Headache Treatment in Concussion Patients

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February 26, 2021

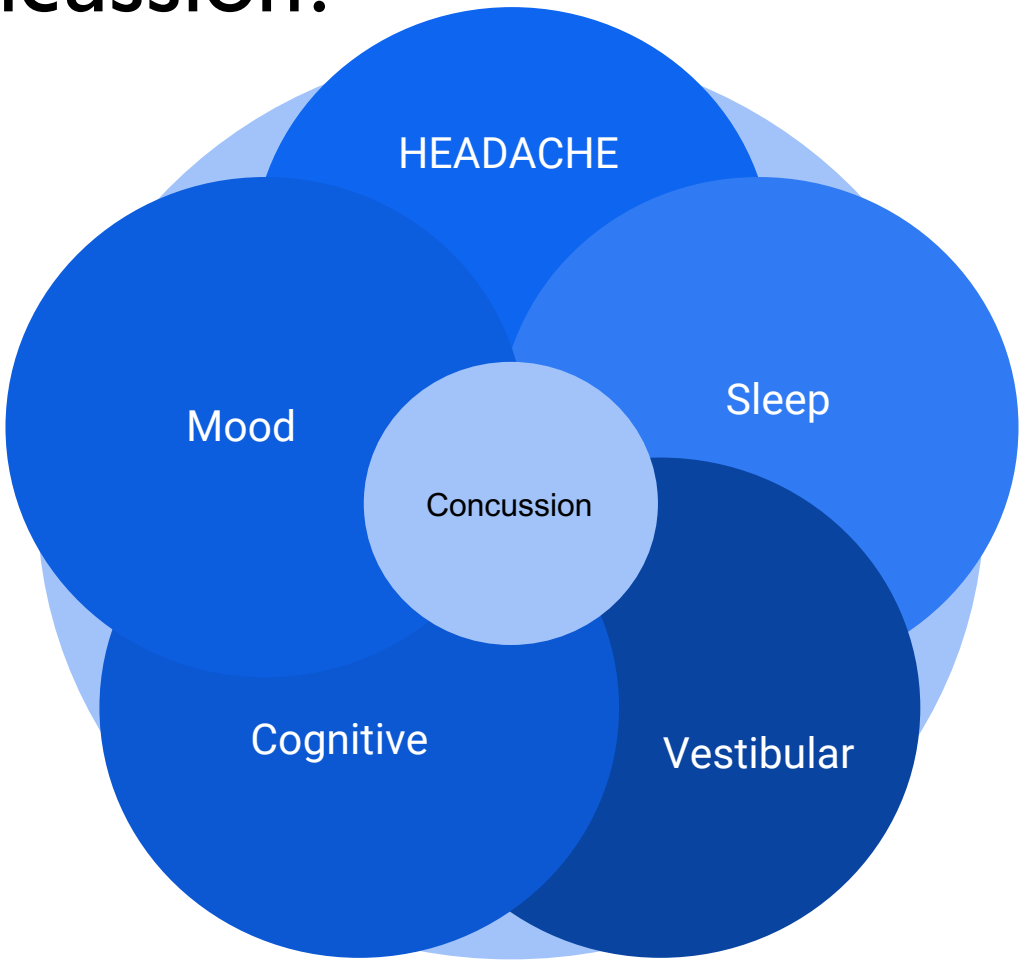
Disclosures

Role	Organization
Advisory Board	Lilly
Speaker	Novartis
Consultant	Aralez, Lundbeck
Grant support	
Support: Clinical trial site PI	
Editorial Board	
Contributing author	

Objectives: Upon completion of this learning activity, the participant will be able to:

- Outline diagnostic criteria for acute and persistent post-traumatic headache (PTH)
- Distinguish phenotypes of PTH
- Formulate an approach to multimodal treatment of headache in patients with concussion

Why Should You Care About Headache After Concussion?



Why Should You Care About Headache After Concussion?

- Headache is COMMON after concussion
  - 25-90% of patients with concussion experience headache
  - Lifetime prevalence of PTH in one study 4.7% in men, 2.4% in women

Ashina et al. *Nat Rev Neurol* 2019;15(10):607-617.
Rasmussen and Olesen *Neurology* 1992;42(6):1225-1231.

