

Celiac Plexus Block in Cancer Pain Management

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YAMAMURO, M., KUSAKA, K., KATO, M. and TAKAHASHI, M. *Celiac Plexus Block in Cancer Pain Management*. Tohoku J. Exp. Med., 2000, **192** (1), 1–18
— The neurolytic celiac plexus block (NCPB) has been recommended for pain relief in patients with upper abdominal cancer by the WHO Cancer Pain Relief Program. In this article, we review the indications, techniques, and adverse effects of NCPB based on the previous findings in the literature and our own experience of 142 NCPBs during the past 11 years. No well-validated indication criteria for the NCPB have been available from invasive trials or non-invasive pain evaluations. Thus, the procedure has been employed using comprehensive pain assessment. Several modified approaches have been described for NCPB with differences in the target space where the alcohol is injected (precrural and retrocrural) and the insertion route of the needle (posterolateral and transdiscal). We have used the retrocrural transdiscal approach because of its simplicity and safety. The efficacy of the resultant pain relief does not differ among these techniques. Therefore, whether a distinction exists between blocks of the celiac plexus and those of the splanchnic nerves is controversial. The term “peri-aortic nerve block” may better describe the feature of this neurolytic intervention. The noteworthy adverse effects of alcoholic neurolysis include regional pain, hypotension, diarrhea, hypoxemia, and acute alcoholic intoxication. Most of them are transient and controllable. The diarrhea may counteract the morphine-induced constipation. NCPB relieves visceral pain in upper abdominal cancer with no serious adverse effects. We recommend this procedure to improve the quality of life of the patients suffering from abdominal cancer pain. ——— celiac plexus block; neurolysis; peri-aortic nerve block; cancer pain © 2000 Tohoku University Medical Press

In the progress of cancer in the abdominal organs, visceral pain in the affected area can result from various mechanical and neurohumoral mechanisms. The

Received March 30, 2000; revision accepted for publication August 9, 2000.

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possible etiology of the pain includes torsion or traction of the mesentery, distention or contraction of hollow viscera, irritation or inflammation of the mucosa and serosa, spasm of the smooth muscle, stretching of the capsule of the solid viscera, obstruction, ischemia, and neurogenic causes (Johnson and Parris 1997). These nociceptive stimuli are transduced into neural impulses and transmitted to the central nervous system via the visceral afferent fibers associated with the autonomic nerves which distribute widely to the abdominal organs. Block or lysis of these fibers, therefore, can diminish the pain perception conveyed by these pathways.

The sensory pathways of the celiac plexus are composed of afferent fibers contained in the thoracic and lumbar splanchnic nerves (sympathetic), the vagal nerves (parasympathetic), and the phrenic nerves (motor). A dramatic reduction of visceral pain by neurolytic celiac plexus block (NCPB) has been reported in patients with upper abdominal cancer for decades (Bonica 1953; Moore et al. 1981). The effectiveness of NCPB on cancer pain relief has been confirmed in several prospective randomized controlled studies (Lillemore et al. 1993; Mercadante 1993; Polati et al. 1998). The WHO Cancer Pain Relief Program has endorsed this procedure as the most suitable invasive intervention in a palliative setting (World Health Organization 1984). However, NCPB is still considered a non-standard procedure in cancer pain management. This is likely because many physicians and other medical personnel hold some misconceptions concerning NCPB such as that it is painful, dangerous, and not effective. Thus, many terminally ill patients are deprived of a potential improvement in their quality of life (QOL). The aim of this article is to review the indications and techniques, and the adverse effects of NCPB based on previous findings in the literature combined with our own experience of 142 NCPBs during the past 11 years (Table 1).

Indications

General concepts. In general, neurolytic interventions are employed in cancer patients when pain cannot be controlled adequately with non-invasive therapies, and when life expectancy is limited (Jain 1997). The issues that should be considered prior to employing neurolysis include the etiology of pain, the patient's condition, patient and family preference, appropriate techniques, the availability of expert physicians, side effects and complications, as well as future problems resulting from progression of the disease. However, these concepts are rather subjective and a clear consensus concerning invasive approaches has not been established (Sharfman and Walsh 1990; Eisenberg et al. 1995).

The timing of induction is an additional issue for neurolytic interventions in palliative medicine. The best pain relief is often obtained with patients who received neurolysis at the early stage of their illness (Jain 1997). Further, successful control of pain with the neurolytic procedure can prolong the lives of

TABLE 1. *Methods of neurolytic celiac plexus block applied and cancer types in our patients*

Method	Number of patient	Types of cancer			
Transaortic	3	Gastric	2		
		Pancreas	1		
Classical transcrural	19	Gastric	6		
		Pancreas	6		
		Colon	3		
		Liver	4		
Classical retrocrural	67	Gastric	16		
		Pancreas	15		
		Colon	10		
		Liver metastasis	10		
		Liver	8		
		Renal/adrenal	3		
		Gynecologic	2		
		Other	3		
		Transdiscal retrocrural	53	Gastric	11
				Pancreas	12
Colon	9				
Liver metastasis	6				
Liver	9				
Renal/adrenal	2				
Gynecologic	1				
Other	3				

cancer patients (Lillemore et al. 1993). On the other hand, the risks associated with neurolysis increase as the progress of the illness (Ogawa et al. 1989). Therefore, referring physicians are encouraged to consider viable options including neurolytic interventions early in the course of terminal illness.

