

Gabapentin prophylaxis for postoperative nausea and vomiting in abdominal surgeries: a quantitative analysis of evidence from randomized controlled clinical trials

S. Achuthan¹, I. Singh^{1*}, S. B. Varthya¹, A. Srinivasan¹, A. Chakrabarti¹ and D. Hota²

¹ Department of Pharmacology, Department of Pharmacology, Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh 160012, India

² Department of Pharmacology, AIIMS, Bhubaneswar, India

* Corresponding author. E-mail: inderhazari@gmail.com

Editor's key points

- The authors examined the evidence base for the effectiveness of gabapentin in preventing postoperative nausea and vomiting (PONV).
- They found support for the use of preoperative gabapentin in PONV prophylaxis, especially in abdominal surgery.
- Interestingly, the benefits of gabapentin appeared reduced in the presence of the use of propofol.

Introduction. Postoperative nausea and vomiting (PONV) is frequently encountered in the surgical recovery room. Abdominal surgery is one important risk factor for increased incidence of PONV. Gabapentin, an anticonvulsant with known postoperative analgesic properties, has shown some activity against PONV. Results from clinical trials evaluating the anti-emetic efficacy of gabapentin are conflicting. The present meta-analysis was performed to examine this issue.

Methods. Seventeen randomized placebo-controlled trials reporting PONV with preoperative gabapentin administration in patients undergoing abdominal surgery were included for analysis. Outcomes evaluated were nausea, vomiting, composite PONV and the use of rescue anti-emetic medication in the postoperative period.

Results. The pooled relative risk (RR), estimated using the random effects model of the metafor package for R, was 0.76 (95% CI 0.58–0.98) for nausea, 0.62 (0.45–0.85) for vomiting, 0.71 (0.39–1.28) for data represented as composite PONV (possibly biased by a single study, as observed in the sensitivity analysis), and 0.6 (0.41–0.89) for rescue anti-emetic use. There was a significant RR reduction for nausea and vomiting when propofol was not used as induction and/or maintenance for anaesthesia. In the abdominal hysterectomy subgroup, there was a significant RR reduction for vomiting but not for nausea.

Discussion. The present analysis provides evidence supporting preoperative gabapentin as a pharmacotherapy for prevention of PONV in patients undergoing abdominal surgeries. Future studies comparing preoperative gabapentin with 5HT₃ antagonists are needed to precisely define its role in PONV.

Keywords: gabapentin; hysterectomy; postoperative nausea and vomiting

Accepted for publication: 19 September 2014

Postoperative nausea and vomiting (PONV) in the surgical recovery room is a common occurrence. Despite being self-limiting, it is associated with substantial distress to patients in the early postoperative period. Its prevention and/or treatment significantly improves patient satisfaction and quality of life.^{1–3} PONV prevention can lead to a substantial reduction in health care costs by reducing the duration of the post-anaesthesia care unit (PACU) stay.^{4–5} It is estimated that each episode of emesis delays discharge from the PACU by approximately 20 min.⁶ Furthermore, serious complications, including retinal detachment, aspiration, wound dehiscence, oesophageal rupture, and subcutaneous emphysema, related to PONV can be prevented. The general incidence of PONV ranges from 25% to 30%,⁷ and in some subsets of high-risk patients it can be as high as 80%,⁸ even after preventive

pharmacotherapy. The pharmacotherapies used in the prevention/management of PONV include 5-HT₃, dopaminergic, histaminic, and NK1 antagonists. Nevertheless, the need for cheaper and more effective therapies cannot be disputed.

Gabapentin, an anticonvulsant, has been shown to be effective as a non-opioid ancillary agent for postoperative pain management.⁹ The safety profile, minimal drug interactions, pharmacokinetics (good oral bioavailability and renal elimination), and relatively flat dose–response relationship with respect to safety and efficacy favour its clinical use.^{10–11} Interestingly, in the recent past, gabapentin's anti-nausea effects were noted when there was a marked improvement in the chemotherapy-induced nausea in breast cancer patients¹² and subsequently was observed to possess activity against PONV. The exact mechanism for gabapentin's efficacy in

PONV is not known. While results of a few studies evaluating the efficacy of preoperative gabapentin as a prophylaxis were promising, the results of others did not reach statistical significance and have been equivocal. Hence the present analysis was performed to define the role of gabapentin as a preventive therapy for PONV.

