Contraception in women with migraine or depression

Further basic information on this topic can be found at www.fptraining.org

Update March 2018

Part 1
Migraine

Contents
Migraine

At the end of this session, participants will be able to understand and explain:

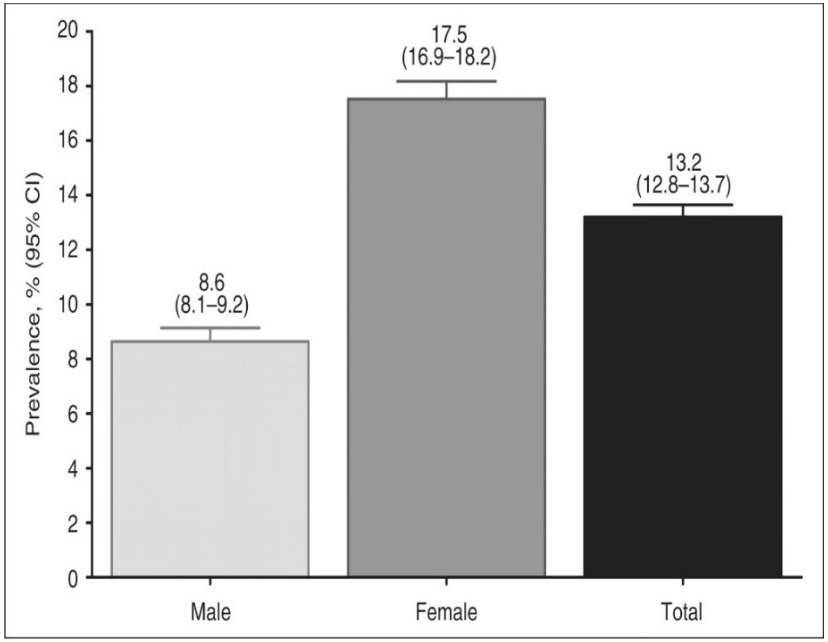
- Sex differences in epidemiology of migraine
- Prevalence of migraine
- Background of hormonal triggers for migraine
- Basics on diagnostic criteria for migraine
- WHO recommendation for CHC use in migraineurs
- The strength of the association between migraine and stroke
- When to stop CHCs in migraineurs
- Benefits and risks of hormonal and non-hormonal contraceptive options for migraineurs

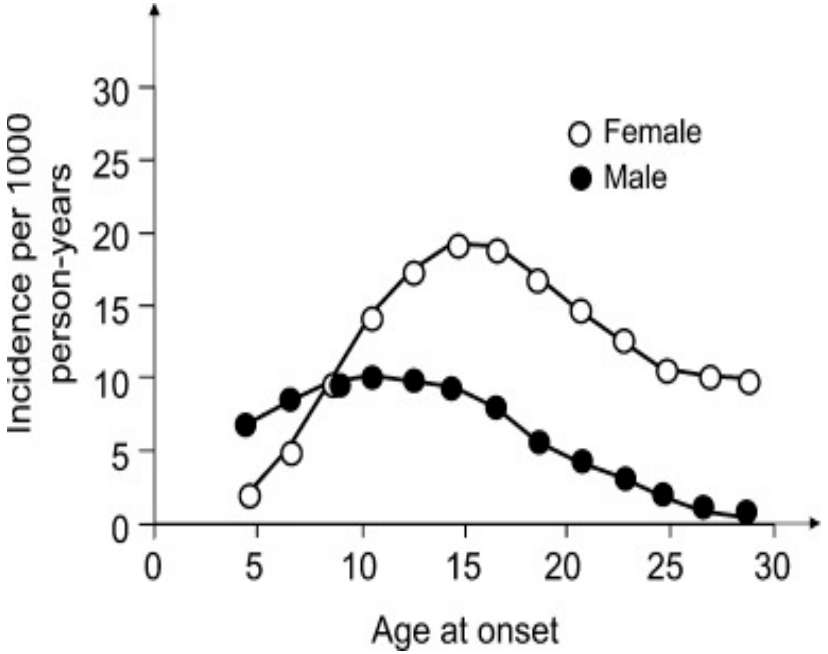
Epidemiology and prevalence of migraine

- Migraine affects around 10–15% of the population
- After puberty the prevalence of migraine is two to three times higher in women than in men (up to 18% of women)
- In women, 50% of migraines are associated with the menstrual cycle
- Estrogen fluctuations during the menstrual cycle play a pivotal role
- Interestingly, the activity of neurotransmitter involved in the pathophysiology of migraine also varies during the cycle

