Analgesia in thoracic surgery: review

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ABSTRACT

Post-thoracotomy pain is one of the most severe types of postoperative pain. It can last up to 2 months and can become chronic in 30% of patients. Pain relief after thoracic surgery is of particular significance, not only for ethical considerations but also for reduction of postoperative pulmonary and cardiac complications. Because of the difficulty in pain control, many approaches have been suggested, but a multimodal therapeutic strategy that provides a central or peripheral block associated with nonsteroidal anti-inflammatory (NSAID) and adjuvant drugs is now the cornerstone of treatment, offering the possibility of reducing opioid requirements and side effects. Thoracic epidural analgesia with local anesthetics and opioids is regarded as the gold standard treatment for post-thoracotomy pain management because it results in early extubation, better ventilatory mechanisms and gas exchange, decreased incidence of atelectasis, pneumonia and chronic postoperative pain. When epidural analgesia is contraindicated or cannot be performed, other regional techniques of analgesia can be used. An alternative method of providing adequate pain relief is a thoracic paravertebral block: continuous paravertebral infusion of local anesthetic via a catheter placed percutaneously or under direct vision during thoracotomy. This is effective in controlling postoperative pain and in preserving pulmonary function. Other techniques, such as intercostal and interpleural blocks, are rarely utilized, whereas a single shot of intrathecal injection of a hydrophilic opioid, such as morphine, appears to be effective. Cryoanalgesia, which is successful in the immediate postoperative period, has been abandoned for its brief duration and increased incidence of chronic pain.

Key words: Thoracotomy - Analgesia - Postoperative complications - Pain, postoperative - Analgesia, epidural - Anesthetic, local - Analgesics, opioid.

Pain following thoracic procedures can occur in >70% of patients and is considered to be one of the most severe types of postoperative pain. Its sequelae can persist for many months and even years, substantially worsening quality of life. Postoperative analgesia is mandatory not only for ethical reasons but also because it can modulate stress response and can preserve respiratory function. Loss of pulmonary parenchyma and postoperative pain negatively influence chest wall mechanics, thus preventing an adequate postoperative physiotherapy, which is essential in patients at high risk for respiratory and cardiac complications. Reduction in lung function is related to preoperative respiratory function, extension of lung resection and degree of pain. The rate of complications is strictly dependent on successful analgesia, which improves cough, depth of breathing and expectoration, thus reducing the incidence and the degree of hypoxia, retention of secretions, atelectasis, pneumonia and respiratory failure. Overall, postoperative pain is a considerable concern even when using a minimally invasive approach, such as video assisted thorascopic (VAT) procedure. Postoperative analgesia is still necessary because VAT, while less invasive and causing less tissue damage than a normal thoracotomy, does not always reduce postoperative pain, espe-
cially immediately after surgery. Moreover, good analgesia may decrease the occurrence of chronic pain syndrome to a non-negligible rate.6, 7

Pathophysiology of acute and chronic pain

The pathogenesis of thoracotomic pain has many factors involving multiple nociceptive and descending modulatory inputs; thus, an adequate postoperative analgesia cannot be determined from knowledge of the concerned factors. Surgical incision, stretch of ligaments, and placement of rib retractors in intercostal spaces to allow for surgery and pleural manipulation, are traumatic events triggering profound sympathetic and inflammatory responses. The inflammatory response activates peripheral nociceptors that transmit nociceptive signals centrally and initiate a larger inflammatory process, amplifying pain transmission and altering pain sensation through central sensitization. Manipulation of pleura/pericardium and bronchi activates visceral pain through the afferences of the vagus and phrenic nerve that seem to be responsible for shoulder pain.8, 9

This pain is also very difficult to treat in cases where an optimal dermatomical analgesia by epidural block is obtained and can be reduced only by phrenic nerve infiltration with local anesthetics or anti-inflammatory drugs.10, 11 When postoperative nociceptive and inflammatory pain disappear, pain can persist in the absence of peripheral noxious stimuli. Current evidence suggests that continued peripheral nociceptive input may maintain central sensitization, amplify postoperative pain and contribute to chronic pain.

