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Acute pain management: assessment and management

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INTRODUCTION

Every year, more than 40 million surgical procedures are performed in the United States, most of which result in significant postoperative pain. Apart from its toll in human terms, unrelieved pain has a sizeable economic impact, through its negative effects on clinical outcome. Traditionally, opioids have been the mainstay of postoperative analgesia, although their dose-limiting side effects (e.g., nausea, vomiting, pruritus, sedation, respiratory depression, constipation) are well recognized. Regional anesthesia/analgesia techniques (RA) offer many clinical and practical advantages, are widely used, and are likely to a strongly influence anesthesia/analgesia treatments in years to come. The advantages gained from the use of RA techniques can be even greater when it is used as part of a multimodal approach to therapy.

IMPROVING PAIN MANAGEMENT, IMPROVING OUTCOMES

Multimodal therapy may include combinations of a variety of agents, such as local anesthetics, opioids, nonsteroidal anti-inflammatory drugs (NSAID), selective cyclooxygenase (COX-2) inhibitors, acetaminophen, and alpha-2 agonists[1-3]. Its effective use is accompanied by a need to consider several relevant issues, such as which drugs to use, and how to combine and administer drug agents over time to achieve continuous pain relief and maximal clinical benefits. In establishing a multimodal treatment plan, one may determine, for example, that combination of RA with a NSAID drug (or alternatively, an opioid or COX-2 inhibitor) may be particularly useful, achieving a lower side effect profile and continuous pain relief. A typical protocol might include a NSAID or COX-2 drug administered preoperatively, followed by a RA technique (e.g., an epidural or regional nerve block) prior to surgery. Postoperatively, the continuous local anesthetic might be combined with non-opioid or opioid drug(s). The addition of a NSAID can reduce the amount of opioid consumed[4-6]. At the same time, improved analgesia is achieved through interruption of nociceptive impulses at multiple sites, central and peripheral, of the pain transmission pathway. At the time of discharge, the transition to oral medications is carefully planned to avoid potential analgesic gaps. Often, different patient populations can benefit from individual specific protocols.

In surgical inpatients, pain management often begins preoperatively, continues intraoperatively, and is extended for a 72-hour period after surgery. A coordinated approach to pain management throughout the perioperative experience is important to elucidate the best methods to combine, administer and time the use of drug agents. Available technologies to provide steady relief of pain through continuous delivery include controlled-release oral drugs or drugs administered by the intravenous, epidural, intrathecal, or transdermal routes, as well as patient-controlled analgesia (PCA), patient-controlled epidural analgesia (PCEA), and regional nerve blocks. Use of oral agents is considered optimal with agents that are dosed once or twice daily. It is well-recognized that more frequent administration is associated with decreased compliance and in turn, a poorer quality of analgesia. With the availability of continuous delivery systems, intramuscular administration of drugs on an intermittent basis is today considered a relatively poor method of pain management.

RA techniques offer continuous pain relief, as well as other clinical benefits that may stem in part from attenuation of the adverse physiological effects of the surgical stress response. The surgical stress response, sympathetically mediated, can have negative consequences on the cardiovascular, pulmonary and endocrine systems. Hypertension, tachycardia and platelet activation can result in adverse cardiac events, (e.g., deep venous thrombosis) or pulmonary embolism. A major

conduction block using local anesthetics can block nociceptive impulses at the surgical site, preventing transmission to the spinal cord. Epidural blockade can prevent impulses from reaching the dorsal horn, and, depending on its level, can also prevent sympathetic outflow (e.g., thoracic epidural anesthesia/analgesia). This can lead to improved outcomes. Reduction of the surgical stress response may reduce major complications such as thromboembolic or cardiovascular events[7], and lead to improved outcomes. A recent review also found that the use of thoracic epidural anesthesia/analgesia with local anesthetic is associated with a significantly earlier return of bowel function[8]. These observations highlight the important role of high quality pain management in improving patient outcomes[9]. The incidence of cardiac or thromboembolic events, or the time of return of bowel function can be taken as surrogate measures of good pain management.

