Headache Treatment in Children, Pregnancy and Lactation, the Elderly, and Renal Disorder

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Use the handout

- General references
- Specific references
- Know the ICHD-II
- You must be secure in the diagnosis before choosing treatment.

Headache treatment in children

- Less data than for adult migraine
- AAN Practice parameter 2004: acute- acetaminophen, ibuprofen, sumatriptan nasal spray (>12yo). Avoid aspirin (Reye syndrome).
- Preventative- flunarizine probably effective. Otherwise conflicting and insufficient data.

Children

- Remember non-pharmacologic measures. Some use propranolol, amitriptyline, cyproheptadine, divalproex, topiramate, zonisamide. No medication has FDA approval.
- Utility of antiemetics (remember children may be more prone to dystonic reactions)

Children

- Abdominal migraine-simple analgesics, fluid replacement, antiemetics. Pizotifen works. ? propranolol, cyproheptadine?
- Cyclic vomiting: Stop vomiting, hydrate, ? erythromycin as a prokinetic agent.
- Benign paroxysmal vertigo- ? antihistamines (betahistine)

Pregnancy and lactation

- Avoid drugs to the extent possible. Many patients (50-80%) improve, usually MWA/MAM by the end of the first trimester.
- Always consider secondary causes of HA (venous sinus thrombsis, stroke, pituitary tumors, eclampsia)

Pregnancy and lactation

- Always consider non-pharmacologic measures
- Medications: acetaminophen (po and pr), NSAIDS until week 32 (effect on ductus arteriosus), opioids judiciously, antiemetics (prochlorperazine, promethazine).
- IV hydration, metoclopramide, magesium
- Steroids
- Occipital nerve blocks

Pregnancy and lactation

- Ergots are category X
- Triptans not FDA-approved but sumatriptan pregnancy registry suggests no increase in birth defects

Prophylactic therapy in pregnancy

- Avoid if possible. May consider amitriptyline, propranolol, verapamil, topiramate (all “C”).
- Consider the possibility of MOH
- Lactation: all drugs get into breast milk. Sumatiptan label (can pump/store, pump discard for 8-12 hours)

Headache in the elderly

- Primary headaches include TTH, migraine, cluster, CDH, SUNCT, hypnic headache. Always consider secondary headaches (like GCA).
- ? Headache related to Parkinson's disease
- Remember age-related liver and renal dysfunction, CAD

GCA ICHD-II 6.4.1

- A. Any new persisting headache fulfilling C and D
- B. At least one of the following:

1. swollen tender scalp artery with elevated ESR and/or CRP
2. temporal artery biopsy demonstrating GCA

GCA ICHD-II

- C. Headache develops in close temporal relation to other symptoms and signs of GCA
- D. HA resolves or greatly improves within 3 days of high-dose steroid treatment

GCA

- Patients usually >50yo, ESR usually >50 mm/hr.
- Any type of headache/location
- Consider for cases of new-onset HA or worsening headache
- Start steroids first, then get biopsy.

GCA

- Risk of blindness, posterior circulation stroke
- Association with PMR
- May present as amaurosis fugax
- Disruption of internal elastic lamina, lymphocytic infiltration

Elderly: cardiac cephalgia

- 10.6 Diagnostic criteria:
- A. Headache, which may be severe, aggravated by exertion and accompanied by N and fulfilling C and D
- B. acute myocardial ischemia has occurred

Cardiac Cephalgia ICHD-II

- C. Headache develops concomitantly with acute myocardial ischemia
- HA resolves and does not recur after effective medical therapy for myocardial ischemia or coronary revascularization

Hypnic Headache ICHD-II

- 4.5 Attacks of dull HA that always awaken the patient from sleep
- A. Dull HA fulfilling B-D
- B. Develops only during sleep, and awakens the patient
- C. At least two of the following ...

Hypnic HA……..

- 1. occurs >15 times/month
- 2. lasts > 15 minutes after awakening
- 3. first occurs after age 50
- D. No autonomic symptoms and no more than one of nausea, photophobia or phonophobia
- E. Not attributed to another disorder

Hypnic headache

- Tx: lithium, caffeine, flunarizine, indomethacin

Trigeminal neuralgia

- ICHD-II 13.1 “classical” vs. 13.1.2 “symptomatic”
- Paroxysms of pain lasting a fraction of a second to 2 minutes; intense, stabbing. Usually in second or third divisions of 5.
- Refractory period in classical not in secondary

Trigeminal neuralgia

- Classical usually due to aberrant blood vessel compressing V
- Must get MRI/MRA with gadolinium to rule out secondary causes
- Treatment: carbamazepine, baclofen, gabapentin, others…or Janetta procedure (microvascular decompression)

