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Role of interventional radiology in upper abdominal cancer pain management

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Abstract

Background The major indication for celiac plexus block is abdominal pain that is nonresponsive to analgesic interventions; often these patients are nonresponsive to high-dose opioid therapies. One of the most common indications for the celiac plexus block is the treatment of abdominal pain associated with pancreatic cancer.

Aim of the work The differences between two techniques (ultrasound and fluoroscopy guided) are highlighted in terms of effectiveness by means of a Visual Analog Scale (VAS), a percentage reduction in daily morphine consumption and any complications are recorded and evaluated at the time of implementation of each technique from start to finish.

Results Through the data that have been recorded and statistically analyzed, we found that the mean values of VAS were decreased in the two groups, and there was statistically significant difference between ultrasound and fluoroscopy groups.

Conclusions It is noticeable and good in conducting this research that there are no major complications that include a large space on the study sample, despite the presence of some minor with no significant differences between ultrasound and fluoroscopy groups. This effective celiac block, regardless of the technique used, produced immediate analgesics that permitted significant opioid decrease in the study sample with a significant improvement in the unwanted adverse effects on account of opioids.

Keywords Pancreatic cancer, Cancer pain, Celiac plexus block, Ultrasound guided block

Background

Despite the tremendous developments in science, especially in reducing the severity of pain, there is still presence of pain, especially in the patients with cancer, as those percentages may range between 14 and 100%. A population study, vanden Beuken-van Everdingen et al. [1], indicated that the idea of controlling severe pain in the disease is no longer sufficient and must be developed, as its percentage did not exceed 42% of the number of patients, especially among the patients with cancer who receive cancer treatments Geffen et al. [2]. On the contrary, many other symptoms may appear in the patients who receive the chemotherapy or radiation after approximately 40 days of receiving treatments, thus the emergence of more pain and resulting in the emergence of more other symptoms [2].

The influence of the sympathetic nervous system as a factor in a diversity of painful states in humans was a part of traditional medical wisdom for more than 100 years. The sympathetic nervous system (SNS) is the part of the autonomic nervous system that controls the body's involuntary activities. It has been involved in the neuropathic pain (NeP), the vascular, and visceral pain. The sympathetic ganglia were the target of local anesthetic block to evaluate the role of the sympathetic nervous system in pain transmission. In spite of the repeated use of minimally invasive sympathetic blocks by pain practitioners, their effectiveness in providing analgesia has been scantly

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reported. Numerous case series and reports have been published, but there are few blinded, placebo-controlled studies. The sympathetic degeneration can be performed with local anesthesia, nerve analyzers, and neurectomy techniques such as radiofrequency lesioning procedure [3].

To block the sympathetic nerve, we inject local anesthetic into the sympathetic chain at different sites. The primary sympathetic ganglia involved in pain include the stellate ganglion, celiac plexus, lumbar sympathetic ganglion, superior hypogastric plexus, and ganglion impar.

The visceral cancer pain may be eliminated from the upper abdominal viscera (pancreas, liver, gallbladder, stomach) by a neurolytic celiac plexus block (NCPB). The celiac sympathetic ganglia are located on both sides of the celiac artery anterior to the aorta and anterior to the crura of the diaphragms [1].

The malignant tumors that are arising from the pancreas, stomach and liver may cause abdominal pain that does not respond to large doses of narcotic analgesics and significantly affect the patient's quality of life. The celiac plexus block (NCPB) was used as an adjuvant therapy in those kinds of cases [5].

The fluoroscopic localization of instruments depends on the indirect information that are obtained from the displacement of contrast-filled structures [6].

The good thing in this study is that, we used the US-guided method that has been used in many studies, such as Bhatnagar et al. [7], who carried out the celiac plexus lysis under US guidance and reported that it offers several advantages in comparison with other proposed procedures because it permits the whole procedure to be observed on a video monitor in the real time. The US-guided procedure exposes neither the patient, nor the doctor to unnecessary radiation, and it takes shorter time [8].

Through certain procedures, where imaging in the real time is necessary, the combination of CT and X-ray fluoroscopy may be of interest. One of the concerns related to the use of CT fluoroscopy is the higher radiation exposure [9]. An additional concern is the scattered exposure of the radiologists' hands and body since they may be very close to the main source of the X-ray during needle manipulation [10].

