The management of cancer pain represents a difficult diagnostic and therapeutic problem for the clinician. In a multidisciplinary approach to the management of cancer pain, neurosurgical methods are an essential part of the therapy. Frequently, patients with advanced cancer suffer from an increasing pain, requesting ever-higher dosage of narcotics, and finally seeming to respond only to high dosage of intravenous narcotics. Gradually, the opioids produce less satisfactory analgesic effects and more serious side manifestations. These patients can be considered for surgical management of pain. Historically, surgery for cancer pain began with destructive procedures (neurectomy, rhizotomy, sympathectomy), often referred to as ablative. In past two decades, with the help of the current knowledge of cancer pain mechanisms and some of the technological developments, such as microsurgical and stereotactic techniques, computerized tomography and magnetic resonance imaging, the majority of ablative procedures have been replaced by new methods. Among them a few are selectively and minimally ablative (microsurgical spinothalamic cordotomy, dorsal root entry zone operation, limited midline myelotomy) and the others ones are neuroaugmentative operations (deep brain structures and spinal cord stimulation, drug-delivery systems).

Key words: cancer pain, surgical management of pain, ablative procedures, neuroaugmentative operations

INTRODUCTION

In a multidisciplinary approach to the management of cancer pain, neurosurgical methods are an essential part of the therapy. As the pain becomes more severe the larger doses of analgetics are required. In time, the medicaments produce less satisfactory analgesic effects and more serious side manifestations. Depending on diagnosis and clinical status, certain patients can be considered for surgical relief of pain. The numerous surgical techniques in cancer pain management are described. In selecting the procedure for a specific patient, one must consider the nature of the pain - nociceptive or neuropathic, visceral or somatic, peripheral or central.

THERAPEUTIC NERVE BLOCKS

Neurolytic blockades are used to treat visceral and somatic pain. Neural tissue can be damaged irreversibly by a variety of chemical agents. Ethyl alcohol and phenol remain the neurolytic agents of choice. They produce protein denaturation and extraction of lipid membrane components. Their action is nonselective as to fiber size and type. Unfortunately, they cause necrosis and glia scarring. Ethyl alcohol is usually used undiluted (95%), although a concentration of at least 35% to 50% may produce neurolysis. Phenol is used in concentration of 5% to 10%.

Paravertebral Somatic Nerve Block - assists in determining the extent of spinal nerve involvement, enable spinal localization of a pain-producing disease process, and give prognostic information prior to neurolytic or surgical ablative procedures in pain from malignancies. The spinal nerve is blocked at its exit...
from the intervertebral foramen, as it crosses the space between two transvers processes. Overlapping innervation usually necessitates blocks of one to two neighboring segments. Because most spinal nerves are mixed nerves, neurolytic agents will affect both, motor and sensory fibers. Alcohol and phenol can cause chemical neuropathy which may become a pain syndrome.

Stellate Ganglion Block (cervicothoracic sympathetic block) – is useful in painful invasive lung tumors involving the head, neck or upper extremity. The stellate ganglion is formed by the fusion of the inferior cervical ganglion and the first thoracic ganglion and lies anterior to the neck of the first rib. Its blockade interrupt the sympathetic outflow from the upper four or six thoracic sympathetic ganglia and at the lower cervical sympathetic ganglion. Successful block will affect the ipsilateral cranium and hemifacies, the upper extremity sympathetic ganglion. Successful block will affect the ipsilateral hemithorax, including visceral pleura and sympathetic supply to the heart.

Celiac Plexus Block - pancreatic cancer and upper abdominal malignancies present the most frequent indications for celiac plexus block. The celiac plexus is a conglomerate of sympathetic ganglia which contain visceral afferent and efferent sympathetic fibers. Parasympathetic fibers may pass through it as well. It receives the splanchnic nerves which are the sympathetic rami communicantes from the T5-T12. Aparasympathetic fibers may pass through it as well. It receives the splanchnic nerves which are the sympathetic rami communicantes from the T5-T12.

