UPDATE ON Craniofacial Pain and Dystonia

North American Neurotoxin Association

North Central Headache Society
Inpatient Treatment of Refractory Headache

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Disclosures

- Speakers Bureau for Allergan, Teva, and Avanir
Headache is best managed in the outpatient department
1-3 million visits to ED annually (US)
ED Chief Complaint

• 4th most common reason adults
  – Approximately two-thirds of these visits were for primary headache disorders, most commonly migraine headaches

• 3rd leading common reason pediatrics
Problem with ED Care of Migraine

• Medications:
  – Variability of treatment ~20 parenteral medications
  – Lack of evidence for therapeutic benefit

• Opioids:
  – Less effective than other medications
  – Carry the risk of adverse CNS side effects, habituation, and addiction

• Headache relief:
  – High frequency of headache recurrence
1.4.1 Status migrainosus
ICHDS-3

- May occur in migraine with or without aura
- Migraine is typical of previous attacks except for its duration and severity
- Characteristics:
  - unremitting for >72 hours
  - pain and/or associated symptoms are debilitating

Chronic daily headache (CDH)

- A group of headache disorders, in which headaches occur daily or near-daily (>15 days per month) and last for more than 3 months.

- CDH subtypes:
  - Chronic migraine
  - Chronic tension-type headache
  - Hemicrania continua
  - New daily persistent headache.
General Principles of Treating HA in the ED

(1) Adequately IV hydration
(2) Treat head pain with nonopioid medications
(3) Provide rapid relief with IV medications
(4) Establish the correct expectations
   - CDH for years: pain reduction
   - Episodic migrainer: pain free
Goals of ED Treatment

• Headache free upon discharge
• Sustained pain freedom 48 hours postdischarge
  – Pain free: 20% to 25% of patients
  – 24 hour recurrence: 30%
• Predictors of poor outcomes:
  – severe pain at baseline
  – presence of nausea
  – longer duration of headache.

Factors that Influence Rx

- Comorbid medical illnesses
  - Vascular Disease
  - GI Bleed
- Hypotension:
  - Dopamine receptor antagonist and magnesium can ↓ BP
  - Past response to treatment (ED, headache infusions) t.
- Current medication list
- What has the pt has already taken prior to the ED visit?
- Try to get contract treating physician
- Past responses to meds in ED or infusion centers
Medication Choices for Acute Treatment of Status Migrainosus

- Glutamate effect must be blocked
- GABA levels enhanced
- Dopamine and histamine effect blocked
- Serotonin levels raised
- CNS inflammation blocked
- The patient must be hydrated
Intravenous Fluids

- Rehydrate patient with uncontrolled vomiting
- Hydrate all migraineurs?
- Harden et al.:
  - IM ketorolac 60 mg, meperidine 50 mg + promethazine 25 mg, and normal saline: all treatments equally produced a significant reduction in head pain

Outcomes

• Balbin et al. (2)
  – Post hoc analysis of 570 patients
  – No evidence of short-term or sustained efficacy among pts who were administered IVF in addition to IV metoclopramide

<table>
<thead>
<tr>
<th></th>
<th>IVF</th>
<th>No IVF</th>
<th>Between-group difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean improvement in 0-10 score between baseline and 1 h</td>
<td>4.5</td>
<td>5.1</td>
<td>0.6 (0.1-1.1)</td>
</tr>
<tr>
<td>Sustained headache freedom a</td>
<td>16/112 (14%)</td>
<td>80/446 (18%)</td>
<td>4% (−4% to 11%)</td>
</tr>
</tbody>
</table>

Babin JEB. American Journal of Emergency Medicine, 2016; 34:(4) 713-716
Dopamine Receptor Antagonist

• Effective:
  – antiemetic effects
  – relief of both pain and aura symptoms
  – sedative

• 3 subclasses
  – Metoclopramide
  – Phenothiazines (prochlorperazine, promethazine, and chlorpromazine)
  – Butyrophenones (droperidol and haloperidol)
Dopamine Receptor Antagonist

Efficacy

- Haloperidol
- Chlorpromazine*
- Droperidol
- Prochlordperazine
- Promethazine**
- Metoclopramide**

