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EDITORIAL

Real-world insights on the use of transversus abdominis plane block with liposomal bupivacaine in the multimodal management of somatic versus visceral pain in the colorectal surgery setting

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Introduction

Multimodal approaches are recommended to achieve effective postsurgical analgesia with reduced opioid reliance and are integral to enhanced recovery after surgery (ERAS) protocols. Transversus abdominis plane (TAP) block is a regional analgesia technique commonly used in colorectal ERAS protocols, particularly in the laparoscopic surgery setting. Clinical trial data demonstrate TAP block with liposomal bupivacaine ([LB]; Exparel®, bupivacaine liposome injectable suspension; Pacira Pharmaceuticals, Inc., Parsippany, NJ, USA) to be an effective opioid-sparing approach for controlling pain after colorectal surgery. However, clinical trials poorly address patient factors that might affect outcomes using this approach. This editorial provides the author's personal experience and opinions regarding the optimal use of LB in multimodal management of somatic versus visceral pain and in complex cases, including patients with ulcerative colitis (UC) or other intense visceral inflammatory processes. Such patients are difficult to manage because of visceral pain, chronic opioid use, and increased opioid requirements and may require epidural analgesia and dose escalation. The author's clinical experience suggests that TAP block with LB may not fully address visceral pain but can improve the somatic component, reducing the necessary epidural analgesia dose and allowing for the safe expansion of treatment options to include modalities that control visceral pain. Additional data are needed to further determine how patient factors such as comorbid disease affect efficacy and safety outcomes with this approach.

Multimodal pain management in colorectal surgery

Effective control of postsurgical pain can reduce the likelihood of complications, improve patient satisfaction and recovery, and decrease hospital length of stay and costs.[1–3] Opioid analgesics are central to pain management in many surgical settings.[1] However, their use puts patients at risk for opioid-related adverse events (ORAEs) and chronic opioid use.[4,5] Multimodal analgesia incorporating systemic therapies, regional anesthesia techniques with local anesthetics, and neuraxial anesthesia techniques with or without opioids is recommended as an opioid-sparing approach to manage postsurgical pain[2,6] and is an important component of ERAS protocols for colorectal surgery, aiming to minimize postoperative ileus and sedation.[7,8]

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Epidural anesthesia and TAP block are commonly used regional anesthesia techniques in ERAS protocols for colorectal surgery.[8] Usage of these techniques is still evolving and varies according to the procedure. Although epidural anesthesia is strongly recommended for open colorectal procedures, its risks are generally considered to outweigh its benefits in laparoscopic procedures.[9] In the laparoscopic setting, alternatives such as TAP block, which provides analgesia to the anterior abdominal wall,[10] may be favored over epidural techniques.[8] There is considerable heterogeneity in studies of TAP block in colorectal surgery, and most studies have involved laparoscopic procedures. However, data support effectiveness of TAP block in reducing opioid reliance after colorectal surgery.[7] Advantages over epidural anesthesia include procedural simplicity; preservation of lower limb motor function, urinary function, and hemodynamic stability; and ability to use in patients with contraindications to epidural analgesia such as anticoagulant use.[7] The optimal local anesthetic for TAP block is not currently agreed upon,[11] but available data suggest that LB, a prolonged-release formulation of bupivacaine,[12] may offer improved effectiveness compared with non-liposomal local anesthetic.[13]

Across a variety of procedural settings, surgical site infiltration with LB has been demonstrated to provide analgesia for up to 72 hours with reduced postsurgical opioid consumption.[14,15] Results of a pooled analysis of 10 clinical studies show a similar safety profile for LB and bupivacaine HCl, with no signs of cardiac or central nervous system (CNS) toxicity; the most commonly reported adverse events were nausea, constipation, and vomiting, which are typically associated with opioid use.[16] As with all local anesthetics, LB carries a risk for local anesthetic systemic toxicity (LAST), a potentially life-threatening event that can occur subsequent to accidental intravascular injection.[17] However, the pharmacokinetic profile of LB, namely, the lower peak plasma bupivacaine concentration,[18] suggests that the risk of acute systemic toxicity may be lower than with bupivacaine HCl.

LB in colorectal surgery

In the colorectal surgery setting, LB has been evaluated primarily for local infiltration analgesia,[15,19–22] with two recent studies in TAP block.[13,23] The first, a retrospective cohort study, demonstrated significant reductions in requirements for postsurgical ketorolac and opioids after colorectal surgery in patients receiving TAP block with LB compared with those receiving TAP block with bupivacaine HCl. No significant difference in length of stay, a secondary outcome, was observed.[13] In the second prospective cohort study, patients who underwent laparoscopic colorectal resection with a standardized ERAS protocol and LB as a TAP block and via local wound infiltration experienced significant reduction in pain scores in the postanesthesia care unit and on postoperative day 2, opioid consumption on postoperative day 0, and length of stay compared with a matched cohort treated using the ERAS protocol without TAP block or wound infiltration.[23] In a chart review of laparotomy patients, local wound infiltration with LB was associated with shorter intensive care unit and hospital length of stay compared with the use of continuous thoracic epidural (CTE) anesthesia.[22] However, comparative efficacy and safety data on LB TAP block and CTE are lacking.