Specific considerations. Possible candidates for NCPB are patients suffering from severe visceral pain caused by cancer in the upper abdominal organs such as the pancreas, stomach, and liver. The assessment of pain for each patient and the results of pre-CPB trial anesthetic block have conventionally facilitated the decision to use NCPB. However, wide variations of pain descriptions by patients and doubts concerning the diagnostic efficacy of the trial block have militated against establishing a consensus on the indication criteria for such patients. This may interfere with the appropriate timing for providing optimal pain relief to terminally ill patients.

Pain assessment

The most frequent indication for NCPB in the literature has been visceral-originated "celiac pain" (Ischia et al. 1992) caused by cancer of the pancreas (Lillemore et al. 1993; Mercadante 1993; Polati et al. 1998) and of the other abdominal organs (Hilger and Rykowski 1994; Ina et al. 1996). Table 2 summarizes the previously reported locations and characteristics of the pain that were described by patients who received NCPB (Ischia et al. 1992; Eisenberg et al. 1995). Variety in the descriptions of pain by the patients, however, may compromise the standardization of induction criteria based on the non-invasive pain assessment. Terauchi et al. (1995) have suggested that the changes in pain perception induced by environmental factors positively predict the subsequent NCPB effects. Bathing or local warming of the affected area often improves cancer pain. Among our patients, 52 out of 71 cases (73.2%) who described a warming-induced pain reduction experienced satisfactory pain relief (pain less than 20 in the visual analog scale) by NCPB. The warming-induced changes in pain perception may be a possible candidate for the induction criteria of NCPB. However, the underlying mechanisms are not fully understood. Further well-controlled studies are needed to clarify the prognostic usefulness of non-invasive pain assessment for predicting the NCPB efficacy.

Trial (or preliminary) block

Since NCPB is highly invasive, a trial (or preliminary) block of the celiac plexus with local anesthetic has been recommended to predict the effects of neurolytic blockade on the targeted pain (Bonica 1990). However, the diagnostic sensitivity and specificity of the pre-NCPB trial block has been questioned (Ischia et al. 1992). Various factors may limit the diagnostic efficacy of the trial block, such as a placebo effect, differences in regional diffusion and the mechanisms of action of the anesthetic and the neurolytic agent, and the systemic effects of local anesthetic.

The epidural block has been used as an alternative prognostic block for NCPB (Ina et al. 1996). Theoretically, the effects of the epidural block are limited on somatic pain, sympathetically maintained pain, and the splanchnic

TABLE 2. *Pain assessment for indication of neurolytic celiac plexus block*

Location	Characteristic
Upper abdominal, epigastric Sometimes hypochondrial Often radiating to the back	Deep»superficial Crampy, boring, gnawing Chronic»episodic Continuous visceral pain Sometimes colic-type pain Frequently accentuated by palpation

afferent component of visceral pain. The diagnostic efficacy of the trial epidural block, therefore, depends upon the etiology of individual pain. In our results (Yamamuro 1997), 52 out of 83 (62%) patients whose pain was controlled with the epidural block experienced satisfactory pain relief with NCPB, indicating the limited efficacy of the trial epidural block for predicting the subsequent NCPB effectiveness.

Since, as discussed above, a highly reliable prognostic procedure has not been available, we have routinely used both the epidural and the anesthetic celiac plexus block prior to alcoholic neurolysis. However, it is possible that patients with negative trial results have needlessly lost an opportunity to receive adequate pain relief. Therefore, the establishment of reliable indication criteria for NCPB should be pursued using invasive trials as well.

Techniques

Safe and reliable techniques for NCPB have been a major topic in the field of pain management (Eisenberg et al. 1995), and various techniques have been described in the literature.

Classification. The celiac plexus is lysed with alcohol directly under laparotomy or percutaneously using a block needle. The percutaneous procedures have been conventionally performed by a posterior approach but an ultrasound-guided anterior approach has also been reported (Caratozzolo et al. 1997). The NCPB techniques most frequently used are based on the percutaneous posterior approach in a palliative setting (Ischia et al. 1992). Several modifications of this approach have been described with regard to the target position of the needle tip, which may be the retrocrural (Boas 1978; Moore et al. 1981) or precrucral space (Singler 1982; Ischia et al. 1984), and the route of the needle insertion, which may be the classic paravertebral (tangential) or transdiscal route (Yamamuro 1989a; Ina et al. 1996) (Table 3; Fig. 1).

Theoretically, the injection of alcohol into the retrocrural space achieves blockade of the splanchnic nerves only, while that into the precrucral space (transcrural approach) produces a comprehensive blockade of the celiac plexus. However, no difference in the resultant pain relief between the two approaches has been found (Ischia et al. 1992). Although the reason for this lack of difference is not clear, previous findings using contrast computed tomography (CT) have suggested that the retrocrural agent spreads periaortically, blocking additional precrucral components of the plexus (Moore et al. 1981; Ito et al. 1987; Fujita 1993). We have also confirmed, using CT, the precrucral spread of contrast medium that was injected retrocrurally (Fig. 2). These findings call into question the rigid distinction between the celiac plexus block (precrucral) and the splanchnic network block (retrocrural). Therefore, we have proposed the comprehensive

TABLE 3. *Classification of neurolytic celiac plexus block using percutaneous posterior approach*

Target space	Transcrural space		Retrocrural space	
Needle tip position in relation to aorta	Anterolateral, ^a	Left lateral	Bilateral	Bilateral posterolateral
Needle insertion route	Tangential line to vertebral body	Tangential line to vertebral body	Transcrural	Tangential line to vertebral body Transdiscal
Number of needles	1	1	2	1 (2 ^b)
Reference	Ischia et al. (1983)	Hilger and Rykowski (1994)	Ina et al. (1996)	Moore et al. (1981) Yamamuro (1984)

^aTransaortic method, ^bif spread of contrast medium is not adequate, the other needle is inserted at the contralateral site.

