Neurolytic blocks: When, How, Why

Nörolitik bloklar: Ne zaman, Nasıl, Niçin

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Summary

Interventional techniques are divided into two categories: neuroablative and neuromodulatory procedures. Neuroablation is the physical interruption of pain pathways either surgically, chemically or thermally. Neuromodulation is the dynamic and functional inhibition of pain pathways either by administration of opioids and other drugs intraspinally or intraventricularly or by stimulation. Neuroablative techniques for cancer pain treatment have been used for more than a century. With the development of imaging facilities such as fluoroscopy, neuroablative techniques can be performed more precisely and efficiently.

Key words: Neuroablative techniques; neurolytic blocks; radiofrequency thermocoagulation.

Özet

Girişimsel teknikler nöroablatif ve nöromodülatör işlemler olarak iki gruba ayrılırlar. Nöroablasyon, cerrahi, kimyasal veya ısı uygulamalarıyla ağrı yolaklarında fiziksel iletinin kesilmesidir. Nöromodülasyon, stimülasyon uygulamasıyla veya intraventriküler ya da intraspinal uygulanan opioidler ve diğer ajanlarla ağrı yolaklarının dinamik ve fonksiyonel inhibisyonudur. Nöroablatif teknikler kanser tedavisinde yüzyıldan fazla zamandır kullanılmaktadır. Fluroskopi gibi görüntüleme araçlarındaki gelişmelerle nöroablatif uygulamalar daha doğru ve etkili bir şekilde gerçekleştirilmektedir.

Anahtar sözcükler: Nöroablatif teknikler; nörolitik bloklar; radyofrekans termokoagulasyon.

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Introduction

Cancer pain is one of the most witnessed pain syndromes throughout the world.[1] The World Health Organization (WHO) analgesic ladder has been reported to be efficacious in controlling pain in approximately 90% of the patients.[2-5] There thus remain quite a number of patients who require interventional treatment of cancer pain.

Interventional techniques are divided into two categories: neuroablative and neuromodulatory procedures.[6] Neuroablation is the physical interruption of pain pathways either surgically, chemically or thermally. Neuromodulation is the dynamic and functional inhibition of pain pathways either by administration of opioids and other drugs intraspinally or intraventricularly or by stimulation.

Patient selection for neuroablation

The use of neuroablative techniques for the control of cancer pain necessitates training of the pain physician, development of facilities for applying these techniques and follow-up of the patients. Patients who are candidates for interventional therapies require special care and follow-up.

Patient selection is very important prior to the interventional pain treatment. A thorough history of the patient related with his disease and pain should be evaluated, including the onset, duration, intensity, localization, and course of the pain. In addition to the knowledge regarding the disease itself, a complete evaluation of the patient related with pain should be done, and should include a general medical and neurological evaluation, laboratory tests and radiographic evaluation. Most of the interventional techniques target the nervous system; thus, a recent radiological evaluation is a must in order to identify the cause of the pain as well as to prevent complications related with the technique. It is also important to verify the objective findings of pain, which will help to clarify the type of intervention to be used.

The emotional and psychological status of the patients should be assessed prior to the intervention. The psychological assessment of the patient will guide the physician in determining if the patient is suitable for an intervention, and if so, which type.

The life expectancy of the patient is another important criterion for selecting the interventional technique. Most of the cancer patients referred for interventional treatment are in the terminal stage with short life expectancy. The interventional technique to be applied should sustain a better quality of life with the least complications or side effects.

Interventional techniques should be applied when more conservative pain modalities fail. Generally, the WHO ladder is applied, and when all drugs included in the ladder are inadequate, interventional techniques are considered. However, in some cases, interventional techniques may be applied earlier, and this will be addressed in a later section.

There should be no general contraindications such as sepsis or coagulopathy while performing the interventional techniques.

Neuroablative techniques for cancer pain treatment

Neuroablative techniques for cancer pain treatment have been used for more than a century. With the development of imaging facilities such as fluoroscopy, neuroablative techniques can be performed more precisely and efficiently.

Neuroablative techniques are used less frequently than before with the improvement in new drugs and use of new routes, such as transdermal application of opioids, and use of long-acting opioids and adjuvant drugs. Although more limited than before, neuroablative techniques still have a certain role in the treatment of intractable cancer pain. These techniques are indicated when administration of analgesics according to the "ladder" is inadequate. Life expectancy of the patient should be limited and the pain should be localized to a part of the body. Neuroablative techniques can be used for somatic or visceral pain. They do not have a real place in neuropathic pain syndromes, except for sympathetic blocks.

