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Postoperative Epidural Bupivacaine-Morphine Therapy

Experience with 4,227 Surgical Cancer Patients

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Background: We prospectively studied surgical cancer patients who received epidural bupivacaine-morphine to determine perioperative morphine use, side effects, and complications.

Methods: All study patients received general-epidural anesthesia followed by epidural analgesia with 0.05% or 0.1% bupivacaine and 0.01% morphine at a rate of 5–10 ml·h⁻¹ to keep the dynamic pain score at less than 5 (of 10). Patients were evaluated daily for pain relief, side effects, catheter migration, accidental removal, hypotension, respiratory rate, mental status changes, nausea and vomiting, and pruritus.

Results: Over 4 yr, 4,227 patients (61% women, aged 68 ± 24 yr) were studied. Lumbar epidural catheters (n = 2,248 or 53.18%) were used more frequently than thoracic catheters (n = 1,979 or 46.82%) (P < 0.00001). Most of the patients were discharged to the surgical wards after the procedures (n = 3,001, 71%). Those patients (n = 1,226, 29%) admitted to the surgical intensive care unit, spent 1.2 ± 0.8 days. Epidural catheter failure occurred in 283 (6.3%) patients. Length of epidural analgesia therapy was 6.3 ± 2.6 days. There were three cases (0.07%) of respiratory depression which were treated with oxygen, intravenous naloxone, and by stopping the epidural infusion for 6 h. Hypotension occurred in 126 patients (3%). There were no apparent cases of catheter migration to either the subdural or subarachnoid space. Nausea or vomiting occurred in 929 patients (22%). Pruritus occurred in 930 patients (22%).

Conclusions: Continuous epidural analgesia with 0.05–0.1% bupivacaine and 0.01% morphine is an effective method of postoperative analgesia with a low incidence of side effects, that can be safely administered on the surgical wards with no special monitoring equipment. (Key words: Analgesia: postoperative. Analgesics, opioid: morphine. Anesthetic techniques: epidural. Anesthetics, local: bupivacaine. Pain: postoperative.)

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THE need for adequate postoperative pain management has been advocated in the acute pain management guidelines recently released by the United States Department of Health and Human Services.[#] This document is timely in light of recent findings suggesting that uncontrolled postoperative pain amplifies the neuroendocrine responses produced by surgery.^{**} Moreover, pain has an adverse effect on postoperative cardiopulmonary and immunologic function possibly prolonging patients' recovery.^{**} Epidural anesthesia followed by epidural analgesia with morphine alone has been shown to be safe and effective.¹ Moreover, the high quality of pain control could justify widespread use of epidural analgesia. A decrease in postoperative morbidity could result in shorter stays in the surgical intensive care unit (SICU) and hospital.²

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Both animal³⁻⁵ and human studies⁶ have documented synergistic analgesic effects of epidural bupivacaine and morphine combination therapy. This combination has resulted in better quality of analgesia as demonstrated by a better control of dynamic pain.⁶ However, the use of epidural analgesia with bupivacaine and morphine in the surgical wards is not widely accepted because of potential complications such as hypotension, respiratory depression, catheter infection, and migration of the epidural catheter into the subarachnoid or subdural spaces.⁷⁻⁹ Thus, we evaluated the safety of this postoperative pain control technique in 4,227 cancer patients treated primarily on the surgical wards at Roswell Park Cancer Institute.

Materials and Methods

This study was conducted during a 4-yr period (1989-1993) after Institutional Review Board Approval and written patient consent were obtained. Inclusion criteria included scheduled cancer surgery of the thorax, abdomen, or lower extremities during epidural-light general anesthesia, and postoperative epidural analgesia for at least 72 h postoperatively. Exclusion criteria included preoperative coagulation abnormalities, refusal of insertion of an epidural catheter, postoperative epidural analgesia for less than 72 h, and a history of allergy to morphine or bupivacaine.

