Critical Evaluation of Chemical Neurolysis of the Sympathetic Axis for Cancer Pain

Oscar A. de Leon-Casasola, MD

Background: Patients with pain caused by cancer frequently experience visceral pain. In addition to oral pharmacologic therapy to manage pain, neurolytic blocks of the sympathetic axis are also effective in controlling visceral cancer pain.

Methods: Four types of neurolytic blocks (interpleural phenol, celiac plexus, superior hypogastric plexus, and ganglion impar) used in the treatment of visceral cancer pain are reviewed.

Results: Several studies have documented the efficacy of neurolytic blocks in reducing pain intensity and opioid consumption. However, the narrow risk-benefit ratio associated with neurolysis techniques requires knowledge of the implications associated with the different neurolytic blocks to minimize undesirable effects.

Conclusions: Neurolysis of the sympathetic axis has been shown to be an effective and safe approach to treat visceral pain in cancer patients and should be incorporated in the armamentarium of the pain specialist as a useful adjunct to oral pharmacologic therapy.

Introduction

Pain associated with cancer may be somatic, visceral, or neuropathic in origin. Approximately 50% of cancer patients experience a combination of pain types at the time of diagnosis. Stretching, compressing, invading, or distending visceral structures can result in a poorly localized noxious pain. Patients experiencing visceral pain often describe the pain as vague, deep, squeezing, crampy, or colicky. Other signs and symptoms include referred pain (eg, shoulder pain that appears when the diaphragm is invaded with tumor) and nausea/vomiting due to vagal irritation.

Visceral pain associated with cancer may be relieved with oral pharmacologic therapy that includes combinations of nonsteroidal anti-inflammatory drugs (NSAIDs), opioids, and coadjuvant therapy. In addition to pharmacologic therapy, neurolytic blocks of the sympathetic axis are also effective in controlling visceral cancer pain and should be considered as impor-
tant adjuncts to pharmacologic therapy for the relief of severe pain experienced by cancer patients. These blocks rarely eliminate cancer pain because patients frequently experience coexisting somatic and neuropathic pain as well. Therefore, oral pharmacologic therapy must be continued, albeit at lower doses. The goals of performing a neurolytic block of the sympathetic axis are to maximize the analgesic effects of opioid or nonopioid analgesics and reduce the dosage of these agents to alleviate side effects.

Since neurolysis techniques have a narrow risk-benefit ratio, undesirable effects due to neurolytic blocks can be minimized with sound clinical judgment and by assessing the probable effect of the technique on each patient. A detailed description of the techniques for these blocks is beyond the scope of this review but is available elsewhere. This report describes several different approaches to achieve neurolysis, including the interpleural phenol block, celiac plexus block, superior hypogastric block, and ganglion impar block.

**Interpleural Phenol Block**

The role of interpleural analgesia in both acute and chronic pain management is still undergoing clinical scrutiny. Original work with this technique showed that interpleural analgesia could provide analgesia in patients with subcostal incisions and fractured ribs. Inserting an interpleural catheter is a relatively easy technique, and an epidural tray can be utilized. Local anesthetics (0.5% bupivacaine or 2% lidocaine) traditionally have been used via intermittent bolus or a continuous infusion. Recently, interpleural phenol therapy has been described as an alternative for the treatment of visceral pain associated with esophageal cancer. Unpublished data suggest that this may be an effective technique to treat visceral pain associated with cancer of the esophagus, liver, biliary tree, stomach and pancreas. A multicenter study is under way to determine the efficacy of this block in the treatment of pain associated with the above-mentioned malignancies (H. Silva, MD, and R. Plancarte, MD, personal communication, 1999).

**Drugs and Dosing**

For neurolytic blocks, increased concentrations of phenol are recommended. Since patients with cancer of the esophagus or the chest wall frequently have pleural effusions, several injections through a catheter are indicated. Initially, 10 mL of 6% phenol is recommended. A subsequent progressive increase in concentration of up to 10% is encouraged, depending on the results, because the pleural effusion acts as a diluting agent. However, further experience with patients with pleural effusions suggests that 5 to 10 mL of 6% phenol may render adequate results (H. Silva, MD, and R. Plancarte, MD, personal communication, 1999).

