Regional Anesthesia and Analgesia in Critically Ill Patients

A Systematic Review

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Abstract: Regional anesthesia has become invaluable for the treatment of pain during and after a wide range of surgical procedures. However, its benefits in the nonsurgical setting have been less well studied. Regional anesthesia is an appealing modality for critically ill patients, providing focused and sustained pain control with beneficial systemic effect profiles. Indications for regional anesthesia in this patient group are not limited to surgical and postsurgical analgesia but expand to the management of trauma-related issues, medical conditions, and painful procedures at the bedside. Patients in the critical care unit present special challenges to the regional anesthesiologist, including coagulopathies, infections, immunocompromised states, sedation- and ventilation-associated problems, and factors potentially increasing the risk for systemic toxicity. This review is intended to evaluate the role of regional anesthesia in critically ill patients, to discuss potential benefits, and to provide a summary of the published evidence on the subject.

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The practice of regional anesthesia and analgesia in the perioperative period has become widespread and is supported by numerous publications that have demonstrated its feasibility and effectiveness.[1,2]

However, the role of regional anesthetic techniques outside the traditional perioperative arena, including in the critical care setting, has been less well established. This is surprising and represents a major opportunity to impact patient care, as pain control in critically ill patients represents a major challenge. Some level of pain is encountered by nearly all patients in this setting. Furthermore, pain in critically ill patients is often difficult to quantify and is frequently not easily treatable without considerable adverse effects,[3,4] which can be particularly cumbersome in patients where, for example, the ability to use enteral nutrition has important outcome implications. Although a fraction of patients receiving surgery under regional anesthesia is considered critically ill, and many are admitted to an intensive care facility postoperatively, there are still very limited data available on the rate of utilization and outcomes associated with regional anesthetic and analgesic techniques among this patient population and in the critical care environment itself.

This comorbidity-ridden patient population might, in theory, reap beneficial effects of regional anesthesia, given its effectiveness, relative lack of systemic adverse effects, and ability to reduce the adverse systemic effects of pain. However, there is conflicting evidence regarding the potential impact of regional anesthesia on outcomes, including morbidity and mortality, partly because most complications occur very infrequently and are thus not easily quantifiable.[5–10] With a relatively high incidence of adverse outcomes in critically ill patients, the potential impact of regional anesthetics could be profound and, from a research perspective, prove easier to measure and study.

Recent shifts in treatment strategies of the critically ill have become apparent over time, including trends toward maintaining a more lucent state, with daily interruption of sedation and targeted analgesia.[11–14] Regional anesthesia has been recognized as a valuable tool to meet this demand in recent guidelines.[15] Published data (some investigational) suggest additional potential benefits, including improved gastrointestinal and hepatic microcirculation,[16–18] anti-inflammatory effects,[19,20] relaxation of bronchial smooth muscle,[21] and antithrombotic effects.[22]

Given the limited attention that this topic has received in the past and the potential implications that expansion of regional anesthesia in the care of the critically ill might have, we sought to systematically evaluate the available evidence on the utilization of regional anesthesia in the intensive care environment. Therefore, we (1) present the various indications for which regional anesthesia can be of special use in the intensive care unit (ICU); (2) place particular emphasis on issues regarding specific complications, contraindications, and limitations applicable to this special patient group; and (3) briefly recapitulate specific regional anesthetic techniques that may be used in critically ill patients.

METHODS

Literature Search

To locate and retrieve available literature, we accessed Ovid MEDLINE (1966 to March 2009, 2012) and the Cochrane Database. A comprehensive search for "regional anesthesia," "neuraxial anesthesia," and "intensive care" or "critical care," respectively, revealed 159 results in MEDLINE (refer to Table 1 for exact terms allowing for different formulations and spelling), but no results in the Cochrane Database. Only 14 studies were found to actually focus on the practice of regional anesthesia in an intensive care setting. Eight of the articles found included reviews focusing on specific issues concerning critically ill patients (5 articles), ultrasound use (1 article), trauma (1 article) or the subgroup of pediatric patients (1 article).[23–29] We performed qualitative analysis on the retrieved literature, searched through the corresponding references to capture related studies, and expanded our search to also include 63 studies that were not primarily designed for critical care, but nevertheless