Intraoperative Management

All patients received premedication with either oral diazepam or intramuscular midazolam. Upon arrival to the operating room, routine monitors were placed. An epidural catheter was then inserted with the patient in the lateral decubitus position titrating intravenous midazolam and sufentanil for sedation. For patients undergoing thoracotomy or upper abdominal procedures catheters were introduced *via* the T4-T5, T5-T6, or T6-T7 interspace. For those patients undergoing lower abdominal or pelvic procedures, catheters were inserted *via* either the upper lumbar or lower thoracic interspaces. For patients undergoing lower-extremity procedures, catheters were inserted *via* the lower lumbar interspaces. All catheters were tested for intravascular or subarachnoid placement with 3 ml of 1.5% lidocaine and epinephrine $5 \mu\text{g} \cdot \text{ml}^{-1}$ and secured to the skin with sterile reinforced strips of paper tape and a self-adhesive transparent dressing. General anesthesia was induced with thiopental or propofol and sufentanil

at doses not controlled by the protocol. Vecuronium $0.1 \text{ mg} \cdot \text{kg}^{-1}$ was used to facilitate tracheal intubation. Bupivacaine 0.5% was then injected through the epidural catheter in 5 ml increments. Patients with thoracic epidural catheters received 5-8 ml and those with lumbar epidural catheters 10-12 ml, depending upon the number of dermatomes that needed to be anesthetized, assuming that 1 ml of local anesthetic would anesthetize one dermatome. Immediately after the first bolus dose of bupivacaine, a continuous infusion of 0.43% bupivacaine and 0.013% preservative free morphine (4 mg of morphine in 30 ml of 0.5% bupivacaine) was started at $5-8 \text{ ml} \cdot \text{h}^{-1}$ and titrated to maintain systolic blood pressure between 90-140 mmHg. Epidural infusions were continued throughout the duration of the case, regardless of the length of the procedure.

If intraoperative hypertension or tachycardia occurred despite administration of the maximum doses of local anesthetics described above or if the amount of sufentanil required to maintain hemodynamic stability reached $1 \mu\text{g} \cdot \text{kg}^{-1}$ during the first 30 min of surgery, malposition of the epidural catheter was assumed. The continuous epidural infusion was discontinued, and general balanced anesthesia was administered, followed by postoperative patient-controlled analgesia (PCA) with intravenous morphine. The patient was then withdrawn from the study. However, the incident was noted to determine the total incidence of catheter malposition.

Postoperative Pain Management

Upon completion of surgery, patients were transferred to either the postanesthesia care unit or the SICU, where postoperative analgesia was started using a 0.05-0.1% bupivacaine and 0.01% morphine solution at $6-8 \text{ ml} \cdot \text{h}^{-1}$, within 15 min after their arrival. Patients that underwent lung resection or gynecologic procedures received the 0.05% bupivacaine concentrations. The rest of the patients were treated with 0.1% bupivacaine. The therapeutic goal was to maintain a dynamic visual analog pain score (VAPS) (pain during coughing or movement) of less than 5 (as evaluated in a 10-cm visual analogue pain scale, where 0 = no pain and 10 = worse imaginable pain). If patients reported a dynamic VAPS equal to or greater than 5 during the first 6-8 h of treatment, 5-15 ml of 0.25% bupivacaine was administered in 5 ml aliquots to determine proper catheter positioning. If no sensory block developed, as tested by the pin-prick technique, the epidural catheter

was removed, intravenous PCA morphine therapy was begun, and the patient was withdrawn from the study. Conversely, if pain relief was achieved, the infusion rate was increased by $1 \text{ ml} \cdot \text{h}^{-1}$ every 30–60 min until the dynamic VAPS was less than 5. Morphine 2–4 mg intravenously every 1–2 h as needed also was administered to achieve this goal.

For the remainder of the treatment period, patients were evaluated every 2–4 h by the nursing staff for their quality of pain control. The Anesthesiology-based Acute Pain Service was contacted (via telephone) if the dynamic pain VAPS exceeded 4, in which case, patients received intravenous morphine 2–4 mg, and the epidural infusion rate was increased by $1 \text{ ml} \cdot \text{h}^{-1}$ every hour until the dynamic VAPS was less than 5. If no analgesia was achieved within 4–6 h, the epidural catheter was tested again with 10 ml of 0.25% bupivacaine and the same protocol described above was followed. Thus, all patients experienced dynamic pain control throughout the study. Epidural infusions were decreased by $1 \text{ ml} \cdot \text{h}^{-1}$ when dynamic VAPSs remained less than 5 for 12 h, and patients did not request breakthrough intravenous morphine during that same period.

