Progestin-only contraception and beneficial effects on migraine

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Conflicts of interest

- Adviser and lecturer for EXELTIS
- Lectures and Advisory boards Bayer
- Lectures and Advisory boards MSD

ESC Teaching Tool
Medical condition session: Migraine and depression

- www.escrh.eu
- http://www.escrh.eu/education/TTTtool

Combined hormonal contraceptives can initiate and worsen migraines and increase the risk for ischemic stroke in migraineurs

What about progestin-only contraception?

Progestin-only methods

Type or dose of progestagen

- 2nd generation
  - levonorgestrel
    - Mirena
    - Kyleena
    - Jaydess

- 3rd generation
  - Desogestrel
  - Cerazette
  - Etonogestrel
    - (3-keto desogestrel)
    - Implanon
Principal aims in the treatment of hormonal migraines

Avoid hormone fluctuations and estrogen withdrawal in the natural cycle and in CHC and HRT users

POC use continuous regimen

Pill with Oestrogen + Progestin

Pill, Implant, Injection, (IUS)

Consequences of this continuous regimen and estrogen-free contraception

- No hormone withdrawal (excluded LNG-IUS)
- No increased risk for stroke
- No increased risk for venous thromboembolism
- Bleeding not predictable
- Frequently amenorrhoea

Levonorgestrel releasing - intrauterine devices
Mirena/Kyleena/Jaydess

- Releases Levonorgestrel into the uterus cavity
- LNG is absorbed only in small amounts
- Can inhibit ovulation, but mostly ovulation occurs
- Can induce ovarian cysts with estrogen production
- Prevents menstrual bleeding (MIRENA)

Levonorgestrel 20 - releasing intrauterine system

The MIRENA LNG-IUS causes highly fluctuating estradiol levels in women with and without bleeding Nielsen 1984. This can promote migraine in predisposed women

Migraine and POC which inhibit ovulation
Inhibits ovulation
• Very low-dosed but as effective as CHC with 20-30mcg EE /150mcg desogestrel)

POP : Desogestrel 75 mcg

Estrogen withdrawal migraine

Hormone-withdrawal migraine are:
• Difficult to treat
• Duration over several days
• Associated with high disability
• Avoid medication overuse headache

What types of migraine are we talking about in the following studies?

It is of importance to consider the issue of:

Clinical trials with migraine and desogestrel 75 mcg

Desogestrel-only pill (Cerazette ®) in women with migraine with aura

Incidence for VTE

• 1.1 / 10 000 FJ Desogestrel-only
• 0.9 / 10 000 FJ LNG-IUP
Desogestrel-only pill (Cerazette ®) in women with migraine with and without aura

<table>
<thead>
<tr>
<th>Days / month</th>
<th>Mean (SD) baseline</th>
<th>Mean (SD) treatment</th>
<th>P-value</th>
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<tbody>
<tr>
<td>Headache days</td>
<td>3.1 (2.8)</td>
<td>2.6 (2.8)</td>
<td>0.459</td>
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<td>Migraine days</td>
<td>3.0 (3.4)</td>
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<td>Mean headache intensity*</td>
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Subanalysis of only females with MO showed very similar results

- reduction in migraine days (p<0.003)
- reduction in all headache days (p<0.02)
- reduction in days with pain medication (p<0.03)
- reduction in pain intensity (0.0001)
- reduction in the number of days with severe pain (p<0.0001)

Positive effects of the progestin desogestrel 75 μg on migraine frequency and use of acute medication are sustained over a treatment period of 180 days.

Table 2: Changes in headache intensity and use of acute medication within 30 days of change from the contraceptive pill (Cerazette) to the progestin-only pill (Desogestrel) 75 μg.

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Improvement of migraine with change from combined hormonal contraceptives to progestin-only contraception with desogestrel: A retrospective pilot diary study

Figure 3: Absolute difference in days of headache compared to baseline in patients taking the progestin-only pill compared to treatment period.

Different in MIDAS grades between baseline and during three months of treatment with desogestrel 75 μg. For each difference (1 to 3) the absolute number of patients is mentioned. Positive differences indicate improvement, 0 means no change, and negative differences indicate worsening.

Merki et al. 2013: The European Journal of Contraceptive & Reproductive Health Care

Desogestrel-only contraception may reduce headache frequency and improve quality of life in women suffering from migraine.

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Reactions on desogestrel 75μg can be very individual

- Improvement of migraine around 70-75% in women, mostly without improvement with prophylactic agents
- Worsening on the longterm 10-15%*
- 20% no improvement but safe and effective contraceptive
- Frequently it is possible to take women off prophylactic agents after longer use of Desogestrel 75μg

Data: G. Merki University Hospital Zurich

Case POP

- 28 year old woman with MO
- Frequency of migraine increased last two years
- Uses CHC since 5 years
- Around 6-8 attacks monthly,
- Particularly strong in the pill-free interval

Progestin implants and injection

Caution with longterm methods, because patients react individually and progestin rarely can act as a migraine trigger as well

Caution, no data

Levonorgestrel 20 -releasing intrauterine system

The MIRENA LNG-IUS causes highly fluctuating estradiol levels in women with and without bleeding Nielsen 1984

Conclusions

- Migraine is a disabling neurologic disease that places an enormous burden on patients
- There is a high unmet need for efficacious therapies and prophylactic agents with fewer side effects
- Migraineurs are at increased risk for ischemic stroke
- This risk multiplies with the use of CHC
- Women suffering from migraine with aura should not use combined hormonal contraceptives WHO-4
- Combined hormonal contraceptive can initiate and worsen migraines and potentially increase the risk for ischemic stroke in migraineurs
- Several studies indicate that desogestrel 75μg has a positive impact on the course of both migraine with aura and migraine without aura
- The POP does not increase the risk for stroke
- Copper-IUDs do not exert negative effects in migraineurs

G. Merki FUSZ