

Menstrual migraine – Diagnosis and management

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Prevalence Menstrual Migraine (MM)

4-8% of all women have menstrual migraine:

- Pure menstrual migraine: 1 %
- Menstrual related migraine: 6-7 %

In women with migraine disorder: 22 % have MM

Global prevalence of migraine

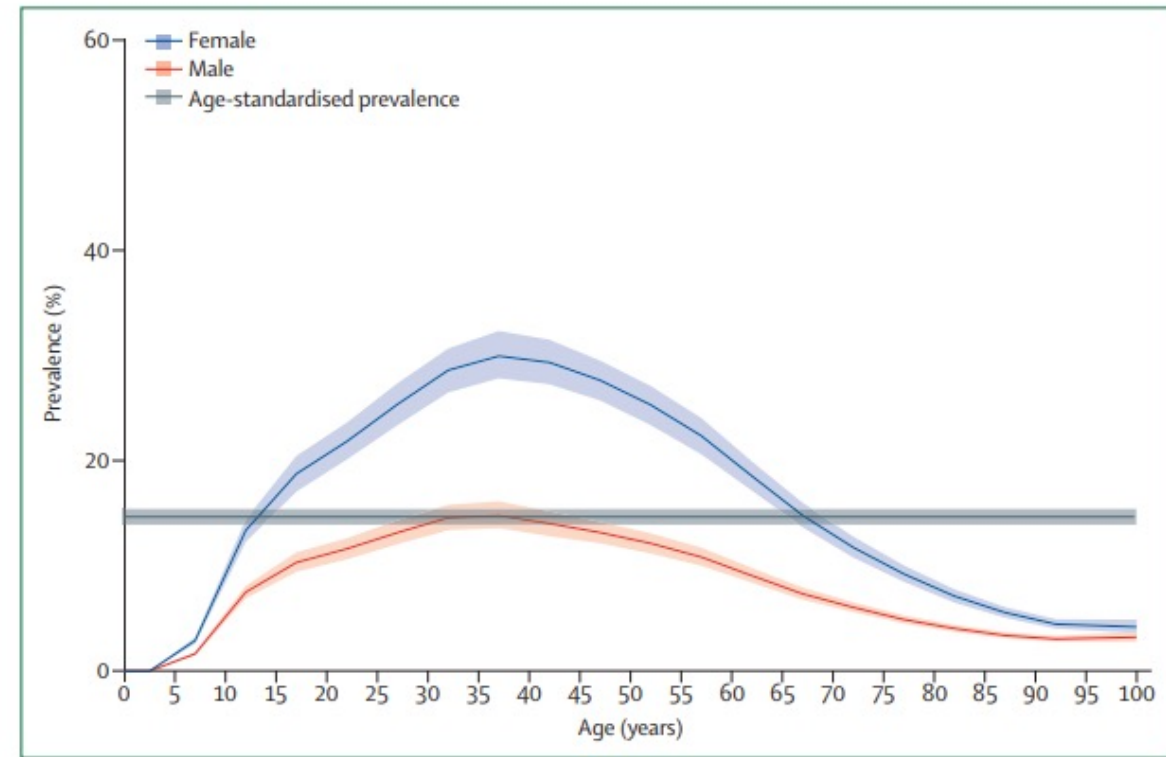


Figure 1: The global age-standardised prevalence and the global prevalence of migraine by age and sex. Reproduced from the GBD 2016 Headache Collaborators' systematic analysis for the Global Burden of Disease Study 2016.¹¹ Global age-standardised prevalence is 14.4% (95% CI 13.8–15.0).

