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Endoscopic Ultrasound Guided Celiac Plexus Neurolysis (EUS-CPN) in Patients with Cancer Pancreas

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Abstract

Introduction: With rising burden of pancreatic cancer that is usually discovered late in Egyptian population, the need to control cancer-related pain is deemed to be a crucial issue. It is well known that pancreatic cancer pain is commonly encountered with intolerable pain that is difficult to control. The presence of pain on initial diagnosis not only impacts the quality of life, but also predicts the prognosis of the disease. With the advent of selective celiac plexus neurolysis, the transmission of pain sensation to the pancreas is selectively inhibited and the potential systematic side effects of narcotics are reduced.

Material and Methods: This study has been conducted in Assiut University Hospitals from June 2015 to June 2016 and was carried out on 20 patients suffering from severe abdominal pain (according to NRS) due to cancer pancreas, who were subjected to endoscopic ultrasound guided celiac plexus neurolysis.

Results: Endoscopic ultrasound guided CPN was effective in alleviation of pain by 73.9%, improving patients sleep rhythm by 68.9% and as regard psychological aspect; also EUS-guided CPN was effective in improving patients psychological aspect by 61.4% in comparison to pre-procedure scores. In the current study we approved the safety of EUS-guided CPN without any reported complications in all cases that have been concluded in the study.

Conclusion: Celiac plexus neurolysis is a technique that can potentially improve pain in pancreatic cancer. EUS-guided CPN is a safe and effective technique in pain alleviation and improving patients' quality of life.

Key Words: *Endoscopic ultrasound – Cancer pancreas – Celiac plexus neurolysis.*

Introduction

WITH the rising burden of pancreatic cancer that is usually discovered late in Egyptian population, the need to control cancer-related pain is deemed to be a crucial issue. It is well known that pancreatic cancer pain is commonly encountered with intolerable pain that is difficult to control [1]. Up to 80% of patients with pancreatic cancer report abdominal pain [2] and 44-70% suffer from severe pain [3]. Difficult-to-control pain is reported in more than 90% of patients with advanced disease. The presence of pain on initial diagnosis not only impacts the quality of life, but also predicts the prognosis of the disease [4]. As a result, systemic analgesic therapy usually including opioid medication is central to the management of unresectable pancreatic cancer. However, pain can often become intractable and refractory to narcotics leading to dose escalation and opioid associated side effects [5]. The usual and initial therapy with non-steroidal anti-inflammatory drugs is often inadequate as pancreatic cancer pain is not only visceral but has also a neuropathic component which is very difficult to treat with these standard analgesic medications [6]. With the advent of selective celiac plexus neurolysis, the transmission of pain sensation to the pancreas is selectively inhibited and the potential systematic side effects of narcotics are reduced [7]. Celiac plexus neurolysis is a technique that can potentially improve pain control in pancreatic cancer while preventing further escalation of opioid consumption [5].

Celiac plexus intervention for pancreatic pain was first described by Kappis in 1914 [8]. The initial approach utilized for injection was posterior and percutaneous, which can nowadays also be performed under fluoroscopic or Computed Tom-

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Abbreviations:

EUS: Endoscopic Ultrasound.
NRS: Numerical Rating Scale.
CPN: Celiac Plexus Neurolysis.

ography (CT) guidance. A modified anterior approach can be performed under guidance of transabdominal ultrasound, CT, intra-operatively or most recently under linear endoscopic ultrasound guidance. EUS is well-suited for identification of the celiac plexus due to the close approximation of the gastric wall with the origin of the celiac artery. It is generally effective, safe and well-tolerated procedure and avoids serious complications [9].

Aim of work: To evaluate the safety and efficacy of endoscopic ultrasound guided celiac plexus neurolysis in patients with intolerable severe pancreatic cancer pain as regard degree of pain alleviation, effect on quality of life as regard sleep rhythm and psychological aspect of patient.

Patients and Methods

A prospective hospital based study has been conducted in Assiut University Liver Hospital, Endoscopy Unit from June 2015 to June 2016. The study was carried on 20 patients with cancer pancreas suffering from abdominal pain (with pain score more than 4, by numerical rating scale) due to cancer pancreas, who were subjected to endoscopic ultrasound guided celiac plexus neurolysis.

