Regional anaesthesia in the ICU

VESNA NOVAK-JANKOVIČ

Clinical Department of Anaesthesiology
and Intensive therapy
University Medical Centre Ljubljana, Slovenia
E-mail: vnjankovic@hotmail.com

INTRODUCTION

Intensivists have become more and more interested in the prevention and the treatment of physiological and psychological stress in critical ill patients. Major surgery and major traumatic injury elicit profound physiological changes including hormonal, metabolic and immunological responses. Many patients with a critical illness are in pain. The alleviation of perioperative pain is primarily provided for humanitarian reasons but also to reduce nociception-induced responses, which may adversely influence organ functioning and contributed to morbidity. Although there are only a few studies that scientifically document this problem, the facts are clear that pain is a major problem for patients hospitalised in intensive care units *(1)*.

A database search offers only a few articles regarding regional anaesthesia and critical ill patients. A pain is widely recognised as the so-called »fifth vital sign« and its assessment in the intensive care unit (ICU) can be difficult. Many patients in the ICU are not able to communicate so alternative assessment tools such as physiological responses to painful stimuli, changes of heart rate and blood pressure, grimacing, sedation Ramsay score and so on might be helpful *(2)*.

Regional anaesthesia and analgesia may result in improvements critically ill patient outcomes.

REGIONAL ANAESTHETIC TECHNIQUES

Animal data have shown that blockade of noxious stimuli from the periphery can reduce the phenomenon of spinal cord excitation, and thus reduce pain and analgesia requirements. After tissue injury or inflammation acute pain messages start with the excitation of primary afferent nociceptors and the excitation of the myelinated (A-δ) or unmyelinated neurons (C-fiber) occurred. Afferent input from large and small-fiber activation is balanced in the dorsal horn. Descending pathways (excitatory and inhibitory) modulate pain transduction by primary afferents. Alteration in the balance of these factors can result in inhibition (analgesia) or stimulation (hyperalgesia)*(3)*. Regional anaesthesia and analgesia refers to techniques that use needles, catheters, and infusion devices to deliver drugs in close proximity to peripheral nerves, plexuses, nerve roots, ganglia, or directly into spinal fluid. Regional analgesia often is defined by the impulse-blocking action of local anaesthetic agents. Local anaesthetic agents interfere with voltage-gated sodium channels impeding or eliminating axonal impulse propagation. Drugs may be applied directly to the site of injury or directed to the nerves that subserve the general area of injury. Targets include nociceptors, mixed nerves, plexuses, ganglia and segments of the spinal cord. Local anaesthetic agents remain the first-line agents used in re-

TABLE 1

Drugs used for regional anaesthesia and analgesia.

Anaesthetics and analgesics	Site of action	Anatomic location
Local anaesthetics	Sodium channel blockers	All locations
Opioid analgesics	G-protein opioid receptors	Peripheral, epidural, subarachnoidal
Clonidine	Alpha-2 adrenergic receptors	Subarachnoidal, epidural, peripheral
Neostigmin	Increases acetylcholine	Subarachnoidal, epidural
Midazolam	GABA receptors	Epidural
Ketamine	NMDA receptor antagonist	Epidural

gional analgesia. Adrenaline is often added to local anaesthetic agents to reduce intravenous uptake and to prolong the effects of the block. The alpha 2 agonists have antinociceptive properties and have been used as adjuncts to local anaesthetic agents at various anatomic levels. Clonidine potentiates opioid analgesia when applied neuraxially (Table 1).

Epidural analgesia

Epidural analgesia is probably the regional anaesthetic technique most often used in the ICU. Epidural anaesthesia is defined as the intraoperative use of local anaesthetics and opioids and epidural analgesia is defined as the postoperative use of local anaesthetics or opioids *(4)*. Indications for epidural analgesia in the ICU include chest trauma, thoracic and abdominal surgery, major vascular surgery, major orthopaedic surgery, acute pancreatitis, paralytic ileus, cardiac surgery and intractable angina pain. Contraindications for the placement of epidural catheters are: current sepsis, bacteremia and coagulopathies (Table 2).

Cardiac morbidity is the most common cause of death after major surgical procedures. Thoracic epidural anaesthesia (TEA) with local anaesthetics can produce a selective segmental blockade of the cardiac sympathetic innervations (T1-T5). Excessive activation of the cardiac sympathetic nervous system by surgical stress has been

demonstrated to increase myocardial oxygen demand, while inducing coronary artery vasoconstriction (decreasing supply), thus resulting in clinical correlates of myocardial ischemia such as ST segment changes, angina and disrrhythmias. TEA blunts these adverse effects of surgical stress with increase of blood flow to ischemic regions of myocardium, so TEA thus improves the balance between cardiac supply and demand.

