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Endoscopic Ultrasound Guided Celiac Plexus Block and Neurolysis in the Treatment of Pancreatic Pain

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INTRODUCTION

Pancreatic diseases are considered to be among the most challenging when it comes to pain control and management. Treatment options can vary remarkably based on the underlying disease process, whether benign or malignant, acute or chronic, and patients frequently require a significant amount of opiates for pain control. Commonly employed methods for pain control include celiac plexus block (CPB) and celiac plexus neurolysis (CPN). Conventionally, these were achieved through a percutaneous approach; however, the endoscopic ultrasound (EUS) approach is increasingly being utilized in current practice. Numerous methods and approaches have been recognized and described in literature, with the efficacy and safety profiles of these procedures being the main topics of controversy. This article will review EUS-guided CPB and CPN, including indication, methods, and treatment outcomes.

BACKGROUND

• Anatomy

The celiac plexus consists of a right and left ganglion that lie anterolateral to the aorta at the level of the celiac trunk, the first main vessel to branch off of the aorta below the diaphragm. The crura of the diaphragm lies posterior to the plexus; the kidneys, adrenals, and inferior vena cava are found laterally, and the pancreas overlies the celiac plexus anteriorly.[1] The celiac plexus is predominantly innervated by sympathetic fibers that transmit both afferent and efferent signals from all upper abdominal viscera including the pancreas, liver, gallbladder, stomach, and the ascending and transverse colon.[2] The celiac plexus receives splanchnic nerves from T5 through T12, which connect at the celiac plexus and pass through the crus of the diaphragm onto the spinal cord.[3,4]

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Celiac Plexus Block (CPB)

CPB typically involves injection of a local anesthetic and a long-acting steroid into or around the celiac plexus. This process usually results in interruption of neuronal transmission from the celiac plexus, and therefore provides pain relief. The relief provided, however, is temporary, usually only lasting weeks to months, with 3 months being a typical duration of effect. Patients with chronic pain usually require repeated procedures if their pain responds to the initial injection.[5] If a patient does not respond to an initial block it can be repeated to see if a second block is beneficial before abandoning further blocks.[6]

Celiac Plexus Neurolysis (CPN)

CPN involves injection of a neurolytic agent, typically absolute or dehydrated alcohol, into or around the celiac plexus, causing destruction of the ganglia. Bupivacaine is typically injected prior to the alcohol in order to provide analgesia, as the alcohol injection can be painful otherwise. CPN causes permanent nerve damage in an attempt to provide long-lasting pain relief. CPN is commonly reserved for patients with advanced inoperable pancreatic cancer or other intraabdominal malignancies.

- **Indications**

Indications for CPB include management of pain associated with chronic pancreatitis. CPN, however, is usually utilized in the treatment of patients with advanced pancreatic cancer-associated pain.[7]

Methods

The principle underlying celiac plexus block (CPB), and celiac plexus neurolysis (CPN) is reducing or even eliminating transmission of pain signals from visceral afferent nerves of the celiac plexus. This is accomplished via injection of agents that reduces the intensity of, or disrupts, signal transmission. CPB and CPN have both been used in the management of pancreatic pain since the technique was first described by Kappis in 1914.[3] CPB and CPN can be performed either intraoperatively or via fluoroscopic, ultrasound, or computed tomography-guidance.[8] Endoscopic ultrasound-guided CPB/CPN was first reported in 1996 and is now widely performed.[9] There are currently multiple approaches in current practice regarding EUS-CPB/CPN. All are performed with a linear echoendoscope (the radial echoendoscope does not properly visualize the ganglia in many cases and cannot perform therapeutic maneuvers). (Figure 1) The classic approach, known as the central technique, involves injection of the therapeutic agents into the potential space just anterior to the origin of the celiac artery (CA) itself. In another approach, the bilateral technique, involves injection of the therapeutic agents bilaterally with regards to the original of the CA.[10] Intraneuronal and perineuronal variations exists as well, as do so-called "extended" blocks that inject agents along the length of the aorta down to, and sometimes