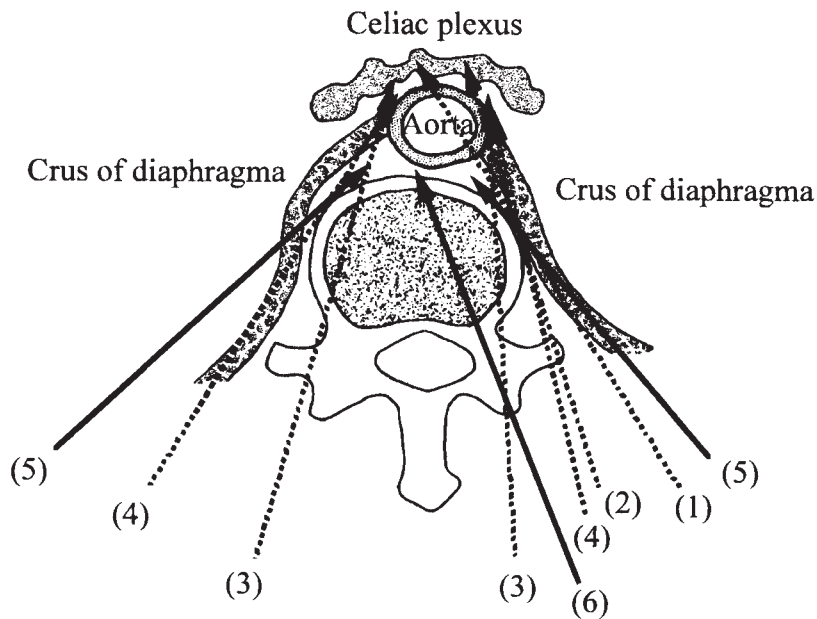


Fig. 1. Needle tip position and insertion route with various methods for neurolytic celiac plexus block.

- (1) The needle protrudes through the aorta and the needle tip is placed in the center portion of the celiac plexus (Ischia et al. 1983).
 - (2) The needle is passed through the left lateral aspect of the aorta and the needle tip is placed in the left portion of the celiac plexus (Hilger and Rykowski 1994).
 - (3) The needles penetrate the intervertebral disc and the needle tips are placed at the bilateral anterolateral aspect of the aorta (Ina et al. 1996).
 - (4) The needles are inserted tangentially to the vertebral body and the needle tips are placed bilaterally at each lateral aspect of the aorta (Singler 1982).
 - (5) The needles are inserted tangentially to the vertebral body and the needle tips are placed bilaterally at the posterior aspect of the aorta (Moore et al. 1981).
 - (6) The needle penetrates the intervertebral disc and the needle tip is placed in the postaortic retrocrural space (Yamamuro 1984).
- ←, transcrural; ←····, retrocrural.

term “peri-aortic nerve block” for this neurolytic procedure (Yamamuro 1989b).

The classical route of the needle insertion is paravertebral with a posterolateral skin puncture (Boas 1978; Moore et al. 1981). In this tangential approach, the needle is advanced while contacting the lateral aspect of the vertebral body. The resultant laterality of the needle position often requires bilateral injections, thereby increasing the discomfort and invasiveness. The neurolysis can be completed with a single injection using the transaortic approach (Ischia et al. 1983) or transdiscal approach (Yamamuro 1989a; Ina et al. 1996). Since the expected efficacy is not different among these techniques, we have recommended the transdiscal retrocrural approach because of its technical simplicity and reduced invasiveness.