Adverse Events

- Haloperidol
- Chlorpromazine*
- Droperidol
- Prochlordperazine
- Promethazine**
- Metoclopramide**

** strong recommendation
* weak recommendation
Dopamine Receptor Antagonist

Risks

- Hypotension
- Prolong QT interval (butyrophenes and chlorpromazine)
- Extrapyramidal effects: akathisia or dystonia
  - Pretreatment with IV benztropine or diphenhydramine (25-50 mg)
  - Post: PO Inderal 10 mg
Dopamine Receptor Antagonists Dosing

- Metoclopramide 10 mg IV
- Promethazine 12.5-25 mg IM or IV (possible tissue injury)
- * Prochlorperazine 10 mg IV (repeat 30 min- max 40 mg /day)
- Droperidol 0.625-2.5 mg IV (ICU restricted)
- Chlorpromazine 2.5- 25 mg IV
IV Promethazine
Black Box Warning

- Risks of severe tissue injury/gangrene associated with IV/SQ administration of this drug
- Preferred route of administration is deep IM
- SQ is contraindicated.

Figure 1. Woman develops Gangrene after Receiving Phenergan IV. Image provided courtesy of ISMP.
Nonsteroidal Anti-inflammatory Drugs

• Ketorolac- 30-60 mg IV or IM
• Contraindications: GI bleed
• Systematic review (34 studies, including 8 trials)
  – Effective: 55% (combined with prochlorperazine ~93%)
  – Similar pain relief to meperidine
  – More efficacious than sumatriptan
  – Not as effective as phenothiazines and metoclopramide.
  – 24 hr recurrence ~30%

Magnesium Sulfate

- 500-1000 mg (up to 5 g)
- Effect: antagonism of N-methyl-D-aspartate (NMDA) receptors, or blockade of cortical spreading depression
- SE: Hypotension
- Caution use with other medication
  - Lamictal: rash
  - Topirimate: hyperammonemia
- Evidence: conflicting, probably better in migraine with aura
Additional Anti-nausea

- Ondansetron- 4 to 8
- Hydroxyzine: 25 to 50 mg IM
Parenteral NSAIDS

- Diclofenac-37.5-50 mg
- Ibuprofen- 400-800 mg
- Lysine acetylsalicylate 1 gm
Corticosteroids

- Meta-analysis (25 studies/ 3989 pts) – does not support the use of dexamethasone for acute treatment but may delay recurrence by 72 hours with fewer repeat physician visits
- 2nd line therapy
- Contraindications: DM, infection
- Risk: Avascular necrosis
- Dosing
  - Methylprednisolone- 100 -1000 mg
  - Dexamathasone- 4-12 mg

Opioids in Headache Rx

• Consensus guidelines: advise against the use of opioids for migraine
• 70% increase in the use of hydromorphone, morphine, and oxycodone in US emergency departments from 2001 to 2010
• Opioids are typically less effective or, at most, equally effective as multiple nonopioid acute migraine treatments (ketorolac, DHE, corticosteroids, and multiple dopamine receptor antagonist compounds)

Valproate sodium (Depacon) -500-1000 mg
• May be efficacious
• Well tolerated: sedation, dizziness
• Avoid if pregnant, liver failure or taking lamotrigine
Opioids

- More side effects
- More likely to need rescue medication
- Increased risk of relapse and need for return to the ED
- May also render acute migraine medications, such as triptans, less effective
- May impair the effectiveness of migraine preventives.
- Have the potential to promote chronic migraine
- Promote medication overuse
- Migraine patients with opioid dependence have more disability, depression, and anxiety issues when compared to those who had not with similar headache frequencies
- Use should be used for rare occasions

Vasoconstrictors

• Sumatriptan (Imitrex)- 6 mg SQ
  – Effective 70% in ED

• DHE (dihydroergotamine)- 1 mg IV (Raskin protocol)
  – Effective 60% -70 %at 1 hour

• Contraindications
  – uncontrolled hypertension
  – stroke or myocardial infarction
  – peripheral vascular disease
  – hemiplegic aura and prolonged aura (> 1 hour)
Triptan
Sumatriptan SQ

