

PAIN RELIEF AND PALLIATIVE CARE IN LEBANON MANAGEMENT OF CANCER PAIN

Different Intervention Techniques

<http://www.lebanesemedicaljournal.org/articles/56-2/doc6.pdf>

Zoher NAJA¹, Mohamad AL-TANNIR², Fouad ZIADE³, Michel DAHER⁴



PAINRELIEFAND PALLIATIVECAREGROUP

Naja Z, Al-Tannir M, Ziade F, Daher M. Management of cancer pain : Different intervention techniques. J Med Liban 2008 ; 56 (2) : 100-104.

Naja Z, Al-Tannir M, Ziade F, Daher M. Différentes techniques interventionnelles pour contrôler la douleur du cancer. J Med Liban 2008 ; 56 (2) : 100-104.

ABSTRACT : A considerable number of patients with cancer suffer considerable pain during their disease. Most of these patients achieve analgesia using opioids and adjuvant medication ; however, 5-10% of them still experience inadequate pain control despite aggressive combined pharmacological therapy and their use is often associated with adverse events.

Providing effective pain management for patients with severe pain that affects quality of life confronts the oncologist or pain specialist with clinical challenges that often require multifaceted therapeutic measures. Interventional pain therapies are a diverse set of procedural techniques for controlling pain that may be useful when systemic analgesics failed to provide adequate control of cancer pain or when the adverse effects cannot be managed reasonably.

Commonly used interventional therapies for cancer pain include neuroaxial, neurolytic including sympathetic block and paravertebral block ; in addition, neurosurgical procedures are used as last rescue once other techniques failed in order to achieve the highest possible success while minimizing potential complications and side effects. The intent of alternative therapies is to provide adequate and effective pain management in the oncology and palliative care arena with improvement in patient quality of life.

RÉSUMÉ : Un nombre considérable de patients atteints de cancer souffrent d'une façon importante durant leur maladie. La plupart de ces patients contrôlent leurs douleurs avec des opiacés et d'autres médicaments adjuvants ; cependant, 5 à 10% d'entre eux n'ont pas un contrôle adéquat malgré une thérapie combinée agressive et souvent associée à des effets indésirables. Le contrôle effectif de la douleur des patients dont la souffrance affecte la qualité de vie mettent l'oncologue et le spécialiste de la douleur devant un défi qui nécessite le plus souvent des mesures thérapeutiques multidisciplinaires. Les traitements interventionnels de la douleur constituent un ensemble de techniques pour contrôler la douleur qui peuvent être efficaces quand l'analgésie par voie générale a échoué dans le contrôle adéquat de la douleur ou lorsque l'analgésie entraîne des effets secondaires difficiles à contrôler raisonnablement.

Les techniques interventionnelles de la douleur cancéreuse comprennent les blocs neurolytiques, neuroaxiaux, incluant les blocs sympathiques et paravertébraux, et les procédures neurochirurgicales qui seront utilisées en dernier recours quand les autres techniques ont échoué à obtenir le résultat escompté avec le moins de complications et d'effets secondaires. Le but de cette thérapie est de fournir un traitement efficace pour la douleur du cancer dans le cadre des soins palliatifs, avec une amélioration notable de la qualité de vie.

INTRODUCTION

Estimates of the prevalence of cancer pain based on published studies range generally from 14% to 100% depending on the stage, severity, and site of cancer [1-2], making pain management a topic of continuing interest. Pain negatively affects the quality of life of patients with

cancer [3-4]. Therefore pain management is crucial to reduce patients' distress and increase productivity and functioning [2, 5].

Inadequate and inappropriate pain management of patients who experienced cancer pain has been documented in several studies [6-8]. This is possibly due to insufficient understanding of pain assessment and management [9-11]. The main barriers concerning adequate cancer pain management include physicians' knowledge and attitudes about opioids, patient reluctance to use opioids for pain relief, and lack of new interventions to improve patient's pain severity [12].

Management of cancer pain has made significant progress in recent years, due to several guidelines suggested for cancer pain therapy [13]. Most patients with solid tumors encounter moderate to severe pain at some

From Beirut, Lebanon, ¹Anesthesia and Pain Medicine Department & ²Research Unit, Makassed General Hospital ; ³Faculty of Public Health, Lebanese University ; ⁴Surgery Department, Saint George Hospital-University Medical Center-University of Balamand.

Correspondence : Zoher Naja MD. Anesthesia & Pain Medicine Department. Makassed General Hospital. POBox 11-6301. Riad El-Solh 1107 2210. Beirut. Lebanon.

