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Treating Migraine Headaches with Compounded Medications

Migraine headaches have significant effects not only on those who suffer from the attacks, but also on society. Approximately 24 million individuals in the U.S. alone are affected by migraines, and the combined indirect and direct costs associated with migraines have been estimated at \$13 billion.¹ Migraine headaches typically begin by the second or third decade of life and are one of the most common reasons for visiting a healthcare practitioner. Migraine occurs in both men and women and is most prevalent in those aged between 35 and 45 years.¹

Clinical Features

Migraine occurs most frequently in the morning. They may occur with or without an aura, experienced by approximately 20% of patients suffering from migraines.¹ The aura is a combination of neurologic symptoms, mostly visual in nature, that accompany or initiate a classic migraine. It may have a sensory, aphasic, or motor component, reflected in symptoms such as blind spots, flashing lights or colors, fortification spectra, paresthesias, hemiparesis, or visual and auditory hallucinations. Individuals who suffer from migraine with aura may find the aura does not always progress to a migraine. A list of some of the precipitating factors for migraine is included.

Four phases of migraine have been established:

1. **Prodromal** – Occurs hours or days before the headache and consists of phonophobia, photophobia, increased sensitivity to odors, difficulty concentrating, and psychological, autonomic, or constitutional symptoms.
2. **Aura** – Typically precedes the headache by an hour or less.
3. **Headache** – Presents as a unilateral, pulsating, or throbbing pain. The individual with a migraine frequently experiences nausea, vomiting, phonophobia, and/or photophobia,

and is often unable to perform normal activities during the headache.

4. **Postdromal** – A phase that is characterized by the malaise and irritability, often present after the migraine has subsided. During this phase, the pain may recur with sudden head movement.

Pharmacology

Drug classes commonly utilized in the treatment of migraines include analgesic and nonsteroidal anti-inflammatory agents (NSAIDs), as well as ergot derivatives. Analgesics and NSAIDs are useful for managing mild or moderate migraines, whereas ergot derivatives are effective for the treatment of moderate to severe migraines. Ergot derivatives are nonselective 5-hydroxytryptamine 1 (5-HT₁) receptor agonists that act by constricting intracranial blood vessels and preventing neurogenic inflammation.

Another class includes the serotonin receptor agonists, often referred to as “the triptans.” These agents are selective 5-HT_{1B/1D} receptor agonists that exert their effects by causing constriction of the blood vessels that distend during a migraine attack. They reduce nerve activation, thus inhibiting release of peptides and decreasing pain neurotransmission.

Treatment

When selecting a medication regimen for the treatment of migraine, the severity of the condition, route of intended administration, side effects, and efficacy of the medication should all be taken into consideration in order to maximize patient compliance, improve the patients well-being as soon as possible, avoid undesirable side effects, and maximize cost-effectiveness. For example, an oral route obviously would be less effective for a patient experiencing nausea and vomiting, and self-injection may not appeal to a patient. In considering acute therapy and the many options available, opiates should be avoided since they are known to lead to addiction and can precipitate a rebound headache. Narcotic analgesics may be used to treat an intractable migraine but should be reserved for patients who have a contraindication to conventional therapy and experience severe infrequent migraines. Opiates are also useful as rescue medication in treating a migraine that has failed to respond to conventional therapy.¹



Acetaminophen – Use of an acetaminophen alone is not recommended.

Barbiturates – Should be monitored and limited, since overuse can lead to additional migraines and withdrawal.

Triptans – Commonly cause adverse drug events, but are usually only mild to moderate in severity and of short duration. *Sumatriptan* has been most studied of all these agents and is available in several dosage forms.

Ergot derivatives – Used for treating moderate or severe migraine. Ergot derivatives have been used for the treatment of migraine for a long time. They are associated with more *ADEs* than the *triptans* and are obtainable at a lower cost. Two commonly used drugs include *ergotamine* and *dihydroergotamine (DHE)*.

Magnesium – Has been reported in a German study involving adults who took 600 mg magnesium daily for a month and had a 42% drop in headache frequency. Magnesium alters the duration, intensity, and frequency of migraines. Italian children given 122 mg to 366 mg magnesium daily had two-thirds fewer migraines after a month.^{2,3}

Compounded Treatments for Migraines

Many pharmaceutical elegant dosage forms and drugs can be compounded for the treatment of migraine; optional compounded formulations are provided. Compounding pharmacists can tailor a specific medication regimen in dosage forms that assist patients with compliance.

References

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2. Peikert A, Wilimiz C, Kohne-Volland R. Prophylaxis of migraine with oral magnesium: Results from a prospective, multi-center, placebo-controlled and double-blind randomized study. *Cephalalgia* 1996; 16(4): 257–263.
3. Castelli S, Meossi C, Domenici R et al. Magnesium in the prophylaxis of primary headache and other periodic disorders in children. *Pediatr Med Chir* 1993; 15(5): 481–488.

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PRECIPITATING FACTORS THAT CAN TRIGGER A MIGRAINE

FACTOR	EXAMPLES
Dietary	Monosodium glutamate, sodium nitrite, alcohol, tyramine-containing foods, citrus fruit, aspartame, chocolate, caffeine
Environmental	Bright lights, tobacco smoke, glare, strong odors, loud noise, flickering lights, weather changes, high altitude
Hormonal	Menstruation, pregnancy, menopause
Lifestyle	Stress, inadequate or excessive sleep, fatigue, dieting, fasting, skipping meals, strenuous exercise, smoking
Medications	Cocaine, oral contraceptives, fluoxetine, H ₂ -receptor antagonists, nifedipine, mestranol, indomethacin, hormone replacement therapy, nicotine, nitroglycerin, reserpine, theophylline
Psychological	Anxiety, stress, depression

COMPOUNDED FORMULAS FOR THE TREATMENT OF MIGRAINE

Rx

Cafergot and Metoclopramide Suppositories

Rx

Dihydroergotamine Mesylate 0.5-mg/mL and Metoclopramide 10-mg/mL Injection

Rx

Dihydroergotamine 2-mg/mL in Pluronic Lecithin Organogel Transdermal

Rx

Ergotamine Tartrate 2-mg Sublingual Tablets

Rx

Ergotamine 1-mg, Caffeine 100-mg, Belladonna 10-mg, and Pentobarbital 30-mg Capsules

Rx

Ergotamine Oral Inhalation Spray (0.36 mg/spray)

Rx

Ergotamine Tartrate 2-mg, Caffeine 100-mg, Atropine Sulfate 0.25-mg, and Butalbital 60-mg Suppositories

Rx

Ketoprofen 12.5-mg, Riboflavin 100-mg, and Caffeine 65-mg Capsules

Rx

Metoclopramide Hydrochloride 5-mg Troches

Rx

Metoclopramide Hydrochloride 10-mg/0.1-mL Nasal Spray

Rx

Naratriptan Hydrochloride 0.5-mg/mL Oral Liquid

Rx

Piroxicam 40-mg Mini-Troches

Rx

Prochlorperazine 5-mg/0.1-mL Nasal Spray

Rx

Prochlorperazine 25-mg/0.5-mL Pluronic Lecithin Organogel Transdermal

Rx

Propranolol 40-mg/mL in Pluronic Lecithin Organogel Transdermal

Rx

Sumatriptan 20-mg Troches

Rx

Verapamil Hydrochloride 40-mg/mL in Pluronic Lecithin Organogel Transdermal