Although neuroablative techniques should be performed when the "ladder" is inadequate in certain cancer pain syndromes, they may be performed at an earlier stage. Localized pain at the innervation of the trigeminal nerve may be interrupted either by neurolytic block or radiofrequency thermocoagulation of the gasserian ganglion. Celiac and splanchnic blocks may also be performed at an earlier stage before the anatomy of the region is distorted.

The advantages of neuroablative techniques are: they require less follow-up of the patient when compared with neuromodulatory techniques, they are more cost-effective, and they may have a place in patients with short life expectancy. Their disadvantages include: greater potential risks such as of permanent motor loss, paresthesia and dysesthesia, their requirement of very well-trained physicians, and their limited use only for localized pain.

Neurolytic nerve blocks

Neurolytic agents

Neurolytic agents are chemical substances that destruct the nerve, including 50-100% alcohol, 5-15% phenol, glycerol, and hypertonic saline.

Alcohol is the oldest agent, generally used for celiac plexus, gasserian ganglion, sympathetic chain, or intrathecally. Several concentrations varying between 50-100% are used. Damage to the nerve is nonselective.

Phenol is more frequently used in glycerine solutions as a hyperbaric solution in concentrations between 5-15%. Damage to the nerve is again nonselective, but is more reversible than with alcohol.

Glycerol is only used for peripheric nerves, but the duration of the effect is much shorter.

Neurolytic blocks

Trigeminal ganglion neurolysis

The percutaneous trans-foramen ovale approach for the trigeminal (gasserian) ganglion using absolute alcohol was first described by Hartel in 1912.[7] In the evolution of treatment, radiofrequency lesioning for this ganglion was described by Sweet and Wepsic in 1965[8] and retrogasserian glycerol injection by Hakanson in 1981[9].

Trigeminal ganglion block is generally used for the treatment of idiopathic trigeminal neuralgia, but it has a place in the treatment of secondary pain due to cancer of the region. It should be performed at an earlier stage, before the anatomy of the region is distorted by the growth of the cancer to obtain a better result. It effect lasts for months to years.

It should be performed under fluoroscopy. The foramen ovale is easily seen under the fluoroscope, and the neurolytic solution, either alcohol or phenol, which should not exceed 1 ml, is given in smaller aliquots. Otherwise, it may spread to the brainstem and cause severe complications. Currently, the use of radiofrequency lesioning is preferred to the neurolytic agents. More precise location of the nerve is possible with radiofrequency lesioning, and there is no risk of spread of neurolytic solution to the brainstem.

Trigeminal ganglion neurolysis is not free of complications.[10] Facial numbness develops as a result of the neurolysis in all cases. The patients should be informed in advance regarding facial numbness. In fact, it may be considered a result of neurolysis rather than a complication. Loss of corneal reflex may occur as a result of the destruction of the ophthalmic branch of the trigeminal nerve. Anesthesia dolorosa is the most severe complication. The pain is relieved but burning pain and dysesthesia develop in the region, and this is difficult to control.

Intercostal nerve block

By 1922, Labat's textbook contained an elaborate description of the intercostal nerve block that is quite similar to our present-day conceptions.[11] Intercostal nerve block is one of the most effective blocks in the treatment of pain. It may be used in the treatment of pain due to fractured ribs and cancer metastasis.

It is much better to perform the block under fluoroscopy. The needle touches the lower edge of the rib and slips down the rib while adjacent to it. It is preferable to perform the block first with a local anesthetic, 2% lidocaine solution. If it is helpful, 6-8% phenol (3-5 ml) may be administered. Pneumothorax and intravascular injection are the main risks. However, careful performance of the block reduces the risk of pneumothorax development.

Intrathecal and epidural neurolytic blocks

Intrathecal neurolysis has been used since 1931, and was first performed by Dogliotti.[12] The use of intrathecal alcohol and phenol has faded in recent years because of the fear of complications such as motor, autonomic and sensorial loss. The concept of the procedure is bathing the posterior, sensory nerve root with the neurolytic solution, either alcohol or phenol. Very small amounts of the neurolytic solution are delivered based on the patient's position: if hypobaric alcohol is used, the painful side is up; if phenol is used, the painful side is down.[13,14] It should be performed by very experienced physicians in order to prevent dreadful complications.