Lumbar Sympathetic Block - is used in therapy of cancer pelvic pain and ureteral involvement. The lumbar sympathetic chain lies on the anterolateral surface of the bodies of the second, third, and fourth lumbar vertebrae.

Pelvic Sympathetic Nerve Block - the superior hypogastric plexus is in the retroperitoneum, bilaterally extending from the lower third of the fifth lumbar vertebral body to the upper third of the first sacral vertebral body. Pelvic cancer pain may be alleviated by blockade of the superior hypogastric plexus. Analgesia to the organs in the pelvis is possible because the afferent fibers innervating these structures travel in the sympathetic nerves, trunks, ganglia, and rami. A sympathetic block for visceral pain has the same effect as a peripheral neurectomy or dorsal rhizotomy for somatic pain. Significant pain relief may be obtained with percutaneous neurolytic blocks of the superior hypogastric plexus.

Ganglion Impar Block – visceral pain or sympathetically maintained pain in the perineal area associated with malignancies of the pelvis may be effectively treated with neurolysis of the ganglion impar. The ganglion impar (or sacroccygeal ganglion) is the most caudal ganglion of the sympathetic trunk.

Subarachnoid Neurololytic Block – segmental injections of small amount of phenol or alcohol are used to produce chemical posterior rhizotomy. The success rate lies between 60 and 70%. Exact positioning of the patient and choice of the injection level and volume allows selective sensory anesthesia with sparing of motor fibers. The duration of analgesia is an average from one week to three months.

Peripheral Neurectomy

Peripheral neurectomy is rarely useful except in the unusual circumstance in which a specific peripheral nerve is involved with tumor.

Dorsal Rhizotomy

The section of dorsal spinal roots is performed for cancer pain of the chest wall. When painful radiculopathy is part of the patient’s clinical picture, satisfactory relief can be achieved by section of the roots invaded with tumor.

Dorsal Root Ganglionectomy

The ganglionectomy may be helpful in the treatment of next nonextremity pain of malignant origin:
- pain of peripheral origin located in the neck, trunk, or abdomen.
- pain due to invasion of the chest wall by pleural-based or other chest wall malignancy.
- perineal pain due to malignancy (if ganglionectomy includes S2 and S3, a neurogenic bowel and an denervated anal sphincter will result).

In the preoperative evaluation a local anesthetic blockade of the spinal ganglia must be carried out under radiographic and fluoroscopic control. The block must be repeated at least twice. Unfortunately, a complete pain relief from an anesthetic block is not a guarantee for success of operation. The reason of that are the ventral root afferent fibers that may not have been divided even after seemingly complete ganglionectomy, or more likely, a more central mechanism for the pain. The dorsal root ganglionectomy means a laminectomy and foraminotomy at appropriate vertebral level and a microsurgical extradural exposure of a targeted sensitive ganglion; then, the dorsal root is divided proximally to the ganglion, sparing the ventral root and the feeding segmental arteries.
region the dorsal and ventral roots can be sacrificed together without producing motor dysfunction or significant atrophy. Usually a minimum of three roots are taken, often as many as four or five

The excellent early results in pain relief have 91% of the patients which fell to 79% of the patients after follow-up of 30 months. Pain control lasted in most patients until death. Complications from extradural ganglionectomy are rare and common to spinal surgery.

**CEPHALIC AND FACIAL CANCER PAIN**

Malignancy arising from the paranasal sinuses, salivary glands, or ear canal may spread directly along nerve sheaths and produce intense pain in the distribution of the nerve. The diagnosis is made in the presence of a known head or neck cancer with evidence of tumor spread along the nerve (CT or MRI). In intractable pain of invasive carcinoma an ablative procedure, as radiofrequency trigeminal rhizotomy, is indicated. In some cases a supra-or infra-orbital neurectomies may be effective in alleviating the pain. Percutaneous injection of glycerol into the Gasserian ganglion may produce pain relief usually. Radiation therapy is also often effective, mainly temporarily. Sometimes, the pain caused by invasive carcinoma is so severe that intrathecal or intraventricular administration of morphine, through an implanted continuous infusion pump, is indicated.

