

Prevention and Management of Postoperative Wound Pain after Thoracic Surgery

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Received date: Jan 29, 2016, Accepted date: Feb 19, 2016, Publication date: Feb 23, 2016

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Early ambulation and management of wound pain lead to decrease of the postoperative complications for especially elderly patients in thoracic surgery [1]. The types of pain frequently observed after thoracic surgery are wound pain, pulmonary apex pain due to the drain, pain caused by intercostal nerve compression, intercostal neuralgia, visceral pain due to manipulation of the pleura/bronchi, and shoulder pain associated with the patient's position for surgery. Since the dominant nerve differs among painful areas, the innervation regions requiring analgesia are extensive, causing difficulty in pain control. During the operation and in the acute postoperative stage, anesthesiologists have conventionally taken the lead in pain control, epidurally administering opioids and local anesthetics including paravertebral block [2]. Pain control after returning to the general ward or after discharge is generally performed by thoracic surgeons, but neuropathic pain, which is due to intercostal nerve damage after intercostal thoracotomy or the use of ports for laparoscopic surgery, often persists. This pain is controlled by the administration of anti-inflammatory analgesics such as NSAIDs, gabapentin (anti-epileptic drug) as a central nervous system drug, or tranquilizers. In some patients showing poor pain control, intercostal nerve block is performed on an outpatient basis at the clinic. In thoracic surgery, there are differences in the incision size among surgical techniques and surgical invasiveness to the chest wall among approaches to the thoracic cavity, such as posterolateral thoracotomy, axillary thoracotomy, median sternotomy, a median incision, a small incision, and conventional video-assisted thoracic surgery (c-VATS) with only a trocar used in VATS. Thus, the intensity of postoperative pain also differs. Even when thoracotomy is performed after the intercostal nerves, veins, and arteries are dissected as minimally as possible, and the ribs are partially resected, or even when c-VATS is performed, some patients occasionally develop marked symptoms of neuropathic pain such as burning, shooting, and tingling sensations and hypesthesia in the area from the precordial region at the intercostal thoracotomy level to the upper abdominal region. Their stress is marked when these symptoms develop.

With the advent of pregabalin, the treatment methods for neuropathic pain used by thoracic surgeons have been changing and improving. This mechanism of action (MOA) of neuropathic pain differs from that of general inflammation-associated pain. The latest definition of neuropathic pain is "pain arising as a direct consequence of a lesion or disease affecting the somatosensory system" [3,4]. Pregabalin is a structural derivative of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA), but does not bind to GABA receptors, and does not inhibit GABA reuptake for metabolism. This

drug neither blocks the sodium channel nor activates opioid receptors. The main MOA of pregabalin is its binding to the $\alpha 2\delta$ subunit of the voltage-gated calcium channel with high affinity. Pregabalin, based on the characteristics of its pharmacokinetics, is considered to infrequently induce interactions with other drugs. The degree of anxiety about pain and pain threshold differ among individuals. In particular, in patients with mental disorders as complications, pain control at the outpatient clinic is sometimes difficult. Pregabalin, which binds to the $\alpha 2\delta$ subunit of the voltage-gated calcium channel as the MOA, was reported to reduce the excessive release of excitatory neurotransmitters by hyper-excited neurons involved in the development of anxiety symptoms, and suggested to have early-onset effects on both somatic and psychological symptoms of anxiety about pain [5].

As described above, the pain threshold differs among individuals, and the fear of and feelings toward postoperative pain also differ among patients. When postoperative wound pain is compared between c-VATS using only the trocar and thoracotomy involving rib resection with a large wound, the degree of surgical invasiveness to the chest wall is often inconsistent with the pain intensity, which supports the above individual differences. Previous studies have suggested the involvement of the activity of the anterior cingulate gyrus in the mechanism of the change from acute to chronic pain [6,7] and, therefore, individual differences in pain might be associated with changes in the activity of this gyrus after surgery [6,7]. At present, for pain, symptomatic therapy according to its intensity is mainly performed. Concerning pregabalin administration methods, its preoperative administration has been reported to reduce postoperative pain [8,9]. Therefore, preoperative pregabalin administration is expected to also have adequate inhibitory effects on postoperative wound pain in patients in whom intercostal thoracotomy is planned and those with a low pain threshold and psychological disorders represented by depression as complications in thoracic surgery.

When nociceptive input into the central nervous system with acute, intense postoperative pain is sustained, a change to chronic pain such as post-thoracotomy pain syndrome (PTPS) [10] can occur. PTPS is defined by the International Association for the Study of Pain as neuropathic pain with dysesthesia that is burning and stabbing, and persists for at least two months following the surgical procedure. Its incidence is 80% at 3 months, 75% at 6 months, and 61% at 1 year after surgery; the incidence of severe pain is 3-5%. PTPS interferes with daily life in 50% of patients [11]. The incidence of PTPS is similar between thoracoscopic surgery and thoracotomy [12-14], and the causes of PTPS include rib fracture, intercostal nerve injury due to compression by the rib retractor, and rib hyperextension. An anxious personality of patients was also reported to tend to be positively

correlated with the incidence of PTPS [15]. In addition, in patients with PTPS, sensory abnormalities such as allodynia (pain induced by normally innocuous, weak stimuli) and hypesthesia sometimes persist around the thoracotomy wound or the anterior axillary line area or upper abdominal area at the thoracotomy intercostal level for a long period after surgery. Since no drugs have been developed to alleviate these symptoms, pain causing discomfort whenever clothes come into contact with the area around the wound may reduce patients' QOL and delay their return to society [16].

In recent years, thoracic operations have become less invasive. Among the less invasive operative procedures, robot-assisted surgery and single-port VATS (SPVATS) are recent topics [17,18]. However, robotic surgery is basically multi-port VATS, and its disadvantages such as stress placed on the intercostal nerve, a high cost, and high complication rate have been shown [19]. SPVATS is thoracoscopic surgery performed using a small thoracotomy wound (3-5 cm). This surgical procedure, which does not require a rib retractor and is performed avoiding contact between surgical instruments and the intercostal nerve, may be the least invasive surgery for patients. However, SPVATS can only be performed by skilled surgeons because of limitations in forceps manipulation and difficulty in performing delicate procedures and, therefore, is used in only some countries. Recently, we learned an SPVATS procedure that does not impose stress on the intercostal space, showed surgical results in patients with early lung cancer, and performed detailed evaluation of this procedure in terms of postoperative pain. Comparison between the SPVATS and multi-port VATS groups showed no significant difference in the blood loss, operative time, postoperative hospital stay, drainage period, or the total number of dissected lymph nodes between the two groups but a definite decrease in the incidence of neuropathic pain for SPVATS [20]. At present, the most preventive and effective methods of postoperative pain control in the thoracic surgery field may be SPVAT that is protective toward the intercostal nerve and pregabalin administration immediately after the development of neuropathic pain. Of course, it is also important that thoracic surgeons actively ask patients about symptoms associated with neuropathic pain and perform appropriate pain assessment.

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