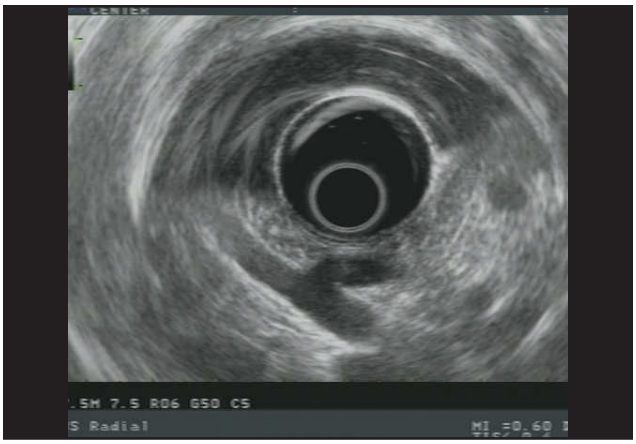

Figure 1. Celiac artery well seen by radial EUS with the vessel splitting into the common hepatic artery and the splenic artery. Celiac ganglia not well seen.

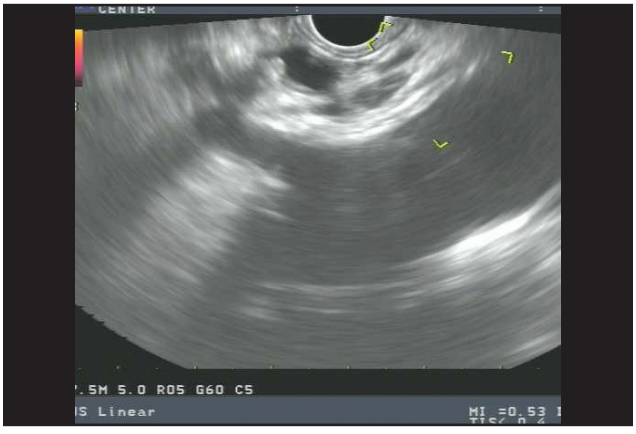

Figure 2a. Intraneuronal central EUS CPN/CPB technique. Note the celiac ganglia just anterior to the origin of the celiac artery.

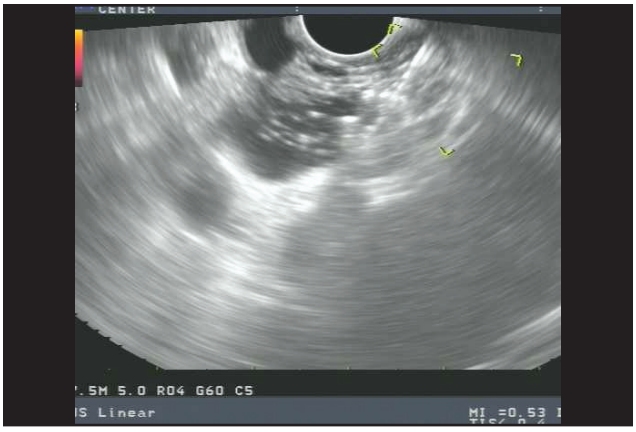

Figure 2b. Celiac needle inserted directly into the ganglia through the esophagus. Note that some of the injectate extravasates around the ganglia despite needle entry into the ganglia itself.

beyond, the origin of the superior mesenteric artery (SMA).[11] It should be noted that, in practice, some CPN or CPB procedures do not fit squarely into the techniques described below given local anatomy and vasculature.

Central Celiac Plexus Block/Neurolysis Technique

An EUS FNA needle or a dedicated celiac plexus needle is advanced, under direct ultrasound guidance and with Doppler ultrasound, towards the origin of the celiac artery. The injectate is then delivered as a bolus into the potential space just anterior and superior to the origin of the CA.[12] (Figures 2 and 3)

Bilateral Celiac Plexus Block/Neurolysis Technique

The bilateral approach involves advancing an EUS FNA needle, or a dedicated celiac plexus needle, into the regions on both sides of the celiac artery and performing injections in these locations in an attempt to reach more nerve branches of the celiac ganglia. The bilateral approach can also be used if the central technique is not feasible due to local anatomy or interposed vasculature.[13]

Celiac Ganglia Neurolysis

Another possible approach is direct injection of the agent into the celiac ganglia, known as Celiac ganglia neurolysis (CGN). EUS-CGN was first described by Levy et al.[27] in 2008. It involves identifying the celiac ganglia between the aorta and left adrenal gland on EUS, and injecting absolute alcohol directly into the ganglia until it becomes hyperechoic and no longer identifiable.[10] The initial trial in 2008 concluded that direct injection into the celiac ganglia was more effective and achieved higher rates of pain relief. Multiple studies following the initial trial also concluded that the direct ganglia injections were more effective in reducing pain when compared to the classic approaches.[27-29] Other studies, however, such as the 2008 trial by Adler et al. revealed no difference in efficacy in intraneuronal injections when compared to perineuronal injections. Whether there is a true difference in outcomes when comparing direct injections to the classic approach remains controversial.

