

ORIGINAL ARTICLE

# Comparison of the Effects of Alcohol and Phenol Used for Celiac Neurolysis with Endoscopic Ultrasound in Patients with Pancreas Cancer: Retrospective Analysis

## Pankreas Kanseri Tanılı Hastalarda Endoskopik Ultrason Eşliğinde Çölyak Nöroliz Ağrı Tedavisi için Kullanılan Alkol ve Fenolün Etkilerinin Karşılaştırılması: Retrospektif Analiz

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### ABSTRACT

**Objective:** In this study we aimed to compare the efficacy of ethanol and phenol used in the EUS-guided celiac plexus neurolysis procedure on pain scores and complications.

**Material and Methods:** Between January 2009 and June 2022, 28 patients who underwent celiac neurolysis under sedation via EUS (endoscopic ultrasonography) guidance at the endoscopy unit were included. We retrospectively analyzed the data of the EUS-guided celiac neurolysis procedures for pain management of patients with pancreatic cancer.

**Results:** Patients in the alcohol group had lower pain scores.

**Conclusion:** When alcohol and phenol-based neurolytic techniques were compared, better analgesic effect was obtained in the alcohol group.

**Keywords:** alcohol, celiac neurolysis, endoscopic ultrasound, phenol

### ÖZ

**Amaç:** Çalışmada amacımız EUS rehberliğinde uygulanan çölyak pleksus nöroliz işleminde kullanılan etanol ve fenolün ağrı skorları ve komplikasyonlar üzerine etkinliklerini karşılaştırmaktır.

**Gereç Yöntem:** Ocak 2009 ve Haziran 2022 tarihleri arasında endoskopi biriminde sedasyon altında EUS (endoskopik ultrasonografi) rehberliğinde çölyak nöroliz uygulanan 28 hasta dahil edildi. Pankreas kanseri tanılı hastaların ağrı tedavisi için uygulanan EUS rehberliğinde çölyak nöroliz girişiminin verilerini retrospektif olarak inceledik

**Bulgular:** Alkol grubundaki hastaların ağrı skorları daha düşük saptanmıştır.

**Sonuç:** Alkol ve fenol bazlı nörolitik teknikler karşılaştırıldığında alkol grubunda daha iyi analjezik etki elde edilmiştir

**Anahtar Kelimeler:** alkol, çölyak nöroliz, endoskopik ultrason, fenol

## Introduction

Pancreatic cancer is usually associated with severe and treatment-resistant pain. Pain may not be adequately controlled with non-narcotic medical treatment agents; in addition, there are various restrictions on the use of opioids due to side effects such as constipation, changes in mental status and respiratory depression (1). The main advantage of the using interventional pain management techniques as celiac plexus neurolysis (CPN) is that both pain control and quality of life can be improved, whereby the incidence of opioid-related side effects can be reduced (2).

CPN is the procedure of destruction of the splanchnic nerve fibers followed by the development of fibrosis by the percutaneous or intraoperative injection of alcohol or a sclerosing agent. It has been shown to be more effective than placebo with its analgesic effectiveness lasting between 6 weeks and 6 months (3).

Performing endoscopic ultrasound-guided (EUS) CPN has become safer than traditional laparotomy, percutaneous ultrasound (US)-guided, and computed tomography (CT)-guided CPN. When EUS is performed instead of traditional techniques, the puncture distance is extremely short, and the high image quality allows for the recognition of small vascular structures and the prevention of probable accidental punctures, which increases patient safety. EUS-CPN application does not expose the patient and interventionalist to radiation and does not require endotracheal intubation and general anesthesia (4).

Two commonly used neurolytic agents for permanent destruction of the celiac plexus are ethanol and phenol. Ethanol causes the precipitation of endoneural lipoproteins and mucoproteins in the celiac plexus, resulting in the extraction of cholesterol and phospholipids from the neural membrane. Phenol causes

neurolysis with protein coagulation and necrosis of neural structures similar to that obtained with ethanol. Although there is limited data comparing ethanol and phenol, it is generally thought that ethanol causes more neurodegeneration (3,5).

When we review the literature, it is noticeable that there have been few clinical studies comparing phenol and alcohol for the EUS-CPN procedure, and patient data is limited. In this retrospective study, our aim is to compare the effectiveness of ethanol and phenol used in the celiac plexus neurolysis procedure under EUS guidance on pain scores and complications.

## Materials and Methods

Approval for our retrospective study was obtained from the local Ethics Committee (Date:25/08/2022 Number:0372 ) of İzmir Atatürk Training and Research Hospital. Thirty patients who underwent celiac neurolysis under sedation under EUS (endoscopic ultrasonography) guidance in the endoscopy unit between January 2009 and June 2022 were included. In our study, we retrospectively analyzed the data of celiac neurolysis intervention under EUS guidance applied for the pain management of patients with pancreatic cancer. Data were obtained from hospital data and patient follow-up documents.

