

Management of Chronic Upper Abdominal Pain in Cancer

Transdiscal Blockade of the Splanchnic Nerves

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Background: The use of celiac plexus block to relieve the intractable pain caused by upper abdominal malignancies is well established. However, its effects are inconsistent for many reasons, mainly because of structural anatomic distortion as a consequence for the malignancy. The splanchnic nerve blockade (SNB) seems to be a useful alternative to the celiac plexus block in upper abdominal pain relief.

Materials and Methods: The pain of 109 patients with unresectable upper abdominal or lower esophageal neoplasms was managed by posterior transdiscal SNBs guided by computed tomography at the Instituto Nacional de Cancerología in Mexico City from January 2004 to June 2007. The study evaluated SNB efficacy with regard to pain relief, its adverse effects/complications, and patient satisfaction.

Results: Splanchnic nerve blockade efficacy with regard to pain relief was exhibited by a marked decrease in the visual analog score and in opioid consumption, with preprocedural mean values dropping from 6.1 ± 2.4 and 102.4 mg/d of morphine to 2.7 ± 2.4 and 53.3 mg/d at the first postprocedural visit, respectively. These results persisted during the 1-year follow-up period or until death. Minor adverse effects (moderate diarrhea and mild hypotension) were frequent ($n = 64$ and $n = 47$, respectively), and severe complications occurred in 1 patient with a transient paraparesis ($n = 1$). No procedure-related mortality was observed.

Conclusions: Splanchnic nerve blockade via a transdiscal approach is a technique that provides analgesia and the alleviation of the secondary undesirable effects of analgesic drugs resulting from the decrease of morphine consumption in patients with upper abdominal malignancies. In experienced teams, the reliability of its analgesic effect is high, with a low rate of severe complications.

Abbreviations: CT - Computed tomography, SNB - splanchnic nerves neurolytic blockade, CPB - celiac plexus block, PSS - patient satisfaction scale, VAS - visual analog score

(*Reg Anesth Pain Med* 2010;35: 500–506)

For cancer patients, pharmacological treatment remains the mainstay of pain management. Since the World Health Organization (WHO) established the 3-step ladder concept,¹ ef-

fective analgesia has become sometimes difficult to institute in cancer patients because the dose-response is unpredictable and because analgesic doses may be poorly tolerated in patients who are debilitated and who are using several other drugs.^{2,3} Thus, the neurolytic sympathetic block has been proposed as an efficient, relatively simple, and repeatable method of management,⁴ bringing both relief of pain and allowing the discontinuation of drugs or a decrease in their dosage.^{5,6}

The celiac plexus originates from the preganglionic sympathetic fibers of the greater (T5-9), lesser (T10-11), and least (T12) splanchnic nerves (SNs). Pain transmitted through the celiac plexus originates primarily in the upper abdomen, including in the pancreas, the diaphragm, the liver, the spleen, the stomach, the small bowel, the ascending and proximal transverse colons, the adrenal glands, the kidneys, the abdominal aorta, and the mesentery. In addition, the greater and lesser SNs innervate the distal thoracic esophagus,^{6,7} which explains the efficacy of splanchnic nerve blockade (SNB) in carcinomas involving the inferior third of the esophagus. Both the celiac plexus and the thoracic SN represent a logical target point for the blockage of nociceptive transmission from the upper abdomen.⁶ Any pain originating from the visceral structures innervated by the celiac plexus, theoretically, can be effectively alleviated by the blockade of 1 of the 2 structures, either the celiac plexus or the SN; this particularity only occurs in this level of the sympathetic axis.⁸

The interventional management of pain for patients with upper abdominal malignancies is classically based in the use of the celiac plexus blockade (CPB).⁷⁻⁹ Indeed, articles reporting the use of SNB are scarce, despite the fact that it can be performed by way of percutaneous,¹⁰ videothoracoscopic,^{11,12} or intraoperative approaches.¹³