Chronic pain syndrome can have multiple components, most likely related to nerve injury and myofascial involvement. The neuropathic component has a distribution beyond the scar and is characterized by sensory loss with areas of hypoand hypersensitivity such as dysesthesia on light touch, burning and aching pain. Major peripheral nerve injury is the trigger that modifies the pain response and can be responsible for development of chronic pain. Nerve damage from surgical incision or direct compression of intercostal nerves by rib retractors is also related to the surgical approach used and type of surgery (i.e., pneumonectomy versus lobectomy versus wedge resection). Numerous factors can decrease the chances of developing pain: accurate skin incision and closure of the thoracotomic wound, and lateral limited thoracotomy incision that avoids splitting the latissimi dorsi and other muscles of the chest wall, all of which can reduce surgical trauma. Also, genetic and psychological factors have an important role: women seem to have higher acute postoperative pain scores than men.12 Preoperative degree of anxiety and depression has been demonstrated to affect postoperative pain perception.13 Therefore, an aggressive analgesic treatment minimizes the rate of chronic pain syndrome development in thoracic surgery where its prevalence is 50% at 1 year, and 30% 4-5 years after the surgery.14, 15

Postoperative analgesia

Several techniques have been employed to treat post-thoracotomy pain, but the best approach requires a multimodal analgesia with a local anesthetic that block nociceptive input from the periphery, opioids administrated intratechally and/or parenterally and, at the end, non-steroidal anti-inflammatory drugs (NSAID), cyclooxygenase (COX) inhibitors or paracetamol in order to reduce opioid requirements. Epidural block is widely used because it provides optimal anesthesia and analgesia with few side effects, but other techniques such as paravertebral and intercostal block, interpleural and subarachnoid administration of drugs and cryoanalgesia can be utilized. Among these techniques, paravertebral block is the most effective alternative when epidural block cannot be performed.16, 17 It has also been reported in previous studies that administration of regional anesthesia or epidural opioid analgesia before the surgery, the so-called preemptive analgesia, may block the sensitizing effects of surgical stimulation with a reduction in acute postoperative pain.

Thoracic epidural analgesia

Clinical effect

The use of thoracic epidural anesthesia in the intra- and postoperative periods have gained great popularity in cardiac, major thoracic and abdominal surgery, because it provides superior analgesia.
when compared with systemic opioids. Moreover, it ensures a rapid extubation and has positive effects on respiratory and cardiovascular functions by reducing postoperative morbidity and mortality. Postoperative pain causes a restrictive pattern of ventilation, and epidural anesthesia is able to partially restore respiratory function by allowing deep breathing and coughing, which are considered effects of an adequate analgesia.\textsuperscript{18-20} In normal subjects, sensory block from T1 to T5 by administration of local anesthetic reduces vital capacity (VC) and forced expiratory volume in 1 s by 5.6% and 4.9%, respectively. These effects are due to the blockage of the intercostal muscles.\textsuperscript{20} At this dermatomeral level, reduction of the ventilatory function is also minimal in subjects with severe chronic obstructive pulmonary disease and the modifications of functional residual capacity (FRC), which are more pronounced in thoracic and abdominal surgery and are less dangerous with anesthetic epidural block as compared to intravenous opioids.\textsuperscript{21} This is mainly because a postoperative pain-free period enhances a caudal displacement of the diaphragm and reduces diaphragmatic dysfunction that occurs during thoracic and major abdominal surgeries.

Postoperative pain produces a reversible restrictive pattern of respiration with a decrease of VC and FRC with shallow and frequent inspiration and possibly compromised gas exchange. Pulmonary complications are frequent when FRC decreases to 60% of the preoperative value and are severe when FRC decreases to 40% of preoperative levels. Pain reduces FRC by 22% and VC by 63%, and epidural analgesia restores the respiratory function partially but significantly, improving oxygenation. An increase of FRC moves tidal volume above closing volume, whereas an increase of VC enhances oxygenation and decreases the risk of atelectasias.\textsuperscript{22, 23}

Epidural analgesia is performed by placing an epidural catheter between the T3-T6 level before induction of general anesthesia. At the thoracic level, the paramedian approach to the epidural space is the most popular technique because the obliquity of the spinous processes often makes it difficult to utilize the classical midline approach. One to 1.5 cm lateral and inferior to the spinous process, a Tuohy needle is advanced perpendicularly and cephalad to make contact with the lamina of the inferior vertebra. The needle is then withdrawn and redirected medially and cephalad with an angulation of 10-20° to reach the epidural space identified with the technique of loss of resistance.