Phone : +961 3 377064 Fax : +961 1 636941
e-mail : zouhnaja@yahoo.com

point during their illnesses [14]. Moreover, pain experiences in patient with cancer are often influenced by psychological stress associated with the disease [15]. An effective multidisciplinary approach to pain management is advocated where physicians need to work with other healthcare professionals [3, 16].

Interventional techniques in cancer pain management become the treatment of choice once oral and parenteral opioids are ineffective [17]. If the World Health Organization step ladder failed in cancer pain management due to tolerance or induced severe side effects such as constipation, nausea and vomiting, drowsiness and cognitive impairment (not even improved upon opioids rotation), other techniques should be considered to control cancer pain. Opioids resistance and toxicity are two major reasons behind seeking an effective interventional technique for cancer pain management [17-18].

Furthermore, adjuvant drugs are necessary in the success of management ; they can promote sleep, relieve anxiety, potentiate pain relief, and decrease side effects [17].

This paper reviews interventional techniques for cancer pain treatment including neuroaxial, neurolytic and neurosurgical procedures.

INTERVENTIONAL TECHNIQUES FOR CANCER PAIN MANAGEMENT

Even though transdermal delivery systems have some advantages over parenteral delivery techniques as being non invasive, avoid hepatic first pass metabolism, provide stable blood levels and are convenient for the patient [14], the currently available transcutaneous delivery system is not considered as the most favorable treatment for cancer pain management.

Patient controlled analgesia (PCA)

PCA was first introduced four decades ago. It became a common technique for managing pain when it is used as prescribed and intended. It can improve pain relief, lesser sedation, and lower opioids consumption ; improve patient satisfaction and pulmonary function. It has made home care particularly easy ; moreover, infusion pumps are commercially available, usually portable, battery-driven and inexpensive with incorporated alarm systems.

A more invasive approach may be needed to control pain and improve quality of life.

Neuroaxial procedures for cancer pain

This intervention is indicated in patients with cancer pain that cannot be controlled with conservative measures. However, this technique is contraindicated in patients with severe bleeding diathesis, septicemia, local cutaneous infection, increased intracranial pressure, and known allergies to the infused medications [19]. On the other hand, if the patient's life expectancy is less than one month, a nylon catheter could be inserted into the epidural or intrathecal space, tunneled laterally, and attached

to an external high-pressure infusion pump. This system can be implanted in an outpatient setting to alleviate the need for hospitalization. Whereas if a patient's life expectancy is from one to three months, a silastic catheter can be inserted and attached to an external infusion pump. This is a monitored anesthesia care procedure that can be performed in an outpatient setting. Experienced nurses can be involved in this intervention by changing the infusion rates and medication mixtures at the patient's bedside. If there is any concern, a temporary trial of opioids in addition to other adjuvant can be administered with a nylon catheter before the silastic catheter is inserted [19].

The most useful adjuvant drugs are : Carbamazepine, Gabapentine, Ketamine, Clonidine, Neostigmine and Calcitonin [20]. In addition, psychotropic drugs such as antidepressants and anticonvulsants can be also helpful in cancer patients to smooth their pain [17].

Requirement of a trial use of spinal medications is recommended before a physician can consider placing a permanent internal pump. The potential benefits and daily dosages should be assessed knowing that internal pump placement usually requires general anesthesia. These techniques of performing an internal pump may be accompanied with the same risks as those of implantable devices and include infection (in 3-5% of patients), drug tolerance, and pump or catheter malfunction.

As the needs of patients with pain change, especially in those with progressive cancer, trained nurses must be accessible to change infusion rates and medications for patients. However, to change medications in the internal infusion pumps, greater physician support and skill is needed compared with the external infusion pumps.

Administration of spinal opioids is usually well tolerated as patients judged for such modality have been already used to opioids and are bearing to their side effects [19].

Tissue destruction or trauma pain in patients with cancer results in the activation of nociceptors. Opioids are usually effective at interrupting nociceptive pain transmission. Antagonizing N-methyl-D-aspartate receptors or enhancing glycine and gamma-aminobutyric acid (GABA) transmission can interrupt spinal pain transmission.

Alternatively, non-opioids spinal analgesics could be applied using Clonidine, baclofen and ziconitide. Clonidine could be capable of reversing the neuroplastic changes in postsynaptic dorsal horn by activating 2 receptors on primary afferent neurons [21]. Baclofen activates GABA neurons on primary afferent and secondary postsynaptic horn neurons. Whereas, ziconitide blocks pain mediated neuro-transmitters [19].