Clinical experience in the use of multimodal therapy, over time, can lead to the evolution of a protocol for pain management which provides optimal analgesia while minimizing undesirable drug effects. The development of an optimal protocol is best achieved through an interdisciplinary approach which incorporates input from members of the clinical care team (surgery, anesthesia, nursing, physical therapy, pharmacy, nutrition)[10]. This helps identify and maximize variables (e.g., better ambulation, greater participation in physical therapy, earlier return of bowel function) that can be used to evaluate outcomes[11]. For example, in orthopedic procedures, the physical therapist plays a role in maximizing outcome by recognizing that the patient is pain-free and encouraging the use of more aggressive physical therapy. A floor nurse can play a role by recognizing that a patient who has had a bowel movement on the first day can be fed orally, facilitating earlier discharge. Continuous quality improvement can be achieved through evaluation of these daily quality indicators, allowing re-examination and adjustment of the protocol to further improve outcome as needed. Ultimately, improvements in clinical care can be realized.

RATIONALE FOR THE USE OF A SELECTIVE CYCLOOXYGENASE INHIBITOR

Effective pain relief with reduced opiate use

It is potentially advantageous to use a COX-2 inhibitor, rather than other NSAIDs, for preoperative medication because of the absence of effects on platelet function. In addition, the synergistic analgesic effects possible with co-administration of NSAIDs and opioids for postoperative pain relief can provide important practical advantages. The expected benefits include a reduction in postoperative opioid requirements, a sustained or enhanced degree of pain relief, and a decreased incidence of adverse effects when lower doses of each drug are used. Indeed, double-blind clinical studies demonstrate that the total dose of opioid can be reduced significantly when NSAIDs and opioids are administered together for the treatment of postoperative pain[4-6]. Moreover, NSAIDs (i.e., ketorolac) are effective in controlling some types of postoperative pain (e.g., thoracotomy pain) that may prove elusive to treatment with epidural opioids or epidural bupivacaine-morphine combinations[16]. It is important to note, however, that these studies failed to show a reduced incidence of adverse effects commonly associated with either NSAIDs or opioids (e.g., nausea, vomiting, gastric irritation, dyspepsia, platelet dysfunction, and renal dysfunction). Concerns over the potential adverse effects of NSAIDs, even when utilized for short periods of time, thus prompted the selection of a COX-2 inhibitor for this study.

RATIONALE FOR THORACIC EPIDURAL ANESTHESIA

A potential key benefit of the use of thoracic epidural anesthesia/analgesia lies in its effects to promote gastrointestinal and bowel motility. This may occur by a variety of mechanisms, including blockade of nociceptive afferent nerves, unopposed parasympathetic efferent nerve activity, blockade of thoracolumbar sympathetic efferent nerves, a reduced need for postoperative opiates, increased gastrointestinal blood flow and systemic absorption of local anesthetics. Through blockade of thoracolumbar sympathetic nerves, while leaving craniosacral parasympathetic nerves undiminished, epidural anesthesia –especially thoracic epidural anesthesia– would be expected to have beneficial effects on gastrointestinal motility.

The use of opiates can have a negative effect on the development of postoperative ileus, a finding observed in both animal and human studies[23,24]. On the other hand, thoracic epidural anesthesia and analgesia with a local anesthetic, especially if opioids are not added, may favorably affect the resolution of postoperative ileus through the substantial reduction or abolishment of postoperative pain, thereby decreasing or eliminating the need for systemic opiates. Additionally, to the extent that increased gastrointestinal blood flow can increase gastrointestinal motility, epidural analgesia may further reduce the duration of postoperative ileus. An increase in gastrointestinal blood flow may also promote anastomotic healing. Systemic absorption of local anesthetic drugs has also been shown to have a positive effect on the resolution of postoperative ileus. Further, epidural anesthesia used intraoperatively, followed by epidural analgesia for postoperative pain, can diminish or completely inhibit the catabolic stress response to surgery occurring below the umbilicus, attenuating cortisol levels and other markers of the catabolic stress response. An important result of this is the inhibition of sympathetic activation, which could potentially result in constipation.