Evaluation and Treatment of Side Effects and Complications

Patients were evaluated daily by the Acute Pain Service and every 2–4 h by the nursing staff for the following side effects or complications:

Respiratory Depression. Respiratory depression was defined as a respiratory rate of less than 10 breaths/min. For patients who exhibited a pattern of decreasing respiratory rates for 4 h, the epidural infusions were turned off for 4 h and they were closely monitored with a pulse oximeter. If the respiratory rate improved and hemoglobin oxygen saturation (SpO_2) remained greater than 95% (room air), the epidural infusion was restarted at $1 \text{ ml} \cdot \text{h}^{-1}$ less than their previous infusion rate. Patients who presented with respiratory rates of less than 10 breaths/min were also monitored by pulse oximeter, and the epidural infusion was turned off for 6 h. Ventilation of these patients' lungs was assisted using 100% oxygen *via* a resuscitative ventilating connected to a face mask until SpO_2 was greater than 95% and intravenous naloxone, 0.1 mg was administered every 5–10 min until a normal breathing pattern was established and patients were fully awake, or until 0.4 mg naloxone had been administered. Follow-up care was provided by nursing staff who evaluated patients every 30 min for 4–6 h. If respiratory depression re-

curred, patients were transferred to the SICU for treatment and closer monitoring.

Mental Status. A sedation scale was used for the evaluation of drowsiness: 0 = alert, 1 = occasionally drowsy and easy to arouse, 2 = frequently drowsy and easy to arouse, and 3 = frequently drowsy and difficult to arouse. Patients at level 2 had their epidural infusions turn off for 4 h and then restarted at $1 \text{ ml} \cdot \text{h}^{-1}$ less than the previous infusion rate. Patients at level 3 had their infusion rates turned off for 6 h, were monitored using a pulse oximeter, and naloxone was administered only if the respiratory rate was less than 10 breaths/min. Epidural infusions were then restarted at $1\text{--}2 \text{ ml} \cdot \text{h}^{-1}$ less than the previous infusion rate.

Nausea and Vomiting. Once adequate functioning of the nasogastric tube was determined (if present), patients were treated with prochlorperazine, 5 mg intravenously over 15 min every 4–6 h as needed.

Pruritus. Patients were asked both to grade their pruritus from mild to severe to determine the need for therapy. Patients with severe pruritus or who otherwise requested medication were treated with 0.1 mg intravenous naloxone followed by 0.2 mg subcutaneously every 2 h as needed.

Hypotension. Hypotension was defined as a blood pressure of less than 90/60 mmHg at any time during therapy or a decrease greater than 30% in the systolic blood pressure recorded on admission. For patients who presented with this clinical picture, the epidural infusion was turned off for 4 h and the source of hypotension evaluated. While the cause (*e.g.*, hypovolemia, extensive epidural blockade, or subdural or subarachnoid catheter migration) was being determined, patients with lumbar and lower thoracic (below T9) catheters received 500 ml crystalloid over 10 min and patients with upper thoracic catheters were treated with dopamine $3\text{--}5 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$. Further therapy was based on evaluation of urine output, specific gravity, central venous pressure, and response to the fluid challenge.

Epidural Catheter Migration. Patients were evaluated for signs of catheter migration into the subcutaneous space (increased use of intravenous opioids associated with no sensory block after a test dose of 0.25% bupivacaine), subdural or subarachnoid catheter migration (sudden and rapid progression of the sensory block with increasing somnolence) as necessary. When there was a clinical suggestion of catheter migration into the subdural or subarachnoid space, the infusion was stopped until patients could be taken to the ra-

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diology suite for definite diagnosis by contrast dye radiographic studies.

Catheter Infection. Catheter insertion sites were evaluated every 24 h by the Acute Pain Service. If frank inflammation was detected during inspection through the transparent sterile dressing, the dressing was removed and appropriate cultures obtained. The epidural catheter was left in place and further therapy was based on progression of the clinical picture. Thus, sterile dressings placed in the operating room were not routinely removed or changed unless they had been partially removed by patient movement.