At the Department of Pain Management and Palliative Care of the Instituto Nacional de Cancerología in Mexico City, the percutaneous technique of transdiscal SNB with a single needle has been adopted as an alternative procedure to CPB. This technique has shown a minor risk of complications (eg, pneumothorax and its consequences) compared with traditional approaches because of the use of a single needle throughout the disk. Compared with CPB, SNB may be more useful for visceral abdominal pain that is secondary to upper visceral neoplasms in which the celiac plexus anatomy may be distorted¹⁴ and can also be used when large lesions complicate the percutaneous plexus blockade. Transdiscal techniques for neurolytic CPB have been previously described,⁹ but the only available report on the transdiscal approach for SNB was published in Spanish.¹⁰ The aim of this article was to describe the benefits (efficacy and safety) of this approach for pain relief treatment in upper abdominal neoplasms.

MATERIALS AND METHODS

This clinical observation study aims to assess the efficacy and safety of transdiscal SNB in the treatment of cancer pain.

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ISSN: 1098-7339

DOI: 10.1097/AAP.0b013e3181fa6b42

Patients

This is a prospective, longitudinal study approved by the institutional review board and conducted at the Instituto Nacional de Cancerología in Mexico City during a period ranging from January 2004 to June 2007. Written informed consent was obtained in which we offered information about the procedure, about its foreseeable complications and about the other available alternatives of pain management.

All the included subjects had been diagnosed with a surgically intractable malignancy of the upper abdominal cavity (including the pancreas, liver, gallbladder, stomach, and duodenum) or of the distal third of the esophagus and were receiving chemotherapy and/or radiotherapy when necessary.

Patients were excluded when they reported accompanying chronic pain caused by another source such as metastases, disease progression, a psychiatric disorder, or a neurologic impairment, or when they were unable or refused to sign an informed consent form. Patients with systemic or local active infectious processes at the site of puncture and patients with hematological conditions such as coagulation disorders were also excluded. All the patients were treated with opioid analgesics according to the WHO's guidelines for cancer patient treatment,¹⁵ with conversion of opioids according to morphine-equivalent conversion displayed in Table 1.

Assessment of the Patients and of the Procedure

All of the subjects were assessed by an independent oncologist and by the interventionist pain physician before and after the procedure.

Before the procedure, both the oncologist and interventionist pain physician evaluated the intensity of the pain with the visual analog scale (VAS).¹⁶ The interventionist pain physician

recorded the use and doses of analgesics (ie, morphine dosage).

After the procedure, both physicians assessed the patient at prescheduled dates (the first week and the first, third, sixth, ninth, and twelfth months) or until death. They recorded and evaluated the following: (1) the degree of analgesia obtained according to the VAS, (2) the daily morphine consumption (mg/d, per os), (3) any complications of the procedure, and (4) patient satisfaction.

Patient satisfaction was evaluated using the patient satisfaction scale (PSS), which recorded the improvement of symptoms, such as somnolence, intestinal function, recovery of appetite, and weight gain.¹⁷ The PSS was assessed by the patient with a linear analog scale (with 0 indicating very satisfied and 10 indicating very dissatisfied).

Statistical Analysis

The results were reported by means of descriptive statistics (mean \pm SD and percentages) and statistical analysis.

The main effectiveness outcome of VAS was tested through both a Student *t* test and a linear generalized model (with analysis of variance [ANOVA] of repeated measures) to probe consistency across these multiple measures over time. We stratified the results according to variables such as primary malignancies.

Technique

All the procedures were performed under sterile conditions, using our previously described technique.¹⁰ The needle entry site in this procedure should be appropriately selected with the help of computed tomography (CT) or fluoroscopy guidance to ensure the accuracy of the puncture. Our procedures were performed by CT guidance because of its institutional

