Post Traumatic Headache: Pearls and Pitfalls

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Disclosures

Advisory and Speaking:

- Abbvie
- Amgen/Novartis
- Biohaven
- Eli Lilly
- Impel Neuropharma

Objectives

- Discuss diagnostic criteria for post-traumatic headache
- Review red flags that could indicate a more complex diagnosis
- Recognize risk factors for post-traumatic headache
- Pearls and pitfalls of management plan

Image Credit: peterschreiber.media / Shutterstock.com

ICHD-3 Diagnostic Criteria

- Post-traumatic headache (PTH): secondary headache with onset within seven days* following trauma or injury, or within seven days after recovering consciousness, or within seven days after recovering the ability to sense and report pain
- One of the most common sequelae of concussion
- Divided into:
  - Acute PTH – lasting less than 3 months
  - Chronic PTH – persisting longer than 3 months

*Appendix criteria allow for headache to begin after 7 days but up to 3 months after the injury

Incidence and Prevalence of PTH

- Headache is the most common physical complaint following mTBI
- Chronic PTH accounts for 4% of all secondary headache disorders.
- Prevalence of PTH in patients with mTBI ranges from 30% to 90%.
  - Of those patients, 18% to 22% of patients reported ongoing post-traumatic headaches after 1 year
- In a large cohort during the first year after TBI:
  - Incidence of new-onset headache was 44%
  - Cumulative incidence of headache at 12 months was 71%
  - 20% incidence of persistent PTH

J Tessler and LJ Horn. Post-Traumatic Headache. StatPearls Jan 2022

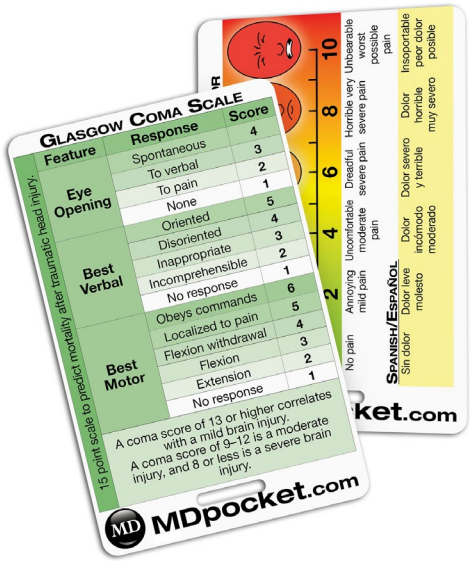
Risk Factors for PTH

- Female gender (2:1)
- Older age
- Presence of headache at the emergency room
- Pre-existing headache history
  - Migraine patients who developed PTH have a 2-fold increase in the frequency and/or intensity of the headache after the injury
  - pre-existing tension-type headache also experience a slight increase in attack frequency
- Family history of primary headache disorders
- Comorbid psychiatric disorders

Labastida-Ramírez, A. et al. *J Headache Pain* 2020
Yilmaz et al. Emerg Med J. 2017
Hoffman J et al. J Neurotrauma. 2011.
Image: flo.health.com

NOT Associated with Increased Risk for PTH

- Severity of headache
- Recovery time
- Race
- Marital status
- Level of education
- Alcohol use at the time of injury
- Etiology of TBI
- Glasgow Coma Scale



Labastida-Ramírez, A. et al. *J Headache Pain* 2020
Yilmaz et al. Emerg Med J. 2017
Hoffman J et al. J Neurotrauma. 2011.

Healthcare Disparity Effects in PTH

Socioeconomic Influence

- Medicaid patients use the ER for concussion care significantly more than private pay and self pay patients
- Children with Hispanic ethnicity and lower SES are highly likely to be associated with a decline in quality of life 3 months after concussion children who present to an ED.
- Lower SES assc with increased risk of long-term sequelae noted 6-12 months from mTBI, ie novel psychiatric disorders, declines in health-related QOL.

Racial Influence

- Black children compared to non-Hispanic white children are less likely to receive a diagnosis of concussion
- African Americans and Hispanics were less likely to receive intensive rehabilitation after a TBI and were more likely to have a lack of post-TBI follow up

Arbogast et al. JAMA Pediatr. 2016;170(7):e160294
Lyons et al. Front Neurol 2019 Jul 2;10:690
Lumba Brown et al. JAMA Pediatr 2018; Nov 1;172(11):e182847.

Red Flags

As always, the history is everything

- History of head or neck injury
- Timing of headache onset
- Preinjury headache history
  - Secondary, primary or both
  - Headache phenotype
  - Migraine-like and probable migraine-like are the most common phenotype

Lucas et al. Cephalalgia. 2014
Ashina et al. Cephalalgia. 2020

Consider Imaging

Panel 1: **Canadian CT Head Rule**

CT Head Rule is only required for patients with minor head injuries with any one of the following:

High risk (for neurological intervention)

- GCS score <15 at 2 h after injury
- Suspected open or depressed skull fracture
- Any sign of basal skull fracture (haemotympanum, 'racoon' eyes, cerebrospinal fluid otorrhoea/rhinorrhoea, Battle's sign)
- Vomiting ⩾two episodes
- Age ⩾65 years

Medium risk (for brain injury on CT)

- Amnesia before impact >30 min
- Dangerous mechanism (pedestrian struck by motor vehicle, occupant ejected from motor vehicle, fall from height >3 feet or five stairs)

Minor head injury is defined as witnessed loss of consciousness, definite amnesia, or witnessed disorientation in a patients with a GCS score of 13–15.