Ref 1–4

Migraine prevalence by age and sex in the USA





Migraine affects around 10–15% of the population. After puberty the prevalence of is two to three times higher in women than in men

Ref 1

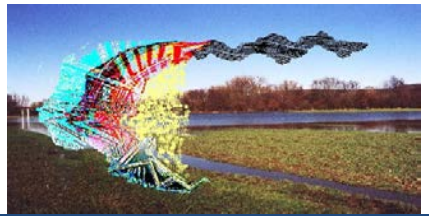
Diagnostic criteria for migraine (adapted from International Headache Society criteria, 2013)

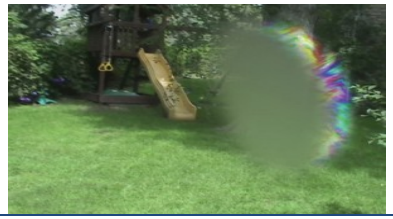
Migraine

- Attacks last 4–72 h
- Unilateral location
- Pulsating quality
- Moderate to severe intensity
- Aggravation by physical activity
- Nausea, photophobia, phonophobia

Aura

- Visual symptoms*
- Sensory symptoms*
- Speech/language symptoms
- Duration >5 min
- Accompanied or followed by headache





* More information in the notes

Ref 1

Migraine, COCs and stroke

	OR*
• **All migraine**	**2.3–3.7**
• **Migraine without aura**	**2.3–3.8**
• **Migraine with aura**	**3.8–8.6**
• **Migraine and COCs**	**13.9–16.9**
• **Migraine, smoking and COCs**	**34.4**

- Migraine with aura is associated with a higher risk of ischaemic stroke compared with migraine without aura
- The risk multiplies with use of COCs

Ref 1–3

WHO recommendation for CHC use in women with migraine

CHC use	**Initiation**	**Continuation**
Migraine without aura • Age <35 years • Age >35 years	 (Yes) No	 No No
Migraine with aura (WHO MEC category 4)	No	No

Migraine and combined hormonal contraceptives (CHCs)

- Use of CHCs is significantly associated with migraine (OR 1.4)
- CHCs increase the risk of ischaemic stroke in migraineurs
- Starting with CHCs can:
  - ➢ Initiate migraine in predisposed women
  - ➢ Worsen migraine
  - ➢ Initiate aura in previous non-aura migraineurs

➢ In all these situations CHCs should be stopped

Ref 1

Migraine
Alternatives to CHCs in contraception

Avoid

- Hormones which increase cardiovascular risk, including risk of stroke (CHCs)
- Hormones which may worsen the migraine (CHCs)
- Estrogen withdrawal, for example by using a method which inhibits ovulation and is used continuously

Use

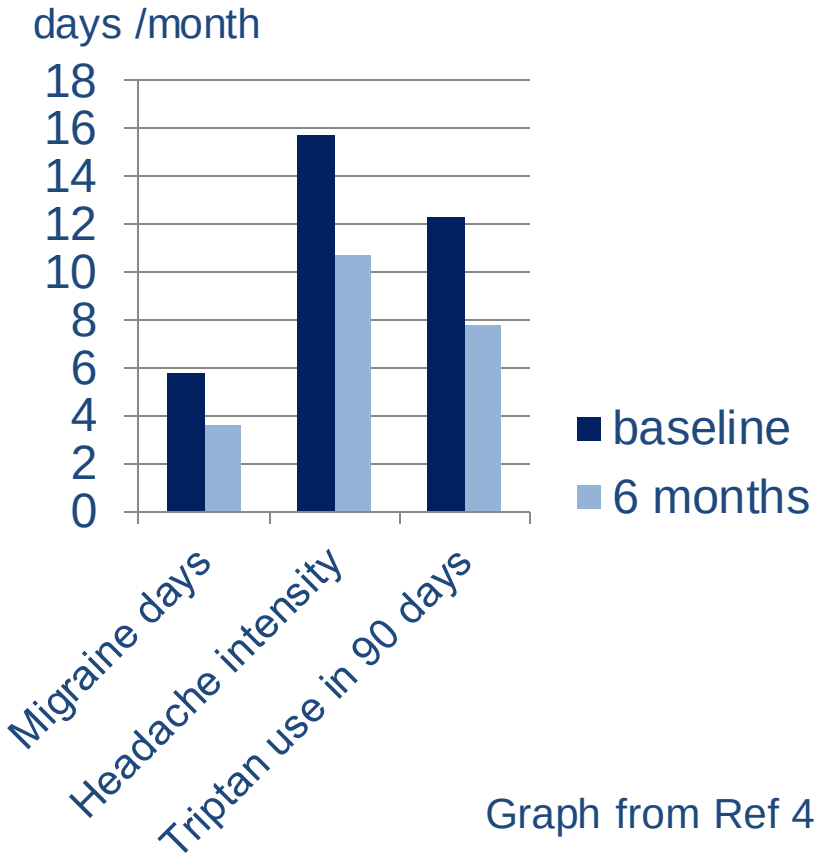
- **Progestin-only pill (POP) with desogestrel → positive impact on migraine**
- Implant
- Depot medroxyprogesterone acetate (DMPA)
- Copper intrauterine device (IUD)