Why Should You Care About Headache After Concussion?

- Headache can be DISABLING after concussion
  - Persistent PTH in 15-75% of those with headache
  - Can be very persistent -- up to 20% of those with headache still have headache at 4 years post-injury

Ashina et al. *Nat Rev Neurol* 2019;15(10):607-617.
Nampiaparampil. *JAMA* 2008;300(6):711-719.

Defining Post-Traumatic Headache

5.1, 5.2: Headache attributed to traumatic injury to the head

A. Any headache fulfilling criteria C and D

B. Traumatic injury to the head has occurred

Direct impact not required

C. Headache is reported to have developed within 7 days of one of the following:

   a. The injury to the head

   b. Regaining consciousness following head injury

   c. Discontinuation of medication(s) impairing ability to sense or report headache

D. Acute vs persistent

   a. Acute: headache resolves within 3 months or 3 months have not yet passed

   b. Persistent: headache persists for >3 months

E. Not better accounted for by another ICHD-3 diagnosis

ICHD-3. Cephalalgia 2018;38(1):1-211

5.3, 5.4: Acute and persistent headache attributed to whiplash

- Not well studied
- Will not be addressed specifically today

ICHD-3. Cephalalgia 2018;38(1):1-211

PTH: Unique entity vs post-traumatic migraine?

- Unique entity?
  - Patients with no history of headache
  - Patients with a very different headache post-injury
  - → Diagnose as PTH
- Post-traumatic migraine?
  - Patients with history of headache in whom headache becomes chronic or at least 2 times more frequent or severe post-injury
  - → Diagnose both disorders

ICHD-3. Cephalalgia 2018;38(1):1-211

Phenotyping PTH

- **Migraine with or without aura**
  - Migraine with aura reported as most common phenotype in sports-related acute PTH
- **Tension-type**
- Other (not an exhaustive list)
  - Trigeminal autonomic cephalalgias (TACs)
    - Hemicrania continua, cluster headache
  - Cervicogenic

Ashina et al. *Nat Rev Neurol* 2019;15(10):607-617.
Seifert T. *Neurology* 2018;91(23 Suppl 1)S28-S29.

International Classification of Headache Disorders (ICHD-3)

Migraine is 5 or more attacks of headache lasting 4-72 hrs with:

Any 2

- ❑ unilateral
- ❑ throbbing
- ❑ worsened by activity
- ❑ moderate or severe

Any 1

- ❑ nausea or vomiting
- ❑ photophobia and phonophobia

2+1 = Migraine

- ❑ not due to any other disorder

ICHD-3. *Cephalalgia* 2018;38(1):1-211.

Migraine versus tension-type headache

MIGRAINE	TENSION-TYPE HEADACHE
May be unilateral	Usually bilateral
Throbbing	Non-pulsatile
Moderate to severe	Rarely disabling
Worse with activity	Not worse with routine physical activity
Photophobia AND phonophobia	Only one of photophobia OR phonophobia
Nausea and/or vomiting	No nausea or vomiting

ICHD-3. *Cephalalgia* 2018;38(1):1-211.

Headache Red Flags (SNOOP)