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TABLE 1. Search Terms

Search term	((“critical care” [title] OR “critically ill” [title] OR “intensive care” [title] OR “ICU” [title]) OR (“critical care” [MeSH terms] OR “critically ill” [MeSH terms] OR “intensive care” [MeSH terms] OR “ICU” [MeSH terms])) AND (“regional anesthesia” OR “regional anaesthesia” OR “regional analgesia” OR “nerve blocks” OR “nerve block” OR “neuraxial anesthesia” OR “neuraxial anaesthesia” OR “spinal anesthesia” OR “spinal anaesthesia” OR “epidural anesthesia” OR “epidural anaesthesia”)
No. records screened (after duplicates removed)	159
No. records excluded	136
Reasons	Not English (56), unrelated subject (79), retracted (1)
No. full text articles assessed for eligibility	23
No. full text articles excluded	9
Reasons	Unrelated subject (9)
No. studies included in qualitative synthesis	14

represented topics of interest when considering regional anesthesia in the critically ill. Studies were categorized according to the Oxford Center for Evidence Based Medicine–Levels of Evidence system.[30] In Table S1 (Supplemental Digital Content 1, http://links.lww.com/AAP/A51), an extracted summary of recommendations, including level of evidence, is listed. Table S2 (Supplemental Digital Content 2, http://links.lww.com/AAP/A52) details all 77 studies included in this systematic review.

INDICATIONS FOR REGIONAL ANESTHESIA IN CRITICALLY ILL PATIENTS

Surgical and Postsurgical Analgesia in the Critically Ill

Regional anesthesia is frequently utilized in the operating rooms for patients who are subsequently admitted to an ICU. Regional anesthesia has been associated with superior, sustained analgesia, reduced nausea, vomiting and sedation, and decreased requirement of supplemental analgesic medication when compared to opioid-based pain management.[2]

Moreover, the use of regional anesthetic techniques may reduce adverse effects of general anesthesia or systemic analgesia.[4] Furthermore, neuraxial techniques have been shown to preserve or even improve gastrointestinal motility and hepatic and intestinal blood flow.[16–18] Consequently, they may possibly avert acute as well as chronic detriments to the digestive and metabolic system and subsequently lead to improved outcome.

Trauma

The mainstay of regional anesthesia in trauma medicine is intraoperative and postoperative pain control.[31] Many of the experiences originate from battlefield medical care, where regional anesthesia has been applied for evacuation and transport of victims.[32] In civilian trauma medicine, numerous indications have been studied thus far.[33–44] Most of the principles established in the trauma setting are also applicable in intensive care situations for critically ill patients. After thoracic trauma and multiple rib fractures, adequate analgesia is critical to alleviate pain associated with breathing, subsequently improving the patient’s ventilatory mechanics, and possibly averting the need for intubation or shortening the period of mechanical respirator support. Thoracic epidural analgesia,[45] thoracic paravertebral analgesia,[46,47] and continuous intercostal nerve block[48–50] have proven effective for this purpose. However, the use of regional anesthesia in trauma patients warrants attention to careful perianesthetic evaluation and documentation of neurologic function, because the techniques can potentially disguise sensory or motor deficits. Other important issues to consider are those associated with the risk for compartment syndrome.[51] In critically ill trauma patients, the incidence of acute compartment syndrome was reported to be higher than in the general patient population and disturbingly may be associated with a disproportionately high mortality rate.[52] However, a systematic review on the subject by Mar et al[53] indicates no association between regional anesthesia and delayed diagnosis of compartment syndrome.[54] Application of a high level of clinical suspicion and utilization of devices, such as transducer-tipped intracompartmental manometers, despite its clinical limitations, are recommended measures to facilitate the diagnosis of compartment syndrome.[55]

Nonsurgical Analgesia, Sympatholysis, and Other Indications

Similar to the operative patient population, nonsurgical patients in the ICU benefit from sustained analgesia and sympatholysis provided by regional anesthetic techniques. Indications for neuraxial anesthesia comprise conditions in which adequate pain control is often difficult to achieve by systemic analgesia, including pancreatitis,[56,57] neoplasia,[58] neuralgia,[59] or regional pain syndromes.[60,61] The sympatholysis conferred by neuraxial techniques, peripheral blockade, or specific methods such as stellate ganglion blockade is probably a key mechanism for providing vasodilation and improving blood flow. A study by Nygard et al[62] demonstrated increased cutaneous blood flow in the corresponding regions after application of thoracic epidural anesthesia. These properties, with regard to vasodilation and increased blood flow, might be of special importance in patients with peripheral vascular disease,[63] angina pectoris,[64–66] or impaired gastrointestinal circulation. Similarly, rates of perioperative myocardial infarction have been reported as lower in patients who received thoracic epidural anesthesia for major surgery, although the magnitude of this protective effect is unclear.[67–69] Reduction in myocardial oxygen demand, along with dilation of coronary arteries, has been proposed as a causative factor that likely originates from thoracic sympatholysis.[70,71]

