

Percutaneous Ultrasound Long Axis (In-plane)-guided Approach: A Novel Technique for Celiac Plexus Neurolysis in Patients with Advanced Pancreatic Cancer

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ABSTRACT

Introduction: The primary objective is to investigate the feasibility of proposed percutaneous ultrasound long axis (LA; in-plane) guided approach for celiac plexus neurolysis (CPN) in patients with advanced pancreatic cancer. The present study also aimed to assess the outcome as well as to document complications specific to the proposed technique if any.

Materials and methods: Celiac plexus neurolysis under LA ultrasound (USG) guidance was performed in thirty one patients (mean age of 58.2 ± 4.7 years) of either-sex (24 men and 7 women) suffering from chronic pain due to pancreatic cancer [visual analog scale (VAS) score > 4] not responding to any pharmacological treatment or in those where opioids-related adverse effects are poorly tolerated. Follow-up was done immediately after injection, first day, 1 week, 4 weeks and 12 weeks following intervention and on an as needed basis thereafter. Post-neurolysis and at each subsequent follow-up visit, pain scores, satisfaction rate and other complications were studied. Level of statistical significance was set at a $p < 0.05$.

Results: At 12 weeks CPN under LA ultrasound guidance was associated with significant pain relief, reduced NSAIDs/opioids consumption and improved patient satisfaction ($p < 0.05$). There were no major peri- and/or postoperative complications.

Conclusion: Celiac plexus neurolysis under LA USG guidance enhances effectiveness and was associated with better pain relief, reduced NSAIDs/opioids consumption and improved patient satisfaction.

Clinical significance: Celiac plexus neurolysis under LA USG guidance enhances effectiveness of pain relief and level of safety in patients with abdominal malignancies.

Keywords: Celiac plexus, Celiac plexus neurolysis, Long axis ultrasound, Pancreatic cancer, Visual analog scale.

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INTRODUCTION

The celiac plexus neurolysis (CPN) is an interventional technique indicated in a setting of intractable abdominovisceral pain resulting from upper abdominal malignancies which is nonresponsive to less aggressive non-narcotic medical therapies; often these patients require high doses of opioids which is associated with serious side-effects and minimal clinical benefit, thus its use is discouraged.¹⁻³ Chronic pain in these patients significantly impairs their families, social and professional environment, causing marked deterioration in the patients' health-related quality of life.³⁻⁵ Palliative care and substantial pain management is treatment of choice in these patients. Thus there is a need to adopt a comprehensive approach to improve the patient's condition and quality of life, while reducing the risk of drug-induced adverse effects. Celiac plexus neurolysis has been widely accepted as an effective therapy delivering long-lasting pain relief and decreased narcotic usage in 70–90% of patients with pancreatic cancer pain.⁶⁻¹⁰ The celiac plexus is web of nerve fibers comprised of the celiac ganglia, aortic-renal ganglia, and superior mesenteric ganglia having both sympathetic and parasympathetic nerves positioned in the retroperitoneum, anterolateral aspects of aorta at the level of L1 vertebrae.^{11,12} It can be approached anteriorly or posteriorly.¹⁰ Celiac plexus neurolysis can be performed under computed tomographic (CT), fluoroscopic or endoscopic ultrasound (EUS)-guidance.^{10,13,14} Although these imaging modalities have a role in the injection of neurolytic agents to the celiac ganglion; these are fraught with some technical drawbacks. In contrast, ultrasonography (USG) provides "real-time"

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imaging technique, that permit for direct visualization of important vascular structures without exposing to hazards of radiations and requirement of any sophisticated armamentarium. All these advantages made CPN under USG guidance as more frequently

utilized technique.^{15,16} Though clinical benefit has been shown we have found that most of the authors have preferentially used the short axis (SA) technique as the preferred approach for CPN. The SA approach attempts to visualize the important vasculatures in cross-section. During injection, the needle may not be seen when it is advanced out of the scanning plane and also during in-plane all the concerned vasculatures will not be visualized in one view. Therefore, positioning of needle tip is entirely based on visualization of tissue movement and assumption. This will lead to frequent attempts to reposition the needle. Furthermore, at times in SA it is difficult to visualize the celiac trunk or even superior mesenteric artery (SMA) owing to their extreme cranial position under sternum. Also the obstructing rib cage restricts the movement of probe cranially. These will results in frequent punctures and/or repositioning of needle while performing the procedure. For these reasons, an impetus exists to develop and validate alternative cost-effective technique under long axis (LA) ultrasound guidance that is capable of replicating the performance of the published literatures significantly while dramatically minimizing the chances of failure and this was the aim of our study. We hypothesized that CPN under LA ultrasound guidance enhances the visualization of target region, reduces chances of failure and thus increases the efficiency.