Aim of the work

There are multiple different techniques of coeliac plexus block. Our study will focus on the comparison between two techniques, the first one is done ultrasound guided. And the second one is done under fluoroscopic guidance. All the patients in the sample of the study are subjected to both methods and are on opioid medical treatment, although it is not sufficient to relieve pain.

The differences between the two techniques are highlighted in terms of effectiveness by means of a Visual Analog Scale (VAS), a percentage reduction in daily morphine consumption and any complications are recorded and evaluated at the time of implementation of each technique from start to finish.

Methods

Ethical considerations

The study group was notified about the nature and the goal of the study. The study group was not exposed to any harm or risk and confidentiality was assured.

Selection of the patients

The following materials and methods were applied to this Randomized Controlled Trial (RCT). This study was carried on forty patients with pancreatic cancer pain from Pain Clinic of the National Cancer Institute, Cairo University. All the patients were given information on the procedure and its probable complexities, and written informed consent was obtained.

The patients with persistent intractable upper abdominal pain even with Opioids treatment), which has been shown to be either ineffective or limited by side effects.

The patients were randomly distributed to two groups using a closed envelope in order to the randomization:

The first group The US group of 20 patients that are scheduled to have Neurolytic celiac plexus block (NCPB) through the ultrasound.

The second group The C-arm fluoroscopy group of 20 patients that are scheduled for (NCPB) through the C-arm fluoroscopic guidance (the control group).

A precise and detailed history of pain was taken and included the following:

- Onset mode.
- Provoke factors.
- Quality (e.g., feeling of burning, aching, faint, cramping or sharp pain, pattern).
- The intensity.
- Duration and progress of symptoms and complaints.
- Steady or intermittent nature.
- Exacerbation of factors (e.g., posture and eating).
- The mitigating factors.
- The efficacy and toxicity of previous drugs.

A thorough physical examination was performed. The abdominal examination was performed to determine the source of the pain and to decide if there were any regional signs of an sharp process (i.e., rebound tenderness).

The patients were interviewed prior to performing (NCPB) to get a baseline pain score using a (VAS).

The inclusion criteria

The patients with pancreatic cancer.

The Patients' age is 25–60 years.

The exclusion criteria

The patient's refusal to participate in the study.

The mentally retarded patients.

The uncorrectable coagulopathy (anticoagulant therapy and bleeding disorders).

The local infection or tumors that can spread because of the needles that are inserted through the infected or malignant infiltrated tissue.

The intestinal obstruction.

Back pain related to spinal metastatic disease.

The lab investigations

Before the procedure, all patients were evaluated regarding their systemic disease and blood tests, i.e., CBC, platelet function and prothrombin time. Also, CT scan was evaluated for the tumor spread and any displacement or distortion in the anatomical structures.

Preparation of patients

The patients have infused lactate Ringer's solution l000 cc via 18G venous catheter before the procedure. The patients' vital parameters (i.e., heart rate, non-invasive blood pressure and oxygen saturation) during the procedure and the two hours that are after the procedure were continuously monitored. The patients were anesthetized prior to surgical intervention with Midazolam 1–2 mg.

Ultrasound-guided celiac plexus block and neurolysis

The patient is in the supine position and the ultrasound transducer is positioned over the epigastrium, just caudal to the xiphoid process scout scanning is performed so the operator will be familiar with the relevant anatomy especially in malignant cases where the anatomy may be distorted and accordingly plan on the safest and shortest path for the needle (usually out-of-plane). We obtain both short-axis and long-axis views to correctly identify the celiac trunk (CT) and the SM 20- or 22-gauge needle is then introduced under direct vision in the short axis or the long axis. We prefer to advance the needle from the lateral side of the transducer (short-axis view) to lie just cephalic to the origin of the CT and not between the CT and SMa, to avoid injury to those vessels or their branches. The injection is carried out with real-time sonography after negative aspiration and negative test dose as ultrasound is not accurate in recognizing intravascular injections at such depth.

