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Post-Thoracotomy Pain: Review Article

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ABSTRACT

Background: Thoracotomy is a very painful surgical procedure that is used to get access into the pleural space, to the lungs, to the heart, to the esophagus or to get access to the thoracic aorta or anterior mediastinum.
Objective: To study different modalities of treatment used for post thoracotomy pain control.
Recent Findings: Inadequate post-thoracotomy analgesia enhances the postoperative stress response with deleterious effects on respiratory, cardiovascular, gastrointestinal, urinary, immune and coagulation systems. In addition to anxiety and increased risk of Post Thoracotomy Pain Syndrome (PTPS), which can interfere with normal life and may persist for years or even for life?
Conclusion: Providing adequate post-thoracotomy analgesia can be challenging, as patients are often elderly or having multiple comorbidities. A multimodal approach is considered in managing post-thoracotomy pain starting with preemptive analgesia and cognitive behavioral modalities in addition to conventional multimodal systemic regimens as opioids, acetaminophen, NSAID, cyclooxygenase (COX)-2-specific inhibitors, gabapentin and pregabalin, steroids, IV lidocaine infusion, ketamine, and many regional analgesic modalities to avoid or decrease adverse effects of systemic regimens. These regional analgesic modalities include thoracic epidural blocks, thoracic paravertebral blocks, intrathecal opioid analgesia, serratus anterior plane blocks, intercostal nerve blocks, interscalene block, erector spinae block and interpleural block.
Keywords: Post-thoracotomy pain, Systemic analgesic treatment, Regional analgesic modalities.

INTRODUCTION

Thoracotomy is a surgical procedure to get access into the pleural space, to the lungs, to the heart, to the esophagus or to get access to the thoracic aorta or anterior mediastinum. Thoracotomy is the first step in thoracic surgeries including pneumonectomy, lobectomy, lung segment resection, biopsies, and decortication or to get access for thoracic exploration in major trauma [1]. Acute postoperative pain is intense, universal and interfering with the recovery of respiratory function requiring the use of opioid analgesics. Later, chronic postoperative pain may develop that may last for years or even for life. Moderate quality evidence was concluded by a Cochrane review that regional analgesia may decrease the risk of chronic postoperative pain persisting at 3 to 18 months after thoracotomy [2].

Acute post-thoracotomy pain:

Thoracotomy is a very painful incision, with significant trauma and distraction forces involving several muscles and fascial layers, ribs, neurovascular bundles and pleura that are exaggerated with continuous movement during patient breathing [3].

Severe acute post-thoracotomy pain may be due to retraction, resection, or fracture of ribs, dislocation of costovertebral joints, injury of intercostal nerves, and further irritation of the pleura by chest tubes [4]. Inadequate post-thoracotomy analgesia has major respiratory effects, as breathing requires stretching of the incision, which is extremely painful. Patients without adequate analgesia try to prevent stretching of the incision by contracting their expiratory muscles (splinting). Thus, minimizing the stretch on the incision during inspiration and reducing forced expiratory volume in 1st second (FEV1) [5].

Diaphragmatic contraction is also impaired by reflex mediated increase in abdominal muscles tone during expiration that results in reduction in pulmonary compliance and inability to breathe deeply or to cough forcefully resulting in possible hypoxemia and hypercarbia, retention of secretions, atelectasis or pneumonia [6]. Postoperative neuroendocrine and metabolic stress response includes increased catecholamine and catabolic hormone secretion and decreased secretion of anabolic hormones. The effects of this process include increased oxygen consumption, mobilization of metabolic substrates from storage depots, sodium and water retention and increased blood glucose, free fatty acids, ketone bodies and lactate. A catabolic state with negative nitrogen balance occurs if the process continued. There is current interest in inhibition of such stress response and its possible consequences by various anesthetic and analgesic methods [7].

Stress response also causes immunological changes as epinephrine and cortisol that induce suppression of the adaptive immune system. It also produces leukocytosis with lymphopenia and reticuloendothelial system depression that predispose patients to infection. Postoperative epidural analgesia has shown valuable effects in decreasing these immunological alterations [7, 8]. On cardiovascular system, sympathetic stimulation by pain causes

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tachycardia and increased stroke volume, cardiac work and myocardial oxygen consumption with increased risk of myocardial ischemia or infarction in vulnerable patients (e.g., patients with preexisting hypertension and congestive heart failure) [9].

