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Is there a role for Gabapentin in preventing or treating pain following thoracic surgery?

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Abstract

A best evidence topic in cardiothoracic surgery was written according to a structured protocol. The question addressed was whether gabapentin, a commonly prescribed neuropathic analgesic and anticonvulsant, is safe and beneficial in patients with post-thoracotomy pain following thoracic surgery. Seventeen papers were identified using the search described below, and five papers presented the best evidence to reach conclusions regarding the issues of interest for this review. Side effects and complications as well as evidence of benefit, typically using various pain-scoring systems, were included in the assessment. The author, date and country of publication, patient group studied, study type, relevant outcomes, results and study weaknesses of the papers are tabulated. The systematic review of two randomized controlled trials (RCTs) demonstrated that the use of a single dose gabapentin does not reduce pain scores or the need for epidural or morphine immediately in hospital following thoracic surgery. One double-blinded RCT used multiple doses of gabapentin perioperatively and showed that oral gabapentin administered preoperatively and during the first 2 days postoperatively, in conjunction with patient controlled analgesia morphine, provides effective analgesia in thoracic surgery with a consequent improvement in postoperative pulmonary function and less morphine consumption. One prospective clinical study comparing a 2-month course of gabapentin with naproxen sodium for chronic post thoracotomy pain following surgery showed significant improvement in both the visual analogue scale (VAS) score and the Leeds assessment of neuropathic symptoms and signs (LANSS) at 60 days in the gabapentin ($P = 0.001$). One prospective study of out-patients with chronic pain (>4 weeks since thoracotomy performed) suggested that gabapentin is effective, safe and well tolerated when used for persistent postoperative and post-traumatic pain in thoracic surgery patients. We conclude that there is no evidence to support the role of a single preoperative oral dose of gabapentin in reducing pain scores or opioid consumption following thoracic surgery. Multiple dosing regimens may be beneficial in reducing acute and chronic pain; however, more robust randomized control studies are needed.

Keywords: Gabapentin • Safety • Thoracotomy • Pain

INTRODUCTION

A best evidence topic was constructed according to a structured protocol. This protocol is fully described in the *ICVTS* [1].

THREE PART QUESTION

Does [gabapentin] reduce the incidence of [pain] experienced by patients post [thoracic surgery]?

CLINICAL SCENARIO

The pain team at your hospital discusses with you the introduction of a new perioperative pain management protocol for patients undergoing thoracic surgery. The protocol includes the use of gabapentin. You are not sure whether gabapentin is a safe and effective drug so you decide to to look up the evidence yourself.

SEARCH STRATEGY

Medline 1950–November 2011 and Embase 1974–June 2011 using the Dialog Datastar interface. ('gabapentin' [Supplementary Concept] AND 'Pain'[Mesh]) AND ('Thoracic Surgical Procedures' [Mesh] OR 'Thoracic Surgery'[Mesh]). This search was repeated in the Cochrane Central Register of Controlled Trials.

SEARCH OUTCOME

A total of 17 papers were identified of which 5 were deemed to be relevant (see Table 1).

RESULTS

Pain experienced post-thoracic surgery can have a major impact on a patient's mobility and recovery. Many factors can affect the analgesic outcome after thoracic surgery, including surgical

