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Gabapentin and postoperative pain: a systematic review of randomized controlled trials

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CRD summary

This review evaluated the efficacy and tolerability of peri-operative gabapentin administration to control acute post-operative pain. Peri-operative gabapentin administration was found to be effective in reducing pain scores, opioid requirements and opioid-related adverse effects in the first 24 hours after surgery. Given the significant differences between the studies and the possibility of bias, the authors' conclusions should be interpreted with caution.

Authors' objectives

To evaluate the efficacy and tolerability of peri-operative gabapentin administration to control acute post-operative pain.

Searching

MEDLINE (1966 to 2006), the Cochrane CENTRAL Register (2006), Scopus and CINAHL were searched; the search terms were reported and no language restrictions were applied. The last search was performed in 2006. In addition, the bibliographies of reviews and reports were checked.

Study selection

Randomised placebo-controlled trials (RCTs) investigating peri-operative gabapentin for post-operative pain management were eligible for inclusion. Eligible outcomes were relevant pain outcomes such as pain scores, time to first analgesic request and post-operative cumulative opioid consumption. The participants in the included studies were patients undergoing various types of surgery and the dose of gabapentin was between 300 and 1,200 mg, administered as a single pre-operative dose in the majority of studies. Studies that incorporated a local anaesthetic technique or nerve block as part of the anaesthetic regimen were excluded. Pain scores were measured using the visual analogue scale and pain verbal rating scale in the included studies. Total analgesic requirement, time to first analgesia and adverse effects were also reported.

One reviewer selected relevant studies for inclusion.

Assessment of study quality

Randomisation, concealment of allocation, double-blinding and flow of patients was assessed using the modified Oxford Scale.

Two reviewers independently assessed the validity of the included studies. Any disagreements were resolved by discussion or consultation with a third reviewer.

Data extraction

Outcome data for analgesia outcomes and adverse effects were extracted. Pain intensity, 24-hour cumulative opioid consumption and time to first request for rescue analgesic were expressed as weighted mean differences (WMDs) with 95% confidence intervals (CIs). Adverse effects were expressed as Peto odds ratios (ORs) with 95% CIs, or relative risks (RRs) with 95% CIs. Authors were contacted for additional information where necessary. Pain scores were documented at different time intervals in the included studies, therefore, to facilitate pooling, pain scores were analysed within 6 hours of the end of surgery and 24 hours from the end of surgery. All post-operative opioid consumption was converted to morphine equivalents. When outcome data were unavailable, authors were contacted; when no response was received, data were extracted from graphs, where available.

A data abstraction form was created for the review. The authors did not state how many reviewers performed the data extraction.

Methods of synthesis

The studies were combined in meta-analysis. WMDs, Peto ORs or RRs were combined using either a fixed-effect or random-effects model for the following subgroups: patients that received a single dose of gabapentin 1,200 mg pre-operatively; patients that received a single dose of gabapentin less than 1,200 mg pre-operatively (the dose range was 300 to 900mg); and patients that received multiple doses of gabapentin peri-operatively. The number-needed-to-treat (NNT) and number-needed-to-harm (NNH) were also calculated for adverse effects when statistically significant differences between treatment groups were found. Differences between studies were investigated using a χ^2 test for statistical heterogeneity and I^2 test.

Results of the review

Sixteen RCTs (n=1,151) were included in the review.

Gabapentin 1,200 mg single dose pre-operatively.

Gabapentin was associated with a statistically significant decrease in pain intensity at rest compared with placebo at 6 hours (6 RCTs; WMD -16.55 mm, 95% CI: -25.66, -7.44, p=0.0004) and 24 hours (3 RCTs; WMD -10.87 mm, 95% CI: -20.90, -0.84, p=0.03). The χ^2 test suggested statistically significant heterogeneity between studies (p<0.00001).