Results

The VAS score was re-evaluated in the two groups at pre block, two hours, post block, two days, two weeks and four weeks later where the median and (IQR) values of the VAS were 8, 2, 3, 4 and 5 in group I, and 8, 4, 4, 5 and 6 in group II, respectively, that are statistically significant drop of VAS score that was observed in the two groups. Also statistically, statistical significance decreases median in group I in comparison with group II regarding VAS between both groups from after 2 h. to after 4 weeks (Tables 1, 2; Fig. 1).

Obvious reduction of the need for opioids was observed in the two groups. The mean value of patient analgesic consumption (MME /day) before treatment in group I and group II, was significantly reduced after neurolysis. Also statistically, significant decrease in morphine in group I compared to group II (Table 3).

There are no significant differences between the study groups according to complications with regard to orthostatic hypotension at 12 h, diarrhea and local pain.

Complications of the study

These complications, which we tried to face as much as possible, can be described in the (study sample) as in Table 3.

It was noted that there is a very small percentage of complications that are related to the procedure and expressed as (transient), including the temporary orthostatic hypotension, diarrhea and also local pain.

Table 1 Comparison between two groups according to VAS score at post block

VAS score	Group I ($n=20$)	Group II ($n=20$)	z-test	*p* value
Pre				
Median (IQR)	8 (2)	8 (2)	0.158	0.875
Range	7–10	7–10		
After 2 h				
Median (IQR)	2 (1)	4 (1)	6.325	< 0.001
Range	1–4	2–6		
After 2 days				
Median (IQR)	3 (1)	4 (2)	4.162	< 0.001
Range	1–5	2–7		
After 2 weeks				
Median (IQR)	4 (1)	5 (2)	3.162	0.003
Range	2–6	3–8		
After 4 weeks				
Median (IQR)	5 (2)	6 (2)	2.481	0.018
Range	3–7	4–9		

Table 2 Comparison between two groups according to morphine consumption (MME)

Morphine (MME/day)	Group I ($n=20$)	Group II ($n=20$)	*t* test	*p* value
Pre	89.95 ± 19.79	91.33 ± 20.09	0.219	0.828
After 2 days	13.49 ± 2.97	25.24 ± 5.55	8.348	< 0.001
After 2 weeks	43.19 ± 9.50	58.76 ± 12.93	4.34	< 0.001
After 4 weeks	62.16 ± 13.68	80.00 ± 17.60	3.579	0.002

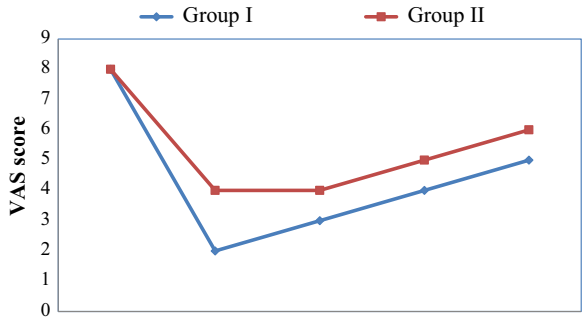

Fig. 1 Changes of the VAS score pre block, 2 h, 2 days, 2 weeks and 4 weeks post block in the two studied groups

Table 3 Comparison between two groups according to complications

Complications	Group I ($n=20$)	Group II ($n=20$)	χ^2	*p* value
Orthostatic hypotension at 12 h				
No	15 (75.0%)	16 (80.0%)	0.143	0.705
Yes	5 (25.0%)	4 (20.0%)		
Diarrhea				
No	14 (70.0%)	15 (75.0%)	0.125	0.723
Yes	6 (30.0%)	5 (25.0%)		
Local pain				
No	15 (75.0%)	13 (65.0%)	0.476	0.490
Yes	5 (25.0%)	7 (35.0%)		

In group I, 25% (5 patients) had transient orthostatic hypotension, i.e., systolic blood pressure less than 33% of basal value or systolic blood pressure below 90mmhg while in group II, 20% (4 patients) had transient orthostatic hypotension.

Orthostatic hypotension was managed by I.V fluids and vasopressors. The incidence of pronounced hypotension was low probably because of routinely ordered infusions of fluids before the procedure.

In group I, 30% (6 patients) had transient mild diarrhea while in group II, 25% (5 patients) had transient mild diarrhea.

Diarrhea was managed by I.V rehydration and antidiarrheal drugs.