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![Fig 1](image1.png)  
**Fig 1.** — Anteroposterior view of a patient with Chiba needles placed to perform a splanchnic nerve neurolysis. Note the contrast medium distribution. The black arrows demonstrate the needles, and the open arrows indicate the contrast medium.

![Fig 2](image2.png)  
**Fig 2.** — Lateral view of a patient with Chiba needles placed for a splanchnic nerve neurolysis. The black arrows demonstrate the needles, and the open arrows indicate the contrast medium.
For analgesia associated with cancer, a continuous infusion of 0.25% to 0.375% of bupivacaine (8 to 10 mL/hr) or intermittent bolus doses of 0.5% of bupivacaine (10 to 15 mL every 8 hours) also provide adequate analgesia. However, if the high concentration of bupivacaine is chosen, the risk of toxicity increases. Thus, a regimen of 0.375% to 0.5% of ropivacaine for a continuous infusion and 0.5% of ropivacaine (10 to 15 mL every 8 hours) is a better choice for patients who need higher doses of bupivacaine.

Complications

Complications from this procedure can be divided into two categories — those produced by traumatic injuries caused by the needle or the catheter and those produced by the neurolytic agent injected in the interpleural space. Pneumothorax may occur in 2% of the patients, and lung injuries have been reported when a rigid catheter is used. Phrenic nerve palsy resulting in respiratory failure may also occur following this block. Therefore, bilateral blocks should be avoided. Systemic effects from drug absorption may also occur since the pleural membranes are highly vascularized. Thus, at our center, doses of phenol are limited to 10 mL of a 10% solution.

Efficacy

No outcome information is available to determine the efficacy of this block for the treatment of visceral pain. Literature describing experience with this block is limited to a case report, and the effects in a large population have not been reported.

Celiac Plexus Block

The celiac plexus is situated retroperitoneally in the upper abdomen. It is at the level of the T12 and L1 vertebrae, anterior to the crura of the diaphragm. The celiac plexus surrounds the abdominal aorta and the celiac and superior mesenteric arteries. The plexus is composed of a network of nerve fibers, from both the sympathetic and the parasympathetic systems. It contains two large ganglia that receive sympathetic fibers from the three splanchnic nerves (greater, lesser, and least). The plexus also receives parasympathetic fibers from the vagus nerve. Autonomic nerves supplying to the liver, pancreas, gallbladder, stomach, spleen, kidneys, intestines, and adrenal glands, as well as blood vessels, arise in the celiac plexus.

Neurolytic blocks of the celiac plexus have been used for malignant and chronic nonmalignant pain. In patients with acute or chronic pancreatitis, the celiac plexus block has been used with significant success. Likewise, patients with cancer in the upper abdomen who have a significant visceral pain component have responded well to this block.

Three approaches to block nociceptive impulses from the viscera of the upper abdomen include the retrocrural (or classic) approach, the anterocrural approach, and neurolysis of the splanchnic nerves. With all of these approaches, the needles are inserted at the level of the first lumbar vertebra, 5 to 7 cm from the midline. Then, the tip of the needle is directed towards the body of L-1 for the retrocrural and anterocrural approaches and to the body of T-12 for neurolysis of the splanchnic nerves. Figs 1-2 illustrate the final position of the needles and the expected spread of contrast medium after successful placement. More recently, computed tomography and ultrasound techniques have allowed pain specialists to perform neurolysis of the celiac plexus via a transabdominal approach. This approach is frequently used when patients are unable to tolerate either the prone or lateral decubitus position or when their liver is so enlarged that a posterior approach is not feasible.

Drugs and Dosing

For neurolytic blocks, 50% to 100% alcohol, 20 mL per side, is used. Injected by itself, alcohol can produce severe pain. Thus, it is recommended to first inject 5 to 10 mL of 0.25% bupivacaine 5 minutes prior to the injection of alcohol or to dilute 100% alcohol by 50% with local anesthetic (0.25% bupivacaine). Phenol in a 10% final concentration may also be used; this has the advantage of being painless on injection. Both agents seem to have the same efficacy.

