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Safety and Efficacy of CT Fluoroscopy in Celiac Plexus Neurolysis in Hepatocellular Carcinoma Related Abdominal Pain

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Abstract

Background: Management of hepatocellular carcinoma related abdominal pain is a complex and challenging issue as most HCC develop on top of liver cirrhosis and the deficient hepatic function obstacle the high-dose narcotic analgesics. Imaging-guided Celiac plexus neurolysis for refractory pain management has been used for almost 100 years in patients with advanced abdominal malignancy and effectively control pain without the noted side effects typical of opioids, however CT guided celiac block is the most accurate method for celiac block guidance the lack of real time visualization, radiation exposure & time consuming call the need for real time CT fluoroscopy guidance.

Aim of Study: To assess the efficacy of CT fluoroscopy in celiac plexus neurolysis in hepatocellular carcinoma related abdominal pain.

Patient and Methods: This study was carried out on 30 adult patients suffering from abdominal pain due to infiltrative or metastatic HCC and pain not controlled by WHO analgesic step ladder. Celiac Plexus Neurolysis (CPN) is achieved with intravenous conscious sedation, prognostic block accomplished by using injecting a near by anesthetic accompanied with the aid of alcohol for celiac plexus block, after 10 minutes, if the injection correctly relieved pain; maximum filling of the retro-pancreatic area with ethanol is a sign of enough neurolysis.

Results: Marked decrease of pain severity in all patients was noted as a sharp fall of the Numerical Rating Scale (NRS) score on the 1 st day post CPN with relatively stationary course for 3 months in the patient survived their primary disease.

Conclusion: Celiac Plexus Neurolysis (CPN) provides an effective technique in decreasing pain severity in HCC patients, and so decreases the analgesic requirement, their side effects and may increase patients' survival, CT fluoroscopy guided CPN is an easy and safe procedure that provides high success rates, markedly decreased patient radiation dose and total procedure time compared with use of conventional CT guidance.

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Key Words: *Hepatocellular carcinoma – Abdominal cancer pain – Celiac plexus neurolysis – CT fluoroscopy.*

Introduction

ABDOMINAL pain is a major problem for patients with HCC **[1,2]**. More than 80% of patients with HCC have underlying liver disease or cirrhosis **[3]**; cirrhosis may change the pharmacodynamics of drugs by influencing changes in drug absorption, distribution, bioavailability, and hepatic and renal clearance mechanisms generating pain management difficulties **[4]**. As deficient hepatic function must be taken into consideration when prescribing pain medications as most analgesics are metabolized in the liver and even standard doses or dosing frequency can induce adverse side impacts such as variceal hemorrhage, ascites, renal failure, and hepatic encephalopathy or even can precipitate liver failure **[4]**. Moreover cancer patient necessitates chronic use of high-dose narcotic analgesics **[5]**.

The celiac plexus is a network of ganglia that relay preganglionic sympathetic and parasympathetic efferent fibers and visceral sensory afferent fibers to the upper abdominal viscera. The visceral sensory afferent fibers transmit nociceptive impulses from the liver, gallbladder, pancreas, spleen, adrenal glands, kidneys, distal esophagus, and bowel to the level of the distal transverse colon. Located in the retroperitoneal space just inferior to the celiac trunk and along the 2 sides of the aorta, between the levels of T12-L1 disc space and L2, the celiac plexus can easily be reached by several different approaches **[6]**.

Methods leading to an inhibition of pain transmission are therefore encouraging alternatives to

alleviate pain and decrease of the danger of side effects caused by drugs. For more than 100 years, imaging-guided celiac plexus neurolysis has been used in patients with advanced abdominal neoplasms. It includes injecting a neurolytic substance (most frequently absolute alcohol) into or around the celiac plexus to inhibit these impulses and efficiently relieve pain without the noted opioid side effects [7].

Imaging guidance for celiac plexus neurolysis is mostly done with multidetector Computed Tomography (CT), which has replaced the use of fluoroscopy or Ultrasonography (US)-guided techniques [8].