Although clinical trials are the gold standard for demonstrating comparative efficacy and safety, they are limited in their ability to address the effects of patient factors on outcomes. In the colorectal surgery setting, patients' pain may be influenced by not only the surgical procedure but also comorbid medical conditions, particularly those that cause chronic visceral pain. A recently published case report by the author and his colleagues[24] suggests that additional patient and clinical factors may need to be considered to optimize postsurgical results when using TAP block with LB in colorectal surgery. Briefly, the case report presented a 24-year-old female with a notably complex medical history, including underlying UC, gastritis, and gastroesophageal reflux disease, and multiple prior procedures (esophagogastroduodenoscopies and colonoscopies) who underwent laparoscopic colectomy that was converted to an open colectomy.[24] A multimodal regimen that included subcostal TAP block with LB (266 mg) following closure of the midline incision and hydromorphone patient-controlled analgesia (0.8 mg) initiated ~5 hours after LB infiltration provided inadequate postsurgical pain control. The patient achieved transient relief (3 hours) with a CTE with lidocaine bolus and subsequent continuous epidural infusion with bupivacaine 0.1%/hydromorphone 10 µg/mL on postoperative day 1. Adequate analgesia was ultimately achieved with an additional 5 mL bolus of bupivacaine/hydromorphone, with subsequent ambulation on postoperative day 3.[24]

Several aspects of the patient's medical history are worthy of consideration. Patients with UC are more likely to have chronic opioid use and high opioid requirements.[25,26] Moreover, UC is a strong predictor of ORAEs.[27,28] Although this patient was not receiving chronic opioid therapy, underlying inflammatory disease may have contributed to increased opioid requirements. Equally important to consider is that patients with UC or other visceral inflammatory disease are likely to have more visceral pain, for which TAP block is generally considered less effective.[29,30]

Although LB has demonstrated efficacy in somatic pain,[13,14,23,31,32] the effectiveness of TAP block with LB in this patient was likely complicated by the underlying UC, and the patient's visceral pain may not have been controlled. Nevertheless, the ability of the TAP block to manage somatic pain would be expected to reduce the needed epidural dose.

Author's updated clinical experience

The author's more recent clinical experience with two additional patients with chronic underlying inflammation further illustrates that TAP block with LB may not fully address visceral pain but can improve the somatic component. The first patient had prolonged abdominal inflammation before surgery and an indolent course of infarcted bowel that presented poorly over 2 weeks and required a return visit to the emergency room after prolonged hospitalization. Computed tomography scans indicated infarcted jejunum. A TAP block with LB and bupivacaine HCl was performed at the onset of surgery. After the procedure, the patient had no tenderness at the abdominal incision but reported significant internal pain, requiring patient-controlled analgesia. The second patient had a history of chronic abdominal pain and opioid use and presented with severe peritoneal inflammation because of perforation, which was not immediately recognized. In response to escalating pain over the course of several days, the patient received TAP and rectus sheath blocks with LB and bupivacaine HCl before an exploratory laparotomy. On postoperative day 1, the area of the abdominal incision was not tender, indicating control of somatic pain, but the patient reported deep visceral pain. The patient received a thoracic epidural rather than a repeat TAP block but still required a significant dose of intravenous analgesic to control pain.

Two additional cases of patients with no acute or chronic inflammatory conditions undergoing elective open hemicolectomies indicate that technique is crucial for achieving optimal results with LB TAP block in colorectal surgery. For each of these patients, there was a desire to minimize or avoid opioid usage, and therefore, TAP and rectus sheath blocks with LB (admixed with 0.25% bupivacaine HCl to facilitate rapid onset of analgesia) were performed post induction utilizing meticulous injection techniques. The first patient received 100 μg of fentanyl on induction, and neither patient received further intraoperative opioids. After surgery, the first patient reported only right shoulder pain and the second patient reported only throat discomfort. These cases exemplify the author's experience with TAP and rectus sheath blocks with LB producing prolonged analgesia and reducing opioid usage when administered in the presurgical period and with proper technique.