Phenol may also be delivered epidurally to the affected route.[15] It should be performed under fluoroscopy and the catheter tip should be visible in order to advance to the root; 6% aqueous phenol may then be injected. The risk of complications such as sensorial or motor loss is less than with intrathecal neurolysis.

Neuroadenolysis of the pituitary
In hormone-related cancer such as thyroid or breast cancer with several metastases throughout the body, neuroadenolysis of the pituitary may be considered. It was first performed by Moricca in the late 1970's.[16] The technique is performed under fluoroscopy. With the patient lying in the supine position, the needle is advanced transnasally and transsphenoidally to the pituitary. Following the verification of the position, 0.5-3 ml of absolute alcohol is injected to destroy the pituitary gland.[17] Cephalalgia, hypothyroidea, hypoadrenalism, and diabetes insipidus are the most frequently seen complications. Currently the technique has lost its popularity.

Neurolytic sympathetic blocks
The relationship of the sympathetic nervous system and several chronic pain syndromes including cancer pain has long been recognized.[18,19] Sympathetic blocks may have a place in cancer pain patients if they have neuropathic pain syndromes due to surgery, chemotherapy or radiotherapy or infiltration of the brachial or lumbosacral plexus, or in visceral pain arising from the upper or lower abdominal organs.

Stellate and thoracic and lumbar sympathetic blocks are used in the treatment of neuropathic pain syndromes related with the cancer, while splanchnic, celiac, hypogastric and impar ganglion blocks are used for the treatment of visceral pain arising from the upper or lower abdominal organs.

a. Stellate ganglion block
Selective block of the stellate ganglion was first described by Sellheim and shortly after by Kappis in 1923, and by Brumm and Mandl in 1924.[19,20]

Stellate ganglion block is useful in cancer patients if the patient has a burning pain radiating to the upper extremity. It is much better to combine it with the thoracic sympathetic block. It is also effective in patients with postherpetic neuralgia.

It is contraindicated if the patient had a pneumonectomy on the contralateral side because of the danger of additional pneumothorax on the ipsilateral side. It is also contraindicated if the patient had a recent cardiac infarction. It should first be performed using a local anesthetic solution, and if effective, the neurolytic solution should then be given. Currently, the stellate gangliolysis may be performed by radiofrequency thermocoagulation.

The two principal complications of stellate ganglion block are pneumothorax and intraspinal injection. A third risk when neurolysis is performed is the possibility of persistent Horner's syndrome. If the neurolysis is performed under fluoroscopy, the potential risk is minimalized.

b. T2-T3 sympathetic neurolysis
Previously, T2-T3 sympathetectomy was performed surgically. With the development of imaging techniques, neurolysis is performed more. In 1979, Wilkinson devised the technique for radiofrequency thermocoagulation with minimal complications.

T2 and T3 sympathetic block is considered for patients who have sympathetically maintained pain. It is contraindicated in respiratory insufficiency or thoracic aortic aneurysm.

It is performed in a prone position under fluoroscopy. 2-3 ml of phenol may be delivered to the sympathetic chain, or radiofrequency thermocoagulation is performed. Pneumothorax is the principal complication. Another side effect of this procedure is intercostal neuritis. This problem can be minimized by meticulously performing sensory and motor stimulation prior to lesioning.[21]

c. Splanchnic nerve block

The first anterior percutaneous approach to splanchnic nerve block was described by Kappis in 1914.[22] The recognition that splanchnic nerve block may provide relief of pain in a subset of patients who fail to obtain relief from celiac plexus block has led to a renewed interest in this technique. It was recently revised by Raj for radiofrequency thermocoagulation.[21]

Splanchnic block is one of the effective blocks in relieving cancer pain in the upper abdominal organs including the stomach and pancreas.

The technique should be performed under fluoroscopy with the patient in a prone position. If the pain is unilateral, the splanchnic nerve on the same side is blocked; however, it is generally bilateral and should be performed for both sides.

Smaller volumes, 5-8 ml of absolute alcohol, are recommended for single needle procedures. Many investigators believe that alcohol as a neurolytic agent is superior to phenol in duration of neural blockade. 6-10% phenol may also be used.[23]

Because splanchnic nerves are contained in a narrow compartment, they are accessible for radiofrequency lesioning. To produce a lesion of the splanchnic nerve, the needle needs to lie on the mid-third portion of the lateral side of the T11-T12 vertebral body. After a sensorial test stimulation in which the patient should report a stimulation in the epigastric region, the radiofrequency lesion is created.

