Managing contraceptive side effects

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Order of presentation

• Definition of side effect

• Contraceptive side effects
  – How common are they
  – What can we do

• “Nocebo effect”

• Background rate of non-specific symptoms

• Counselling
Definition of side effect:

Noun

A secondary, typically undesirable effect of a drug or medical treatment

http://www.oxforddictionaries.com/definition/english/side-effect
Choice study
Continuation rate at 12 months

Peipert et al. 2011 Obstet Gynecol
COC discontinuation/side-effects

Percentage

- Bleeding irregularities
- Nausea
- Weight gain
- Mood changes
- Breast tenderness
- Headaches

Rosenberg MJ and Waugh MS Am J Obset Gynecol 1998
On discontinuation of pills

• Many choose less effective methods (or no method at all)

• Women unhappy with COC:
  – inconsistent users
  – breakthrough bleeding
Summary of product characteristics

• Undesirable effects

• Include all adverse reactions from:
  – clinical trials
  – post-authorisation safety studies
  – spontaneous reporting

If a causal relationship between medicinal product and adverse event is a reasonable possibility
The average drug has about 70 listed side effects!
## Undesirable effects (COC)

<table>
<thead>
<tr>
<th>Adverse events</th>
<th>Common (&lt;1/10, &gt;1/100)</th>
<th>Uncommon (&lt;1/100, &gt;1/1000)</th>
<th>Rare (&lt;1/1000)</th>
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</table>
Evidence from blinded RCT
COC versus placebo

• Very few studies

• **Nonspecific** side effects – not significantly more common with COC

• Only evidence of associated COC side-effects:
  – Bleeding irregularities especially with low dose pills
  – Nausea, vomiting and headaches in high dose pills (50µg EE)

*Goldzieher JW et al. Fertil steril 1971*
*Coney P et al. Contraception 2001*
Undesirable effects
Combined hormonal ring / patch

• Combined hormonal ring:
  – Common – vaginal infection, acne, genital pruritis

• Combined hormonal patch:
  – Very common (>1/10) – headache, nausea and breast tenderness
  – Common – migraine, dizziness, abdominal distension, skin irritation, acne, malaise and fatigue
Dealing with most common COC S/E

- Nausea/vomiting – time of pill taking
- Headache – exclude migraine
- Breast discomfort - EPO
- Mood changes
- Acne (Cochrane 2012)
- Breakthrough bleeding – exclude other causes
- Weight gain – no evidence (Cochrane 2014)
Undesirable effects (POP)

<table>
<thead>
<tr>
<th>Adverse events</th>
<th>Common (&lt;1/10 to &gt;1/100)</th>
<th>Uncommon (&lt;1/100 to &gt;1/1000)</th>
<th>Rare (&lt;1/1000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal disorders</td>
<td>Nausea</td>
<td>Vomiting</td>
<td></td>
</tr>
<tr>
<td>Metabolism</td>
<td>Weight increase</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td>Headache</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reproductive system and breast disorders</td>
<td>Breast pain/tenderness, irregular bleeding, amenorrhoea</td>
<td>Dysmenorrhoea, ovarian cyst</td>
<td></td>
</tr>
<tr>
<td>Skin</td>
<td>Acne</td>
<td>Alopecia</td>
<td>Rash, urticaria, Erythema Nodosum</td>
</tr>
<tr>
<td>Psychiatric disorders</td>
<td>Altered mood, depressed mood, libido decrease</td>
<td></td>
<td>Anxiety, insomnia</td>
</tr>
<tr>
<td>Infections</td>
<td></td>
<td>Vaginal infection</td>
<td></td>
</tr>
<tr>
<td>General</td>
<td></td>
<td>Fatigue</td>
<td></td>
</tr>
</tbody>
</table>
Very common side effects of Depo Provera (>1/10)

• Abdominal pain or discomfort

• Headaches
# Undesirable effects (Depo)

<table>
<thead>
<tr>
<th>Adverse events</th>
<th>Common (&gt;1/100)</th>
<th>Uncommon (&gt;1/1000,&lt;1/100)</th>
<th>Rare (&lt;1/1000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal disorders</td>
<td>Nausea, bloating</td>
<td>Vomiting, diarrhoea, distention</td>
<td>Rectal bleeding</td>
</tr>
<tr>
<td>Metabolism</td>
<td>Appetite increase/decrease</td>
<td>Weight increase/decrease, fluid retention</td>
<td></td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td>Dizziness</td>
<td>Migraine, somnolence, convulsions</td>
<td>Paralysis</td>
</tr>
<tr>
<td>Reproductive system and breast disorders</td>
<td>Breast pain/tenderness, vaginitis, IMB, HMB, amenorrhoea, pelvic pain, leucorrhoea</td>
<td>PV discharge, vv dryness, PMS, dysmenorrhoea, dyspareunia, ovarian cyst,</td>
<td>Breast lumps, nipple bleeding</td>
</tr>
<tr>
<td>Vascular</td>
<td>Hot flushes</td>
<td>Hypertension, PE, varicose veins, thrombophlebitis</td>
<td></td>
</tr>
<tr>
<td>Skin</td>
<td>Acne, alopecia, rash</td>
<td>Chloasma, dermatitis, bruising, hirsutism, pruritis, melasma,</td>
<td></td>
</tr>
<tr>
<td>Psychiatric</td>
<td>Anorgasmia, depression, nervousness, emotional disturbance, libido decrease</td>
<td>Anxiety</td>
<td></td>
</tr>
</tbody>
</table>
Dealing with Depo Provera S/E