Exclusion criteria:

- Patients who refused to give an informed legal consent for the protocol of the study.
- Severe co-existed cardiopulmonary and/or renal disease.
- Abnormal coagulation profile (international normalized ratio ≥ 1.5).
- Low platelet count < 50000/ tL.
- Presence of co-existed gastric and/or esophageal varices.
- History of previous CPN.
- Presence of more than moderate ascites.
- Patients with disturbed conscious level.
- Diabetic patients.

Each patient was subjected to:

- Full history and clinical examination.
- Laboratory and imaging investigations:
  - Blood picture.
  - Liver function tests; bilirubin, AST, ALT, alkaline phosphatase, prothrombin time, prothrombin concentration and INR.
  - Renal function test; serum urea and creatinine.
  - Serum amylase.
  - CEA and CA 19-9.
  - MSCT or MRI abdomen.
- Pain, sleep and psychological scores assessment before the procedure.

Technique of endoscopic ultrasound guided CPN:

By using Pentax linear echoendoscope (EG-3870 UTK, Pentax, Japan) and ultrasound (Hitachi prius, Tokyo), a EUS-guided FNA needle (Echotip ultra-3, 22-gauge, cook medical, USA) has been used. The EUS under endoscopic view was passed into the proximal stomach, just distal to the gastro-esophageal junction and along the posterior wall of the stomach, the aorta and the celiac axis (first vessel arising from the aorta below the diaphragm) were identified. Then a 5ml of sterile saline-filled syringe has been loaded into the needle and check aspiration was done to test the position of the needle tip. Through the needle a 20ml of 0.5% bupivacaine (Hospira, USA) has been injected followed by 10ml of 98% alcohol. Bilateral injections were done by clockwise and counter clockwise.

Patients follow-up:

Assessment of EUS-guided CPN impact on quality of patient life by calculating pain, sleep and psychological scores at baseline, after first, second, third and fourth weeks by:

- Sleep score (0-5): Normal rhythm (5), interrupted (4), insufficient (3), disturbed (2), hard by hypnotic (1), or no sleep (0) (10).
- Psychological score (0-5): Balanced (5), worried (4), anxious (3), hypochondriac (2), depressed (1), or nervous breakdown (0) (10).
- Pain score, NRS (0-10): Where 0=no pain and 10 is worst pain ever (11).

This study was approved by the Faculty's Ethics Committee and permission was obtained from the ethics committee to assure confidentiality.

Statistical analyses:

The collected data was entered, and edited using SPSS Version 20 statistical software (IBM Corporation and its licensor 1989, 2011). Descriptive statistics of the collected data was done for most variables in the study using statistical measurements. Frequency tables, graphs, percentages, means and standard deviations were used.

Results

The current study included 20 patients. Their mean ± SD age was 59.65 ±6.7 years (median = 59.5). Male sex was predominant (55%). There were 13 males and 7 females.

All patients were presented by pancreatic cancer pain with pain score mean ± SD was (9.20±0.7). EUS-guided CPN was applied for all patients.

There were significant pain reduction, improvement of sleep rhythm and psychological aspect of patients who were subjected to EUS-guided CPN compared to pretreatment scores.

As regard pain score assessment, the overall percentage of pain reduction after EUS-guided CPN in patients with cancer pancreas was (73.9%) as shown in (Table 3).

Pain score before procedure = (pain 0), at first week after procedure = (pain 1), at second week = (pain 2), at third week = (pain 3) and at fourth week = (pain 4).

As regard sleep score assessment, the overall percentage of improvement in sleep scores after EUS-guided CPN was (68.9%) as shown in (Table 4). Sleep score before procedure = (sleep 0), at first week after procedure = (sleep 1), at second week = (sleep 2), at third week = (sleep 3) and at fourth week = (sleep 4).

And as regard psychological score assessment, the overall percentage of improvement in Psychological Score in EUS-guided CPN group was (61.4%) as shown in (Table 5).

Psychological score before procedure = (psychological 0), at first week after procedure = (psychological 1), at second week = (psychological 2), at third week = (psychological 3) and at fourth week = (psychological 4).

