Reports of Original Investigations

Gabapentin does not reduce post-thoracotomy shoulder pain: a randomized, double-blind placebo-controlled study

[La gabapentine ne réduit pas la douleur à l'épaule post-thoracotomie : une étude randomisée, à double insu et contrôlée par placebo]

Marie-Pierre Huot MD,* Philippe Chouinard MD FRCPC,* François Girard MD FRCPC,* Monique Ruel RN CCRP,* Edwin R. Lafontaine MD FRCSC,† Pasquale Ferraro MD FRCSC†

Purpose: Despite adequate epidural analgesia, up to 97% of patients undergoing thoracotomy experience ipsilateral shoulder pain. In this setting, this study evaluated the safety and the efficacy of pre-emptive gabapentin.

Methods: A double-blind, placebo-controlled study was undertaken in 51 patients randomized into two groups. Two hours before surgery, 23 patients received gabapentin 1200 mg *po* (Group G), and 28 patients received placebo (Group P). Shoulder pain and postoperative pain, at the surgical site, were monitored every four hours for 24 hr, using a numerical rating scale. Subcutaneous hydromorphone was administered for rescue analgesia against shoulder pain.

Results: Forty-four patients complained of shoulder pain (prevalence of 86%). Demographic and surgical data were similar between the two groups. There were no significant differences in the total cumulative doses of hydromorphone administered at eight, 16, and 24 hr, nor were there differences in individual numerical rating scale scores for shoulder pain. The groups were similar with respect to the degree of pain at the surgical site. The frequency of side effects between groups at corresponding time intervals was also similar, with the exception of sedation. At four hours, the incidence of sedation scores > 1 was greater in Group G (21/23 patients), compared to Group P (18/28 patients; $P = 0.025$). In contrast, by 24 hr, 5/18 patients in Group P had sedation scores > 1, compared to 0/28 patients in Group G ($P = 0.05$).

Conclusion: Pre-emptively administered gabapentin, 1200 mg, does not reduce the incidence, or the severity, of post-thoracotomy shoulder pain in patients receiving thoracic epidural analgesia.

CAN J ANESTH 2008 / 55: 6 / pp 337–343

Objectif *: Malgré une analgésie péridurale adaptée, jusqu'à 97 % des patients subissant une thoracotomie éprouvent de la douleur à l'épaule ipsilatérale. Dans ce contexte, notre étude a évalué l'innocuité et l'efficacité de la gabapentine administrée de façon préventive.*

Méthode *: Une étude à double insu et contrôlée par placebo a été menée ; elle évaluait 51 patients randomisés en deux groupes. Deux heures avant la chirurgie, 23 patients ont reçu de la gabapentine 1200 mg oralement (groupe G) et 28 un placebo (groupe P). La douleur à l'épaule et la douleur postopératoire au site chirurgical ont été évaluées toutes les quatre heures durant 24 h à l'aide d'une échelle d'évaluation numérique. De l'hydromorphone sous-cutanée a été administrée en analgésie de secours contre la douleur à l'épaule.*

Résultats *: Quarante-quatre patients se sont plaints de douleur à l'épaule (prévalence de 86 %). Les données démographiques et chirurgicales étaient semblables dans les deux groupes. Il n'y a pas eu de différence significative dans les doses cumulatives totales d'hydromorphone administrée à huit, seize et 24 h, ni dans les*

From the Department of Anesthesiology* and Thoracic Surgery Division,† CHUM, Hôpital Notre-Dame, Montréal, Québec, Canada.
Address correspondence to: Dr. Philippe Chouinard, Department of Anesthesiology, CHUM, Hôpital Notre-Dame, 1560 Sherbrooke East, Montréal, Québec H2L 4M1, Canada. E-mail: philippe.chouinard.chum@ssss.gouv.qc.ca
Accepted for publication June 13, 2007.
Revision accepted March 17, 2008.