Complications

Complications associated with celiac plexus blocks appear to be related to the technique used: retrocrural, transcrural, or transaortic. In a prospective, randomized study of 61 patients with cancer of the pancreas, Ischia et al compared the efficacy and incidence of complications associated with these three approaches to celiac plexus neurolysis. Orthostatic hypotension occurred more often when the retrocrural (50%) or splanchnic (52%) technique was used than when the anterocrural approach (10%) was used. In contrast, transient diarrhea was more frequent with the anterocrural approach (65%) than with the splanchnic nerve block technique (5%) but not the retrocrural approach (25%). The incidence of dysesthesia, interscapular back pain, reactive pleurisy, hiccups, or hematuria was not statistically different among the three groups.
The incidence of complications from neurolytic celiac plexus blocks was recently determined by Davis11 in 2,730 patients having blocks performed from 1986 to 1990. The overall incidence of major complications (eg, paraplegia, bladder, and bowel dysfunction) was 1 in 683 procedures. However, the report does not describe which approach or approaches were used to perform the blocks.

Following are several aspects in the diagnosis and management of specific complications.

**Malposition of the needle** is avoided with radiologic imaging prior to the injection of a neurolytic agent, as the tip of the needle may be intravascular, in the peritoneal cavity, or in a viscus. Imaging techniques currently used include biplanar fluoroscopy, computed tomography, or ultrasound guidance. However, no study has evaluated the superiority of one technique over the others. Wong and Brown12 suggest that the use of radiologic imaging does not alter the quality of the block or the incidence of complications based on a retrospective study of 136 patients with pancreatic cancer pain treated with a celiac plexus block with or without radiologic control of the position of the needle's tip. However, it is not clear how many of those patients had radiologic imaging. Assuming that half of the patients did not, the upper 95% confidence limit for complications is 5%.13

**Orthostatic hypotension** may occur up to 5 days after the block in 1% to 3% of patients. Treatment includes resting in bed, avoiding sudden changes in position, and replacing fluids. Once compensatory vascular reflexes are fully activated, this side effect disappears. Wrapping the lower extremities from the toes to the upper thighs with elastic bandages has been successful in patients who developed orthostatic hypotension and thus needed to walk during the first week after the block.

**Backache** may result from local trauma during the needle placement resulting in a retroperitoneal hematoma, from alcohol irritation of the retroperitoneal structures, or from injury to the lumbar plexus. Patients with a backache should have at least two hematocrit measurements at a 1-hour interval. If there is a decrease in the hematocrit, radiologic imaging is indicated to rule out a retroperitoneal hematoma. A urine analysis positive for red blood cells suggests renal injury.

**Retroperitoneal hemorrhage** is rare; however, in patients who present with orthostatic hypotension, the possibility of hemorrhage must be ruled out before assuming that it is a physiologic response to the block. Patients who present with backache and orthostatic hypotension after a celiac plexus block should be admitted to the hospital for serial hematocrit monitoring. If the hematocrit level is low or decreasing, patients should undergo radiologic evaluation to rule out injury to the kidneys, the aorta, or other vascular structures. A surgical consult should be obtained as soon as feasible.

**Diarrhea** may occur due to the sympathetic block of the bowel. Treatment includes hydration and antidiarrheal agents. Oral loperamide is a good choice, although any anticholinergic agent may be used. Matson and colleagues14 reported near-fatal dehydration from diarrhea following this block. In debilitated patients, diarrhea must be treated aggressively.

**Abdominal aortic dissection** has also been reported.15,16 The mechanism of aortic injury is direct damage with the needle during the performance of the block. As expected, the anterocrural approach is more frequently associated with this complication. Thus, this approach should be avoided if atherosclerotic disease of the abdominal aorta is present.

