Has postoperative pain been eradicated?

Sabaratnam Sabanathan FRCS
Consultant Thoracic Surgeon
Department of Thoracic Surgery, Bradford Royal Infirmary, Bradford

Key words: Thoracotomy; Postoperative pain; Analgesia; Pre-emptive analgesia; Continuous extrapleural intercostal nerve block; NSAID; Balanced analgesia

Recent evidence suggests that surgical trauma induces a process of central nervous system sensitisation that contributes to and enhances postoperative pain. These changes are also thought to be the underlying cause of much chronic pain. Central sensitisation is generated not only during surgery, but also postoperatively as a result of the inflammatory response to the damaged tissue. This knowledge provides a rational basis for pro-active, pre-emptive and postoperative analgesic strategies to reduce the neuronal barrage associated with tissue damage. Reduction or elimination of postoperative pain is therefore possible.

We advocate the use of continuous extrapleural intercostal nerve block for postoperative analgesia in patients undergoing thoracotomy. When this is begun pre-emptively (by precutaneous, pre-incisional paravertebral block) it is combined with an opiate and a non-steroidal anti-inflammatory drug premedication.

In a randomised study of 56 patients, pain scores of less than 0.5 cm on a 10 cm scale were produced, postoperative lung function was preserved and glucose and cortisol responses were significantly unchanged from preoperative values. Evidence that effective perioperative analgesia reduces the incidence of chronic post-thoracotomy chest wall pain was found in a retrospective study of 1000 consecutive thoracotomies. The endpoints of a zero pain score, complete preservation of preoperative lung function and prevention of the stress response to trauma are currently achievable and should be provided for virtually all patients undergoing chest surgery.

Pre-empting pain must be the goal for all those involved in the postoperative care of patients.

The cruel and callous disgrace of inadequate attention by the medical profession towards acute postoperative pain has been highlighted by lay people and doctors alike who have found themselves at the receiving end of a surgeon’s scalpel. Despite lurid descriptions, editorials and surveys, progress in acute pain management has been painfully slow, only recently attention being paid by government agencies (1) and professional organisations (2). Against this apparent stagnation must be set great advances in the understanding of underlying pathophysiological mechanisms of pain.

Major alterations in ventilatory mechanics and pulmonary gas exchange occur in all patients after anaesthesia and thoracotomy because of a decrease in the functional residual capacity (FRC) with minimal changes in the closing volume. Shallow monotonous breathing without periodic maximal inflation occurs as a consequence of the postoperative pain and these changes are most severe in the elderly, the obese, smokers and in those with pre-existing cardiopulmonary disease (3). These factors lead to airway closure during tidal breathing producing hypoxaemia as a result of venous admixture from regional ventilation perfusion inequality and shunting of pulmonary capillary blood through closed alveoli (3). Mucous plugs and infection develop secondarily to alveolar collapse and airway closure.

Postoperative hypoxaemia is associated with complications such as myocardial insufficiency and infarction, pulmonary complications, cerebrovascular accidents, thromboembolism, delirium, delayed wound healing and prolonged convalescence with fatigue and inability to work (4–6). My work and that of others has shown effective postoperative analgesia will improve and even reverse the adverse effects of surgery on the pulmonary mechanics (3,5–8). Such analgesia may reduce the nutritional and immunological consequences of the endocrine–metabolic response to surgical trauma (7,8).

Recent emphasis on a multimodal approach (9) to the treatment of postoperative pain has come about by better understanding of its pathophysiological mechanisms.
Peripheral tissue injury can lead to hyperexcitability and neuronal plasticity in the spinal cord dorsal horn, that is responsible for the maintenance of postoperative pain (9–12). Wall (12) has pointed out that these findings provide a rational basis for pre-emptive measures which might reduce the peripheral neuronal barrage associated with tissue damage and thus reduce or eliminate postoperative pain.

Although recent clinical papers suggest the effectiveness of pre-emptive analgesia (13–16), this has not so far proved to be of major clinical importance (15,17–19), as the inflammatory reaction to tissue damage during operation provides a source of sensory signals that could induce central sensitisation, even if it had been prevented during operation (19). It follows that the postoperative analgesic regimen should be continued until these sensory signals have subsided as a result of normal wound healing. Furthermore, a truly effective analgesic regimen, by preventing the prolonged sequelae of central sensitisation, ought to be able to reduce the incidence and severity of chronic post-thoracotomy neuralgia, responsible for prolonged pain in up to 60% of patients in one survey (20), by preventing or reducing the development of any ‘memory’ of the pain stimulus in the central nervous system (CNS). This concept has never been tested clinically.