- S ystemic symptoms (e.g., fever, weight loss) or

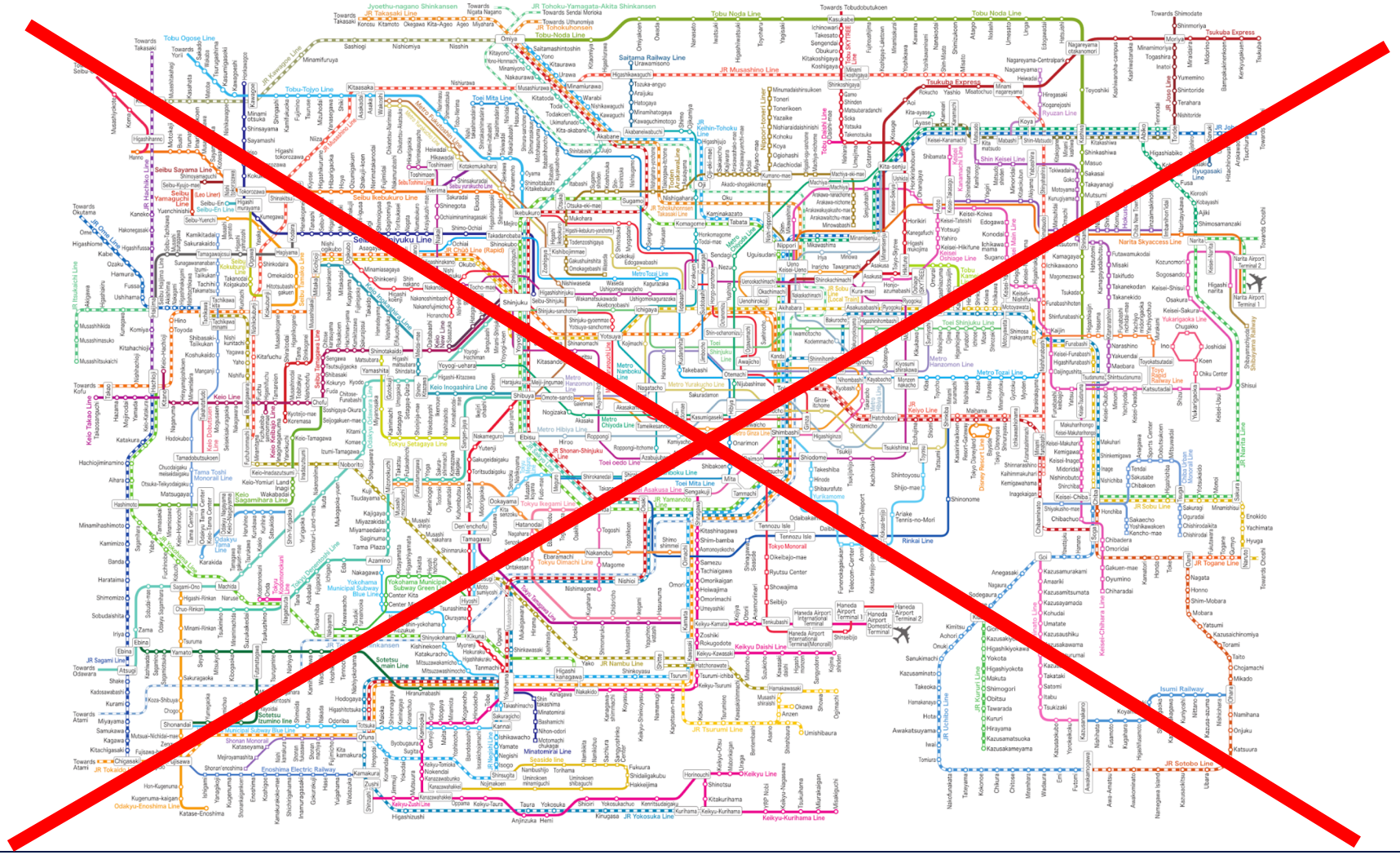
  [S]econdary risk factors (e.g., HIV, cancer, pregnancy)
- N eurologic symptoms/signs (altered level of consciousness, focal neurological deficits such as weakness, papilledema, meningismus)
- O nset (sudden, split-second, “thunderclap”)
- O lder (new-onset or progressive headache especially in a patient over 50)
- P revious headache history (change in frequency, severity, or clinical characteristics, or first headache of a new type)

  [P]recipitated by cough/Valsalva

  [P]ositional

Modified from Dodick *Adv Stud Med* 2003;3:87-92.

Treatment of PTH



Treatment of PTH

Ontario Neurotrauma Foundation 2018 Guidelines:
https://braininjuryguidelines.org/concussion/

Treatment of PTH: Take-Home Spoilers

- Evidence is overall poor
- Everything is off label
- Treat the phenotype

Multimodal PTH Management

- Treating EARLY can reduce central sensitization and lessen risk of progression to chronic headache
  - Early = within weeks
- Hyperacute treatment may inappropriately mask headache which can be an important warning sign

Multimodal PTH Management

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

Eigil Lindekilde Larsen, Håkan Ashina, Afrim Iljazi, Haidar Muhsen Al-Khazali, Kristoffer Seem, Messoud Ashina, Sait Ashina & Henrik Winther Schytz

The Journal of Headache and Pain **20**, Article number: 98 (2019) | Cite this article

Larsen et al. *J Headache Pain* 2019;20(8):1-211.

