%)</td>
</tr>
<tr>
<td>Italy</td>
<td>253</td>
<td>0</td>
<td>0.00%</td>
<td>(0.00%- 1.38%)</td>
</tr>
<tr>
<td>Egypt</td>
<td>200</td>
<td>4</td>
<td>2.00%</td>
<td>(0.69%- 5.03%)</td>
</tr>
<tr>
<td>Netherlands</td>
<td>55</td>
<td>0</td>
<td>0.00%</td>
<td>(0.00%- 5.93%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>7,034</strong></td>
<td><strong>10</strong></td>
<td><strong>0.14%</strong></td>
<td><strong>(0.08%- 0.25%)</strong></td>
</tr>
<tr>
<td><strong>Total w/o Egypt</strong></td>
<td><strong>6,834</strong></td>
<td><strong>6</strong></td>
<td><strong>0.09%</strong></td>
<td><strong>(0.04%- 0.19%)</strong></td>
</tr>
</tbody>
</table>

Cleland et al. 2011
Pregnancy Rates 5 days after LNG: Pooled WHO Studies

Pregnancy rates by day since unprotected sex and use of Ulipristal

Moreau and Trussell, 2011

Sustained efficacy over time elapsed since UPI, $P=0.91$
Ulipristal *versus* Levonorgestrel

- Meta-analysis of two randomized studies found ulipristal superior to levonorgestrel
  - in multivariable analyses

- 0-24 h: OR=0.35 (95% CI, 0.11-0.93)
- 0-72 h: OR=0.58 (95% CI, 0.33-0.99)
- 0-120 h: OR=0.55 (95% CI, 0.32-0.93)

Ulipristal *versus* Levonorgestrel

- In RCT, all 3 pregnancies with use 73-120 h were in the LNg group
- Significantly more pregnancies prevented in the UPA group (p=0.037)
- Why?

Glasier AF et al. *Lancet* 2010;
Schwarz and Trussell. *Contraceptive Technology* 2011.
Ulipristal *versus* Levonorgestrel

Preventing ovulation/follicular rupture

- Leading follicle=15-17 mm, levonorgestrel no more effective than placebo

- Leading follicle=18-22 mm, ulipristal still prevents follicular rupture in 59% of cycles (vs. 0% for placebo)

Croxatto HB et al. *Contraception* 2004
Brache V et al. *Hum Reprod* 2010
Ulipristal Acetate

- Follicular rupture within 5 days of ulipristal
  - 0% women treated before onset of the LH surge
  - 21% of women treated after the onset of the LH surge but before the LH peak
  - 92% of women treated after the LH peak

Brache V et al. *Hum Reprod* 2010
ECPs and Obesity

ECP Failure among obese versus non-obese women

- LNg: OR = 4.41, 95%CI 2.05-9.44
- Ulipristal: OR = 2.62, 95%CI 0.89-7.00

The limits of efficacy of EC pills

- For Lng: Weight=70 kg (154 lb)
- For UPA: Weight=88 kg (194 lb)

On average, American women weigh 166 lbs…

Glasier A et al Contraception 2011
Repeated unprotected intercourse

<table>
<thead>
<tr>
<th>Repeated UPI</th>
<th>Ulipristal</th>
<th>LNg</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>1.0%</td>
<td>1.9%</td>
</tr>
<tr>
<td>Yes</td>
<td>5.6%</td>
<td>7.3%</td>
</tr>
</tbody>
</table>

A drop of EC in the ocean of UPS
Pregnant within 3 months (Pittsburgh data)

“trying to avoid pregnancy for 6+ months”

- Levonorgestrel pills: 7% (3%-15%)
- Ulipristal pills: 30% (10%-60%)
- ParaGard: 0% (0%-12%)
Take-Away Points on Effectiveness:

- IUD is most effective EC option

- Especially with repeated unprotected intercourse with obesity (weight >155lbs for Lng)
Safety and Side Effects
Is Same-Day IUD placement Safe?