MATERIALS AND METHODS

Study Design

The present study was a prospective, single-blind analysis on the safety and efficacy of USG guided CPN a novel technique as a modality to treat chronic pain in patients with pancreatic cancer enrolled at our institution during period from September 2018 to September 2019. The study was approved by the Scientific Review

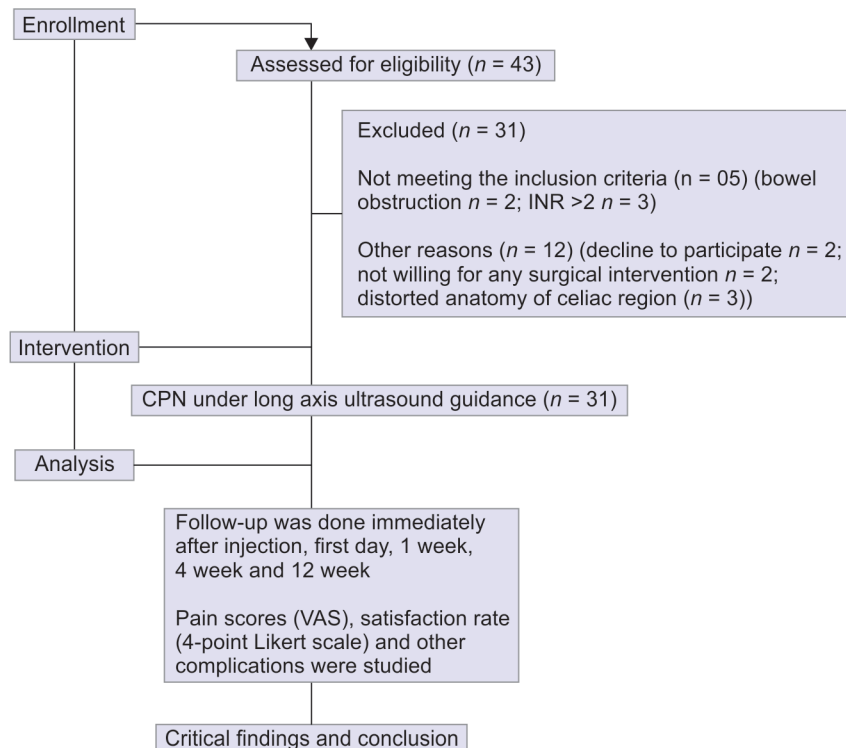
Committee and the Institutional Review Board of the participating health service. Written informed consent (about the technique, risks, partial pain relief and other potential complications) was provided according to the declaration of Helsinki and obtained from all participating patients.

Inclusion and Exclusion Criteria

The inclusion criteria were as follows: patients of either-sex suffering from chronic pain due to pancreatic cancer [visual analog scale (VAS) score >4] not responding to any pharmacological treatment or in those where opioids-related adverse effects are poorly tolerated. Patients with INR >2; with colonic gas distention; severe coagulopathies, patients with bowel obstruction; patients on disulfiram therapy for alcohol abuse, those who refused and patients where the anatomical variation of celiac trunk was found during screening due to aberrant anatomy or metastatic mass or non visualization of plexus were not considered for the study. Similarly, those with psychiatric diagnosis and/or any other circumstances that would make participation not in the best interest of the cohort or could prevent the protocol-specified outcome evaluation were also excluded.

During the study period, a total of 43 patients suffering from abdominal pain due to pancreatic cancer reported to our institution were screened. Among 43 patients screened twelve patients were excluded because of potential confounders, including patients did not fulfill inclusion criteria ($n = 5$); decline to participate ($n = 2$), not willing for any intervention ($n = 2$) and distorted anatomy of celiac region ($n = 3$). The remaining 31 patient's providing informed consent for participation were recruited in the study. The cohort included 24 men and 7 women with the mean age of 58.7 ± 4.45 years. The consort flowchart for the study is shown in Flowchart 1.

