Women, Hormones & Migraine-What is the Connection?

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MIGRAINE AND MENARCHE

• Beginning with puberty, migraine is more common in girls

• Menstrually-associated migraine begins at menarche in 33% of women with migraine

• 60-70% of female sufferers experience migraine in association with menses

Silberstein SD. Neurology. 1991; 41:786-793
Migraine Prevalence: US Female Population

SPECIFIC QUESTIONS FOR WOMEN

**Do you often have a headache with menses?**

**What happened to your headaches during pregnancy, after delivery, and during breast-feeding?**

**Any current chance of pregnancy?**

**Are you planning on pregnancy near future?**

**What are you doing now for birth control?**
MENSTRUAL MIGRAINE - WHY IMPORTANT TO RECOGNIZE & TREAT

• More disabling than non-menstrual migraine for many women
• Tends to last longer, be more refractory to treatment
• Often associated with nausea & morning (wake-up) headache
• Predictable so treatment can be preemptive
DIAGNOSIS

• Menstrual migraine is migraine that occurs in the perimenstrual window of -2 to +3 of the menstrual cycle and occurs at least 66% of the time in a patient; i.e. the migraine begins sometime in that time frame

• Day 1 is first day of bleeding; there is no Day 0

• Prospective diary recommended but not mandatory to make the diagnosis
ESTROGEN WITHDRAWAL HEADACHE

- ICHD-3 8.3.3 defined as headache or migraine developing within 5 days after 3 or more weeks of exogenous estrogens is interrupted (for example during placebo week of oral contraceptive pills) and headache/migraine resolves within 3 days in absence of further exogenous estrogen.

- [ICHD 8.3 Headache attributed to substance withdrawal]

- ichd-3.org accessed 1/04/2020
A headache calendar or diary is THE MOST IMPORTANT TOOL to diagnose menstrual migraine and then to classify as pure menstrual migraine (PMM) vs. menstrual related migraine (MRM).

The patient MUST mark down the first and last day of menses on the calendar as well as all headache days.

Day 1 of cycle=first day of bleeding
WHY SO IMPORTANT TO DIFFERENTIATE PMM VS. MRM?

• For women with PMM (pure menstrual migraine) her treatment can be targeted to her vulnerable time of the cycle
• For women with MRM (menstrual related migraine) her treatment will need to be expanded to looking at all her triggers and risk factors and a broader preventive approach
HORMONE INFLUENCE

- Drop in estrogen is a strong migraine trigger
- Late luteal injections of estradiol postponed migraine occurrence
- Late luteal injections of progesterone postponed bleeding but not migraines
# Treatment Approaches

## Menstrual Migraine

- **NSAID’S**
- **MAGNESIUM**
- **HORMONAL**
- **STANDARD MIGRAINE PREVENTIVES**
- **RESCUE OPTIONS IF SEVERE**

- **TRIPTANS INCLUDING NON-ORAL AND SHORT-TERM PREVENTIVE DURING VULNERABLE TIME**
SHORT-TERM PREVENTION: NAPROXEN SODIUM

- Naproxen sodium 550 mg BID versus placebo (n=35)
  - Day -7 to Day +6 (start of menses=Day 1) for 3 cycles
  - Significantly reduced headache intensity, duration, number of headache days compared to baseline, p<.05
  - Naproxen was only superior to placebo at 3 months of treatment, p<.05
  - 33% were headache free (none with placebo)

Magnesium (Mg) is postulated to affect pain threshold. Magnesium pyrrolidone carboxylic acid 360 mg/day or placebo from Day 15 to start of menses for 2 cycles (n=20). Mg treatment reduced number of headache days (P<.01) and reduced Total Pain Index (P<.005). Facchinetti F et al. Headache. 1991;31:298-301.
HORMONAL TREATMENT OPTIONS

- Add-back estrogen-perimenstrually: e.g. estradiol patch .1 mg the week of menses
- Continuous OCP’s-monophasic
- Continuous contraceptive ring (NuvaRing)
SHORT-TERM PREVENTION WITH ESTRADIOL GEL

