Women, Hormones & Migraine-What is the Connection?

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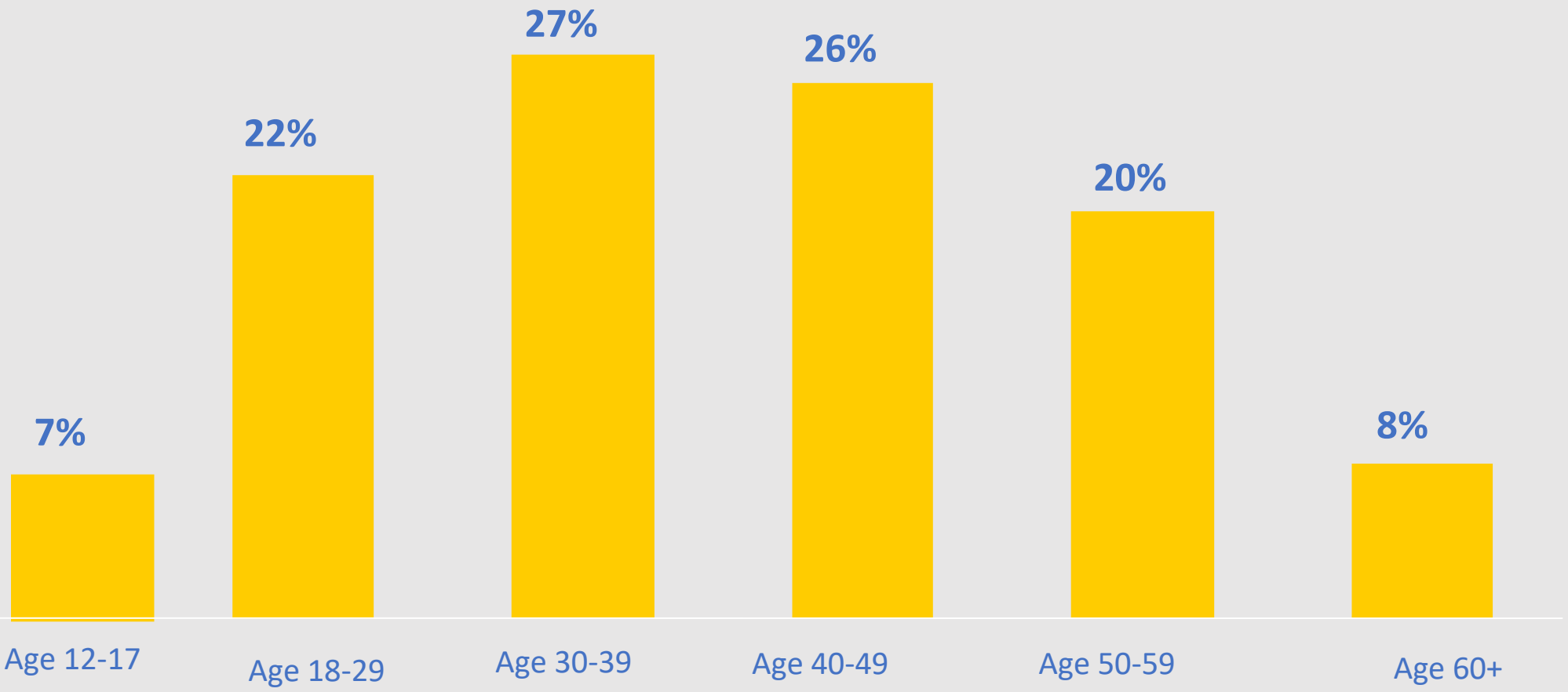
MIGRAINE AND MENARCHE

- 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
MacGregor EA. *Neruologic Clinics*. 1997; 15(1): 125-141
Benedetto, C et al. *Cephalalgia.* 1997; 20: 32-34

Migraine Prevalence: US Female Population



Lipton RB et al. *Headache*. 2001;41:646-657.

SPECIFIC QUESTIONS FOR WOMEN

DO YOU OFTEN HAVE A HEADACHE WITH MENSES?

ANY CURRENT CHANCE OF PREGNANCY?

WHAT HAPPENED TO YOUR HEADACHES DURING PREGNANCY, AFTER DELIVERY, AND DURING BREAST-FEEDING?

ARE YOU PLANNING ON PREGNANCY NEAR FUTURE?

WHAT ARE YOU DOING NOW FOR BIRTH CONTROL?

MILES FOR MIGRAINE

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

DIAGNOSTIC TOOL

- 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
- Somerville BW, Neurology, 1972:22:355-365.

Treatment Approaches Menstrual Migraine

NSAID'S
MAGNESIUM

- HORMONAL

- TRIPTANS INCLUDING NON-ORAL AND SHORT-TERM PREVENTIVE DURING VULNERABLE TIME

- STANDARD MIGRAINE PREVENTIVES
- RESCUE OPTIONS IF SEVERE

MILES FOR MIGRAINE

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)

Sances G et al. Headache. 1990;11:705-709.