Flowchart 1: Consort flowchart



Methodology

With the patient supine a preliminary scan was done to confirm an adequate course to the celiac plexus region and also to rule out any direct invasion of the plexus by the underlying tumor.

Just prior to therapeutic block, the patient is asked to rate their pain on a scale from 0 to 10. This baseline parameter and any significant change after temporary block is an important predictor for confirming the optimal needle placement. A convex transducer was placed over epigastric area in LA of the aorta as it exit the thorax and enter the abdominal cavity to delineate the entire course of common celiac trunk and SMA. The probe was rapped with a sterile sheath, and the sterile gel was applied to the inside of the sheath. With all aseptic precautions under local anesthesia (5 mL lidocaine 2%) in supine, under sonographic guidance a Stimplex B-Braun 10 cm 22 G needle was introduced in-plane (LA) from caudal to cephalad (to the celiac axis). Mostly we have encountered the left lobe of liver as the needle advances and this also gives a good acoustic window with better visualization of needle. With the LA of the scanning beam view, the entire length of the needle was visualized as it advances gradually as close as possible to aorta between two vessels SMA and celiac trunk (CT) until showed a pattern of a classical “trident pattern of lord Shiva” (Fig. 1). Authors coined this specific pattern as “trident sign of lord Shiva” was very much appreciated in USG (LA in-plane) formed by SMA, celiac trunk and block needle placed between these two vessels (Fig. 2). Once the needle is in position aspiration was recommended to rule out intravascular placement. Once confirmed, an injection of 10 mL of 1% lignocaine with 8 mg Decadron was given slowly in 2 mL aliquots over 5–10 minutes as temporary block and scan reviewed. Doppler was used continuously to assess the dispersion of fluid (Fig. 3). Confirmation of fluid spreading around the celiac trunk, SMA and aorta is desired; failure to find such dispersion locally the authors advised to reposition the needle aiming to maximize the spread. Fifteen minutes following successful temporary block, under LA USG guidance 10 mL of 99.9% absolute alcohol was injected with negative aspiration after every 2 mL of alcohol administration. Alcohol appears echogenic in ultrasound. Adequate filling of the retropancreatic space with alcohol as indicated by the loss of “trident sign” in scan is an indication of satisfactory neurolysis.

Before the needle was removed, 2 mL of lidocaine 2% was injected to minimize the burning sensation produced by alcohol. The patient kept under observation at the hospital and critically monitored for complications if any and assessment of pain levels.

Follow-up Assessment

Follow-up was done immediately after injection, first day, 1 week, 4 weeks and 12 weeks following intervention and on an as needed basis thereafter. Post-neurolysis and at each subsequent follow-up visit, pain scores, satisfaction rate and other complications were studied.

The patients selected were assessed by use of the following instruments: the visual analogue scale (VAS) of pain, according to which patients classify their pain in a 0–10 numeric scale, the highest score corresponding to the worst pain possible.¹⁶ The assessments were performed at the baseline (V_b), immediately (V_{im}), day after (V_d), at the fourth weeks (V_4) and at the twelve weeks (V_{12}) of intervention. Patient’s perspective was assessed based on a transitional four-point Likert scale.¹⁷ The items include patients’ overall satisfaction with procedure and the extent of pain relief, mental health (ability to enjoy life as before) and social functioning (ability to attend social functions as before). Items are scored on a 4-point Likert scale with response categories consisting of: very satisfied (100 points), somewhat satisfied (75 points), somewhat dissatisfied (50 points) and very dissatisfied (25 points). The current scale score is the unweighted mean of the scores from the individual items, ranging from 25 to 100 per item (with 100 being very satisfied). Face validity was assessed by having the scale reviewed by a panel of independent experts in the field of pain management. All data collection and critical evaluation using validated scoring instruments was performed by assessor who was blinded to the treatment received by each patient.