**PERCUTANEOUS TRIGEMINAL TRACTOTOMY**

This procedure means the use of stereotactic techniques for creating percutaneous radiofrequency lesions in the trigeminal tract or nucleus in the upper cervical spinal cord or medulla. Extension of the lesion more posteriorly and medially in the medulla allows incorporation of lower cranial nerves. The relief of facial cancer pain is 87% of the patients.

**DREZ lesions**

DREZ – otomy (dorsal root entry zone) is indicated for treatment of cancer pain (nociceptive or neuropathic) located in upper or lower extremities which are preoperatively functionally preserved. These are the patients with malignant tumors and compression or infiltration of the brachial plexus or lumbosacral plexus.

The large and small axons in a dorsal root are randomly dispersed through most of the length of the root. However, near the entry of the dorsal root into the spinal cord (DREZ), the large fibers (A-beta, transmitting the tactile sensibility) tend to become segregated from the small ones (A-delta and C, responsible to nociceptive sensibility. The larger myelinated axons are situated medially and the poor myelinated and unmyelinated fibers more laterally in the dorsal rootlets. The major somatic and visceral nociceptive input from the periphery is distributed to Rexed layers I, II, and V of the medullary dorsal horn; the secondary neurons from these layers give rise to the spinothalamic tract destined to the contralateral thalamus. The precise lesion in the region of ventrolateral area of “dorsal root entry zone” and superficial Rexed layers may selectively destroy (1) the nociceptive fibers, (2) Lissauer’s tract, and (3) their synapses with secondary sensory neurons, sparing other sensitive pathways. The chronic central pain (deafferentation pain) is due to pathological lesions that isolate the centrally located secondary neurons in the dorsal horn. Because these central neurons are isolated from their normal peripheral sensory input, they function abnormally, causing pain. Therefore, the DREZ lesion result not only in relief of nociceptive pain but in elimination of neuropathic central pain, as.

The DREZ lesions may be done by controlled radiofrequency heating and coagulation, or with a laser, or microsurgical section.

Sindou used DREZ lesions in treatment of cancer-related pain in tumors of superior pulmonary sulcus, the brachial plexus, the axillary region, and pelvic floor. At an average of 10 months of follow-up, approximately 85% of the patients sustained good pain relief.

The postoperative morbidity after unilateral cordotomy transient or persistent, appear in 44% of the patients. The most common transient is a ipsilateral weakness of legs in 11% of the patients, while the persistent is a contralateral dysesthesia in 4% of the patients. In our series of 56 patients suffering of cancer pain localized in upper extremities and shoulder we applied cervical DREZ-otomy. A total pain relief immediately after surgery was achieved in 88% of the patients.

**SPINOthalamic CORDOTOMY**

a) microsurgical anterolateral high thoracic cordotomy

Open high thoracic spinothalamic cordotomy should be considered in cancer patients suffering of unilateral intractable pain caused by compression of lumbosacral plexus, untreatable by all other conservative methods, whose general condition permits a surgical procedure and whose life expectancy is six months or longer.

The spinothalamic (or anterolateral) cordotomy means a section of fibers of spinothalamic tract situated in ventrolateral segments of spinal cord. Typical anterolateral cordotomy severs spinothalamic, spinoreticular, spinotectal, and dorsal and ventral spinocerebellar long tracts.
A successful section results in anesthesia for pain and temperature on the opposite side of the body at a level one to two segments below the area section. The spinothalamic tract decussates either within one or several segments rostrally from the cell bodies. The sensation of touch, vibration, and position is preserved.