Timing Matters

- Estradiol gel or placebo on tenth day following the first day of peak fertility and continued daily until, and including, day +2
- Percutaneous estradiol was associated with a 22% reduction in migraine days, \( p=0.04 \)
- The migraines were less severe and had less nausea
- However, there was a 40% increase in migraine in the 5 days following rx!
- Benefit during treatment was offset by deferred estrogen withdrawal, triggering post-dosing migraine immediately after the gel was stopped

MacGregor EA et al. Neurology 2006;67:2159–2163
SHORT-TERM PREVENTION:
TRANSDERMAL ESTROGEN
Dose Matters

- No benefit observed in placebo-controlled trial with 50 µg 17-beta-estradiol

- Reduced frequency (ns) and use of rescue medication (P<.05) with 100 µg dose compared with 25 µg dose

- No long term safety data from these studies

Migraine is an independent risk factor for stroke in women < 45 years old

- 2-fold increase in ischemic stroke compared to women without migraine
- *This increase primarily driven by the subgroup of women who have migraine with aura*
- Approximately 1.5 increased risk hemorrhagic stroke in women with migraine
- Other risk factors such as smoking amplify this risk
To date, there is no consensus on guidelines for prescribing combined oral contraceptives in women who have migraine with aura. The International Headache Society advises that low-dose estrogen may be prescribed in women who have simple visual aura. The American College of Obstetricians and Gynecologists recommends using progestin-only intrauterine or barrier contraception. Meanwhile, the World Health Organization states that estrogen-containing contraception is an absolute contraindication in all women who have migraines with aura.

CLINICAL PRACTICE

• Low dose estrogen dose CHC’s are appropriate in the majority of women with migraine without aura who do not smoke

• CHC’s may be an option for women with migraine with aura if the benefits outweigh the risks (individualized approach)

• Use of the vaginal ring contraceptive decreased aura frequency in women with migraine with aura in one study

CONTRACEPTIVE OPTIONS: THE YOUNGER WOMAN WITHOUT AURA

- Regular menses
- Low-dose, monophasic
- Dose of ethinyl estradiol 10-35 mcg
- Oral or vaginal ring delivery

Contraceptive Options for Women with Aura

- Progesterone only oral contraceptive
- IUD (Progesterone (3 dosages) & copper IUD)
- Progesterone implant
- Progesterone Injection
- Low dose estrogen containing contraception if non-smoker and benefits>risks
TRIPTANS

• Acute or short-term preventive

• None are FDA approved for short-term prevention of menstrual migraine

• Frovatriptan 2.5 mg and Naratriptan 2.5 mg are most suited due to long half-life and low chance of medication overuse

• Can be dosed once daily or twice daily for 5-7 days beginning 1-2 days prior to expected onset of menstrual migraine
RESCUE OPTIONS - MENSTRUAL MIGRAINE

- Sumatriptan injectable (3, 4, 6 mg)
- Sumatriptan or Zolmitriptan nasal delivery
- Ketorolac 60 mg IM injectable
- Anti-emetic suppository
- Occipital Nerve Block
- Sphenopalatine Ganglion Nerve Block (SPG)
- Infusion Center IV orders (Ketorolac 30 mg, Odansetron 4 mg, Magnesium 1-2 gram)
New Migraine Treatments

- CGRP mAB’s for prevention
- Oral “gepants” for acute treatment (Ubrelvy; Nurtec)
- Oral “ditan” for acute treatment (Reyvow)
- Non-invasive neurostimulators (newest Nerivio)
- Coming: an oral CGRP antagonist (gepant) for daily prevention of migraine
- None are FDA approved specifically for menstrual migraine; unknown effects on pregnancy & BF
RESOURCES FOR PREGNANCY AND BREAST-FEEDING


  User friendly (put in name of medication-all current information that is known comes up)
RESOURCES FOR WOMEN WITH MIGRAINE

1. International Headache Society www.ihs-headache.org
2. Migraine Research Foundation www.migraineresearchfoundation.org
   Numerous international speakers; live event to educate worldwide-free
   www.migraineworldsummit.com
   - Diamond Headache Clinic Research & Educational Foundation
   Connection to find Hope and Wellness Published 2013
   Geared for the female migraine patient to be better educated about migraines
   and better able to communicate with her health care providers
   Available on Amazon (Paperback or e-book) [Author Hutchinson, S.]
Thank you

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