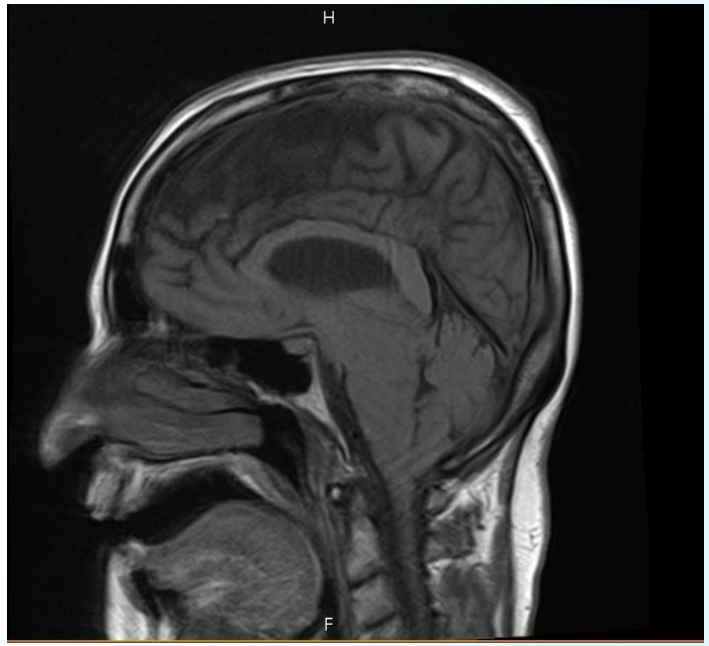
Additional Orange Flags

- Focal neurologic symptoms and signs
- Orthostatic headache
- Progressively worsening headache

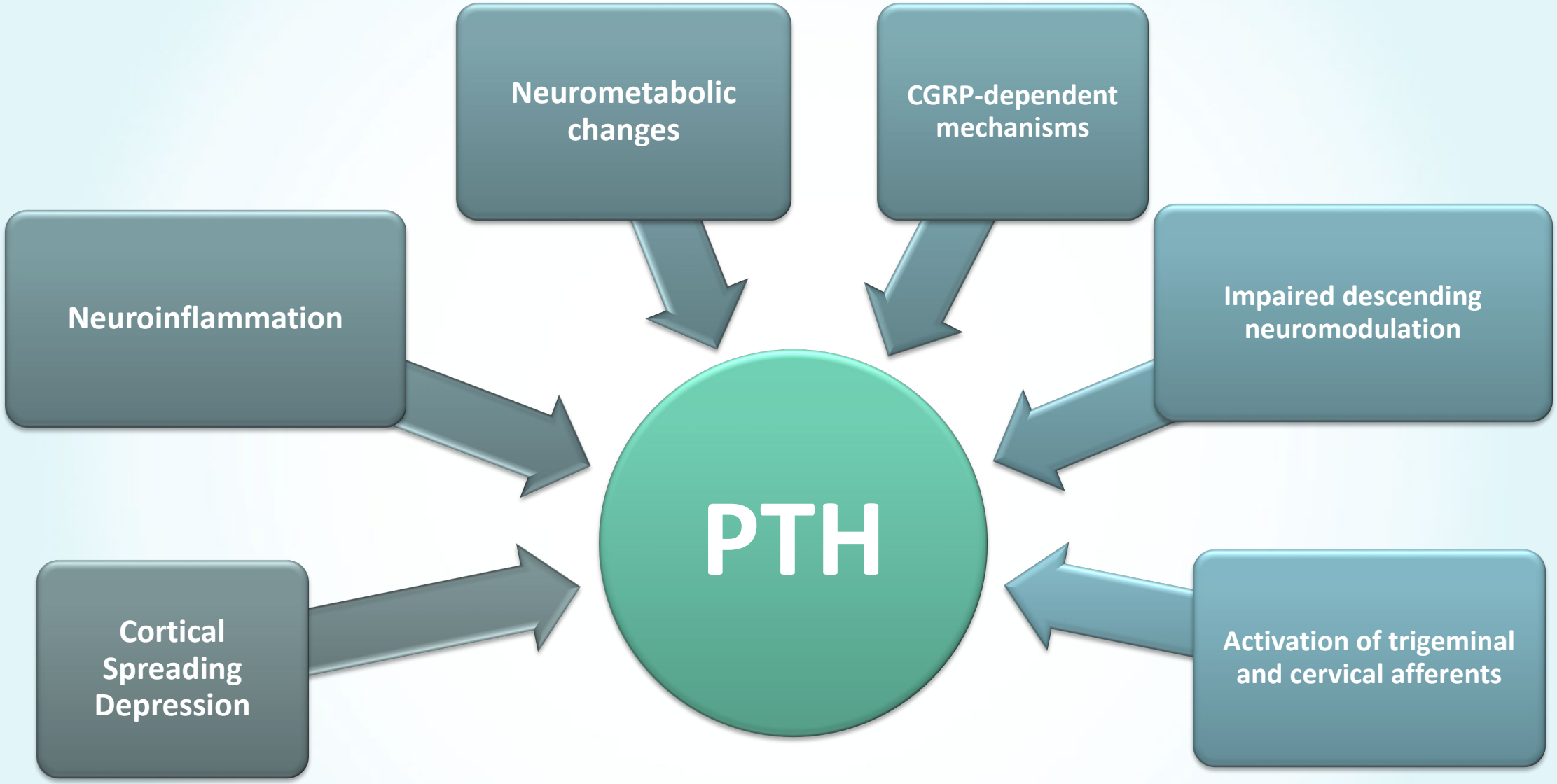
J Emerg Trauma Shock. 2011 Oct-Dec; 4(4): 472–476.
Lucas et al. Cephalalgia. 2014
Ashina et al. Cephalalgia. 2020

Intracranial Hypotension

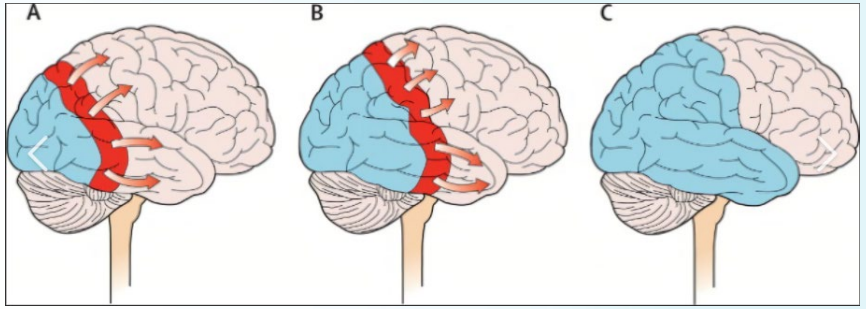
- Once thought to be rare, but more likely underdiagnosed
- Acute or delayed CSF leak, spinal > skull base
- Often positional but can lose positional quality over time
- Pathophysiology: loss of CSF volume → compensated by subdural fluid collections + increase in intracranial venous blood → MRI findings
  - pachymeningeal thickening and sometimes enhancement,
  - enlarged pituitary,
  - engorgement of cerebral venous sinuses
  - Midbrain sagging
- Treatment: empiric EBP, repeat if needed



Headache. Volume53, Issue7 July/August 2013


Neurometabolic changes
CGRP-dependent mechanisms
Neuroinflammation
Impaired descending neuromodulation
PTH
Cortical Spreading Depression
Activation of trigeminal and cervical afferents

Overlapping Mechanisms



1. Impaired descending modulation

   DAI → structural remodeling of cortical and subcortical regions in the somatosensory and insular cortex →impaired neuromodulation of descending pain-modulating pathways

2. Trigeminovascular system activation

   nociceptive signaling from upper cervical afferents → convergence between cervical afferents and trigeminal nerve pathways → supports the observation that treatments to cervical neck pain generators can help alleviate PTHA.

