Review: anticonvulsants are better than placebo for reducing the frequency of migraine attacks


Clinical impact ratings GP/FP/Primary care ★★★★★☆☆ IM/Ambulatory care ★★★★★☆★ Neurology ★★★★★☆☆

Q In patients with migraine, are anticonvulsants more effective than placebo for preventing or reducing the intensity of migraine attacks?

METHODS

Data sources: Medline (up to April 2003); the Cochrane Central Register of Controlled Trials (up to April 2003); review articles; books on headache; contact with drug companies, authors, and experts; and hand searches of Headache and Cephalalgia.

Study selection and assessment: randomised controlled trials (RCTs) that compared anticonvulsants given regularly during headache free intervals in adults >18 years of age with placebo, no intervention, other drug treatments, or behavioural or physical therapies. Methodological quality was assessed using the Jadad 5 point scale.

Outcomes: headache frequency (number of migraine attacks measured at 28 d), headache index measures (frequency and intensity or duration), and adverse events.

MAIN RESULTS

15 RCTs met the selection criteria. Anticonvulsants investigated were divalproex sodium (500–1500 mg daily [4 RCTs]), topiramate (50–200 mg daily [3 RCTs]), sodium valproate (800–1500 mg daily [2 RCTs]), gabapentin (1200–2400 mg daily [2 RCTs]), carbamazepine (dose not reported [1 RCT]), clonazepam (1 mg daily [1 RCT]), and lamotrigine (200 mg daily [1 RCT]). Mean duration of the maintenance phase of trials was 9.6 weeks (range 4–18 wk). The median quality score of studies was 4 (range 1–5). Compared with placebo, anticonvulsants as a class reduced mean migraine frequency by 1.4 attacks per 28 days (8 RCTs, weighted mean difference [WMD] −1.43, 95% CI −2.2 to −0.65) and increased the number of patients in whom migraine frequency is reduced by ≥50% (10 RCTs) (table). For individual anticonvulsants compared with placebo, migraine frequency was reduced by sodium valproate (2 RCTs, WMD −4.31, CI −8.32 to −0.30), topiramate (3 RCTs, WMD −1.27, CI −1.74 to −0.79), and gabapentin (1 RCT, WMD −1.89, CI −2.35 to −1.43). The results of individual anticonvulsants for the number of patients in whom migraine frequency is reduced by ≥50% are in the table. Lamotrigine or clonazepam did not differ from placebo for reducing migraine frequency. The most common adverse events were nausea (number needed to harm [NNH] 6.6, CI 5.0 to 9.8), asthaenia or fatigue (NNH 12.3, CI 7.6 to 31.8), tremor (NNH 12.4, CI 8.9 to 20.1), weight gain (NNH 16.0, CI 8.5 to 154.4), and dizziness or vertigo (NNH 16.3, CI 9.5 to 57.9).

CONCLUSIONS

In patients with migraine, anticonvulsants as a class reduced the frequency of migraine attacks.

Abstract and commentary also appear in ACP Journal Club.

Anticonvulsants v placebo for number of patients who responded with ≥50% reduction in migraine frequency at mean 9.6 weeks *

<table>
<thead>
<tr>
<th>Number of trials (n)</th>
<th>Comparisons</th>
<th>Weighted event rates</th>
<th>RBI (95% CI) NNT (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 (1341)</td>
<td>Anticonvulsants as a class v placebo</td>
<td>49% v 20%</td>
<td>71% (63 to 80)</td>
</tr>
<tr>
<td>4 (579)</td>
<td>Divalproex sodium v placebo</td>
<td>47% v 21%</td>
<td>74% (57 to 91)</td>
</tr>
<tr>
<td>1 (68)</td>
<td>Sodium valproate v placebo</td>
<td>29% v 18%</td>
<td>68% (47 to 89)</td>
</tr>
<tr>
<td>3 (498)</td>
<td>Topiramate v placebo</td>
<td>48% v 22%</td>
<td>74% (66 to 82)</td>
</tr>
</tbody>
</table>

*Abbreviations defined in glossary; weighted event rates, RBI, NNT, and CI calculated from data in article using a random effects model.
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