

VCU

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Headaches in Women: Mechanisms and Management

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The burden of headache in women

- The public health burden of recurrent headache is enormous
 - Almost entirely due to chronic primary headache disorders, especially migraine
 - Migraine is ranked 11 among causes of disability in women

World Health Organization Fact Sheet #277. Available online at:
<http://www.who.int/mediacentrefactsheetsfs277/3n>

IHS Diagnostic Criteria For Migraine Without Aura

- A. Lasting 4 to 72 hours
- B. Two of the following
 - Unilateral location
 - Pulsating quality
 - Moderate or severe intensity
 - Aggravation by routine physical activity
- C. At least one of the following:
 - Nausea and/or vomiting
 - Photophobia and phonophobia
- D. At least five attacks fulfilling the three bullet points above
- E. No evidence of organic disease



IHS Diagnostic Criteria For Tension-Type Headache

- A. Lasting 30 minutes to 7 days
 - Steady, pressing quality
 - Bilateral location
 - Mild to moderate intensity
 - No aggravation by routine physical activity
- C. No associated symptoms (mild nausea allowed)
- D. At least five attacks fulfilling the three bullet points above
- E. No evidence of organic disease



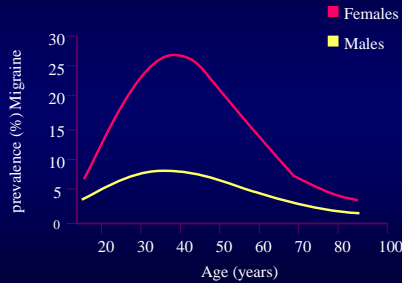
Options for acute therapy

- | | |
|------------------------|---------------------|
| • Nonspecific | • Specific |
| NSAID analgesics | Ergot derivatives |
| Opioid analgesics | Triptans |
| Sedatives | (CGRP antagonists?) |
| Combination analgesics | (NO inhibitors?) |

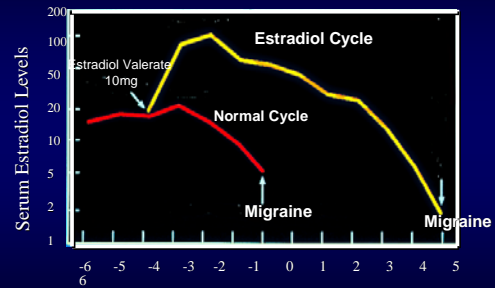
Migraine Preventive Medications Categories of medication typically prescribed

- Beta adrenergic blockers*
- Antidepressants
- Antiepileptic drugs (AEDs)*
- Serotonin antagonists
- Calcium channel blockers
- Nonsteroidal anti-inflammatory drugs (NSAIDs)

Migraine Prevalence in Women and Men



Estrogen and migraine: Somerville's work



Additional Evidence Linking Estrogen Fluctuations to MM

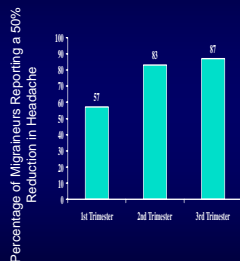
- Migraine more likely to occur during the pill-free or placebo week of traditional OCs (Whitty et al., *Lancet* 1966)
- MM often improves during pregnancy (Stein, *Headache* 1981)
- MM often returns postpartum (Neri et al., *Maturitas* 1993)
- MM often improves with onset of menopause (Neri et al., *Maturitas* 1993)
- Migraine common with supraphysiologic estrogen decline seen in infertility regimens (in press)

Migraine Activity During the Female Lifecycle¹

	Estrogen Levels	Migraine Prevalence
Menarche and menstruation	Cyclic	↑
Pregnancy	Consistently high	↓
Perimenopause	Irregular fluctuations	↑
Menopause	Consistently low	↓

1. Lucas S. *Migraine in Women*. BC Decker Inc; 2004.

Migraine and Pregnancy



50% to 85% of migraine patients report an improvement in headaches during early pregnancy, particularly when¹

- Migraine is not accompanied by aura
- Migraine began at menarche
- Migraine has been related to menses

Sances G et al. *Cephalalgia*. 2003;23:197-205.

A cautionary note

- Women with ongoing headache at the end of the first trimester are unlikely to experience further reduction of headache²
- Migraine headaches generally recur soon after delivery¹
- Postpartum headache must be carefully evaluated. Differential diagnosis includes migraine, but also...
 - Ischemic and hemorrhagic stroke
 - Cerebral venous thrombosis
 - Preeclampsia
 - Pituitary apoplexy
 - Low volume headache

1. Brandes JL et al. *Migraine in Women*. BC Decker Inc; 2004.
2. Marcus DA et al. *Headache*. 1999;39:625-632.

Gestational hypertension

- A large population-based study compared CHD risk profile of migraineurs to non-migraine population.
- Migraineurs had increased likelihood of several classic risk factors
- Women with migraine more likely to have been diagnosed with gestational hypertension, even after taking into account age and number of pregnancy
- Diagnostic and treatment implications

Scher AI, Terwindt GM, Picavet HS, et al. Cardiovascular risk factors and migraine: The GEM population-based study. *Neurology* 2005;64:614-620.