3. Neurometabolic changes
   1. Neuronal injury → metabolic stress (lactate and free radicals) → axonal damage
   2. Cortical spreading depression (CSD) → Excessive glutamate and potassium release → increased neuronal excitability → trigeminal sensory activation

Acute Management of PTH

PTH Treatment Considerations

- Caveats:
  - There are no FDA approved treatments
  - There are no agreed-upon guidelines
  - Recent systematic review found “lack of high-quality evidence-based studies on the treatment of PTH”
- Main ideas:
  - Treat by phenotype
  - Attempt to break the headache cycle
  - Initiate acute treatment early, and preventive treatment within weeks
  - Monitor for medication overuse

Consider: Comorbidities, Activity requirements (i.e., Return to learn or work, Return to play, Professional vs Recreational athlete, etc.), Non-pharmacologic treatment-Behavioral, Physical therapy

Irwin et al. Headache 2020
Larsen et al. J Headache Pain 2019
Murray et al. Seminars in Pediatric Neurology 2021

Multiple Phenotypes

Multiple paths and responses to treatment

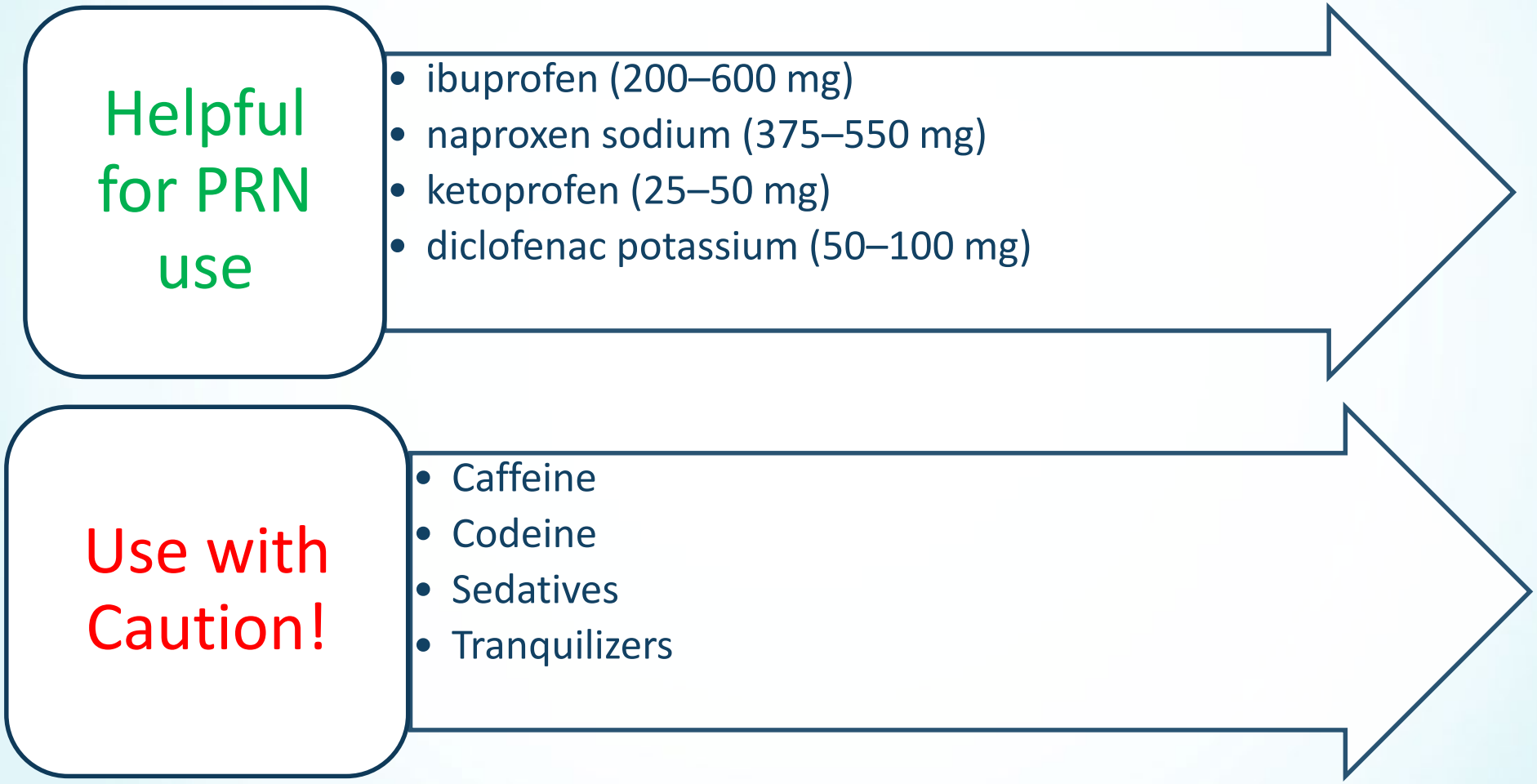
TTH Diagnostic Criteria

A. At least 10 episodes of headache fulfilling criteria B through D. Infrequent and frequent episodic subforms of TTH are distinguished as follows:
Infrequent episodic TTH: Headache occurring on <1 day per month on average (<12 days per year).
Frequent episodic TTH: Headache occurring on 1 to 14 days per month on average for >3 months (≥12 and <180 days per year).
B. Headache lasting from 30 minutes to seven days.
C. At least two of the following four characteristics:
Bilateral location.
Pressing or tightening (nonpulsating) quality.
Mild or moderate intensity.
Not aggravated by routine physical activity such as walking or climbing stairs.
D. Both of the following:
No nausea or vomiting.
No more than one of photophobia or phonophobia.
E. Not better accounted for by another ICHD-3 diagnosis.

