CHRONIC HEADACHE PAIN, CO-MORBIDITIES, AND EVIDENCED BASED MANAGEMENT

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The objectives of this presentation are to understand chronic headache presentations, review evidence for the treatment of chronic pain, (including behavioral approaches, injections and neurostimulation) and to consider a multidisciplinary approach that includes lifestyle interventions, preventive treatments, physical therapy, psychological support, sleep and anxiety interventions

Statement of Problem: Migraine headaches are common, affecting 2-5% of preschool age children, 1 in 10 school age children, and16-30% of young women. The typical migraine patient will have 2 attacks/month. Often, it is difficult to find totally effective treatment for our patients.

Chronic Daily Headaches (CDH) Are Common: CDH is defined as greater than 15 headache days per month for longer than 3 months. In adults CDH affects 4% of women, and 2% of men. A study by Wang et al (Neurology 2006) looked at 7900 middle school children, age 12-14 and found that 2.4% of middle school girls and 0.8% of middle school boys had CDH. Of those, 67% had chronic migraine, yet only 4% consulted a neurologist. In an even younger aged sample, Arruda et al (Neurology 2010, 2012) studied 5671 children aged 5-12 in Brazil. At that early age 2.2% of girls, and 1.1 % of boys had daily headache, and 0.6% had chronic migraine.

Chronic Daily Headache Prognosis is not totally bleak. Wang et al, (Neurology 2009) in follow-up of a community-based sample of adolescents documented that 50% improved after 1 year, and 75% improved after 2 years. Unfortunately, 12% had chronic daily headaches 8 years latter. Some vacillated between chronic and episodic headache conditions.

Types of Chronic Daily Headache include Chronic Migraine (the most likely type that will be seen in the office). New Daily Persistent Headache is characterized by no prior headache history, and a sudden onset of symptoms, often associated with infection. Chronic Tension Type Headache is notable for the absence of migrainous features. Hemicrania continua is a one-sided, side locked headache disorder that by definition is responsive to indomethacin

What is Chronic Migraine (CM)? According to International Headache Society (IHS) criteria, headaches occur15 days/month, for more than 3 months, lasting more than 4 hours a day. At least 8 days/month has features of a migraine, including unilateral (bilateral in children) location, pulsating quality, moderate or severe intensity, worse with activity, nausea and/or vomiting, photo- or phonophobia, and relief by sleep.

Chronic Migraine may have Multiple Headache Types. Patients often described severe intermittent headaches with migrainous features. And some will describe a low-grade daily, continuous headache, which is bothersome but not always debilitating. Both headache types often seem to be on a continuum of migraine.

Idiopathic stabbing headaches are a third headache type, occurring in 2% of adolescents. These headaches are described as severe, stabbing or ice pick, occurring in multiple spots on their head, and will last for seconds to minutes. They may occur once to multiple times each day, and are often responsive to indomethacin

Does Medication Overuse Cause CM? In a study by Bigal, Lipton et al (Neurology 2008) called the American Migraine Prevalence and Prevention Study 24,000 headache sufferers were identified from the general population. This sample has been followed up with annual surveys for the diagnosis of episodic migraine and chronic migraine. As a part of the survey, subjects were asked to report the specific medications used for their most severe headaches, as well as level of satisfaction with treatment. One of the questions this study asked if frequent medication use led to chronic headaches.

Important findings are as follows:
1) Opiates are associated with migraine progression; critical dose of exposure is around 8 days per month, and the effect is more pronounced in men.
2) Barbiturates are also associated with migraine progression. Critical dose of exposure is around 5 days per month and the effect is more pronounced in women.
3) Triptans induced migraine progression in those with high frequency of migraine at baseline (10-14 days per month), but not overall.

Migraine Prophylaxis: Prophylaxis medications are given on a daily basis to reduce the headache burden. This could mean either the reduction of headache frequency or severity or both. The pragmatic goals of therapy are to reduce headache frequency by at least 50%. It may be rare to get to zero headaches, and 1-2 headaches per month is often great control.

Amitriptyline (up to 1 mg/kg/day) was used in an uncontrolled retrospective study (Hershey et al, Headache 2000) looking at 192 children with migraine. 84% of children reported feeling better, with a reduction in mean headache days from 17 to 9 days per month. The severity of headaches was also decreased.

Powers et al, (JAMA 2013) looked at **Amitriptyline plus Cognitive Behavioral Therapy (CBT)** in children aged 10 to 17 with chronic migraine with a baseline of 21 headache days/month. Amitriptyline plus CBT reduced by 12 headache days per month while the control group of Amitriptyline plus headache education reduced 7 headache days per month.

In adults (Silberstein et al Headache, 2009), **topiramate** showed a reduction in headache days, the worst daily severity of migraine, and improvement in quality of life. Still the effect was mild, with only 37% of topiramate treated patients (versus 28% of placebo treated) showing a greater than 50% reduction in the number of headache days. Lewis et al, (Pediatrics, 2009) looked at topiramate in adolescents with episodic migraine, it was shown that 100 mg/day of topiramate was effective in reducing monthly migraine days (72% vs 44%), whereas 50 mg/day was no different than placebo.

Recently, the Child and Adolescent Migraine Prevention Study (Powers et al, 2017 NEJM) compared **amitriptyline vs topiramate vs placebo** in an NIH funded prospective, randomized controlled trial. There were surprisingly no differences in efficacy (p=0.49) >50% reduction in HA days, and side effects occurred in >30% of the active med groups.