Statistic Analysis

Data were entered in Microsoft office excels and statistical analysis was done with the help of SPSS (software package for social sciences) version 20. Quantitative variables were presented as mean and standard deviation and qualitative variables were presented in frequency and percentage. Friedman test is used to compare VAS score at different point of time. p value less than 0.5 was considered

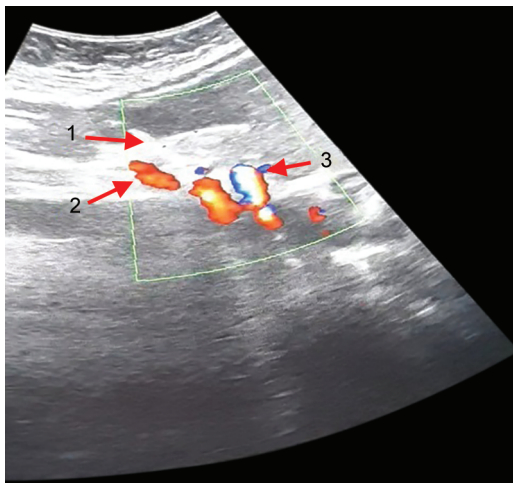


Fig. 1: Under ultrasonography long axis the needle (the entire length of needle shown) advances until a typical pattern appears “Trident”, i.e., needle shown by arrow between (1) two vessels superior mesenteric artery shown by arrow (2) and CT shown by arrow (3)

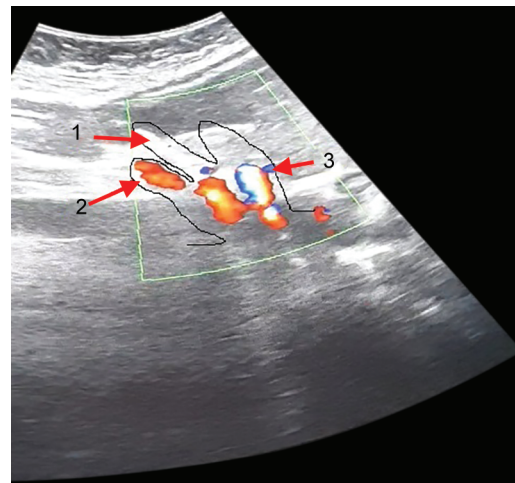


Fig. 2: Under ultrasonography “Trident sign of Lord Shiva” in ultrasonography (long axis in-plane) formed by three components superior mesenteric artery (2), celiac trunk (3) and block needle (1) placed between these two vessels

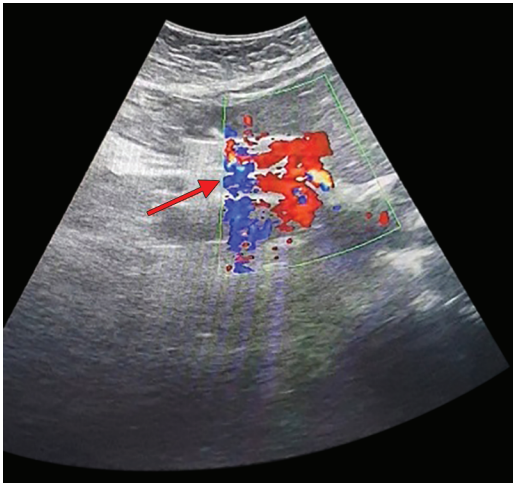


Fig. 3: Under ultrasonography long axis showing dispersion of fluid and disappearance of classical “Trident sign” (shown by arrow)

to be statistically significant. The internal consistency (reliability) of the scale was assessed using Cronbach’s α coefficient.

RESULTS

The clinical and demographic variables showed a significant higher incidence of pancreatic cancer in males ($p > 0.05$); the age did not show any significant difference ($p > 0.05$) (Table 1). All the patients with pancreatic cancer reported significantly less pain scores than at baseline (V_b) ($p < 0.05$) following CPN. We found significant differences with regard to the levels of pain immediately after procedure (V_{im}) ($p < 0.0001$), and day after (V_d) ($p < 0.0001$), at the 4th weeks (V_4) ($p < 0.0001$) and at the 12 weeks (V_{12}) ($p < 0.0001$) of intervention (Table 2). At 12 weeks they were significantly different with regard to the NSAIDS drug consumption during the study period ($p < 0.05$) (Table 3). With regard to subjective satisfaction, all patients were satisfied. At 4 weeks 26 patients (83.871%) were very satisfied while four patients (12.90%) were somewhat satisfied and one patient (3.228%) was somewhat dissatisfied with the procedure (Table 4). At 12 weeks 27 patients (87.096%) were very satisfied with the procedure (Table 4). Cronbach’s α coefficient for internal consistency of the satisfaction scale is 0.942 at 4 weeks and 0.9137 at 12 weeks of follow-up (Table 5). Patients reported one or more complications in the present series but there were no major peri- and/or postoperative complications. However, local irritant/burning pain occurred in 15 patients (48.38%), increased defecation occurred in 20 patients (64.51%), backache occurred in 16 patients (51.61%) and 10 patients (33.25%) reported hypotension

(Table 6). Furthermore, there has been no infection at the site of injection.