Episodic tension-type headache diagnostic criteria

Description: Episodes of headache, typically bilateral, pressing or tightening in quality and of mild to moderate intensity, lasting minutes to days. The pain does not worsen with routine physical activity and is not associated with nausea, but photophobia or phonophobia may be present. Increased pericranial tenderness may be present on manual palpation.

Acute Treatment of TTH



Ashina. *Curr Pain Headache Rep.* 2003;7:466–74.

167 mTBI Patients: Treatment Outcomes

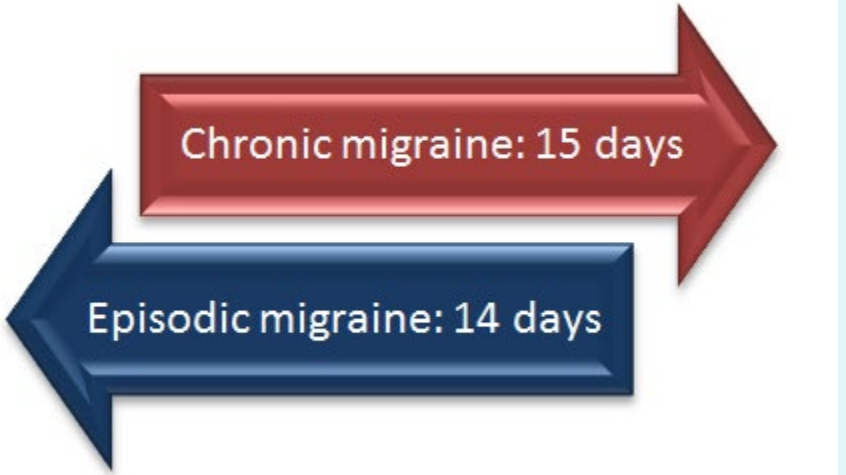
Retrospective analysis of treatment based on PTH phenotype

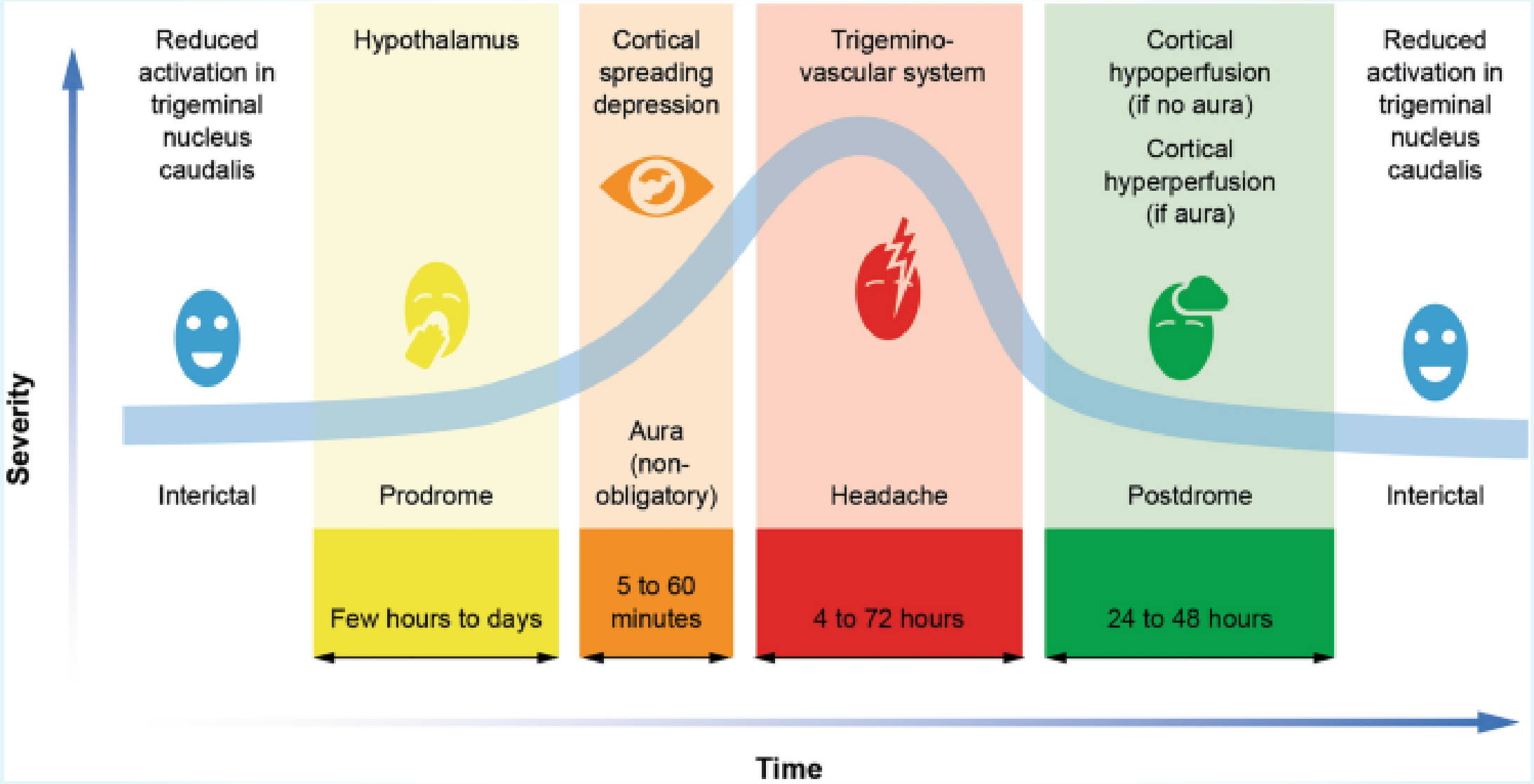
- Patients often take OTC medications which provide minimal benefit
- TTH-like phenotype-70% relief
- Migraine-like phenotype-26% relief

DiTommaso et al. J Head Face Pain 2014

Migraine Diagnostic Criteria

A	≥5 attacks fulfilling features B to D
B	Headache attack lasting 1 to 72 hours
C	Headache has at least 2 of the following 4 features: (1) Bilateral or unilateral (frontal/temporal) location (2) Pulsating quality (3) Moderate to severe intensity (4) Aggravated by routine physical activity
D	At least one of the following accompanies headache: (1) Nausea and/or vomiting (2) Photophobia and phonophobia (may be inferred from their behavior)