- Peak concentration (Tmax): 12 minutes
- Bioavailability: 97%
- Migraine relief:
  - 6 mg SQ: 63% at 30 min; 75% at one hour
  - 100 mg oral: ~60% 2 hr; 78% 4hr)
- Pain free at 2 hr: 65%
Diphenhydramine as Adjuvant Therapy

- IV diphenhydramine 50 mg + IV metoclopramide 10 mg
- 208 patients
- Conclusion:
  - Adjuvant therapy did not improve migraine outcomes
  - Also did not decrease the rate of akathisia
  - No reason to co-administer

Friedman BW et al.
## Outcomes

<table>
<thead>
<tr>
<th>Variable</th>
<th>Metoclopramide+Diphenhydramine</th>
<th>Metoclopramide+Placebo</th>
<th>Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improvement in 0–10 pain score between baseline and 1 h</td>
<td>5.1 (n=104)</td>
<td>4.8 (n=101) *</td>
<td>0.3 (–0.6 to 1.1)</td>
</tr>
<tr>
<td>Required rescue medication in ED (%)</td>
<td>31/104 (30)</td>
<td>40/104 (38)</td>
<td>9% (–4 to 21%)</td>
</tr>
<tr>
<td>Sustained headache freedom (%) †</td>
<td>17/101 (17)</td>
<td>14/102 (14)</td>
<td>3% (–7 to 13%)</td>
</tr>
<tr>
<td>Want same medication again (%) ‡</td>
<td>84/99 (85)</td>
<td>77/102 (76)</td>
<td>9% (–2 to 20%)</td>
</tr>
<tr>
<td>Functional impairment at 1 h; unable to perform usual activities (%) §</td>
<td>27/103 (26) *</td>
<td>30/98 (31) *</td>
<td>4% (–8 to 17%)</td>
</tr>
</tbody>
</table>
"Our nation is needlessly losing thousands of people to a preventable epidemic, and we must take action for our patients."
By The Numbers

Over 249,000,000 prescriptions for opioids were written in 2013 — enough for every adult in America to have a bottle of pills.

300% increase in opioid prescription sales since 1999 — without overall change in reported pain.

As many as 1 in 4 receiving long-term opioid therapy (in primary care settings) struggles with opioid addiction.

Source: CDC
TURN THE TIDE
OUR PLEDGE

AS HEALTH CARE PROFESSIONALS, WE BELIEVE WE HAVE THE UNIQUE POWER TO END THE OPIOID CRISIS. WE PLEDGE TO:

1. Educate ourselves to treat pain safely and effectively.

2. Screen our patients for opioid use disorder and provide or connect them with evidence-based treatment.

3. Talk about and treat addiction as a chronic illness, not a moral failing.

MaryAnn

Mays
Nerve Blockade

- Greater occipital nerve blocks
- Cervical facet blocks
- Cervical epidural steroid injections
- Suriculotemporal blocks
- Supraorbital nerve blocks
- Supratrochlear nerve blocks
• Strongly recommended:
  – Sumatriptan
  – Prochlorperazine
  – Metoclopramide
  – Ketorolac

• Strongly not recommended:
  – IV haloperidol
  – IV dexamethasone.

AHS Guidelines

• Level B- Should be offered as first line
  – Metoclopramide
  – Prochlorperazine
  – Sumatriptan SQ
  – Dexamethasone- to prevent recurrence of HA

• Level C- Best to be avoided as first line
  – Parenteral morphine
  – Parenteral hydromorphone

AHS Guidelines

- Level C – May offer
  - IV acetaminophen
  - IV acetylsalicylic acid
  - Parenteral chlorpromazine
  - Intravenous dexketoprofen
  - Intravenous diclofenac
  - Parenteral droperidol
  - Parenteral haloperidol
  - Intravenous ketorolac
  - Intravenous valproate
AHS Guidelines

• Level C- May avoid
  – IV Diphenhydramine
  – IV Hydromorphone
  – IV Morphine
  – IV Lidocaine
  – IV Octreotide
AHS Guidelines

• No Recommendation (Level U)
  – IV Dexamethasone (acute)
  – IV DHE
  – Parenteral ergotamine
  – IV Ketamine
  – IV Lysine clonixinate
  – IV Magnesium (except migraine with aura)
  – IV Meperidine
  – IV Nalbuphine
  – IV Propofol
  – IV Promethazine
  – IV Tramadol
  – IM Trimethobenzamide
Emergency Department Treatment Strategy

