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"This is a description of an individual expert practitioner's approach, presented to give the learner some practical ideas. These treatment recommendations have not been endorsed by the American Headache Society® (AHS). For some of the statements and recommendations there is little formal evidence."

### How Do I Do It Reference for Menstrual Migraine

Menstrual migraine is migraine without aura that occurs in at least 2/3 of menstrual cycles during the 5-day perimenstrual period from day -2 through day +3 (day 1=first day of flow). The best way to make the diagnosis is by review of a headache diary that the woman keeps for at least 3 months. Over 50% of women migraineurs suffer from menstrual migraine.

Menstrual migraine is divided into 2 types:

1. **Pure Menstrual Migraine:** migraine without aura that occurs exclusively during the 5-day perimenstrual window of -2 through +3. This affects approximately 14% of female migraineurs.
2. **Menstrually Related Migraine:** migraine without aura that occurs during the 5-day perimenstrual window of -2 through +3 but occurs at other times of the cycle as well. This is present in approximately 50% of female migraine patients.

Treatment approaches include acute, preventive and short-term regimens. Options include OTC preparations; prescription medications including hormonal manipulation; herbal supplements; and non-pharmacologic modalities. Much of what we do in the treatment of menstrual migraine is off-label. In fact, there are no prescription medications that have been given specific FDA approval for acute treatment or prevention of menstrual migraine.

### ACUTE TREATMENT

Treatment for acute menstrual migraine is similar to non-menstrual migraine acute treatment. However, many women report that their menstrual migraines are more difficult to treat. The clinical desired end-point of headache-free in 2 hours is a reasonable treatment goal for evaluating the effectiveness of acute therapy. The following is a list of commonly used treatment options:

1. Acetaminophen-Aspirin combinations with and without caffeine (e.g. brand name Excedrin; the caffeine can potentiate the analgesic effect)
2. Naproxen (Aleve) 250 mg 1-2 every 8-12 hours prn
3. Ibuprofen (Advil/Motrin) 800 mg every 8-12 hours prn
4. Naproxen (Naprosyn) Rx strength 500 mg every 12 hours prn
5. Ketorolac (Toradol) 30-60 mg IM prn to rescue (NSAID)
6. Triptans-oral; nasal spray; injectable.
  - a. Almotriptan (Axert) 12.5 mg every 2 hours; max 25 mg in 24 hrs
  - b. Naratriptan (Amerge) 2.5 mg every 4 hours; max 5 mg in 24 hours
  - c. Frovatriptan (Frova ) 2.5 mg every 2 hours; max 7.5 mg in 24 hours
  - d. Sumatriptan (Imitrex) 50-100 mg every 2 hours; max 200 mg in 24 hours
  - e. Rizatriptan (Maxalt) 10 mg every 2 hours; max 30 mg in 24 hours
  - f. Eletriptan (Relpax ) 40 mg every 2 hours; max 80 mg in 24 hours
  - g. Zolmitriptan (Zomig)) 2.5-5 mg every 2 hours; max 10 mg in 24 hours
  - h. Sumatriptan (Imitrex) 20 mg nasal spray 1 spray 1 nostril; may repeat in 2 hours to max of 40 mg in 24 hours
  - i. Zolmitriptan (Zomig) 5 mg nasal spray 1 spray 1 nostril; may repeat in 2 hours to max of 10 mg in 24 hours
  - j. Sumatriptan (Imitrex) 4-6 mg injectable; may repeat in 1 hour to max of 12 mg in 24 hours
7. Triptan/NSAID combination such as Sumatriptan (Imitrex) 100 mg & Naproxen 500 mg (Naprosyn)
8. DHE/dihydroergotamine (Migranal) 1 spray each nostril; repeat in 15 minutes
9. Butalbital-containing products with or without codeine such as Fiorinal plain or Fiorinal with codeine; not a good choice unless patient can't tolerate the triptans and the ergots/ergot alkaloids which are more migraine specific
10. Narcotic such as Hydrocodone (Vicodin) sparingly to rescue only: 1-2 of the 5 mg every 6 hours prn severe migraine only (suggest limit max 15/month)

**Recommendations:**

1. Mild-moderate menstrual migraine: OTC NSAID/combination product; Rx NSAID, e.g. Naproxen 500 mg prn
2. Moderate-severe: triptan +/- NSAID
3. Rescue: Sumatriptan 4-6 mg sq; Ketorolac 30-60 mg IM; DHE .5 mg NS each nostril; repeat in 15 minutes; DHE-45 .5-1 mg IM or IV every 8 hours

