

Wiffen PJ, McQuay HJ, et al. Gabapentin for acute and chronic pain. Cochrane database of Systematic Reviews 2005, Issue 3, Art No CD005452.

Design: Meta-analysis of randomized trials

PICOS:

- Patients: Adults with a wide variety of neuropathic pain conditions, including diabetes, postherpetic neuralgia (PHN), phantom limb pain, Guillain Barre, and spinal cord injury
- Interventions: Gabapentin by any route at any dose for analgesia
- Comparison: Placebo or active alternative treatment
- Outcomes: Pain intensity or pain relief, with a hierarchy of (1) 50% relief, (2) patient global impression of change (PGIC), (3) pain on movement, (4) pain at rest, (5) any other pain related measure
- Study types: Randomized trials with full journal publication (not abstracts)

Study search and selection:

- MEDLINE, EMBASE, SIGLE (a grey literature database), and the Cochrane Library through November 2004
- 38 reports of 39 studies were identified; 24 were excluded and 14 were included for further analysis
- Quality was rated on a 5 point scale for randomization, blinding, and attrition, but quality scores were not used to weight the studies which were included
- All studies were read by all authors, and agreement was reached by discussion
- Publication bias was not explored, as the authors judged that current methods are not reliable

Results:

- For acute pain, gabapentin was not superior to placebo
- For diabetic neuropathy, a daily dose of 900 mg was not better than placebo, but studies using 1200 mg or more reported that gabapentin was superior to placebo
- Gabapentin was compared to amitriptyline in 2 small studies which did not show a difference between treatments
- For PHN, two placebo-controlled studies with doses up to 3600 mg per day showed a relative benefit for moderate or better pain improvement of 2.5 in favor of gabapentin (patients on gabapentin 2.5 times more likely to improve than patients on placebo)
- For mixed neuropathic pain, gabapentin at a dose up to 2400 mg/day showed 50% pain relief in 21% of gabapentin and 14% of placebo groups; this was not statistically significant
- Studies of cancer pain, phantom limb pain, Guillain Barre syndrome, and spinal cord injury pain were small, and no conclusions were drawn from them
- Pooling of data from 7 studies (4 diabetes, 2 PHN, 1 mixed neuropathic pain) yielded a number needed to treat (NNT) of 4.3 for improvement, with a relative benefit of 2.2 for gabapentin over placebo

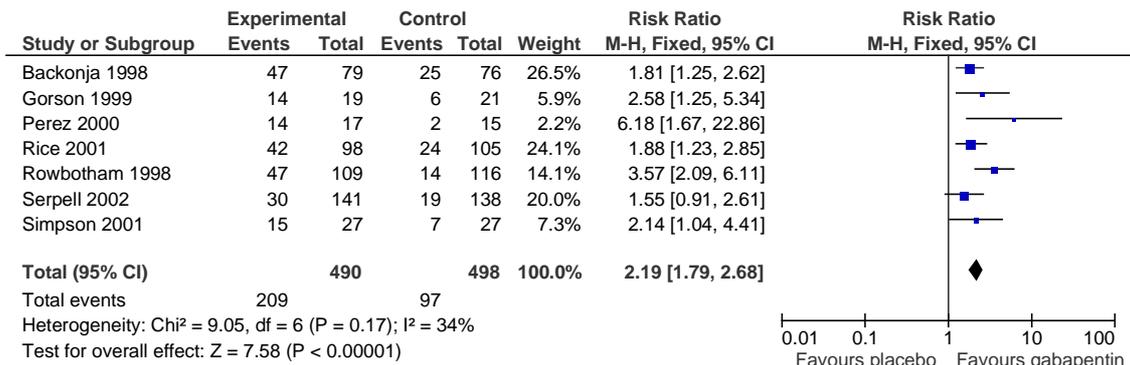
- Adverse effects were frequently reported, but the numbers were not always available; dizziness was the most common (24%) followed by somnolence (20%) and headache or diarrhea (10%)

Authors' conclusions:

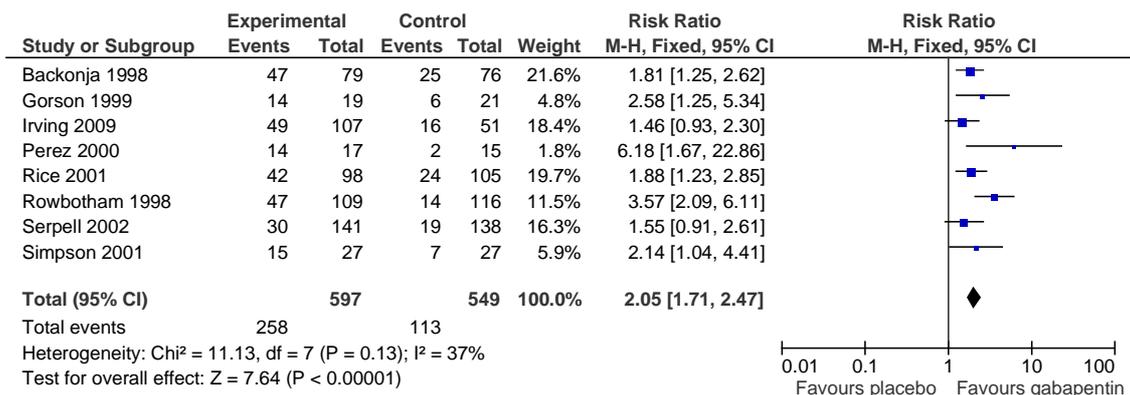
- Gabapentin is effective for neuropathic pain, with an NNT of about 4.3 for moderate or better improvement, compared to an NNT of 2 for amitriptyline (work in progress)
- Gabapentin is not effective for acute pain
- Some studies used enriched enrollment (excluding patients who had not previously responded to gabapentin); excluding them did not appreciably alter the estimated effect of gabapentin
- Gabapentin may not be better than some less expensive alternatives such as amitriptyline; the latter should be considered as an effective and more affordable alternative

Comments:

- NNT from meta-analyses should be interpreted with caution, since their reliability depends on having a fixed response rate in the placebo group; the studies pooled for this meta-analysis had considerable variation from 0.13 to 0.33 (overall placebo response rate was 19.5%)
- Only a minority ($209/409 = 43\%$) of gabapentin patients had moderate or better improvement in the 7 studies which were combined to give the NNT of 4.3; for most patients, gabapentin was not successful
- The authors state that the review will be updated in 2009 to account for more recent studies of gabapentin; as of October 2010, this had not been done
- Most recent trials of gabapentin are crossover trials, and the Cochrane Handbook recommends that crossover trial data for dichotomous outcomes should not be combined with parallel group trials without consulting a statistician
- One article, by Irving et al 2009, was a parallel group trial of extended release gabapentin for postherpetic neuralgia, and it can be combined with the 7 studies that were combined in the current meta-analysis
- The estimate of gabapentin's effect is not changed when data from Irving 2009 is added to the current analysis. The forest plot from the 7 studies included in the current meta-analysis are below:



The addition of Irving et al 2009 yields the following forest plot:



The pooled relative benefit changes from 2.19 to 2.05

Assessment: High quality meta-analysis produces strong evidence that gabapentin is more effective than placebo for neuropathic pain, even though it provides complete pain relief to a minority of patients.