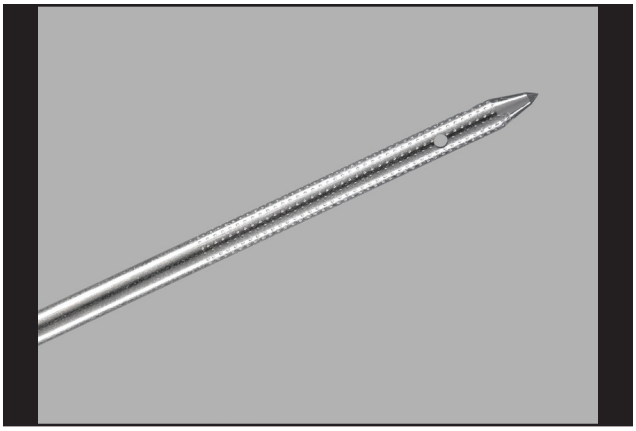

Figure 3a. Dedicated celiac plexus needle with multiple sideholes for performing CPB and CPN. the celiac plexus needle.
Figures 3a and 3b courtesy of Cook Endoscopy.

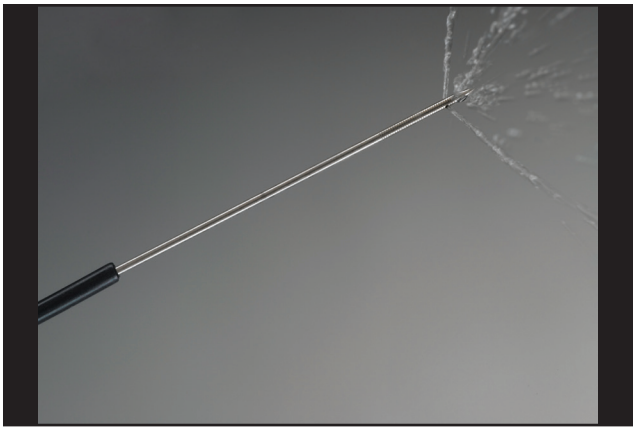

Figure 3b. Note wide fluid dispersion when using the celiac plexus needle.
Figures 3a and 3b courtesy of Cook Endoscopy.

Results

- **Efficacy**

CPN for Treatment of Pancreatic Cancer Pain

A meta-analysis conducted in 2010 by Kaufman et al.[14] showed that EUS-CPN is effective at controlling pain in patients with pancreatic cancer in 73% of cases. There were 2 studies, however, that reported no significant change in narcotic usage after the procedure.

Additionally, Catalano et al.[15] concluded that the location of the cancer plays a role in the responsiveness to treatment. It was observed that patients with pancreatic cancers in the body or tail were more likely to respond to CPN, as opposed to patients with cancers in head of the pancreas.[14]

Another prospective randomized study by Ischia et al.[16] observed that the efficacy of CPN and the degree of pain relief were significantly impacted by the stage of the underlying cancer.[17] It should be noted, however, that CPN rarely provides patients with absolute pain relief. The more common outcome is for patients to experience a reduction in their opiate consumption, rather than elimination of pain.[17]

CPB for Pancreatitis and Benign Diseases

A prospective randomized trial conducted by Leblanc et al. in 2009[18] found that CPB for chronic pancreatitis pain was effective in about 60% of cases. Effectiveness was measured as reduction of pain to less than 50% of the patient's baseline pain score, with the average effect lasting about 3 months.[7] Other studies such as a retrospective study by Sey et al.[19] reported efficacy rates as high as 78%, which the authors defined as subjective pain relief. A significant consideration is that the response observed following the initial procedure is predictive of the efficacy of repeated procedures to follow.[19] Therein, the Leblanc study there was no difference between the central and the bilateral approach when applied to patients with chronic pancreatitis.[18] Conversely, a study conducted by Sahai et al.[12] concluded that the short term response initially was superior when the bilateral technique is performed. This superiority was thought to be due to the fact that the bilateral approach allows more medication to be injected and, therefore, potentially have a more rapid onset of action. Long term response, however, was not measured. One adverse event reported was trauma to the adrenal artery, and resulted in a self-limited bleed. This consequently led to the preference for the central technique on the part of these authors for patients with a bleeding diathesis.[12]