The cost of implanting a nylon catheter is approximately \$ 500, and a silastic catheter approximately \$ 2000. An internal infusion pump can cost \$ 15,000. Hassenbusch et al. [22] found that if the life expectancy of a patient with cancer is longer than three months, the overall cost of intrathecal delivery and the personnel to manage the infusions may be less than that of tunneled catheters.

NEUROLYTIC PROCEDURES FOR CANCER PAIN

Most peripheral neurolytic blocks for cancer pain are performed on sympathetic nerves. In addition, peripheral blocks have been performed, although infrequently, on the trigeminal ganglion, brachial plexus, and intercostal nerves.

Spinal infusions, neurolytic blocks and radiofrequency lesions have replaced peripheral neurectomy as methods of cancer pain management rather than ablative procedures that should not be applied if patient could be relieved by other means.

Sympathetic nerve blocks

The sympathetic block can be performed at pre- and paravertebral sympathetic ganglia such as stellate ganglia (cancer pain of head, neck and upper extremity), cervico-thoracic ganglia, thoracic ganglia, celiac plexus (pain due to intra-abdominal cancer), lumbar ganglia, hypogastric plexus (pain of cancer pelvic organs – uterus, cervix, bladder, prostate, urethra, testes and ovaries) and ganglion impar depending on the pain site and its extension [23].

Celiac block

The celiac plexus innervates most of the abdominal viscera, including the stomach, liver, pancreas, small intestine and the proximal half of the large intestine. Pain caused by gastric, biliary, hepatic and other gastrointestinal malignancies are treated well from celiac plexus.

Furthermore, celiac block is mainly indicated in pancreatic carcinoma [19]. Pancreatic carcinoma is one of the most important leading causes of cancer death, because it has increased steadily in incidence and it still has a very poor prognosis [24], resulting in the death of more than 98% of the patients [25]. Pain is one of the most frequent symptoms, affecting more than 75% of patients [25-26].

Two approaches of celiac block guided by fluoroscopic and computed tomography (CT) are the most common methods used to perform celiac plexus :

➤ *Transaortic celiac plexus block*

A simple approach to the celiac ganglia, which does not require the use of CT guidance, is the transaortic technique described in 1983 by Ischia et al. [27].

➤ *Transcrural celiac plexus block*

This is a CT-guided transcrural approach, described by Singler in 1982 [28]. In practice, this technique requires a bilateral needle insertion at the level of the origin of the celiac artery, using the CT scan to calculate insertion points and trajectories that ensured avoidance of renal parenchyma and major vessels to reach the target.

However, in 1994, Hilgier and Rykowski modified the technique, introducing the one-needle transcrural technique : the needle is inserted 4 to 6 cm from the

midline on the left, at the lower edge of L1 vertebral body [29].

Paravertebral block

Paravertebral block is an effective intervention to control cancer pain and enable patient to return to normal daily activities [30]. During the last 30 years, the value of paravertebral block has been re-established [31-32]. In the early decades of this century, thoracic paravertebral blockade was made using neurolytic agents, mostly alcohol and phenol [33-34]. At present such agents have not generally been used for paravertebral analgesia [31]. No complications are normally seen in such blockade [30]. Moreover, continuous peripheral nerve block was selected for tumor invasion after metastatic spread of breast cancer to the axilla provided an effective means of pain control [35]. Furthermore, paravertebral block can be effective in controlling pain due to primary and metastatic cancer of the spine [36].

Neurolytic CNS blockade is beneficial for patients with advanced cancer whose pain is unilateral and involves a limited number of spinal segments. Patients with widespread cancer pain are not good candidates for this procedure, but they may be administered phenol or alcohol. Phenol has local anesthetic properties and denatures proteins. Accidental intravascular injection can cause CNS depression, convulsions, and cardiovascular collapse. Similarly, ethyl alcohol injections can be painful, dehydrate and denature protein. This technique can offer excellent pain relief for 60% of patients.

Extensive counseling and trials with local anesthetics need to be practiced before performing the neurolytic procedure. Physicians must be trained to perform these procedures correctly. Neurolysis of peripheral nerves can be accomplished by using radiofrequency probes. An insulated needle with an uninsulated tip and high frequency current creates a small thermal lesion. Radiofrequency neurolysis is thought to be safer than chemical neurolysis and less expensive than surgical neurolysis.