CLINICAL STUDIES

A 1998 review evaluated 16 studies published since 1977 comparing the effects of epidural anesthesia/analgesia with systemic analgesia (e.g., IV opioids via PCA and other delivery systems) on bowel function recovery. In eight studies in which the epidural catheter was placed above T12, bowel function recovered significantly more rapidly when epidural analgesia was used than when systemic analgesia was used. In the remaining eight studies, in which the epidural catheter was positioned at or below T12, or in which the position was not specified, patients who received epidural analgesia or systemic analgesia were equally likely to show a more rapid recovery of gastrointestinal function. In this review, 7 studies were evaluated that compared postoperative gastrointestinal recovery in patients who had received epidural local anesthetics or epidural opioids. Again, in all studies with the catheter placed above T12, gastrointestinal recovery was more rapid with local anesthetics than with opioids. These studies were generally limited by relatively small numbers of subjects and other factors specific to trial design. Nonetheless, these data suggest that thoracic epidural anesthesia used intraoperatively, with thoracic epidural analgesia used postoperatively can have a beneficial effect on postoperative pain and recovery of bowel function after major abdominal surgery. Lumbar epidural blockade was not as consistently effective in this regard. Local anesthetics and local anesthetic-opioid mixtures appeared to be more effective with fewer undesirable side effects than epidural opioids alone[8].

A more recent study not included in the above review evaluated the effect of thoracic epidural anesthesia on the return of bowel function in 40 patients who underwent radical prostatectomy. One group of patients received general anesthesia intraoperatively, followed by intravenous PCA morphine postoperatively. Another group of patients received thoracic epidural anesthesia intraoperatively followed by epidural morphine analgesia postoperatively. The thoracic epidural catheter was inserted at T10/T11 or T11/T12. Patients who received thoracic epidural anesthesia had an earlier return of bowel function, as measured by criteria including first bowel sounds, first flatus, first bowel movement, and first intake of liquids and solids. Intraoperative blood loss was also significantly lower (mean, 34%) in the thoracic epidural anesthesia group. No significant differences were noted in the duration of anesthesia or surgery, the quality of postoperative analgesia, adverse effects or time to discharge. There was no deep venous thrombosis in any patient. These investigators suggested that patients undergoing surgeries that involve greater trauma to the bowel than during radical prostatectomy, (e.g., bowel resection), who may have, potentially, postoperative ileus of greater duration, may benefit to an even greater degree from the use of epidural anesthesia[25].

Anastomotic disruption may be an issue of concern when early bowel movements occur follow colonic surgery, although it was not a significant clinical issue in the pilot study reported here. It has been suggested that continuous infusion of an epidural local anesthetic may lead to an increased risk of anastomotic leakage, although available data do not indicate an increased risk. A recent review of controlled, randomized clinical trials evaluated the incidence of postoperative complications in patients scheduled for colorectal surgery with an anastomosis and who had received postoperative epidural analgesia with a local anesthetic. In twelve trials enrolling a total of 562 patients, anastomotic leakage occurred in 6% of patients receiving postoperative epidural local anesthetic or epidural local anesthetic-opioid mixtures, compared with 3.4% of patients who received epidural or systemic opioid-based analgesia. The authors noted that the number of patients studied to date are relatively few[26]. A retrospective review of patients undergoing gastrointestinal surgery over a period of 12 years also found a very low incidence of anastomotic disruption. In this review, the incidence was higher among patients who had received intravenous opioids than among those who had not[27].