Table (1): Socio-demographic data (age and sex) of EUS-guided CPN group in current study.

	EUS CPN (N=20)
Age:	
Mean ± SD	59.65±6.7
Median (range)	59.5 (49-75)
Sex:	
Male	13 (59.1 %)
Female	7 (38.9%)

SD: Standard Deviation.
N : Number.

Table (2): Laboratory data of EUS-guided CPN group in current study.

Variable (mean ± SD)	EUS CPN (No=20)
CBC:	
Haemoglobin (mg/dl)	11.05±1.5
RBCs (10^9/L)	4.33±0.5
WBCs (10^9/L)	6.88±1.9
Platelets (10^9/L)	284.30±68.1
Reticulocytes (%)	0.81±0.5
MCV	87.10±2.8
MCH	27.90±1.1
Renal functions:	
S. creatinine (mg/dl)	81.64±28.5
Blood urea (mg/dl)	6.60±2.4
Bleeding parameter:	
PT (per second)	11.68±0.9
PC (%)	92.80±7.1
INR	1.06±0.1

Table (3): Patients' pain score assessment pre and post EUS-guided CPN.

	EUS CPN (N=20)
Pain score-0:	
Mean ± SD	9.20±0.7
Median (range)	9 (8-10)
Pain score-1:	
Mean ± SD	2.55±1.6
Median (range)	2.5 (0-5)
Pain score-2:	
Mean ± SD	2.15±1.5
Median (range)	2 (0-5)
Pain score-3:	
Mean ± SD	2.20±1.4
Median (range)	2 (0-5)
Pain score-4:	
Mean ± SD	2.40±1.8
Median (range)	2 (0-6)
Overall % of pain reduction	73.9%

Table (4): Patients' sleep score assessment pre and post EUS-guided CPN.

	EUS CPN (N=20)
Sleep score-0:	
Mean ± SD	1.35±0.5
Median (range)	1 (1-2)
Sleep score-1:	
Mean ± SD	4.15±0.9
Median (range)	4 (2-5)
Sleep score-2:	
Mean ± SD	4.60±0.7
Median (range)	5 (3-5)
Sleep score-3:	
Mean ± SD	4.65±0.7
Median (range)	5 (2-5)
Sleep score-4:	
Mean ± SD	4.35±0.9
Median (range)	5 (2-5)
Overall % change in sleep scores	68.9%

Table (5): Patients' psychological score assessment pre and post EUS-guided CPN.

	EUS CPN (N=20)
Psychological score-0:	
Mean ± SD	1.60±0.9
Median (range)	2 (0-3)
Psychological score-1:	
Mean ± SD	4.15±0.9
Median (range)	4 (2-5)
Psychological score-2:	
Mean ± SD	4.55±0.8
Median (range)	
Psychological score-3:	
Mean ± SD	
Median (range)	5 (3-5)
Psychological score-4:	
Mean ± SD	4.15±0.9
Median (range)	4.5 (2-5)
Overall % change in psychological score	61.4%

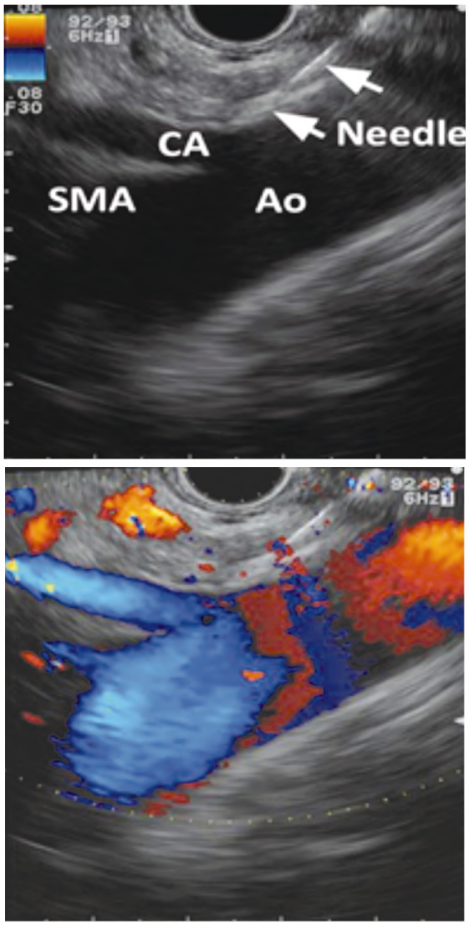

Fig. (1): EUS view of celiac plexus and needle position.