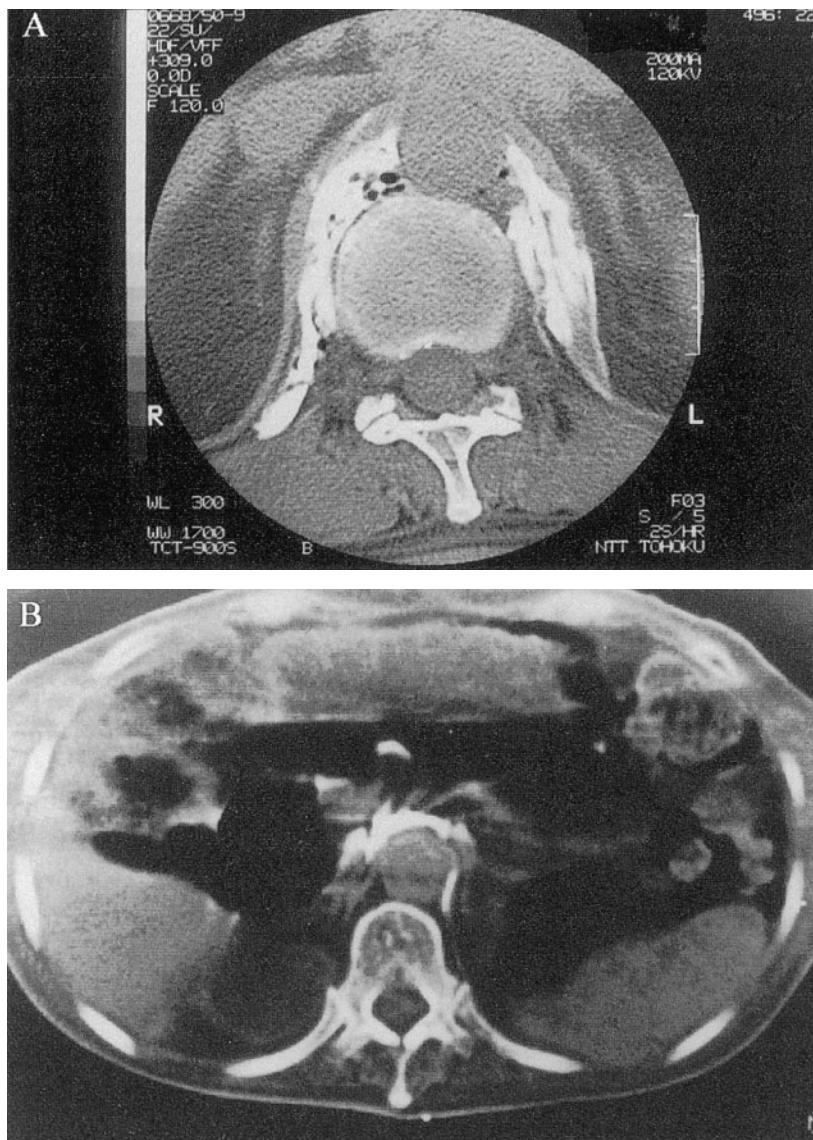


Fig. 2. Computed tomographic findings of contrast medium injected in the retro-crural space.

A: Contrast medium remains posterior to the crura of the diaphragm.

B: Most of the contrast medium spreads anterior to the aorta.

Technical considerations.

Pre-estimation of the needle insertion route and target space

Possible insertion routes for the needle and the target point for the agent injection are estimated using CT imaging at the appropriate vertebral levels (Th12-L2) prior to NCPB. The needle angle with reference to the sagittal plane, the distance from the skin to the target, and the relative dimensions of the needle and the surrounding organs should be taken into consideration. Later contrast imaging is also considered.

Insertion of the needle

The block needle is placed at the target point according to the image under fluoroscopy or CT guides. In the transdiscal approach, we recommend the loss of resistance method using a 10 ml syringe filled with saline containing antibiotics for confirming by feeling that the needle tip reaches the anterior aspect of the intervertebral disc. Although the CT-guided needle placement may be most reliable, no significant differences have been found in the efficacy between NCPB under CT guide and that under fluoroscopy (Ischia et al. 1992; Eisenberg et al. 1995).

Contrast fluoroscopy

Accurate positioning of the needle tip can be confirmed using contrast radiography (Yamamuro et al. 1984). In the transcrural approach, a “butterfly-wing” shadow is often observed in the anteroposterior view (Fig. 3). In the retrocurural method, a “wedge-shaped” shadow in the lateral view is characteristic (Fig. 4).

Trial block with local anesthetics

The prognostic power of the pre-NCPB anesthetic block has been discussed (Ischia et al. 1992). However, since preliminary epidural block has only limited diagnostic efficacy, a trial block with local anesthetic still remains essential to predict effects of the subsequent neurolysis (Bonica 1990). In order to verify changes in the pain symptoms, no sedative or analgesic agents should be given for the trial block.

Injection of alcohol

Yabuki et al. (1988) has recommended injecting more than 25 ml of alcohol with a concentration higher than 75% to obtain the best results. Ina et al. (1996) also reported that using of alcohol with a higher concentration resulted in better pain relief. We have used 20 ml of 99.5% alcohol in most cases.

Advantages and disadvantages of the different approaches

We have used the transcrural approach in 22 patients and the retrocurural approach in 120 patients. In the transcrural group, 3 cases were blocked by the transaortic method described by Ischia et al. (1983) and 19 cases were performed by the tangential direction method described by Singler et al. (1982). In the retrocurural group, the needle was advanced by slipping off the anterolateral aspect of the vertebral body (Moore et al. 1981) in 67 cases, while the transdiscal approach was used in 53 cases (Table 1). Table 4 summarizes the technical difficulties of each approach based on our experience.