In comparison to conventional fluoroscopy and Ultrasonography (US), CT has been limited as an interventional guidance method due to absence of real-time capability. While conventional CT enables the determination of optimal puncture sites, the direction of needle insertion and the assessment of needle positioning after insertion, it needs the time-consuming acquisition of multiple single or helical images and does not enable real-time assessment during the puncture operation [9].

The development of slip ring technology and the continuously rotating X-ray tube has made acquisition of CT images. The evolution of new image reconstruction algorithms and high-speed array parallel processor systems for real-time raw data reconstruction and display paved the way for the development of real-time CT fluoroscopy (also known as continuous imaging CT). Also, the introduction of X-ray tubes with much improved heat capacity and more sensitive semiconductor detectors contributed to evolution of CT fluroscopy [10].

The use of CT fluoroscopy for the guidance of interventional radiologic procedures markedly decreased patient radiation dose and total procedure time compared with use of conventional CT guidance [11].

Aim of the study: To assess the safety and efficacy of CT fluoroscopy in celiac plexus neurolysis in hepatocellular carcinoma related abdominal pain.

Patients and Methods

Thirty patients (12 females, 18 males), (age range 49-68 years) (mean age, 53.4 ±3.83 years), suffering from uncontrolled upper abdominal pain due HCC (5 local disease, 10 infiltrative and 15 extra hepatic and nodal metastatic hepatocellular carcinoma) were enrolled in this study between January 2018 to June 2019 in Radiology Department at our university hospitals, referred from outpatient clinic.

Inclusion criteria include abdominal pain due to liver cancer, pain not controlled by WHO analgesic step ladder or patients suffering from side effects of analgesic drugs.

Exclusion criteria include patient refusal of the study, patients with coagulopathy or patients suffering from marked ascites.

The study was approved by the Medical Ethical Committee of Faculty of Medicine of our University.

Imaging procedures will be operated on 160-slice CT scanner with CT fluoroscopy.

Celiac plexus neurolysis technique:

All patients underwent real time CT fluoroscopy-guided celiac plexus neurolysis, after informed consent was obtained, good history taking, general examination, pre procedure investigation (including abdominal US/CT, coagulation profile and chest X-ray), patients should stop analgesics overnight and fasting for about 8 hours.

The first essential step in real time CT fluoroscopy-guided celiac plexus neurolysis is preprocedure planning.

Celiac plexus neurolysis is performed under intravenous conscious sedation with agents such as midazolam and fentanyl. Cardiorespiratory monitoring, including electrocardiography, blood pressure, and pulse oximetry, is an essential component of the procedure. Oxygen masks if needed for old or obese patients.

Patient position:

Posterior paravertebral approach was done in 18 patients (5 of them with mild to moderate ascites, 7 patients with locally infiltrative left lobe subcapsular masses with no safe anterior passage & 6 patients with extensive para aortic extra hepatic nodal metastasis) while patients were in prone or oblique position. Anterior approach was done in (12 patients) while patients were in supine position.

Unilateral injection was sufficient in 27 patients however 3 patients need bilateral approach.

A control axial scanning of the abdomen was taken to localize the region of interest which covers the course of the needle to the celiac plexus.

The video monitor was used inside the scanning room. The panel was used in the scanning room.

Exposures were activated by using a footswitch. The X-ray tube current is adjusted to be 30-50mA to reduce the patient radiation exposure, compared with conventional CT with 150-400mA.