Discussion

Up to 80% of patients with pancreatic cancer report abdominal pain and 44-70% suffer from severe pain [2,3]. Difficult-to-control pain is reported in more than 90% of patients with advanced disease. The presence of pain on initial diagnosis not only impacts the quality of life, but also predicts the prognosis of the disease [4].

There is increasing evidence in oncology that pain management contributes to a broad quality of life improvement [12].

As a result, analgesic therapy usually including opioid medication is central to the management of unresectable pancreatic cancer. However, pain can often become intractable and refractory to narcotics leading to dose escalation and opioid associated side effects but selective celiac plexus neurolysis can selectively inhibit the transmission of pain sensation to the pancreas and the potential systematic side effects of narcotics are reduced.

All patients were diagnosed as cancer pancreas and presented by severe abdominal pain with pain score mean (9.20±0.7) according to numerical rating scale and they underwent EUS-guided CPN. There were significant pain reduction, improvement of sleep rhythm and psychological aspect of patients who were subjected to EUS-guided CPN compared to pretreatment scores.

As regard pain alleviation, the overall percentage was 73.9% after EUS-guided CPN and this result was in agreement with those reported by Wiechowska-Kozlowska et al., 2012 [9] when they studied the efficacy and safety of endoscopic ultrasound-guided celiac plexus neurolysis for treatment of pain in twenty nine patients with pancreatic cancer with severe pain and they found that 86% of these patients showed decrease in pain score using numerical rating scale by at 1-2 weeks following the procedure and also was concordant with that reported by Wyse et al., 2011 [13] in their randomized, double-blind, controlled trial of early endoscopic ultrasound guided celiac plexus neurolysis to prevent pain progression in patients with newly diagnosed, painful and inoperable pancreatic cancer which was done on 96 patients, half of them were subjected to EUS-CPN and they concluded that pain relief was greater in the EUS-CPN group at 1 month and significantly greater at 3 month by about 80%.

In the current study, pain score has been decreased from the first week after procedure with more decrease and improvement of pain alleviation at the second and third weeks. The same also has been noticed as regard the increase in sleep and psychological scores with improvement of patients' quality of life when compared to the pretreatment scores.

The inability to completely control the pain in all patients as well as reduction in pain relief over time as noticed at the fourth week was also observed by Wyse et al., 2011 and Hao et al., 2014 **[13,14]**. The reason why alcohol injection into the plexus did not completely eliminate pain may be explained by pathologic studies of the plexus following treatment.

The EUS-guided CPN was effective in improving patients' quality of life and survival as improvement of sleep rhythm was 68.9% and regarding improvement of psychological aspect, it was 61.4%.

Our data as regard improvement of sleep rhythm and psychological aspects of patients were 68.9% and 61.4% respectively after EUS-guided CPN and to our knowledge there are no previous studies that record the effect of EUS-CPN on quality of life, although it has been suggested to improve survival of patients as described by Larissa et al., 2015 **[15]**.

In the current study we used the bilateral injection technique in EUS-guided CPN. The effectiveness of bilateral EUS-CPN was evaluated by Iwata et al., 2011 **[16]** who concluded that ethanol should be injected on both sides of the celiac axis to obtain greater pain relief.

There were no reported any complications in the current study and this may be due to:

- Safety of EUS-guided CPN technique due to availability of real-time visualization so this avoids trauma or injury of blood vessels or false injection in spinal cord also the availability of Doppler US.
- The technique of EUS-guided CPN was done by expert personnel.

Although the efficacy of EUS-CPN has been established, there are still many controversies surrounding its use and because pain relief by EUS-CPN is not guaranteed, it is necessary to predict a favorable or unfavorable outcome of this treatment in order to enable rational selection of the therapeutic strategy. For example, it should be recommended earlier and with assurance in patients expected to have favorable outcomes. In contrast, it should be recommended on a limited basis for patients suspected of having unfavorable outcomes. predictive factors must be divided in to two categories; factors related to patient characteristics as site of cancer and its staging, duration of pain and pain degree, and those related to the procedure as the technique itself, site of injection, visualization of the ganglia and/or plexus and assessment of diffusion degree.