TABLE 1. Morphine Equivalent Conversion Table

(Converting From) Current Opioid	(Converting to) New Opioid and/or New Route of Administration	Divide 24-hr Dose* of Current Opioid (Column 1) by Relevant Figure Below to Calculate the Initial 24-hr Dose of New Opioid and/or New Route (Column 2)
Oral-to-oral route conversions		
Oral codeine	Oral morphine	Divide by 10
Oral tramadol	Oral morphine	Divide by 5
Oral morphine	Oral oxycodone	Divide by 2
Oral morphine	Oral hydromorphone	Divide by 7.5
Oral-to-transdermal route conversions		
Oral morphine	Transdermal fentanyl	Refer to manufacturer's information†
Oral morphine	Transdermal buprenorphine	Seek specialist palliative care advice
Oral-to-subcutaneous route conversions		
Oral morphine	Subcutaneous morphine	Divide by 2
Oral morphine	Subcutaneous diamorphine	Divide by 3
Oral oxycodone	Subcutaneous morphine	No change
Oral oxycodone	Subcutaneous oxycodone	Divide by 2
Oral oxycodone	Subcutaneous diamorphine	Divide by 1.5
Oral hydromorphone	Subcutaneous hydromorphone	Seek specialist palliative care advice
Other route conversions rarely used in palliative medicine		
Subcutaneous or intramuscular morphine	Intravenous morphine	No change
Intravenous morphine	Oral morphine	Multiply by 2
Oral morphine	Intramuscular morphine	Divide by 2

*The same units must be used for both opioids and routes, for example, milligrams of morphine to milligrams of oxycodone.

†The conversion ratios of oral morphine–transdermal fentanyl specified by the manufacturer(s) vary from around 100:1 to 150:1.

availability. All of the patients received adequate hydration by way of an intravenous access, were managed under conscious sedation, and were noninvasively monitored with regard to blood pressure, heart rate, electrocardiogram, and O₂ saturation. Resuscitation equipment was available throughout the procedure.

When the patient lies prone on the table, the scout view allows the physician to identify the interspinous spaces of T9-10 and T10-11 by tracing their external markers. After asepsis, the skin and subcutaneous tissue are infiltrated with local anesthetics at the site of puncture. We usually used a 22-gauge needle with a curved tip, which facilitated navigation through the disk (Fig. 1, top right). This needle is manually slightly curved like the tip of a Tuohy needle (Fig. 1, mid right). The needle is inserted with 40 degrees of oblique angulation from the sagittal plane, and the point of entry is approximately 5 cm lateral to the midline (Fig. 2A), preferably on the left side to minimize the risk of aortic puncture. The tip is advanced pointing toward the midline, verifying the correct position within the intervertebral disk (Fig. 2B). When the tip is bent, the angle will allow the needle to modify its direction and to reach the targeted position. The needle tip crosses through the discal annulus and localizes at the retromediastinum anterolateral level. The aspiration should be negative for blood, cerebrospinal fluid, or lymph before any injection is attempted.

The core of the procedure has 3 steps. The first is the use of 1 mL of contrast liquid to make sure the tip of the needle has reached the posterior mediastinum. The second is the injection of 20 mL of air, progressively injected in amounts of 5 mL, thus creating a real cavity with a double contrast image (air/liquid) to create a plasty in the retromediastinum (Figs. 2, C–E). The third is the injection of 8 to 10 mL of 10% aqueous phenol. The neurolytic contrast medium should remain between the air (upper) and the diaphragm (lower). Finally, the needle is retrieved and rinsed with physiologic serum, and 0.3 mL of ceftriaxone is injected in the disk to prevent postprocedural infectious complications into the disk.

RESULTS

Patients' Demographics

One hundred nine patients with upper abdominal or esophageal cancer were included in the study, a group composed of 71 women and 38 men. The age of the patients ranged from 23 to 82 years, with a mean age of 54.2 ± 12.9 years. The neoplasms were pancreatic in 48 patients, hepatic or gallbladder in 29 patients, gastric in 27 patients, and esophageal (lower third) in 5 patients. Concerning the extension of the cancer, 14 patients had only a local spread, 42 patients had a regional dissemination, and 53 patients had metastases elsewhere. Visceral pain alone