Postoperative pain with increased sympathetic tone also increases sphincter tone and decrease intestinal and urinary motility, promoting ileus and urinary retention. Inhibition of pain and efferent sympathetic activity by regional analgesia and anesthesia may enhance recovery or prevent ileus [10]. Postoperative hypercoagulability is related to stress-mediated increase in platelets adhesiveness, reduced fibrinolysis and activation of the coagulation cascade. Data propose that the use of perioperative epidural analgesia results in less platelet activation and better fibrinolytic function causing significant protection against thromboembolic complications. This protection also may be related to the systemic effect of local anesthetics, which may have an antithrombotic effect. Inadequate analgesia causes prolonged immobility, which is an additional risk factor for postoperative hypercoagulability [11]. In addition, perioperative pain is a major source of fear and anxiety in hospitalized patients. Insomnia may accompany the process, adding another determinant to recovery [12].

Chronic post thoracotomy pain:

Post-thoracotomy pain syndrome (PTPS) is defined by the International Association for the Study of Pain (IASP) as 'pain that recurs or persists along a thoracotomy incision at least two months following the surgical procedure'. It is generally a burning and stabbing pain with dysesthesia and shares many features of neuropathic pain [6]. Despite a common belief that post-thoracotomy pain is transient, there is no evidence that the pain decreases significantly over time. Incidence of reported post-thoracotomy pain was 80% at 3 months, 75% at 6 months, and 61% at one year postoperative with incidence of severe pain is 3–5%, and pain that interferes with normal life is 50% of patients. Clearly, post thoracotomy pain can be the commonest complication of thoracotomy. For many patients, the gentlest stimulation provokes intense pain interfering with participation in routine daily activities [13]. Although some authors concluded that the incidence of chronic pain and disability is less with using video assisted thoracic surgery for pulmonary resection compared to thoracotomy [14], other authors found no difference, and even variation in surgical techniques or incisions has not been shown to reduce subsequent PTPS [15]. Factors and mechanisms involved in developing chronic pain after thoracotomy include intercostal nerve damage, as surgery routinely crushes the intercostal nerve, as the nerve is exposed on the caudal side of the rib.

The nerve also can be totally severed or included in a suture when closing the chest or mechanically damaged during rib resection by compression with a retractor. Additionally, incidental rib fractures can damage the intercostal nerve or entrap an intercostal nerve during healing, causing neuropathic pain symptoms. The hyperalgesia or allodynia accompanied by numbness is diagnostic for nerve injury. These symptoms frequently occur along the innervation area of the intercostal nerves and are the most common feature of PTPS [16, 17]. Increasing pain may be also an early sign of disease (e.g., tumor) recurrence [18]. Personality traits are strong determining factors in the overall post thoracotomy pain experience. Also, anxiety plays a major role [16].

Different modalities to control post-thoracotomy pain:

Providing analgesia for thoracic surgery can be challenging as patients are often elderly with multiple comorbidities. Preemptive analgesia pharmacologically induces an effective analgesic state before the surgical trauma leading to decrease in postoperative analgesic needs. This involves wound infiltration with local anesthetic, the administration of adequate doses of opioids, ketamine or NSAID or central neural blockade. A multimodal approach looks beneficial in managing postoperative pain [19].

Cognitive behavioral modalities:

Cognitive behavioral modalities are recommended as a part of multimodal management, like guided imagery and intraoperative suggestions and other relaxation techniques to reduce anxiety seem to have some benefits on postoperative anxiety, pain and analgesic requirements. Playing music and limiting noise level on anesthetic induction is encouraged [20].

Systemic analgesic treatment:

1) ***Opioids:*** The value of opioids analgesic properties in the treatment of intense, acute pain after major or minor surgery is well known. Morphine is the most popular analgesic used in patients after thoracotomy surgery, while other synthetic opioids, like fentanyl, alfentanil, sufentanil and remifentanil, may be used as well. However, other systemic drugs, such as NSAID or COX-2 inhibitors, lidocaine and steroids or regional analgesic techniques are used to reduce opioid use and subsequently its side effects [21]. Transdermal fentanyl is a simple noninvasive modality. However, the steady release of fentanyl does not allow flexible dose adjustment to ensure adequate analgesic effect or avoid adverse effects. Narcotic-based patient-controlled analgesia (PCA) may not provide adequate pain relief, as the side effects of respiratory depression, sedation, constipation and altered mental status frequently outweigh its benefits [22].
2) ***Acetaminophen and NSAID:*** Parenteral, oral and rectal acetaminophen (paracetamol) and parenteral and oral NSAID can share as effective elements of multimodal anesthesia. The analgesic effect of acetaminophen is less by 30% compared to that of NSAID, but with fewer side effects. Acetaminophen with a NSAID can be used as an adjunct to PCA to improve postoperative analgesia and to reduce morphine requirements. Hepatotoxicity is the primary

concern when using acetaminophen with elderly patients and chronic alcohol consumers. Ketorolac is the most common parenteral NSAID used. Common oral NSAID available include ibuprofen and diclofenac. There is no difference in postoperative pain reduction between IV vs. oral NSAID. NSAID are associated with increased risk of gastrointestinal bleeding and ulcerations, renal dysfunction and cardiovascular events [23].