Data Collection and Statistical Analysis

Demographic data collected included age, sex, success rate, lumbar *versus* thoracic catheter, accidental removal of catheters, patients transferred to the SICU or to surgical wards immediately after surgery, length of SICU stay when applicable, daily epidural and intravenous morphine consumption, rest and dynamic VAPs, length of therapy, and incidence of complications. Values are reported as the mean plus standard deviation and median interquartile range when suitable. Chi-squared tests were used to determine differences between the number of lumbar and thoracic epidural catheters, and the gender distribution of patients. The null hypothesis was rejected at the $P < 0.05$ level. The predicted maximum risks of complications was calculated using the upper bounds of the 95% confidence interval.¹⁰

Results

During the 4 yr, 4,510 patients were enrolled in the study. However, 283 (6.3%) patients experienced intraoperative malposition of their epidural catheters, and were withdrawn from the study. Thus, 4,227 patients were included in the analysis.

Mean age was 68 ± 24 yr. Women (61%) were more frequently treated than were men ($P < 0.00001$). Lumbar epidural catheters ($n = 2,248$, 53.18%) were used more frequently than thoracic catheters ($n = 1,979$, 46.82%) ($P < 0.00001$). Most of the patients were discharged to the surgical wards after the procedures ($n = 3,001$, 71%). However, a large portion of patients ($n = 1,226$, 29%) were scheduled to be admitted to the SICU, where they spent 1.2 ± 0.8 days (table 1).

Patient distribution by site of surgery was 1,268 thoracic (30%), 711 upper abdominal (17%), 1,873 lower

abdominal (44%), and 375 lower-extremity cases (9%). All patients received the same rate of epidural infusion, regardless of the site of epidural catheter insertion.

Patients received epidural analgesia for 6.3 ± 2.6 days (range, 2–19 days). Daily mean epidural doses of morphine were 14.4 ± 2.1 , 12.0 ± 1.3 , 9.6 ± 0.8 , 8.4 ± 0.6 , 7.1 ± 0.3 , and 6.0 ± 0.2 $\text{mg} \cdot \text{day}^{-1}$, respectively. Daily mean breakthrough doses of intravenous morphine were 6.2 ± 2.2 , 4.8 ± 2.8 , 4.0 ± 2.0 , 0, 0, and 0 $\text{mg} \cdot \text{day}^{-1}$, respectively, over the 6 days (table 2).

Nausea or vomiting was experienced by 929 patients (22%), with 790 (85%) patients sustaining only one or two episodes and the rest (139 patients) three or more. Most of the nausea and vomiting episodes occurred during the first 24 h of therapy (92%) when patients first sat up. All patients responded to intravenous prochlorperazine therapy. Pruritus occurred in 930 patients (22%), 40 (4.3%) of whom required therapy (table 3). All episodes occurred during the first 48 h of therapy. Patients responded well to intravenous and subcutaneous naloxone therapy. However, they required several doses for the first 24 h to obtain relief.

One hundred thirty-one patients experienced level 2 mental status changes. They were treated by turning off their epidural infusions for 4 h. Three patients experienced level 3 sedation (table 3). They are described under the respiratory depression section.

There were three cases (0.07%) of respiratory depression (< 10 breaths/min) which were successfully treated as per protocol. Patients adequately recovered after receiving 0.4 mg of naloxone. These three patients continued receiving epidural therapy in the surgical ward without further complications. Pulse oximetry monitoring for the next 24 h failed to show a further decrease of Sp_{O_2} less than 90% in all three patients. Moreover, no transfer to the SICU was required for closer monitoring or further treatment for respiratory depression.

