

Appendix 6.7

Prophylactic Therapy

Note that all therapies utilized for the prophylaxis of post-traumatic headaches are off-label. Prophylactic therapies should be utilized using a “start-low and go slow” approach. Patients should be advised that prophylactic therapies are not a cure and they may not perceive any benefit for weeks and maximal benefit may take up to 12 weeks to be realized.

A therapeutic trial of a prophylactic therapy should last 12 weeks unless there are intolerable medication side-effects. The only useful way to evaluate the effectiveness of a prophylactic therapy is review of the patient’s headache and medication calendar. If the prophylactic therapy is efficacious, it should be continued for a minimum of 3-6+ months and then consideration could be given to gradually weaning off, if possible.

It should be made clear to the patient that the goal of prophylactic therapy is to try to decrease the individual’s headache frequency and/or headache intensity and/or headache duration and/or acute medication requirements. Patients should also be advised that there are no “designer” drugs for headache prophylaxis – all medications utilized were created for other reasons and were subsequently found to be effective in headache prophylaxis in some, but not all, patients.

If the headaches are tension-type in nature or unclassifiable, first-line therapy is Amitriptyline or Nortriptyline (starting at 10 mg po qhs and increasing by 10 mg q1-2 weeks as necessary/tolerated to a maximum of 50- (and occasionally up to 100 mg po qhs). Amitriptyline is more sedating than Nortriptyline so should be utilized if there are concomitant sleep disturbances. Second-line therapy to consider is Gabapentin (starting at 100-300 mg po qhs and increasing by 100-300 mg q5 days as necessary/tolerated on a TID schedule to a maximum of approximately 600 mg po TID).

From the Canadian Headache Society Guideline for Migraine Prophylaxis**

General Principles of Migraine Prophylaxis

When should Migraine Prophylaxis Be Considered? (Expert Consensus)

- i. Migraine Prophylactic therapy should be considered in patients whose migraine attacks have a significant impact on their lives despite appropriate use of acute medications and trigger management/ lifestyle modification strategies.
- ii. Migraine prophylactic therapy should be considered when the frequency of migraine attacks is such that reliance on acute medications alone puts patients at risk for medication overuse (rebound) headache. Medication overuse is defined as use of opioids, combination analgesics, or triptans on ten days a month or more, or use of simple analgesics (acetaminophen, acetylsalicylic acid [ASA], non-steroidal anti-inflammatory drugs [NSAIDs]) on 15 days a month or more.
- iii. Migraine prophylaxis should be considered for patients with greater than three moderate or severe headache days a month when acute medications are not reliably effective, and for patients with greater than eight headache days a month even when acute medications are optimally effective because of the risk of medication overuse headache.
- iv. Migraine prophylaxis may be considered in some patients with relatively infrequent attacks according to patient preference and physician judgement, for example in patients with hemiplegic migraine.
- v. Migraine prophylaxis may be particularly useful for patients with medical contraindications to acute migraine therapies.

When should Migraine Prophylactic Therapy Be Stopped? (Expert Consensus)

- i. A prophylactic medication trial should consist of at least two months at the target or optimal dose (or at the maximum tolerated dose if the usual target dose is not tolerated) before a prophylactic drug is considered ineffective.
- ii. A prophylactic medication is usually considered effective if migraine attack frequency or the number of days with headache per month is reduced by 50% or more, although lesser reductions in migraine frequency may be worthwhile, particularly if the drug is well tolerated.
- iii. In addition to reduction in migraine attack frequency or in the number of days with headache per month, reductions in headache intensity and migraine-related disability need to be considered when judging the effectiveness of prophylactic therapy.
- iv. Patients on migraine prophylaxis require periodic reevaluation both to monitor potential side effects and to assess efficacy.
- v. Because of its utility in assessing the effectiveness of prophylactic therapy, patients should be strongly encouraged to keep a headache diary/calendar.
- vi. After 6 to 12 months of successful prophylactic therapy, consideration should be given to tapering and discontinuing the prophylactic medication in many patients, although others may benefit from a much longer duration of prophylactic therapy. If headache frequency increases as the prophylactic drug dosage is reduced, the dosage can be increased again or the drug restarted if it has been discontinued.**

If the headaches are migrainous in nature:

- a) First-line therapy would be a Tricyclic Antidepressant (i.e. Amitriptyline or Nortriptyline starting at 10 mg po qhs and increasing by 10 mg q1-2 weeks as necessary/tolerated to a maximum of 50-100 mg po qhs) or a beta-blocker (i.e. Nadolol starting at 20 mg po BID and increasing by 20 mg q5days as necessary/tolerated to 40-80 mg po BID or Propranolol 20 mg po TID and increasing by 20 mg q5days as necessary/tolerated to a maximum of 80 mg po TID).
- b) Second-line therapy includes Topiramate (starting at 12.5 mg po qhs and increasing by 12.5 mg po qhs qweekly as necessary/tolerated to a maximum of 100 mg po qhs) or, failing this, Gabapentin (starting at 100-300 mg po qhs and increasing by 100-300 mg q5 days as necessary/tolerated on a TID schedule to a maximum of approximately 600 mg po TID).
- c) Third-line therapies would include Verapamil (starting at 40 mg po TID and titrating to 80 mg po TID as necessary/ tolerated), Pizotifen (starting at 0.5 mg po qhs and increasing by 0.5 mg qweekly as necessary/tolerated to 3.0 mg po qhs) and Flunarizine (starting at 5 mg po qhs and increasing to 10 mg po qhs after 10-14 days).
- d) Notably, should trials of a couple oral prophylactic agents prove ineffective, or should oral prophylactic medications be contraindicated by concomitant medical issues or by significant polypharmacy, consideration could certainly be given to interventional therapy. Botulinum Toxin Type A (onabotulinum toxin) up to 200 units q3months using a fixed- dose, follow-the-pain treatment paradigm has proven beneficial in recent phase 3 RCT trials for the prophylaxis of chronic migraine and is an approved treatment for chronic migraine.
- e) Nerve blocks (i.e. occipital nerve blocks) should be restricted to intractable daily post-traumatic headache and should be discontinued if the repetitive nerve blocks are ineffective after weekly treatment for 4-6 weeks.

The choice of prophylactic therapy depends on comorbid symptoms (i.e., consider Amitriptyline if concomitant insomnia, a Beta-blocker if concomitant hypertension, Topiramate if concomitant obesity) and contraindications (avoid Beta-blocker/ Calcium-channel blocker if hypotensive, Tricyclic if excessive fatigue, Topiramate if excessive cognitive symptoms, Flunarizine if depression etc).

**Pringsheim T, Davenport W, Mackie G, Worthington I, Aube M, Christie SN, Gladstone J, Becker WJ, Canadian Headache Society Prophylactic Guidelines Development Group. Canadian Headache Society guideline for migraine prophylaxis. Can J Neurol Sci. 2012 Mar;39(2 Suppl 2):S1-59