• Adverse Events

EUS-CPB and EUS-CPN are considered to be safe procedures. A large case series conducted by O'Toole et al. showed that the overall complication rate for EUS-CPN was 3.2%, with no major complications.[20] EUS-CPB had a 1.6% overall complication rate, with a major complication rate of 0.5%. Major complications were defined as bleeding events, perforations, neurologic sequelae, or deaths. Minor complications that were generally reported included temporary increase in pain, oxygen desaturation, anesthetic induced hypotension, and most commonly, diarrhea. Of note, the study conducted by O'Toole[20] also revealed that rates of minor complications observed by the EUS approach were lower when compared to the percutaneous approach. The lower rate of complications, along with the ease of use may be why the EUS approach has been largely replacing the percutaneous approach.

For instance, paraplegia is a catastrophic complication that has been reported following the percutaneous approach to CPN, due to neurolytic agents tracking into the spinal cord. This adverse event was thought to be non-existent in the EUS approach. Nevertheless, a case report by Koker et al.[21] described a patient that suffered from spinal cord ischemia following EUS-CPN using the bilateral injection technique, resulting in permanent paraplegia. This procedure was performed on a patient with advanced poorly differentiated ductal adenocarcinoma, and the extensive local invasion made identification of the injection sites difficult. Conversely, a 2013 literature review by Alvarez-Sanchez et al.[22] reported 4 cases of retroperitoneal abscesses, and 3 cases of empyema that occurred after EUS-CPB. A brain abscess managed with IV antibiotics and antifungals in an immunocompromised host was the only infectious complication observed after EUS-CPN.[22]

Discussion

EUS approaches to CPB and CPN were first introduced in 1996 and were described as a safer alternative to the percutaneous approach. This is attributed to multiple factors, one of which is that the EUS method allows access to the celiac plexus from a direction that is anterior to the plexus itself, which minimizes the risk of trauma to spinal nerves and vasculature. In addition to the less invasive approach, the utilization of a doppler US for the procedure causes a significant reduction in injury rates to nearby vascular structures. In percutaneous CPN procedures, serious complications occurred in 1-2% of cases. The serious complications observed included paraplegia, paresthesia, aortic dissection, and pneumothorax.[2,6,9,23,24] Nevertheless, most studies concluded that major complications

occurring after EUS-CPB or CPN were extremely rare, and the complications observed were usually minor and self-limited such as diarrhea and transient hypotension.[8,17] Another factor to consider is that the EUS approach allows for a more cost effective management, as it provides the endoscopist the opportunity to perform the procedure at the time of biopsy, staging or during other procedures such as endoscopic retrograde cholangiopancreatography (ERCP).[6,17]

The efficacy of both procedures was reported to be similar in terms of outcomes and pain relief in most studies.[6,17,25] Some studies, such as the literature review by Sachdev, even reported higher efficacy rates in the EUS approach.[7] Nonetheless, given the fact that the EUS approach has a significantly higher safety profile, and the fact that it may be more cost effective, the EUS approach has gained increased popularity in clinical practice.

Although several studies have shown CGN to be more efficacious at achieving pain relief as opposed to CPN, a randomized controlled trial (RCT) conducted by Fujii-Lau et al.[26] observed that patients who underwent CGN had a shorter survival rate when compared to cases that underwent CPN. However, whether these findings were related to the technique of the procedure performed versus the natural progression and extent of the underlying disease remains controversial and will ultimately need more trials to reach a more accurate conclusion.

CONCLUSION

In conclusion, the EUS approaches to CPB and CPN are in widespread use. Most studies have concluded that it is a safe procedure with a relatively low risk of major complications when compared to the classic percutaneous approach. Most of the complications observed after EUS procedures were minor and self-limited. Several different EUS approaches have been introduced into clinical practice, and the various studies conducted have yielded similar results when it comes to efficacy and safety profile. Further trials performed on a larger scale are needed to adequately demonstrate the procedure's efficacy and to compare the efficacy between various approaches, and at this time no specific method of performing EUS CPB or CPN has been shown to be ideal. ■

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