This article is accompanied by an editorial. Please see Can J Anesth 2008; 55: 6 323–7.

scores individuels sur l'échelle d'évaluation numérique pour la douleur à l'épaule. Les groupes ont présenté des résultats semblables concernant le degré de douleur au site chirurgical. La fréquence des effets secondaires, comparée entre les groupes à des intervalles correspondants, était également similaire, à l'exception de la sédation. À quatre heures, l'incidence de scores de sédation > 1 était plus élevée dans le groupe G (21/23 patients), comparé au groupe P (18/28 patients; P = 0,025). En revanche, à 24 heures, 5/18 patients du groupe P présentaient des scores de sédation > 1, comparé à 0/28 patients dans le groupe G (P = 0,05).

***Conclusion** : La gabapentine 1200 mg administrée de façon préventive ne réduit pas l'incidence ou la sévérité de la douleur à l'épaule post-thoracotomie chez les patients recevant une analgésie péridurale thoracique.*

THIRTY-ONE to 97% of patients, undergoing a thoracotomy, experience ipsilateral shoulder pain, despite adequate thoracic epidural analgesia. Patients complain of a constant, moderate to severe, aching pain, in the posterior deltoid and in the suprascapular region, ipsilateral to the surgery.[1–6] The most plausible mechanisms, amongst several proposed to explain the occurrence of post-thoracotomy shoulder pain (PTSP),[2,7,8] appear to be pain referred from an irritation of the pericardium or pleural surfaces.[5] Different pharmacological agents have been used to alleviate PTSP, but few of these modalities have proven attractive, notably because of their side effects and their relatively short half-life.[9]

Acute postoperative pain is increasingly believed to have a transient and reversible neuropathic component.[10] Recent scientific evidence shows the effectiveness of pre-emptive administration of gabapentin (a structural analog of γ-aminobutyric acid) in decreasing postoperative pain and opioid analgesic requirements after various types of surgeries.[11] Gabapentin has an elimination half-life of six to eight hours, and the drug is safe in therapeutic doses, with only minimal side effects and few interactions with concurrent medications.[9,10] The efficacy of gabapentin for PTSP has, however, never been investigated.

We designed this randomized, placebo-controlled, double-blind study to assess the effect of a single, pre-emptive dose of 1200 mg, oral gabapentin *vs* placebo on the prevalence and severity of PTSP, during the first 24 hr following thoracotomy for pulmonary resection. We hypothesized that the administration of gabapentin would result in a reduction in the incidence of PTSP, compared to placebo. Secondarily, we evaluated the impact of gabapentin on postoperative opioid requirements and the occurrence of its side effects.

Methods

After receiving institutional Review Board approval and written informed consent, 60 patients, aged 18 to 80 yr, were recruited. Subjects, ASA physical status II–III, were scheduled to undergo elective thoracotomy in the lateral decubitus position, with thoracic epidural analgesia (TEA). Exclusion criteria were: 1) a known or suspected allergy to local anesthetics, gabapentin, or hydromorphone; 2) a contraindication to the placement of an epidural catheter; 3) a previous ipsilateral thoracotomy (with or without a diaphragmatic resection); 4) the presence of preoperative shoulder pain, or any chronic pain syndrome; 5) the concurrent use of analgesics in the immediate preoperative period [e.g., opioids, non-steroidal anti-inflammatory drugs (NSAIDs), antidepressants, antiepileptics, corticosteroids]; 6) a history of drug or alcohol abuse; and 7) the inability to understand a numerical rating scale (NRS) for pain assessment.

On the day of surgery, patients were randomly assigned to receive gabapentin, 1200 mg *po* (Group G), or a placebo (Group P), approximately two hours before surgical incision. The hospital research pharmacy provided identical gabapentin and placebo capsules, with respect to shape, size, and colour, for patients who had been randomized using a computerized table of random numbers. The investigators, as well as the surgical and anesthesia personnel involved in patients' care and data collection, were blinded to the group assignment.