Hypotension occurred in 126 patients (3%), 95 patients in the upper thoracic epidural group, 18 in the lower thoracic epidural group, and the rest in the lumbar epidural group. All hypotensive episodes occurred during the first 24 h of therapy. All patients in the upper thoracic epidural group had undergone thoracic surgery and lung resections. At the time of hypotension they were still being treated in the SICU where dopamine infusions could be easily administered. In all of these thoracic patients, lowering the epidural infusion rate, and optimizing intravascular volume resulted in

Table 1. Demographic Data

Parameter	n	Percentage
Age (yr)	68 ± 24	NA
Sex (F)	2,579	61.0
Lumbar catheters	2,248	53.2
Thoracic catheters	1,979	46.8
Failure rate	283	6.3
To surgical ward	3,001	71.0
To surgical intensive care unit	1,126	29.0
Surgical intensive care unit stay (days)	1.2 ± 0.8	NA
Rest pain score	1 (3)	NA
Dynamic pain score	4 (4)	NA
Duration of therapy (days)	6.3 ± 2.6	NA

Age, surgical intensive care unit stay, and duration of therapy are expressed as mean ± SD. Rest, pain, and dynamic pain scores are expressed as median and interquartile range (in parentheses).

stopping the dopamine infusions within 6 h of therapy, as blood pressure normalized. The rest of the patients were treated successfully by administering crystalloid or colloid therapy and by decreasing the rate of infusion by 1 ml · h⁻¹. No adverse results were attributable to this transient hypotension.

Twenty four patients (0.57%) had infection at the site of catheter insertion. Twelve patients (0.28%) developed purulent secretions that resolved after removal of the epidural catheter. One patient who had a carbuncle near the catheter site, developed a subcutaneous abscess requiring a small (2-cm) incision and drainage at the site of insertion, and antibiotic therapy for staphylococcus epidermidis infection. The rest (11 patients) required no further therapy and were closely observed until removal of catheter and for an additional 48 h.

There were no cases of apparent catheter migration to either the subdural or subarachnoid space despite a mean duration of therapy of 6.3 days. No cases of epidural abscesses associated with the long-term use of the epidural catheters were detected. Catheters were

accidentally removed during mobilization in or out of bed in only 68 (1.6%) patients, and occurred early in the study when nursing staff was less familiar with this therapy. However, because all 68 incidents occurred after 72 h of therapy, information from these patients was included in the final analysis (table 3).

One patient accidentally received 1 g cefazolin epidurally, with no sequelae, and another patient received 20 ml of epidural solution (20 mg bupivacaine and 0.2 mg morphine) over 20 min, with no hypotension or respiratory depression. These two events, which oc-

Table 3. Side Effects and Complications

Event	Incidence (n (%))	Maximum Risk at 95% Confidence (%)
Nausea, vomiting	929 (22)	23.30
Pruritus	930 (22)	23.30
Requiring therapy	40 (4)	5.80
Hypotension	126 (3)	3.54
Sedation		
level 2	131 (3)	3.55
level 3	3 (0.07)	0.20
Respiratory depression	3 (0.07)	0.20
Local inflammation	24 (0.57)	0.84
Purulent secretion	12 (.28)	0.50
No further changes	11 (0.26)	0.47
Abscess	1 (0.02)	0.13
Neurologic injury	0	0.07
Catheter migration	0	0.07
Catheter-related epidural hematoma	0	0.07
Accidental removal of catheter	68 (1.6)	2.04
Mortality	0	0.07

Table 2. Daily Milligrams of Morphine Use

Day	Epidural	Intravenous
1	14.4 ± 2.1	6.2 ± 2.2
2	12.0 ± 1.3	4.8 ± 2.8
3	9.6 ± 0.8	4.0 ± 2.0
4	8.4 ± 0.6	0
5	7.1 ± 0.3	0
6	6.0 ± 0.2	0

Values are mean ± SD.

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curred in the early phases of the study, resulted from our use of the same type of pumps as those used for intravenous infusions. No further accidents occurred after the inception of dedicated epidural infusion pumps clearly labeled "epidural catheter."

Discussion

In 1979, 6 yr after Pert and Snyder's discovery of opioid receptors,¹¹ Wang *et al.* demonstrated the superior analgesic properties of spinal morphine delivery.¹²

Epidural morphine provide more complete analgesia than intravenous morphine PCA.¹³ Current data indicate that use of epidural opioids^{14,15} or combinations of epidural opioids and local anesthetics¹⁶ may improve outcome and decrease hospitalization time.² We elected to administer subanesthetic concentrations of bupivacaine and morphine by continuous infusion to avoid large bolus doses of either drug. Moreover, epidural catheters were placed closer to the site of nociceptor modulation to decrease drug requirements and improve analgesic effects.