**Patient selection:** Numeretic rating scale (NRS) >4 patients who were diagnosed with pancreatic cancer over the age of 18 and applied to the algology outpatient clinic and did not benefit from opioid treatment were included in the analysis. The data of 2 patients whose pain score was not followed up or documented were defined as incomplete data and the data of these patients were excluded from the analysis.

**Pain assessment:** standard 11-point NRS (numerical rating scale) The patient was asked to score as "0" no pain and "10" the most severe pain, and it was evaluated and recorded by the anesthesiologist during the follow-up days and after the procedure.

**Grouping and data collection:** The patients included in the analysis were divided into two groups according to the agent use during the procedure. It consisted of patients who were administered 10 ml of alcohol in group 1, and patients who were administered 10 ml of 7% phenol in group 2. Although the drug preference was the personal preference of the endoscopy practitioner, no intervention was made.

NRS scores of the patients in the groups were obtained from the examination of the patient records, which were kept as a result of face-to-face interviews or telephone interviews, after coming to the Algology outpatient clinic on the 1st, 15th and 30th days after the procedure. In routine clinical practice, additional pain treatment is started when NRS>4, and pain is considered to be absent if NRS<4. NRS values and additional analgesic requirements of the patients

were also obtained from the patient follow-up charts.

**Anesthesia and endoscopic intervention process:** During the endoscopy procedure, an anesthesiologist administered intravenous propofol for sedation according to the anesthetic care principles monitored by the anesthesiologist. The patients were placed in the left lateral decubitus position during the procedure. During the procedure, all patients were given oxygen and their blood pressure and heart rate were monitored. EUS-CPN procedure was performed with a linear echoendoscope probe (Pentax EPK-100, Hitachi Inc., Hamburg, Germany). Sagittal images of the aorta were followed up to the celiac trunk and superior mesenteric artery of the aorta by turning the echoendoscope probe counterclockwise after obtaining appropriate images at the junction of the stomach fundus and the lesser curvature body.

Under the guidance of real-time EUS, a 20 gauge 4 cm neurolysis needle prepared with normal saline solution was placed just anterior to the aorta at the level of the celiac trunk. After injecting 2 mL of saline solution to clean the needle, the aspiration test was performed. When no blood was observed, it was planned to inject 10 mL of alcohol or phenol solution according to the practitioner's preference. The aspiration test was repeated and when blood flow was not observed, 10 mL of neurolytic solution was injected. The needle was then washed with 3 mL of saline solution and withdrawn from the patient.

## Statistical analysis:

Statistical analyzes were performed using IBM SPSS Statistics for Windows (Version 22.0; IBM Corp., Armonk, NY, USA). Descriptive statistics are expressed using mean and standard deviation or median-[IQR] for continuous variables, and numbers and percentages for categorical variables. Before all analyses, whether the data conformed to the normal distribution was evaluated using skewness-kurtosis values, Shapiro-Wilk test and histogram graphics. In determining the differences in mean values between groups, independent variables T test or dependent variables T test was used for variables with normal distribution; The Mann-Whitney U test was used for the variables that did not fit the normal distribution. Chi-square test or Fischer's exact test was used to determine the differences of categorical variables between groups. In all analyses, p<.05 was considered statistically significant.

## Results

Demographic data of the patients are shown in Table 1. NRS scores before and after the procedure are shown in Table 2, and the pain scores of the patients in the alcohol group were significant at each follow-up. It was observed that the procedure was successfully performed in all 28 patients who underwent endoscopic ultrasonography-guided celiac ganglion blockade, and major complications such as mortality,

paraplegia, pneumothorax, peritonitis, loss of anal and bladder sphincter were not observed. Minor complications such as hypotension, diarrhea, back and epigastric pain were observed in 2 patients. These minor complications were observed in the second group (phenol) (Table 3).

**Table 1:** Demographic data

	Alcohol n:14	Phenol n:14	p
Gender (Female/Male)	3/11	7/7	0.236
Age (years)	68(64-80)	65(62-76)	0.734
Operation	1	3	0.298
Chemotherapy	8	5	0.449
Radiotherapy	4	1	0.163

Chi square test n,% Median [IQR] Mann Whitney -U test. p<0.05

**Table 2:** NRS scores

	Alcohol n:14	Phenol n:14	p
Before the procedure	9(8-9)	9(8-9)	0.462
1st day	6(6-8)	9(7-10)	<b>0.002</b>
15th day	4(3-6)	7(4-8)	<b>0.024</b>
30th day	3(2-4)	6(3-8)	<b>0.016</b>

Median [IQR] Mann Whitney -U test p<0.05

**Table 3:** Side effects

	Alcohol n:14	Phenol n:14	p
Diarrhea	0	2	0.481
Temporary back/ epigastric pain	0	0	
Hypotension	0	0	

Chi square test n,%

## Discussion

When alcohol and phenol use compared in the study in terms of reducing pain scores, it was determined that, more effective analgesia was provided and less side effects were observed in the group that used alcohol.