Standard, noninvasive monitors were placed; a thoracic, epidural catheter was inserted, under local anesthesia, between the fourth and the ninth thoracic, spinous processes, and general anesthesia was induced. Correct placement of the epidural catheter was assessed by infusing a bolus of 5 mL of lidocaine (1.5%) with epinephrine 1:200,000. If no decrease to cold sensation was displayed over at least two thoracic dermatomes, a higher concentration, 5 mL, testing bolus of lidocaine (2%) was given after ten minutes. If a decrease to cold sensation was still not detected after ten minutes, the epidural catheter was reinserted and managed using the same protocol. After induction of anesthesia and after placing the patient in the lateral, decubitus position, the epidural infusion (bupivacaine 0.1% and fentanyl 2 $\mu g \cdot mL^{-1}$) was started at a rate of 0.1 $mL \cdot kg^{-1} \cdot hr^{-1}$. Adjustments were made between 4 to 16 $mL \cdot hr^{-1}$, with boluses of 0.1 $mL \cdot kg^{-1}$ of solution, as needed (at the discretion of the attending anesthesiologist, in order to maintain blood pressure and heart

rate within ± 20% of the preinduction values). Postoperatively, the infusion rate was adjusted to maintain a pain score at the surgical site of ≤ 3 on the NRS.

General anesthesia was induced with propofol 1 to 2 mg·kg^{-1} *iv* and fentanyl 2 to 5 μg·kg^{-1} *iv* or sufentanil 0.2 to 0.5 μg·kg^{-1} *iv*. Endotracheal intubation was facilitated with rocuronium 0.6 to 1.2 mg·kg^{-1} *iv* or succinylcholine 2 mg·kg^{-1} *iv*. Anesthesia was maintained with desflurane or sevoflurane (0.6 to 1.2 MAC) in O_2/air 50:50 or O_2 100%. Patients received supplemental boluses of fentanyl or sufentanil, as needed (whenever optimal use of the epidural catheter failed to maintain blood pressure and heart rate within ± 20% of the preinduction values). Rocuronium was given, as required, to maintain a single twitch response using a nerve stimulator. All patients were maintained in the lateral decubitus position, with a padded roll placed under the dependent axilla. Special care was taken to avoid strain on the ipsilateral shoulder joint, by means of an arm rest kept at < 90° of anterior flexion and eliciting no abduction; the elbow flexion was maintained at 45°. Surgical incisions were standard, lateral thoracotomies performed between the fourth to sixth intercostal spaces. The types of procedures are presented in Table I. Except for patients who underwent pneumonectomy, one or two chest tubes were inserted into the pleural space at the end of the surgery. The patients' tracheae were extubated in the operating room, and, afterwards, all subjects were transferred to a postanesthesia care unit (PACU).

Pain at the surgical site, at rest and while coughing, and shoulder pain, at rest and during movement (90° abduction of the ipislateral arm), were assessed by the PACU nursing staff at four-hour intervals for 24 hr (total of seven assessment periods). The level of pain was evaluated using a ten-point NRS, where 0 refers to "no pain" and 10 refers to "the worst possible pain imaginable". At any time, individuals experiencing moderate to severe pain (NRS > 3) at the surgical incision site received a bolus of 0.1 mL·kg^{-1} of epidural solution, and the infusion rate was increased in 2 mL·hr^{-1} increments, to a maximum infusion rate of 16 mL·hr^{-1}. If pain was still not alleviated, the epidural solution was changed to bupivacaine (0.125%) with fentanyl 2 μg·mL^{-1}, restarted at 10 mL·hr^{-1}, and was readjusted using the same protocol. Patients complaining of shoulder pain, despite adequate incisional analgesia, received rescue medication (hydromorphone 1–2 mg *sc* every four to six hours). Nausea, vomiting, pruritus, and sedation (scaled from 0 to 3) were evaluated concurrently with the pain assessments.

The following information was recorded: demographic data; the duration of anesthesia, from induction to extubation; the duration of surgery, from the time of skin incision to closure; the total time maintained in the lateral, decubitus position; the duration of the epidural infusion; the cumulative dosage of administered hydromorphone; and the need for treatment of nausea and vomiting.

TABLE I Demographic and surgical data

	Group G (gabapentin)	*Group P (placebo)*
Patients (*n*)	23	28
Gender (male:female)	11:12	17:11
Age (yr)	60.1 ± 13.6	60.0 ± 8.7
Weight (kg)	71.2 ± 15.9	70.1 ± 13.8
Height (cm)	168.7 ± 8.2	167.9 ± 9.3
Creatinine clearance (mL·min^{-1})	80.3 ± 29.4	83.8 ± 23.6
Duration of surgery (min)	108.8 ± 30.6	91.6 ± 28.4
Duration of lateral decubitus position (min)	133.4 ± 30.4	117.4 ± 28.1
Type of surgery		
Pneumonectomy	4	2
Lobectomy	13	17
Segmentectomy/ wedge/biopsy	6	6
Exploratory thoracotomy	0	3