There is evidence that postoperative epidural analgesia with morphine can be used with a low incidence of life-threatening complications.¹ However, reports of severe postoperative respiratory depression,^{8,17,18} urinary retention,¹⁹ hypotension,⁷ and epidural catheter migration to the intrathecal or subdural space⁹ have limited the use of postoperative epidural analgesia, particularly outside the critical care setting. All of these studies used epidural opioid analgesia administered by bolus techniques.

Several questions can be raised. How high must the incidence of adverse complications be to justify using epidural catheters, instead of switching to intravenous PCA analgesia when patients are transferred to the surgical wards? Is the incidence of respiratory depression associated with intravenous PCA analgesia lower than that experienced with epidural opioid or local anesthetic analgesia?²⁰ Are there data suggesting that the risk-benefit ratio supports the use of long term postoperative epidural analgesia in the surgical wards?

Epidural Versus Intravenous Patient-controlled Analgesia

It has been demonstrated that the incidence of hypoxemia, as an indicator of respiratory depression, associated with epidural or intravenous PCA morphine

administered to produce the same quality of analgesia is similar.¹⁸ However, patients receiving epidural morphine had more prolonged episodes of oxyhemoglobin desaturations, despite receiving smaller bolus doses than patients studied during the initial trials with the epidural technique. In this study, by Wheatly *et al.*,¹⁸ epidural bolus doses of morphine amounted to 3.6 mg every 6 h ($14.4 \text{ mg} \cdot \text{day}^{-1}$, range 7–18). Ready *et al.*¹ reported an incidence of respiratory depression of 0.2% in 1,106 patients using morphine doses of 7–13 $\text{mg} \cdot \text{day}^{-1}$ adjusted for the surgical site and patients' age. Although criteria for respiratory depression was not defined, a single bolus dose of 3 mg epidural morphine resulted in a normal respiratory rate and oxygen level but high arterial carbon dioxide tension in one of their patients.

These two studies illustrate the difficulty in analyzing existing data regarding respiratory depression because respiratory rate, Sp_{O_2} , arterial carbon dioxide tension, and decreased ventilatory responsiveness to inhaled carbon dioxide all have been used to define this problem. Thus, patients may exhibit normal respiratory rates and Sp_{O_2} values and yet experience high arterial carbon dioxide tension. Conversely, patients may have normal respiratory rates with arterial oxygen desaturation. Current data do not adequately define which of these parameters have the greatest prognostic importance.

Respiratory Depression

In our study we defined respiratory depression as a respiratory rate lower than 10 breaths $\cdot \text{min}^{-1}$. With these criteria, the incidence of respiratory depression was only 0.07%. Based on our favorable outcomes, we continue to use this criterion and to treat patients at risk (*e.g.*, those who are morbidly obese or who have a history of sleep apnea) with more frequent clinical evaluations, prophylactic oxygen, and pulse oximetry.

However, we favor continuous epidural infusions over intermittent bolus for epidural analgesia for the following reasons. First, studies evaluating cephalad migration of morphine in the cerebrospinal fluid suggest that respiratory depression occurs as a result of significant amounts of the drug reaching the respiratory center in the brain stem after the administration of a bolus dose in the lumbar epidural area.^{21,22} Although not tested in our protocol, the concentrations of morphine available for rostral spread in the cerebrospinal fluid in patients receiving continuous infusions of morphine may be lower. This could potentially affect the incidence of respiratory depression and other opioid-

induced side effects. Second, continuous infusions allow for intraoperative use of bupivacaine-morphine which results in excellent analgesia in the early postoperative period. In patients undergoing lower abdominal surgery, this practice has resulted in decrease postoperative analgesic demands suggesting that there may be a value to preemptive analgesia with neuroaxial blockade with local anesthetics.²³ Third, the synergy between bupivacaine and morphine³⁻⁶ reduces the postoperative epidural morphine requirements. This combination has clinically resulted in a better quality of dynamic pain control.⁶

The concurrent use of parenteral opioids, particularly in large doses, and epidural morphine has been implicated as a significant risk factor for delayed respiratory depression.¹ Patients in the study received small doses of intravenous morphine for breakthrough pain with no significant incidence of respiratory depression. This suggests that with dilute infusions, administration of small doses of intravenous morphine may be acceptable therapy in the surgical wards. Alternative modes of therapy include epidural PCA and parenteral nonsteroidal antiinflammatory agents. However, their safety has yet to be confirmed.