DISCUSSION

Neurolytic blocks are a keystone in the armamentarium available to clinicians in cancer pain management, particularly with intractable pain from advanced malignancies. The CPN can be performed using a variety of approaches with the use of ultrasound, fluoroscopy, and endoscopic and CT guidance.^{10,13,14} Currently the posterior and anterior are the most commonly practiced approach to perform the CPN.¹⁰ Authors preferred USG guided anterior approach owing to its relative ease, rapidity and minimal periprocedural discomfort as compared with posterior techniques.^{12,18} It is well tolerated by patients with advanced malignancies, ileostomies and colostomies.^{12,18} Furthermore, the needle neither makes it way through the paraspinal musculature nor it impinges on either periosteum or nerve roots. Also there is less risk of any iatrogenic neurological injury owing to its precural placement.¹² In anterior approach the needle passage will inevitably encounter abdominal viscera. The most commonly traversed organs are the liver, stomach and small bowel loops. Though there are chances of organ injury; surprisingly, these are exceedingly rare.^{12,13,19–23} It is better to avoid traversing fecal-filled colonic loops. Furthermore authors stated that coagulation profile should be within normal parameters to prevent bleeding.²² In current study with anterior approach we have not encountered any injury to the abdominal viscera. The authors attribute this to use of 22 G needle under real time imaging in performing the CPN. Also wide experience with trans-abdominal FNA biopsy has established the relative safety of anterior approach. Authors articulated that to draw a definitive conclusion further experience with anterior approach in larger cohort is required. Though clinical benefit has been shown we have found that most of the authors have preferentially used the SA technique as the preferred approach for CPN. The SA approach attempts to visualize the important vasculatures in cross-section. During injection, the needle may not be seen when it is advanced out of the scanning plane and also during in-plane all the concerned vasculatures will not be visualized in one view. Therefore, positioning of needle tip is entirely based on visualization of tissue movement and assumption. This will leads to frequent attempts to redirection the needle. Furthermore, at times in SA it is difficult to visualize the celiac trunk or even SMA owing to their extreme cranial position under sternum. Also the obstructing rib cage restricts the movement of probe cranially. These will results in frequent punctures and/or repositioning of needle while performing the procedure. A major drawback of SA is that due to extreme proximity to thorax the respiratory movements affects the position of aorta with every breath and makes injection technique arduous and unsafe. In view of these critical matters authors used LA USG for performing CPN. In LA all the concerned vessels can be visualized in one view. Further with the use of Doppler the vascular area becomes extremely safe for any injection if the needle can also be fully visualized. When the needle was advanced under LA as it reaches between the CT and SMA it gave the classical pattern of “Trident.” This pattern indicates that it covers almost all major ganglion of the celiac plexus; this in

Table 1: Demographic and clinical variables

	Characteristic		p value
1	Pancreatic cancer	Male 24 (77.41%) Females 7 (22.58%)	<0.05
2	Age	Male 58.2 ± 4.2 years Females 59.2 ± 4.7 years	0.5931

Table 2: Visual analog scale

Sample	Tool	Baseline	Immediate (V_{im})	Day after procedure (V_d)	At the 4th week (V_4)	At the 12th week (V_{12})	p value
31	VAS	8.3 ± 0.71	0.17 ± 0.37	0.60 ± 0.49	1.43 ± 0.56	1.97 ± 0.61	<0.001

Table 3: Analgesic consumption

S. no.	Analgesics	Baseline consumption (%)	Immediate after the procedure (consumption decrease in percentage)	At the 4th week (decrease in percentage)	At the 12th week (decrease in percentage)	p value
1	NSAIDS	100	90 ↓	70 ↓	70 ↓	<0.001
2	Opioids	100	100 ↓	100 ↓	85 ↓	<0.001