Ref 1–6

Desogestrel 75 µg POP
Positive impact on migraine

It reduces:

- Frequency of MA
- Frequency of MO
- Number of triptans used
- Headache intensity
- Days missed at work
- Days missed for social activities



Graph from Ref 4

MA, migraine with aura; MO, migraine without aura

Ref 1–5

Migraine
Implant and DMPA

1. Implant

No data available, probably similar positive effects to those of POP. However, if migraine worsens, which may be expected in a small subgroup (15% with POP), removal of the implant is more expensive and uncomfortable than stopping a pill

2. DMPA

No data available, no negative impact on migraine expected or reported. However, if migraine worsens, which cannot be excluded in a small subgroup (<15%), it takes rather longer until DMPA is completely eliminated

These methods do not increase the risk of ischaemic stroke

Migraine
Copper IUD and LNG-IUS

Copper IUD

No data available, no negative impact expected

Levonorgestrel-releasing intrauterine system (LNG-IUS)

No data available, high fluctuation of estradiol levels might not be tolerated in women with hormone-related migraine. Clinical experience suggests better not to use. A prospective study is ongoing

Advantage in migraineurs: neither of these methods further increase the risk of ischaemic stroke

Part 2
Depression

Contents
Depression

At the end of this session, participants will be able to understand and explain:

- Definition of depression
- Prevalence in Europe
- How not to miss depression, when taking a history
- Potential effects of contraceptive methods on the course of depression in women with depression as a pre-existing condition
- Which contraceptives may cause depressed mood

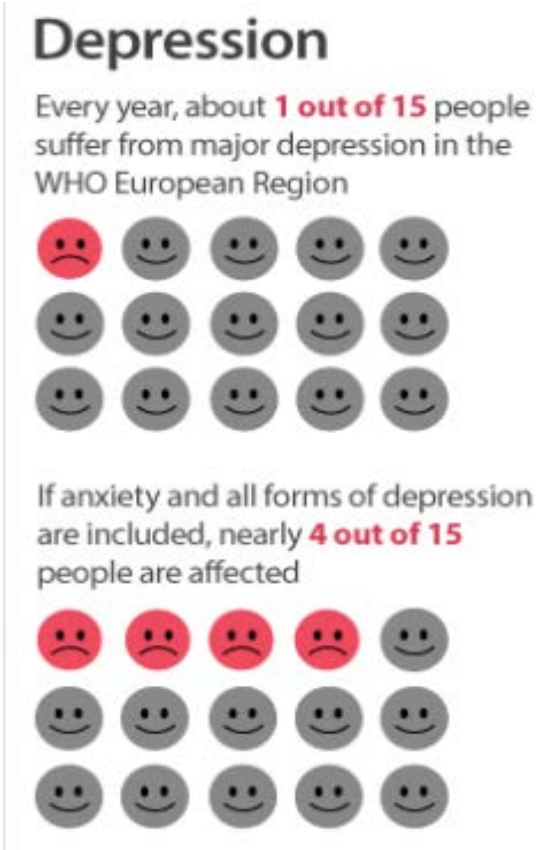
Depression
Prevalence and definition

Definition

Depression is a disorder that may make a person feel sad, empty or irritable, and may in turn affect the person's ability to function in normal activities

Prevalence in women

- During reproductive age 14%
- Postpartum depression 15%



Graph from Ref 3

Ref 1–3

Depression
Recognise depression

Recognise depression

Women often do not report depression because they are ashamed.
Some hormonal treatments can influence the course of the condition

During counselling

Many women will have already been diagnosed and will be on a course of treatment. These women can be identified by conducting a thorough medication history

Ask twice

Check that the patient has not omitted to mention anything
Plan enough time to discuss her personal life, including her private and working life. Ask actively about earlier episodes of negative moods and ever use of anti-depressants.
Does the patient feel she is functioning well in her normal activities?