Multimodal PTH Management

Conclusion

We found that there is a lack of high-quality evidence-based studies on the pharmacological treatment of PTH. Future studies are highly needed and must emphasize open-label studies with rigorous methodology or RCTs with a placebo-controlled design.

- So now what?
- Some of these studies were in children where placebo response rates are high
- Authors note that patients also often have other comorbid symptoms which should also be addressed
- Headache does not exist in a vacuum!

Larsen et al. *J Headache Pain* 2019;20(8):1-211.

Multimodal PTH Management

- Target phenotype and keeping brain out of chronic pain state in general
- Lifestyle
- Behavioural
- Vitamins
- Acute
- Preventative

Multimodal PTH Management

- Treat underlying issues that can worsen headache
  - Sleep apnea
  - Iron deficiency
  - Anemia
  - Vitamin D deficiency
  - Bruxism
- Avoid exacerbating medications e.g. amlodipine

Santos et al. *J Clin Med* 2020;9(3);691.

Multimodal PTH Management: Lifestyle

- Sleep: consistent routine including weekends, limit technology before bed
- Diet: Breakfast with 12-15g protein <1hour of awakening, don't skip meals, avoid artificial colors/preservatives
- Hydration: 1.5-2L water per day
- Caffeine: less than 200mg/day
- Exercise regularly as tolerated, increase green space time
- Keep a headache diary

Multimodal PTH Management: Behavioral

- Mindfulness/meditation >5 minutes per day
- CBT, CBTi if insomnia
- Progressive muscle relaxation
- Biofeedback

Multimodal PTH Management: Marijuana YEA or NAY

- Evidence for cannabis in headache is limited
- We do not typically recommend marijuana for headaches
- There may be benefits for other symptoms/diagnoses
- Pre-clinical models suggest cannabis may contribute to a medication overuse phenotype in animals
- Marijuana does carry risks e.g. reversible cerebral vasoconstriction, neurodevelopmental concerns < age 30

Kopruszinski et al. *Cephalalgia* 2020;40(1):68-78.

Multimodal PTH Management: Vitamins

*****Risk of liver toxicity if impure pyrrolizidine alkaloids - ensure brand does not contain (Flora, Weber etc)**

- Vitamin B2/Riboflavin 200mg twice daily
- Magnesium citrate 300-600mg daily (try qhs)
- CoQ10 100mg three times daily
- Butterbur 75mg twice daily**
- Vitamin D 1000 IU daily (emerging evidence)
- Melatonin 3-5mg qhs 2-3 hours before bed

Multimodal Migraine Management: Acute

Goal: headache-free within 2 hours

- Treat early to maximize efficacy and minimize side effects
- Triptans (7 different triptans, oral, intranasal, subcutaneous)
- NSAIDs
- Anti-emetics: metoclopramide
- Neuromodulation: Cefaly device
- Avoid combination analgesics, opioids, butalbital (Fiorinal)

Medication Overuse Headache (MOH)

- Formerly called rebound headache
- MOH: Headache >15 days per month with 3 months medication overuse
- Present in 42-44% of patients with PTH at time of referral to a headache specialist in Danish studies

Ashina et al. *Nat Rev Neurol* 2019;15(10):607-617.
ICHD-3. *Cephalalgia* 2018;38(1):1-211.

Medication Overuse Headache

- "Overuse" varies by medication, days are additive between meds
  - Triptans: 10 days/month
  - Simple analgesics (acetaminophen, ibuprofen): 15 days
  - Combination analgesics: 10 days
  - Opioids: as little as 3 days!
  - Long-acting NSAIDs (naproxen, nabumeto

    thought to cause medication overuse

Medication Overuse Headache

- Can lead to dull, featureless, daily headache that is resistant to treatment
- Treatment strategies typically combine multiple modalities
  - Detox - wean or cold turkey
  - Bridge with long-acting NSAID or nerve blocks
  - Prophylaxis