CPN has been developed as an alternative method to reduce visceral abdominal pain and narcotic drug use by disrupting the transmission of pain signals from the afferent nerves to the spinal cord. CPN, which was first reported by Kappis in 1914, was defined by open surgery, and then fluoroscopic or computed tomography (CT) guided methods were developed (6,7).

It is generally thought that alcohol causes more neural destruction than phenol and that phenol has a shorter duration of action than ethanol. Many studies have suggested adding a local anesthetic agent to ethanol

to prevent burning pain after CPN using ethanol; It is accepted that there is no procedural pain due to the local anesthetic effect of phenol (8).

In our study, injections were performed with the central single puncture technique. The results of the randomized prospective study showed that the procedure performed with bilateral injection was more effective than the procedure with single puncture (9). In addition, a retrospective study showed a decrease in similar pain scores in procedures performed with single puncture and bilateral puncture. It is still a matter of debate whether the bilateral approach is superior to the single (central) puncture approach in terms of pain relief (10). Theoretically, EUS-CPN permanently relieves the pain of cancer patients, but in clinical observations the analgesic effect is only 8 to 12 weeks. The mechanisms that limit the duration of analgesia have not been fully elucidated. However, a longer-lasting effect has been reported to be strongly associated with the appropriate distribution of the neurolytic agent in the celiac plexus (11–13).

Although pain scores decreased in both groups, pain scores were significantly lower in the alcohol group. Among the 4 studies that evaluated pain scores during the 4-week observation period similar to our study, one study showed that the CPN group showed positive results with statistical significance, while these positive results could not be shown in the other 3 studies. A general difference in favor of CPN was noted in the VAS score in pooled data analysis using a fixed-effect model (8,14–16).

Opioids, percutaneous interventional methods directed to the celiac plexus, and neurodestructive methods under the guidance of EUS continue to be applied and developed in the treatment of pain associated with pancreatic cancer. According to the results of a randomized controlled study comparing patients who underwent EUS-CPN for pancreatic cancer patients and those using oxycodone and/or fentanyl, no significant difference was observed in pain scores at 4, 8, and 12 weeks compared to baseline values. In addition, no difference was observed between the two groups in quality of life scores and opioid consumption values. Although EUS-CPN may be an option for patients with unbearable or uncontrollable pain, there are currently insufficient scientific data to make it a routine procedure for all patients with cancer-related pain (2).

The results of the clinical study comparing EUS-CPN with the celiac plexus radiofrequency ablation (RFA) method under the guidance of EUS, which has been implemented recently, suggest that EUS RFA may be superior to EUS-CPN in terms of palliation of pain and improvement in the quality of life in patients with pancreatic cancer. However, the radiofrequency technique needs to be standardized (17).

According to the results of the EUS-CPN study using a high-viscosity phenol-glycerol solution, the authors

argue that it provides an excellent analgesic effect by providing the appropriate distribution of the neurolytic agent. In addition, the authors stated that further studies are needed and some changes are necessary, but they stated that this approach has the potential to be an effective treatment for pancreatic cancer-related pain (18).

Common complications reported regarding EUS-CPN are transient diarrhea (23.4%), transient pain increase (36%), transient hypotension (33%) (19). In this study, which included 28 patients, only 2 patients had minor complications and no major complications were observed. A recent review of 20 reports involving 142 patients showed that complications occurred in 7% of 481 EUS-CP block procedures and 21% of 661 EUS-CPN procedures. The most common complications were related to blockade of sympathetic efferent activity (7% of patients had transient diarrhea, this resolved spontaneously, and hypotension was observed in 4% of patients). Transient increase in pain occurred in 2% of EUS-CPB cases and 4% of EUS-CPN cases. It is still controversial whether direct injection into the ganglia causes more pain or whether the sudden pain during the procedure is associated with longer-term pain relief (20). In addition, serious side effects such as retroperitoneal bleeding, abscess, and paraplegia have been reported (19,21).

A case of paraplegia was also reported by Minaga et al. The resulting vascular injuries and ischemic complications have been interpreted as possible as a result of injecting alcohol into an inappropriate anatomical site or administering excessive numbers of EUS-CPN (22).

In a review of complications, the possible mechanism of spinal cord injury includes vasospasm due to diffusion of alcohol into the radicular arteries. This complication occurred after bilateral EUS-CPN and no cases of paraplegia have been reported with the single puncture (central) EUS-CPN technique (20).

### Limitations

The limitations of our study include the retrospective nature of our study design, the relatively small number of patients, the documentation of only pain scores, but the lack of use of scales to measure quality of life and patient satisfaction, and short patient follow-up period.

### Conclusion

When alcohol and phenol-based neurolytic techniques were compared, better analgesic effects were obtained in the alcohol group. The fact that we observed only transient minor complications during the study proves that celiac ganglion blockade with EUS-guided approach is also a reliable method. Celiac ganglion neurolysis procedure is an effective, suitable, low complication rate, and successful method for

short-medium-term pain control, which is used to reduce pain associated with pancreatic cancer that does not respond to narcotic analgesics.

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