Author's recommendations for use of TAP block with LB

Adequate spread of the local anesthetic within the anatomical plane is essential to achieving an effective TAP block.[10] Meticulous placement of the injectate is particularly important to achieve optimal results with LB, which, owing to its viscosity, has more limited ability to spread compared with bupivacaine HCl.[33,34] The importance of optimal infiltration technique to achieving effective analgesia with LB has been well demonstrated in total knee arthroplasty,[35,36] and optimal techniques are evolving in other surgical settings.[37] In TAP block, accurate identification of the anatomical plane and adequate spread of local anesthetic are critical to achieving analgesic efficacy.[10] Whereas clinical experience has shown that good outcomes can be achieved when bupivacaine HCl is deposited in near approximation to targeted nerves, LB will remain where it is deposited because the liposomes are unable to diffuse across tissue planes.[34]

The author's technique of TAP block with LB has evolved with clinical experience and includes bupivacaine bridging using separate syringes for LB and bupivacaine HCl. Initial injection of bupivacaine HCl facilitates visualization of the plane and confirmation of correct needle placement. The injected volume should be sufficient for hydrodissection of the potential space. Subsequently, LB can be injected. Adequate injection volume is essential, and flushing of the tubing with bupivacaine HCl can further ensure optimal deposition of LB. Presurgical administration of TAP block is ideal to minimize ultrasound interference from surgical dressings and subcutaneous emphysema from laparoscopy and to reduce intraoperative opioid requirements while allowing adequate time for the block to become effective before the conclusion of surgery. Efficiency is also critical to minimize any perception of operating room delay.

Infiltration technique may have contributed in part to the lack of efficacy described in the previously published case report.[24] TAP block was administered in the late intraoperative period. In addition, independent laboratory results showed a total plasma LB concentration of <0.2 μg/mL, and physical examination showed no apparent relief of somatic pain. The same patient underwent an additional abdominal surgery 1–1.5 years later and, despite her previous experience, elected to have TAP and rectus sheath blocks with LB instead of a thoracic epidural. The blocks were performed immediately after induction of anesthesia, and the patient had good postsurgical pain control, minimal supplemental opioid requirement, and high satisfaction and was able to engage in conversation. At no time following surgery was a thoracic epidural considered.

In addition to TAP block, an increasing number of alternatives to epidural have become available. However, research on these newer techniques is still evolving, whereas epidurals are supported by extensive research and history.[38] In clinical scenarios for which more extensive abdominal wall coverage or visceral pain relief is needed, a 4-point TAP block or quadratus lumborum (QL) block may be effective.[11,39] Multiple QL block variations have been described.[11] It is thought that spread into the paravertebral space could translate to better relief of visceral pain using QL blocks.[40] However, there is no consensus regarding which infiltration site is optimal with respect to either somatic or visceral pain, and questions also remain regarding dose and spread of local anesthetic. The author's recent experience using a posterior approach to TAP block with extension to the lateral QL block location has been promising with regard to control of somatic and visceral perioperative pain. Comparative studies (eg, QL vs 4-point TAP and QL vs rectus sheath block) and best practices are needed to inform these new approaches, and absent compelling evidence that benefit outweighs risk and cost, clinicians may be resistant to change their approach.

In the previously published case study, pain control and ambulation were ultimately regained with additional bupivacaine HCl.[24] Importantly, LB did not preclude safe use of other treatment options. The prescribing information for LB states that formulations of bupivacaine other than LB should not be administered within 96 hours after LB administration.[12] However, laboratory testing conducted just before epidural placement and again 20.5 hours after the start of the bupivacaine/hydromorphone epidural infusion confirmed that total plasma bupivacaine levels were well below the threshold for potential toxicity.[24]

Conclusion

There is a continued need for measures to counter the prescription opioid epidemic,[41] including opioid-sparing strategies for postsurgical pain management, particularly for patients with an increased risk of chronic opioid use such as those with underlying visceral disease.[5,25,42] An optimal multimodal approach controls pain and minimizes supplemental opioid consumption, which can aid recovery. Although TAP block with LB has demonstrated effectiveness as part of a multimodal pain management approach for colorectal procedures,[13,23] as with any pain management approach, it is important to consider patient medical history. In particular, patients undergoing colorectal surgery may have comorbid inflammatory disease that can complicate postsurgical pain management. UC/indeterminate colitis pain is difficult to manage for several reasons, including the presence of visceral pain, chronic opioid use, poor response to opioids, and high opioid requirements. Although TAP blocks[29,30] and even opioids[43] may be less effective in addressing visceral pain, it is important to note that TAP block with LB does not limit the ability to safely expand treatment options (including epidural bupivacaine) and can be part of an effective multimodal approach when administered using a proper technique, especially during the presurgical period. Because TAP block with LB can address the somatic pain component and thereby reduce the dose needed in epidural analgesia, it should be offered to patients undergoing colorectal procedures, with supplementation as needed with other modalities that can address visceral pain.

Implementation of ERAS protocols has helped to improve patient outcomes in the colorectal surgery setting. Given the expanded options for postsurgical analgesia in ERAS protocols, it is important to address data gaps regarding the comparative efficacy and safety of epidural anesthesia, TAP block, QL block, and rectus sheath block, with or without LB. Further data are also needed to determine how patient factors, such as comorbid diseases, affect outcomes. This knowledge can help to inform Phase IV and pragmatic trials and further guide patient selection for various multimodal pain management protocols.

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