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# Ipsilateral Shoulder Pain Following Thoracic Surgery

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AGGRESSIVE postoperative pain management following major surgical procedures may play an important role in reducing postoperative morbidity and mortality.[1,2] Epidural opioid analgesia, with or without local anesthetics, has become a standard at many centers for postthoracotomy pain control.[3,4] For most patients, epidural opioid analgesia provides a virtually pain-free convalescence during the early postoperative period.

Unfortunately, not all postthoracotomy patients obtain satisfactory pain control with epidural analgesia.[5,6] This often occurs despite intense analgesia and even anesthesia of the involved sensory dermatomes. Affected postthoracotomy patients frequently will describe pain symptoms involving sites remote from the incisional area, often radiating to the ipsilateral shoulder, upper abdomen, or arm.[5] These symptoms usually are attributed to irritation of the pleural surface by the surgical procedure or by the thoracostomy drainage tubes.

To better characterize the nature of this shoulder pain, 45 patients undergoing posterolateral thoracotomy, with planned postoperative thoracic epidural analgesia were evaluated prospectively for complaints of pain, at sites remote from the incision site, in the immediate postoperative period.

## Case Reports

With the approval of the Clinical Investigation and Human Use Committees of the authors' institution, 45 consenting adult patients scheduled for thoracic surgery were identified on the day prior to surgery. Each subject underwent insertion of a thoracic epidural catheter, between the fifth and seventh thoracic spinous processes, before induction of general endotracheal anesthesia. General anesthesia was induced with intravenous thiopental or etomidate, supplemented with 0.25–0.5 μg/kg intravenous sufentanil. The total dose of sufentanil was limited to less than 1 μg/kg for the entire case.

Anesthesia was maintained with isoflurane, air, and oxygen. Epidural anesthesia was provided with 10 ml 0.25% bupivacaine. Each patient was assigned randomly to receive a continuous epidural infusion containing fentanyl 4 μg/ml, alone or in combination with 0.03%, 0.0625%, or 0.125% bupivacaine at 10 ml/h as part of an ongoing clinical study. All patients, with one exception, had their tracheas extubated in the operating room.

The continuous epidural infusions were adjusted by the nursing staff, under the supervision of the authors' Acute Pain Service, to maintain patient comfort during the postoperative period. Individuals experiencing significant discomfort (pain score ≥5 using a visual analog pain scale in which 0 is no pain and 10 is unbearable pain) received supplemental epidural injections of 1 μg/kg fentanyl, in addition to adjustment of the infusion rate (epidural infusion limits 0–22 ml/h, 0–88 μg/h fentanyl). The epidural infusions were increased to 20 ml/h for pain scores of ≥3, then gradually decreased at a rate of 2 ml/h to maintain a pain score of 1 or 2.

Following surgery, each patient was interviewed and examined by one of the investigators in the postanesthesia recovery area prior to transfer to a critical care ward and again 24 h later. Each patient was questioned as to the presence of pain over the incision site, the severity of the incisional pain, whether they were experiencing pain elsewhere, and whether the pain was mild, moderate, or severe.[7] Patients acknowledging pain in areas other than the incision site

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were asked to describe the location, the quality of the discomfort (sharp, dull, electric, burning, throbbing, or aching), the presence of radiating pain, and the effect of positional changes on the pain. On postoperative day 1, each patient was again interviewed, and any favorable response to interim intervention was noted.

All assessments were made by one of the investigators. The patients and assessors were not blind to the surgical procedure. With the availability of parenteral ketorolac, 10 of the 19 patients complaining of shoulder pain were treated empirically with 15 or 30 mg intramuscular ketorolac every 6 h, following a 30- or 60-mg loading dose. The dose of ketorolac was determined by the patient's age and general medical condition. Shoulder pain severity was assessed immediately before the administration of ketorolac, and at 1 and 24 h after the initiation of ketorolac therapy. When appropriate, the data are expressed as the median (range). Between-group comparisons were performed using the chi-square test and the *t* test for nominal and continuous variables.

Of the 45 patients who underwent a thoracotomy, 19 complained of moderate to severe discomfort at locations remote from the incision site (table 1). In all of the 19 patients complaining of shoulder pain symptoms, the discomfort was localized primarily to the superior/posterior aspect of the ipsilateral shoulder. The discomfort was constant, aching in quality, unrelieved by position change, and was neither aggravated nor relieved by palpation, massage, or deep inspiration. Upon reviewing the similarities among those afflicted, it became evident that a relationship existed between the occurrence of shoulder pain and the transection of a major bronchus (lobectomy or pneumonectomy).