Although the administration of neurolytic blocks may relieve pain in patients with cancer, pain relief may end if the cancer grows beyond the level of anesthesia, the most common being the celiac plexus.

NEUROSURGICAL PROCEDURES FOR PAIN CONTROL

As 70% of cancer patients will be referred to an anesthesiologist for a nerve block or spinal medications, the left 30% will be referred for a neurosurgical procedure to interrupt pain pathways. Neurosurgical procedures namely rhizotomy and thalotomy can be ablative.

Dorsal rhizotomy involves severing sensory input at particular spinal levels ; however, it preserves motor function. This procedure is performed frequently for patients with cancer who have Pancoast tumors of the lungs or head and neck tumors. However, extensive rhizotomies can cause motor dysfunction. Other potential complications include sexual, bowel, and bladder dysfunction.

Thalatomy, which is the cutting of sensory fibers in the thalamus, can relieve midline or bilateral pain caused by metastatic disease. Initial pain relief can be as high as 80%, but pain can recur in 30% of patients one year after the procedure is performed. Side effects can include confusion, cognitive deficits, and disorientation. Contralateral paresthesia and ipsilateral cervical motor responses must occur before the electrode is used. The applied procedure is up to 93% of initial analgesic pain relief decreasing to 61% after one year. Major complications include respiratory failure, sleep apnea, hemiparesis, bladder dysfunction, and hypotension.

CONCLUSION

Assessments of medical concerns, any physical limitations and psychological status of patients are needed to evaluate patient cancer pain. Interventions with beneficial management of cancer pain should be considered seriously to be administered providing comfortable life to such patients regardless of disease prognosis.

Permanent destruction of neural pathways should be reserved for patients with cancer who have a limited life expectancy and whose pain has not been controlled by conservative methods. If injections are administered to properly selected patients, their quality of life can improve. In addition, they may experience fewer side effects than from systemic medications. Risks such as motor weakness, sphincter incompetence, or loss of position sense must be considered carefully.