Depression and Hormonal contraception
Is there a causal relationship ?

- Only one study indicates, that there might be a very small association between hormonal contraception and depression (2 cases in 10000 wy)
- This Danish study has **strong limitations** and has to be interpreted with caution: No information on the social background of affected women and on family history for depression (RR 2.8)
- The depression evolved typically within 3-6 months after newstart

Result: First diagnosis of depression	RR users vs non-users
CHC	1.1 s.
POC	1.2 s.
LNG-IUS	1.4 s.
Desogestrel POP	1.2 s.

Ref 1

Depression and CHCs

- CHCs can be used for contraception in women with depression
- Compared with placebo, no significant mood worsening was observed with a CHC containing estradiol/nomegestrol acetate; indeed, a premenstrual improvement in mood was observed
- A 24/4 regimen of drospirenone 3 mg/ethinylestradiol 20 µg improves premenstrual dysphoric disorder
- One study reported an improved depression score 3 months after CHC start in comparison with placebo

Depression can very rarely evolve in CHC users, typically newstarters. If healthy women report symptoms for depression after newstart of CHC, stop CHC and follow-up. Mood frequently improves within 2-4 weeks

Ref 1,2

Depression and DMPA

- No data indicate that DMPA initiates depression in healthy women
- In women with diagnosed depression no differences were found in psychiatric hospitalisation in comparison with non-DMPA users
- Few studies report that DMPA users have an increased likelihood of reporting depressive symptoms
- Depressive symptoms subsided after discontinuation of DMPA

Ref 1,2

Postnatal depression
IUD/IUS vs DMPA

- Data on the effect of DMPA on postnatal depression are inconsistent
- One trial found more women with major depression in the DMPA group than in the copper IUD group (Ref 1)
- The authors concluded that women diagnosed with postnatal depression should be counselled against use of DMPA (Ref 1)
- One study indicates that the LNG-IUS very rarely might be associated with depression, more data are needed.
- Another study did not confirm this result (Ref 2)

Ref 1,2,3

Contraception in women with depression Conclusion: POC

Based on limited evidence and clinical experience:

- Progestin-only contraception (POC) might rarely have a negative impact on the course of pre-existing depression
- Better options are CHCs, copper IUDs or permanent methods
- If no other option is available, the patient should be informed that mood may worsen and she should come back immediately if this happens (start a method which can easily be stopped)
- This is also true for the LNG-IUS

Case 1: Depression

- 38-year-old teacher, migraine with aura (eight attacks/month), hormonal component
- Many migraine treatments have been unsuccessful
- Contraception: condoms
- Two children
- Was started on the desogestrel-only pill to stop hormone withdrawal, improve migraine and for contraception

Case 1: Depression

- Six weeks later, the patient reported that she felt she was becoming depressed
- She stayed in bed all day and cried
- Her neurologist had started her on an antidepressant 3 days earlier
- Her migraine had strongly improved for the first time in years
- Recommendation: Stop the POP (however, no other option to treat her migraine with a POC is available)
- Her mood improved within 3 weeks after stopping the POP

Case 2: Depression

- 36-year-old woman in stable relationship
- Heavy smoker
- Would be happy without menstruation
- Decided to have the LNG-IUS, after counselling

Case 2: Depression

- Returned 2 weeks later (between Christmas and new year), because she felt depressed
- Reported that during the past she had experienced long periods of hospitalisation because of depression and using antidepressant medication
- The doctor told her that the LNG-IUS could not be the cause of the worsening of depressive periods, as the hormone was only locally released and had no systemic effects
- She returned to the clinic again 2 weeks later and insisted on removal of the LNG-IUS, because in the patient information leaflet she had read that the LNG-IUS can cause depression
- In between she had been hospitalised in a closed ward, as she was suicidal
- The LNG-IUS was removed
- **10 days later, she was feeling much better**