Painful Procedures in the ICU

Depending on the location of a planned intervention, peripheral nerve blocks, plexus blocks, neuraxial anesthesia, placement of catheters, or local infiltration should be considered when attempting to manage painful procedures carried out at the bedside. Examples for this include burn treatments,[72,73] wound debridement,[74] chest tube placement or semiflexible thoracoscopy,[75] and procedures involving instrumentation of the upper airway or pharynx.[76–78]

SPECIAL CONSIDERATIONS IN THE CRITICALLY ILL AND IN THE ICU

Some specific characteristics of critically ill patients must be taken into account when considering regional anesthetic techniques, including a number of contraindications related to the patients' multisystem disease. Additional challenges, such as space limitations or patient positioning, may be encountered. Because of subcutaneous edema and anasarca after massive fluid resuscitation, locating the appropriate block site can be complicated by distorted anatomy, increased skin-to-site distance, and impaired ultrasound imaging. Patient positioning can be difficult because of the presence of multiple catheters, tubes, and monitoring equipment. Moreover, special considerations with regard to the maintenance of neuraxial and regional catheters should be applied. Appropriate labeling, fixation, and dressing, along with frequent inspection of catheters, can potentially prevent numerous complications, including administrating route confusions, catheter dislocation or disruption, and infectious complications.[79–81] Subcutaneous tunneling of catheters has been proposed as a potential measure to reduce bacterial invasion from the skin.[82,83]

Coagulopathies

A very common issue is altered state of coagulation, either iatrogenic, hereditary, or secondary, to associated medical conditions, possibly limiting the use of regional anesthesia techniques. Pharmacologic anticoagulation is prominent among critically ill patients because of the presence of numerous risk factors for thromboembolic events, including immobility, surgery-related hypercoagulability, indwelling catheters, and patient-related risk factors, such as advanced age, obesity, or neoplastic disease.[84,85] The appropriate management is outlined in the American Society of Regional Anesthesia (ASRA) guidelines on regional anesthesia in patients receiving antithrombotic or thrombolytic therapy. It is suggested that the same approach to both neuraxial and peripheral nerve blocks be used.[86]

In addition to iatrogenic disorders of coagulation, acquired coagulation abnormalities reflected as thrombocytopenia ($<100 * 10^9 L^{-1}$) or prolonged coagulation time can be seen in up to 30% to 50% and 14% to 28% of critically ill patients, respectively.[87] To date, evidence on outcomes of neuraxial anesthesia or peripheral nerve blocks during coagulopathic states is scarce. Some considerations might be derivable from evidence on patients experiencing iatrogenic anticoagulation, or with parturients suffering from thrombocytopenia associated with the hemolysis, elevated liver enzymes, and low platelet count disease complex (HELLP).[88] However, it is difficult to draw conclusions for critically ill patients with coagulopathy because of different underlying conditions. Thus, performance of regional anesthesia still remains subject to critical weighing of benefits and risks on a case-by-case basis.

Infection and Immunocompromise

There is a high prevalence of infectious states in the ICU,[89] including sepsis and nosocomial infections.[90] Recent studies suggest a relatively low risk of central nervous spread and abscess formation, even in patients showing signs of systemic infection, provided that adequate antimicrobial therapy was initiated.[91,92] Yet, cautious deliberation about the use of regional anesthesia and careful monitoring is recommended, because common signs of neurologic complications, including headache, meningitis, pain, neurologic impairment, and altered state of consciousness, can be concealed in critically ill patients.

Local anesthetics might exert intrinsic bactericidal and bacteriostatic effects, which have been demonstrated in vitro and in animal models.[19,20,93,94] However, no large-scale clinical studies have translated these results into clinical practice.