Epidural and to a lesser extent, intraspinal opioid delivery has become a common method for pain control in surgical intensive care. Evidence indicates that the dorsal horn is the site of action for regional opioid activity. Studies indicate that the onset of analgesic action from epidural or subarachnoid opioids is proportional to the lipid solubility of the opioid administered. Hydrophilic opioids are transported in the cerebrospinal fluid stream.

Opioid analgesics

All opioids in clinical use produce analgesia with the same molecular mechanism, binding to G-protein coupled opioid receptors with subsequent inhibition of adenylate cyclase, activation of inwardly rectifying potassium channels, and inhibition of voltage-gated sodium channels, all of which decrease neuronal excitability. A large part of the explanation for pharmacologic differences among opioids lies in the fact that opioids differ in their ability to reach opioid receptors. Epiduraly administered opioids must traverse the dura and arachnoid mater, diffuse through cerebrospinal fluid, traverse the pia mater to reach the surface of the spinal cord, diffuse through the white mater and than the gray mater so reach opioid in the dorsal horn.

Studies demonstrate that the only mechanism by which drugs redistribute from the epidural space to the spinal cord is diffusion through the spinal meninges. The precise mechanism involved in epidurally administered lipid-soluble opioids is a matter of controversy. The blocking of pain by lipid-soluble opioids after epidural administration is more the result of systemic uptake than a direct effects on spinal opioid receptors. Continuous fentanyl infusion as the sole agent for epidural analgesia appears to produce analgesia by systemic uptake and redistribution to brain. Continuous fentanyl infusion produced the same quality analgesia, the same side effects, required the same fentanyl dose and produced the same fentanyl

TABLE 2

Indications and contraindications for epidural analgesia in ICU.

Indications	Contraindications
Chest trauma	Patient refusal
Thoracic surgery	Coagulopathy
Abdominal surgery	Thrombolytic therapy
Paralytic ileus	Increased ICP
Pancreatitis	Sepsis
Intractable angina	Local infection at puncture site
Vascular surgery	Severe hypovolemia
Orthopaedic surgery	Acute haemodynamic instability
Trauma of lower extremities	Obstructive ileus

plasma concentration whether the drug was infused intravenously or epidurally. Approximately 10% more sufentanyl infusion is needed for postoperative analgesia by the epidural than by the intravenous route. Morphine clearly produces analgesia by spinal mechanism whether administered epidurally or intrathecally and it should probably be considered the »gold standard« for spinally administered opioids. Morphine is hydrophilic and spreads quickly in the cerebrospinal fluid and it is therefore able to produce analgesia in thoracic region even when it is injected into the caudal epidural space. Only ¼ as much morphine is required epidurally as intravenously for postoperative pain relief. Morphine remains the drug of choice for epidural administration because its decreased dose, improves pain relief and may diminish serious morbidity and mortality in high risk surgical patients compares with standard parenteral administration. However, spinal pharmacokinetics of these drugs are complex and, in some ways, counterintuitive.

Clonidine is a selective alpha-2 adrenergic agonist with some alpha-1 agonist property (200:1). Clonidine produces analgesia through stimulation of alpha-2 adrenoceptors located in the dorsal horn of the spinal cord. The combined epidural administration of clonidine (1–4 mg kg-1) with a local anaesthetic improves the block and prolongs postoperative analgesia.

Ketamine has recently been utilised in spinal anaesthesia. Ketamine provides deep analgesia by acting as antagonist at the level of NMDA receptors present throughout the central nervous system. Epidural ketamine gives longer lasting analgesia than intramuscular ketamine while the blood levels are similar.

Local anaesthetic agents

Bupivacaine, racemic mixture of two enantiomers is the most commonly used local anaesthetic agents for epidural anaesthesia and analgesia. The dose of local anaesthetic in the thoracic region and in the pregnant, obese and elderly patients is reduced about 15–30%.

Ropivacaine is chemically related to mepivacaine and bupivacaine, but differs in its molecular structure and being the first marketed enantiomeric local anaesthetic.