In group I, 25% (5 patients) had back pain while in group II, 30% (7 patients) had back pain. Back pain is transient local pain associated with local spread of neurolytic agent and lasted for few hours and be controlled with mild analgesic.

The previous minor complications were not statistically significant in both procedures.

It is distinguished in this study that, there are no complications of great value within the study sample of any kind (hemiplegia, pneumothorax, hematoma formation or injury of the kidneys).

Discussion

Cancer pain control and maintenance of an enhanced quality of life in preterminal patients remains a therapeutic challenge. Many cancer patients often complain about the severity of the pain and thus it may affect their lives and the society in which they live [11].

The World Health Organization (WHO) has proposed the use of combination of non-steroidal anti-inflammatory drugs (NSAIDs), oral or transdermal opioids.

Auxiliary medications are primarily used to manage cancer pain. These medications are chosen based on the type and severity of that pain. The role of this treatment is to control cancer pain in 70–90% of patients [12]. However, the use of NSAIDs and opioids in general is connected to adverse [13]. It reduces quality of life mainly in patients with cancer [14].

Since Kappis (1919) reported the first percutaneous neurolytic celiac plexus block, the technique has been refined by a number of authors and several neurolytic celiac plexus block (NCPB) techniques have been used with the aim of avoiding complications and improving outcome [15].

Anterior or posterior celiac plexus blockade was performed [5]. Each method has its advantages and disadvantages, and this is evident by comparing the two methods with each other. The anterior approach is easy to carry out and the patient is in a supine position that causes the patient less discomfort than the posterior approach. It is considered the most appropriate method for patients, especially those who suffer from severe pain,

or difficulty lying prone, and the potential injury to the kidney. Also, avoiding posterior retro-crural injection, lead to lack of drug spread to the somatic nerve roots, and the risk of epidural and subarachnoid spaces spread [16].

The desired goal of the technique is always to relieve pain by determining the optimal place for placing the needle, thus improving the diffusion of the neurolytic solution in the plexus area, providing comfort to patients and reducing the incidence of complications [17].

Until 1979, celiac plexus block was performed blindly. In 1979, Hegedus stressed the importance of using radiological guidance in order to determine the axis of celiac. A block of the abdominal plexus can also be performed through imaging techniques, such as computed tomography, magnetic resonance, ultrasound as well as endoscopic ultrasound [5].

The advantage of this research is that the ultrasound-guided celiac plexus degeneration (USG) technology produced a distinct and very wonderful pain relief for longer periods that may reach months, and this appears when compared to fluoroscopy. And the reason for this may be on account of the correctness of the real time of USG technology that provided better Visualizations of the needle trajectory as well as the accurate and effective diffusion of the neurolytic drug to the target. This is consistent with [18].

A study was conducted by Jimenez et al. about the degeneration of the celiac plexus neurolysis (CPN) under the ultrasound. There was a high rate of pain relief in approximately 61% of the study sample starting from the first week and within six months, and it reached 39% for a whole year. These patients recorded periods longer than the duration of our current study [19].

In this study, as regards patient's position, the USG technique was more comfortable than posterior fluoroscopic guided technique because the patients have lied in supine position with mild sedation (IV midazolam (0.01 mg/kg) and this has provided an easy accessibility and a management of their airway while patients in fluoroscopic guided have lied in prone position with a difficult accessibility and a management of their airway, and so they have required deep sedation (IV midazolam 0.01–0.02 mg/kg).

In this study, the USG technique is a real time technique with better visualization of the blood vessels and soft tissue that is better than the fluoroscopy technique that had relation to the bone only (and this a poor anatomy accuracy), and does not distinguish the abdominal plexus from its neighbor structures, such as the pancreas, blood vessels and lymph nodes and that is a defect in the fluoroscopy technique.

Akhan et al. explained in a study that the ultrasound is safe and effective in the abdominal celiac plexus neurolysis, because it eliminates the risk of unintended injection of ethanol into the blood vessels or intradural since the tip of the needle is in front of the spinal arteries and the spinal canal [20].