Immunocompromise is a frequent finding in the critically ill, warranting a conservative approach to regional anesthesia.[95] It should be noted, however, that in deliberately immunosuppressed patients undergoing lung transplantation, thoracic epidural anesthesia has not been associated with elevated risk of infection, even after the catheter has been in place for long periods.[96,97]

Sedation-/Ventilation-Related Problems

Sedation, general anesthesia, and ventilation can pose additional risks to the performance of regional anesthesia in the intensive care patient. The ASRA Practice Advisory on Neurologic Complications in Regional Anesthesia and Pain Medicine recommends avoiding regional anesthesia in heavily sedated patients, except when the benefit clearly outweighs the risk, for instance, in patients with dementia or developmental delays, or to prevent injury by patient movement.[98]

Ventilation-associated changes in distribution of local anesthetics applied by the epidural route have been reported. After epidural injection of lidocaine at cervicothoracic or low thoracic levels, Visser et al[99,100] noticed an increased spread of sensory blockade in cranial or caudad directions, respectively, in subjects breathing spontaneously at 7.5 cm H_2O continuous positive airway pressure, compared with those breathing at ambient pressure. The influence of altered levels of intrathoracic pressure as well as other factors, including patient position, speed of injection, and substance volume on spread of neuraxial anesthesia, should be taken into account in patients requiring respiratory support.[101]

Finally, respiratory motor function can be affected by regional anesthesia, specifically interscalene blocks. The appearance of hemidiaphragmatic paresis, although mostly without clinical repercussions, seems to be relatively independent of technique and local anesthetic volume used.[102,103] Without conclusive studies in the critically ill, special attention should be given to patients with pulmonary comorbidities, including chronic obstructive pulmonary disease, emphysema, or acute lung injury. In this population, hemidiaphragmatic paresis may lead to impaired ability to wean from the respirator and may delay extubation. The risk of this occurrence must be weighed against the negative effects of pain on respiratory mechanics.

Local Anesthetic Systemic Toxicity

Continuous or bolus administration of high dosages of local anesthetics in conjunction with the absence of specific warning signs makes sedated patients in the ICU potentially more prone to local anesthetic systemic toxicity (LAST).[104] In addition, inadvertent injection of local anesthetics into incorrect catheters can lead to systemic toxicity. Details on preventive measures and treatment are outlined in the most recent ASRA advisory.[105,106] Furthermore, special attention should be devoted to the frequent finding of acidosis in critically ill patients, because it is known to potentially aggravate LAST-associated cardiotoxicity.[107]

Electrolytes, Acid-Base Disturbances, and Renal Failure

Electrolyte imbalances or disruptions of the acid-base homeostasis are frequent findings in patients admitted to the ICU. Although these disorders are known to have significant impact on effect and toxicity of local anesthetics,[104] clinical evidence is surprisingly scarce. One study by Al-Mustafa et al[108] found no significant association between onset and intensity of infraclavicular plexus block and serum electrolytes. In another study by Rodriguez et al,[109] axillary plexus block in end-stage renal failure patients did not exert toxicity despite high intravascular concentrations of mepivacaine. Furthermore, ropivacaine metabolism was recently reported to be relatively unaffected in patients with chronic renal failure.[110]

Inadvertent Confusion of Infusion Route

Another important safety prerequisite that often receives little attention is the clear and unambiguous identification of catheters and their locations. The effects of accidental drug injection into the epidural or intrathecal space instead of intravenously, or vice versa, can range from unpleasant to catastrophic.[111] Case reports of these incidents involve epidural or spinal injection of ephedrine, etilefrine, neostigmine, atropine, thiopental, midazolam, vecuronium, suxamethonium, bicarbonate, antibiotics, acetaminophen, potassium chloride, chlorhexidine, and others.[112–115] Most cases were duly recognized and resolved without permanent damage; however, some did lead to permanent paraplegia. Conversely, inadvertent intravenous infusion of epidural drugs can lead to development of LAST with all its consequences (see above).[116] Strategies to prevent these occurrences include, above all, explicit labeling of lines, syringes, vials, pumps, and so on; introduction of noninterchangeable line connectors; and implementation of an organizational culture of safety and error reporting systems.[111,117]