The use of a mixture of a local anesthetic with opioid or opioid alone reduces the amount of opioids administered intravenously, making possible early extubation in the operating room and avoiding ventilator-associated complications without modifying hypoxic vasoconstriction and intraoperative gas exchange during one-lung ventilation. A loading dose of 5-8 mL of local anesthetic and an opioid is usually administered before the induction of anesthesia. Afterwards, local anesthetic is generally administered together with an opioid in epidural space by continuous infusion or by patient-controlled analgesia for 48-72 postoperative hours. It has been reported that continuous infusion of low doses of levobupivacaine 0.125% combined with a lipophilic opioid such as sufentanyl are highly effective for postoperative pain relief. The synergy between these two different categories of drugs in producing segmental analgesia has been well documented, with levobupivacaine facilitating the entry of the opioid from the epidural space into the cerebrospinal fluid.\textsuperscript{24, 25} Ropivacaine has the same analgesic effectiveness as levobupivacaine at equianalgesic dosage and both demonstrate a long-lasting action and a cardiotoxicity lower than bupivacaine.\textsuperscript{26} As demonstrated by Dernedde et al., an adequate analgesia depends more on the administered dose and less on its concentration and volume. In this study, the same quality of analgesia could be obtained with different volumes, but the same amount of local anesthetic regardless of concentration.\textsuperscript{27}

All opioids at the appropriate dose have been utilized epidurally, but lipophilic drugs are preferred to long-lasting hydrophilic morphine, because its cephalic spread is more limited and the reported incidence of sedation and respiratory depression is lower. Intrathecal opioid administration, however, is not without side effects. Nausea, vomiting, pruritus, urinary retention, hypotension and respiratory depression (incidence is low but not negligible) can depend on many factors such as the patient’s age and level of epidural-
al administration, and the time of occurrence may be related to the opioid used. A major concern in epidural block is the risk of hematoma that can be associated with devastating sequelae and occurs more frequently since the introduction of low molecular weight heparin (LMWH) for the prophylaxis of peripheral vein thrombosis.

It was suggested that the neuraxial blockade can not be run if the administered drug does not spend two half-lives in subjects with normal renal function, and that administration of LMWH should be resumed after removal of the catheter, keeping in mind that the peak effect of the drug is reached after 8 h, when the clot is consolidated.

Thoracic paravertebral nerve block

Administration of local anesthetics in paravertebral spaces to anesthetize both dorsal and ventral rami of spinal nerves is useful in patients with pain originating from the thoracic spine, thoracic cage or abdominal wall. It can be utilized in all situations in which epidural blockade is not possible or contraindicated or wherever the afferent input is predominantly unilateral, i.e., thoracotomy, cholecystectomy and nephrectomy.

The concept of the use of paravertebral block was initially introduced by Sellheim in 1905 to produce analgesia during abdominal surgery and subsequently used by Lawen in 1922 for the differential diagnosis of abdominal pain. Many years later, Eason et al. have emphasized the use of paravertebral block, now largely utilized, in thoracic and abdominal surgery. Because the input of pain after thoracotomy is almost always unilateral using this form of regional anesthesia, a block can be performed unilaterally with the opportunity to avoid the sympathetic nervous blockade implicated in causing a significant incidence of side effects such as hypotension and urinary retention that complicate patient’s discharge.

Anatomy

The thoracic paravertebral space (TPVS) is a wedge-shaped anatomical compartment adjacent to the vertebral bodies. The vertebral body, intervertebral disk and intervertebral foramen form the base of the space, parietal pleura is the anterolateral area, while the posterior boundary is the transverse process and superior costovertebral ligament. The fibro-elastic endothoracic fascia of the thorax lies between the superior costovertebral ligament and the parietal pleura and is anchored to the ribs and vertebral bodies. A loose areolar space, the subserous fascia, interposed between the parietal pleura and the endothoracic fascia splits the TPVS into two compartments: an anterior extrapleural and a posterior subendothoracic compartment. The paravertebral space contains fatty tissue, spinal nerve, its dorsal rami, rami communicantes, the anterior sympathetic chain and the intercostal vessels.

The effectiveness of the block is enhanced by three factors: injecting local anesthetic near the spinal nerves, which loses the fascial sheath that envelopes the nerves, segmentation of the spinal nerves in small bundles and the systematic involvement of the sympathetic and of posterior primary rami. The block of these intercostal nerves is fundamental because it prevents pain originating from rib traction, stretch of costovertebral and costotransverse joint and posterior spinal muscles.