HA in renal disease

- HA occurs in CRF (? due to low magnesium levels)
- HA occurs frequently in hemodialysis (up to 70% in some series, the most frequent patient complaint)
- Can be seen with disequilibrium syndrome (cerebral swelling, HA, stupor, seizures, coma)

Renal disease ICHD-II

- 10.2 Dialysis HA
- A. At least 3 attacks of acute HA fulfilling C and D
- B. The patient is on hemodialysis
- C. HA develops during at least ½ of the hemodialysis sessions
- D. HA resolves within 72 hrs after each session and/or ceases after successful transplantation

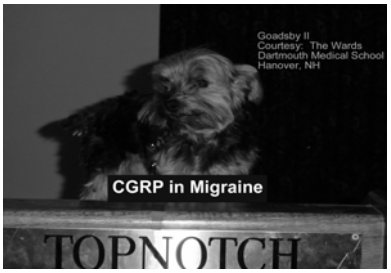
Hemodialysis HA

- Usually bilateral, dull or throbbing, moderate to severe. Mean duration about 5 hrs.
- Consider caffeine withdrawal HA
- Risk factors: HTN, low serum osmolality, high BUN, low magnesium

Hint:

- Gabapentin not metabolized by either liver nor kidney, but is excreted by the kidney
- Pregabalin similar.....

Thank you and good luck



Advanced Treatment for Headache: Procedures and Inpatient Treatment

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This lecture material covers procedures for headache treatment and inpatient therapy for headache patients.

Procedures for Headache Treatment

When medications and non-pharmacologic treatments provide inadequate effect there are various “procedures’ which can be utilized to help alleviate headache. This lecture will focus on the various neurosurgical options and pain procedures/anesthetic blockade. These options vary from relatively non-invasive procedures (e.g. neural blockade) to choices which are destructive and/or invasive to a significant degree. They rarely cure headache by themselves; medical management is often still necessary. All carry some degree of risk and therefore the age and general medical condition of the patient must be kept in mind.

Cluster Headache

Cluster headache is thought to be the most painful of all conditions. Pharmacologic therapy has been covered by me in a separate lecture. Most cluster patients, fortunately, have the episodic form (with bouts and remissions). The unfortunate minority have chronic cluster currently defined in ICHD-II as cluster headache occurring without significant remissions (for > 1 year with either no remissions of with remissions lasting < 1 month). Many such patients still achieve significant relief with vigorous medical therapy. For those who do not, surgical procedures become a consideration. As understanding of cluster pathogenesis has advanced, treatment options have expanded. Cluster also serves as a useful example of various procedures that may be employed for head pain. These procedures are typically performed by neurosurgeons or Pain specialists.

Anatomy and Neurophysiology

The trigeminal nerve (CN V) is an important part of the cluster headache story. Cluster pain is usually most prominent in the first, and less often, the second division of V. Trigeminal fibers pass via the Gasserian (trigeminal) ganglion in Meckel’s cave to the brainstem and reach the trigeminal nucleus caudalis. Indirect (polysynaptic) connections involve the superior salivatory nucleus in the pontine tegmentum. This trigemino-autonomic reflex may help explain the cranial parasympathetic symptoms that occur during a cluster attack (e.g. lacrimation, rhinorrhea). The autonomic fibers travel in the nervus intermedius (sensory VII) and then with the greater petrosal nerve to the sphenopalatine ganglion. Postganglionic fibers then run to the various glands. Also, of note, there are bilateral pathways descending from the hypothalamus to both the superior salivatory nucleus and the trigeminal nucleus caudalis. These *bilateral* projections may explain why cluster pain sometimes switches sides, especially after a procedure.

One of the most important findings now known about cluster pathophysiology is the abnormal activity (previously postulated) and anatomy shown by functional imaging and voxel-based MRI morphometry that occurs in the posterior hypothalamic gray matter.

Procedures for Cluster

Nervus intermedius section was pioneered by Dartmouth neurosurgeon Ernest Sachs, Jr. MD. The procedure is invasive and involves a suboccipital craniectomy. This nerve usually runs between the VIIth and VIIIth cranial nerves in the cerebellopontine angle; it is not always a separate bundle but may run admixed with the fibers of CN VIII. While Dr. Sachs reported generally good outcomes on a very smalls series of patients, other series have been less favorable. Adverse events include hearing loss, vertigo, loss of taste, and facial weakness.

Further along the autonomic pathway, the greater superficial petrosal nerve has been sectioned. Radiofrequency lesioning of the sphenopalatine ganglion has also been performed. While less invasive, results tend to be disappointing due to fairly frequent failures and recurrences.