High thoracic anterolateral corodotomy is performed using a microsurgical techniques. The patient were under general anesthesia. The laminectomy seize the T1-T2 vertebrae. Rarely it is necessary to remove more than two laminae, even for the bilateral corodotomy. Under a operating microscope, the dorsal roots, dentate ligaments and ventral roots are readily identified by an extra-arachnoid approach. All dentate attachments in the operative area are divided from its lateral insertion on the dura. The divided dentate ligament may be grasped with a forceps or a needle holder to rotate the spinal cord contralaterally. Usually the cord can be rotated up to 60 degrees and the anterior spinal artery can be seen.

The section by a sharp pointed blade with a measured distance between 4-5 mm is made, depending on the diameter of the cord. The blade is inserted into the pial opening such a manner as to make an angle of about 15 degrees anteriorly with the transverse diameter. A lesion encompassing the entire anterior quadrant of the spinal cord, thereby the spinothalamic tract.

In our series of 86 patients who underwent spinothalamic cordotomy a total pain relief immediately after surgery was present in 86% of the patients and after follow-up of six months in 79% of the patients.

b) percutaneous corodotomy

This procedure is recommanded to the patients suffering of pain below the junction of the C4 to C5 dermatomes, because the procedure does not reliably produce persistent analgesia higher than this. Preferably, pain should be predominate on one side, ideally in one leg, but bilateral corodotomy can be considered for bilateral pain.

The percutaneous corodotomy minimizes surgical impact and increases precision of spinothalamic lesion. This procedure is usually performed under intravenous sedation, but can also be performed under general anesthesia (in children, confused patients, or others not likely to cooperate). In the patients with previously performed myelography, the contrast medium identify The dentate ligament at the C1 and C2 space is identified by previously performed myelography. The laterally advanced corodotomy electrode, always aimed at the center of the C1 and C2 space, enters the subarachnoid space. The deeper penetration of electrode, into the spinothalamic tract, is checking by measurement of electrical impedance and by electrical stimulation. Computed tomography guidance has been described by Kanpolat and is also used by Izumi. The lesion can be made once the electrode is located in the spinothalamic tract. Because coagulating pia is painful, this stage require deep sedation or even brief anesthesia. The corodotomy lesion is made by radiofrequency current.

Postcorodotomy dysesthesia, paresis, ataxia and bladder dysfunctions occur from 5% to 20% of the patients. Patients who undergo a high cervical corodotomy are at risk for respiratory insufficiency. The reticulospinal tract lies adjacent to the spinothalamic fibers of the upper cervical dermatomes. The high level of analgesia requiring to relieve the pain of the patient with Pancoast syndrome, almost certainly damage the reticulospinal tract. Percutaneous cervical corodotomy affords a rate of 64-79% of complete and 75-96% of significant relief of cancer nociceptive pain.

MIDLINE COMMISSURAL MYELOTOMY

It is an alternative to bilateral anterolateral corodotomy for bilateral pain syndromes located below shoulders. The decussation of spinothalamic fibers across medline commissures provides the anatomic basis for this procedure. The introduction of operative microscope allows the complete division of both, the anterior and the posterior commissures, sparing the touch and motor fibers that decussate at the higher levels, in the brainstem and upper cervical cord. The successful pain relief after one year is about 59% in malignant pain syndromes. Complications include dysesthesias and lower extremity proprioceptive deficits in up to 75% of cases.

STEREOTACTIC CENTRAL MYELOTOMY

Stereotactic central midline lesion in limited longitudinal extent interrupts not only the spinothalamic tract fibers crossing locally but also the spinoreticular tracts and some other structures involved in nociceptive transmission and pain modulation. The result is the relief of pain in segments caudal to the lesion without producing a lasting deficit in pinprick discrimination. The satisfactory pain relief is achieved in 78% of the patients.

MESENCEPHALIC TRACTOTOMY

Stereotactic mesencephalic tractotomy has long been a popular operation for relief of intractable chronic cancer pain. In this procedure the radiofrequency lesion is applied by stereotactic technique on the mesencephalic spinothalamic tract. The procedure is associated with a 5% mortality and 37% morbidity,
including oculomotor disturbances (1-5%) and dysesthesias (5%)\textsuperscript{102}. A long-term pain relief after mesencephalotomy is achieved in 76\%\textsuperscript{103} to 83\%\textsuperscript{104} of the patients.