TPVS seems to spread cranially and caudally from the column cervicalis to the psoas muscle as demonstrated radiologically by the extent of spreading of contrast medium. However, the real anesthetic diffusion is under debate. Some authors have pointed out that medial communication with the epidural space and contralateral paravertebral space may be relevant, whereas other authors have demonstrated that the effect of local anesthetic is restricted to paravertebral space since, at computed tomographic scan, the radio-opaque contrast medium injected into the paravertebral space remains confined to this space. This is why thoracic paravertebral block (TPVB) produces mainly unilateral somatic and sympathetic nerve block.

Techniques

Many techniques are used to perform paravertebral block. It can be performed with the patient in a prone, sitting or lateral position. For thoracic surgery, the appropriate dermatomes are from T4 to T7, and the site injection can be single or multiple. A 22-G spinal needle, or a 18-20 Tuohy needle if a catheter must be placed, is advanced horizontally to make contact with the transverse...
process of the vertebra, 2-3 cm lateral to the spinous process of the superior vertebra. This landmark is very important to prevent pleural puncture. Afterwards, the needle is redirected cranially or caudally to the transverse process until a loss of resistance to air or saline is felt. The distance from the skin to the paravertebral space depends on the level selected and on the patient's body mass index (BMI). For example, the paravertebral space is deeper in subjects with increased BMI and more superficial in the mid-thoracic region. As the perception of the loss of resistance that localizes the entrance in the paravertebral space can be difficult to determine, some authors prefer to advance the needle 1-1.5 cm to the superior edge of the transverse process and report a low incidence of pneumothorax. Due to the difficulty in finding the paravertebral space and the high rate of failure (about 10%), some authors have thought to simplify this method by measuring pressure while the needle is advanced. In the erector spinae muscle, the pressure is higher during inspiration than during expiration. An inversion of pressure can be visualized after traversing the costovertebral ligament with a reduction of pressure during inspiration and an increase during expiration, whereas a negative pressure during both respiration phases indicates entrance in the interpleural space.

Other techniques used to perform paravertebral block have been suggested, but they are less frequently utilized. An example is the medial approach with the needle inserted 1 cm lateral to the midline and advanced to make contact with the lamina and then directed laterally to overcome the bone and enter into TPVS. Sabanathan et al. have described a technique to insert a paravertebral percutaneous catheter under direct vision before chest closure: in a pocket created surgically by peeling medially away the parietal pleura until the vertebral bodies and form two superior intercostal spaces, the surgeon places the catheter at the angle of the rib. Generally, a bolus of 15-20 mL of local anesthetic, levobupivacaine, bupivacaine, or ropivacaine is injected to obtain TPVB before induction of the anesthesia. A continuous infusion of 0.1 mL/kg/h or 5-8 mL/h of long acting anesthetic can be started as soon as the catheter is introduced in the space, or a bolus of 15 mL is administered if the catheter is positioned at the end of surgery. A single site thoracic paravertebral injection seems as effective as a multiple site injection, but if a larger area of block is desired, administration of local anesthetic in three or more contiguous sites may be preferable. It can be carried out before the percutaneous incision or before chest closure. In the first case, the advantage is to obtain an analgesic block before incision, the so-called preemptive analgesia, while in the second case, the catheter can be positioned correctly under direct visual control. TPVS is a relatively simple technique and is an effective alternative to epidural analgesia. The analgesia has been variously reported to be as effective, better or inferior to epidural analgesia. The response to stress and postoperative ventilatory function is better than intravenous analgesia and seems to overlap with the epidural analgesia, whereas it was not possible to evaluate the effectiveness of the technique on the incidence of chronic pain.

However, paravertebral block is still rarely used in thoracic surgery even if it seems to be quite effective and represents the better choice when epidural analgesia is unfeasible. Low incidence of adverse effects has been reported: neurologic complications are rare, and hematoma is also usually easy to deal with in patients treated with anticoagulants; the overall occurrence of hypotension, urinary retention, vascular and pleural puncture and pneumothorax is low. Moreover, the unilateral nature of the block induces only a 4.6% hypotension because it involves only few dermatomes.