SPECIFIC BLOCKS IN THE ICU

Neuraxial Anesthesia

Epidural catheters are commonly used in patients scheduled to be admitted to the critical care unit. In addition to improving pain control,[7,9] epidural anesthesia has been reported to facilitate weaning from the ventilator and pulmonary improvement after lung surgery, lung transplantation, and thoracic trauma.[45,118] In a recent study regarding sedative effects of epidural anesthesia, Lu et al[119] reported decreased levels of cortical arousal in postsurgical ICU patients receiving epidural lidocaine, as measured by auditory evoked potentials, but no difference on the Ramsay Sedation Scale. Continuous spinal anesthesia has undergone alternating popularity. Although patients at high risk for circulatory failure have been shown to benefit from the superior controllability associated with its use, it might not be feasible in many cases.[120–123]

Peripheral Nerve Blocks

Provided the patient can be positioned for the procedure and no contraindications are present, virtually any peripheral nerve block is applicable in critically ill patients. Yet, special caution is in order if the patient is under heavy sedation, especially regarding the interscalene block.[124] Nerve stimulator and ultrasound imaging are valuable adjuvants for the correct placement of needle and catheter.[29,125]

Possible techniques with particular relevance in the ICU include nerve blocks to the upper or lower extremity, the performance of which has been extensively reviewed in the literature.[126,127] These blocks can be used for pain control after fractures or surgery and painful bed-side procedures or to achieve sympatholysis and increase perfusion to the affected extremity. A number of blocks to the trunk can also be of use. Transversus abdominis plane block has emerged as a useful, albeit controversial, option for postoperative pain control after major abdominal surgery involving laparotomy or laparoscopy. Niraj et al[128] reported satisfactory analgesia and enhanced recovery after using transversus abdominis plane block in the ICU.[129] This block may theoretically be useful for placement of suprapubic bladder catheters or other procedures requiring penetration of the abdominal wall. As mentioned previously, after major insult to the thoracic cavity or the adjacent upper abdomen, regional anesthesia provides both excellent pain control and advantages in respiratory mechanics. Therefore, this may allow for improved spontaneous ventilation and pulmonary rehabilitation. Possible techniques include thoracic epidural anesthesia as well as paravertebral, intercostal, and intrapleural nerve blocks. Although the former 3 appear highly effective to achieve these improvements, the latter is still subject to controversy.[48–50,118,130] To allow for early tracheal extubation and facilitate respiratory rehabilitation, epidural analgesia has reportedly been used successfully over several days after lung transplantation.[131] Similar to epidural anesthesia, continuous peripheral nerve catheters provide prolonged analgesia for patients admitted to the ICU; maintenance of catheters is important and includes observation for signs of infection or bleeding and monitoring of coagulation status. Although infection of a peripheral nerve catheter is a rare event, special attention to this complication is advisable in critically ill patients.[132,133]

Interest in the modality of stellate ganglion blockade has recently surged. Applied for a large variety of vastly different conditions, from chronic pain syndromes to posttraumatic stress disorder,[60] blocking the stellate ganglion provides unilateral sympatholysis to the thoracic, neck, and head regions. However, most significantly for the ICU setting, reports of its successful application include salvage of ischemic limbs in patients with peripheral vascular disease and in the treatment for vasopressor extravasation.[134] In addition, it has been used to reduce vasospasm of intracranial and extracranial arteries after subarachnoid hemorrhage or aneurysm coiling,[135,136] treatment of highly detrimental ventricular arrhythmias, sustained ventricular fibrillation, and electrical storm[137] or cardiac rhythm stabilization after ventricular assist device application.[138]

FUTURE DIRECTIONS

In light of the many advantages regional anesthesia could have in critically ill patients, systematic research is needed to further clarify its effects with regard to efficacy and safety, both in the hospital and over the long term. Although numerous randomized controlled trials and large cohort studies have been performed to study the intraoperative and postoperative effects of various neuraxial and peripheral techniques, only grade 4 or 5 evidence is available for many aspects regarding the application of regional anesthesia or analgesia in the critically ill.

CONCLUSIONS

Regional anesthesia can be useful in the management of a large variety of conditions and procedures in critically ill patients. Although the attributes of regional anesthetic techniques could feasibly affect outcomes, no conclusive evidence supporting this assumption exists to date, and research needs to be directed toward this entity. Given current epidemiologic trends among patients seeking healthcare, specifically increasing comorbidity burdens, the proportion of patients admitted to critical care units is likely to increase significantly in the future, mandating that our specialty expand to meet their needs.[139] Recent findings promote the safe use of most regional and neuraxial techniques in many situations, but further research is warranted to gain a better understanding of their use in the critically ill or injured.

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