The sample size requirement was determined by drawing on a study, with a similar design, that was previously completed in our hospital. That particular study examined the efficacy of acetaminophen for PTSP.[3] Considering a 97% prevalence of PTSP,[2] a reduction of 25% was deemed to be clinically significant and, consequently, would require 80 patients. This estimate provides a power of 90% with an α of 0.05. Paired Student's *t* and Chi-square tests were used to assess differences in demographic and intraoperative variables. Between-group differences in NRS scores for shoulder pain were evaluated at corresponding time intervals using the unpaired Student's *t* test.[12] Because of a non-normal distribution, between-group differences in NRS scores for incisional pain were compared at corresponding time intervals using the Wilcoxon test. Differences in the prevalence of adverse effects were compared using the Chi-square statistic. Analysis was by intention-to-treat. Results are reported as the mean ± SD, except when stated otherwise. A *P* value < 0.05 was considered significant.

Results

Of the 60 patients randomized in the study from April 2005 to March 2006, nine were excluded. Reasons

TABLE II Postoperative data

	Group G (gabapentin)	*Group P (placebo)*
Total dose of epidural solution (mL)	281.1 ± 75.8	318.1 ± 94.8 ($P = 0.06$)
Bupivacaine 0.1% + fentanyl 2 $\mu g \cdot mL^{-1}$		
Patients who received rescue medication (hydromorphone) (n)	17	17
Cumulative hydromorphone dose (mg/24 hr)	2.36 ± 2.5	2.65 ± 3.2 ($P = 0.36$)

TABLE III Severity of pain at the site of surgical incision

NRS		*Group G (gabapentin)*	*Group P (placebo)*
0 hr	Rest	0 [0-6]	0 [0-10]
	Cough	0 [0-10]	0 [0-10]
4 hr		0 [0-8]	0 [0-5]
8 hr		0 [0-7]	0 [0-5]
12 hr		0 [0-7]	0.5 [0-6]
16 hr		0 [0-4]	0 [0-5]
20 hr		0 [0-5]	0 [0-5]
24 hr	Rest	0.5 [0-8]	0 [0-2]
	Cough	3 [0-10]	1.5 [0-8]

Median [range]. NRS = numerical rating scale, where 0 represents no pain and 10, the worst possible pain.

for exclusion were: impossibility to insert the epidural catheter ($n = 1$); epidural not properly functioning in PACU ($n = 4$); postoperative respiratory arrest ($n = 1$, Group G); prolonged, intraoperative hypotension, with rates of epidural solution below the minimum allowed ($n = 1$); addition of morphine in the epidural solution ($n = 1$); and postoperative agitation ($n = 1$). A total of seven and two patients were excluded from groups G and P, respectively.

Of 51 patients, whose data were available for analysis, 23 were in Group G and 28 were in Group P. Demographic and surgical data (Table I), as well as the total amount of epidural solution and the total dose of hydromorphone administered at eight, 16, and 24 hr (Table II), were similar in the two groups. No differences were observed between groups, with respect to pain at surgical site (Table III). For the entire postoperative period and at each time interval, there were no between-group differences in the NRS scores for shoulder pain (Figure). Twenty-three patients (82%) in Group P experienced shoulder pain compared to 21 (91%) in Group G. The frequencies of nausea, vomiting, and pruritus were similar in the two groups. A similar proportion of patients in the two groups received antiemetic treatment; seven patients in Group G (30%) and eight patients in Group P (29%). At four hours, the incidence of sedation scores > 1 was greater in Group G (21/23 patients), compared to Group P (18/28 patients; $P = 0.025$). In contrast, by 24 hr, 5/18 patients in Group P had sedation scores > 1, compared to 0/28 patients in Group G ($P = 0.05$).