Vetvik, K et al. Prevalence of menstrual migraine: A population-based study. *Cephalalgia*. 2014

Ashina et al. Migraine: epidemiology and systems of care. *Lancet*. 2021

Definitions used for menstrual migraine

Pure Menstrual Migraine

- Attacks fulfill criteria for migraine with or without aura
- Occur only on days –2 to +3 of menstruation in at least 2 out of 3 menstrual cycles *and at no other times of the cycle.*

Menstrually Related Migraine

- Attacks fulfill criteria for migraine with or without aura
- Occur on days –2 to +3 of menstruation in at least 2 out of 3 menstrual cycles, *and additionally at other times of the cycle.*

Adapted from the International Classification of Headache Disorders, 3rd edition - Appendix

MM - characteristics

MM attacks are mostly without aura

- even in women who have attacks with aura at other times of the cycle.

The MM attacks compared with other attacks in the cycle are:

- more severe and disabling
- last longer
- are less responsive to symptomatic medication

Association between MM and dysmenorrhea

Migraine frequency and severity often increase during perimenopause – particularly in women with MM

Diagnosing MM

- A diagnosis fulfilling the diagnostic criteria for migraine with or without aura
- Diagnosis should be restricted to women in whom there is a greater than chance association between migraine and menstruation
- A prospective headache diary – also recording menstrual periods
 - To confirm diagnosis
 - Harder to confirm in patients with very frequent migraine
 - – statistical association between migraine and menstruation has been shown also in this patient group

Barra et al. J. Headache Pain 2019

Huvudvärksdagbok

Namn: _____

År: _____

	Dag	Dag	Dag	Dag	Dag	Dag	Dag	Dag	Dag	Dag	Dag	Dag	Dag	Dag	Dag	Dag	Dag	Dag	Dag	Dag	Dag	Dag	Dag	Dag	Dag	Dag	Dag	Dag	Dag	Dag	
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
Januari																															
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Maj																															
Juni																															
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Augusti															2	2*	3	3	2	2											
September	3	1														1	3*	3	3	2	2							3	1		
Oktober											3	3*	3	2																	
November																															
December																															

Markera de dagar du har huvudvärk. Ange svårighetsgrad: 1 = lätt (hämmar ej aktivitet), 2= medelsvår (hämmar men hindrar ej aktivitet) , 3=svår (hindrar aktivitet).