Because we have observed postprocedural bleeding from the aorta in one

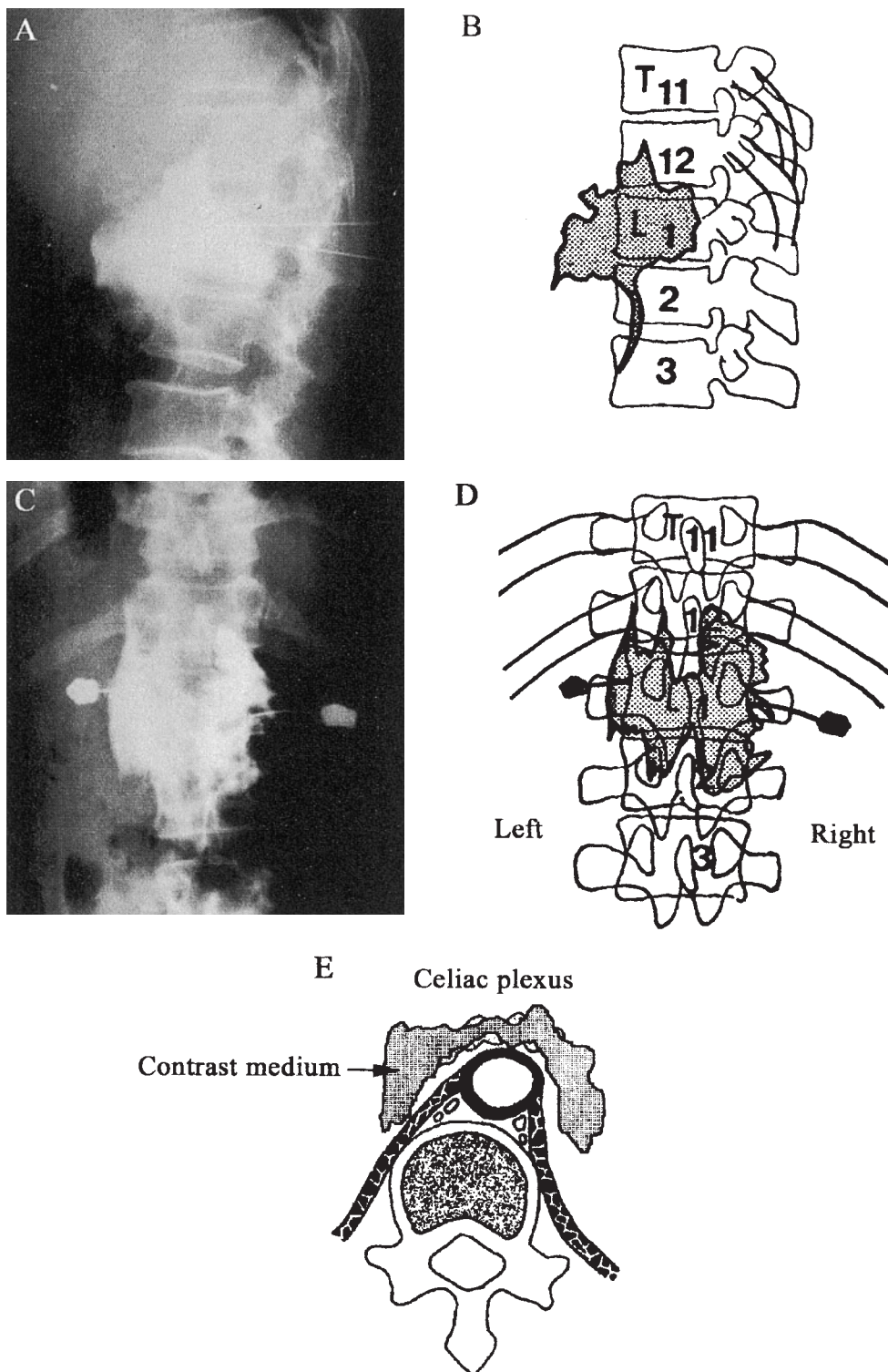


Fig. 3. Spread of contrast medium in the transcubital method.

A, B: Lateral view.

C, D: Anteroposterior view.

E: Cross section.

Contrast medium spreads anterior to the crura of the diaphragm. The lateral view (A, B) shows no typical shape. The anteroposterior view (C, D) shows a "butterfly-wing" appearance with a narrow isthmus.