The above studies indicate that, to maximize the advantages available through use of thoracic epidural anesthesia/analgesia, the location of the epidural catheter and the use of a local anesthetic perioperatively are of key importance. The clinical benefits obtained include decreased morbidity and potential cost savings. A lower incidence of ileus is associated with a higher level of patient comfort, and decreased use of nasogastric intubation and intravenous hydration. Cost savings are associated with a lower need for additional nursing care and laboratory tests as well as shorter lengths of stay. A 1990 study estimated that the prolongation of hospitalization due to ileus costs $1,500 per patient per day, or $750,000,000 annually nationwide. Cost estimates for the current day would expected to be much higher[28].

NEW TECHNIQUES IN POSTOPERATIVE ANALGESIA: PERIPHERAL NERVE BLOCKS

The major advantage of multimodal pain control derives, at least partly, from the use of RA techniques. Both epidural and peripheral nerve block RA techniques are a focus of the multimodal approach. Compared to intravenous and epidural PCA, RA provides postoperative analgesia that is both effective and specific to the site of surgery. Peripheral neuronal blockade, when combined with long-acting local anesthetics can provide excellent anesthesia and postoperative analgesia through a single technique. In addition, continuous neuronal blockade can be achieved by infusion of a local anesthetic through a perineural catheter. This extends analgesia even longer, beyond the duration of a single injection. In practice,

optimal utilization includes the use of rescue analgesia (e.g., intravenous PCA) in addition to the continuous RA technique employed, to protect against breakthrough pain that may result from accidental dislodgement of the catheter. Overall, however, clinical experience with these techniques demonstrates a very high degree of patient and physician satisfaction. This section presents practical guidance on use of a few peripheral nerve block techniques for common surgical procedures. Further detailed information on these and other techniques is available online (The New York School of Regional Anesthesia; *www.NYSORA.com*).

PARAVERTEBRAL BLOCK

Paravertebral blockade, a somatic block of the mixed nerve just distal to the intervertebral foramina, provides a unilateral sympathetic, sensory and motor block and is an excellent choice for thoracic, chest wall or breast surgery. In particular, thoracotomy often results in severe postoperative pain that may be difficult to control. Use of a paravertebral block can be an excellent alternative to the postoperative use of opioids, which can lead to respiratory depression, or thoracic epidural analgesia, which may lead to hypotension. In addition, the unilateral blockade of intercostal muscles at the chosen level can promote ventilation and facilitate mobilization of secretions. Paravertebral blockade is also useful for other procedures, including total mastectomy, axillary dissection, minimally invasive cardiac surgery, ventral or inguinal hernia repair and iliac crest bone graft.

CONTINUOUS INTERSCALENE BRACHIAL PLEXUS BLOCK

This technique is useful for several types of shoulder surgery, including arthroscopy, rotator cuff repair and, in particular, shoulder replacement surgery. It is also indicated for postoperative pain management. The continuous interscalene technique is an advanced technique and requires a considerable experience level with single injection interscalene brachial plexus block. Compared to single injection interscalene block, in the continuous technique the needle is inserted at a much more acute angle to the skin, 45 *vs* 90°, to facilitate insertion of the catheter.

Clinical experience indicates that with adequate volume of local anesthetic, twitches of the deltoid, arm or forearm muscles are all reliable, and result in equally successful procedures. With intermittent aspiration for blood, 30-45 mL of local anesthetic is injected. At this location, frequent aspiration is crucial to prevent inadvertent intravascular injection. Once the local anesthetic is injected, the catheter is carefully inserted 5 cm beyond the tip of the needle.

For continuous infusion of local anesthetic to manage postoperative pain, the use of 0.2% ropivacaine 4-5 mL/h with 2 mL PCA bolus every 20 min. is suggested. Alternatively, one may bolus with 0.2% ropivacaine, 20 mL and remove the catheter at this time. For many patients, this provides excellent analgesia of very long duration. The duration of the block may be extended up to 70% longer than would otherwise be observed and can allow early discharge for ambulatory surgery patients. In a pilot study, after open shoulder surgery using continuous interscalene block anesthesia, patients were discharged with a disposable, fixed-rate controlled infusion pump for ambulatory recovery at home, and visited by a home health nurse for 3 days. This pump delivered a 72 h infusion of ropivacaine 0.2% at 10 mL/h. Patient satisfaction with this technique was extremely high[37].