Hypotension

The addition of bupivacaine to morphine for postoperative epidural analgesia resulted in a high incidence of hypotension in one study⁷ but few or no episodes in two others.^{6,24} Our low incidence of hypotension (3%) may be related to aggressive fluid management in patients undergoing abdominal and lower-extremity procedures and to the placement of the epidural catheter in the middle of those dermatomes involved in the skin incision. Infusion of lower doses of bupivacaine are required, in contrast to patients having lower lumbar epidural catheters for upper abdominal surgery. Most of the observed hypotensive episodes (95 patients) occurred in patients undergoing thoracotomies and lung resections. Perioperative fluid replacement is traditionally below calculated requirements to prevent postoperative pulmonary edema. The response of all patients to the administration of intravenous fluids underscores the need for adequate perioperative fluid replacement in these patients.

Nausea and Vomiting

Nausea and vomiting occurred in 22% of our patients. Ninety-two percent of these episodes occurred when patients first got out of bed. It has been suggested that

postoperative nausea and vomiting may be due to increased sensory or vagal input from the viscera or to stimulation of the chemoreceptor trigger zone either by the vestibular apparatus or by high concentrations of opioid in plasma or cerebrospinal fluid.²⁵ The pattern of occurrence suggests that activation of vestibular reflexes *via* the eighth cranial nerve may have been the underlying cause in our patients. However, patients may have experienced a contributing effect from early mobilization and morphine migration in the cerebrospinal fluid to the chemoreceptor trigger zone. Nevertheless, all patients responded well to prochlorperazine treatment.

Pruritus

Pruritus was experienced by 22% of the patients, but only 4% (40 of 930) required therapy because of its severity. The incidence of pruritus after epidural or intrathecal opioids may be as high as 100%.²⁶ Opioid-induced pruritus may be caused by the local excitatory effects of high morphine concentrations in the posterior horn of the spinal cord.^{27,28} A more recent study has corroborated this hypothesis by demonstrating that the medullary dorsal horn (the brainstem homologue of the spinal dorsal horn) is the site where morphine acts to produce facial scratching in monkeys.²⁹ This may explain the effectiveness of naloxone in treating morphine-induced pruritus.

Infection

The incidence of infection associated with catheter insertion was also low. Thirteen patients (0.3%) developed purulent secretions at the site of catheter insertion. All patients had the catheters in place for more than 7 days. Catheter removal resulted in control of the local process without further need for antibiotics. Only one of these patients developed a small subcutaneous abscess which required incision and drainage at the bedside, and antibiotic therapy which did not prolong hospital stay. There were no cases of epidural abscesses detected in this study population. The solutions for epidural infusion were and continue to be prepared by the Institute's pharmacy. We are not currently using antibacterial filters during the infusion periods. Despite some patients experiencing disconnections at the junction of the epidural catheter and the connecting hub, it is our policy to continue the infusion therapy after cutting 2-3 cm of catheter (empiric conduct), and reinsert it into a new sterile hub connector. However, the nursing staff and the Acute Pain Service

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members continue to follow these patients very closely for the development of signs and symptoms of epidural abscesses.

Mortality

There were no perioperative deaths associated with the use of this technique. This underscores the need for trained nursing staff to recognize and treat potential life-threatening complications early.

In conclusion, epidural anesthesia and analgesia by continuous infusion of bupivacaine-morphine can be safely used in older patients with a low incidence of complications and bothersome side effects. Both supplemental intravenous morphine dosing and naloxone therapy appear to offer the important benefit of having the ward nursing staff treat breakthrough pain and side effects.

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