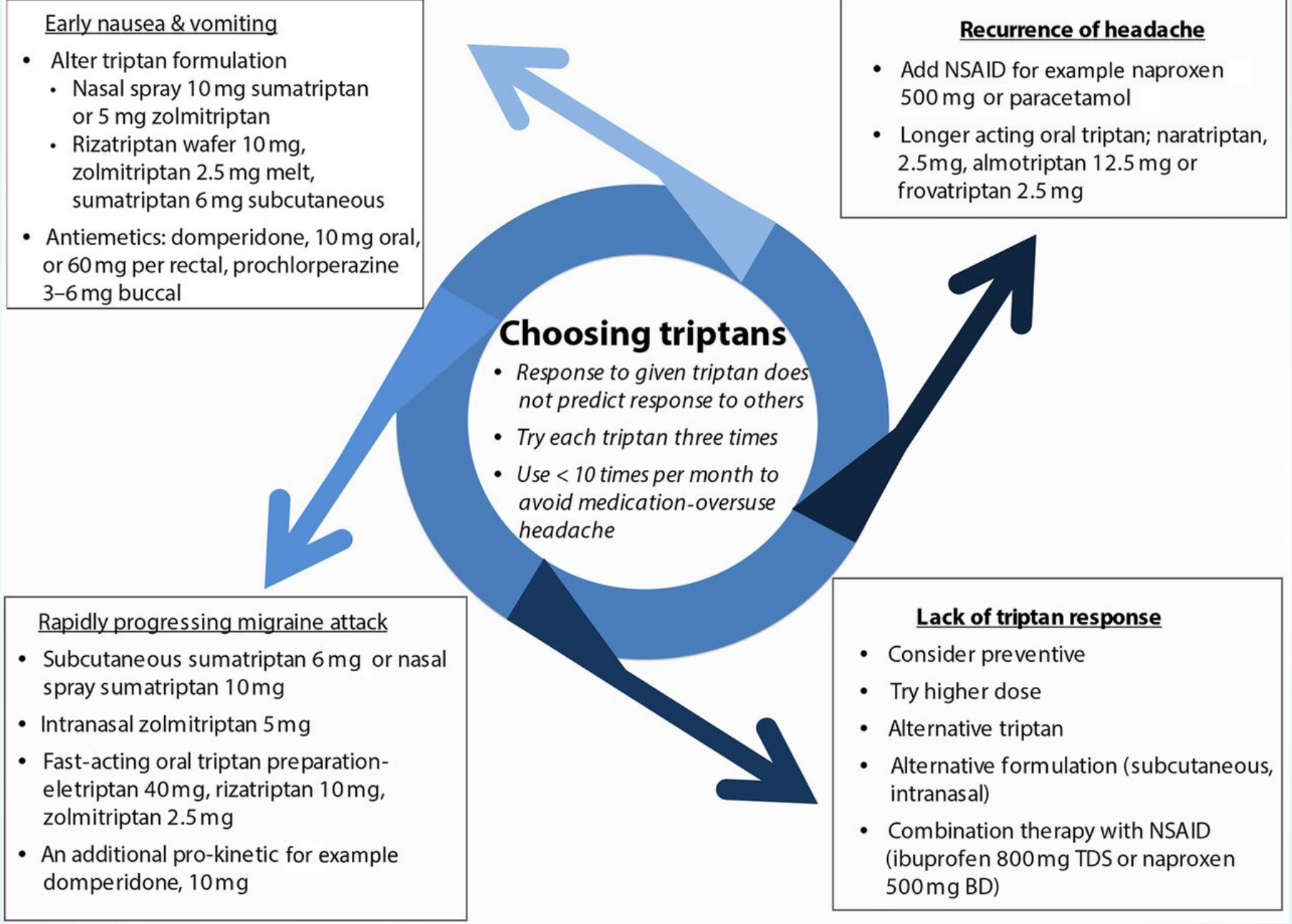




Blumenfeld et al Neurol Ther Dec;10(2):469-497 2021

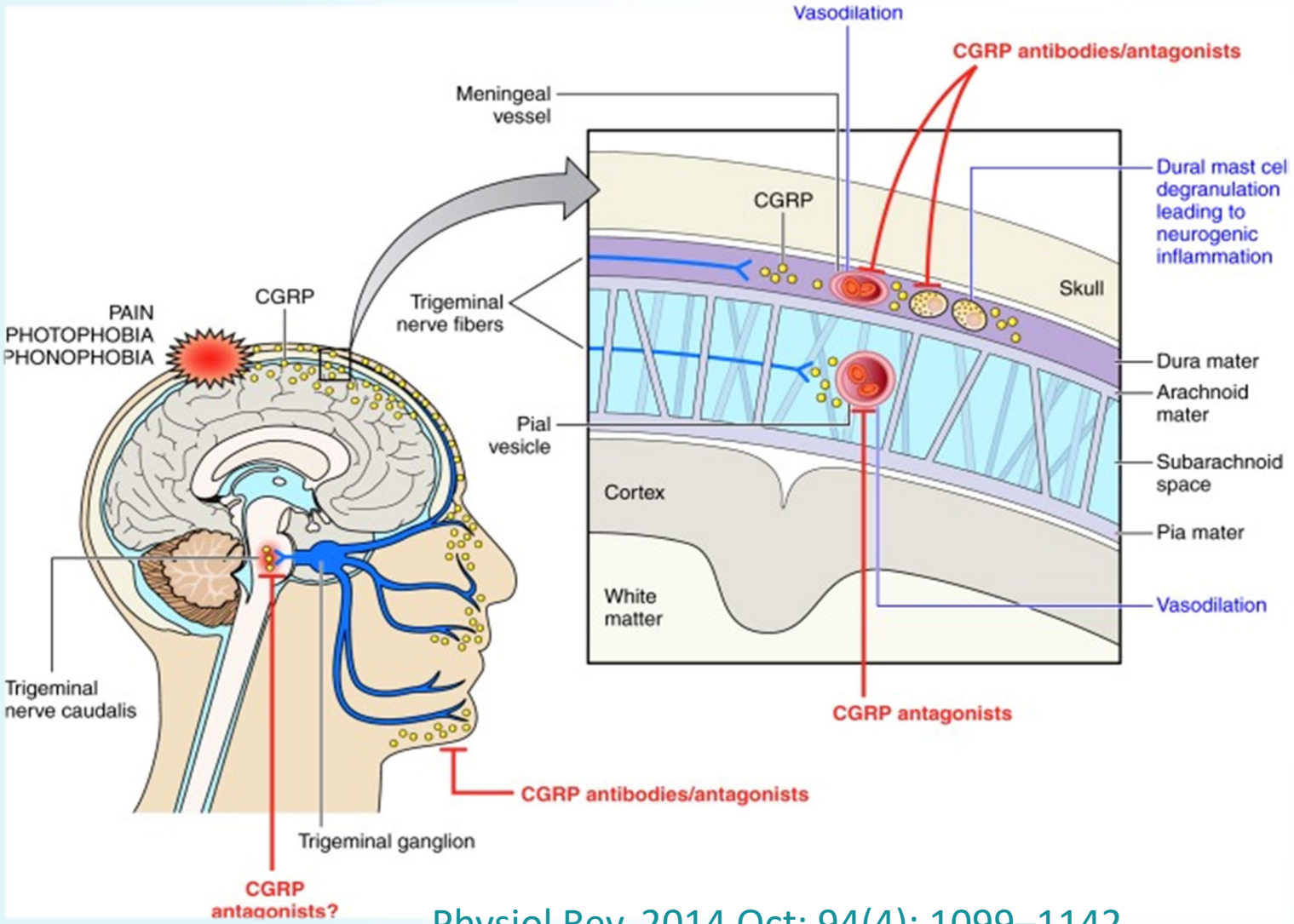
Acute Migraine Treatment

- Monotherapy: single agent: triptan, NSAID, gepant, ditan, device
- Combination therapy: triptan+NSAID +/- antiemetic
- NSAIDs
  - Aspirin 600–900 mg (ideally effervescent)
  - Ibuprofen 600–800 mg
  - Naproxen 500 mg
  - Diclofenac 50–75 mg (powder or tablet)
  - Celecoxib oral solution 120 mf