SHORT-TERM PREVENTION: MAGNESIUM

- 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)

-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

MILES FOR MIGRAINE

SHORT-TERM PREVENTION: TRANSDERMAL ESTROGEN

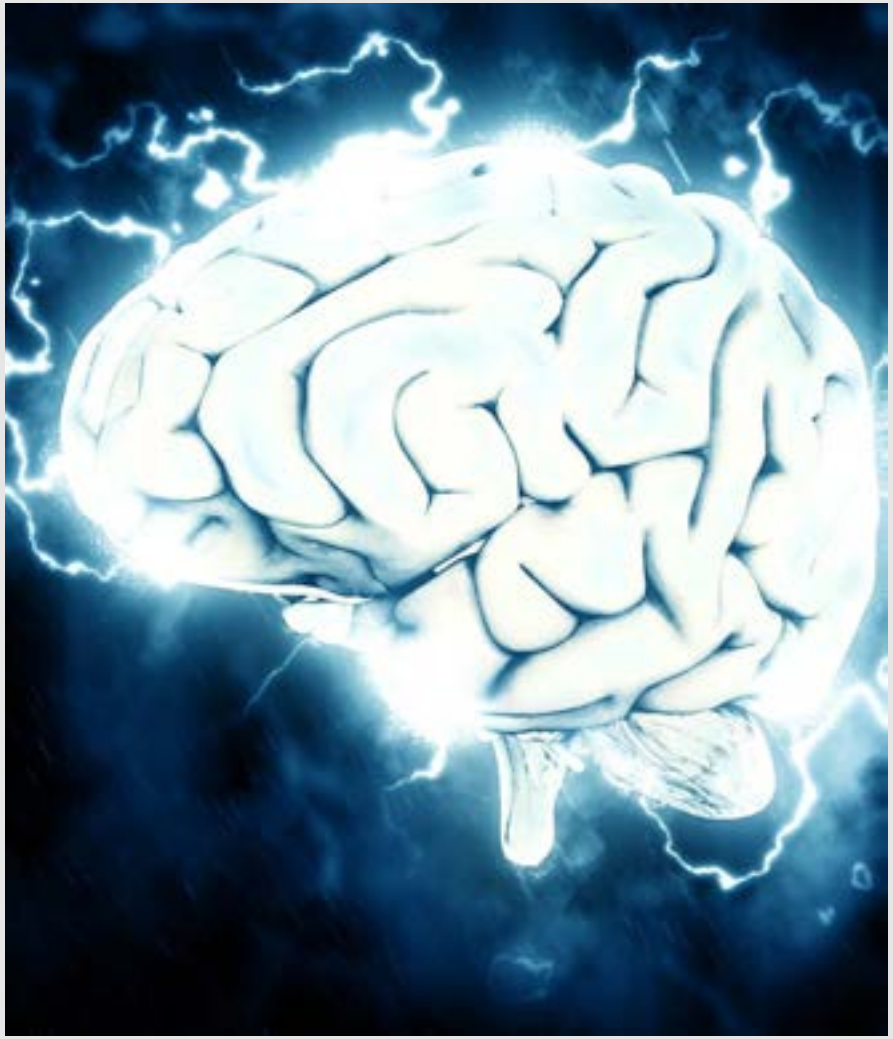
Dose Matters

-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

1. Smite MG et al. Headache. 1994;34:103-106. 2. Pradalier A et al. Proc 10th Migraine Trust Symp. 1994;129-132.



MIGRAINE AS RISK FACTOR FOR STROKE

- 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

ESTROGEN CONTROVERSY

- 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.1 The American College of Obstetricians and Gynecologists recommends using progestin-only intrauterine or barrier contraception.2 Meanwhile, the World Health Organization states that estrogen-containing contraception is an absolute contraindication in all women who have migraines with aura.3

1. International Headache Society Taskforce. Recommendations on the risk of ischaemic stroke associated with use of combined oral contraceptives and hormone replacement therapy in women with migraine. Cephalalgia. 2000;20:155-6. 2. ACOG Committee on Practice Bulletins-Gynecology. ACOG practice bulletin. No. 73: Use of hormonal contraception in women with coexisting medical conditions. Obstet Gynecol. 2006;107(6):1453-72. 3. World Health Organization. Medical Eligibility Criteria for Contraceptive Use. 3 rd ed. Geneva: Department of Reproductive Health and Research, WHO; 2004.

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

Calhoun A, Ford S, Pruitt A. The impact of extended-cycle vaginal ring contraception on migraine aura: A retrospective case series. Headache. 2012;52:1246-1253.

CONTRACEPTIVE OPTIONS: THE YOUNGER WOMAN WITHOUT AURA

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

Chavanu et al. Pharmacotherapy. 2002;22(11):1442-1457.

MILES FOR MIGRAINE

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 of 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

MILES FOR MIGRAINE

RESOURCES FOR PREGNANCY AND BREAST-FEEDING

- Drugs in Pregnancy and Lactation Book. Authors Briggs, Freeman, et al. Updated regularly. Most recent edition 2018. Hard copy and on-line

- Hales Medications and Mother's Milk. Updated regularly. Most recent edition 2019. App available.

- Free data base called LactMed (app available)

https://www.ncbi.nlm.nih.gov/books/n/lactmed

- 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
3. Migraine World Summit (Dates 3/18-3/26/2020)

   Numerous international speakers; live event to educate worldwide-free

   www.migraineworldsummit.com
4. Migraine Education On-line www.dhc-fdn.org/pages/cme

- Diamond Headache Clinic Research & Educational Foundation

5. American Headache Society www.americanheadachesociety.org
6. The Woman's Guide to Migraine Management: Understanding the Hormone 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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www.ocmigraine.org