Choosing an Acute Migraine Treatment

Rapid-onset or wake-up attacks	**Nasal or sc triptan (zolmitriptan, sumatriptan), eletriptan, diclofenac K powder, dissolved alka-seltzer (aspirin)**
Significant nausea or vomiting	**Nasal or sc triptan, metoclopramide, prochlorperazine, ondansetron**
Prolonged attacks	**Long-acting triptan (frovatriptan, naratriptan)**
Menstrually-related	**Long-acting triptan or long-acting NSAID x 5-7 days, starting 1 day before headache**
Aura	**Magnesium at aura onset**
Triptan side effects	**Lower side effect profile triptan e.g. almotriptan, rizatriptan**
Next-day headache recurrence	**Eletriptan, frovatriptan, naratriptan**

Long-acting NSAIDs = naproxen, nabumetone

Multimodal Migraine Management: Acute

Red headache: "I have to **STOP**"

Yellow headache: "I have to **SLOW DOWN**"

Green headache: "I can still **GO**"

- Red: Triptan + NSAID
- Yellow: Triptan or NSAID
- Green: NSAID

Lagman-Bartolome and Lay.
Headache 2019;59:250-252.

Multimodal Migraine Management: Preventative

- Consider preventative if:
  - 4+ headache days/month (risk for transformation to chronic migraine)
  - Disabling headaches despite acute treatment (e.g. prolonged or hemiplegic aura)
  - Contraindication, side effect, or overuse of acute treatment

Multimodal Headache Management: Preventative

- Goal: at least 50% reduction in headache frequency/severity
- With daily pain, target of reduced severity may be more realistic

Multimodal Headache Management: Preventative

- Start low, go slow
- Tailor prevention to the patient
- Avoid side effects if these would be dangerous e.g. avoid topiramate if history of glaucoma or kidney stones
- Consider dual benefit, e.g. mood benefit, but do not undertreat a coexisting disorder - may be better to treat both problems separately

Multimodal Migraine Management: Oral Preventatives

- Blood pressure agents: **candesartan**, lisinopril, **beta-blockers**, verapamil
- Antiepileptics: **topiramate**, gabapentin
- Mood agents: amitriptyline***, venlafaxine
- Others: SSRIs, valproate, flunarizine, pizotifen, memantine

*****Recent concerns about long-term cognitive side effects of anti-cholinergics e.g. TCAs**

Larsen et al. *J Headache Pain* 2019;20(8):1-211.
BMJ 2018;361:k1315

Multimodal Migraine Management: Other Preventatives

- Botulinum toxin PREEMPT protocol (chronic migraine only)
- CGRP mAbs (erenumab/galcanezumab/fremanezumab)
- Cefaly device (other neuromodulatory options not available in Canada at this time)
- Nerve blocks: Can be used as an acute treatment for status migrainosus, weekly for 4-6 weeks to break a headache cycle, or every 4+ weeks as preventative

Larsen et al. *J Headache Pain* 2019;20(8):1-211. Charles JA. *Journal of Concussion* Jan 2019. Yerry et al. *Headache* 2015;55(3):395-406. Ashina et al. *J Headache Pain* 2020;21(1):62. Zirovich et al. *Military Medicine* 2020;usaa391.

Tension-Type Pharmacological Treatment

- Acute
  - Non-steroidal anti-inflammatories (NSAIDs)
  - Acetaminophen
- Preventative
  - Tricyclic antidepressants
  - Venlafaxine
  - Gabapentin
  - ?Tizanadine

Preventatives in PTH: Stop? Add? Continue?

- Reasonable oral preventative trial = 2-3 months at therapeutic dose
- Onabotulinum toxin = 3 cycles (9 months)
- CGRP monoclonal antibodies = 6 months

Preventatives in PTH: Stop? Add? Continue?

- No benefit after reasonable trial, or intolerable side effects → STOP
- Some benefit, incomplete response at highest dose or unable to tolerate higher dose → ADD a second agent
- Good benefit and medication tolerable → CONTINUE
  - Consider attempt to wean once well x 3-12 months
  - Stay at lowest effective dose if unable to wean

Take-Home Points

- Headache is common and disabling in patients with concussion
- Most PTH displays a migraine-like or tension-like phenotype
- Treat early and avoid factors that may prolong headache such as medication overuse
- Treat the headache phenotype

Questions?

Additional References

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