And finally, we should admit that this current study had many limitations. The first potential limitation was the small sample we selected for the study. The second limitation was the lack of data collected about the patients as regard type and doses of analgesics used prior to the procedures and hence we could not determine the degree of efficacy of both procedures on decreasing dose of analgesics previously used. The third limitation was the short duration of follow-up, so we recommend for a larger study with a larger sample of patients and longer duration of follow-up with more sufficient collected data.

Conclusion and Recommendation:

Based on the results of this study we concluded that CPN is a technique that can potentially improve pain in pancreatic cancer. EUS-guided CPN is a safe and effective technique in pain alleviation and improving patients' quality of life. A larger study sample with longer duration of follow-up is recommended.

Conflicts of interest:

No conflict of interest has been declared.

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تدمير الضفيرة العصبية البطنية بواسطة منظار الموجات فوق الصوتية فى مرضى سرطان البنكرياس

مع إزدياد عبء سرطان البنكرياس فإن الحاجة إلى السيطرة على آلام السرطان باتت آمرا هاما. وآنه من المعروف آن سرطان البنكرياس فى مراحلة المتآخرة يصاحبه آلام لا تحتمل ولا يسهل تخفيفها وإن إستخدام الآدوية المضادة للإلتهابات غير السيترويدية كعلاج إبتدائى لم يعد بالقدر الكافى للتحكم فى آلام سرطان البنكرياس وبالتالى يلجآ المريض إلى الآدوية المخدرة والتى تقضى على الآلم تدريجيا ولكن على النقيض تعرضه إلى آعراض جانبية كثيرة ولكن بإمكانية تدمير الضفيرة العصبية البطنية فإن الإحساس بالآم البنكرياس آصبح آقل بالإضافة إلى تجنب المزيد من الآعراض الجانبية للآدوية المخدرة.

الهدف من العمل: تقييم كفاءة تدمير الضفيرة العصبية البطنية عن طريق منظار الموجات فوق الصوتية فى المرضى الذين يعانون من آلام سرطان الينكرياس الغير محتملة من حيث درجة تخفيف الآلم وآيضا من حيث التآثير على معدل النوم وتحسن سيكولوجية المرضى.

المرضى والآساليب: آجريت هذة الدراسة على ٢٠ مريضا بسرطان البنكرياس، خضعوا جميعهم لتدمير الضفيرة العصبية البطنية من خلال منظار الموجات فوق الصوتية وسوف يتم تقييم التآثير الناتج عن هذا الإجراء الطبى على حياة المرضى آسبوعيا ولمدة آربعة آسابيع من حيث الحالة النفسية للمريض وتآثيره على نومه ونتائجه فى السيطرة على الآلم.

نتيجة البحث: آثبتت هذه الدراسة مدى فعالية تدمير الضفيرة العصبية البطنية بواسطة منظار الموجات فوق الصوتية حيث تخفيف الآلم الناتج عن سرطان البنكرياس والتحسن المصاحب فى معدل النوم وتآثيره على الحالة النفسية للمريض. حيث آنه وجد آن نسبة تحسن درجة الآلم وصلت إلى ٧٣.٩٪ فى الحالات التى تعرضت لتدمير الضفيرة العصبية البطنية بواسطة منظار الموجات فوق الصوتية ووجد آن نسبة التحسن فى معدل النوم وصلت إلى ٦٨.٩٪. ومن حيث تحسن نفسية المرضى، فلقد آثبتت الدراسة فعالية منظار الموجات فوق الصوتية حيث وصلت نسبة التحسن ٦١.٤٪.

التوصيات: آثبتت هذه الدراسة آن تدمير الضفيرة العصبية البطنية بواسطة منظار الموجات فوق الصوتية يعتبر وسيلة آمنة وفعالة فى تخفيف الآلم الناتج عن سرطان البنكرياس وتحسين الحالة النفسية للمرضى.