Gabapentin was also associated with a statistically significant decrease in cumulative opioid consumption compared with placebo, (3 RCTs; WMD -27.9 mg, 95%: -31.52, -24.29, p<0.00001) and a statistically significant delay in the time to first request for analgesia (2 RCTs; WMD 7.42 minutes, 95% CI: 0.49, 14.34, p=0.04). Statistically significant heterogeneity was not indicated. Gabapentin was associated with a lower risk of vomiting (6 RCTs; Peto OR 0.42, 95% CI: 0.24, 0.76; NNT 8) and less risk of urinary retention (figures not reported; NNT 7). There was no statistically significant difference in any other adverse effects between gabapentin and placebo.

Gabapentin <1,200 mg single dose pre-operatively.

Gabapentin was associated with a statistically significant decrease in pain intensity at rest compared with placebo at 6 hours (5 RCTs; WMD -22.43 mm, 95% CI: -27.66, -17.19, p<0.00001) and 24 hours (4 RCTs; WMD -13.18, 95% CI: -19.68, -6.68, p<0.0001). There was evidence of statistically significant heterogeneity at 24 hours (p<0.00001) and 6 hours (p=0.009), (I^2=64.8%). Post-operative opioid consumption reduction was significantly reduced with gabapentin compared with placebo (4 RCTs; WMD -15.98, 95% CI: -23.45, -8.50, p<0.0001). There was evidence of statistically significant heterogeneity (p<0.00001). Sedation risk was statistically significantly higher in the gabapentin group compared with placebo (2 RCTs; Peto OR 6.95, 95% CI: 3.96, 12.20; NNH 4). There was no statistically significant difference in other adverse effects between placebo and gabapentin.

Gabapentin given as multiple doses peri-operatively.

There was no statistically significant difference between placebo and gabapentin in pain intensity (2 RCTs) or time to first request for analgesia (1 RCT). One RCT showed a 24% reduction in 24-hour cumulative opioid consumption in the gabapentin group compared with placebo.

There was a statistically significant lower incidence of nausea (5 RCTs; Peto OR 0.54, 95% CI: 0.31, 0.95; NNT 9) and pruritus (3 RCTs; Peto OR 0.21, 95% CI: 0.05, 0.87; NNT 13) in the gabapentin group compared with placebo. The difference between these two groups was not statistically significantly different for any other adverse effects, except constipation (OR 0.12, 95% CI: 0.02, 0.9).

Further analyses were reported in the paper.

Authors' conclusions

Peri-operative gabapentin administration is effective in reducing pain scores, opioid requirements and opioid-related adverse effects in the first 24 hours after surgery. No serious side-effects were observed, though sedation was associated with gabapentin use.

CRD commentary

The review question was clearly stated and the inclusion criteria were clear in terms of the intervention, outcomes and study design. No inclusion criteria were stated for the participants, which might have led to subjective decisions regarding inclusion. Four relevant electronic databases were searched without any language restrictions. However, there was no attempt to identify unpublished studies, which might have increased the possibility that some relevant studies were not included in the review. It was reported that one reviewer selected the studies but not how the data were extracted; this might have increased the possibility of error and bias. The validity of the primary studies was assessed. Heterogeneity of the studies was investigated, however, for some outcomes the studies were pooled despite statistically significant heterogeneity. The studies also appear to be clinically heterogeneous, as there was a wide variety of type of surgery, gabapentin regimen and type of post-operative rescue analgesic. Given that there were a number of possible sources of bias and the possibility of inappropriate pooling of studies, the authors' conclusions should be interpreted with caution.

Implications of the review for practice and research

Practice: The authors did not state any implications for practice.

Research: The authors stated that future clinical trials should examine the analgesic efficacy of gabapentin in major or painful surgery, to better evaluate the opioid-sparing effect of gabapentin. Trials should also include long-term follow-up to investigate the influence of peri-operative gabapentin on preventing chronic pain syndromes. Also, trials should be adequately powered to detect differences in pain outcomes and adverse effects. There should also be a focus on the possible impact of sedation on recovery profile. The optimal regimen for the peri-operative administration of gabapentin needs to be investigated through adequately powered dose-response studies, and possible pharmacokinetic and pharmacodynamic interactions with other drugs also require exploration.

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Bibliographic details

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Record Status

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CRD has determined that this article meets the DARE scientific quality criteria for a systematic review.

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