Table 4: Likert scale

S. no.	Items/criteria	4-point Likert scale	Assessment (satisfaction) (n = 31)	
			1 month (%)	3 months (%)
1	Overall satisfaction with procedure	Very satisfied	83.871	87.096
		Somewhat satisfied	12.90	9.6774
		Somewhat dissatisfied	3.228	3.228
		Very dissatisfied	–	–
2	How satisfied are you with the outcome of procedure for improving your pain (in patient own language—अब पहले जैसा दर्द तो नहीं होता)?	Very satisfied	83.871	83.871
		Somewhat satisfied	12.90	12.90
		Somewhat dissatisfied	3.228	3.228
		Very dissatisfied	–	–
3	How satisfied are you with the outcome of procedure for mental health (ability to enjoy life as before: in patient own language—अब इस दर्द को लेकर कोई चिंता तो नहीं)?	Very satisfied	83.871	83.871
		Somewhat satisfied	12.90	12.90
		Somewhat dissatisfied	3.228	3.228
		Very dissatisfied	–	–
4	How satisfied are you with the outcome of procedure for social functioning (ability to enjoy socialism as before: in patient own language—जबसे दर्द में आराम है पंचायत शादी, दूसरो के घर में जाते हो)?	Very satisfied	58.064	45.161
		Somewhat satisfied	38.709	51.612
		Somewhat dissatisfied	3.228	3.228
		Very dissatisfied	–	–

Table 5: Cronbach's a coefficient for internal consistency (reliability) of the satisfaction scale

S. no.	Follow-up	n	Items	Cronbach's a coefficient
1	4-week satisfaction	31	4	0.9424
2	12-week satisfaction	31	4	0.9137

Table 6: Complications statistic

S. no.	Complications	Percentage/frequency
1	Local irritant/burning pain	15 (48.38)
2	Increased defecation	20 (64.51)
3	Backache	16 (51.61)
4	Hypotension	10 (33.25)

turn enhances the effectiveness of the block. Also in contrast to SA, the effects of respiration on major vessels while injecting becomes extremely low especially when moving from caudal to cranial side. Mostly we have encountered the left lobe of liver as the needle advances and this also gives a good acoustic window with better visualization of needle.

Although different agents are available, in present scenario neurolysis is most often performed with ethanol and phenol.¹⁸ Authors articulated that the choice of neurolytic medication can appropriately be left to the treating physician. Local anesthetic properties made phenol injection as painless and is not accompanied by typical burning sensation as produced by ethanol. Review of literature has shown that a less intense and

shorter duration of action with greater complication rate limits the use of phenol as choice of neurolytic agent.^{18,24} Ethanol neuroablation is widely known in providing long-lasting chronic malignant pain relief and is the most commonly used neurolytic agent in current practice. Ethanol infiltration causes damage of axonal and Schwann cell from phospholipid extraction in the cell membrane and precipitation of the lipoprotein resulting in Wallerian degeneration.^{25,26} In the present series we have used 10 mL of 99.9% absolute alcohol. The current study has shown that there was adequate analgesia in all patients during the study tenure. On critical analysis it was found that a greater percentage of patients in our study experienced a significant pain improvement than the other similar studies ($p < 0.05$).²⁷⁻²⁹ Possible etiologies for failure to produce adequate pain relief in other studies could be technical fault owing to aberrant anatomy or advanced disease; or it could be due to existence of other several sources of significant pain. The technical success rate of present technique were similar to the results reported by Marcy et al. performed celiac plexus block under CT guidance, as the proposed "trident sign of lord Shiva" under LA USG ensured the precise placement of needle and thus adequate spread of neurolytic agent resulting in long-lasting pain relief with the proposed technique.²⁷

In the present series we have found that after neuroablation, the need for opioids and NSAIDS decreased significantly by about 85% and 70% at 12 weeks respectively that are consistent with findings of previous studies. Alcohol induced Wallerian degeneration interrupting the transmission of sensory pathways for 3–6 months; improved the pain scores resulting in the decreased consumption of the analgesics by the patients.³⁰