A potential **Chronic Migraine Rx Strategy** is as follows: First, **limit analgesic use** to no more than 2 headache days per week. Find a **preventive** medication, which may include amitriptyline, topiramate, propranolol (atenolol), or OnabotulinumtoxinA. Set **appropriate expectations such as improving sleep (**Typical adolescent needs 9.5 hours/night) **and functioning** with use of CBT, biobehavioral techniques, 504 school plan (late start, access to nurses office).

What to do when this strategy doesn't work? Not all patients will respond to the above suggestions. When that happens it is useful to question the diagnosis of Chronic Migraine, treat co-morbidities that are interfering with recovery, and consider Onabotulinumtoxin A, Trigger Point Injections, Neurostimulation, or Behavioral Programs that focus multiple targets symptoms and return to functioning

Other diagnostic considerations for CDH: Assuming that major secondary causes of headaches have been ruled out with a normal neuroimaging study and normal neurological exam, several entities should additionally be considered. In **Idiopathic Intracranial Hypertension,** most (but not all) patients have papilledema, and an opening pressure >28 cm H20. Eye pain, visual obscurations, pulsatile tinnitus are frequent symptoms in addition to the headache. **Hemicrania Continua** is a side-locked unilateral headache with autonomic features that is responsive to indomethacin. **Occipital/Supraorbital Neuralgia** often will have a positive Tinel's sign and can be responsive to nerve blocks, or gabapentin. **Nummular Headache** is a coin shaped, silver dollar size headache that is often responsive to Botox.

Onabotulinumtoxin A for CM In adults, double-blind placebo-controlled trials of 155 IU onabotulinumtoxin A (Aurora, Diener, Dodick et al Cephalalgia 2010) has shown a decreased number of headache days (-7.8 versus -6.4 days/28) in adults with chronic migraine. Treatments vary in price, but are approximately $3500 per treatment, which is effective for 3 months. Typically insurance preapproval is needed, which is facilitated by a diagnosis of Chronic Migraine, and evidence of trials of > 3 preventives.

Onabotulinumtoxin A: Peds Studies Ahmed et al, (Pediatric Neurology, 2010) used a retrospective chart review of a 100 IU protocol to document a positive response in 50% patients who have failed multiple (>8) previous preventative medications. This treatment was effective in other HA types, such as NDPH, and nummular headache. The results of a prospective RCT funded by Allergan comparing a single dose of 75 IU vs 150 IU vs placebo are pending.

Commonly seen Co-Morbidities include problems with sleep (67%), anxiety (85%), fibromyalgia and muscle pain (40%), chronic abdominal pain (40%), and dizziness and lightheadedness (60%).

Comorbidities: Sleep, School Two of the most commonly identified triggers for worsening headaches are stress (use the term busy rather than stress when talking to teens) and lack of sleep. Migraines are frequent during school year. Teenagers tend to be “night owls”, and are challenged by early school start time. Most teens will need 9-10 hours per night, and a good way to assess this is to ask “do you feel rested in the morning”. Treatments can consist of melatonin, CBT, turning off electronics prior to bedtime.

Comorbidities: Anxiety 50% of adults with episodic migraine, and 85% in Teens with CDH will endorse anxiety symptoms. This can include an anticipatory anxiety of getting a headache in certain situations, like school or sports. CBT can be very effective.

Comorbidities: Dizzy and Lightheaded In patients with daily headaches, the lightheadedness may have multiple etiologies. Migrainous Vertigo tends to be worse during migraine attack, and when the headaches are worse. Orthostatic Intolerance is position dependent, and responds to fluids, salt, and exercise. Chronic Subjective Dizziness is position independent, and patients report feeling “like on a boat”. This is often seen with anxiety, and responds to CBT, SSRIs or SNRIs.

The best evidence for the therapeutic use of **nerve blocks** is seen in post-traumatic headaches. Seeger et al (J Child Neuro 2015) reported on 15 patients who received occipital nerve block for chronic post traumatic headaches. Follow-up in 14 patients at 5 months post injury, 64% reported long-term response to the occipital nerve blocks. Sphenopalatine ganglion nerve blocks have been used by some physicians with the availability of three devices recently came to market. There is no childhood study evaluating efficacy in chronic headaches, and in this author's experience, is of limited value.

Neurostimulation can include the FDA approved (for adults with chronic migraine) Cefaly Anti-migraine device. This device is worn for 20 minutes a day, and provides electrical stimulation over the forehead. Patients with significant allodynia find it uncomfortable, but others can find it helpful. This author demonstrates it and recommends it to many of my CM patients. The eNeura Transcranial Magnetic Stimulator is a single pulse magnet that generates a 0.9 T magnetic field for 1/100 of a second. It is FDA approved for use in migraine with aura.

Biofeedback has been demonstrated to reduce pain levels and frequency of headaches. Multidisciplinary behavioral programs, utilizing expertise in physical medicine, psychology, and neurology, are helpful in returning patients to functioning and improving pain control.

CGRP, a 37 amino acid peptide/Neurotransmitter associated with pain is the target of future therapies under development. Initial studies used small molecule (talcagepant), but were associated with liver problems. Anti-CGRP antibodies being developed to use as preventive therapy. Positive effects are seen early adult studies.

In Conclusion,
Chronic headaches cause significant pain and functional disability.
There is a not a single treatment to help everyone.
Pharmacology helps, but often a more holistic approach is needed.