We undertook a review of the effects of a continuous extrapleural intercostal nerve block balanced analgesic regimen on 1000 consecutive patients who underwent a posterolateral thoracotomy at the Bradford Royal Infirmary.

We have previously demonstrated the effectiveness of a continuous extrapleural intercostal nerve block for post-thoracotomy analgesia (5,21). As the paravertebral space is catheterised just before chest wall closure this technique is unable to provide intraoperative analgesia. In order to extend this method of pain relief into the intraoperative period we commenced the block with pre-incisional percutaneous paravertebral injection of local anaesthetic. In a randomised study we assessed the efficacy on postoperative pain and pulmonary function of pre-emptive analgesia in conjunction with postoperative extrapleural continuous intercostal nerve block and rectal diclofenac compared with on-demand opiates.

**Postoperative acute pain study**

**Study design**

All patients undergoing elective thoracotomy who were able to give informed consent were admitted to the trial. The study was approved by the hospital ethics committee. Before operation, patients were instructed in the use of a hand-held spirometer and a linear visual analogue scale for pain assessment. Those who were treated with non-steroidal anti-inflammatory drugs (NSAID) and opiates before operation, and those who had an additional incision or procedure were excluded. Also excluded were patients with a known allergic reaction to anti-inflammatory drugs, a history of peptic ulceration, impaired renal function and those with spontaneous bleeding tendencies. All patients had standard general anaesthesia using a double lumen endobronchial tube and single lung ventilation.

The patients were allocated by random permuted blocks to one of eight groups (Table I). Premedication was administered 1 h before the estimated time of surgery. The non-steroidal anti-inflammatory premedication was diclofenac sodium (100 mg) given in the form of a suppository (Groups 1, 2, 5, 6). The opiate premedication used was morphine sulphate 10 mg intramuscularly (Groups 1, 2, 3, 4). Pre-incisional paravertebral blockade (Groups 1, 3, 5, 7) using 10 ml of 0.5% bupivacaine was performed at the proposed level of incision with the patient in the lateral position fully anaesthetised, 10 min before incision. An identical postoperative analgesic regimen was used in all patients throughout the study period of 48 h: continuous extrapleural intercostal nerve block, 12 hourly diclofenac suppositories (100 mg) and on-demand opiates. No attempt was made to withhold requested analgesia. The technique of insertion of the extrapleural cannulas has been described previously (21,22). A bolus injection of 10–20 ml (10 ml to those who had pre-incisional block and 20 ml to those who did not) of 0.5% bupivacaine was first given. This was followed by a continuous infusion of the same solution at a rate of 0.1 ml/kg body weight per hour for 5 days (5).

### Table I. Pre-emptive analgesia used according to groups

<table>
<thead>
<tr>
<th>Groups</th>
<th>Pre-incisional block</th>
<th>Opiate</th>
<th>NSAID</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>2</td>
<td>—</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>3</td>
<td>Yes</td>
<td>—</td>
<td>Yes</td>
</tr>
<tr>
<td>4</td>
<td>—</td>
<td>—</td>
<td>Yes</td>
</tr>
<tr>
<td>5</td>
<td>Yes</td>
<td>Yes</td>
<td>—</td>
</tr>
<tr>
<td>6</td>
<td>—</td>
<td>Yes</td>
<td>—</td>
</tr>
<tr>
<td>7</td>
<td>Yes</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>8</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

**Postoperative assessment**

**Subjective pain relief**

Postoperative pain was assessed by the patients on a 10 cm linear visual analogue scale. Pain scores were recorded at 4 h intervals for the first 48 h after operation. The requirement for additional analgesia was recorded for each patient.

**Objective respiratory function**

Before operation and 12 hourly during the first 48 h after operation, peak expiratory flow rate (PEFR), forced expiratory volume in 1 s (FEV₁) and forced vital capacity (FVC) were measured with the patient in a sitting position using the spirometer. The best of three measurements was recorded. PEFR, FEV₁, and FVC were expressed as a percentage of the preoperative values.
Hormonal response (group 1)

Blood samples for analysis of cortisol and glucose were taken before induction of anaesthesia, at surgical incision, and at 1, 4, 8, and 24 h after surgical incision. Glucose was analysed using a Yellow Springs Glucose Analyser (Clandon Scientific Ltd, Sheffield, UK) and cortisol was estimated by radioimmunoassay (ADL, Amersham, Bucks, UK).