3) ***Cyclooxygenase (COX)-2-specific Inhibitors:*** Preoperative dose of oral celecoxib as a part of multimodal preemptive analgesia is suggested, because it helps in reduction in postoperative opioid requirements and postoperative pain leading to earlier bowel function and resuming normal activities. Ultimately, increases patient satisfaction with quality of recovery and pain management [22, 23].

4) ***Gabapentin and Pregabalin:*** Both when used as a part of multimodal preemptive regimen or immediately postoperatively are associated with reduced opioid requirements and lower postoperative pain scores. They also help in preventing chronic postoperative pain persisting beyond 2 months. Sedation and dizziness are common adverse effects. Lower doses should be used in elderly or patients with impaired renal function [24].

5) ***Steroids:*** Steroids decrease the inflammatory response to the stress of surgery by blocking the lipoxygenase and COX enzymes. A single preoperative or intraoperative dexamethasone dose decreases opioid requirements and postoperative pain without significant adverse effects [25].

6) ***IV Lidocaine Infusion:*** IV lidocaine infusion when used intraoperative and/or postoperative were associated with reduced opioid requirements and postoperative pain helping to improve bowel function recovery. The suggested dosing in adult is 1.5 mg/kg bolus induction followed by 2 mg/kg/hour infusion. Rare adverse effects include dizziness, arrhythmias, light headedness, drowsiness and visual disturbances [26].

7) ***Ketamine:*** Ketamine, a NMDA receptor antagonist, is associated with less postoperative opioid requirements and decreased postoperative pain scores when given IV. The recommended dose is 0.5 mg/kg bolus with or without 10 μg/kg/min infusion. It has an increased risk of nightmares and hallucinations [27].

8) **Regional analgesic modalities:**

Conventional multimodal systemic regimens (oral and parenteral) may be difficult or sometimes impossible to institute because of patient safety/appropriateness concerns, especially in elderly frail patients with multiple comorbidities. Many modalities of regional analgesia were implemented trying to avoid adverse effects of systemic opioids and other elements of multimodal systemic regimens [22].

1) ***Thoracic Epidural Blocks:*** Thoracic epidural is generally considered the gold standard for post-thoracotomy pain control and usually provides excellent analgesia. A high/mid-level thoracic (T4–5) epidural is usually required. Although thoracic epidural advantages are numerous, there are number of limitations to the procedure, including being challenging to place for an inexperienced anesthesiologist and associated serious risk of inadvertent dural puncture and spinal cord injury. The risk of massive bleeding in the neuraxial space causing spinal cord compression and paraplegia (temporary or permanent) is another limitation. It's contraindicated in patients on anticoagulants or antiplatelet medications and/or with preexisting coagulopathies or localized infection at epidural placement site or with significant systemic infections. Also, the anatomic challenges of elderly patients' thoracic spine may require the use of alternatives to the usual midline spinal approach used by anesthesiologists in epidural and hemodynamic side effects, like hypotension, resulting from the local anesthesia-related sympathetic blockade are other concerns [22, 28].

2) ***Thoracic Paravertebral Blocks (PVB):*** PVB is effective and non-inferior to TEA for the management of pain following thoracotomy and can significantly improve postoperative pulmonary function [29]. A Cochrane review of 14 studies including a total of 698 patients undergoing thoracotomy concluded that PVB was as effective as TEA in controlling acute pain with less risk of developing minor complications [30]. Complications after thoracic PVB is relatively low and varies from 2.6%–5%. These include vascular puncture (3.8%), hypotension (4.6%), pleural puncture (1.1%) and pneumothorax (0.5%). Unlike with thoracic epidural anesthesia, hypotension is rare in normovolemic patients after thoracic PVB because the sympathetic blockade is unilateral. However, thoracic PVB may lead to hypotension in hypovolemic patients. Therefore, thoracic PVB should be used with caution in patients who are hypovolemic or hemodynamically labile. Life threatening complications from thoracic PVB have occurred as a result of accidental injection into the intrathecal or epidural space, or into a blood vessel. In addition to pneumothorax, these are the greatest risks associated with PVB [31].

3) ***Intrathecal opioid analgesia:*** In intrathecal opioids analgesia, much smaller opioid doses are used than in TEA and IV opioid analgesia due to multicompartmental mechanism. Opioids spread cephalad within the CSF, bind to opioid receptors in the dorsal horn in addition to the white matter of spinal cord and enter the systemic circulation via vascular uptake. The duration of action, speed of onset, and degree of rostral spread are related to the lipophilicity of the opioid in each compartment. As morphine is hydrophilic, it is commonly used in thoracotomy as it crosses the dura slowly leading to little binding to epidural fat and delayed entry to systemic circulation. So, large CSF morphine concentrations result in an onset of action around 1–2 h after administration and to last up to 24 h. Intrathecal opioids analgesia can be combined with a PVB as an alternative to TEA.

