Changing pills
Managing COC / POP side effects

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Kingston Hospital
BASHH / FSRH meeting
17.1.20
Order of presentation

• What to choose if patient using CHC complains of:
  • Nausea/vomiting
  • Headache
  • Breast discomfort
  • Mood changes
  • Acne
  • Breakthrough bleeding
  • Weight gain

• POP
• Nocebo effect
• Background symptoms
LARC and oral contraceptives by age in primary care patients in the UK

Note: Patients could be counted more than once in this analysis if they have changed therapy during the course of the time period

1. Patient Data, IQVIA Solutions UK Limited, Nov 2017
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!
In the SPC for COC which side effect is not listed as common (<1/10 – >1/100)?

1. Nausea
2. Headache
3. Reduced libido
4. Weight gain
In the SPC for COC which side effect is not listed as common (<1/10 – >1/100)?

1. Nausea
2. Headache
3. Reduced libido
4. Weight gain
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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<tbody>
<tr>
<td>Gastrointestinal</td>
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<tr>
<td>disorders</td>
<td>Nausea</td>
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<td>abdominal pain</td>
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<td>Weight</td>
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<td>Decrease</td>
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<td>Nervous system</td>
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<td>disorders</td>
<td>Headache</td>
<td>Migraine</td>
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<tr>
<td>Reproductive system</td>
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<td>Breast pain</td>
<td>Breast tenderness</td>
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<td>and breast disorders</td>
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<td>Vaginal discharge</td>
<td>Breast discharge</td>
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<td>Erythema nodosum</td>
<td>Erythema multiforme</td>
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<td>Rash, urticaria</td>
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<td>Psychiatric disorders</td>
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<tr>
<td></td>
<td>Depressed mood</td>
<td>Libido decreased</td>
<td>Libido increased</td>
</tr>
</tbody>
</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*
### Possible causes of possible side effects

<table>
<thead>
<tr>
<th>Side effect</th>
<th>Oestrogenic</th>
<th>Progestogenic</th>
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<tbody>
<tr>
<td>Acne</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Anxiety</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Bloating</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Breast swelling</td>
<td>+</td>
<td>-</td>
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<tr>
<td>Breast tenderness</td>
<td>+</td>
<td>+/- (assoc. with depression)</td>
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<tr>
<td>Decreased libido</td>
<td>+</td>
<td>+/- (assoc. with depression)</td>
</tr>
<tr>
<td>Depression</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Headache</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Hirsutism</td>
<td>-</td>
<td>+</td>
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<tr>
<td>Irregular bleeding</td>
<td>+/-</td>
<td>+</td>
</tr>
<tr>
<td>Mood swings</td>
<td>+/-</td>
<td>+</td>
</tr>
<tr>
<td>Nausea</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Weight gain</td>
<td>+/- (water retention: cyclical gain)</td>
<td>+/- (increased appetite)</td>
</tr>
</tbody>
</table>
## Progestogen properties

<table>
<thead>
<tr>
<th></th>
<th>Progestogenic</th>
<th>Oestrogenic</th>
<th>Androgenic</th>
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</thead>
<tbody>
<tr>
<td>Progesterone</td>
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<td>-</td>
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<tr>
<td>Levonorgestrel</td>
<td>++</td>
<td>-</td>
<td>+</td>
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<tr>
<td>Desogestrel</td>
<td>+</td>
<td>-</td>
<td>+</td>
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<td>Norgestimate</td>
<td>++</td>
<td>-</td>
<td>+</td>
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<tr>
<td>Gestodene</td>
<td>++</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Drospirenone</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Dienogest</td>
<td>+++</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Norethisterone</td>
<td>+++</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Cyproterone acetate</td>
<td>+</td>
<td>-</td>
<td>-</td>
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</table>
## Progestogen properties cont.