- Antiemetics - for nausea and/or as prokinetics
  - Metoclopramide 10 mg
  - Prochlorperazine 10 mg
  - Promethazine 25 mg



Alex J Sinclair et al. Pract Neurol 2015;15:411-423

Gepants for Acute Migraine



Rimegepant 75 mg every 24 hours at onset of headache

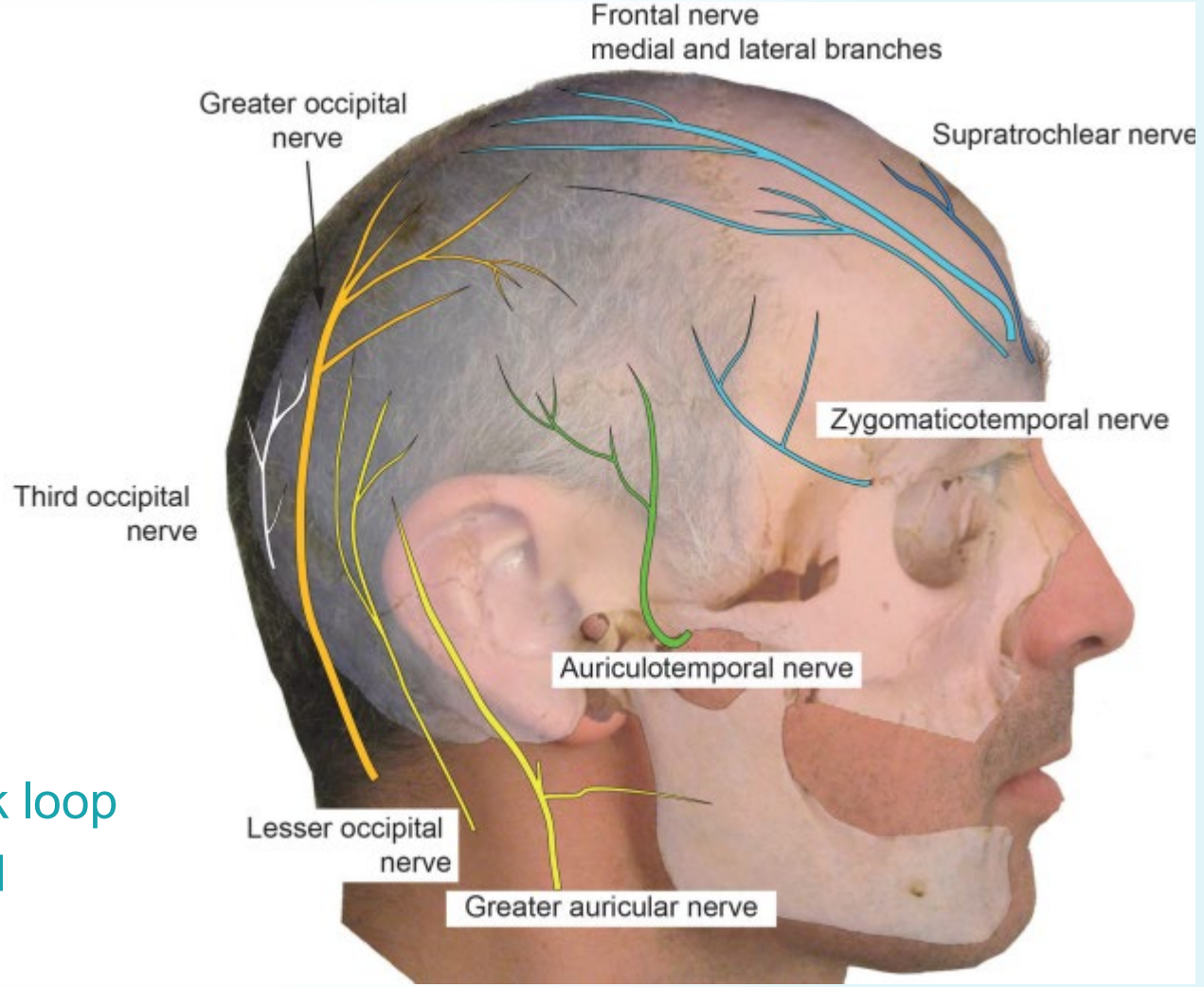
Ubrogepant 50-100 mg at onset of migraine, repeat once in 2 hours prn

SE profile – 2% nausea, otherwise similar to placebo. No MOH or vasoconstriction.