The majority of procedures for alleviating cluster headache pain are directed against the sensory trigeminal nerve. Sometimes these are combined with procedures directed against the cranial parasympathetic pathways. Minimally invasive procedures on the supra- and/or infra-orbital nerves can be helpful. These nerves can be blocked temporarily with a local anesthetic such as lidocaine or bupivicaine. Longer benefit might be achieved using alcohol injection. Yet longer results may be seen with neurectomy (avulsing the nerves). These procedures are minimally invasive and have fewer side effects but recurrence rates are quite high. These options are most appropriate for older patients and others who are not suitable candidates for more invasive (but potentially more durable) procedures.

Procedures directed against the trigeminal ganglion are certainly much more invasive but may result in more durable outcomes. Injections of alcohol have given disappointing results and are rarely employed anymore. Glycerol may also be injected, with fairly high initial success rates but also fairly high recurrence rates. Perhaps 75% experience pain relief, but nearly half have recurrence often with the year. It is fairly safe so it can be done in elderly patients and does not require general anesthesia. It results in a mild sensory deficit which patients generally tolerate. It can be repeated but may cause arachnoiditis which then renders further such treatments ineffective.

The Gasserian ganglion may be “treated” with heat (radiofrequency). The device is inserted through the cheek and passed through the foramen ovale and the procedure is performed. The operator can control the amount of neural damage by assessing the amount of sensory deficit produced. Less deficit generally results in fewer side effects (which can be serious) but at thetherapeutic cost of lower efficacy .About 50% of patients do very well, 20% less well, and about 30% fail to benefit. Side effects include corneal anesthesia (with the risk of corneal abrasions) and anesthesia dolorosa which may become a more serious problem than the cluster pain was.

Sensory rhizotomy involves sectioning the trigeminal nerve at the root entry zone. Jarrar et al. at the Mayo Clinic reported their experience; 88% of patients had complete or near-complete symptom relief (and mean follow-up was > 6 years). Complete section gave better results than did partial sectioning. Adverse events included CSF leak, weakness of masticatory muscles, and one case of (mild) anesthesia dolorosa. Some surgeons have added nervus medius sectioning to this procedure.

Gamma knife radiosurgery has also been employed against the trigeminal nerve and/or the nervus intermedius. Response may occur after days to weeks (or longer). There are few published reports and long-term consequences are not yet known. Mis-targeting has been reported when used for other indications and would therefore be possible in this situation.

Analagous to the “Janetta” procedure for trigeminal neuralgia, microvascular decompression has been applied to both the trigeminal nerve and nervus intermedius for cluster headache. Both arterial and venous compressive lesions have been reported. In Lovely’s series, the initial

success rate was about 75% but recurrences lowered the longer-term success rate to slightly less than 50%. Repeat procedures were ineffective.

Trigeminal Neuralgia

Medically-refractory trigeminal neuralgia may be treated with some of the same procedures as for cluster headache. These options can be directed against the peripheral nerve, the trigeminal ganglion, or the root entry zone. The old procedure of “medullary tractotomy” has been abandoned. Lost procedures are directed against the root entry zone or Gasserian ganglion. Trigeminal nerve cryosurgery, alcohol blockade, or neurectomy are less invasive but also less efficacious. The four major procedures are ballon compression of the ganglion in Meckel’s cave, glycerol “gangliolysis” in the trigeminal cistern, radiofrequency lesioning of the fibers for the appropriate division of the Vth nerve (“retrogasserian”), and stereotactic radiosurgery directed at the root entry zone (this may require several months or longer to work while the other methods have a much sooner onset of benefit). All these procedures tend to provide temporary relief with recurrence in ≥ 50% of patients within 3 years Side effects include masseter weakeness, corneal ulcerations, and anesthesia dolorosa. The microvascular decompression procedure of Janetta has also been advocated. When performed, about 80% are without symptoms at 1 year. The offending vessel is often found to be the superior cerebellar artery compressing the root entry zone of the Vth nerve. Adverse events include death, CSF leak, VIIIth nerve damage, and stroke (cerebellar infarction).

Intracranial Hypertension

Surgical procedures may be necessary for medically-refractory intracranial hypertension. In idiopathic intracranial hypertension surgery is considered when vision is deteriorating. Optic nerve sheath fenestration may not only preserve vision but sometimes ameliorates the head pain. It may be a preferable option to ventricular shunting. Shunts may be very efficacious but have numerous drawbacks including the need for shunt revision/shunt failure, infection (which may be deadly), low pressure headache, and acquired Chiari. Medical management may still be required.