**Paraplegia and transient motor paralysis** have occurred after celiac plexus block.16,22 These neurologic complications may occur due to a spasm of the lumbar segmental arteries that perfuse the spinal cord.23 In fact, canine lumbar arteries undergo contraction when exposed to low concentrations of alcohol.24 Thus, empirical data suggest that alcohol should not be used if there is evidence of significant atherosclerotic disease of the aorta, suggesting that the circulation to the spinal cord may also be impaired. However, there is also a report of paraplegia after phenol use,17 thus suggesting that other factors (eg, direct vascular or neurologic injury or retrograde spread to the spinal cord) may come into play. These complications further support the use of radiologic imaging during the performance of the block.

**Efficacy**

To date, only two randomized, controlled trials25 and one prospective study26 have evaluated the efficacy of celiac plexus neurolysis in pain due to cancer of the upper abdomen. In a prospective, randomized study, Ischia et al7 evaluated the efficacy of three different approaches to celiac plexus neurolysis in pancreatic cancer. Of 61 patients with pancreatic cancer pain, 29 (48%) experienced complete pain relief after the neurolytic block. The remaining 32 patients (52%) required further therapy for residual visceral pain due to technical failure in 15 patients and neuropathic/somatic pains in 17 patients. The second trial,25 which compared the procedure with oral pharmaco-
logic therapy in 20 patients, concluded that celiac plexus neurolysis resulted in an equal reduction in visual analog pain score (VAPS) as therapy with a combination of NSAIDs and opioids. However, opioid consumption was significantly lower in the group of patients who underwent neurolysis when compared to the group receiving oral pharmacologic therapy during the 7 weeks of the study. Moreover, the incidence of side effects was greater in patients who received oral pharmacologic therapy when compared to those who underwent neurolysis block.

The prospective, nonrandomized study compared 41 patients treated according to the World Health Organization (WHO) guidelines for cancer pain relief with 21 patients treated with a neurolytic celiac plexus block. The authors concluded that this technique can play an important role in managing pancreatic cancer pain.

Since one of the two studies that used a randomized, controlled design compared different approaches to the celiac plexus and had no control group and the other study compared the procedure with an analgesic drug, it is not possible to estimate the success rate of this technique. In contrast, the results of a meta-analysis that evaluated the results of 21 retrospective studies in 1,145 patients concluded that adequate to excellent pain relief can be achieved in 89% of the patients during the first two weeks following the block. Partial to complete pain relief continued in approximately 90% of the patients who were alive at the 3-month interval and in 70% to 90% of the patients during the 3-month interval before death. Moreover, the efficacy was similar in patients with pancreatic cancer than in those with other intra-abdominal malignancies of the upper abdomen. However, these results are based on retrospective evaluations that may not yield reliable information or may be subject to publication bias. In addition, statistical techniques used for the analysis must account for the heterogeneity produced by the patients' selection criteria, technical differences in the performance of the blocks, choice of neurolytic agents and doses, diversity in the tools for the evaluation of pain, goals of therapy, etc. Thus, the meta-analysis must be interpreted with caution as the reports may be overly enthusiastic.

**New Perspectives**

As previously discussed, oral pharmacologic therapy with opioids, NSAIDs, and coadjuvants is frequently used for the treatment of cancer pain. However, evidence suggests that chronic use of high doses of opioids may have a negative effect on immunity. Thus, analgesic techniques that lower opioid consumption may have a positive effect on patient outcomes. Lillemoe and colleagues showed in a prospective, randomized trial that patients with non-resectable cancer of the pancreas who received a splanchnic neurolysis lived longer than patients who did not. These findings may be the result of lower opioid use in the neurolysis patients who not only had better-preserved immune functions, but also experienced fewer side effects (eg, nausea and vomiting), thus allowing them to eat better. This hypothesis is currently being tested in a prospective, randomized trial.

**Superior Hypogastric Plexus Block**

Cancer patients with tumor extension into the pelvis may experience severe pain that is unresponsive to oral or parenteral opioids. Also, excessive sedation or other side effects may limit the acceptability and usefulness of oral opioid therapy. Therefore, a more invasive approach is needed to control pain and improve the quality of life of these patients.

