In 25 minutes we will provide course participants with the description of evaluating refractory headache patients, then discuss treatment options and finally cover three illustrative cases. This presentation will also include references which can be reviewed to help appropriately utilize these treatment options whether on an outpatient or inpatient basis.

Let us begin with the definition of “refractory”. It may mean intractable or unmanageable or resistant to ordinary treatment. It can be considered a relative term for in some hands such headaches may be actually quite treatable once a diagnosis is made and the correct treatments are done. Many things can go wrong in therapy. The wrong drug may be chosen or given at the wrong dose, or not trialed for long enough or the patient may be non-compliant. Medication overuse may be unrecognized and when present it may nullify or reduce the effectiveness of preventive therapies. The patient and/or the provider may have unrealistic expectations of therapy.

First and foremost a clear diagnosis must be made. “Headache” is a symptom; there are > 300 different types of headaches. Is the headache a primary headache disorder? Is there a secondary (i.e. due to something else) headache disorder? Is there more than one type of headache? If it is chronic migraine, why is it worsening? Medication overuse can confound any type of headache and migraineurs seem particularly prone to be affected by it.

The ICHD-IIIbeta definition of chronic migraine now allows for the presence of medication overuse headache (MOH) and there is no longer a requirement for the patient to improve after MOH is curtailed. According to the ICHD-IIIbeta patients may either develop a new type of headache or a worsening of their pre-existing headache as a consequence of regular overuse of acute medications. These medications may include triptans, ergots, opioids, simple and combination analgesics. While some of these medications may be stopped or tapered on an outpatient basis, there are situations (including patients taking substantial amounts of opioids or butalbital) where detoxification under medical supervision may be advisable.

Risk factors for worsening of migraine include obesity, medication overuse, snoring and sleep apnea, caffeine intake above 100mg daily, psychiatric comorbidity and stressful life events, head trauma and thyroid disorders. Of these it is only known to be therapeutic to curtail medication overuse and correct thyroid disorders. We do recommend addressing the other issues but doing so has not (yet) been proven to improve headache.

The best approach to evaluating patients with chronic migraine is first to make a diagnosis (diagnoses) and address risk factors for chronification. Imaging is appropriate, lab testing such as thyroid tests and consider performing a lumbar puncture for a careful opening pressure and routine studies. High intracranial pressure without papilledema is not a rare condition. For treating chronic migraine
preventatively topiramate and onabotulinumtoxinA have the best evidence of efficacy, perhaps somewhat even in the presence of MOH. Acutely, longer half-life NSAIDs and dihydroergotamine are preferable to short half-life triptans. MOH must be addressed and opioids should not be continued.

Chronic migraine treatment strategies may include outpatient treatment alone, infusion therapy (outpatient or inpatient) and a comprehensive multidisciplinary program (outpatient or inpatient). Patients who have failed outpatient therapy may then become candidates for inpatient treatment. Certain emergency situations such as a dehydrated pregnant headache patient or a patient with severe psychiatric decompensation may require admission. Also, patients who cannot get off their opioids as outpatients (and they often fail to come off these in the outpatient setting) may need to be admitted for treatment under medical supervision. If admission is chosen by the patient and provider it is important to choose a therapeutic target, i.e. a goal that is agreed upon in advance.

Most patients who end up being admitted for “intractable headache” and then subsequently improve turn out to have analgesic rebound headache/medication-overuse headache. The “therapeutic goal” is to remove the offending medications (and not to initiate other analgesic-rebound-inducing medications) and to control the ensuing withdrawal headache and associated symptoms until they subside. The duration of withdrawal symptoms due to triptan drugs is usually brief (1-2 days) while the period for analgesics especially those containing butalbital is longer (several days). Abruptly stopping butalbital, at higher doses, carries a risk of provoking delirium and/or seizures so it can either be tapered or replaced with a bedtime dosage of phenobarbital which has a much longer half-life (100mg of butalbital is approximately equal to 30 mg of phenobarbital) and which then can be slowly tapered.