After sterilization of the skin, setting the local cutaneous and subcutaneous anesthesia with lidocaine 2% (20mg/ml). A 20-cm long 20-gauge Chiba needle was used for procedure. The needle tip was inserted to the right side or to the left side of the celiac trunk under the guidance of serial CT cuts. When the tip of the needle appears to be properly positioned, a suction has been introduced to ensure that the tip of the needle is not inside a blood vessel, and a "prognostic block" was performed by injecting a local anesthetic (9-12ml of lidocaine 2%) mixed with 2ml contrast agent (ultravist) to show the distribution of the lidocaine under the CT cuts. Local anesthesia should always be injected before alcohol to decrease ganglion neurolysis pain & to perform a diagnostic celiac plexus block. 15-30ml of 90% ethanol mixed with 3ml contrast, indicate the distribution of alcohol after 10 minutes if effectively relieved pain (successful block). Ethanol spread has been assessed. An indication of adequate neurolysis is the maximum retropancreatic space by ethanol. 3ml of lidocaine 2% were injected before the needle was removed to reduce ethanol irritation.

The serial CT scans were acquired immediately after needle removal covering the region from the upper border of the 12 th thoracic to the lower border of the 1 st lumbar vertebrae to display the spread of the neurolytic solution. The patient stays in the hospital for 4 hours under observation.

The degree of pain relief was assessed subjectively using the Numerical Rating Scale (NRS) which is an 11 points scale from 0 to 10 where 0 indicates no pain & 10 indicates the worst pain and objectively by the change in daily analgesic doses; before the procedure, immediately after injection, 1 week, 1 month and 3 months post-neurolysis. A decrease in NRS score to 50% or more of the baseline value was considered significant. Also, analgesic intake and complications were documented.

Statistical methods:

Statistical analysis was done by IBM personal computer (SPSS Inc., Chicago, Illinois, USA) software package version 25.0. Two types of statistics were done: Descriptive statistics, for example, percentage, mean, SD, and range, and analytic statistics. p-value that measures less than 0.05 statistically significant.

Results

CT-guided CPN was carried out for 30 adult patients. The technique was successfully performed in 30 patients (100%), of whom 21 (70%) were males and 9 (30%) were females with mean age 50.4±4.83.

According to the accessibility and the ease of entrance:

Right celiac ganglion: 18/30 patients (60%).

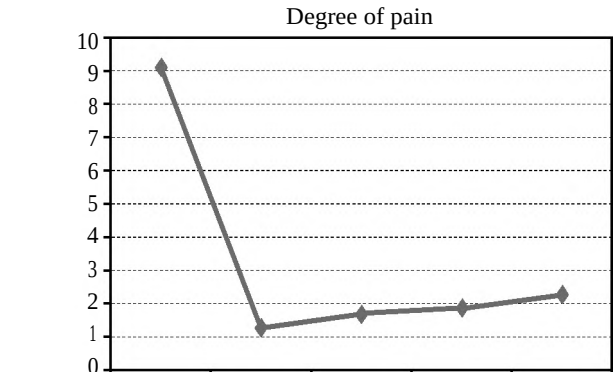
Left celiac ganglion: 9/30 patients (30%).

Bilateral needle insertion: 3/30 patients (10%).

Degree of pain was assessed by Numerical Rating Scale (NRS) score before and after CPN.

A marked decline in pain intensity was observed in all patients as a sharp drop in the NRS score on the 1 st day after CPN with a relatively stationary 3-month course in which the patient survived their main illness.

Baseline NRS score was 9.1 ±0.85. One day after CPN, pain intensity decreased markedly to 1.3±0.71, one week after CPN the decrease in pain intensity maintained at the same level 1.7 ±0.89, one month after CPN the decrease in pain intensity maintained at the same level 1.9±0.79 and 3 months after CPN pain intensity still decreased significantly to 2.3± 1.02. The decrease in pain intensity at its average before and at different sequences after CPN recorded high significant statistical difference (p-value <0.001) Fig. (1).



	Before procedure	One day after procedure	One week after procedure	One month after procedure	Three months after procedure
Degree of pain	9.1	1.3	1.7	1.9	2.3

Fig. (1): Linear graph shows the degree of pain before & after procedure.