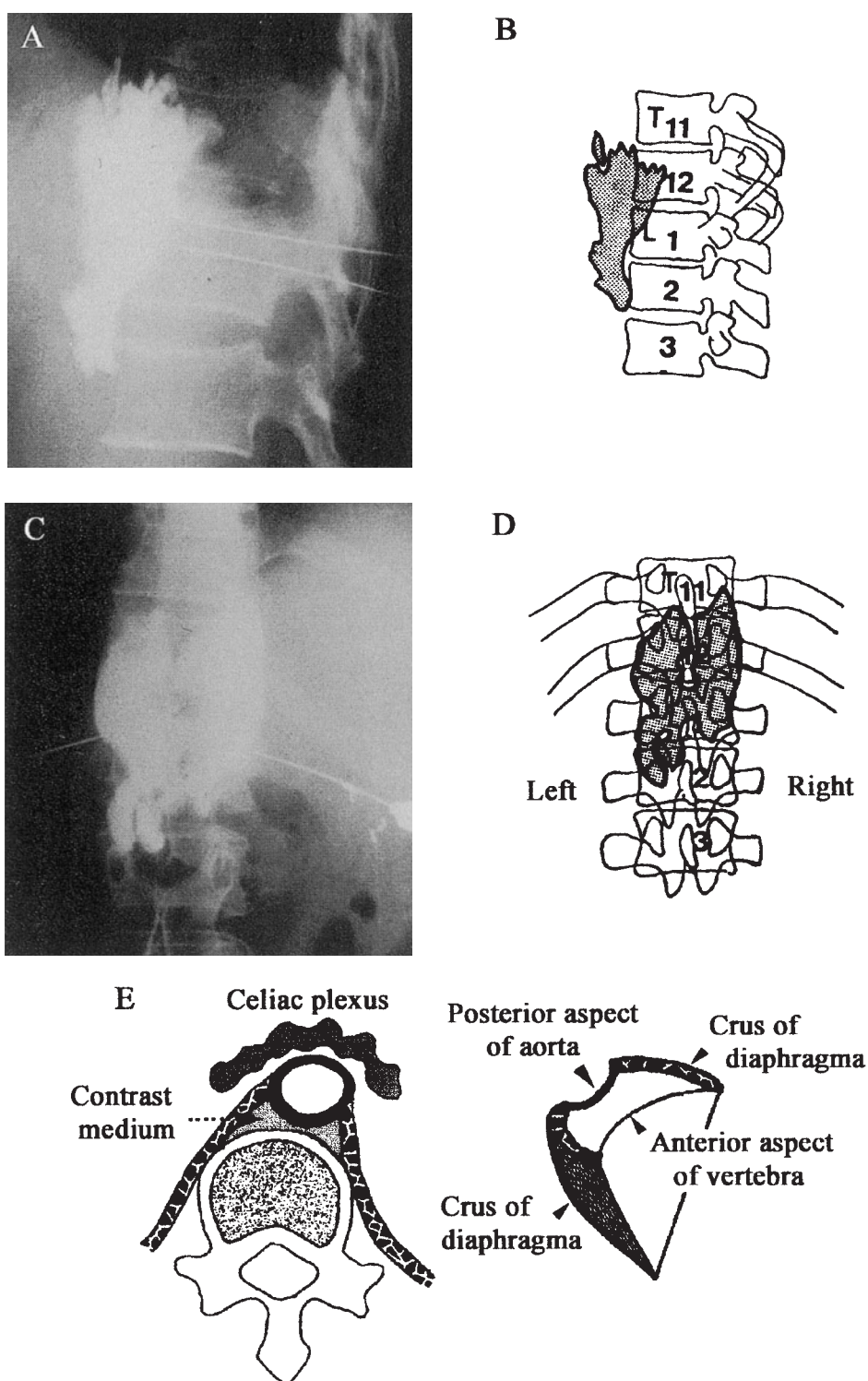


Fig. 4. Spread of contrast media in the retrocrural method.

A, B: Lateral view.

C, D: Anteroposterior view.

E: Cross section.

Contrast medium spreads posterior to the diaphragm. The lateral view (A, B) shows a “wedge-shaped” appearance as contrast medium spreads in the compartment surrounded by the posterior of the aorta, the crura of the diaphragm and anterior aspect of the vertebrae. The anteroposterior view (C, D) is similar to that of the transcral method.

TABLE 4. Comparison of the degree of difficulty in the techniques for the neurolytic celiac plexus block

	Transcrural method			Retrocrural method		
	Transaortic	Tangential	Transdiscal	Transdiscal	Tangential	Tangential
Route estimation on CT	Easy	Difficult (right side)	Easy	Easy	Difficult (encountering kidney or liver on the right)	Difficult
Needle insertion	Difficult (aortic protrusion)	Difficult (often too lateral)	Easy (loss of resistance method)	Easy	Slightly difficult (often intracranial on the right)	
Needle tip positioning	Easy (preaortic space)	Difficult (bilateral anterolateral aspect of aorta)	Easy (anterior aspect of intervertebral disc)	Easy	Easy (postaoptic and retrocrural space)	
Fluoroscopic finding	Lateral view : nontypical Anterolateral view : "butterfly-wing"	Lateral view : "wedge-shaped" Anterolateral view : "butterfly-wing"				

patient who received the transaortic block, we stopped using this approach. Coagulopathy is often observed in terminally ill patients. Chemo- and radiotherapy also compromise the coagulatory function. Intraabdominal bleeding may be potentially hazardous in patients whose sympathetic response is inhibited by NCPB. Therefore, we disagree with Ischia et al. (1983) who suggested the safety of the transaortic approach.

A wide spreading of the agent can be obtained with the tangential transcruval approach when the needle tip is placed at the anterolateral aspect of the aorta. However, the surrounding organs, especially on the right side, often interfere with the appropriate positioning of the needle. Inappropriate placement of the needle tip may result in insufficient pain relief. Fig. 5 shows a typical contrast image in such a case.

The tangential retrocruval approach requires the needle to be the widest insertion angle from the sagittal plane (Fig. 1) so that the needle often encounters the surrounding organs especially on the right side. Further, the wide laterality of the puncture points often restricts the position of the patient during the block procedure.