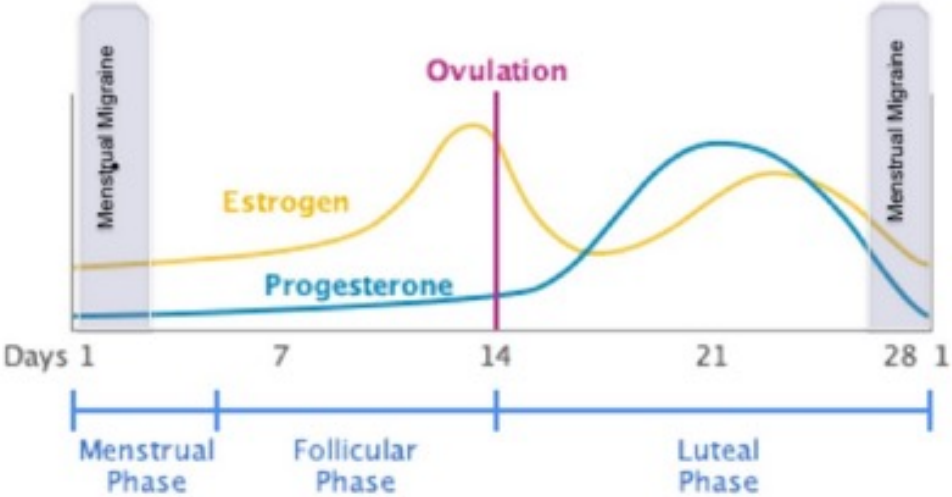
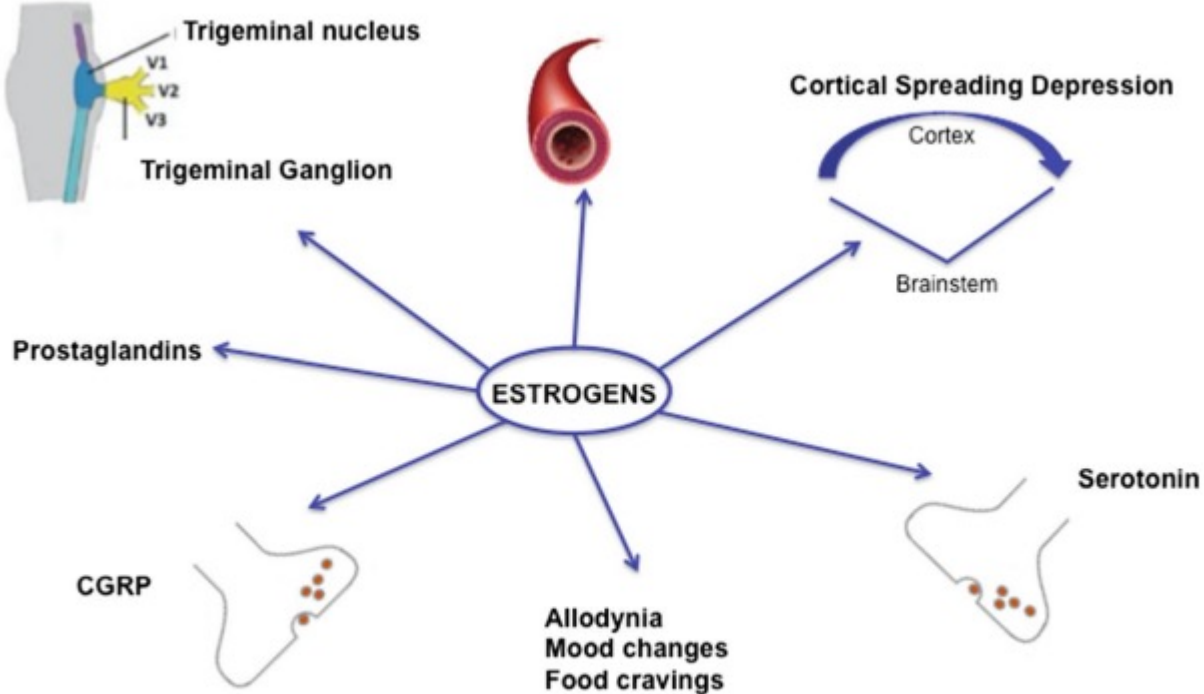
Mediciner:

Ange vilka läkemedel du tar i listan nedan. Skriv sedan bokstaven i din dagbok.

A.	C.	E.
B.	D.	F.

* First day of bleeding

Estrogen influences on menstrual migraine



Cupini, L.M et al. Menstrual migraine: what it is and does it matter?. *J Neurol* **268**, 2355–2363 (2021)

MM – when during the menstrual cycle?

- migraine is significantly more likely to occur in association with falling estrogen in the late luteal/early follicular phase of the menstrual cycle
- supports the hypothesis of estrogen “withdrawal” triggering migraine