During inpatient treatment great attention must be paid to detail. Small errors in treatment protocols may result in treatment failure. Clonidine and especially neuroleptics can help suppress withdrawal symptoms allowing for cessation of narcotics. Medications which can cause rebound must be avoided. Sedating medications can be especially useful during the withdrawal period. Strict bedrest may be necessary (e.g. iv chlorpromazine can cause impressive orthostatic hypotension) and if so, then measures must be instituted to lessen the risk of deep venous thrombosis. Serial EKGs to follow QTc intervals may be advisable especially with iv chlorpromazine. Remember methadone can prolong QTc intervals dramatically and obtaining a baseline level prior to admission in such patients may be reasonable.

The Pain service may be utilized to administer blocks (e.g. for neck pain, low back pain) if narcotics are being stopped which were being used to treat pain from those chronic conditions. Occipital nerve blocks can be dramatically effective, particularly for unilateral headaches with neck pain.

The “Raskin” protocol uses repetitive iv metoclopramide 10mg or 5mg of intravenous prochlorperazine followed by the effective subnauseating dose of dihydroergotamine (0.25-1mg) tid. Dystonic reactions can be ameliorated or prevented by iv diphenhydramine 25 mg or benztrtopine mesylate 1-2 mg. The regimen is given tid, not Q8h (to avoid awakening sleeping headache patients, you cannot have a headache when you are asleep!!!!). Three days of therapy is typical, although some patients may benefit from longer stays. Most if not all analgesics must be stopped (a common error is to initiate or continue meperidine which renders the protocol ineffective). Meperidine, by the way, is a potent serotonin uptake inhibitor and there is data which suggests it is potentially dangerous in our headache patients, who are often on multiple drugs which effect serotonin. Prochlorperazine 5-10 mg iv can be substituted for the metoclopramide, especially if sedation is desired. Akathisia (motor
restlessness due to neuroleptics can be treated with low dose iv benzodiazepines such as 1-2 mg iv diazepam). Dihydroergotamine must be avoided in pregnancy (Category X) and should also be avoided in coronary artery disease. There is also a “continuous iv infusion” protocol for DHE (Ford and Ford, 1997).

Intravenous chlorpromazine (preceded by iv diphenhydramine or benztropine mesylate) titrated to a dose that renders the patient lightly asleep is quite useful. 10 mg tid is a reasonable initial dose. If the patient becomes hypotensive during therapy iv boluses of saline may be helpful; sometimes rather than advancing the doses of iv chlorpromazine a dose of oral clonazepam 0.5-1mg may be added to tip the patient into unconsciousness. Strict bedrest is advised as this medication can cause impressive orthostatic hypotension. Deep venous thrombosis prophylaxis is usually initiated.

Intravenous valproate has been advocated for acute headache therapy. 300-500 mg is run in rather rapidly over 5-10 minutes. This may be repeated. A serum pregnancy test prior to administration would be appropriate in females of childbearing potential (this would also apply prior to the initiation of dihydroergotamine which is category X).

Intravenous magnesium makes good sense to utilize although there is little evidence to support its use. It is certainly reasonably safe and there are anecdotal reports of efficacy. In pregnant patients it has been used but there are now some concerns about bone effects in the fetus, and in hemiplegic migraine it can easily be justified as safe and if it doesn’t work it does not preclude trials of other measures. 1 gram initially is given over 5-10 minutes. Some have used up to 2 grams iv BID (serum magnesium levels should be followed although ionized magnesium levels would be more relevant but are generally unavailable).

Intravenous ketorolac 30mg Q 6 hours as needed for several days can be a helpful addition for breakthrough headaches during inpatient treatment. Sometimes steroids may provide benefit. While we are treating patients acutely we also typically begin prophylactic medication(s) so we know patients can tolerate them. We also educate patients about reasonable expectations of the therapy. Prior to discharge they are given an action plan for how to deal with acute headache attacks after discharge and a rescue plan to let them stop vomiting and achieve sleep when their usual acute therapy may fail. They are discharged with instructions to keep a headache calendar and to keep a rather soon headache clinic appointment (1-3 weeks after discharge).

With meticulous attention to detail, approximately 70% of such difficult patients are either headache-free or substantially improved upon discharge. Failure to improve portends a bad prognosis but some of those patients do improve (some require more pronged hospitalizations beyond the average 3 day stay of most of our patients). Failure to improve mandates a reassessment of the diagnosis and some patients end up having more invasive treatments such as occipital nerve stimulators or surgery for causes of headaches (such as upper cervical root entrapments).

During the presentation we will discuss several cases to which you may apply this information and see how the patients fared.

References