**SHORT-TERM PREVENTIVE STRATEGIES**

This treatment approach is ideal for many women who suffer from menstrual migraine. The majority of women report they have migraines outside of the menstrual window; however, their non-menstrual migraines are often easier to

treat. Many may report that their normal acute treatment for migraine does not work for menstrual migraine. Additionally, many are afraid they will take the full allotted amount of triptan medication for their menstrual migraine which can last 3-7 days. An effective short-term preventive approach should lessen both the severity and duration of the menstrual migraine. Common short-term preventive strategies:

1. Magnesium 360-400 mg during the luteal phase of the cycle; i.e. begin around day 14 of the cycle. Limiting potential side-effect: diarrhea.
2. Naproxen 500 mg twice a day; begin several days before the anticipated onset of menstrual migraine; continue until at least day 3 of cycle. Advantage: low cost. Potential side-effect: nausea/GI.
3. Triptan (one of the 7) dosed in a bid fashion. Begin several days before anticipated onset of menstrual migraine. Use the highest dose of the triptan. May combine with a NSAID such as naproxen 500 mg. Use for 5 days in most cases. Be aware, this extended duration use of triptans is not FDA-approved and information on long-term safety is not available for triptans when dosed in this mini-prophylaxis manner. Advantage: can be very effective. Disadvantage: Cost; not enough triptan Rx left for non-menstrual migraine.
4. Increase does of daily preventive that the woman is already on; e.g. if on topiramate (Topomax) 50 mg hs to prevent headache, increase to 75-100 mg during her vulnerable menstrual migraine time of cycle. Advantage: the patient does not feel they are taking an unnecessary dose of their preventive during their non-menstrual time of month.
5. Estradiol patch .1 mg (name brand Climara .1 mg; Vivelle dot .1 mg) to wear for at least 1 week to prevent the drop in estradiol that is often a catalyst for the menstrual migraine; the women should apply the patch on approximately day -3 and stop when menses complete. This can be done in conjunction with an oral contraceptive if the contraceptive is taken cyclically. The transdermal estradiol patch can also be used in women who don't take contraception as it will help prevent the natural endogenous drop in estradiol.
6. Oral estradiol tablets the week of menses. However, they don't give as even a level of estradiol as the transdermal patch and are only recommended if women can't tolerate the transdermal estradiol patch. Dose: Estradiol 1 mg dose dosed qd or bid.

#### **Recommendations:**

1. Magnesium 360-400 mg qd; Naproxen 500 mg bid; begin day 14 of cycle; continue through completion of menses
2. Triptan for 5-6 days; e.g. Frovatriptan (Frova) 5 mg loading dose followed by 2.5 mg bid for 5 days; begin -2 of cycle
3. Alternative triptan: Naratriptan (Amerge) 2.5 mg bid or ½ tablet bid for 5 days

4. Increase dose of preventive, e.g. increase topiramate by 25-50 mg qd day 14 through menses.
5. Estradiol .1 mg transdermal patch begin day -2; wear through day 5

## PREVENTIVE TREATMENT

This approach is ideal for women who suffer from a lot of non-menstrual migraine as well as menstrual migraine or for women who are suffering despite optimal acute and short-term treatment. Preventive treatment can be broken into 2 categories: traditional daily preventive medication and hormonal manipulation.

### Most common preventive treatment (traditional):

1. AED's (Anti-epileptic) medication such as topiramate (Topomax) and divalproex sodium (Depakote). For Topomax, start with 25 mg qd; increase by 25 mg/week until 100 mg or until clinical desired end-point. If necessary increase up to 200 mg daily dose. Dose bid or all at bedtime if sedation noticed. Most common side-effects: paresthesias (usually mild and transient); sedation; word-retrieval problems; appetite suppression and weight-loss. **Category C for pregnancy.** For divalproex sodium (Depakote): start with 500 mg as the 500 mg ER on 250 mg bid; may increase to 1000 mg a day. Most common side-effects: tremor, weight-gain, hair loss, and nausea. **Category D for pregnancy.** Other AED's may be used such as Gabapentin but only topiramate (Topomax) and divalproex sodium (Depakote) are FDA approved for migraine prevention.
2. TCA's such as Amitriptyline (Elavil) and Nortriptyline (Pamelor). Begin as 10 mg hs; increase by 10 mg/week until 50-75 mg total daily dose or until clinical desired end-point noted. Most common side-effects: sedation; dry mouth; constipation; weight-gain. Both: **Category C for pregnancy.**
3. Beta-blockers such as Propranolol (Inderal LA) and Atenolol. For Propranolol (Inderal LA): start with 60 mg LA; may increase to 80-240 mg a day. For Atenolol, start with 25 mg a day; may increase to 50-100 mg a day. Most common side-effects: sedation, hypotension; depression and weight-gain. May aggravate asthma. Beta-blockers are **Category C for pregnancy.**
4. Others: SSRI's; Calcium channel blockers; Ace inhibitors; ARB's. None of these categories of preventive are as effective as the AED's, TCA's and Beta-blockers. The SSRI's can help PMDD and mood disorders but are not very effective when used as a single agent for h/a. **All SSRI's are Category C except Paroxetine (Paxil): Category D.**

