Gabapentin for postoperative pain relief

Gabapentin was developed 20 years ago to treat muscle spasms but has since been found to be useful in both the treatment of epilepsy and also increasingly in the management of chronic pain, especially neuropathic pain. There has been a recent flurry of articles describing the use of gabapentin for acute pain. This article discusses the case for and against its use as a postoperative analgesic.

Introduction

Gabapentin's name leads to some confusion. Gabapentin is a structural analogue of γ-aminobutyric acid (GABA), but does not have any direct action at GABA receptors and does not block GABA uptake or metabolism. Although its exact mechanism of action is still unknown, laboratory studies have suggested some plausible hypotheses. Gabapentin has been shown to modulate glutamate receptors. These receptors have a role in the process of central sensitization (wind-up), producing an increased response to painful stimuli, suggesting that gabapentin may reduce hyperalgesia following tissue trauma (Rose and Kam, 2002). Gabapentin also binds with high affinity to pre-synaptic voltage-gated calcium channels on neurons in pain pathways, inhibiting calcium influx and subsequent release of excitatory neurotransmitters, potentially directly reducing the transmission of pain signals.

Dosage and administration

Gabapentin is only available as oral preparations. It has a relatively short half-life, therefore a three times a day administration schedule is recommended. There is wide variation in the bioavailability and side-effect rates, and so when used in the chronic pain setting the dose is built up over a few weeks, titrated to effect. The recommended starting dose for neuropathic pain is 300 mg on day 1, 300 mg twice daily on day 2 and then 300 mg three times daily thereafter. This dose is often insufficient and doses up to a maximum of 3600 mg per day may be required.

This kind of dose titration is not possible when used perioperatively and there is currently no consensus on the best acute dosing regimen. Most studies have used a large single preoperative dose (1200–1800 mg), but some have also continued the administration for 48 hours postoperatively. Starting with a large dose may theoretically increase the incidence of side effects, but so far no serious side effects have been reported in acute pain studies.

The case for gabapentin for postoperative analgesia

The effectiveness of established postoperative analgesics (non-steroidal anti-inflammatory drugs and opiates) is well known, and so are their contraindications and side effects. Novel analgesics may augment the action of the existing analgesics, improve the quality of the analgesia and lower the total dose of drugs used, thereby minimizing side effects. Gabapentin, with its unique mode of action, offers the possibility of analgesic benefits and the initial trials in patients are encouraging.

A randomized, double-blind, placebo-controlled study of 70 women undergoing mastectomy receiving a single preoperative dose of 1200 mg of oral gabapentin demonstrated a significant and substantial reduction in postoperative total morphine consumption (median 29 mg *vs* 15 mg; $P<0.0001$) and movement-related pain at 2 hours postoperation (41 mm *vs* 22 mm on a 100 mm visual analogue scale; $P<0.0001$) (Dirks et al, 2002).

Turan et al (2006) used a randomized, double-blind, placebo-controlled design to study the effects of gabapentin (1200 mg/day before and 2 days after surgery) in 40 patients undergoing lower extremity procedures who were also receiving patient-controlled epidural analgesia (PCEA). Patients randomized to the gabapentin group had decreased postoperative pain scores (8 cm *vs* 4 cm at 1 hour postoperation, and 3 cm *vs* 2 cm at 24 hours on a 10 cm verbal rating scale (VRS); $P<0.001$), reduced PCEA requirements (14 *vs* 21 PCEA bolus doses delivered in the first 24 hours; $P<0.05$) and higher patient satisfaction (85.5 *vs* 63.5 on a 1–100 VRS scale).

The case against gabapentin for postoperative analgesia

Gabapentin is not without side effects. Up to 50% of patients starting gabapentin experience one or more of nausea, sedation, ataxia or dizziness. Dizziness was reported by 35% of patients taking gabapentin in the Turan et al (2006) study. Stevens–Johnson syndrome is a rare problem which has been linked to gabapentin, although not when used acutely.

Gabapentin has only been used in a few perioperative trials in varying dosage regimens. It is not yet clear what the optimum dose and duration of treatment are. As gabapentin is only available in an oral preparation, and its bioavailability varies widely, its perioperative use may be limited. We need large, high-quality evidence-based trials to be sure of gabapentin dose, division of dose, duration of treatment, its efficacy and safety before prescribing gabapentin for routine postoperative pain.

Conclusions

Gabapentin in the acute setting offers some interesting possibilities, particularly in patients where other analgesics are contraindicated, or for procedures with a high incidence of long-term neuropathic sequelae (e.g. inguinal hernia repair). Before gabapentin can be used for routine postoperative pain considerable work needs to be done, particularly on the optimal dosage schedule. A clear picture of its routine use and usefulness will emerge with time. **BJHM**

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Dirks J, Fredensborg BB, Christensen D, Fomsgaard JS, Flyger H, Dahl JB (2002) A randomized study of the effects of single-dose gabapentin vs placebo on postoperative pain and morphine consumption after mastectomy. *Anaesthesiology* **97:** 560–4

Rose MA, Kam PCA (2002) Gabapentin: pharmacology and its use in pain management. *Anaesthesia* **57:** 451–62

Turan A, Kaya G, Karamanlioglu B, Pamukcu Z, Apfel CC (2006) Effect of oral gabapentin on postoperative epidural analgesia. *Br J Anaesth* **96:** 242–6

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