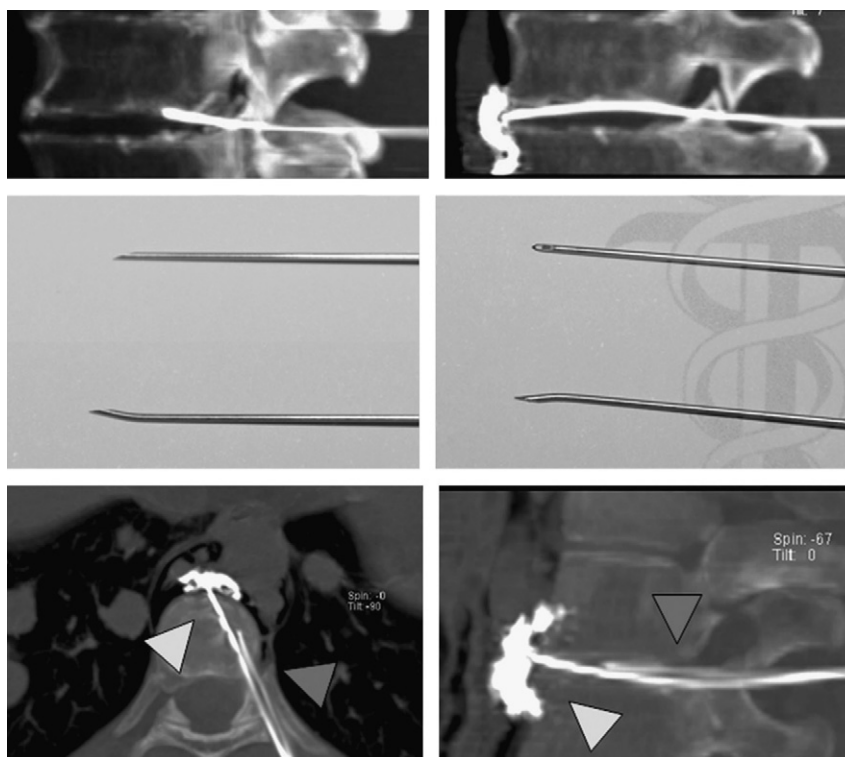


FIGURE 1. Instructions for the curved needle technique. Comparison with the straight needle technique. Top left and top right: Sagittal view of the CT scan of the 2 types of needles. Top left, A straight tip may render difficult a smooth navigation through the disk if it bumps into the vertebral plateau. Top right, A bent tip allows the needle to cross the disk more easily and to continue its navigation into the prevertebral space (contrast). Mid left, Lateral view comparing the tips of 2 actual needles: classic straight (on top) and modified curved (on bottom). Mid right, Lateral and frontal view of a curved needle showing how the curvature at the bevel does not interfere with the bore at the tip. Bottom left and bottom right: Computed tomographic scan of a patient where 2 parallel needles were inserted, one with a straight end (red arrowhead) and another one with a curved end (yellow arrowhead). Bottom left, The bent needle is able to reach the posterior mediastinum, whereas the straight does not (axial view). Bottom right, The straight tip bumps against the vertebral plateau, but the curved end navigates through the disk (sagittal view).