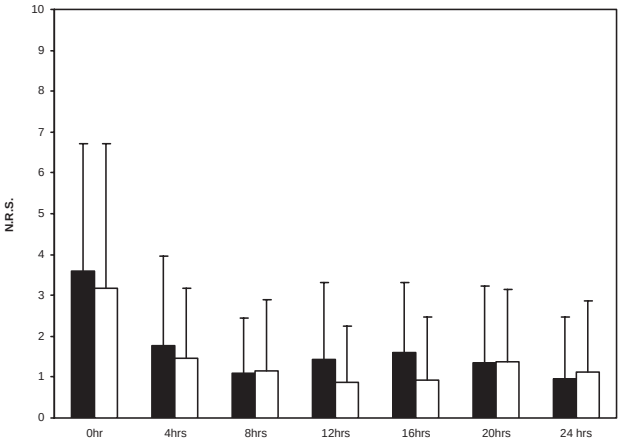

FIGURE Severity of post-thoracotomy shoulder pain. NRS = numerical rating scale (where 0 represents no pain and 10, the worst possible pain); black bars = gabapentin group; white bars = placebo group. Data are mean ± SD.

Discussion

This study shows that gabapentin, compared to a placebo, does not reduce the incidence or the severity of PTSP. Hydromorphone requirements, in the first 24 hr, postoperatively, were also comparable between the two groups. The 86% prevalence of PTSP, amongst all patients in this study, is within the 60% to 97% range of that reported in recent literature.[3–6] This confirms that most post-thoracotomy patients will experience shoulder pain in the early postoperative period.

Burgess *et al.*[2] was one of the first groups to describe and better characterize PTSP in an open, prospective study that included 45 patients undergoing posterolateral thoracotomy. They reported an overall incidence of 43% for PTSP and recommended the postoperative use of ketorolac. Because of a higher prevalence of PTSP after major pulmonary resection, it was suggested that transection of a major bronchus was the mechanism involved in this kind of pain. In a prospective study, Barak *et al.*[1] showed that intrarectal indomethacin reduced the intensity of PTSP, implying that inflammation may play an active role in the process. However, the side effects associated with

NSAIDs, such as platelet inhibition, gastro-intestinal bleeding, and potential renal toxicity, render these drugs questionable for routine use in this population of patients. Although there was no difference between the two groups, in terms of the total dose of hydromorphone administered as rescue medication, Mac *et al.*[3], from our institution, recently demonstrated that the administration of intrarectal acetaminophen, pre-emptively, and in the postoperative period, also attenuated the intensity of PTSP for the first 16 hr postoperatively. The most plausible etiology for PTSP was proposed by Scawn *et al.*[5] in a randomized, placebo-controlled study, where it was demonstrated that there is a marked reduction in the prevalence of pain with the intraoperative infiltration of the phrenic nerve with lidocaine. The authors hypothesized that PTSP was a referred pain transmitted via the phrenic nerve from an irritation of the pericardium or pleural surfaces during the surgery. Several case reports showed that blocking the stellate ganglia and the interscalene, brachial plexus (often in association with the phrenic nerves) decreases the prevalence of PTSP.[7,13,14] The diaphragmatic paresis and potential compromise in pulmonary function associated with these techniques is, however, a concern in regards to patient safety.[13] The incomplete efficacy of supraclavicular nerve blocks to suppress shoulder pain[6] suggests that the shoulder capsule is unlikely to be involved as a mechanism for PTSP.

In recent years, gabapentin has been evaluated for the management of acute, postoperative pain. The efficacy of a single, pre-emptive dose of gabapentin for postoperative analgesia, has yielded inconsistent results. In spinal surgery, two studies showed a positive effect of gabapentin on pain scores and on opioid requirements in the postoperative period.[15,16] In contrast, Radhakrishnan *et al.*[17] did not show any benefit of gabapentin in the same surgical setting. In patients scheduled for total abdominal hysterectomy, 1200 mg of gabapentin, administered pre-emptively, resulted in better pain relief than placebo and decreased postoperative, tramadol consumption.[18] The same regimen also resulted in a reduction in the incidence of postoperative nausea and vomiting in patients who underwent elective, vaginal hysterectomy.[19] Recently, Turan *et al.*[11] published the first investigation demonstrating the efficacy of gabapentin, when used in combination with postoperative epidural analgesia. In a randomized controlled trial, the authors showed that gabapentin, administered before surgery and for two days thereafter, decreased patient-controlled epidural analgesia consumption and postoperative pain scores after lower extremity surgeries. In addition, there was an improvement in patient satisfaction scores and a lower incidence of motor block.