Table 2 illustrates the presence of ipsilateral shoulder pain in 86% of the patients who underwent either lobectomy or pneumonectomy. Only 1 patient out of the remaining 24 undergoing open thoracotomy, without a subsequent lobectomy or pneumonectomy, complained of shoulder pain. Pain scores relating to the incision site, in patients suffering from shoulder pain, were not significantly different from those without shoulder pain. The median postoperative incisional pain score in patients with shoulder pain was 0 (range 0–4) and 1 (range 0–3) at 1 and 24 h, respectively. Shoulder pain symptoms appeared to be unrelated to the epidural analgesic mixture.

Prior to the availability of parenteral ketorolac, interventions to alleviate severe shoulder pain symptoms included the administration of local anesthetic *via* a thoracic epidural catheter (2 patients), supplemental epidural fentanyl injections (2 patients), trigger-point injection (1 patient), instillation of local anesthetic *via* the thoracostomy tubes (1 patient), and supplementation with intravenous morphine (2 patients). None of these interventions effectively eliminated the shoulder pain symptoms.

Good to excellent analgesia and, in one patient, frank sensory anesthesia were obtained over the entire chest wall and extending to the shoulders (C4 dermatome) following supplemental epidural injections of 1% lidocaine. In this same patient, a presumed trigger pint was identified by palpation on the superior border of the trapezius muscle. However, infiltration with 0.5% bupivacaine failed to alleviate the pain. Furthermore, the patient could not sense the insertion of the infiltrating needle secondary to the sensory anesthesia provided by the epidural anesthetic.

With the availability of parenteral ketorolac tromethamine (Toradol, Syntex, Palo Alto, CA) at our institution, it was found that 30–60 mg intramuscular ketorolac or 15–30 mg intravenous ketorolac, beginning in the recovery area and continuing with 15–30 mg intramuscularly every 6 h, completely eliminated the ipsilateral shoulder pain in 8 of 10 patients treated. In one patient (#27), treatment with ketorolac was not instituted until 24 h after surgery. In this individual, ketorolac proved to be only partially effective at alleviating the shoulder pain. Among individuals not treated with parenteral ketorolac, eight of nine patients experienced no change in the severity of their shoulder pain symptoms at the 24-h postoperative evaluation.

**Table 1. Postoperative Shoulder Pain after Thoracotomy**

| Patient No. | Surgery | Shoulder Pain Severity* |
|---|---|---|
| 1 | Wedge | — |
| 2 | Wedge | — |
| 3 | Wedge | — |
| 4 | Lobectomy | Severe |
| 5 | Pleurodesis/wedge | — |
| 6 | Pleurodesis/wedge | Severe |
| 7 | Biopsy of pleural mass | — |
| 8 | Wedge | — |
| 9 | Lobectomy | Moderate |
| 10 | Lobectomy | Mild |
| 11 | Wedge | — |
| 12 | Lobectomy | — |
| 13 | Lobectomy | — |
| 14 | Lobectomy | Severe |
| 15 | Lobectomy | Severe |
| 16 | Lobectomy | Mild |
| 17 | Wedge | — |
| 18 | Wedge | — |
| 19 | Lobectomy | Severe |
| 20 | Wedge | — |
| 21 | Biopsy | — |
| 22 | Wedge | — |
| 23 | Biopsy | — |
| 24 | Lobectomy | Severe |
| 25 | Lobectomy | Moderate |
| 26 | Pneumonectomy | Severe |
| 27 | Lobectomy | Moderate |
| 28 | Lobectomy | Severe |
| 29 | Wedge | — |
| 30 | Wedge | — |
| 31 | Pneumonectomy | — |
| 32 | Lobectomy | Severe |
| 33 | Pneumonectomy | Severe |
| 34 | Biopsy of mediastinal mass | — |
| 35 | Biopsy | — |
| 36 | Biopsy | — |
| 37 | Biopsy | — |
| 38 | Wedge | — |
| 39 | Wedge | — |
| 40 | Pneumonectomy | Moderate |
| 41 | Lobectomy | Moderate |
| 42 | Decortication | — |
| 43 | Lobectomy | Moderate |
| 44 | Lobectomy | Severe |
| 45 | Biopsy | — |

* Patients were asked to grade their shoulder pain as none, mild, moderate, or severe.

**Table 2. Incidence of Shoulder Pain by Surgical Procedure**

| Surgical Procedure | Incidence |
|---|---|
| Pneumonectomy | 3/4 (75%)* |
| Lobectomy | 15/17 (88%)† |
| Wedge resection | 1/15 (7%) |
| Biopsy | 0/8 (0%) |

* $P < .05$ *versus* biopsy and wedge resection groups.

† $P < .001$ *versus* biopsy and wedge resection groups.

## Discussion

Postoperative epidural analgesia provides excellent pain control for the majority of patients undergoing open thoracic surgical procedures. Unfortunately, not all patients achieve satisfactory pain control with epidural analgesics and some often require supplemental systemic pain medication.[5] Exposure to additional systemic opioid carries the potential for increased sedation, cough impairment, respiratory depression, and subsequent pulmonary complications.