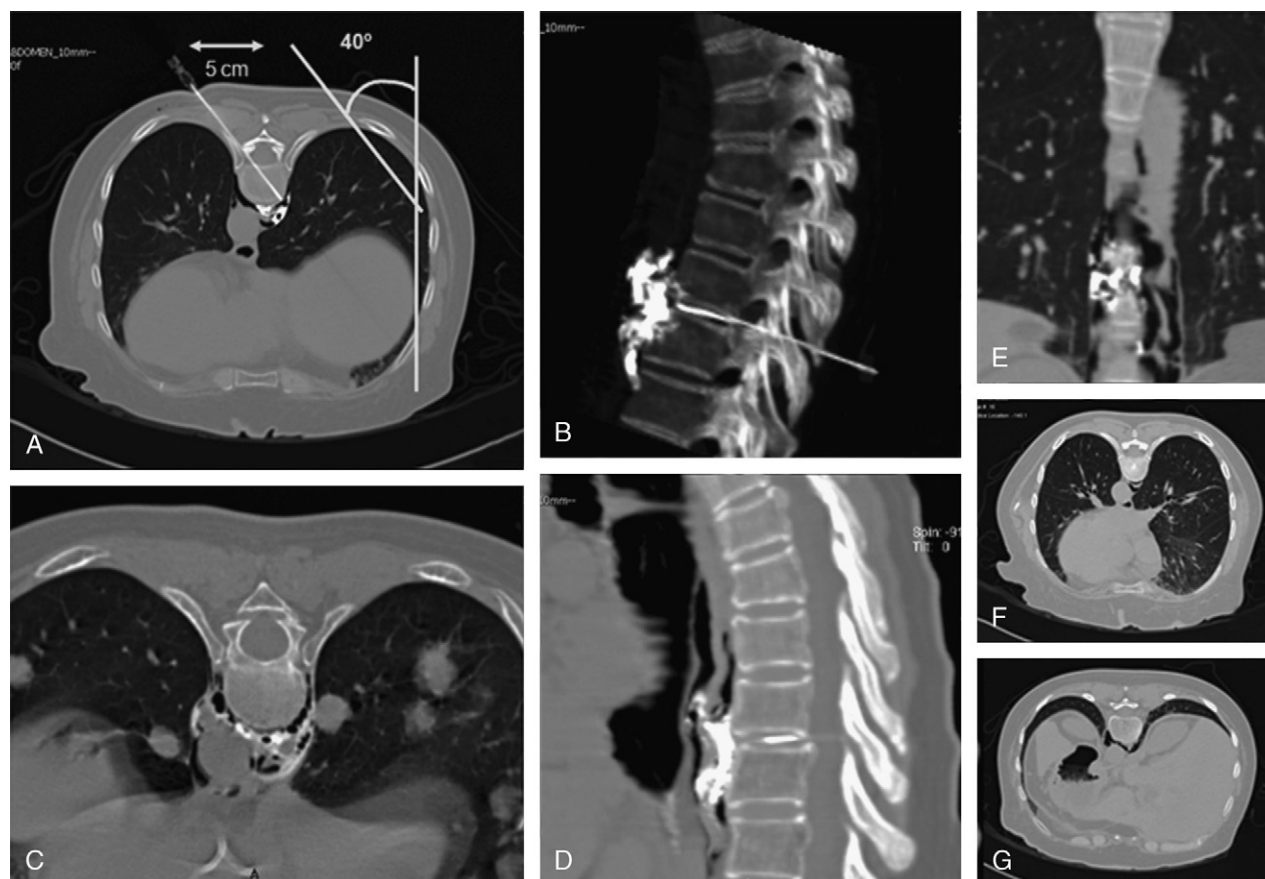


FIGURE 2. Illustration of the technique. Axial view and coronal 3-dimensional reconstructions of a transprocedural CT scan. A, Axial view centered in the T9-10 intervertebral disk: transdiscal injection may be performed safely if the pathway of the needle remains strictly within the limits of the disk. An angle of 40 degrees and an entry point 5 cm away from the midline are the average landmarks for needle placement. B, Lateral view confirming the intradiscal pathway. C, Double-contrast image (air contrast) of both sides with a unilateral puncture. The dissection produced by the pneumomediastinum covers the whole vertebral body surface on both sides. Multiple lung metastases can be appreciated. D, Parasagittal view showing the adjuvant posterior pneumomediastinum: the distribution of air includes at least 4 vertebral levels (2 above and 2 below the punctured disk). E, Coronal view confirming the bilateral spread of air, contrast and lytic agent (in a longitudinal and transversal fashion). F and G, Axial views of the uppermost (F) and lowermost levels of the distribution of air (G).

was present in 73 patients, and the other 36 patients presented both visceral and somatic pain. In 51 patients, the distribution of pain was localized to the upper abdominal region, and in

58 patients, patients had diffuse abdominal pain. The overall survival rate at 6 months was 26 of 109 patients, and at 12 months, it was 9 of 109 patients.