Statistics

The data for each criterion were analysed statistically by the methodology of analysis of variance. Pain data were divided into two 24 h periods and then analysed as above. Pulmonary function data fitted into a general linear model by multiple regression for statistical analysis. Changes in plasma glucose and cortisol were analysed by two-way analysis of variance. A P value <0.05 was taken as statistically significant.

Results

There was no significant difference between the groups regarding age distribution, surgical procedure, sex ratio, smoking habits, body weight, height, and duration of the operation. There were no complications related either to the infusion or the use of diclofenac sodium.

Pain relief (Fig. 1)

The balanced analgesia group (Group 1) had consistently significantly better pain relief (P<0.05) compared with the other groups. Only one patient required a dose of opiate postoperatively (P<0.05). Those patients who had pre-incisional block had better pain relief (P<0.001) and significantly less postoperative opiate requirement in the immediate postoperative period (P<0.02). Premedication with opiates and NSAIDs provided better pain relief only as part of the balanced analgesia regimen. None of the patients in this study required additional opiate analgesia after the first 24 h.

Postoperative pulmonary function (Figs 2–4)

Throughout the study the balanced analgesia group (Group 1) had significantly better pulmonary function than any other group (FEV1, P=0.02; FVC, P=0.04). These patients uniquely maintained their preoperative pulmonary functions postoperatively and often exceeded the baseline values. Those groups of patients who had pre-incisional block had significantly better pulmonary function at 12 h than those without pre-incisional block (FVC, FEV1, P<0.001; PEFR, P<0.02). Opiate premedication and NSAID premedication alone or in combination had no advantage unless as part of a balanced analgesic regimen. Maximal reduction in effort-dependent lung volumes occurred at 12 h in all patients. No pulmonary complications occurred during the 48 h study period.

Plasma levels of cortisol and glucose

There was no significant change in the plasma levels of glucose or cortisol throughout the study period. The mean (SEM) preoperative levels of plasma cortisol and glucose were 452 (41) mmol/l, 5.2 (0.6) mmol/l compared with postoperative maximum levels of 474 (45) mmol/l, 5.91 (0.6), respectively.

---

![Figure 1](https://via.placeholder.com/150)  
*Figure 1. Mean pain scores during the first 48 h after operation. The accumulated pain scores were significantly lower in the balanced analgesia group (Group 1).*
Has postoperative pain been eradicated?

Twelve Hourly F.V.C. Recordings

Figure 2. 'Box and whisker' plot of forced vital capacity (FVC) values as a percentage of preoperative values. Balanced analgesia group (Group 1) maintained their preoperative pulmonary function postoperatively, uniquely exceeding the baseline values.

Twelve Hourly FEV1 Recordings

Figure 3. 'Box and whisker' plot of forced expiratory volume in 1 s (FEV₁) values as a percentage of preoperative values.
Post-thoracotomy neuralgia study (PTN)

Patients and methods

A series of 1000 consecutive thoracotomies were reviewed retrospectively to assess the incidence of post-thoracotomy neuralgia and to identify and evaluate possible risk factors. Post-thoracotomy neuralgia was defined as chest wall pain unrelated to recurrent or persistent tumour or infection, but persisting beyond or recurring 2 months or more after thoracotomy. Insufficient information eliminated 117 patients from the study. For the remaining 883 we analysed age, gender, ethnicity, diagnosis, type and side of surgical procedure, rib removal, reoperation, insertion of chest drain, adjuvant therapy and perioperative analgesia.

Statistics

All data were entered into a Smartware® statistical software database. Most analyses of the significance of the difference in various characteristics were analysed by means of the $\chi^2$ test and contingency tables. Unpaired $t$ tests were used for comparison of means. A $P$ value $<0.05$ was considered significant.