**Intercostal block**

Intercostal block allows an adequate analgesia for fractured ribs and for postoperative pain control after thoracic, breast and some types of abdominal surgery. The block is easy to perform, and the technique uses a needle placed 6-8 cm out from spinous process at the angle of the rib proximal to midaxillary line before the lateral cutaneous nerve splits up in anterior and posterior branch, which supplies the skin and muscles of the torso and abdomen. A 23-25 G needle slides 2-3 mm underneath the inferior border of the rib with a cephalic angle of 20° to reach the subcostal groove. At this point, 3-5 mL of local anesthetic is injected where the nerve lies between the internal and intimus intercostal muscles and where the costal groove is broad.
Two spaces at the upper and lower incision must be anesthetized to obtain analgesia after thoracotomy. Although the procedure is very difficult to perform, a catheter can be positioned percutaneously through a Tuohy needle to provide continuous infusion of local anesthetic, or the block can be performed by the surgeon under direct vision. Complications are very rare. Pneumothorax is not a very relevant problem to deal with in thoracic surgery, and coagulation abnormalities are not a strong contraindication to performing it. However, it must be remembered that high and rapid absorption of anesthetic can produce a toxic reaction, and there is the possibility that the dural sheath can extend 8 cm laterally, conditioning the appearance of a spinal anesthesia.

Interpleural analgesia and cryoanalgesia

Interpleural analgesia is performed by injecting local anesthetic in the pleural space compared with paravertebral analgesia, which is the result of injection outside the parietal pleura. The efficacy of analgesia obtained by interpleural administration of local anesthetic in thoracic surgery is controversial because of drug loss from the drainage tubes, heap in costophrenic angle and high absorption of anesthetic with risk of systemic toxicity. Prospective studies have demonstrated the poor analgesia obtained in comparison with other techniques and the reduced effect on ventilatory function. Today, the cryoanalgesia used for many years to block the nervous conduction has been abandoned because the incidence of chronic neuralgia is increased and the analgesia is present only in the first 6 months.

Anti-inflammatory and adjuvant drugs

Non-narcotic analgesics, NSAIDs, and α₂ agonists can be useful when administered in combinations with opioids as part of a multimodal therapeutic strategy to reduce the need for opioids and to produce or ameliorate analgesia. Non-narcotic drugs are extensively used in the postoperative period, but they must be utilized at recommended dosages because the analgesic effect has a plateau and the increase of dosage augments only the occurrence of side effects, such as gastrointestinal bleeding or perforation and renal failure. The analgesic response is quite different in each patient, a problem that can be solved by changing the drug if an effect is not obtained with a product. The analgesic effect of NSAID is related to inhibition of the two isoforms of the enzyme COX1-2. Recently, selective inhibitors of COX2 have been introduced with the same analgesic effect, but lower side effects compared to non selective COX inhibitors. Clonidine, an α₂ agonist, is administered epidurally at a dosage of 1-4 µg/kg every 8 h or in continuous infusion. However, though it cannot replace opioids, it will eventually improve the quality and duration of analgesia because high doses induce side effects such as sedation, bradycardia and hypotension.

Intrathecal morphine

Intrathecal morphine is a technique of analgesia that is easy and quick to perform with low side effects, except the possibility of late respiratory depression reported after 6-12 h after the administration, a phenomenon caused by the rostral diffusion of the opioid. Morphine assures a good postoperative analgesia for several hours, reduces the rescue dose of intravenous opioids and ameliorates the respiratory function.

Conclusions

Thoracotomy is a painful intervention and is characterized by a high incidence of acute and chronic pain that can be reduced with an aggressive analgesic therapy. A multimodal approach with local anesthetics, opioids and NSAIDs is usually required and is now considered the best choice. High intensity of postoperative pain justifies the use of thoracic epidural analgesia with opiates and local anesthetics for their efficacy and the relatively high benefits, compared with the rare but sometime serious injury at the level of spinal cord, especially after the introduction of LMWHs. This method of analgesia is considered the gold standard for thoracic and abdominal surgery due to efficacy and reduced rates of complications. However, paravertebral block is an efficacious alternative in terms of analgesia because it preserves respiratory function.
function with a low incidence of side effects even in subjects with coagulopathies or other pathological conditions that contraindicate the epidural approach. The other techniques, such as interpleural or cryoanalgesia, appear obsolete, whereas intercostal block can still play a role in some cases, as the intrathoracic administration of morphine that can assure long lasting analgesia.

References

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