In our opinion, the retrocruval transdiscal approach may be technically the most simple. The loss of resistance method can be used for the placement of the needle at the target point. Although the right lateral position is preferable, any other position can be used. Fewer organs exist in the needle insertion route compared to the other approaches. A single puncture completes the neurolysis in most cases. When a semilateral diffusion of contrast medium is found, an additional neurolysis of the inferior mesenteric plexus can be performed using the same transdiscal approach in the lower intervertebral space. This modification is

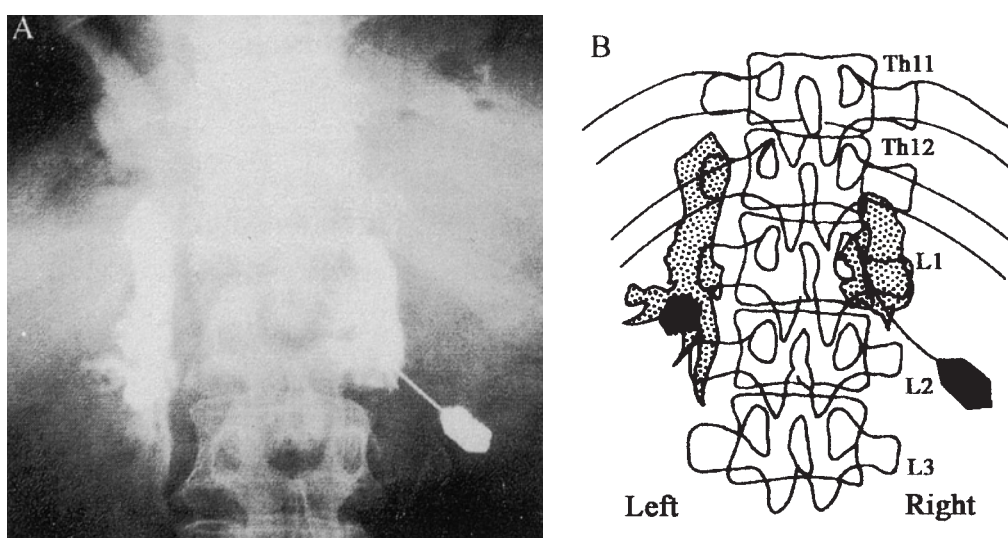


Fig. 5. Spread of contrast medium when needle tips are placed too lateral using the transcruval approach.

The needles were inserted too lateral after slipping off the vertebral body. Contrast medium did not spread into the central portion of the vertebrae (A, B).

supported by a previous report suggesting that superior pain relief can be obtained with the simultaneous neurolysis of the celiac and the inferior mesenteric plexus ("expansive NCPB") in abdominal cancer patients (Tsukamoto et al. 1992). Possible complications specific to this approach include inflammation, degeneration, and dislocation of the intervertebral disc. However, no such case has been observed among our patients or in previous studies (Flangan and Chung 1986; Ina et al. 1996).

Adverse effects and complications

Based on a meta-analysis, Eisenberg et al. (1995) described three minor adverse effects that include puncture-related regional pain (99%), diarrhea (44%), and hypotension (38%) for NCPB. All of those were transient and not serious. Life-threatening complications are rare. They reported a low rate of 2% (13 out of 628 patients) for complications such as motor nerve disturbance and pneumothorax. We have not experienced such problems among the 142 patients.

Regional pain. The puncture-related local pain is transient and requires no treatment in most patients. In cases of severe pain, non-steroidal anti-inflammatory drugs are effective.

Diarrhea. NCPB increases the motility of the intestine by its desympathetic effects, resulting in severe diarrhea in some patients (Dean and Reed 1991; Mercadante 1995). However, this is often beneficial for patients suffering from morphine-induced constipation. Effective NCPB reduces the required dose of morphine. We are aware that withdrawal from morphine can also produce constipation. Weinstable et al. (1993) reported successful control of the decreased intestinal motility after brain surgery with NCPB. NCPB may be used for counteracting the morphine-induced constipation if it compromises adequate pain control.

Hypotension. The decline of the blood pressure can reliably indicate the sympathetic blockade induced by NCPB. Alcohol decreases the blood pressure more profoundly than does local anesthetic. The hypotension is usually transient and can be treated using adequate fluid replacement and vasopressive agents. Hypoglycemia prolongs the NCPB-induced hypotension (Kawanishi 1985). Orthostatic hypotension is an additional concern related to sympathetic denervation. Therefore, special attention should be given to hemodynamics of patients during and after NCPB.

Acute alcoholic intoxication-like symptoms. The injected alcohol is immediately absorbed in the blood and reaches a peak after about 15 minutes. Some patients develop alcoholic intoxication-like symptoms in this period, such as rapid pulse, face flushing, and cold sweating. However, the measured alcohol concentration in the blood has been reported to be much lower than the toxic level (Sato et al. 1992, 1993). Noda et al. (1986) suggested that the metabolic products of

alcohol, rather than alcohol itself, account for such symptoms. In most cases, the symptoms disappear in a couple of hours and do not require any specific treatment.

Hypoxemia. Kusaka (1988) reported the changes in the blood alcohol concentration and the arterial blood gases during NCPB. The neurolysis was completed in 10 patients (9 men and 1 woman) with a single injection of 99.5% alcohol at a volume of 10 ml using the tangential retrocrural approach. The PaO₂ before the alcohol injection was 85.1 mmHg on average. After injection, PaO₂ decreased significantly and the lowest value (73.9 mmHg) was observed at 50 minutes post-injection (Fig. 6A). A significant decrease was also observed in PaCO₂ at 20-30 minutes post-injection (Fig. 6A). The trial block with local anesthetic did not produce such changes in the patients. The decrease in PaO₂ and the increase in the alcohol concentration in the blood were statistically correlated (Fig. 6B). However, the author found no such decrease in PaO₂ in 13 male volunteers who received the same dose of alcohol orally while the blood concentration of alcohol reached six times higher than that observed in the patients receiving NCPB. Therefore, the decrease in PaO₂ is likely to be specific to alcohol but cannot to be explained by its concentration in the blood. The underlying mechanisms of these changes have not been clarified. Nevertheless, possible hypoxemia is a concern during the NCPB procedure.