INFRACLAVICULAR BRACHIAL PLEXUS BLOCK

Continuous or single injection infraclavicular brachial plexus block can be used for any type of surgery on the hand, wrist, elbow or distal arm, for postoperative pain management, and for pain management for elbow or wrist rehabilitation therapy. The infraclavicular approach to brachial plexus block is well-suited to the insertion of a catheter and a continuous infusion, as the needle insertion site is located on the upper chest and the catheters do not kink. In addition, the catheter insertion site is easily approachable for maintenance and inspection, and inadvertent catheter removal is much less likely than with interscalene, supraclavicular or axillary approaches, because the brachial plexus is encountered at a relatively deep location. As with other continuous RA techniques, continuous infraclavicular brachial plexus block is an advanced technique, and is recommended for those who have first mastered the single injection technique.

COST-EFFECTIVENESS ISSUES

In clinical settings, uncontrolled pain must be dealt with as an urgent, immediate concern by skilled staff at any time it may occur, and this is associated with inherent added costs. Monitoring costs are higher for patients who are in the ICU, are receiving individual nursing care, or are being monitored with pulse oximetry. On the other hand, frequent patient monitoring by an acute pain management nurse greatly facilitates effective pain control, which contributes to improvement in patient outcome, and in turn, appropriate hospital bed utilization. A higher degree of patient participation in activities such as physical therapy, ambulation and pulmonary toileting can improve recovery and directly impacts patient satisfaction. For example, the patient's ability to complete incentive spirometry could be beneficial in preventing the development of postoperative pneumonia. A dedicated nursing service can bolus epidural catheters as necessary, allowing the patients to achieve a level of comfort to allow participation in such

chores. Hospital bed utilization can be improved if fewer patients require a high degree of monitoring.

CONCLUSIONS

Pain management delivered through a nursing-based model can provide important benefits to the pain management service, to the institution, and ultimately to patients. Excellent postoperative pain management is best achieved through frequent, periodic assessment and reassessment of the patient's comfort level and side effects. It is a natural step to expand the traditional role of nurses, providing care and advocacy for the patient, to include clinical pain management. Unlike physicians, nurses provide continual care to the patient, are present around-the-clock, and have a greater awareness of subtle changes in the patient's status. A nursing-based acute pain management model allows a greater degree of control over the adjustment of medications to optimize the patient's level of analgesia and reduce the incidence of side effects, and is expected to produce more satisfactory outcomes. In evaluating the total cost of therapy, the quality of analgesia and incidence of side effects are important variables, highlighting the potential significance of utilizing a more cost-effective nursing-based model for pain management. In addition, optimal postoperative pain management may significantly improve outcome measures. Improvements resulting in earlier return of bowel function, earlier oral feeding, earlier aggressive physical therapy, greater participation in daily activities, or potential reductions in post-surgical complications can contribute favorably and significantly both to costs and to patient care.

In clinical practice, an interdisciplinary team approach realized through synergistic relationships between departments of surgery, anesthesiology, nursing and pain management is key to the adequate treatment of postoperative pain, providing for better integration of care. The attainment of patient treatment goals and optimal outcomes requires input and participation by the patient, physician, primary caregiver, and, often a specially trained nurse[41]. Within this context, aggressive pain management through use of a nursing-based model often leads to better pain relief for the patient, resulting in greater participation in daily activities, greater patient satisfaction, and decreased health care costs.