In our study, we found that US-guided block was safer, because it has avoided the unnecessary exposure of the patient and the physician to the radiation of fluoroscopy. Also, ultrasound guidance was quicker and economical since it has provided a real-time imaging in contrast to fluoroscopy that carries the risk of exposure to the hazards of radiation, moreover, it is time-consuming and expensive.

This study was designed to compare the effectiveness of ultrasound and fluoroscopic technique in trans-aortic approach; forty patients were randomly selected from the pain clinic suffering from pancreatic cancer pain. We divided them into two equal groups. We performed anterior ultrasound guided approach in group (I), and posterior trans-aortic approach fluoroscopy guided in group (II).

We compared the VAS immediately pre-block, two hours, three days, two weeks and four weeks post-block, reduction in daily morphine consumption, complications and time of the block. We found that no significant difference between both groups in complications. But, there is a significant difference between both groups in time of the block with p value less than 0.05.

Polati et al. [21] and Hendry [22] found that patients with NCPB reported significant pain relief compared with those treated by pharmacotherapy, but long-term results did not have any difference between the groups. This finding could be related to the fact that pancreatic cancer pain infrequently remains of visceral type in the long-term developed stages of the disease, but acquiring many features and sites because of the neoplastic involvement of somatic or nervous structures.

Reduction in analgesic consumption is an indirect method to estimate pain strength and effectiveness of accompanied treatments. So, the mean values of the daily analgesic consumption were significantly reduced after neurolysis in both groups. This coincide with the result of Kawamata et al. [24] who reported that, NCPB was shown to decrease narcotic requirement and limit narcotic dose related to side effects [23].

In this study, time of doing each technique from its beginning till the end was recorded where US group required significantly shorter time in comparison with the other fluoroscopy group. The difference in soft tissue definition between US and fluoroscopy is perhaps an advantage in US guided neurolysis.

Failure of the procedure can be explained by multiple reasons assuming the anatomical changes or the lack of a sufficient neurodegenerative factor as well as the incorrect position of the tip of the needle because of the presence of fibrosis, malignant infiltration or super add inflammatory changes that distort the anatomy and thus limit the access to the celiac plexus [24], and therefore limit the delivery of the neuroleptic agent to the whole plexus region that is innervated by De Cicco et al. [25] the presence of ascites preventing the spread of the neurolytic agent ideally [26]. It can also be attributed to concomitant somatic component involvement with alternative pain pathways [24] and extensive local metastases beyond the targeted plexus innervations abdominal wall or other viscera with innervations outside the celiac plexus, and the resultant inflammation as disease progression is a dynamic process.

In this study, we have found that there is no statistically significant relationship between age of onset of illness and treatment resistance.

Conclusions

It is noticeable and good in conducting this research that there are no complications that include a large space on the study sample, despite the presence of some minor complications for NCPB, including localized pain, transient orthostatic hypotension, and diarrhea as well as no significant differences within the fluoroscopy and US groups. This effective NCPB, regardless of the technique used, produced good analgesia that permitted significant decrease in opioid in the study sample with a significant improvement in the unwanted opioids adverse effects.

The time for inducing the block was significantly shorter for US group in comparison to fluoroscopy group mostly on account of the difference in soft tissue definition between US and fluoroscopy that is an advantage for US. Of course, each of the existing technologies has its own advantages and disadvantages. However, US is better imaging technique to document the correct position of the needle tip as well as avoiding major injury of the organs. In addition, the ultrasound scan is very useful for determining the anatomy, especially when the anatomical relations of the organs are more distorted, whether because of tumor or because of scars of previous operations.

Abbreviations

CBC	Complete blood count
CT	Celiac trunk
MME	Morphine milligram equivalent
NCPB	Neurolytic celiac plexus block
NSAID	Non-steroidal anti-inflammatory drugs
NeP	Neuropathic pain
RCT	Randomized controlled study
SMa	Superior mesenteric artery
SNS	Sympathetic nervous system
USG	Ultrasound guided
VAS	Visual analog scale

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Author contributions

KEA and YIA gave the idea. HGM put study design. MAE collected the Patients data and analyzed them as well as wrote the paper with revision. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the Research Ethics Committee of the Faculty of Medicine at Ain Shams University in Egypt on 18 September 2019; reference number of approval: 4/4/2019. All patients included in this study gave written informed consent to participate in this research.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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