### Categories of Medication Risk in Pregnancy-US FDA

A=Controlled human studies show no risk

B=No evidence of risk in humans, but no controlled studies

C=Risk to humans has not been ruled out (Risk vs. benefit in prescribing)

D=Positive evidence of risk to humans from human or animal studies  
X=Contraindicated in pregnancy

### Most common hormonal preventive regimens:

1. Continuous oral contraception: monophasic low-dose formulation. Monophasic: same dose of ethinyl estradiol/synthetic progesterone in every active pill in the pack. Low-dose is generally considered to be any contraceptive containing 35 mcg or less of ethinyl estradiol. Favorites in my practice: 30 mcg ethinyl estradiol/3 mg drospirenone (Yasmin); 20 mcg ethinyl estradiol/3 mg drospirenone (Yaz); 35 mcg ethinyl estradiol/.4 mg norethindrone (Ovcon 35). Have the patient take only the active pills in each pill pack; i.e. she will take 21-24 active pills, depending on brand used, and then will skip the placebo pills and go immediately into her next pill pack.
2. Ethinyl estradiol 15 mcg/etonogestrel 120 mcg (Nuvaring): vaginal contraceptive ring; insert and wear for 4 weeks; take out and put a new one in. This can give a very steady state of estradiol in many women.
3. Ethinyl estradiol 20 mcg/norelgestromin 150 mcg (OrthoEvra): NO LONGER recommended since has variable amounts of estradiol and can aggravate menstrual migraine instead of helping
4. Ethinyl estradiol 30 mcg/levonorgestrel .15 mg (Seasonale): first FDA-approved extended release oral contraceptive: contains 84 active pills (12 weeks) followed by 1 week of placebo. **Seasonique** is the same except it contains “add-back” ethinyl estradiol (10 mcg) instead of placebo for the last 7 days.

### Recommendations:

1. Oral or vaginal contraceptive in continuous fashion for those needing/wanting contraception and screened appropriately
2. Use low-dose estrogen containing formulations: 35 mcg or less ethinyl estradiol
3. Transdermal estradiol .1 mg when cycling off
4. Avoid estrogen-containing contraception in migraine with aura; in women who develop new-onset aura; or women with other risk factors for stroke/cardiac disease such as smoking, uncontrolled HTN; clotting problems

### Discussion:

For women who need or want contraception, using an oral or vaginal contraceptive method in a continuous fashion may help prevent menstrual migraine in preventing the drop in estradiol that occurs either endogenously from a woman's own ovaries or exogenously when she goes from the active to the placebo pills in her birth control pack. The woman should be screened to make

sure she is a candidate for estrogen-containing contraception. Contraindications include the presence of aura; smoking; and family or personal history of stroke. **There is no “magic” to the currently approved extended dosage formulations: from my experience, break-through bleeding is a common complaint on these 2 formulations.** These brands are currently among the few that are FDA-approved for extended dosing and are often recommended by name. However, ANY monophasic oral contraceptive can be dosed in a continuous (no placebo) fashion. How often to suggest that a patient cycle off continuous oral contraceptives and have a withdrawal bleed is an individual decision best made by the patient and her provider. Cycling off every 3 months seems to be the most common approach. When cycling off, consider utilizing the short-term preventive strategy of wearing a transdermal .1 mg estradiol patch the week of the placebo. There is no progesterone in the estradiol patches so bleeding can still take place.

The decision on which traditional oral preventive to use depends on the patient including what side-effects she is willing to put up with. Most common in my practice: topiramate (Topomax) with usual dose ranging from 50-150 mg total daily dose; others often used include Nortriptyline (Pamelor) and Propranolol (Inderal LA). For refractory cases, I may consider Botulinum A (Botox) injection:100 units. (on the average) This is an expensive option, non evidence based and it typically is not covered by insurance; however, it can be an option for refractory cases. **There was a recent FDA-advisory pointing out some risks have been associated with Botulinum injections.** Infrequent but important systemic adverse effects, including severe difficulty swallowing and difficulty breathing have occurred in patients with neuromuscular disorders after local injection of botulinum toxin. **These cases usually involved much larger doses than are typically used for migraine prophylaxis.**

#### **NON-PHARMACOLOGIC TREATMENT:**

This can include biofeedback; acupuncture; physical therapy; and psychological therapy including cognitive-behavioral therapy. Exercise; not skipping meals; good sleeping habits; avoiding known trigger such as alcohol: these are all important in the management of menstrual migraine and should be discussed in conjunction with the other pharmacologic treatments discussed in this hand-out.

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