Complications of splanchnic block can be regarded as minor, moderate or severe. Those considered relatively minor such as hypotension and diarrhea are readily reversible. Moderate complications like pneumothorax should not occur if performed under fluoroscopy, but again are transient. Major complications such as paraplegia are rare.

d. Celiac plexus block

In 1914, Kappis introduced the percutaneous technique for the celiac plexus block.[22] The celiac plexus lies anterior to the aorta and epigastrium. It is just anterior to the crus of the diaphragma. Postganglionic nerves from these ganglia innervate all abdominal viscera, with the exception of part of the transverse colon, the left colon, the rectum and pelvic viscera.

Any pain originating from the visceral structures and innervated by the celiac plexus can be effectively relieved by the block of the plexus. These structures include the pancreas, liver, gallbladder, omentum, mesentery, and alimentary tract from the stomach to the transverse portion of the large colon.

Celiac plexus block increases the gastric motility. This may be beneficial in patients with chronic constipation due to analgesics. Diarrhea has been reported in a few patients as well as concomitant decrease in the incidence of nausea and vomiting. However, the celiac plexus block should be avoided in patients with bowel obstruction.[24]

50-100% alcohol is the agent generally used for the neurolysis It should be performed under fluoroscopy guidance to prevent any complication. It may either be performed by single needle technique by transaortic approach or by double needle technique. In the hands of an experienced physician, serious complications rarely occur. Because of the proximity of other vital structures, coupled with large volumes of neurolytic drugs, side effects and complications may be seen.

Minor complications include hypotension, diarrhea and back pain, which fade within days. Moderate complications are mechanical or chemical disturbance of the organs in the proximity of the ganglion and irritation of the genitofemoral nerve. Major complications include paraplegia due to the incorrect placement of the needle near the spinal nerves or subarachnoid/vascular injection of the neurolytic solution, renal injury, perforation of cysts of tumors, and peritonitis.

In spite of its risks and complications, celiac plexus block is one of the most effective neurolytic blocks if performed properly. Time to maximal pain relief is variable. In most patients, relief is immediate and complete, while in others it will accrue over a few days. In addition, pain relief is re-established with repetition. Its effect lasts for months.[25,26]

e. Hypogastric plexus neurolysis

The first attempts to interrupt the sympathetic pathways in the pelvic region date back to the end of the 19th century, with Jaboulay in France and Ruggi in Italy in 1899.[27,28] In 1990, Plancarte described the technique for hypogastric plexus block.[29]

The superior hypogastric plexus is the extension of the aortic plexus in the retroperitoneal space below the aortic bifurcation. It contains almost exclusively sympathetic fibers. The anatomic location of the superior hypogastric plexus, the sympathetic predominance of the fibers of the plexus, and its role in the transmission of most of the pain signals from the pelvic viscera make this structure an ideal target for neurolysis in the cancer pain arising from the pelvic viscera.

It may be performed by lateral approach using double needle technique trying to reach to the L5-S1 level. It may also be performed with the intra-discal approach under fluoroscopy. Long-lasting pain relief with this procedure has been achieved in patients with pelvic cancer pain.

f. Ganglion impar block

The first report of interruption of the ganglion impar for the relief of perineal pain came from Plancarte in 1990.[30]

The ganglion impar is also known as the ganglion of Walther or the sacrococcygeal ganglion and it is the most caudal ganglion of the sympathetic trunk. Visceral pain or sympathetically maintained pain in the perineal area associated with malignancies of the pelvis may be treated with neurolysis of the ganglion impar. Patients with colostomy with tenesmic-like pain and patients with a clinical picture of vague, burning localized pain may benefit from this block, but the duration is shorter than with other sympathetic blocks.

There are multiple approaches to this block such as lateral approach and trans-discal approach. All approaches should be performed under fluoroscopy. Rectum puncture, neurolytic injection into the nerve roots and rectal cavity and neuritis due to nerve root injection are the potential complications.

Radiofrequency thermocoagulation for the treatment of cancer pain

The use of current lesions for the treatment of pain is not new. Kirschner was the first to describe the use of percutaneous current lesions for the treatment of trigeminal neuralgia using direct current delivered to a needle placed in the gasserian ganglion. Since then, the technique and equipment have been developing.