Results (Fig. 5)

PTN was much more common in Asians and Afro-Caribbeans ($P=0.05$). Age and sex were irrelevant. There was a strong association with benign oesophageal disease, less so with malignant oesophageal disease or benign lung disease. The least association was after operations for malignant lung disease. Postoperative adjuvant radiotherapy increased the likelihood of PTN ($P=0.01$). Rib removal at operation reduced it ($P=0.02$). The relationship of acute pain management to the development of PTN was also examined. Cryoprobe neurolysis of intercostal nerves increased the incidence of pain ($P=0.01$), whereas continuous extrapleural intercostal nerve block with bupivacaine, especially when combined with NSAIDs, reduced the incidence ($P=0.01$). NSAIDs reduced chronic pain when used in simple combination with opiates ($P=0.02$).

Figure 4. 'Box and whisker' plot of peak expiratory flow rate (PEFR) values as a percentage of preoperative values.

Figure 5. Chronic pain related to histology and site.
Discussion

Postoperative pain control is finally receiving the attention that it deserves. It is particularly important in thoracic surgery in view of the damaging effects of chest wall pain and the high-risk population coming to thoracotomy. As complete pain control cannot be achieved with a single agent or technique without significant serious side-effects or the need for surveillance, a balanced analgesic regimen is more appropriate (9). 'Pain prophylaxis' is by opiate premedication together with a NSAID followed by pre-incisional afferent blockade, the most effective and logical postoperative technique being continuous paravertebral analgesia. Regular NSAIDs postoperatively are an essential part of pain management.

After thoracotomy, patients are unable or unwilling to inspire deeply. The reduced inspiratory capacity limits the ability to cough effectively. Impaired lung volumes, particularly FRC, ventilatory mechanics and oxygenation are the consequences of this shallow monotonous breathing without periodic maximal inflation (3). Sighing reverses these changes (3). The accepted view of the literature is that these changes in the pulmonary mechanics can be minimised but not prevented (3). Our finding of preserved preoperative lung function postoperatively in Group 1 patients in this study disputes this contention. These patients had a balanced pre-emptive and postoperative analgesic regimen. The effectiveness of total afferent blockade was confirmed by the absence of hormonal and metabolic response to surgery as measured by plasma cortisol and glucose levels. The data presented here suggests that postoperative mechanical abnormalities of pulmonary function are not an inevitable consequence of thoracotomy. Effective postoperative analgesia will improve and even reverse the adverse effects of surgery on the pulmonary mechanics.

The peripheral neuronal barrage resulting from tissue damage can be blocked with pre-incisional regional anaesthetic techniques (13,14,23,24). Afferent blockade must be continued during and for several days after operation to ensure that neuronal plasticity is prevented and not simply delayed (14). Evidence suggests that the peripheral afferent block is more effective than the central block in preventing noiceptive impulses from entering the central nervous system (14,25,26). Paravertebral block would also reduce neurogenic inflammation of traumatised tissues that is dependent on efferent functions of peripheral nerves (24).

The mechanism of action of the continuous intercostal nerve block is via the paravertebral spread of a local anaesthetic agent (27). The results presented here show that a pre-incisional afferent block significantly decreases the intensity of the postoperative pain and more importantly significantly reduces the early loss of postoperative pulmonary function. Postoperative opiate consumption was also less in patients who had pre-incisional paravertebral block. These findings provide further support to the pathophysiological mechanism of pain proposed by Woolf (10) and Woolf and Thompson (11).

Small doses of opiates given before incision prevent central sensitisation by diminishing the sustained hyperexcitation of the central nervous system caused by intraoperative painful stimuli (12,25,28), whereas suppression of established neuronal hyperexcitability requires very large doses (12). In our study, opiate premedication was found to minimise the loss of postoperative lung function and was effective in reducing the immediate postoperative pain only when it was combined with a NSAID premedication.

Suppression of prostaglandin synthesis is probably the basis of the analgesic mechanism of action of NSAIDs (29). Prostaglandins alone are weak stimulators of afferent pain-transmitting nerves, but they facilitate the response to other stimuli (29). Total afferent blockade is not likely to be achieved by prostaglandin synthesis inhibition, and thus NSAIDs have a synergistic effect with other analgesics (29). To prevent prostaglandin-mediated sensitisation of nociceptors during surgery it seems logical to administer NSAIDs prophylactically and then to maintain them postoperatively (30). In the literature, pretreatment with NSAIDs has been found to provide variably effective postoperative analgesia. We were unable to demonstrate any advantage of NSAID premedication in respect of postoperative pain and pulmonary function unless it was part of the balanced analgesic regimen.