IVF (2-3 L bolus or 80-100 cc/hr)
IV diphenhydramine 25-50 mg
IV Metoclopramide 10 mg or prochlorperazine 10 mg
IV Magnesium Sulfate 1 gm
IV Ketorolac 30 mg

IV Sodium Valproate 500-1000 mg
Or
Methylprednisolone 200 -1000 mg

IV DHE 0.5 -1 mg

Rozen TD. Continuum (Minneap Minn). 2015 Aug;21(4 Headache):1004-17 (modified)
Problem with Guidelines

- Some drugs are studied poorly- Class III (highest risk of bias)
- Older drugs- fewer studies
- Lack of evidence does not mean lack of efficacy
Strategies at ED Discharge
ED Success?

- 22% of patients were pain free on discharge
- 64% of patients discharged with improvement had a return of severe headache within 24 hours

Gupta MX, Silberstein SD, Young WB, Hopkins M, Lopez BL, Samsa GP. Less is not more: underutilization of headache medications in a university hospital emergency department. Headache 2007; 47 (8) 1125-1133
Strategies at ED Discharge

• Headache free:
  – At home treatment triptan, naproxen, antiemetic

• Residual pain
  – Reassurance
  – Encourage sleep
  – Additional DHE or phenothiazine prior to d/c
  – NSAID bridge
Why Admit?

- Patient doing poorly with OP withdrawal
- Emergency (suicidal, dehydrated)
- Failed outpatient therapy
- Patient desperate
- Family desperate
- Doctor desperate
- Not getting better
Hospital Admissions

- 50,000 patients were hospitalized for migraine in the USA (2008)
- $375 million, roughly $7500 per patient

Hospital Admission

- Daily use of opioids or butalbital-containing compounds (Caution ≥ 3 tabs/day)
- Daily use of triptans, simple analgesics, or ergotamines with a failed trial of outpatient discontinuation (rare)
- Failed 3 days of OP infusion therapy
- Patient continues with intractable daily head pain after a single or multiple visits to the ED
- Home rescue therapies failed with no access to outpatient infusion therapy
Inpatient Treatment

• 2004 meta-analysis: >50 % headache improvement (mean LOS 4-14 days)
  – CDH (<6 months): 81%
  – CDH (>6 months): 60.5%

• 2009 retrospective study: 78 % of patients had moderate to significant pain reduction + improvement in mood, function, and behavior

• Factors associated with a good outcome
  – Dx MOH (84 vs. 69 %)
  – Absence of personality disorder (81 vs. 68%)

Goals for Inpatient Treatment
Chronic Migraine

- Multidisciplinary program
- Reduce daily pain intensity and possibly introduce pain-free time
- Detoxify acute medication overuse
- Identify response to IV medications so an outpatient treatment program can be established
- Educate about chronic pain and MOH
- Psychiatric/psychological eval/ behavioral Rx
Overall all Goals

- Decreasing disability
- Reducing the use of rescue medications
- Reduce the numbers of office and ED visits
- Improving quality of life
Typical Inpatient Protocol

- IVF: 80 cc/h
- IV diphenhydramine 25 mg every 8 hours
- IV metoclopramide 10 mg every 8 hours
- IV magnesium sulfate 500 mg every 8 hours
- IV DHE: 0.5 -1 mg every 8 hours
- IV ketorolac 30 mg q 8 hours
- IV Depacon 1 gram daily
- If no response:
  - IV levetiracetam,
  - IV methylprednisolone,
  - other dopamine receptor antagonists such as prochlorperazine or droperidol.
DHE Raskin protocol

- Repetitive IV DHE titrated to the effective sub-nauseating dose (1 mg IV tid)
  - Typically 3 days
- Antiemetic 25 minutes prior:
  - Metoclopramide 10mg or prochlorperazine 10 mg or ondansetron 8 mg
- Can precede with diphenhydramine 25mg IV or po
- Stop other analgesics
- Side effects respond to dose reduction: leg cramps, diarrhea
- SQ: patients can inject DHE 1 mg SQ q 8 hours until headache free 24 hours
- Avoid in CAD, pregnancy

Other IV

• IV Propofol
  – 20- to 30-mg IV push, which is repeated every 5 minutes until light sedation is induced
  – Close monitoring of respirations and airway protection is essential.