After CPN, analgesic drug intake decreased markedly for three months after CPN. After one week, all patients on opioids stopped them and 5 patients (16.6%) took NSAIDS. After one month, all patients stopped opioids and 7 patients (23.4%) took NSAIDS. While after three months, 12 patients (40%) continued on NSAIDS and 3 patients only (10%) took opioids again but with smaller dose than the pre block doses Fig. (2).

There were no significant complications (vascular or neurological), however local irritant pain appeared in 18 patients (60%), post-CPN hypotension appeared in 5 patients (16.6%) who all responded to I.V fluid treatment while diarrhea appeared in 22 patients (73.4%) after CPN and all responded to I.V fluid treatment & Diosmectite sachets.

The patient dose exposure during the procedure of CT fluoroscopy was 2.99±0.22mGy using low mA (30-50mA). The dose exposure during CT fluoroscopy was 91% less than conventional CT using (150-400mA), radiation dose exposure sheet was reviewed the DLP (dose-length product) in (mGy.cm) was calculated at the end of the procedure & compared to the radiation summary sheet of the disgnostic study for the same patient Figs. (3,4).

The mean radiation dose DLP used to complete the CT fluoroscopy procedure was 48.2mGy.cm .

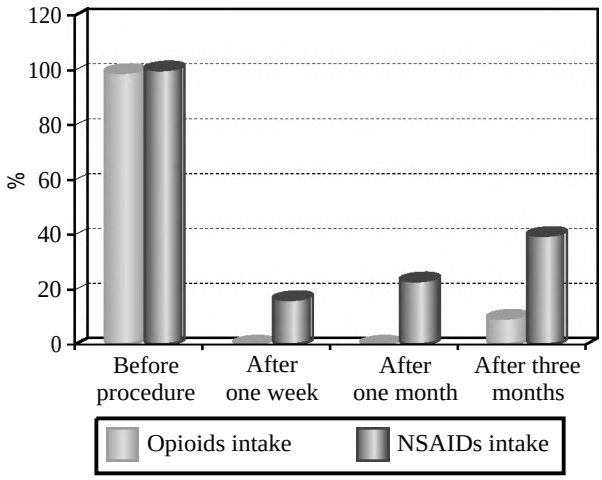


Fig. (2): Bar graph shows opioids & NSAIDs intake before & after procedure.