TABLE 2. Preprocedural and Postprocedural Behavior of the Studied Population

Time, mo	Assessed	Deceased	Lost to Follow-Up	VAS Mean	<i>P</i>	Morphine Consumption, mg/dL	PSS
Before procedure	109	0	0	6.1 ± 2.4		102.4	7.5
After procedure							
1 wk	109	0	0	2.7 ± 2.4	<0.0001	53.3	4.3
1 mo	83	26	0	2.4 ± 2.2	<0.001	52.7	4.3
3 mo	45	58	6	3.1 ± 3.1	<0.001	47.8	4.9
6 mo	26	80	3	2.1 ± 2.1	<0.002	44.9	5.4
9 mo	13	92	4	2.7 ± 2.6	0.13	44.0	5.6
12 mo	9	98	2	2 ± 2.1	0.13	50.0	6.0

Repeated-measures ANOVA shows consistency, $P < 0.05$.

Shown are the number of patients, mean VAS, P values, morphine consumption, and PSS at follow-up visits (NB: reported P values are P baseline/corresponding follow-up visit).

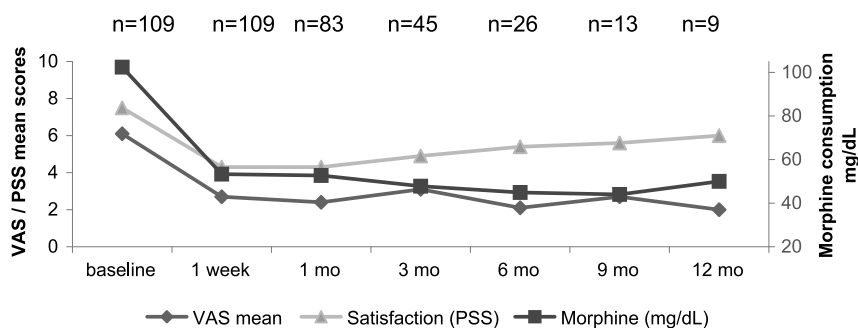


FIGURE 3. Graphical representation of the evolution of measured parameters (with baseline value and values at follow-up visits). Pain is rated by VAS, and patient comfort is rated by PSS (no units, numerical values from 0 to 10). Morphine requirements are measured in milligrams per day.

Technical Data of Procedures

The approached intervertebral disk was the T9-10 in 72 patients and the T10-11 in 37 patients. The side punctured was the left in 85 patients and the right in 24 patients. The procedures failed at first attempt in 5 patients because of the technical inability of the operator to reach the correct site, but all of the patients were ultimately successfully blocked.

Pain Scores and Evaluation of the Procedure

The VAS differences (difference of the postprocedural values at the established dates from the baseline values) were significant ($P < 0.001$) when compared using the Student *t* test for related samples and ANOVA for repeated measures. The respective values of the mean VAS at the preprocedural assessment and at the follow-up visits (1, 3, 6, 9, and 12 months), and the reported *P* values are displayed in Table 2. Before the blocks, the analgesic drug use, expressed as oral morphine consumption, had a median baseline value of 102.39 mg/d, which decreased to 53.34 mg/d at the 1-week visit. The PSS paralleled these results, decreasing from a median value of 7.54 to 4.25 on the first postprocedural evaluation. In 2 cases, no effect on pain relief was observed, and these 2 cases are considered as clinical failures. Further results obtained at the follow-up visits are summarized in Table 1 and are graphically displayed in Figure 3.

Satisfaction of Patients Compared With Preprocedural Status

The PSS improved in 107 patients and did not improve in the 2 other patients (clinical failures); its mean values are reported in Table 1. The most frequently alleged reasons for patient satisfaction were pain relief (98%), reduced somnolence or dizziness (40%), improved intestinal function (30%), recovery of appetite (20%), and weight gain (5%).

