LARC: responding to side effects

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Sita, 29

• Sita had a single-rod contraceptive implant inserted 18 months ago
• She would like it removed today
• Why?
  • Mood disturbance last 3 months
  • Mother suggested removing implant, as it’s “well known to cause mood problems”
Sita – extra information

• Happy with implant otherwise
• Extra pressures at work last 6 months, does not feel can cope much longer
• Partner has commented on her irritability, & suggested she change jobs
• Low mood, lowered self esteem and disrupted sleep patterns
• *Time course and other possible reasons for mood disturbance suggest it’s not due to implant*
Could this be a side effect?

**Table:** Percentages of subjects with at least one experience classified by body system and reported as related to the study drug pre-marketing in clinical trials performed by MSD.

<table>
<thead>
<tr>
<th>Body System (WHO System Organ Class)</th>
<th>Implanon&lt;sup&gt;(2)&lt;/sup&gt; Related AE’s (&gt; 2.5%) N= 1326</th>
<th>Norplant&lt;sup&gt;®&lt;/sup&gt; (levonorgestrel releasing implants) Related AE’s (&gt; 5%) N= 184</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychiatric disorders</td>
<td></td>
<td></td>
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<tr>
<td>Emotional lability</td>
<td>5.2</td>
<td>7.6</td>
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<tr>
<td>Depression</td>
<td>3.2</td>
<td>4.9</td>
</tr>
<tr>
<td>Nervousness</td>
<td>2.9</td>
<td>3.3</td>
</tr>
<tr>
<td>Libido decreased</td>
<td>3.2</td>
<td>5.4</td>
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Evidence for side effects – provider perspective

• Mood
  • Limited data, impact unclear

• Weight gain
  • Limited data, impact unclear

Amico et al, 2015; Lopez et al, 2016
Side effects – patient perspective

- Reasons for removal of implant
  - bleeding irregularities
  - mood swings
  - headaches
  - weight gain
- May be a combination of factors

Hoggart et al, 2013
Responding to possible side effects

• Qualitative studies outline patients’ difficult experiences after reporting side effects to health professionals

Hoggart et al 2013
Provider resistance

‘I think she thought that maybe I was going to go out and then like be sexually active and not have any protection then get pregnant and then come back and blame somebody. So I think she was trying to protect herself while doing it, but I don’t know, I thought that wasn’t really any of her business at that stage in time’
Sita

- Discussed low chance that mood problems, in this case, were likely due to other causes
- Reassured that implant could be removed if desired
- Sita accepted referral to counselling, and kept her implant
- Mood problems resolved in time
Dealing with other side effects
Initial consultation

- Provide accurate information about expected bleeding patterns, emphasising that troublesome bleeding is likely to improve with time:
  - **Implant**: 1/5 amenorrhoea, 3/5 infrequent, irregular bleeding, 1/5 frequent or prolonged bleeding; approximately 1/2 with frequent or prolonged bleeding will improve after three months.
  - **Hormonal IUD**: frequent spotting/bleeding common in first 3-5 months; either amenorrhoea, light irregular or light regular bleeding common after six months.
  - **DMPA Injection**: 1/2 amenorrhoea, 1/6 infrequent irregular bleeding, 1/3 frequent or prolonged bleeding; amenorrhoea increases over time.

- Be proactive in offering management advice for troublesome bleeding. Actively encourage review of troublesome bleeding.

Management of troublesome bleeding

1. **Exclude other causes**
   - Pregnancy, sexually transmitted infections (STIs) including chlamydia, liver-enzyme inducing medications (implant only) and vaginal, cervical or uterine pathology

2. **If no suspicion of another cause for bleeding**
   - Reassure this is ‘normal’ and not harmful

3. **Advise medication management**
   - Ensure no contraindications and explain risks and side effects

4. **Advise that the implant or hormonal IUD can be removed any time or the depot medroxyprogesterone acetate (DMPA) injection discontinued.**

**First line options:**

- A combined hormonal contraceptive\(^1\) taken continuously or cyclically for three months
- Five day course of NSAID\(^2\) such as mefenamic acid 500mg bd-tds
- Five day course of tranexamic\(^3\) acid 500mg bd, particularly if bleeding is heavy

**Second line options**

- With low level, anecdotal or conflicting evidence:
  - Tranexaminc acid 500mg bd for five days for lighter bleeding
  - Norethisterone\(^4\) 5mg tds for 21 days
  - Levonogestrel\(^5\), progestogen only pill, 30 mcg bd for 20 days
  - Early removal and replacement of implant or hormonal IUD, or shortening interval between injections from 12 to 10 weeks

Contraindications include:

\(^1\) migraine with aura, personal and family history of venous thromboembolism, risk factor for cardiovascular disease and smoking >35 years of age, active breast cancer. For other conditions see: www.lrm.org/pdfs/UKMEC-SummarySheets2009.pdf

\(^2\) upper gastrointestinal inflammation or ulceration, renal conditions

\(^3\) active thromboembolic disease and subarachnoid haemorrhage

\(^4\) active thromboembolic disease and subarachnoid haemorrhage

\(^5\) at high risk of venous thromboembolism, ischemic heart disease or stroke

\(^6\) active breast cancer

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FPAA Guidance for management of troublesome vaginal bleeding with progestogen-only long-acting reversible contraception (LARC) November 2015
Bleeding – contraceptive implants

- Anticipatory counselling, reassurance
- Combined hormonal contraceptive continuously or cyclically for three months
- NSAID eg mefenamic acid 500mg bd-tds 5 days
- Tranexamic acid 500mg bd 5 days
- (Ulipristal 15mg daily 7 days)

- Alternatives (lower level evidence):
  - Norethisterone 5mg tds for 21 days
  - Levonogestrel POP, 30 mcg bd for 20 days
  - Early removal and replacement

FPAA 2015; Villavicencio et al, 2016; Zigler 2018
Bleeding - IUDs

• Progestogen IUD
  • Anticipatory counselling, reassurance
  • Similar to contraceptive implants

• Copper IUD
  • Anticipatory counselling
  • Reassurance (may reduce with time)
  • NSAID, tranexamic acid

FPAA 2015; Villavicencio et al, 2016
Practical suggestions

• Prepare patients for expected changes
• What’s the impact of the problem?
• Could it be a side effect?
• Could it be caused by anything else?
  • Investigate further as needed
• Discuss uncertainties with patient
• Provide patient with options
• Respect their decisions
Questions?
References


• Hoggart L Newton VL, Dickson J. "I think it depends on the body, with mine it didn't work": explaining young women's contraceptive implant removal. Contraception 2013 Nov;88(5):636-40.
• *ImplanonNXT Product Information* 24 November 2016 [https://secure.healthlinks.net.au/content/msd/pi.cfm?product=mkpimnxt](https://secure.healthlinks.net.au/content/msd/pi.cfm?product=mkpimnxt)


• Polis C, Hussain R, Berry, A. There might be blood: a scoping review on women’s responses to contraceptive-induced menstrual bleeding changes. Reproductive Health 2018 15:114
References