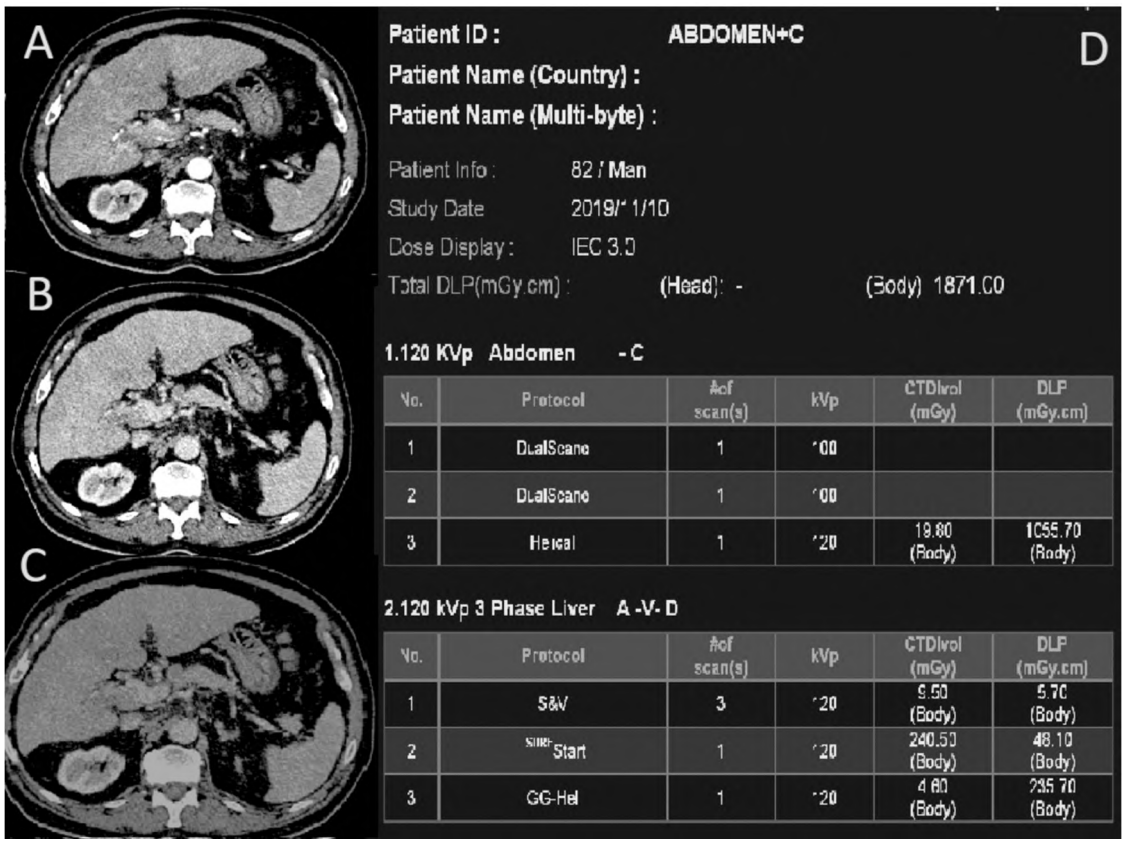


Fig. (3): (A, B, C) 55 male patient presented with elevated serum alpha feto protein and sever abdominal pain axial full dose diagnostic Triphasic CT reveled right lobe liver infiltrative HCC, (D) Total radiation exposure dose of the patient was 1871mGy.cm . Analgesics: Tramadol tablet: two times daily. Pain degree by VAS scores (before CPN).