REFERENCES

1. Horlocker TT, Hebl JR, Kinney MA, et al. Opioid-free analgesia following total knee arthroplasty– a multimodal approach using continuous lumbar plexus (psoas comparatment) block, acetaminophen, and ketorolac. Reg Anesth Pain Med 2002;27:105-108.
2. Rosaeg OP, Krepski B, Cicutti N, et al. Effect of preemptive multimodal analgesia for arthroscopic knee ligament repair. Reg Anesth Pain Med 2001;26:125-130.
3. Brodner G, Van Akren H, Hertle L, et al. Multimodal perioperative management– combining thoracic epidural analgesia, forced mobilization, and oral nutrition reduces hormonal and metabolic stress and improves convalescence after major urologic surgery. Anesth Analg 2001;92:1594-1600.
4. Gillies GW, Kenny GN, Bullingham RE, et al. The morphine sparing effect of ketorolac tromethamine. A study of a new, parenteral nonsteroidal anti-inflammatory agent after abdominal surgery. Anaesthesia 1987;42:727-731.
5. Grass JA, Sakima NT, Valley M, et al. Assessment of ketorolac as an adjuvant to fentanyl patient-controlled epidural analgesia after radical retropubic prostatectomy. Anesthesiology 1993;78:642-648.
6. Sevarino FB, Sinatra RS, Paige D, et al. The efficacy of intramuscular ketorolac in combination with intravenous PCA morphine for postoperative pain relief. J Clin Anesth 1992;4:285-288.
7. Kouraklis G, Glinavou A, Raftopoulos L, et al. Epidural analgesia attenuates the systemic stress response to upper abdominal surgery: a randomized trial. Int Surg 2000:85:353-357.
8. Steinbrook RA. Epidural anesthesia and gastrointestinal motility. Anesth Analg 1998;86:837-844.
9. Sartain JB, Barry JJ. The impact of an acute pain service on postoperative pain management. Anaesth Intensive Care 1999;27:375-380.
10. Miaskowski C. Monitoring and improving pain management practices. A quality improvement approach. Crit Care Nurs Clin North Am 2001;13:311-317.
11. Henriksen MG, Jensen MB, Hansen HV, et al. Enforced mobilization, early oral feeding, and balanced analgesia improve convalescence after colorectal surgery. Nutrition 2002;18:147-152.
12. Kehlet H, Mogensen T. Hospital stay of 2 days after open sigmoidectomy with a multimodal rehabilitation program. Br J Surg 1999;86:227-230.
13. Scott DA, Chamley DM, Mooney PH, et al. Epidural ropivacaine infusion for postoperative analgesia after major lower abdominal surgery– a dose finding study. Anesth Analg 1995;81:982-986.
14. Muldoon T, Milligan K, Quinn P, et al. Comparison between extradural infusion of ropivacaine or bupivacaine for the prevention of postoperative pain after total knee arthroplasty. Br J Anaesth 1998;80:680-681.
15. Wilkes NJ, Woolf R, Mutch M, et al. The effects of balanced versus saline-based hetastarch and crystalloid solutions on acid-base and electrolyte status and gastric mucosal perfusion in elderly surgical patients. Anesth Analg 2001;93:811-816.
16. de León-Casasola OA, McClintock E, Harrison P. The addition of intramuscular ketorolac to epidural morphine-bupivacaine for postthoracotomy analgesia. Reg Anesth 1993;18:2S-74.
17. Reuben SS, Connelly NR. Postoperative analgesic effects of celecoxib or rofecoxib after spinal fusion surgery. Anesth Analg 2000;9:1221-1225.
18. Silverstein FE, Faich G, Goldstein JL, et al. Gastrointestinal toxicity with celecoxib vs nonsteroidal anti-inflammatory drugs for osteoarthritis and rheumatoid arthritis: the CLASS study: a randomized controlled trial. Celecoxib long-term arthritis safety study. JAMA 2000;13:284:1247-1255.
19. Bombardier C, Laine L, Reicin A, et al. Comparison of upper gastrointestinal toxicity of rofecoxib and naproxen in patients with rheumatoid arthritis. VIGOR Study Group. New Engl J Med 2000;343:1520-1528.
20. Mukherjee D, Nissen SE, Topol EJ. Risk of cardiovascular events associated with selective COX-2 inhibitors. JAMA 2001;286:954-959.
21. Harris RC. Cyclooxygenase-2 inhibition and renal physiology. Am J Cardiol 2002;89:10D-17D.
22. Masferrer J. Approach to angiogenesis inhibition based on cyclooxygenase-2. Cancer J 2001;7:S144-150.
23. Frantzides CT, Cowles V, Salaymeh B, et al. Morphine effects on human colonic myoelectric activity in the postoperative period. Am J Surg 1992;163:144-148.