• Change in appetite

• Change in bleeding
## Undesirable effects (Nexplanon)

<table>
<thead>
<tr>
<th>Adverse events</th>
<th>Very Common (&gt;1/10)</th>
<th>Common (&lt;1/10&gt;1/100)</th>
<th>Uncommon (&lt;1/100&gt;1/1000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal disorders</td>
<td></td>
<td>Abdo pain, nausea, flatulence</td>
<td>Vomiting, constipation diarrhoea</td>
</tr>
<tr>
<td>Metabolism</td>
<td></td>
<td>Increased appetite</td>
<td></td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td>Headache</td>
<td>Migraine</td>
<td></td>
</tr>
<tr>
<td>Reproductive system and breast disorders</td>
<td>Breast pain/tenderness, irregular bleeding</td>
<td>Dysmenorrhoea, ovarian cyst</td>
<td>Vaginal discharge Breast discharge, vv discomfort, galactorrhoea, breast enlargement, genital pruritis</td>
</tr>
<tr>
<td>Skin</td>
<td>Acne</td>
<td>Alopecia</td>
<td>Hypertrichosis, rash, pruritis</td>
</tr>
<tr>
<td>Psychiatric disorders</td>
<td></td>
<td>Depressed mood, nervousness, libido decrease</td>
<td>Anxiety, insomnia</td>
</tr>
<tr>
<td>Infections</td>
<td>Vaginal infection</td>
<td></td>
<td>Pharyngitis, rhinitis, UTI</td>
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Dealing with common SDI S/E

- Irregular bleeding
Implanon - bleeding patterns

Three-monthly assessments

Percentage

- Amenorrhoea
- Infrequent bleeding
- Frequent bleeding
- Prolonged bleeding

FSRH 2003
# Undesirable effects (Mirena)

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<th>Adverse events</th>
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<tr>
<td>Gastrointestinal disorders</td>
<td>Abdo pain, nausea</td>
<td>Abdo distension</td>
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<tr>
<td>Metabolism</td>
<td>Weight increase</td>
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<tr>
<td>Nervous system disorders</td>
<td>Headache, migraine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reproductive system and breast disorders</td>
<td>Ovarian cysts, pelvic pain, dysmenorrhaea, vaginal discharge, vulvovaginitis, breast tenderness/pain</td>
<td>PID, endometritis, cervicitis</td>
<td>Uterine perforation</td>
</tr>
<tr>
<td>Skin</td>
<td>Acne, hirsuitism</td>
<td>Alopecia, pruritis, eczema</td>
<td>Rash</td>
</tr>
<tr>
<td>Psychiatric disorders</td>
<td>Depressed mood, nervousness, decreased libido</td>
<td>Altered mood</td>
<td></td>
</tr>
<tr>
<td>Infections</td>
<td>Vaginal infection</td>
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<td>Pharyngitis, rhinitis, UTI</td>
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Dealing with common IUS S/E

- Ovarian cysts
- Acne
- Mood change
The “Nocebo effect”

• Latin “I will harm”

• Harmful, unpleasant or undesirable effect
  – After receiving an inert drug or placebo
    that the patient believes to be an active drug

• Approx ¼ patients taking placebo report S/E

Shepherd M. Psychol Med. 1993
The “Nocebo effect”

• Symptoms related to expectation of outcome
  – Patients who expect side effects are more likely to develop them

• The power of suggestion

• 2 studies:
  – Aspirin for unstable angina and GI side effects
  – Nebulised saline (containing an “allergen”)

McFadden E et al. Psychosom Med 1969*
Background noise of non-specific complaints

• Background prevalence (German medical students)
  – 65% fatigue
  – 30% nasal congestion
  – 25% headache
  – 13% muscle pain
  – 12% joint pain
  – 9% irritability

  11% free of symptoms

• More common in women than men

Meyer et al. Clinical Pharmacology and Therapeutics 1996
Background noise of non-specific complaints

• Non-medical respondents (n=128)
  – 37% fatigue
  – 23% excessive sleepiness
  – 17% irritability
  – 13% headache
  – 13% nasal congestion
  – 11% muscle pain
  – 10% insomnia
  – 3% urticaria

Reidenberg and Lowenthal NEJM 1968
• If women are told to expect noxious side effects
  – They will get them

• Clinicians should err on the side of optimism!
IF THE DRUGS DO CAUSE A PROBLEM THEN WE'VE GOT SOME PILLS THAT MIGHT HELP...

AND SOME OTHER PILLS FOR THE SIDE EFFECTS OF THE PILLS YOU TAKE FOR THE PROBLEMS THE DRUGS CAUSE...
Counselling about CHC side-effects

• Very, very small increased VTE risk
  – Briefly explain symptoms of DVT, PE

• Very, very small increased risk of cerebrovascular disease (higher in smokers)

• Very small risk of migraine

• Very, very small risk of jaundice

• Risk of breakthrough bleeding
  – Especially in first few months

“Read the FPA leaflet, not the PIL in the COC packet”
Counselling regarding side-effects

• Listen
• Find out more information of contraceptive problems in the past
• Explore myths
• Discuss pros and cons for each method
  – Don’t dwell too much on the cons but be honest!
Summary

• No contraceptive method is perfect

• "Nocebo effect"

• High prevalence of background non specific symptoms
Why are there never any "GOOD" side-effects?

Just once I'd like to read a medication bottle that says

"MAY CAUSE EXTREME SEXINESS".

-Unknown Author