Candidates for prophylactic treatment

- Prophylactic migraine therapy may be considered in the following patients:\(^1\)
  - Four or more days with migraine headaches per month
  - Fewer than four migraine headaches per month but with severe pain refractory to all migraine-specific acute therapies
  - Complicated migraines (e.g., migraine associated with focal neurologic signs such as nystagmus or hemiplegia)

Goals of prophylactic therapy

- It is important for patients to have a realistic expectation of treatment. Goals of preventative therapy are to:\(^2\)
  - Decrease migraine attack frequency by 50% or more
  - Decrease pain and disability with each individual attack
  - Enhance response to acute, specific, anti-migraine therapy.

Summary of medication treatment options

- Two recent meta-analyses suggest that propranolol, topiramate & valproate have the best evidence for the treatment of migraine prophylaxis when considering efficacy, safety and tolerability.\(^3,4\)

Table 1: Evidence summary for medications with best evidence of efficacy\(^4-7\)

<table>
<thead>
<tr>
<th>Medication</th>
<th>Initial dose</th>
<th>Study Outcomes</th>
<th>P-value</th>
<th>Difference in (50%) response*†</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propranolol</td>
<td>40 mg BID</td>
<td>Difference in mean headache frequency*</td>
<td>1 to 1.3</td>
<td>NR</td>
<td>23%</td>
</tr>
<tr>
<td>Topiramate</td>
<td>25 mg QPM</td>
<td>1.2</td>
<td>&lt;0.001</td>
<td>24%</td>
<td>4</td>
</tr>
<tr>
<td>Divalproex DR</td>
<td>125 mg BID</td>
<td>NR</td>
<td>NA</td>
<td>21%</td>
<td>4</td>
</tr>
</tbody>
</table>

* difference between treatment & placebo from baseline to study endpoint; †response = 50% reduction in headache frequency; NR = not reported; NNT = number needed to treat

- Other medication treatments with positive evidence for efficacy include: metoprolol and fluoxetine\(^4\)
- Complementary and alternative therapies are often also used as adjunctive treatments in patients with migraine. While the evidence for these options is less robust, the safety profile is favorable to medications. The best evidence for efficacy includes (in alphabetical order):\(^8-11\)
  - Coenzyme Q10 100 mg TID
  - Magnesium 300 mg (elemental) daily
  - Riboflavin 400 mg daily

Patient Counseling Points\(^1,2\)

- Reduction in migraines may take 2-4 weeks. Three months is considered an adequate trial.
- Reinforce avoidance of triggers and lifestyle management (stress reduction, regular eating & sleeping schedules, regular exercise)
**Medication: Placebo-controlled Trials**

**Propranolol**
- In one meta-analysis, the difference between propranolol and placebo in mean monthly headache frequency from baseline to study endpoint ranged from -1 to -1.3, depending upon the duration of the study.\(^4\)
- In another meta-analysis, a higher 50% reduction in migraine frequency was observed with propranolol compared to placebo (45.1% vs 22.3%) with a NNT of four.\(^5\)
- The difference in the rate of treatment discontinuation due to adverse effects was 7.6% for propranolol compared to placebo.\(^5\)

**Topiramate**
- A Cochrane review and meta-analysis evaluating the evidence for topiramate found that:\(^6\)
  - The difference between topiramate & placebo in mean headache frequency from baseline to study endpoint was -1.2 per month, \(p < 0.001\).
  - Patients with a 50% reduction in migraine frequency: 47% topiramate vs 23% placebo, \(p < 0.001\), NNT = 4.
  - The NNH for 100 mg/day treatment groups were as follows: 11 for any adverse event, 17 for anorexia, 25 for fatigue, 25 for memory problems, 3 for paresthesia, 14 for taste disturbance and 17 for weight loss.

**Valproate**
- A Cochrane review and meta-analysis evaluating the evidence for valproate found that:\(^7\)
  - **Divalproex sodium**
    - None of the trials reported sufficient data to calculate mean differences for headache frequency.
    - Patients with a 50% reduction in migraine frequency: 42% divalproex vs 21% placebo, \(p < \), NNT=4.
  - **Sodium valproate**
    - In two cross over trials, the difference between sodium valproate & placebo in mean headache frequency from baseline to study endpoint was -4.3 per month, \(p < \).
    - Patients with a 50% reduction in migraine frequency: 50% sodium valproate vs 18% placebo, \(p , NNT=3\).
  - The NNH were as follows: 14 for dizziness/vertigo, 7 for nausea and 14 for tremor.

**Complementary & alternative therapies**

**Coenzyme Q10**
- **RCT\(^8,9\)** comparing coenzyme Q10 100 mg TID or placebo for 3 months, \(n = 43\)
  - 1.19 fewer attacks per month in Q10 group vs 0.09 in placebo group
  - Patients with 50% reduction in migraine frequency: 48% Q10 vs 14% placebo

**Magnesium**
- **RCT\(^8\)** comparing 600 mg elemental magnesium daily or placebo for 3 months, \(n = 81\)
  - 1.5 fewer attacks in last month of treatment in magnesium group vs 0.58 in placebo group
  - Patients with 50% reduction in migraine frequency: 53% magnesium vs 34% placebo

**Riboflavin**
- **RCT\(^8,10\)** comparing riboflavin 400 mg daily to placebo for 12 weeks, \(n = 55\)
  - Two fewer attacks per month in riboflavin group vs no change in placebo group (\(p=0.0001\))
  - Patients with 50% reduction in migraine frequency: 56% riboflavin vs 19% in placebo

**References**