Physiol Rev. 2014 Oct; 94(4): 1099–1142.

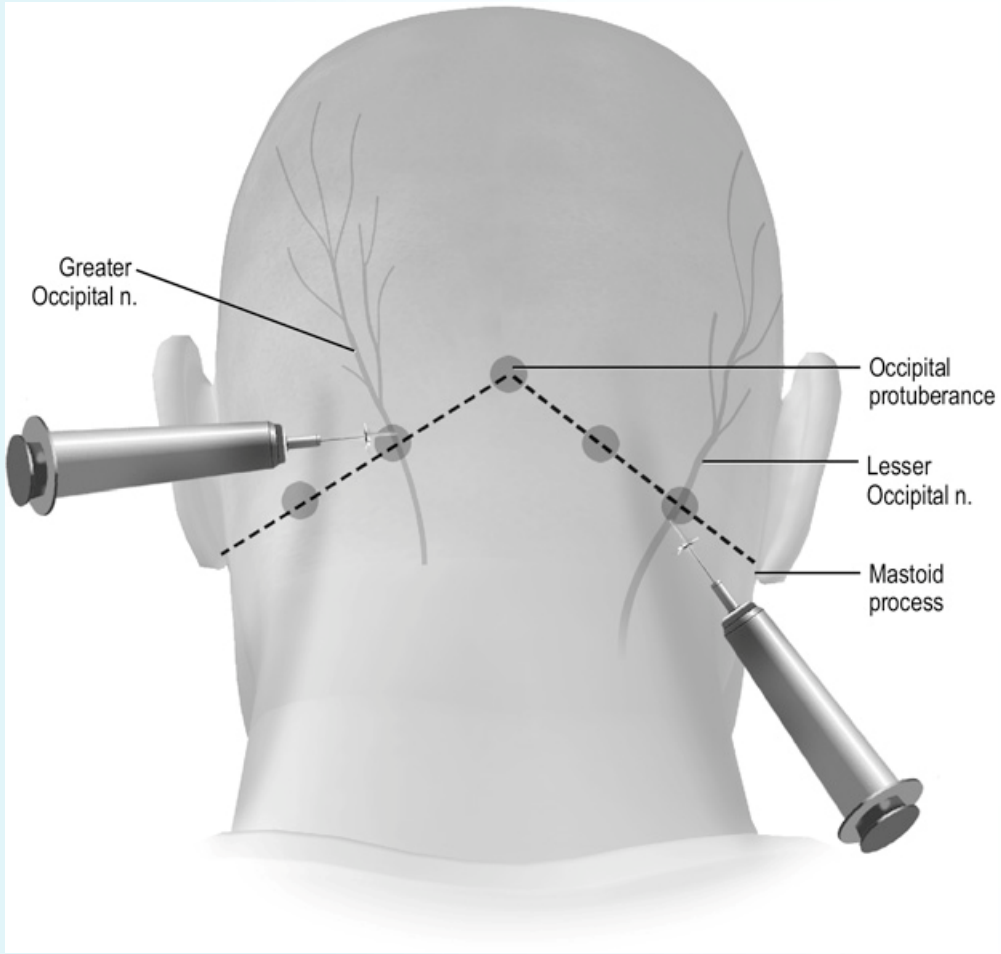
Pericranial Nerve Blocks

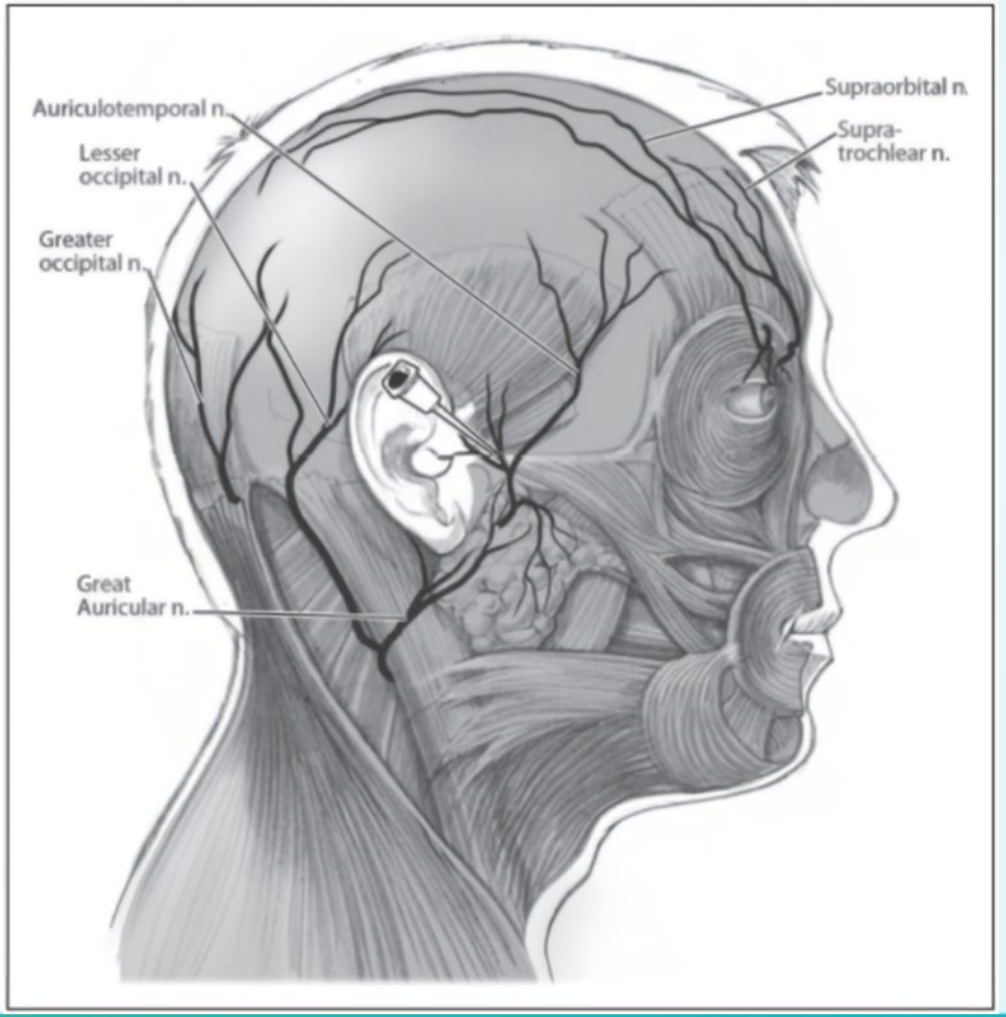
- Common sites:
  - greater occipital nerve
  - lesser occipital nerve
  - auriculotemporal nerve
  - supraorbital nerve
  - supratrochlear nerve
  - sphenopalatine ganglion (SPG)
- Bupivacaine, ropivicaine, or lidocaine (2%)
  - No better with steroids in one RCT
- Volumes ranging from 0.5 to 2 cc per site
- Local anesthesia breaking nociceptive feedback loop
- Reversibly inhibits Na channels in unmyelinated C-fibers and thinly myelinated Aδ fibers