Table 1: Summary table

Author, date, journal and country Study type (level of evidence)	Patient group	Outcomes	Key results	Comments
Huot *et al*. (2008), Can J Anaesth, Canada [2] Thoracic non-oncological (level 1b)	Randomized double-blind study *n* = 51 Gabapentin 23 Placebo 28 9 patients excluded due to epidural difficulties or perioperative complications Single dose of 1200 mg 2 h preprocedure All patients had bupivacaine epidural 0–10 scale used to evaluate pain every 4 h until 24	Preoperative gabapentin does not reduce post-thoracotomy pain	Gabapentin did not reduce the need for epidural ($P = 0.06$) or PRN morphine ($P = 0.36$) use at 8, 16 and 24 h 91 percent in the gabapentin group and 82% in the placebo group experienced pain (quoted as no significant difference but *P*-value not recorded)	Small treatment group with large number of patients excluded Only patients with epidural included One-off dose (several doses required to achieve peak plasma concentration) Short follow-up At least half of patients in almost all categories had pain score of 0 within 24 h
Kinney *et al*. (2012), Pain Pract, USA [3] Thoracic non-oncological (level 1b)	Randomized double-blind study *n* = 120 Gabapentin 57 Placebo 63 26 patients excluded due to logistical problems in medication administration, no thoracotomy, epidural problems Single dose of 600 mg within 2 h preprocedure All patients had bupivacaine + hydromorphone epidural 0–10 scale every 4 h until 48 Any pain at 3 months	A single preoperative oral dose of gabapentin does not reduce pain scores or opioid consumption following elective thoracotomy	No significant difference in epidural use on Day 1 ($P = 0.08$), but significantly lower on Day 2 ($P = 0.02$) No difference in length of epidural use between the gabapentin and placebo groups (60 vs 62 h) ($P = 0.54$) No significant difference in length of stay ($P = 0.054$), or side effects except pruritis increased in the gabapentin group ($P < 0.001$) Pain scores in first 48 h showed no significant differences between the two groups ($P = 0.98$) No significant difference in pain at 3 months ($P = 0.72$)	Only patients with epidural included with large number of patients were excluded from analysis One-off dose (several doses required to achieve peak plasma concentration)
Sihoe *et al*. (2006), Eur J Cardiothorac Surg, China [4] Thoracic non-oncological (level 3b)	Prospective study of out-patients with pain persisting at >4 weeks *n* = 60 prescribed gabapentin Follow-up of 45 patients for median of 21 months (12 = 28) Variable postoperative analgesia protocol	Gabapentin is effective, safe and well tolerated when used for persistent postoperative and post-traumatic pain in thoracic surgery patients	33 patients (73.3%) noted reduction of pain Chest wall paraesthesia distinguishable from wound pain was relieved in 24 (75.0%) of 32 affected patients Severe initial pain was significantly correlated with pain relief using gabapentin ($P = 0.009$) Minor side effects (somnolence and dizziness) occurred in 18 patients (40.0%), causing 3 patients (6.7%) to discontinue gabapentin Satisfaction with gabapentin use was expressed by 40 patients (88.9%)	No randomization and follow-up of only 75% of patients Diverse patient group as procedures included thoracotomy, VATS, sternotomy and blunt chest trauma No consistent perioperative analgesic protocol Initiation of gabapentin therapy at a mean of 5.7 months after surgery

Continued

Table 1: (*Continued*)

Author, date, journal and country Study type (level of evidence)	Patient group	Outcomes	Key results	Comments
Solak *et al*. (2007), Eur J Cardiothorac Surg, Turkey [5] Thoracic non-oncological (level 2b)	Prospective clinical study comparing the gabapentin to naproxen sodium *n* = 40 Consecutive patients with chronic post-thoracotomy pain Gabapentin 20 Naproxen sodium 20 Gabapentin given for 60 days with an incremental stepwise dosage Naproxen sodium 500 mg twice per day for 60 days VAS and the LANSS scorings were performed Pretreatment (Day 0) and on the 15th, 30th, 45th and 60th days	Gabapentin is safe and effective in the treatment of chronic post-thoracotomy pain with minimal side effects and a high patient compliance	The mean pretreatment VAS scores (VAS0) were 6.4 ± 0.6 and 6.8 ± 0.6, respectively ($P > 0.05$) Significant improvement in VAS score at 60 days in the gabapentin group 17 (85%) compared with the naproxen group 3 (15%) ($P < 0.001$) The mean pretreatment LANSS scores (LANSS0) were 18.85 ± 1.6 and 20.75 ± 2.6 in GP and NS groups, respectively ($P > 0.05$) Significant improvement in the LANSS scores at 60 days in the gabapentin group 17 (85%) compared with the naproxen group 0 (0%) ($P = 0.001$) Minor adverse events were noted in 7 (35%) patients in the gabapentin group and in 4 (20%) patients in the naproxen group	Small number of patients The group defined chronic pain as pain that recurs or persists along a thoracotomy incision for at least 2 months following the surgical procedure which can include acute and chronic patients Study does not include details about analgesia protocol and whether gabapentin or naproxen where given solely or as part of multimodality pain protocol
Omran *et al*. (2005), Eg J Anaesth, Egypt [6] Thoracic non-oncological (level 2b)	Randomized double-blind control study *n* = 50 Gabapentin 25 Placebo 25 Single dose of 1200 mg 1 h preprocedure and further 600 mg doses every 12 h post-procedure for 48 h All patients had epidural and IV morphine PCA for 48 h Pain scale every 6 h until 48 FVC and PEFR at 24 and 48 h post-procedure If pain > epidural increased and given IV fentanyl PCA	Oral gabapentin administered preoperatively and during the first 2 days postoperatively, in conjunction with PCA morphine, provides effective analgesia in thoracic surgery with a consequent improvement in postoperative pulmonary function and less morphine consumption	Patients in the gabapentin group had significantly lower VAS scores compared with the control group throughout the postoperative period ($P < 0.05$) Morphine consumption was significantly lower in the gabapentin group in the first and second postoperative days ($P = 0.005$) Patients in the gabapentin group had significantly greater FVC and PEFR values compared with those in the control group at 24 and 48 h postoperatively The incidence of vomiting and urinary retention was significantly higher in the control group ($P < 0.05$)	Small number of patients included Method of randomization unknown Short follow-up