24. Weisbrodt NW, Sussman SS, Stewart JJ, et al. Effect of morphine sulfate on intestinal transit and myoelectric activity of the small intestine of the rat. J Pharmacol Exp Ther 1980;214:333-338.
25. Stevens RA, Mikat-Stevens M, Flanigan R, et al. Does the choice of anesthetic affect the recovery of bowel function after radical prostatectomy? Urology 1998;52:213-218.
26. Holte K, Kehlet H. Epidural analgesia and the risk of anastomotic leakage. Reg Anesth Pain Med 2001;26:111-117.
27. de Medicis E, de León-Casasola OA. Anastomotic disruption after epidural or intravenous analgesia: is there a difference? Reg Anesth (in press).
28. Livingston EH, Passaro EP Jr. Postoperative ileus. Dig Dis Sci 1990;35:121-132.
29. Whiteside R, Jones D, Bignell S, et al. Epidural ropivacaine with fentanyl following major gynecological surgery: the effect of volume and concentration on pain relief and motor impairment. Br J Anaesth 2000;84:720-724.
30. Groban L, Deal DD, Vernon JC, et al. Ventricular arrhythmias with or without programmed electrical stimulation after incremental overdosage with lidocaine, bupivacaine, levobupivacaine, and ropivacaine. Anesth Analg 2000;91:1103-1111.
31. Groban L, Deal DD, Vernon JC, et al. Cardiac resuscitation after incremental overdosage with lidocaine, bupivacaine, levobupivacaine, and ropivacaine in anesthetized dogs. Anesth Analg 2001;92:37-43.
32. Rennie MJ, Bennegard K, Eden E, et al. Urinary excretion and efflux from the leg of 3-methylhistidine before and after major surgical operation. Metabolism 1984;33:250-256.
33. Wernerman J, Von der Decken A, Vinnars E. Protein synthesis in skeletal muscle in relation to nitrogen balance after abdominal surgery: the effect of total parenteral nutrition. J Parenteral and Enteral Nutrition 1986;10:578-582.
34. Vinnars E, Bergstrom J, Furst P. Influence of the postoperative state on the intracellular free amino acids in human muscle tissue. Ann Surg 1975;182:665-671.
35. Carli F, Webster J, Pearson M, et al. Protein metabolism after abdominal surgery: effect of 24-h extradural block with local anesthetic. Br J Anaesth 1991;67:729-734.
36. Carli F, Halliday D. Continuous epidural blockade arrests the postoperative decrease in muscle protein fractional synthetic rate in surgical patients. Anesthesiology 1997;86:1033-1040.
37. Klein SM, Grant SA, Greengrass RA, et al. Interscalene brachial plexus block with a continuous catheter insertion system and a disposable infusion pump. Anesth Analg 2000;91:1473-1478.
38. Mather CMP, Ready LB. Management of acute pain. Br J Hosp Med 1994;51:85-88.
39. Coleman SA, Booker-Milburn J. Audit of postoperative pain control: influence of a dedicated acute pain nurse. Anaesthesia 1996;51:1093-1096.
40. Rawal N. 10 years of acute pain services– achievements and challenges. Reg Anesthesia Pain Med 1999;24:68-73.
41. Viscusi ER, Correll DJ, Witkowski TA, Jan R, Bell SD, Schmidt M, Kane HL. The organization of an acute pain management service: an efficient and cost effective model. Department of Anesthesiology, Jefferson Medical College, Thomas Jefferson University, Philadelphia, PA.