Patients should be observed for the occurrence of delayed respiratory depression or urinary retention [32].

4) ***Serratus Anterior Plane Blocks (SAPB):*** Ultrasound guided SAPB is a relatively new, easy and superficial block technique that provides analgesia for thoracic wall surgeries by blocking the lateral branches of the intercostal nerves (T2–T9). SAPB is performed by approaching either of two fascial planed, either deep to the serratus anterior muscle between the muscle and the thoracic wall or superficial to the serratus anterior muscle underneath the latissimus dorsi, injecting local anesthetic with or without catheter insertion. It's technically easy with very few contraindications and can be performed with patients either supine or in lateral position, so it is suitable for patients with associated spinal trauma or head injuries where paravertebral and epidural blocks are contraindicated. Also, it can be performed in anticoagulated or thrombolysed patients. Patient refusal, allergy to local anesthetics and local infection are absolute contraindications. Relative contraindications include distorted anatomy making landmarks difficult to be identified by ultrasound, for example, surgical emphysema, intercostal drain placement and previous surgery at the insertion site and morbid obesity. Complications include pneumothorax, vascular puncture, nerve damage, failure/inadequate block, local anesthetic toxicity and infection [33].
5) ***Intercostal Nerve Blocks:*** Intercostal nerve blocks are easy to perform and can provide potent analgesia in a fast, reliable manner. It can be performed either under direct visualization in the pleural cavity in the field by the surgeon or percutaneous by the anesthesiologist. If done using liposomal bupivacaine, these blocks may be more effective with extended duration of action up to 72 hours. Disadvantages include an increased risk of systemic local anesthetic toxicity if not performed properly either due to inadvertent intravascular injection, overdose or due to enhanced absorption of local anesthetics from the intercostal space compared to other body areas. Also, due to the circumscribed nature of the intercostal nerves innervating the chest wall, multiple levels injections are required to ensure adequate analgesia. Some of the additional risks include significant bleeding from trauma to the intercostal artery, block failure and pneumothorax [22].
6) ***Interscalene Block:*** Even in case of functioning well placed thoracic epidural with appropriate dermatome spread resulting in standard dermatomal sensory analgesia, patients may still show referred shoulder pain **(Kehr's sign)** related to chest tubes placement that irritates the diaphragm. This referred pain is signaled by the phrenic nerve arising from cervical nerves C3 through C5, as pain in the area above the clavicle. So, an appropriately working thoracic epidural may not cover this particular nerve distribution. However, a peripheral nerve block targeting supraclavicular bundled nerves may be effective in relieving this symptom in such patients. Diluted ropivacaine is used (0.1 to 0.2%) to avoid significant motor block and potential unilateral diaphragmatic weakness [22].
7) ***Erector Spinae Block:*** This new regional technique can be performed as a single shot with an appropriate volume of local anesthetic or by placing a catheter for continuous infusion of local anesthetic superficial to the transverse process and deep to the erector spinae fascia under ultrasound guidance. The local anesthetic then can spread and provide coverage from C7 to T10 dermatomes unilaterally. The mechanism of action is still to be elucidated, but is supposed to be from diffusion of the anesthetic into the paravertebral space. There, it is able to act on the dorsal and ventral thoracic spinal nerves. It is considered as a peripheral nerve block with its associated benefits and risks compared to neuraxial anesthesia. Benefits include lack of significant sympathetic blockade and associated hemodynamic effects, ability to be done under sedation and/or GA, being a single injection that is able to cover the entire chest wall, and the elimination of the risk of an epidural related hematoma in a patient with or without anticoagulation medications. The use of this technique is also promising in trauma patients with rib fractures and in abdominal surgery [34].
8) ***Interpleural block:*** Injecting local anesthetic in the pleural cavity via the chest drain is no longer recommended and has fallen out of favor due to its suboptimal pain relief and many other concerns [35].

CONCLUSION

A multimodal approach is considered in managing post-thoracotomy pain starting even before the surgical trauma in the form of preemptive analgesia and cognitive behavioral modalities. Conventional multimodal systemic regimens (oral and parenteral) as opioids, acetaminophen, NSAID, cyclooxygenase (COX)-2-specific inhibitors, gabapentin, pregabalin, steroids, IV lidocaine infusion and ketamine play a major role in post-thoracotomy analgesia.

Even though, it may be difficult to be used in elderly frail patients with multiple comorbidities. So, many modalities of regional analgesia were implemented to the multimodal approach to avoid or decrease adverse effects of systemic regimens. These modalities include thoracic epidural blocks, thoracic paravertebral blocks, intrathecal opioid analgesia, serratus anterior plane blocks, intercostal nerve blocks, interscalene block, erector spinae block and interpleural block.

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