FVC: forced vital capacity; PEFR: peak expiratory flow rate; PCA: patient controlled analgesia; PRN: pro re nata.

technique, choice of analgesic modality, postoperative level of care, ongoing input from acute pain and physiotherapy services and the patient factor. The current evidence base tends towards a multimodal approach to pain control, targeting a range of different pathways and neurotransmitters.

Our search identified three randomized control studies that compared the effectiveness of preoperative administration of gabapentin to placebo.

Kinney *et al*. carried out a prospective, randomized, double-blinded, placebo-controlled study in adults undergoing elective thoracotomy. Patients were randomly assigned to receive a single dosing regime of 600 mg gabapentin or active placebo orally within 2 h prior to surgery as a one-off dose. Standardized management included thoracic epidural infusion, intravenous patient-controlled opioid analgesia, acetaminophen and ketorolac. One hundred and twenty patients (63 placebo and 57 gabapentin)

were studied. This study revealed that pain scores did not significantly differ at any time point ($P = 0.53$). Parenteral and oral opioid consumption were not significantly different between groups on postoperative day 1 or 2 ($P > 0.05$ in both cases). The frequency of side effects such as nausea and vomiting or respiratory depression was not significantly different between groups, but gabapentin was associated with decreased frequency of pruritus requiring treatment with an antihistamine or termination of opiate analgesia (14% gabapentin vs 43% control group, $P < 0.001$). The frequency of patients experiencing pain at 3 months post-thoracotomy was also comparable between groups (70% gabapentin vs 66% placebo group, $P = 0.72$). The authors concluded that a single preoperative oral dose of gabapentin did not reduce pain scores or opioid consumption following elective thoracotomy, and did not confer any analgesic benefit in the setting of effective multimodal analgesia that included thoracic epidural infusion. Similar outcomes were reported by Hout *et al*. in a previous randomized, double-blinded, placebo-controlled study.

Omran *et al*. however, reported that the administration of a single dose of 1200 mg 1 h preprocedure and further 600 mg doses every 12 h post-procedure for 48 h in conjunction with patient controlled analgesia (PCA) morphine provides effective analgesia in thoracic surgery with a consequent improvement in postoperative pulmonary function and less morphine consumption.

Similar results were reported by Solak *et al*. in a prospective study that used gabapentin for 60 days with an incremental stepwise dosage (300 mg/day for the first 3 days, then 900 mg/day until the 15th day, 1800 mg/day between the 15th and 30th days and finally 2400 mg/day between the 30th and 60th days).

The role of gabapentin in chronic post-thoracic surgery pain management was addressed in a prospective study by Sihoe *et al*., and suggested that gabapentin is safe and well tolerated when used for persistent postoperative and post-traumatic pain in thoracic surgery patients. This study, however, has many limitations, and the follow-up included only 75% of the patients. The patients enrolled had a wide range of procedures included thoracotomy, VATS, sternotomy and blunt chest trauma. There was no consistent perioperative analgesic protocol and initiation of gabapentin therapy was started at a mean of 5.7 months following surgery.

CLINICAL BOTTOM LINE

There is no evidence to support the role of a single preoperative oral dose of gabapentin in reducing pain scores or opioid consumption following thoracic surgery. Multiple dosing regimens may be beneficial in reducing acute and chronic pain; however, more robust randomized control studies are needed.

Conflict of interest: none declared.

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