• IV Lidocaine
  – 2 to 4 mg/min in D5W, starting at 1
  – Cardiac telemetry and blood pressure monitoring aiming to keep systolic blood pressure between 90 to 160 mm Hg, diastolic between 45 to 95 mm Hg, and pulse 50 to 120 bpm.
  – Side effects include nausea, hypotension, arrhythmias, and occasional hallucinations
  – 6 to 14 days.
MOH Treatment

- **1st Step:** Withdrawal of medication
- Education- habituated inadvertently
- Cognitive behavioral therapy
  - increasing problem-solving skills
  - changing the functional approach to pain in order to cope more effectively with disability, discomfort and distress
- “A willingness to experience continuing pain without needing to reduce, avoid or otherwise change it”
- Effective preventative migraine medications
Withdrawal – What to expect

• Main withdrawal symptoms:
  – worsening of the headache, nausea, vomiting, arterial hypotension, tachycardia, sleep disturbances, restlessness, anxiety, and nervousness

• Duration: typically 2 and 10 days (up to 4 weeks)

• Duration of withdrawal headache:
  – triptans (mean 1-4 days)
  – ergotamine (mean 6-7 days)
  – NSAIDs (mean 5-9 days)
Butalbital Withdrawal

- Oral clonazepam: 0.25 mg - 0.5 mg bid-tid
- Phenobarbital orally or IV 60 mg to 120 mg per dose
- 100mg butalbital = 30 mg phenobarbital
Management of Opioid Withdrawal

- Slow taper over a few days
- Opioid substitution: methadone or buprenorphine, followed by a gradual taper
- Abrupt opioid discontinuation with the use of clonidine (0.1 mg q8 hrs prn)
- Clonidine-naltrexone detoxification
Posthospital Planning

• Realistic expectations
• Improvement in pain might only be apparent following hospitalization
• Prophylactic and acute medication with instructions
• Follow-up appointment within 2-4 weeks
Posthospital Planning

• Nonpharmacologic strategies
  – Relaxation techniques
  – Exercise
  – Meal and sleep regulation
  – Avoidance of sedatives and other substances
  – Good psychological support
  – Support systems (family and friends)
Outpatient Alternative?

- Yes!
- Address medical, psychological, social and physical problems
- Alternative to more expensive inpatient treatment and is associated with:
  - Significant reductions in pain
  - Improved functional activity over the period of follow-up
  - Diminished depression
  - Diminished reactivity to stress
IMATCH (Interdisciplinary Method for the Assessment and Treatment of Chronic Headache)

CDH

Nursing Coordination and Education

Medical Therapy  Psychological Treatment  Physical Therapy
IMATCH is an Outpatient Program

**Physician visits**
- 1 initial IMATCH evaluation
- 6 established visits

**Psychological visits**
- 1 new evaluation
- 37 group sessions
- 2 team feedback mtgs
- 2 individual established visits
- 2 biofeedback session

**Nurse Visits**
- 5 RN visits

**Infusion Room**
- 4 days of 4-6 hours each day

**Physical Therapy visits**
- 1 new evaluation
- 6 individual visits
- 14 group sessions
Standard of Care vs IMATCH

Outcomes of Treatment in Chronic Migraine Patients (N = 530)

2014 - 2015

Patients (%)

0 20 40 60 80 100

Pain Rating 152

HIT-6 302

PHQ-9 118

Improved Stable Worsened

Outcomes in IMATCH Patients (N = 115)

2014

IMATCH

Patients (%)

0 10 20 30 40 50 60 70 80 90 100

Pain Rating (N=101)

HIT-6 (N=110)

PDI (N=97)

Worsened Stable Improved

54 45 2

95 14 1

86 10 1

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Conclusion

• Acute and chronic headache are frequent causes of ED visits
• Inpatient admission may be necessary to effectively treat headache and associated disability
• Utilize evidence based guidelines to support clinical judgment
• Success depends on continued OP successful treatment program
References