Migraine treatment in pregnancy

- Recommendations based on expert consensus
- Avoid medicine if possible in 1st trimester
- Use lowest effective doses
- Acute treatment: opioids, hydration, anti-emetics, acetaminophen
- Preventive treatment: most experts recommend propranolol

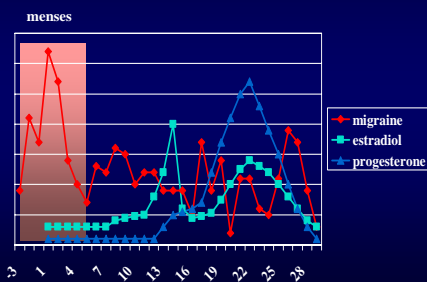
Sumatriptan pregnancy registry

- As of Oct 2005, 15 birth defects in 359 outcomes in 1st trimester, excluding spontaneous losses, fetal deaths and voluntary terminations without reported defects. 4.2% (95% CI 2.4-6.9%)
- No pattern to malformations

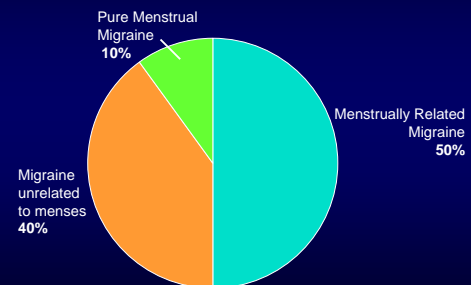
Migraine treatment in lactation

- Breast-feeding should be encouraged
- Lactation does not affect headache activity
- Check AAP lactation rating if medicines are needed
 - Sumatriptan and zolmitriptan compatible with nursing

Migraine and the menstrual cycle



Relationship of Migraine Attacks to the Menstrual Cycle



1. Loder EL et al. *Migraine in Women*. BC Decker Inc; 2004.

What is menstrual migraine?

- Provisional criteria suggest interval of -2 to +3 days
- Distinguish between
 - “Pure” menstrual migraine
 - Menstrually-related” migraine

Menstrual Migraine: Treatment

- Begin with standard therapy
 - Identify and avoid other triggers
 - Use acute, preventive, and nonpharmacologic treatment as indicated
- Proceed to short-term prevention strategies

Short-term prevention of menstrual migraine: grading the evidence

- Level A (Multiple randomized, controlled trials supporting efficacy)
 - Estradiol gel 1.5 mg applied daily days -2 through +5
 - Naratriptan 1 mg po twice daily days -2 through +3
 - Frovatriptan days -2 through +3
- Loading dose of 5 mg po twice daily followed by 2.5 mg po twice daily

Martin VT. Menstrual migraine: a review of prophylactic therapies. Curr Pain Head Reports 2004;8:229-237.

Short-term prevention of menstrual migraine: grading the evidence

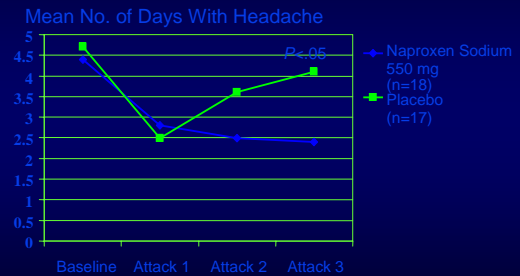
- Level B (Single randomized, controlled trial suggesting efficacy)
 - Naproxen sodium 550 mg po bid

Martin VT. Menstrual migraine: a review of prophylactic therapies. Curr Pain Head Reports 2004;8:229-237.

Short-term prevention regimens

- Timing is everything
- Diary information necessary to determine timing of headache and periods
- Ovulation prediction kits may be useful for women with irregular periods
 - Interval from ovulation to subsequent period is fixed at 14 days

Mean No of Headache Days



Sances et al. Headache. 1990;30:705-709.

Migraine and Menopause

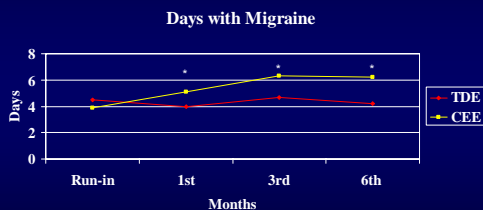
- Migraine can improve or worsen near menopause¹
 - Symptoms generally increase during perimenopause
 - One study showed 29% prevalence at a specialty clinic (nearly 60% reported some type of headache)²
- Clinical pattern depends upon type of menopause³
 - 67% improve with physiologic menopause
 - 67% worsen with surgical menopause
- ERT/HRT have unpredictable effects on migraine headache, dependent on dose and regimen used¹

1. Silberstein SD et al. *Migraine in Women*. BC Decker Inc; 2004.
2. MacGregor EA et al. *Climacteric*. 1999;2:219-223.
3. Neri I et al. *Maturitas*. 1993;17:31-37.

Two Practical Questions

- Are OCs or HRT *safe* for women with migraine?
 - Major concern is stroke
- Do OCs or HRT *affect the clinical course* of migraine?
 - Altered frequency or severity of headache
 - Altered frequency or severity of non-headache symptoms of migraine

HRT and headache: Preparation Used/Route of Delivery



Nappi R, *Maturitas* 38: 157-63, 2001

Constancy of Dosing/ Progestins

- Constancy of dosing
 - Continuous better than cyclic¹
- Use with progestin
 - Progestins can aggravate headache or have little effect²

¹Kudrow L. *Headache* 15: 36-40, 1975

²Magos A. *BJOG* 93: 1290-96.

Best advice

- Current evidence insufficient to recommend use of OCs or ERT solely as *treatment* for migraine
- Risks and benefits to individual woman must be considered
- Migraine without aura is not a contraindication to use of OCs or ERT. Constancy and route of administration *may* make a difference. Discontinuation of OC in women with stable, well-managed headaches probably not reasonable.
- Increased stroke risk and differential impact on clinical course of OCs and ERT in MA dictate caution in these women.

Questions & Answers