REFERENCES

- Patrick DL, Ferketich SL, Frame PS et al. National Institutes of Health State-of-the-Science Panel. National Institutes of Health State-of-the-Science Conference Statement : Symptom management in cancer : Pain, depression, and fatigue, July 15-17, 2002. *J Natl Cancer Inst* 2003 ; 95 : 1110-17.
- Gilson AM, Joranson DE, Maurer MA. Improving state pain policies : recent progress and continuing opportunities. *CACancer J Clin* 2007 ; 57 : 341-53.
- Stearns L, Boortz-Marx R, Du Pen S et al. Intrathecal drug delivery for the management of cancer pain : a multidisciplinary consensus of best clinical practices. *J Support Oncol* 2005 ; 3 : 399-408.
- Sloan PA. Neuraxial pain relief for intractable cancer pain. *Curr Pain Headache Rep* 2007 ; 11 : 283-9.
- Xue Y, Schulman-Green D, Czaplinski C, Harris D, McCorkle R. Pain attitudes and knowledge among RNs, pharmacists, and physicians on an inpatient oncology service. *Clin J Oncol Nurs* 2007 ; 11 : 687-95.
- Cleeland CS, Gonin R, Hatfield AK et al. Pain and its treatment in outpatients with metastatic cancer. *N Engl J Med* 1994 ; 330 : 592-6.
- Desbiens NA, Wu AW, Broste SK et al. Pain and satisfaction with pain control in seriously ill hospitalized adults : findings from the SUPPORT research investigations. For the SUPPORT Investigators. Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatment. *Crit Care Med* 1996 ; 24 : 1953-61.
- Weiss SC, Emanuel LL, Fairclough DL, Emanuel EJ. Understanding the experience of pain in terminally ill patients. *Lancet* 2001 ; 357 : 1311-15.
- Bressler LR, Geraci MC, Schatz BS. Misperceptions and inadequate pain management in cancer patients. *DICP* 1991 ; 25 : 1225-30.
- McMillan SC, Tittle M, Hagan S, Laughlin J, Tabler RE. Knowledge and attitudes of nurses in veterans hospitals about pain management in patients with cancer. *Oncol Nurs Forum* 2000 ; 27 : 1415-23.
- O'Brien S, Dalton JA, Konsler G, Carlson J. The knowledge and attitudes of experience oncology nurses regarding the management of cancer-related pain. *Oncol Nurs Forum* 1996 ; 23 : 515-21.
- Gilson AM, Maurer MA, Joranson DE. State policy affecting pain management : recent improvements and the positive impact of regulatory health policies. *Health Policy* 2005 ; 74 : 192-204.
- Zekry HA, Reddy SK. Opioid and non-opioid therapy in cancer pain : The traditional and the new. *Curr Rev Pain* 1999 ; 3 : 237-47.
- Burgess FW, Haworth K. Developing techniques and strategies for the management of cancer pain. *Curr Rev Pain* 1999 ; 3 : 178-82.
- Thielking PD. Cancer pain and anxiety. *Curr Pain Headache Rep* 2003 ; 7 : 249-61.
- Tumber PS, Fitzgibbon DR. The control of severe cancer pain by continuous intrathecal infusion and patient controlled intrathecal analgesia with morphine, bupivacaine and clonidine. *Pain* 1998 ; 78 : 217-20.
- Eidelman A, White T, Swarm RA. Interventional therapies for cancer pain management : important adjuvants to systemic analgesics. *J Natl Compr Canc Netw* 2007 ; 5 : 753-60.
- De Leon-Casasola OA. Interventional procedures for cancer pain management : when are they indicated ? *Cancer Invest* 2004 ; 22 : 630-42.
- Lordon SP. Interventional approach to cancer pain. *Curr Pain Headache Rep* 2002 ; 6 : 202-6.
- Mercadante S. Neuraxial techniques for cancer pain : an opinion about unresolved therapeutic dilemmas. *Reg Anesth Pain Med* 1999 ; 24 : 74-83.
- Romero-Sandoval A, Eisenach JC. Perineural clonidine reduces mechanical hypersensitivity and cytokine production in established nerve injury. *Anesthesiology* 2006 ; 104 : 351-5.
- Hassenbusch SJ, Paice JA, Patt RB, Bedder MD, Bell GK. Clinical realities and economic considerations : economics of intrathecal therapy. *J Pain Symptom Manage* 1997 ; 14 : S36-S48.
- Chaturvedi A, Dash HH. Sympathetic blockade for the relief of chronic pain. *J Indian Med Assoc* 2001 ; 99 : 698-703.
- Ischia S, Polati E, Finco G, Gottin L. Celiac block for the treatment of pancreatic pain. *Curr Rev Pain* 2000 ; 4 : 127-33.
- Lillemo KD. Current management of pancreatic carcinoma. *Ann Surg* 1995 ; 221 : 133-48.
- Kalser MH, Barkin J, MacIntyre JM. Pancreatic cancer. Assessment of prognosis by clinical presentation. *Cancer* 1985 ; 56 : 397-402.
- Ischia S, Ischia A, Polati E, Finco G. Three posterior per

- cutaneous celiac plexus block techniques. A prospective, randomized study in 61 patients with pancreatic cancer pain. *Anesthesiology* 1992 Apr ; 76 (4) : 534-40.
28. Singler RC. An improved technique for alcohol neurolysis of the celiac plexus. *Anesthesiology* 1982 ; 56 : 137-41.
 29. Hilgier M, Rykowsky JJ. One needle transcrural celiac plexus block. Single shot or continuous technique, or both. *Reg Anesth* 1994 ; 4 : 277-83.
 30. Antila H, Kirvelä O. Neurolytic thoracic paravertebral block in cancer pain. A clinical report. *Acta Anaesthesiol Scand* 1998 ; 42 : 581-5.
 31. Eason MJ, Wyatt R. Paravertebral thoracic block – a reappraisal. *Anaesthesia* 1979 ; 34 : 638-42.
 32. Richardson J, Sabanathan S. Thoracic paravertebral analgesia. *Acta Anaesthesiol Scand* 1995 ; 39 : 1005-15.
 33. Swetlow GI. Paravertebral alcohol block in cardiac pain. *Am Heart J* 1926 ; 1 : 393-412.
 34. Swetlow GI. Alcoholic injections into nerve tissues for relief of pain. *Am J Med Sci* 1926 ; 171 : 397-407.
 35. Borene SC, Rosenquist RW, Koorn R, Haider N, Boezaart AP. An indication for continuous cervical paravertebral block (posterior approach to the interscalene space). *Anesth Analg* 2003 ; 97 : 898-900.
 36. Sundaresan N, Galicich JH, Bains MS, Martini N, Beattie EJ Jr. Vertebral body resection in the treatment of cancer involving the spine. *Cancer* 1984 ; 53 : 1393-6.