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Migraine Summary

Principles of initiating therapy:

For patients with > 2 migraine attacks per week - Consider initiating therapy with one of the following agents. 50 to 75% of patients will notice a 50% reduction in the frequency of Migraines

Expectations of therapy – initial results noted at 4 weeks but improvement can be realized up to 3 months.

Initiate at low dose and increase to target or until side effects are noted.

Medication overuse headaches (MOH) may occur with triptans, analgesics and ergots

- *MOH*: headache occurring on ≥ 15 days/month in those with pre-existing primary headache and developing as a result of regular overuse of headache medication for more than 3 months
  - Ergotamine-overuse: regular intake on ≥ 10 days/month for > 3 months
  - Triptan-overuse: regular intake on ≥ 10 days/month for > 3 months
  - Opioid-overuse: regular intake on ≥ 10 days/month for > 3 months
  - Non-opioid analgesic-overuse: regular intake of 1 on ≥ 15 days/month for > 3 months
- *Treatment of MOH*: discontinue offending agent
  - Symptoms will worsen before they improve

Migraine prophylaxis treatment options

Medication	Dose	ADR	Efficacy
Amitriptyline	10 mg qhs (to target of 20 to 50 mg qhs)	Sedation dry mouth constipation tachycardia palpitations orthostatic hypotension weight gain blurred vision urinary retention	≥ 50% reduction in headache frequency vs. placebo (1) → @8 weeks: **NNT 5** → @ 16 weeks: **NNT 3** → @ 20 weeks: NSS
Bottom Line: Shorter trials that were done in the 1980's showed promising results. 2010 trial documented above (~ 400 patients) showed similar benefit although efficacy lost with time.			
Beta blockers (metoprolol, propranolol, etc)	Metoprolol 25 mg BID (to target of 50 to 200mg/day) Propranolol 20 mg BID (to target of 40 to 160 mg/day) Nadolol 20 mg daily (to target of 20 to 240 mg/day) Atenolol 25 mg daily (25 to 100 mg/d)	Drowsiness Reduced exercise tolerance Bradycardia Hypotension Impotence Sleep disturbance Bronchospasm Depression	≥ 50% decrease from baseline in migraine days/month (2) → Propranolol 160mg vs. placebo @12 weeks **NNT 6** *No clear difference among beta blockers in terms of efficacy
Bottom Line: Trial with 72 patients showed statistically significant benefit with propranolol at 12 weeks. *Beta-blockers remain a first line choice considering efficacy and tolerability.*			

Verapamil	120 mg/day (40 mg TID if short acting) to target of 120-240 mg/day	Constipation Dizziness Hypotension Peripheral Edema	*Treatment of choice in pregnancy
Bottom Line: Limited efficacy data. Small trials in the 1980's including 10-20 people demonstrated potential benefit.			
Candesartan	4 mg daily (to target of 16 mg daily)	Hypotension Dizziness Hyperkalemia	≥ 50% reduction in headache frequency (2) → Candesartan 16 mg vs. placebo @ 12 weeks **NNT 6**
Bottom Line: Efficacy similar to beta-blockers and potentially better tolerated. Limited by few trials completed.			
Venlafaxine XR	37.5 mg daily (to target of 75 to 150 mg daily)	Nausea/vomiting Sexual dysfunction Drowsiness Dizziness Blurred vision Insomnia Nervousness	**Efficacy similar to amitriptyline and potentially better tolerated** (3)
Bottom Line: No placebo controlled trials including 50% responder rate outcomes. Small 12 week trial (n=52) comparing venlafaxine to amitriptyline showed no statistically significant difference between the two agents.			
Pizotifen	1.5 mg daily (to target of 1.5 mg to 3 mg daily)	Weight gain Sedation	**Insufficient evidence to make strong recommendation for use**
Bottom Line: No placebo controlled trials including 50% responder rate. Insufficient evidence.			
Flunarazine	5-10 mg at bedtime (to target 10mg at bedtime)	Weight gain Depression Drowsiness EPS	≥ 50% reduction in headache frequency (4) → Flunarazine 10mg vs. topiramate 50mg @ 8 weeks **NNT 3** *Comparator under dosed ≥ 50% reduction in headache frequency → Flunarazine 5/10mg vs. propranolol 160mg NSS (5) *Treatment option for pregnant women

Bottom Line: 16 week trial (n=808) comparing flunarazine to propranolol showed similar efficacy. No placebo controlled trial available to show responder rate.			
Valproate/Divalproex	500 mg to 1500 mg/day	Nausea, somnolence, tremor, dizziness, weight gain, and hair loss	≥ 50% reduction in headache frequency (6) → Divalproex vs. placebo @12 weeks **NNT 5** *Do not use in pregnancy
Bottom Line: 12 week trial (n=176) demonstrated consistent benefit with all three doses of divalproex (500mg vs. 1000mg vs. 1500mg), while adverse events increased with dose escalation. *Considered as a first line option.*			
Topiramate	25 mg daily (target 100 to 200 mg/day)	Paresthesia, fatigue, anorexia, diarrhea, weight loss, hypesthesia, memory difficulty, language problems, difficulty with concentration, nausea, and taste perversion	≥ 50% reduction in migraine days @26 weeks (7) → 50mg/d**: NNT 8** → 100mg/d: **NNT 4** → 200mg/d: **NNT 4**
Bottom Line: 26 week trial (n=469) showed significant improvement in migraine frequency with 100mg/day being the optimal dose considering longer term efficacy and side effects. *Considered as a first line option*			
Simvastatin + vitamin D	Simvastatin 20 mg twice daily + Vitamin D 1000 units twice daily	Myalgia Abdominal pain Increased transaminases	≥ 50% reduction in migraine days (8) → simva+vitD vs. placebo @24 weeks **NNT 4**
Bottom Line: Small 24 weeks trial (n=57) demonstrated significant benefit. Investigational data, further research needed to confirm results.			
Erenumab (Aimovig)	70 mg sc monthly (may increase to 140 mg)	URTI/nasopharyngitis Injection site reaction Nausea Hypertension, severe constipation, hypersensitivity reactions	≥ 50% reduction in migraine days (9) Erenumab vs placebo @24 weeks **NNT 6** Average reduction of 1-2 migraines per month
Bottom Line: NNT 6 to reduce 50% migraine days (equals 1 to 2 migraines per month). Cost per year $7000, post marketing concerns with hypertension, hypersensitivity reactions, severe constipation			
Natural health products to be considered:			
Butterbur	75 mg BID (150 mg/day)	**Hepatotoxicity** Nausea Flatulence Belching	150 mg/day effective but 100 mg/day not effective Limited data
Coenzyme Q10	100 mg TID	Stomach upset Tiredness Change in urine color	Some limited data *Caution use with warfarin

Feverfew (Tanacetum partheniumdan)		Nausea/vomiting Oral ulcers Contact dermatitis Palpitations	Some limited data
		Inflammation of mouth gums and tongue	
Magnesium Citrate	600 mg daily	Diarrhea	Some limited data
Riboflavin	400mg daily	Well tolerated	Some limited data
Melatonin	3mg qhs	Well tolerated	2 mg not effective

Therapies with little to no evidence to support use: Gabapentin, botulism toxin

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