Risk of PID equivalent for:

• Nonscreening vs. any screening

• Same-day screening vs. prescreening
  ▪ Equivalence persisted when adjusted for age and race

EC IUD Safety

Safe

- Benefits outweigh risks for most situations
- If worried about STI, test
- Can treat STI and PID with IUD in place

CDC Selective Practice Recommendations 2013
IUDs in Adolescents

@ clinic 4 EC. Getting IUD instead! Mom will think I’m planning ahead

ACOG 2007.
ECP Safety

- Benefits outweigh risks
- Safer than pregnancy
- No increased risk of birth defects
- No increased risk of ectopic pregnancy
- Breastfeeding women may use either ECPs or IUD
- Short duration of exposure and low total hormone content of EC pills

Trussell J, Raymond EG. 2011; Trussell J, Schwarz EB. Contraceptive Technology 2011; CDC MMWR 2010.
Possible Side Effects of EC pills

- Nausea and vomiting
- Abdominal pain
- Breast tenderness
- Headache
- Dizziness
- Fatigue
- Short-term cycle changes

Question 1:

Is there a limit to how many times you can safely prescribe ECPs for the same person?

A. No
Risk Taking
Question 2:

In your opinion, what effect will increased availability of ECPs have on adolescent risk-taking behaviors?
Do ECPs Increase Risk Taking?

Studies conducted around the world

- Nevada
- Pittsburgh
- Scotland
- San Francisco
- China
- Los Angeles
- North Carolina
- Hong Kong
- Nevada
- Pittsburgh
- Scotland
- San Francisco
- China
- Los Angeles
- North Carolina
- Hong Kong

Advance Provision of EC

Women who received ECPs in advance were not more likely to:

- Use ECPs repeatedly
- Have unprotected sex
- Change to less effective contraception
- Use contraception less consistently
- Acquire an STI

but...

Reanalysis of one trial suggested easier access to ECPs may have increased frequency of sex with potential for pregnancy
- substitution of ECPs for other contraceptives

Mechanisms of Action for ECPs
How MIGHT EC pills Work?

Inhibit or delay ovulation

Prevent sperm and egg from meeting

Prevent implantation by disrupting the uterine lining

Davidoff F, Trussell J. *JAMA* 2006; ICEC and FIGO statement. 2011; Trussell J, Raymond E. 2011; Gemzell-Danielsson K. *Contraception* 2010
Clinical Evidence: LNG ECPs

- Can inhibit ovulation, though not always
  - May be only mechanism of action
- Have no effect on the quality of cervical mucus or on the penetration of spermatozoa into the uterine cavity
- Can shorten the luteal phase
- Do not alter endometrium

Clinical Evidence: Ulipristal ECPs

Can inhibit ovulation, though not always
- May be only mechanism of action

Do not alter endometrium

What can we say about EC Pills?

Primarily stop or delay ovulation

Best available evidence indicates they do not interfere with any post-fertilization events.

Fertilization without implantation has not been documented

What about EC IUDs?

Copper is toxic to sperm

Copper may prevent implantation

This is a great option for women who really want to avoid pregnancy
Additional Resources

• EC Hotline and Website
  www.not-2-late.com  888-NOT-2-LATE

• Bedsider.org

• Kwikmed.com
Advance provision of EC pills has not been shown to reduce rates of unintended pregnancy.

Community intervention in Scotland

No change in abortion rates

- 78% of women who got pregnant did not use ECPs they were given
- Provider bias may have deprived women most at risk from getting EC pills

Why No Reduction in Pregnancies?

Among women who received progestin-only ECPs in advance

45% of women who had UPI did not use ECPs they were provided

San Francisco

33% of women had UPI at least once without using ECPs they were provided

Nevada/NC

more…

Use and Underuse of ECPs

Women underestimate their risk of pregnancy

- Education is needed to encourage women to use ECPs every time they are needed

ECPs are not used frequently enough

- Underuse of ECPs means major public health impact is unlikely

Advance Provision of ECPs

Women who receive ECPs in advance:
• Take ECPs sooner after sex
• Use other methods of contraception equally well
• Advance provision is recommended
• IUDs are more effective than EC pills!

Studies of ECP Use & Risk Taking

Women randomized to receive either:

1. Counseling and ECPs on demand

OR

2. ECPs in advance for later use

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