Theoretically, gabapentin would be an attractive drug to use for co-analgesia in acute postoperative pain, where diverse nociceptive mechanisms, such as sensitization of peripheral nociceptors and central neurons leading to hyperalgesia and allodynia, are involved.[10,21] Gabapentin is actually an antihyperalgesic drug which has been shown to act on this central sensitization process.[10,22] Despite the fact that PTSP appears to be a referred pain, with a possible component of central sensitization, our study failed to show any beneficial effect of this medication on pain scores, opioid consumption, and side effects.

A single, preoperative dose of 1200 mg of gabapentin was chosen for this study, as it is the dose most frequently reported as alleviating pain without substantial side effects.[15,18,19,21,23] No previous, dose-response study has been performed. In the current investigation, gabapentin was administered two hours prior to surgery, based on the concept of pre-emptive analgesia, where administration of a drug, before the surgical trauma, may attenuate central nervous system wind-up and the resulting allodynia and hyperalgesia.[10,24] The ineffectiveness of gabapentin to reduce PTSP in this study could, in part, be explained by the fact that, on average, the patients reported only a moderate pain intensity in the postoperative period (NRS only ranged from 3.2 to 3.6). An interaction with the thoracic epidural analgesia was unlikely, as the nociceptive pathways of the PTSP (presumably the phrenic nerve) are not implicated. A 24-hr study period of evaluation was deemed adequate, based on the natural history of shoulder pain and its tendency to decrease after 24 hr.[3] Another explanation for this lack of efficacy might be that central sensitization, which is a process that is increasingly advocated in postoperative pain and believed, by some, to be influenced by gabapentin, may not be a mechanism playing a major role in the pathophysiology of PTSP. Finally, gabapentin was administered as a single, preoperative dose. Given the duration of surgery and the expected half-life of gabapentin (six to eight hours),[25] it is possible that additional postoperative doses could have led to different results.

At four hours, patients in the gabapentin group experienced more sedation than those in the placebo group. This is one of the most commonly reported side effects of gabapentin.[9] One patient in the gabapentin group was excluded from the study because of a respiratory arrest. The 74-yr-old male, with no notable, medical history, underwent a thoracotomy for a left upper lobectomy without intraoperative

complication. The patient was found unconscious and bradypneic in the evening, approximately nine hours after the administration of the gabapentin dose, but approximately three hours after he had received hydromorphone 1 mg *sc*. Tracheal intubation and ventilatory assistance were provided, and the patient completely recovered within 24 hr, without sequelae. In contrast with hydromorphone, respiratory depression is not a commonly reported side effect of gabapentin: there is only one case of coma and respiratory arrest found in the literature, where a patient had been subjected to a massive overdose, in association with concurrent administration of quetiapine.[26]

In conclusion, and contrary to our primary hypothesis, gabapentin does not reduce the incidence and/or the intensity of PTSP. Dose response studies are warranted for the use of gabapentin in acute postoperative pain. Additional studies are also required to better characterize the physiopathology of PTSP.

References

1 *Barak M, Ziser A, Katz Y.* Thoracic epidural local anesthetics are ineffective in alleviating post-thoracotomy ipsilateral shoulder pain. J Cardiothorac Vasc Anesth 2004; 18: 458–60.

2 *Burgess FW, Anderson DM, Colonna D, Sborov MJ, Cavanaugh DG.* Ipsilateral shoulder pain following thoracic surgery. Anesthesiology 1993; 78: 365–8.

3 *Mac TB, Girard F, Chouinard P, et al.* Acetaminophen decreases early post-thoracotomy ipsilateral shoulder pain in patients with thoracic epidural analgesia: a double-blind placebo-controlled study. J Cardiothorac Vasc Anesth 2005; 19: 475–8.

4 *Pennefather SH, Akrofi ME, Kendall JB, Russell GN, Scawn ND.* Double-blind comparison of intrapleural saline and 0.25% bupivacaine for ipsilateral shoulder pain after thoracotomy in patients receiving thoracic epidural analgesia. Br J Anaesth 2005; 94: 234–8.