Conclusions

Pain relief by NCPB has been verified in patients with upper abdominal cancer. However, definite indications (or contraindications) for patient selection are not available at present. Comprehensive assessment of pain and careful planning of treatment are required for the induction of NCPB.

Several modified techniques for NCPB have been described in the literature. The efficacy for pain relief does not differ among these techniques. Therefore, we recommend the transdiscal retrocrural approach because of its technical simplicity and safety. This technique also allows the additional block of the inferior mesenteric plexus with minimal invasiveness.

Although NCPB often causes post-procedural adverse changes such as local pain, hypotension, and diarrhea, most of them are transient and not severe. The diarrhea may counteract constipation that is often caused by morphine. Hypoxemia is an additional concern. Possible severe complications include motor disturbance and injury of the organs surrounding the target. However, these are rare when the adequate safety measures are taken.

Taken together, NCPB can be expected to provide superior QOL in patients suffering from intractable cancer pain. Because of its well-validated techniques and low incidence of serious complications, we believe that NCPB can make a significant contribution to cancer pain management.

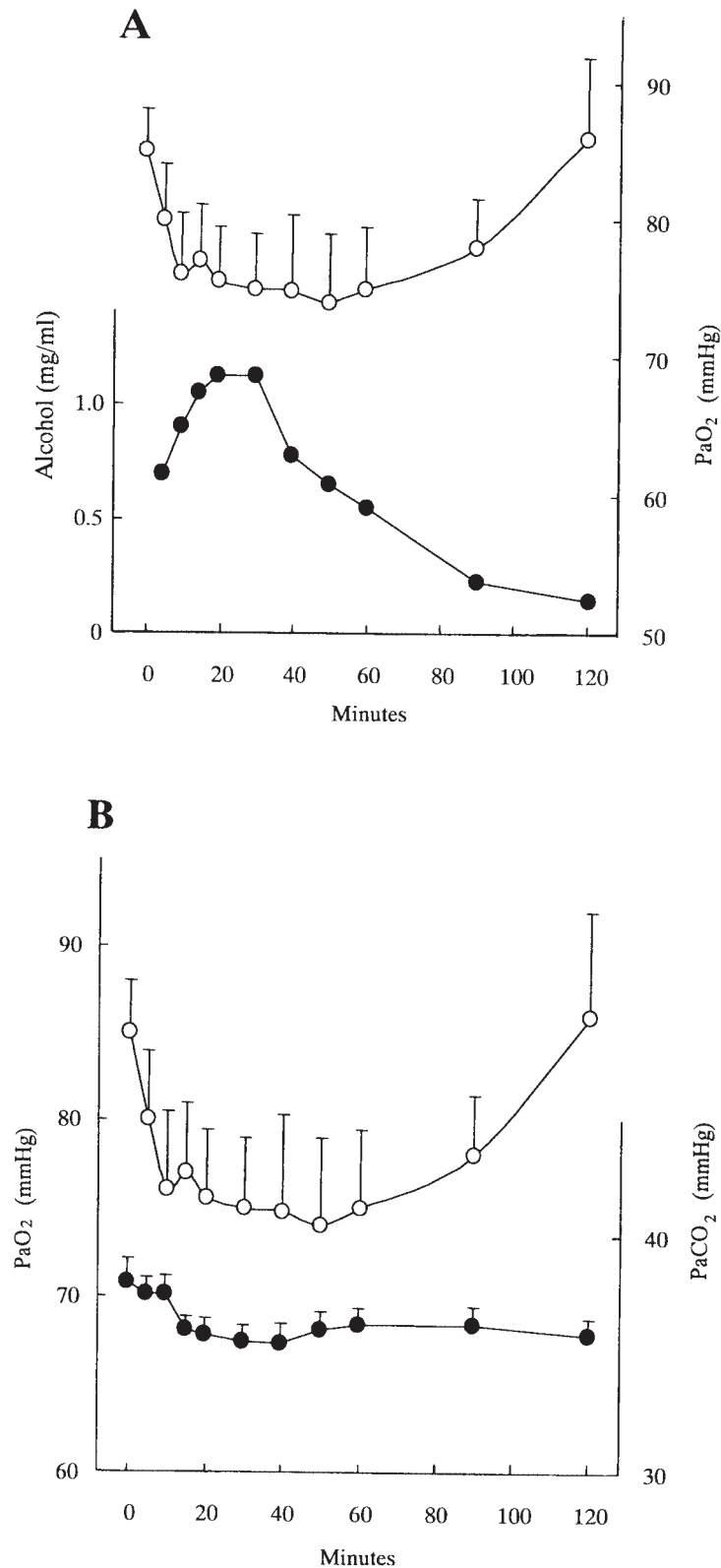


Fig. 6. Changes in plasma alcohol concentration and blood gases after injection of alcohol (Kusaka 1988 with author's permission).

A: Changes in plasma alcohol concentration and PaO₂ following alcohol injection ($n=10$). Data are presented as mean \pm s.e..

●, Alcohol; ○, PaO₂.

B: Changes in PaO₂ and PaCO₂ following alcohol injection ($n=10$). Data are presented as mean \pm s.e.. ●, PaCO₂; ○, PaO₂.

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