Pelvic pain associated with cancer and chronic nonmalignant conditions may be alleviated by blocking 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. Thus, a sympathectomy for visceral pain is analogous to a peripheral neurectomy or dorsal rhizotomy for somat-
vic pain. A recent study suggests that visceral pain is an important component of the cancer pain syndrome experienced by patients with cancer of the pelvis, even in advanced stages. Thus, percutaneous neurolytic blocks of the superior hypogastric plexus should be considered more often for patients with advanced stages of pelvic cancer.

The superior hypogastric plexus is situated 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. The technique for the blockade has been described elsewhere. Fig 3 shows adequate needle placement and contrast medium spread prior to neurolysis of the superior hypogastric plexus.

Complications

The combined experience of more than 200 cases from the Mexican Institute of Cancer, Roswell Park Cancer Institute, and M.D. Anderson Cancer Center indicates that neurologic complications do not occur as a result of this block.

Efficacy

The effectiveness of the block was originally demonstrated by documenting a significant decrease in pain via VAPS scores. In this study, Plancarte et al. showed that this block was effective in reducing VAPS scores in 70% of the patients with pelvic pain associated with cancer. The majority of the enrolled patients had cervical cancer. In a subsequent study, 69% of the patients experienced a decrease in VAPS scores. Moreover, a mean daily opioid morphine reduction of 67% was seen in the success group (736 ± 633 reduced to 251 ± 191 mg/day), and 45% in the failure group (1,443 ± 703 reduced to 800 ± 345 mg/day). In a more recent multicentric study, 159 patients with pelvic pain associated with cancer were evaluated. Overall, 115 patients (72%) had satisfactory pain relief after one or two neurolytic procedures. Mean opioid use decreased by 40% from 58 ± 43 reduced to 35 ± 18 equianalgesic mg/day of morphine 3 weeks after treatment in all the studied patients. This decrease in opioid consumption was significant for both the success group (56 ± 32 reduced to 32 ± 16 mg/day) and the failure group (65 ± 28 reduced to 48 ± 21 mg/day). Success was defined in these two studies as the ability to reduce opioid consumption by at least 50% in the 3 weeks following the block and a decrease in the pain scores below 4/10 in the VAPS scores.

In a recent case report, Rosenberg and colleagues reported on the efficacy of this block in a patient with severe chronic nonmalignant penile pain after transurethral resection of the prostate. Although the patient did not receive a neurolytic agent, a diagnostic block performed with 0.25% bupivacaine and 20 mg of methylprednisolone acetate was effective in relieving the pain for more than 6 months. The usefulness of this block in chronic benign pain conditions has not been adequately documented.

Fig 4. — Anteroposterior view of the pelvis showing contrast medium distribution (arrow) prior to ganglion impar neurolysis.

Fig 5. — Lateral view of the same patient in Fig 4.
Ganglion Impar Block

The ganglion impar is a solitary retroperitoneal structure located at the level of the sacrococcygeal junction. This unpaired ganglion marks the end of the two sympathetic chains. Visceral pain in the perineal area associated with malignancies may be effectively treated with neurolysis of the ganglion impar (Walther’s). Patients who will benefit from this block frequently present with a vague, poorly localized pain that is frequently accompanied by sensations of burning and urgency. However, the clinical value of this block is not clear as the published experience is limited.

This block may be performed with the patient in the left lateral decubitus position with the knees flexed, in the lithotomy position, or in the prone position. The easiest approach is with the patient in the prone position, where a 20-gauge 1.5-inch needle is inserted through the sacrococcygeal ligament in the midline. The needle is then advanced until the tip is placed posterior to the rectum. Figs 4-5 illustrate adequate needle placement and contrast medium spread.

No complications have been reported with this block.

Conclusions

Neurolysis of the sympathetic axis appears to be a safe, cost-effective approach to treating visceral pain associated with cancer. The benefits include improved analgesia, reduced opioid consumption, favorable economic implications, and superior clinical effects due to the deleterious properties of high-dose chronic opioid therapy. Current knowledge and techniques to perform these blocks allow these procedures to be performed safely and expeditiously. Pain practitioners should consider the role of these blocks in adjuvant therapy for the optimal treatment of cancer pain.

References