As illustrated in tables 1 and 2, postoperative thoracotomy patients may experience pain unrelated to the chest wall incision that is not readily blocked by epidural or systemic analgesics. It was possible to have complete analgesia of the chest wall and still experience shoulder pain symptoms. From the data presented here, there appears to be a close relationship between the shoulder pain and the transection of a major bronchus (lobectomy or pneumonectomy). In all of the patients developing a postoperative pain involving the ipsilateral shoulder, good to excellent analgesia (visual analog pain score $\leq 2$) was provided by the epidural infusion over the incisional area.

There were no significant differences in the incision area visual analog pain scores between patients with shoulder pain symptoms and those without. This implies that the pain fibers conducting this nociceptive input do not travel *via* the thoracic spinal cord. Many clinicians frequently ascribe the shoulder pain to pleural irritation produced by the thoracostomy drainage tube rubbing against the parietal pleural surface. However, a major argument against this reasoning is the absence of shoulder pain among the patients undergoing wedge resection and biopsy procedures. Chest tube placement was standardized for all procedures, one directed apically, and another directed inferiorly toward the posterior diaphragmatic angle. Thus, if pleural irritation by the thoracostomy tubes were the primary source of the shoulder pain, a more random distribution among the operative procedures would be expected. Furthermore, thoracostomy tubes were not placed in the four patients who received a pneumonectomy; however, three of those four patients experienced some degree of shoulder pain in the postoperative period.

The phrenic nerve (C3–C5), innervates portions of the pericardial and diaphragmatic pleural surface and could conduct nociceptive impulses that would not be blocked easily by thoracic epidural analgesia. Surgical disruption of the pleural reflection along the pericardial surface may be a common factor in lobectomy and pneumonectomy procedures and may initiate a nociceptive stimulus *via* phrenic sensory fibers. An argument against this explanation is represented by several patients who underwent biopsy or resection of perihilar masses and failed to experience shoulder pain. Another patient underwent a pericardial dissection during an aborted attempt at a radical pneumonectomy and did not develop shoulder pain. Although the source of the shoulder pain remains unclear, there appears to be a remarkable association between its appearance and transection of a major bronchus.

Prior to the availability of ketorolac, most patients pain was managed unsuccessfully by adjustments of the epidural analgesia, resulting in some cases of considerable distress to the patients and their health care providers. Supplemental systemic opioids failed to alleviate the severity of the shoulder pain but commonly produced sedation and sleep.

The individuals treated with supplemental intravenous morphine reported that their shoulder pain persisted unabated when awake. In an effort to avoid sedation and the potential for respiratory depression, ketorolac tromethamine was administered empirically to several patients complaining of shoulder pain after thoracotomy, resulting in complete relief of their shoulder pain symptoms. Two individuals obtained only partial relief with ketorolac. In one patient, this may have been related to the 24-h delay prior to the initiation of ketorolac therapy following surgery. For ketorolac to be completely effective, early administration may be necessary. However, it is important to recognize that this trial was neither placebo-controlled nor blinded. Controlled clinical trials are needed to confirm the beneficial effects of ketorolac on ipsilateral shoulder pain and to account for interpatient variability.

Thoracic surgical procedures involving the transection of a major bronchus are associated with ipsilateral

shoulder pain, that is not well-controlled with thoracic epidural fentanyl, or fentanyl/bupivacaine continuous infusions. This shoulder pain is variable in intensity and may be severe in many patients. An uncontrolled clinical trial appears to support the early institution of parenteral ketorolac therapy to control these pain symptoms. Future studies are needed to compare the relative efficacy of epidural morphine *versus* fentanyl, with and without ketorolac, on the incidence of shoulder pain following thoracic surgical procedures.

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# High-titer Protamine-specific IgG Antibody Associated with Anaphylaxis: Report of a Case and Quantitative Analysis of Antibody in Vasectomized Men

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PROTAMINE, which is used to reverse the anticoagulating effects of heparin, may cause several adverse reactions, including bronchospasm, pulmonary artery hypertension, and systemic hypotension.[1] The mechanisms underlying protamine reactions are not understood completely and appear to be multifactorial.

Several putative high-risk populations for serious protamine reactions have been identified. One such population is vasectomized men.[2–5] Within a year after vasectomy, 50–60% of men develop agglutinating autoantibodies against spermatozoa[3–6] and 22–30% develop autoantibodies against human protamine.[2,3]

Commercial protamine preparations are made from the sperm of salmon and related fish species.[7] Although protamines of different species can be heterogeneous,[8] fish and human protamines are similar and immunologic cross-reactivity is possible.[4]

We have shown previously that, in protamine-insulin dependent diabetic persons, the presence of either protamine-specific IgE or IgG is a significant risk factor for severe, life-threatening reactions when intravenous

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