Methods

Randomized placebo-controlled clinical trials comparing preoperative gabapentin administration were identified for evaluation for inclusion in the analyses. The criteria for inclusion were (i) patients undergoing abdominal surgery (open or laparoscopic) under general anaesthesia, (ii) preoperative administration of gabapentin irrespective of dose and timing of the dose with respect to surgery, and (iii) trials reporting nausea, vomiting, postoperative nausea and vomiting, or a proportion of patients requiring rescue anti-emetic medication irrespective of the objective of evaluation were included in the final analysis. Trials evaluating postoperative dosing alone or in addition to preoperative gabapentin were excluded from the final analysis. A literature search using the terms 'gabapentin', 'postoperative nausea and vomiting', 'abdominal surgery', and 'postoperative pain' was performed in Medline, Embase and the Cochrane library. Additional studies were identified through cross-references and meta-analyses conducted for evaluation of gabapentin in postoperative pain. All human studies published in full-text or abstract forms were initially screened for inclusion without applying any language restrictions. Titles and abstracts from the electronic search were reviewed. After initial review of the abstracts, the relevant studies were identified and a detailed evaluation of the full text was done. All data with regard to authorship, year of publication, study design, study population (i.e. type of abdominal surgery), baseline patient characteristics, gabapentin dose, type of surgery, type and duration of anaesthesia (when data were not available, the duration of surgery was taken as the duration of anaesthesia), number of patients, and relevant outcomes were extracted from the selected studies. The methodological quality of the included studies was assessed using the Downs and Black score.¹³ The whole process was undertaken independently by two authors and all the conflicts were resolved by discussion among all authors.

Outcomes

The outcomes evaluated were postoperative nausea, vomiting, composite of nausea and vomiting (PONV, as some studies had reported a composite outcome of nausea and vomiting), and the proportion of patients requiring rescue anti-emetic medication.

Statistical analyses

Statistical analyses were performed using the metafor package for R.¹⁴ For each individual study the relative risk (RR) was calculated using the reported events of relevant outcomes. Pooled RR for individual outcomes was estimated using the random effects model of the metafor package.

Heterogeneity was assessed based on the calculated I^2 (the proportion of total variability explained by heterogeneity), estimated using the restricted maximum likelihood-based method. A moderator analysis was performed using the mixed effects modelling approach (incorporating weighted least squares regression for the moderator in the random effects model) to assess the contribution of study level covariates to the overall heterogeneity and their impact on the effect size. Age, percentage of females in each study, postoperative opioid consumption, and duration of anaesthesia were the continuous variables, while surgery type and anaesthetic agent used, dose of gabapentin, and timing of the dose were the categorical variables used as covariates in the mixed effects model. The effect of postoperative opioid consumption was evaluated after computing the standardized mean difference between the placebo and gabapentin groups. To assess the publication bias we plotted the log relative risk vs the standard error of the individual studies. The symmetry of the plot was assessed using Egger's test. The trim and fill method was used to estimate the number of studies missing from the meta-analysis due to the suppression of the most extreme results on one side of the funnel plot. A Galbraith plot was also plotted to assess the same. A sensitivity analysis was conducted using leave-one-out analysis. Briefly, in this procedure individual studies were excluded from the model and the influence of the exclusion of that study on the model parameters was assessed.

Results

Seventeen studies were included in the final analysis. The literature search and study selection is represented in Fig. 1. The characteristics of the included studies are shown in Table 1. The included studies differed with respect to the type of surgery and the gabapentin dose evaluated. The selected studies contained a total of 1605 patients, with 810 in the gabapentin group and 795 in the placebo group. Eight studies were conducted in patients undergoing hysterectomy, three studies each for open and laparoscopic cholecystectomy patients, and one study each with donor nephrectomy, major bowel surgery, and laparoscopic-assisted reproductive surgery patients. Gabapentin was administered either 1 or 2 h prior to surgery in all the studies. In two studies an additional dose of gabapentin was administered the night before surgery. The data primarily collected from the studies were the study design; gabapentin dose; number of nausea, vomiting, and PONV events; number of rescue anti-emetic events; and also the induction and maintenance agents used for anaesthesia.

Outcomes

Postoperative nausea

Ten studies comprising a total of 632 patients (324 in the gabapentin group and 308 in the placebo group) were included for pooling the RR for postoperative nausea. The pooled RR was 0.76 (95% CI 0.58–0.98). I^2 was 5.8% and the test for heterogeneity was not significant ($P=0.36$) (Fig. 2).

Download English Version:

<https://daneshyari.com/en/article/8931987>

Download Persian Version:

<https://daneshyari.com/article/8931987>

[Daneshyari.com](https://daneshyari.com)