A strong association between distress and cancer pain is evident across the course of disease.^{4,31} Patient satisfaction is an integral part of modern chronic malignant pain management. To the best of our knowledge we are unaware of any validated self-report scale that evaluates patient satisfaction after CPN. In our setting the majority of responses were in the very satisfied or somewhat satisfied categories (Table 4). At 12 weeks, more patients were very satisfied with overall satisfaction (87.096%), pain relief (83.871%) and their mental health (83.871%). Although the patients were satisfied with the procedure 3.228% of patients were somewhat dissatisfied and 51.612% were somewhat satisfied concerning with their social functioning. This difference could be attributed to their frank advanced disease that leads to limited mobility and social interaction (Table 4). Further, authors observed that the total satisfaction scores were gradually improved over the subsequent follow-up visits (87.096%: very satisfied; 9.6774%: somewhat satisfied) (Table 4). The authors attribute this to adequate analgesia and decreased opioids requirement in patients. In present series, Cronbach's α coefficient for internal consistency of the satisfaction scale is 0.9424 at 4 weeks and 0.9137 at 12 weeks of follow-up, suggesting excellent reliability (Table 5).

Complications were limited to increased defecation, transient hypotension; backache and burning pain in the present series (Table 6).^{12,32} Transient hypotension and diarrhea were secondary to unopposed stimulation of parasympathetic fibers due to sympathetic chain neurolysis within the plexus. Bed rest with legs raised along with monitoring of vitals and administration of appropriate intravenous fluids when necessary can relieve hypotension. All patients were responded well to therapy without need of any vasopressor support. Increased defecation following CPN is mostly self-limiting, and resolved with symptomatic treatment. Alcohol is an irritant and thus causes burning pain along the nerve's distribution which was managed with 10 mL of 1% lignocaine. Authors speculated about the use of local anesthetic prior to injection of alcohol as the resulting burning pain is a positive indicator that significantly enhances the precision and effectiveness of the procedure. This may hold true for blind approach. Presently improvements in radiological guidance technology and the proposed "*trident sign of lord Shiva*" have led the precise needle placement resulting in successful block. Also the successful temporary block enhances the effectiveness of therapeutic block. Authors always preferred to use lidocaine before ethanol infiltration as even for fraction of second ethanol induced burning pain in patient causes severe discomfort that may lead to multiple puncture and frequent needle placement. In contrast to other studies sixteen patients in the present series have reported backache which responded to symptomatic therapy.²⁷⁻²⁹ The backache following neurolysis is attributed to alcohol induced irritation of the retroperitoneal structures. Though retroperitoneal hemorrhage is a rare complication but it should be suspected in cases of persistence backache and hypotension postprocedure and serial hematocrits should be performed to rule out any retroperitoneal bleed and imaging as indicated.^{12,32} None of the patient in the present series has reported neuritis. This could be due to two factors: first we have used steroids along with lidocaine as one of the component of temporary block that relieve the symptoms if any and secondly the neuritis and other severe neurological symptoms were attributed to the dose of alcohol used. Studies showed that complications particularly neurological ones associated to alcohol intoxication, was directly proportional to the alcohol mass injection

and higher dose.³³ Mean administered volume, regardless of the technique, is approximately 15 mL.³⁴ In current study we have used 10 mL of 99.9% absolute alcohol. Furthermore ethanol should not be injected in mass rather it should be pulsatile to avoid acute alcohol intoxication. Regardless of technique used authors recommended that patients should be kept in observation and monitored critically for few hours postprocedure to detect potential complications.³⁵ No major complications were noted in the current study.

CONCLUSION

The present approach has shown that CPN was associated with better pain relief, reduced NSAIDs/opioids consumption and improved patient satisfaction. We have conclusively demonstrated the feasibility and effectiveness of the CPN under LA USG guidance. With the proposed approach good to excellent pain relief was achieved in almost all patients and none of them required a repeat session for suboptimal analgesia. The critical outcome of the present study made it now possible to put forward the view that the CPN under LA USG guidance is safe and effective.

LIMITATIONS

The present study is nonrandomized and does not include any control groups and small sample size further limits the generalization of findings of present study.

CLINICAL SIGNIFICANCE

Celiac plexus neurolysis under LA USG guidance enhances effectiveness of pain relief and level of safety in patients with abdominal malignancies.

ETHICAL APPROVAL

The study was approved by the Institutional Ethics Committee.

ACKNOWLEDGMENTS

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