The immediate postoperative period is a potentially high-risk period for the occurrence of hypoxaemia which may be persistent or episodic. Persistent hypoxaemia is due to ongoing abnormalities in pulmonary mechanics induced by operation, while the episodic hypoxaemia occurs exclusively during sleep and is often opiate induced in susceptible individuals (31). Because of the deleterious effect of hypoxaemia on cardiac, neurological and psychiatric status of the patients, systemic opiates should no longer be used as the mainstay of treatment in the postoperative period (31). Furthermore, a significant proportion of postoperative pain is caused by the pain arising from chest drains transmitted via the sympathetics from the pleura and Aδ and C fibres in the intercostal nerve. As opiates are primarily just C fibre inhibitors, pain due to the chest drains would not be expected to be prevented by reliance upon this method of analgesia (32). Regional analgesia is logical and more effective.

Epidural techniques using either narcotic or local anaesthetic agents provide effective analgesia and improve respiratory mechanics (33), but are difficult to apply to large numbers of surgical patients because of the difficulty in providing sufficient staff for the necessary monitoring. These limitations would be acceptable if a profound afferent block was being effected. Unfortunately, this is not the case for lumbar epidural blockade with 26.9 ml of 0.5% bupivacaine, despite dermatomal analgesia, results in suppression of somatosensory evoked potentials in only 50% of patients (26). This is probably the explanation for the failure of epidural techniques to prevent stress responses in anything more rostral than lower abdominal surgery (9).

Cryoprobe neurolysis of intercostal nerves does not include the posterior primary rami and sympathetic fibres and so does not provide complete postoperative pain relief
and may cause prolonged anaesthesia or dysaesthesia (2,3,34). As repeated multiple intercostal blocks performed postoperatively are painful and time-consuming, continuous infusion techniques are more appropriate. Paravertebral infusion of a local anaesthetic agent effectively blocks not only the intercostal nerves but also the thoracic sympathetic chain and the posterior primary rami which mediate pain from straining of the ligaments of the costovertebral and costotransverse joints and the posterior spinal muscles (3). Unilateral blockade of the sympathetic nervous system is important as it is involved in each stage of the nociceptive response to acute injury (35). Paravertebral block was thought to be comparable to epidural block in respect of pain relief and restoration of pulmonary mechanics (36). We have demonstrated in this study that as part of balanced analgesia beginning pre-emptively it is superior. The side-effects of hypotension after thoracic epidural instillation of local anaesthetic, of urinary retention and the fear of respiratory depression with neuaxial opiates are not a problem (36).

Although there have been some surveys of the problem of post-thoracotomy neuralgia (37), data on this condition remain scant and anecdotal owing to lack of defined diagnostic and therapeutic criteria. Our finding that almost one-quarter of patients (22.3%) were still complaining of pain 2 months after thoracotomy and that 13.9% were still in pain at 12 months, compares favourably with other surveys of this condition.

An increase in incidence of post-thoracotomy neuralgia with cryotherapy has been noted in this study, which is similar to several other studies reported in the literature (2,3,34), and hence only a few enthusiasts continue to advocate its use (2).

In this survey, a large group of patients received continuous extrapleural intercostal nerve blocks with bupivacaine. They were found to have significantly reduced chronic pain (P<0.01); moreover the addition of a NSAID produced a further reduction in the incidence of post-thoracotomy neuralgia (P<0.02). The implication of this is that the afferent barrage on the central nervous system has been prevented and therefore stimulus for dorsal horn hyperexcitability and hence chronic pain avoided (20,38).

The first clear clinical evidence that management of acute pain has a major effect on the development of chronic pain is provided in our findings. The highly effective analgesic regimen of continuous extrapleural intercostal nerve block and NSAIDs prevented not just the acute post-thoracotomy neuralgia but to a significant extent led to the avoidance of chronic pain.

I believe that continuous extrapleural intercostal nerve block used pre-emptively (by percutaneous paravertebral block) and used as part of a balanced analgesic regimen profoundly affects the outcome after thoracotomy. Acute pain is prevented, pulmonary function is preserved and chronic pain is prevented. We have the knowledge and the analgesic agents necessary to prevent postoperative pain. What we need now is logical, rational, and universal application of this information. The principle of an effective afferent blockade as part of a balanced analgesic regimen beginning preoperatively and maintained until wound healing is established deserves to be considered for all surgical procedures.

References


Received 31 August 1994