Adverse Effects and Complications

Minor adverse effects included diarrhea ($n = 64$, 58%), hypotension ($n = 47$, 43%), transient paresthesias in the corresponding dermatome during the procedure ($n = 40$, 37%), pain at the site of puncture ($n = 32$, 29%), nausea ($n = 27$, 25%), and vomiting ($n = 18$, 16%). Only 5 patients presented none of these effects (4%). Diarrhea and hypotension in these cases were mild, without any hydroelectric or hemodynamic disturbances. Nausea and vomiting were transient (limited at most to the first 72 hrs), as was diarrhea (not beyond 48 hrs) and responded to symptomatic treatment. Moderate complications were aortic puncture ($n = 4$, 4%), osseous puncture ($n = 4$, 4%), asymptomatic pneumothorax ($n = 2$, 2%), and hepatic puncture ($n = 1$, 1%). All these were diagnosed either by aspiration of blood (aortic puncture) or required no specific treatment (liver or pleural puncture). No discitis was observed. Severe complications

TABLE 3. Splanchnic Nerve Blockade for the Relief of Pain in Cancer—Summary of Published Series

Author(s), y	n	Lost to Known Follow-Up	Used Technique	Patients Who Did Not Respond to Treatment, %	Morphine Consumption Evaluated	Patient Satisfaction Evaluated	Reasons for Being Satisfied Quantified	Severe Complications
Fujita, ¹⁹ 1993	27	—	SNB	5	—	—	—	0
Fields, ²⁰ 1996	10	—	SNB	40	—	—	—	0
Cariati et al, ¹⁸ 1997	21	—	SNB	5	—	—	—	1
Marra et al, ²¹ 1999	144	—	SNB/CPB*	20	—	—	—	0
Plancarte et al, ¹⁰ 2003	64	—	SNB	NA	+	—	—	0
Suleyman, ⁸ 2004	20	—	SNB	NA	+	+	—	0
Kang et al, ¹¹ 2007	21	—	Thoracoscopy	24	+	—	—	0
Present series	109	+	SNB	1.8	+	+	+	1

*The series of Marra et al is quoted because it is the largest series including patients who underwent SNB; however, they performed CPB and/or SNB, both methods are mixed and definitive conclusions cannot be drawn.

NA indicates not available; +, yes; —, no.

occurred in 1 patient with a transient paraparesis ($n = 1$, 1%). No mortality was observed.

DISCUSSION

Splanchnic nerve blockade was effective for the management of patients with upper abdominal malignancies, producing significant decreases in pain scores (VAS 6.11 ± 2.36 before and 2.13 ± 2.06 after the procedure and during 6 months of follow-up) and in drug use. The reasons we outlined above help to explain this patient satisfaction. The quality of analgesia in SNB is excellent, and pain relief was obtained in the present study in 98% of the cases, supporting the data reported by Cariati et al¹⁸ and Fujita¹⁹ (95%) and by Fields²⁰ and Marra et al²¹ (80%).

The recognition that SNB may provide relief of pain in a subset of patients who fail to obtain relief from CPB has led to a renewed interest in SNB.²² The reports on the application of SNB for the relief of pain in cancer are summarized in Table 3.^{9–11,14,18–20} A few articles report comparatively on the experience of CPB versus SNB for the management of pain in upper abdominal cancer. Splanchnic nerve blockade more successfully relieves pain,²¹ reduces morphine consumption, and improves patient satisfaction.⁸ Those results confirm our previously published experience¹⁰ and support the use of SNB instead of CPB, especially when the celiac plexus anatomy has been modified by inflammation, fibrosis, or tumor involvement because of the limited spread of phenol.^{8,10,18,24–26}

Many studies on CPB/SNB for cancer are limited to pancreatic neoplasms,⁸ a population with a short mean survival rate. In these studies, the reduction of opioid consumption seems to be more evident within 4 weeks after neurolysis,²⁷ but there are reports of such efficacy for up to 7 weeks¹⁷ or 3 months²⁸ after the procedure.

In our study, we decided to include a more heterogeneous population because the opioid requirements of patients with primary malignancies or metastatic disease in the visceral upper abdominal region have deleterious effects. The previously reported techniques are modifications of the technique from Abram and Boas²⁹ and are laterovertebral approaches,^{8,19} more prone to visceral puncture than the technique that we used.