**THALAMOTOMY**

The most effective targets for treatment of pain within the thalamus are the inferior posteromedial thalamus, the basal thalamus, medial thalamus, and dorsomedian thalamus. Although thalamotomy is usually reserved for non-cancer pain, it can be effective for cancer pain. For very precise lesion making the stereotactic surgery is used\textsuperscript{105}.

**HYPOPHYSECTOMY**

This procedure is recommended in the treatment of pain from bone metastases associated with carcinoma of the breast and prostate, regardless of whether the individual tumor is hormonally responsive or unresponsive. The percutaneous stereotactic approach with alcohol installation, radiofrequency thermal lesion, cryotherapy, the interstitial placement of radioactive seeds, or the Gamma knife lesion are used\textsuperscript{106,107,108}.

**IMPLANTED DRUG DELIVERY SYSTEMS**

Unfortunately, many of neurosurgical operations have limited effectiveness and are inappropriate invasive for debilitated patients. The discovery of opioid receptors in the substantia gelatinosa of the spinal cord led to the recognition that the administration of opioid analgesics in the intrathecal space of spinal cord provides an effective modality for patients with cancer-related pain\textsuperscript{109,110,111}.

The programmable pump consists of a battery module, an electronic module for programming and pump control, and a peristaltic pump motor that pulls infusate out of reservoir. The rate of drug infusion is determined by the rate of revolution of the pump motor, which is controlled by the program in the microprocessor of the electronic module. Dosing changes are determined by using an external computer-programmer\textsuperscript{112,113,114}. Before an implanted pump is used it is important to perform an appropriate trial to assure does the patient have side effects with the administered drug and does the patient demonstrate pain relief. Single intrathecal bolus dosing, epidural infusion, and intrathecal infusion are the predominant screening methods\textsuperscript{115,116}.

Cancer pain of all types remains an excellent indication for use of intrathecal opioids, especially with the programmable pump, which can aid in matching pain relief to progression of disease. Many studies have demonstrated the efficacy of intrathecal administration of opiates for cancer pain. About 80\% of the patients have good to excellent pain relief. The complications are rare and may be surgical (hematoma, wound infection, meningitis, neurological injury), device-related complications (failure in the catheter system, pump failure), or drug-related complications (inappropriate drug concentration, overdosage)\textsuperscript{117,118,119}.

**REZIME**

**BOL KOD MALIGNIH TUMORA (neurohirurško lečenje)**


Neurohirurška kancerskog bola se u početku zasnivala isključivo na neuroablativnim procedurama, odnosno destruktivnim lezijama koje su nanošene na odredjene delove perifernog ili centralnog nervnog sistema (neurogomija, rizotomija, simpatektomija). Njihov nedostatak se ogleda ne samo u relativno slaboj efikasnosti u pogledu uklanjanja bola, već i neadekvatno visokom procentu postoperativnog morbiditya (naročito neurološkog) i mortaliteta. Tokom poslednje dve decenije, uporedu sa otkrićem značajnih saznanja u oblasti patofiziologije bula, usavršavale su se dijagnostičke metode (komputerizovana tomatografija, nuklearna magnetna rezonanca) i neurohirurška tehnika (mikrohirurška, stereotaksija, evocirani potencijali, radiofrekventne lezije i dr.). Danas smo u mogućnosti da uklonimo ili znatno umanjimo bol pomoću selektivnih, minimalno destruktivnih, lezija na CNS-u (mikrohirurška hordotomija, DREZotomija) ili savremenih, neuroaugmentativnih procedura, koje isključuju svaku destrukciju nervnog tkiva a zasnovane su na modulaciji nociceptivnih mehanizama (spinalna i moždana elektrostimulacija).

Ključne reči: bol kod malignih tumora, neurohirurško lečenje bola, ablativne procedure, neuroaugmentativne procedure

**REFERENCES**