The Journal of Headache and Pain volume 21, Article number: 55 (2020)

Pericranial Nerve Blocks






CAUTION:
OPIOID
RISK OF OVERDOSE
AND ADDICTION


DO
NO
HARM
THE OPIOID
EPIDEMIC

The Journal of Headache and Pain

BMC

J Headache Pain. 2019; 20(1): 98.
Published online 2019 Oct 21. doi: 10.1186/s10194-019-1051-7

PMCID: PMC6802300
PMID: 31638888

Acute and preventive pharmacological treatment of post-traumatic headache: a systematic review

Eigil Lindekilde Larsen,[#1] Håkan Ashina,[#1] Afrim Iljazi,[1] Haidar Muhsen Al-Khazali,[1] Kristoffer Seem,[1] Messoud Ashina,[1] Sait Ashina,[#2] and Henrik Winther Schytz[✉#1]

Acute Treatment of PTH: Pediatrics

Outcome: ≥50% reduction in pain intensity

- Acetaminophen or Ibuprofen
- Ketorolac plus metoclopramide or prochlorperazine 89%; Metoclopramide or prochlorperazine only 93%; Ondansetron only 78%

Outcome: HA relief lasting longer than 24 hours

- GON block (2% lidocaine with epi) 93% - Lesser ON and supraorbital nerve

Outcome: ≥ 50% reduction in HA frequency

- GON block (2% lidocaine +methylprednisolone or triamcinolone) 64%

J Headache Pain. 2019; 20(1): 98.

Acute Treatment of PTH: Adults

Outcome: Sustained HA relief at 48 hrs

- IV-metoclopramide + diphenhydramine 63%

Outcome (military): HA relief within 2 hours

- Triptans 70%
- Non-triptans 42% (NSAIDs; Acetaminophen; Opioids; Combination)

J Headache Pain. 2019; 20(1): 98.

Medication Overuse Headache (MOH)

- Aka “rebound headache”, analgesic overuse headache
- Worsening of a pre-existing headache disorder
- Overuse defined:
  - Triptans or combo analgesics ≥ 10 days/mo for 3 months
  - Simple NSAIDS ≥ 15 days/mo x 3 mo

Medication Overuse Headache (MOH)

- About half of people with >15 HA days per month have MOH
- Pre-existing HA disorder needed
- Alterations in cortical neuronal hyperexcitability, downregulation of 5HT-1 and upregulation of 5HT-2a receptors, increase in CSD
- Withdrawal of offending agent usually results in improvement of the headache (2/3 of the time)

Preventive Management of PTH

PTH Non-Pharmacologic Prevention

- Multidisciplinary treatment course seems most effective
- Based on presentation, consider:
  - cognitive-behavioral therapy (CBT)
  - biofeedback
  - progressive muscle relaxation therapy
  - acupuncture
  - physical therapy
- Evidence based supplements:
  - Magnesium (migraine and PTH),
  - Riboflavin, feverfew, butterbur, CoQ10 (migraine)

Fraser F, Matsuzawa Y, Lee YSC, Minen M. Behavioral Treatments for Post-Traumatic Headache. Curr Pain Headache Rep. 2017 May;21(5):22.

Migraine Phenotype Preventive Options

- AEDs: topiramate, valproic acid, zonisamide, levetiracetam, gabapentin, lamotrigine
- BP drugs: propranolol, timolol, verapamil, atenolol, nadolol, candesartan
- Antidepressants: nortriptyline, amitriptyline, venlafaxine, duloxetine, fluoxetine
- Supplements: B2, CoQ10, Magnesium, feverfew, butterbur
- Devices: e-TNS / Cefaly, sTMS / SpringTMS “mini”
- Onabotulinum toxin A
- CGRP monoclonal antibodies: erenumab, galcanezumab, fremanezumab

*FDA approved for use

TTH Phenotype Preventive Options

- First line - TCAs:
  - Amitriptyline > nortriptyline > protriptyline
- 2nd and 3rd line:
  - mirtazapine or venlafaxine,
  - tizanadine,
  - gabapentin,
  - topiramate,
  - lidocaine nerve blocks

Preventive Management of Adults with PTH – Systematic Review

Outcome (military): # of HA days per month

- Topiramate (significant decrease in frequency)
- Amitriptyline or nortriptyline
- Propranolol
- Valproate

Outcome: Self-reported HA score

- Amitriptyline
- Gabapentin

Some additional treatments, since the systematic review:

- Erenumab
- Repetitive transcranial magnetic stimulation (TMS)

J Headache Pain. 2019; 20(1): 98.

Consider Co-morbidities

- Caution with tricyclic antidepressants in patients with autonomic symptoms
  - Caution with sedating medications in patients with fatigue
- Caution with topiramate in patients with cognitive domain symptoms
- Caution with beta-blockers in athletes
- Caution with steroids in patients with significant emotional and sleep domain symptoms
  - Steroids may violate anti-doping rules in professional, elite and college athletes

Key Concepts Review

- **Post-Traumatic Headache is common and debilitating**
- **Risk factors in PTH: Minimal evidence**
- **Use a systematic approach for the management of PTH**
  - Look for red flags
  - Until there is better evidence, treat based on phenotype
  - Treat PTH early and adequately
  - Monitor and set strict limits on acute medication use
  - Consider comorbidities when choosing a preventive
- **The science of PTH is advancing steadily**
- We need randomized, double-blind treatment trials

Thank you!