<table>
<thead>
<tr>
<th>Progestogen</th>
<th>Antiandrogenic</th>
<th>Antimineralcorticoid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Progesterone</td>
<td>+</td>
<td>+</td>
</tr>
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<td>−</td>
</tr>
<tr>
<td>Desogestrel</td>
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<td>−</td>
</tr>
<tr>
<td>Norgestimate</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
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<td>−</td>
<td>(+)</td>
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<tr>
<td>Drospirenone</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Dienogest</td>
<td>+</td>
<td>−</td>
</tr>
<tr>
<td>Norethisterone</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>Cyproterone acetate</td>
<td>+++</td>
<td>−</td>
</tr>
</tbody>
</table>
Nausea

• Pregnancy test

• Timing of pill
  • Take with food
  • Take in evening

• Reduce oestrogen dose
• Try PO method
Is it a migraine or a headache?

• Check BP

• PIN diagnosis for migraine:
  • Photophobia – does light bother you when you have a headache?
  • Impairment – do you experience headaches that impair your ability to function?
  • Nausea – do you feel nauseated when you have a headache?

MacGregor A BMJ 2016
What is the % chance that the diagnosis is migraine with all 3 of the “PIN” symptoms?

1. 87

2. 89

3. 91

4. 93
What is the % chance that the diagnosis is migraine with all 3 of the “PIN” symptoms?

1. 87

2. 89

3. 91

4. 93
Migraine cont.

- 98% aura are visual

- Have you ever had visual disturbances lasting 5 – 60 mins followed by headache?
Headache management

• Lifestyle changes, hydration, reduce caffeine, analgesia

• Reduce / omit PFI if headache during PFI
• Reduce oestrogen
• Consider change to DSG containing COC
• Change to POP
Breast discomfort

• Exclude pathology
• Bra support
• High strength evening primrose oil capsules
• Persevere 3/12

• Reduce oestrogen
• Change progestogen consider DSG if persists
• Consider POP
Mood changes

- Explore lifestyle and alternative causes
- History – PMS, postnatal depression
- Exclude suicidal ideation

- Change progestogen – consider DSG / DRSP
Reduced libido

• Explore medical and psychosexual history
• Explore relationship (ask about DV and GBV)

• Change to more androgenic progestogen (NET or LNG)
• (Reduce oestrogen)
• Change to patch - less effect on SHBG
• Change to POP (NET containing)
Acne

- Diet
- Skincare advice
- Less androgenic 3\textsuperscript{rd} generation progestogen
  - DSG / GSD / DRSP
  - Dianette (CPA)
- 30 / 35mcg EE
- Omit PFI
Breakthrough bleeding

• Check compliance, pregnancy
• Check interactions (St. John’s Wort, Modafinil)
• Screen for STIs
• Cervical examination if >3/12
• Cervical cytology if due

• If low dose pill, increase EE
• Change progestogen to GSD / DSG
• Qlaira or Zoely
• Consider Nuvaring
Weight gain

- Explore diet / lifestyle

- No evidence that alternative COC is advantage

- Consider another method (not DMPA)
## Undesirable effects (POP)

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<td>Nausea</td>
<td>Vomiting</td>
<td></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</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reproductive system and breast disorders</td>
<td>Breast pain/tenderness,</td>
<td>Dysmenorrhoea, ovarian</td>
<td></td>
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<tr>
<td></td>
<td>irregular bleeding,</td>
<td>cyst</td>
<td></td>
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<tr>
<td></td>
<td>amenorrhoea</td>
<td></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</td>
<td></td>
<td>Anxiety, insomnia</td>
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<tr>
<td></td>
<td>mood, libido decrease</td>
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<tr>
<td>Infections</td>
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<td>Vaginal infection</td>
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<tr>
<td>General</td>
<td></td>
<td>Fatigue</td>
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</tr>
</tbody>
</table>
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*
In a study of 130 healthy German medical students, what % had no symptoms in the preceding 72 hours?

1. 41
2. 31
3. 21
4. 11
In a study of 130 healthy German medical students, what % had no symptoms in the preceding 72 hours?

1. 41
2. 31
3. 21
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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
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”
Any questions?

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