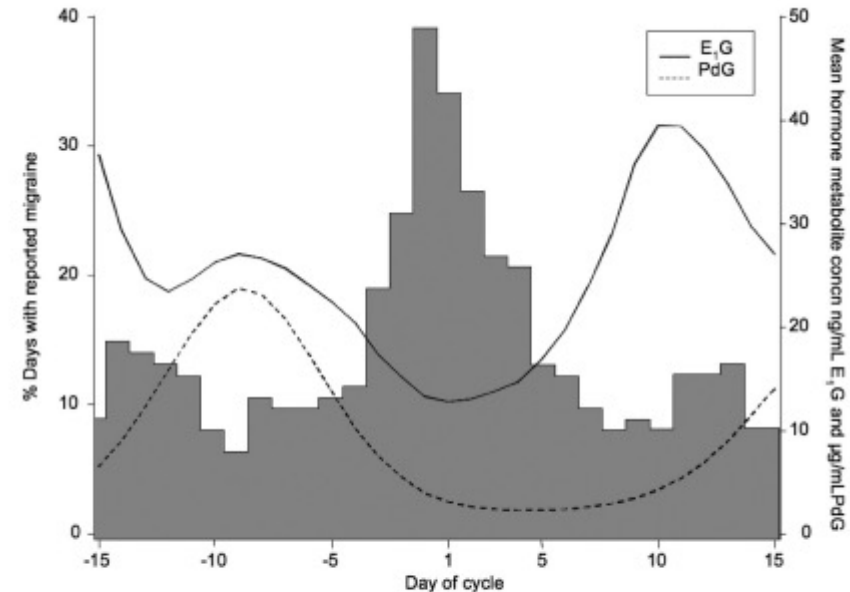


Figure 2. Incidence of migraine, urinary estrone-3-glucuronide (E_1G) and pregnanediol-3-glucuronide (PdG) levels on each day of the menstrual cycle in 120 cycles from 38 women.

Incidence of migraine relative to menstrual cycle phases of rising and falling estrogen

A. MacGregor et al. Neurology 2006, 67 (12) 2154-2158

Other differences reported in menstrual migraine compared with control groups

- changes in aldosterone levels
- intracellular magnesium
- platelet homeostasis
- prostaglandin release
- withdrawal of oestrogen and progesterone -> the endometrium breaks down and prostaglandins are released

Different methods of treatment for menstrual migraine - Medications that can be used

Mini-prophylaxis

Triptans:

Frovatriptan (level A)*

Zolmitriptan (level B)*

Naratriptan (level B)*

Eletriptan

Sumatriptan

NSAIDs:

Naproxen

Mefenamic acid

Nabumetone

Hormonal therapy:

Higher doses of estrogen such as 100- μ g patch or 1.5-mg gel are often required.

Nutraceuticals:

Magnesium

Medical devices:

Non-invasive vagal nerve stimulation

Long-term prevention

Standard medications used for migraine prevention*

Hormonal therapy:

Continuous hormonal therapy either via continuous oral contraceptive pill without a break for menses or extended-cycle dosing of a transvaginal ring contraceptive.

Gonadotropin-releasing hormone (GNRH) analogues

Acute therapies

Triptans:

Sumatriptan

Rizatriptan

Zolmitriptan

Frovatriptan

Almotriptan

Eletriptan

Naratriptan

Sumatriptan-naproxen

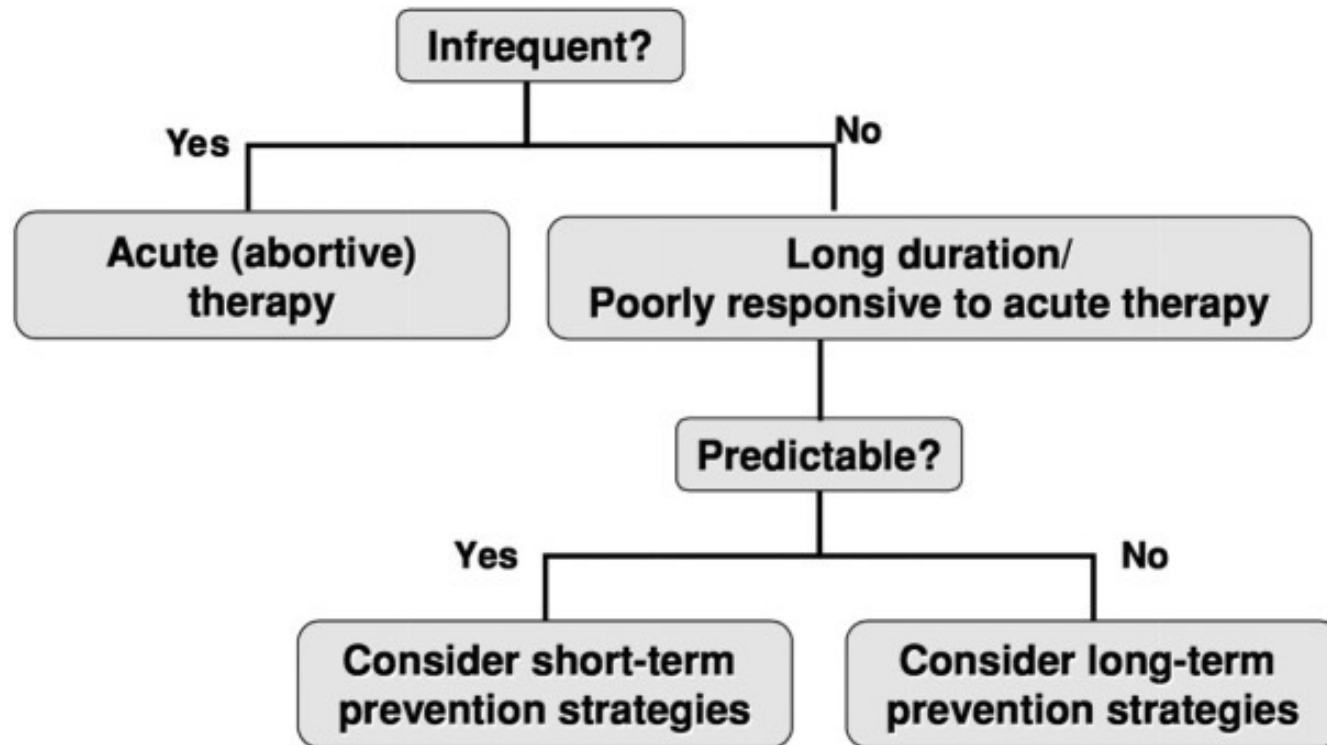
NSAIDs:

Naproxen

Mefenamic acid

Ansari, T. *et al.* Management of Menstrual Migraine. *Curr Neurol Neurosci Rep* (2020).

Menstrual migraine – treatment



Consider:

- Regularity of menstruation?
- Migraine with or without aura – vascular risk factors?
- Presence or absence of menstrual disorder? Depression? Sleep disturbances?
- Need for contraception?
- MM + frequent attacks in between?
- Personal preference?

Summary: Menstrual migraine - treatment

1.) Acute treatments in MM: **Triptans**

Table 2.—Comparison of Effectiveness of Various Triptans Using Statistically Significant Results From Studies Discussed Above

	2 hour pain relief	2 hour pain free	Sustained pain relief 2 to 24 hours	Sustained pain free 2 to -24 hours
Sumatriptan 100 mg		61%	31%	
Rizatriptan	33-73%	63%	63%	32%
Naratriptan	43%		42%	
Zolmitriptan		28-48%		
Almotriptan		48%	36%	

Only statistically significant results are reported in the table.

Maasumi K et al. Menstrual Migraine and Treatment Options: Review. *Headache*. 2017

Summary: Menstrual migraine - treatment

2.) Short term prophylactic treatments around time for menstruation – start 2 days before bleeding starts

Naproxen 500mg x 2 (total 7 days)

Triptans

Frovatriptan 5 mg x 2 – day -2 then 2,5mg x 2 for another 5 days

Zolmitriptan 2,5mg x 3 (total 7 days)

Naratriptan 1x2 (total 5-6 days)

(Estraderm patch days before menses up to 3 days after start of menses)

(Magnesium – 360 mg daily from day 15 to day 30)

Summary: Menstrual migraine - treatment

3.) Prophylactic treatment:

Pure menstrual migraine:

Hormonal treatment (CHC, transdermal estrogen, levonorgestrel intrauterine system or contraceptive implant – talk with a gynecologist)

Menstrual related migraine:

Traditional prophylactic treatments (Note: interactions, teratogen effects)

Maasumi K et al. Menstrual Migraine and Treatment Options: Review. *Headache*. 2017

Review Burch R. *Headache* 2020;60:200-216

Riktlinjer Svenska Huvudvärkssällskapet www.huvudvarkssallskapet.se