Nerve Blocks and Neurostimultation

Anesthetic nerve blocks and neurostimulation are useful for treating some types of headache. There are no adequate controlled data supporting their use but there is ongoing research. Occipital nerve blocks are easy to perform. Afridi et al. reported that 26/57 injections in 54 migraine patients resulted in either a complete or partial response with a median duration of benefit of 21 days. A tender occipital nerve predicted response; the presence or absence of medication overuse did not. Obviously, duration of response outlasts presence of the local anesthetic. They postulated an alteration in CNS nociceptive pathways. These blocks also may lessen central sensitization/cutaneous allodynia. These blocks may work in hemicranial migraine/status migrainosus and in cluster as well as other headache types. They seem to be ineffective in tension-type headaches and paroxysmal hemicrania. It is uncertain if they work in hemicrania continua (in this author’s experience they *sometimes* do). Sometimes supra-orbital nerve blocks may be useful. Atlanto-axial joints may also be blocked. Deep CT-guided C2 and C3 root blocks may be diagnostic as well as (briefly) therapeutic.

“Neurostimulation” is an exciting development for treating some intractable headaches. Occipital nerve stimulation has been studied by numerous investigators including Goadsby and Dodick. It may work in chronic/transformed migraine, posttraumatic headache, intractable cluster headache, new daily persistent headache and hemicrania continua. Prior response to occipital nerve blockade is *not* reliably predictive of response to occipital nerve stimulation. A trial of a temporary stimulator is usually undertaken prior to placing a “permanent” device. Stimulation may be unilateral or bilateral. PET scan changes during stimulation are noted in the anterior cingulated cortex and dorsal pons. Complications include lead migration, wire breakage, and infection.

Vagal nerve stimulation (VNS) has been reported, also anecdotally, to help some refractory headache patients. Transformed migraine and chronic cluster have been reported to sometimes respond. The total number of cases reported has been very small. VNS is known to have analgesic effects, and has been used to treat seizures and depression (both known to be comorbid with migraine).

Finally, the most exciting reports of all have been on the use of deep brain stimulation for refractory cluster (Leone, Schoenen, Bartsch) and also for SUNCT. Complications include infection and there has been one death reported due to hemorrhage.

Inpatient Headache Treatment

Headache patients are usually managed on an outpatient basis. Under certain circumstances, however, inpatient treatment may be appropriate. There is limited literature about this in part because few physicians and few facilities provide this option.

Patients who are doing poorly as outpatients may benefit from admission. Emergency situations due to psychiatric decompensation, refractoriness to adequate trials of outpatient therapy, or if the patient and/or family and/or provider are at “wits’ end all are scenarios which suggest inpatient therapy might be a reasonable option. Before considering an admission, various possible reasons for failure of outpatient therapy must be looked at. Noncompliance with recommended treatment regimens may not be recognized. Medication overuse/analgesic rebound is often not recognized as well and renders patients refractory to preventative medications and worsens the overall headache pattern. Side effects of medications may be causing headache (e.g. proton pump inhibitors) or preventing compliance (such as GI side effects from indomethacin). Confounding or comorbid medical conditions, such as the emergence of coronary artery disease in a patient who had responded well to triptans, may lead to therapeutic dilemmas. Occasionally medical mismanagement is the problem including incorrect therapeutic selection leading to treatment failure (e.g. propranolol chosen to treat cluster headache). Beyond this, inadequate or improper medication trials and unreasonable expectations on the part of both patients and providers may lead to outcomes that are incorrectly perceived as “poor”. Prior to admission for inpatient headache treatment it is often advisable to obtain second opinions and consultations to ensure that outpatient therapy has been optimized.

If outpatient therapy has been ineffective an admission may therefore be an option. Most importantly, a therapeutic target for the admission, a “goal” or objective, needs to be identified. The doctor and patient must be in agreement on what the goal actually is. Some goals include controlling the anticipated withdrawal headache that occurs upon stopping/lessening medications perpetuating analgesic rebound, rehydrating a dehydrated patient with intractable headache and vomiting, obtaining multiple consultations rapidly (Pain service, Psychiatry, Behavioral Medicine), and to obtain further testing (TSH, MRI, lumbar puncture (including an opening pressure !!!! (look for increased intracranial pressure or low CSF pressure)).

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 seizures and/or delirium so it should 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).

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.

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. Lidocaine may also be administered by transdermal patch.Occipital nerve blocks can be dramatically effective, particularly for unilateral headaches with neck pain.

The “Raskin” protocol uses repetitive iv metoclopramide 10mg followed by the effective subnauseating dose of dihydroergotamine (0.25-1mg) tid. Akathisia or dystonic reactions can be ameliorated by iv diphnehydramine 25 mg or benztropine mesylate. Benzodiazepines may be even more effective for akathisia. 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. Dihydroergotamine must be avoided in pregnancy and should also be avoided in coronary artery disease.

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 intravenous 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. The benzodiazepine is also an effective antidote to akathisia if it occurs.

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 duhydroergotamine which is category X).

Intravenous magnesium makes good sense to utilize although there is little high level evidence to support its use. It is certainly safe and there are anecdotal reports of efficacy. In pregnant patients 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 30 mg Q 6-8 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).

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