In 1965, Mullan and Rosomoff described the percutaneous lateral cordotomy for unilateral malignant pain.[31,32] A few years later (1974), Sweet used radiofrequency lesions for the treatment of trigeminal neuralgia.[8]

In 1975, Shealy used a radiofrequency probe to interrupt the posterior primary ramus of segmental nerves. Uematsu in 1977 described the technique for the radiofrequency of the dorsal root ganglion.[33] The development of a small diameter (22 gauge) electrode system facilitated the safer use of the radiofrequency procedures. In recent years, Slujter has been the pioneer of developing newer techniques like pulsed radiofrequency.

What is radiofrequency treatment?

Radiofrequency is an alternating current with an oscillating frequency of 500,000 Hz. The heat produced by radiofrequency creates circumscript lesions by which selective nerve lesioning is possible. The effect of heat on neural tissue becomes destructive after 45° C. Lesions are generally created with heat over 60° C.

Currently, radiofrequency thermocoagulation is used for the treatment of various non- malignant and malignant pain syndromes.

The main procedures of radiofrequency lesioning used in the treatment of cancer pain are:

a. percutaneous cordotomy
b. radiofrequency thermocoagulation of the gasserian ganglion

c. percutaneous rhizotomy
d. percutaneous radiofrequency sympathectomy

a. Percutaneous cordotomy

At present, percutaneous cervical cordotomy is one of the most important neuroablative techniques in the treatment of cancer pain. In recent years, use of the technique has been declining. The number of patients referred for cordotomy has decreased dramatically since the introduction of intraspinal techniques. There are only very few experts in the world who perform cordotomy. Nevertheless, it still has a place in the treatment of severe cancer pain. The aim of percutaneous cordotomy is to interrupt the spinothalamic tract in the anterolateral quadrant, the most prominent ascending nociceptive pathway in the spinal cord.

The cordotomy is performed at the cervical level between C1-C2 where the fibers of the lateral spinothalamic tract are closely compact in the anterolateral quadrant and present a precise somatotropy. The fibers coming from the lumbosacral segments lie in the dorsolateral position, whereas those of thoracic-cervical origin are more ventral.

The cordotomy is performed with the patient awake and able to collaborate so as to have a continuous control of precise positioning of the electrode in the spinal cord.

It may be performed under either fluoroscopy- or CT-guided technique.

Percutaneous cordotomy is indicated for strictly unilateral pain of malignant origin. It is contraindicated in bilateral pain, pain extending to levels cranial to C5, in patients with a life expectancy of more than one year, in those with poor lung function, and in vertebral and epidural metastasis.

Percutaneous cordotomy carries the risk of very serious complications. There is risk of motor loss if the lesion has been made too close to the pyramidal tract. Paraplegia may also develop. Transient urinary retention may develop for the first 48 hours following the procedure. Ondine syndrome, in which a patient can breathe voluntarily but in whom respiration stops during sleep, may develop. Dysesthesia is the most unpleasant complication, in which the patient defines an unpleasant sensation on the originally painful side of the body. This usually develops after several months.

Percutaneous cordotomy is the most dangerous of all percutaneous neuroablative techniques. It should be performed only by highly experienced experts.

b. Percutaneous radiofrequency lesioning of the trigeminal ganglion

Generally, neurolysis of the gasserian ganglion is used for the treatment of cancer pain related with the trigeminal nerve. However, radiofrequency lesioning is less risky than neurolysis. If phenol or glycerol is used, the solution may spread to the brainstem, resulting in serious side effects like nausea and vomiting for several days. Lesioning of the nerve is more precise with thermocoagulation.

In cancer pain, all three branches of the trigeminal nerve are generally affected. Thus, all branches should be thermocoagulated. The complications are the same as with neurolysis.

c. Percutaneous dorsal root ganglion rhizotomy

A diagnostic block before rhizotomy is a requirement. One of the biggest concerns is damaging the nerve root while positioning the electrode or during radiofrequency lesioning. It is seldom used.

d. Lumbar and thoracic sympathetic radiofrequency lesioning

Lumbar or thoracic sympathetic radiofrequency lesioning may be used; however, neurolytic agents are generally preferred.

Conclusion

Neurolytic blocks should only be considered when less invasive methods are inadequate, and the procedures should be performed in well-established centers. Pain practitioners should consider the role of these blocks in adjuvant therapy for the optimal treatment of cancer pain.

Unfortunately, long-term follow-up and results are still lacking for all the methods. However, the clinical perspective offered by interventional pain techniques opens a challenging field for the management of pain in cancer. Finally, this topic represents an important opportunity for new research, and multicenter studies can be carried out on this subject.

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