The level of puncture was chosen based on classic anatomic landmarks and personal experience, supported by the recent work of Yang et al.³⁰ They confirm that the participation rates of T8 and T9 to the greater SN are above 80%, the rates of T10 and T11 to the lesser SN are about 80%, and those of T11 and T12 to the least SN are about 66%. Thus, our level of puncture had been adequately chosen.

Concerning the different steps for the visualization of the posterior mediastinum, we would like to emphasize that we have chosen the injection of air because there is no evidence of air embolism occurring in a transdiscal approach SNB in our experience.

The adjuvant artificial pneumomediastinum has been used in thoracoscopic surgery for several years.^{31,32} The amount of air in these cases is between 400 and 600 mL. The addition of a small volume of air (20 mL) has several advantages: the virtual space where the SN normally lies becomes a true cavity (Figs. 2, C–E) of the retromediastinum, and the created image of the double contrast is produced by the interface of air and dye, yielding an easily noticeable marker. The created cavity allows a better distribution of the neurolytic substance, which need not be diluted because the amount of liquid medium contrast is insignificant (1 mL). Our observation of actual cases have led us to think that the neurolytic agent remains somehow

trapped between an inferior boundary (such as the superior surface of the diaphragm) and a superior limit (the volume of injected air).

Some authors report on procedures that require a bilateral approach,¹⁸ with iterative punctures produced by unsuccessful positioning in almost 20% of these cases.¹⁹ However, our technique needs only a unilateral puncture to place the needle tip adequately for a clinically effective procedure. The dissection of the cavity produced by air injection ensures a homogeneous distribution of the neurolytic agent across different metameric levels on both sides (Figs. 2, C–E), and we are using a readily available adjuvant contrast medium (air), whereas other authors have used carbon dioxide as the contrast agent.³³ This is not a mere theoretical consideration: our clinical experience confirms that a unilateral puncture allows a bilateral block; our radiologic findings have confirmed that the cephalocaudal distribution of contrast includes at least 3 vertebral levels in the sagittal (Fig. 2C) or in the frontal (Fig. 2E) reconstructions.

The use of fluoroscopy is in widespread in interventional pain management, but the number of indications and procedures that can be performed with CT has progressively increased. The accuracy of this imaging modality is high, the visualization and definition of the anatomic structures are adequate, and real-time procedures can be performed.³⁴

No cases of definitive paraplegia were encountered in our series. Only 1 case of transient paraparesis was observed, and the patient had completely recovered a few hours after the procedure. Kumar et al²³ reported a case of reversible paraparesis after CPB. They hypothesized that a direct injection of alcohol into the artery or the subarachnoid space is unlikely and remote but that mechanical damage to the arteries is possible. Masuda³⁵ performed an anatomic study in cadavers to determine the optimal needle placement for preventing ischemic injury to the spinal cord during CPB and SNB. He found that the intervertebral discs and the upper third of the anterolateral vertebral region are the safer routes for the needle tip pathway to avoid traumatic injury to the arteries branching to the artery of Adamkiewicz. Thus, the transdiscal posterior approach in SNB reduces the risk of traumatic damage to the major segmental arteries that might perfuse the spinal cord. In previous reports, our team had already recommended a transdiscal technique at alternative levels of the sympathetic axis as a procedure safer than the more traditional approaches.³⁶

The main advantage derived from SNB that was shown in our study was that, despite the lack of control or the lack of the traditional approach (CPB), it gives both physicians and patients an effective alternative for the management of chronic upper abdominal pain in cancer patients. These results rely on one of the largest case studies of pain intervention literature. In the near future, we hope to begin a comparative research in this area, with a study prospectively designed to compare CPB and SNB, taking into account the transdiscal approach and other important aspects, like those recommended by the IMMPACT (Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials) core outcomes.

ACKNOWLEDGMENTS

The authors thank the subjects who participated in the study for their consent and cooperation. The authors also thank their colleagues from the Department of Radiology of the Instituto Nacional de Cancerología in Mexico City, Mexico, for their devotion in the care of patients and their fundamental contributions to the illustrations and the realization of this article.

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