5 *Scawn ND, Pennefather SH, Soorae A, Wang JY, Russell GN.* Ipsilateral shoulder pain after thoracotomy with epidural analgesia: the influence of phrenic nerve infiltration with lidocaine. Anesth Analg 2001; 93: 260–4.

6 *Tan N, Agnew NM, Scawn ND, Pennefather SH, Chester M, Russell GN.* Suprascapular nerve block for ipsilateral shoulder pain after thoracotomy with thoracic epidural analgesia: a double-blind comparison of 0.5% bupivacaine and 0.9% saline. Anesth Analg 2002; 94: 199–202.

7 *Garner L, Coats RR.* Ipsilateral stellate ganglion block effective for treating shoulder pain after thoracotomy. Anesth Analg 1994; 78: 1195–6.

8 *Mark JB, Brodsky JB.* Ipsilateral shoulder pain following thoracic operations. Anesthesiology 1993; 79: 192.

9 *Mao J, Chen LL.* Gabapentin and pain management. Anesth Analg 2000; 91: 680–7.

10 *Dahl JB, Mathiesen O, Moiniche S.* 'Protective medication': an option with gabapentin and related drugs? A review of gabapentin and pregabalin in the treatment of post-operative pain. Acta Anaesthesiol Scand 2004; 48: 1130–6.

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

12 *Dexter F, Chestnut DH.* Analysis of statistical tests to compare visual analog scale measurements among groups. Anesthesiology 1995; 82: 896–902.

13 *Ng KP, Chow YF.* Brachial plexus block for ipsilateral shoulder pain after thoracotomy. Anaesth Intensive Care 1997; 25: 74–6.

14 *Urmey WF, Mcdonald M.* Hemidiaphragmatic paresis during interscalene brachial plexus block: effects on pulmonary function and chest wall mechanics. Anesth Analg 1992; 74: 352–7.

15 *Turan A, Karamanlioglu B, Memis D, et al.* Analgesic effects of gabapentin after spinal surgery. Anesthesiology 2004; 100: 935–8.

16 *Pandey CK, Sahay S, Gupta D, et al.* Preemptive gabapentin decreases postoperative pain after lumbar discoidectomy. Can J Anesth 2004; 51: 986–9.

17 *Radhakrishnan M, Bithal PK, Chaturvedi A.* Effect of preemptive gabapentin on postoperative pain relief and morphine consumption following lumbar laminectomy and discectomy: a randomized, double-blinded, placebo-controlled study. J Neurosurg Anesthesiol 2005; 17: 125–8.

18 *Turan A, Karamanlioglu B, Memis D, Usar P, Pamukcu Z, Ture M.* The analgesic effects of gabapentin after total abdominal hysterectomy. Anesth Analg 2004, 98: 1370–3.

19 *Rorarius MG, Mennander S, Suominen P, et al.* Gabapentin for the prevention of postoperative pain after vaginal hysterectomy. Pain 2004; 110: 175–81.

20 *Pandey CK, Priye S, Singh S, Singh U, Singh RB, Singh PK.* Preemptive use of gabapentin significantly decreases postoperative pain and rescue analgesic requirements in laparoscopic cholecystectomy. Can J Anesth 2004; 51: 358–63.

21 *Dirks J, Moiniche S, Hilsted KL, Dahl JB.* Mechanisms of postoperative pain: clinical indications for a contribution of central neuronal sensitization. Anesthesiology 2002; 97: 1591–6.

22 *Gilron I.* Is gabapentin a "broad-spectrum" analgesic? Anesthesiology 2002; 97: 537–9.

23 *Al-Mujadi H, A-Refai AR, Katzarov MG, Dehrab NA, Batra YK, Al-Qattan AR.* Preemptive gabapentin reduces postoperative pain and opioid demand following thyroid surgery. Can J Anesth 2006; 53: 268–73.
24 *Dahl JB, Moiniche S.* Pre-emptive analgesia. Br Med Bull 2004; 71: 13–27.
25 *Bennett MI, Simpson KH.* Gabapentin in the treatment of neuropathic pain. Palliat Med 2004; 18: 5–11.
26 *Spiller HA, Dunaway MD, Cutino L.* Massive gabapentin and presumptive quetiapine overdose. Vet Hum Toxicol 2002; 44: 243–4.

Random Passage Set - *Newfoundland*