Ropivacaine is less cardiotoxic than equimolar concentrations of bupivacaine and epidural ropivacaine is less potent than epidural bupivacaine when the two drugs are administered at the same concentration. Nevertheless, higher doses of ropivacaine than bupivacaine are generally required to elicit equivalent anaesthetic effects. Ropivacaine is reported to demonstrate a greater degree of separation between motor and sensory blockade compared to bupivacaine. Ropivacaine provides effective analgesia with minimal motor block and early mobilisation during labour and after surgery.

Levobupivacaine is the pure S-enantiomer of bupivacaine. In preclinical *in vitro* and *in vivo* animal studies, levobupivacaine has demonstrated the potency similar to bupivacaine which exerting significantly less central nervous system and cardiovascular system toxicity (5).

Subarachnoid analgesia

Although subarachnoid anaesthesia is commonly used for many surgical procedures, analgesia from a single injection of local anaesthetics does not last long enough to be useful for postoperative pain relief. The use of continuous subarachnoid analgesia has been reported. Subarachnoid catheters are effective means for delivering medications to the spinal fluid for distribution to the spinal cord. Preservative free nontoxic preparations must be used to avoid the potential for pathologic alteration of the spinal cord. Spinal administration ensures transport of medications to the spinal fluid and reduces the mass of the medication needed. Catheters can be used safely for days to months. The risk for infection is substantial, however *(6)*.

Paravertebral blocks

Paravertebral blocks (PVB) produce unilateral trunk anaesthesia by blocking the segmental nerves of the spinal cord. Thoracic PVB was first performed in 1906 by Selheim and is thus amongst the oldest of local anaesthetic techniques. In 1912 Kappis used lumbar PVB for urological surgery. Eason and Wyatt stimulated renewed interest for PVB when they described the insertion of a catheter into the thoracic paravertebral space (PVS). The new enthusiasm for PVB has occurred to decrease cardiovascular and respiratory effects of central neuraxial blocks, and to decrease side effects associated with general anaesthesia and narcotics. The PVS is bounded by the vertebral body medially, the transverse process and costotransverse ligament superficially and parietal pleura laterally. The lumbar PVS is not continuous with thoracic PVS. The PVS contains the dorsal and ventral rami of the spinal roots as well as sympathetic fibers of the ventral rami. Thus local anaesthetic introduced into the PVS can provide a unilateral motor, sensory and sympathetic block.

PVB can provide anaesthesia and excellent postoperative analgesia for breast surgery, thoracic surgery (lung, rib resections), abdominal surgery, minimal invasive cardiac surgery, rib fractures, and can be used for treatment of chronic pain.

Inadvertent intravascular injection of excessive doses of local anaesthetics can result in toxicity. Because of the close ralationship of the paravertebral space to the parietal pleura, inadvertent needle placement can cause pneumothorax.

Incorrect medial needle insertion can result in epidural or spinal blockade.

Intrapleural analgesia

Intrapleural analgesia may be used for postthoracotomy pain. Its use has also been described following laparoscopic cystectomy, cholecystectomy, herpes zoster and nephrectomy. Intrapleural catheters relly on local anaesthetic spread throughout to intrapleural space and therefore require significant volumes of local anaesthetic. Patinets with chest tubes often drain a significant portion of medication before the medication is delivered to the active site.

Brachial plexus blockade

There are number of approaches to blocking the brachial plexus to provide anaesthesia or analgesia to the upper extremity. The interscalene block involves injecting local anaesthetic immediately lateral to the exiting C6 nerve route. This block provides excellent pain relief to the shoulder and upper arm. Supraclavicular approach for brachial plexus blockade can provide excellent analgesia throughout to entire upper extremity including the shoulder. There is a significant risk for pneumothorax and frenic nerve block is also common with this technique. Axillary block is considered one of the safest approaches to the brachial plexus but axillary approaches do not provide analgesia to the shoulder consistently.

Femoral block and schiatic nerve blocks

Femoral nerve blocks with catheter technique can provide adequate analgesia for the anterior thigh or more distal pain in the saphenous nerve distribution without the haemodynamic changes associated with neuraxial blocks. Sciatic nerve blocks can provide good analgesia to the posterior thigh and the distal lower extremity not in the saphenous distribution.

SURGICAL OUTCOME

Multiple comparisons of neuraxial blockade to general anaesthesia and a recent meta-analysis of these comparisons shows a significant reduction in mortality and morbidity with regional techniques. The first study on this topic suggesting that postoperative epidural opioid use may decrease patient mortality by Yeager *et al.* appeared in 1987 *(7)*. The results of this study showed that intraoperative epidural anaesthesia with local anaesthetics followed by postoperative epidural narcotic analgesia in high risk patients significantly decreased patient mortality, cardiac failure, infections, hospital and physician costs. Raggi *et al.* have shown that a combination of the epidural technique using local anaesthetics intraoperatively and morphine postoperatively offers many advantages. These benefits include inhibition of the surgical stress response, decreased cardiorespiratory depression, blood loss, intubation time and pulmonary infection, thromboembolism, hyperglycemia, hypertensive response, nitrogen sparing, prevention of immunosupression, and enabled earlier ambulation and hospital discharge *(8)*.

Although epidural anaesthesia and analgesia may improve the outcome in high-risk patient population, potential benefits in low-risk population remain poorly defined because of the low rate of morbidity in these patient groups. Significant beneficial effects of epidural analgesia have been observed only for intermediate outcomes not for ultimate patient outcome. Future studies require formation of multicenter study groups and necessitate enrolment of thousands of patients.

However regional anaesthesia is not a panacea, but in the right patients and the right situations it can improve surgical outcome *(9)*.

A more complex , multimodal approach to perioperative treatmant is widely accepted and recommended by many. After colonic operations, combined approach of optimal pain relief with balanced analgesia,enforced early mobilisation,and oral feeding, may reduce the length of covalescence and hospital stay after colonic operations *(10)*. Recovery after abdominothoracic oesophageal resection may be improved by the introduction of intraoperative TEA, postoperative PCEA, earlier extubation,and early mobilisation of the patient *(11)*.

CONCLUSIONS

Nociception is a complicated process and only in recent years have the neural pathways and mediator of pain transmissions been unravelled. Used wisely, the regional techniques, can provide excellent pain control and may have significant role in improving overall patient outcome. Well-conducted regional analgesia offers the best opportunity to provide substantional analgesia without significant central opioid effects. Regional analgesia using single injection regional blocks and continuous neuraxial and peripheral catheters can play a valuable role in a multimodal approach to pain management in the criticaly ill patients to reduce physiologic and psychological stress.

REFERENCES

1. SCHULZ-STÜBNER S, BOEZAART A, HATA S 2005 Regional analgesia in the critically ill. *Crit Care Med 33*: 1400–7

2. SCHULZ-STÜBNER S 2006 The critically ill patient and regional anesthesia. *Current Opinion in Anaesthesiology 9:* 538–44

3. ClaRK F, GILBERT H C 2001Regional analgesia in the intensive care unit. Principle and practice. *In:* Vender J S V, Szokol J W, Murhy G S *(eds)* Critical Care Clinics. Sedation, analgesia and neuromuscular blockers in critical care medicine. W.B. Saunders Company, Philadelphia, London, Toronto etc., p 943

4. LIU S, CARPENTER R L, NEAL J M 1995 Epidural anesthesia and analgesia. Their role in postoperative outcome. *Anesthesiology 82*: 1474–506

5. NOVAK-JANKOVIČ V 2005 Analgesia in major abdomiothoracic surgery. *Liječ Vjesn 127(Suppl.2)*: 6–10

6. STEVENS D S, EDWARDS W T 2002 Management of pain in the critically ill. *In:* Irwin R S, Rippe J M *(eds)* Irwin and Rippe's Intensive care medicine. Fifth edition. Lippincott Williams & Wilkins, Philadelphia, Baltimore, New York etc., p 1732

7. YEAGER M P, GLASS D D, NEFF R K *et al.* 1987 Epidural anesthesia and analgesia in high risk surgical patients. *Anesthesiology 66*: 729–36

8. RAGGGI R, DARDIK H, MAURO A L 1987 Continuous epidural anaesthesia and postoperative epidural narcotics in vascular surgery. *Amer J Surg 154*: 192–7

9. BALLANTYNE J 2001 Does regional anaesthesia improve outcome after surgery. Refresher course lectures. Gothenburg. 9th ESA Annual Meeting, p 41

10. MOINICHE S, BULOW S, HESSELFELDT P *et al.* 1995 Convalescence and hospital stay after colonic surgery with balanced analgesia, early oral feeding, and enforced mobilisation. *Eur J Surg 161*: 283–8

11. BRODNER G, POGATZKI E, VAN AKEN H *et al.* 1998 A multimodal approach to control postoperative pathophysiology and rehabilitation in patients undergoing abdominothoracic esophagectomy. *Anesth Analg 86:* 228–34