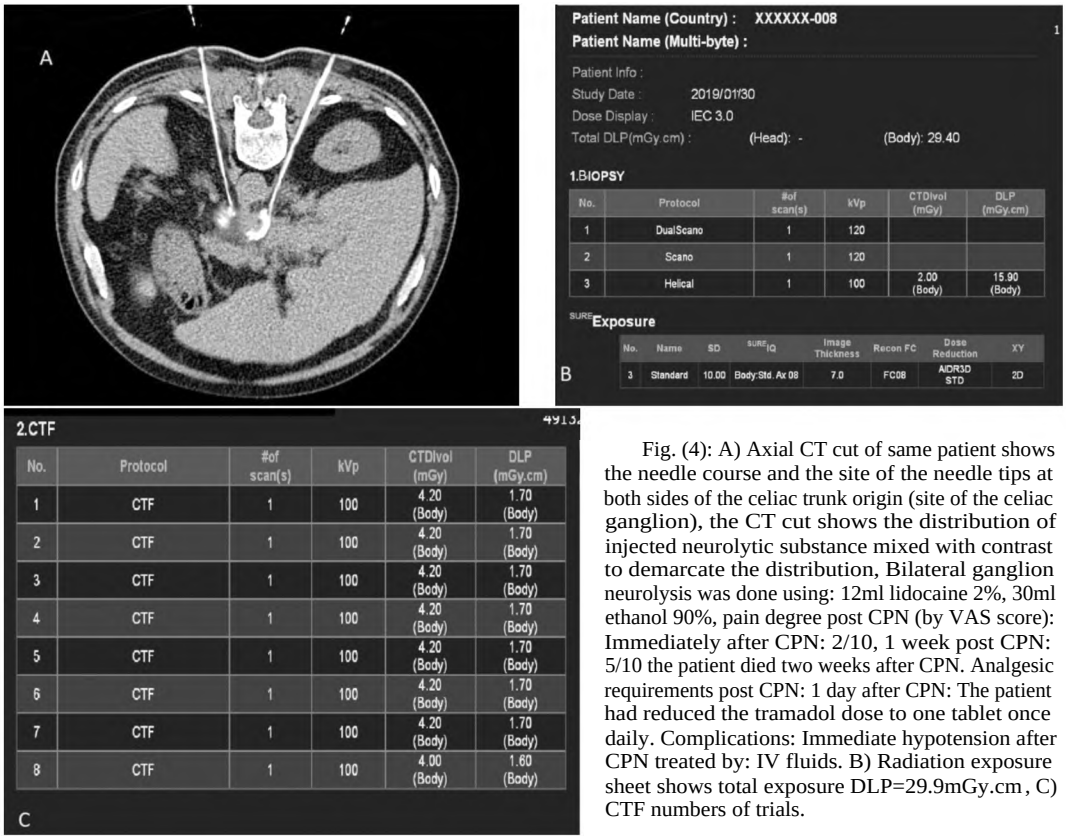


Fig. (4): A) Axial CT cut of same patient shows the needle course and the site of the needle tips at both sides of the celiac trunk origin (site of the celiac ganglion), the CT cut shows the distribution of injected neurolytic substance mixed with contrast to demarcate the distribution, Bilateral ganglion neurolysis was done using: 12ml lidocaine 2%, 30ml ethanol 90%, pain degree post CPN (by VAS score): Immediately after CPN: 2/10, 1 week post CPN: 5/10 the patient died two weeks after CPN. Analgesic requirements post CPN: 1 day after CPN: The patient had reduced the tramadol dose to one tablet once daily. Complications: Immediate hypotension after CPN treated by: IV fluids. B) Radiation exposure sheet shows total exposure DLP=29.9mGy.cm , C) CTF numbers of trials.

Discussion

Treatment of pain is one of the most significant palliative treatment problems in patients with hepatocellular carcinoma. Although opioids efficiently alleviate pain, the problem is amplified and intervention-based pain control, particularly for patients with HCC infiltration or metastasis outside the liver, due to numerous side effects and complications associated with opioids.

Celiac Plexus Neurolysis (CPN) was defined by many studies as an interventional method used to control abdominal visceral pain associated with abdominal malignancies **[12,13]**.

Although the use of CT fluoroscopy carries the hazard of radiation exposure to the patient and operator, the recently used ultra-low dose exposure during the procedure decreased the radiation hazard concern. It provides practitioners with reliable information on the needle position with the real time imaging and the multiplanar reconstruction that makes it less operator dependent, more accurate and less time-consuming tool of guidance than the previously mentioned methods **[14]**.

Approaches and ways used to place the needle either single unilateral or bilateral para median on both sides of celiac trunk, the choice between the single or bilateral methods is still difficult, counting on the personal skills and the experience of every operator. In this study we used single unilateral approach in 80% of patients, while bilateral approach was done in 20% of patient as pain was not relieved by single approach. We found it easy with great pain relief in all patients with no major complications happened.

Decicco et al., (1997) stated that despite different approaches and methods used to place the needle, the success of the block depends on adequate spread of the injected neurolytic agent in the celiac plexus area.

In this study, CT-guided CPN was done by injection of 15-30ml of 90% ethanol. We achieved adequate pain resolution longed for 3 months for all patients in comparison with Bhatnagar et al., (2012) that performed CPN for 30 patients by 15-20ml of 50% ethanol injected bilaterally **[15,16]**. They reported successful CPN for all patients with notable pain relief only for 2 months.

We found that this technique successful rate was 100%. All of the studied patients experienced effective immediate pain relief with NRS scores of pain markedly reduced to less than 2. We observed highly significant (p<0.001) variance in the NRS scores of pain in all studied patients before

and after CPN. The peak reduction of the pain was observed in the first day after the CPN.

Numerical Rating Scale (NRS) is an 11 points scale from 0 to 10 where 0 indicates no pain & 10 indicates the worst pain perceived. NRS was more practical than graphic Visual Analogue Scale (VAS), easier to perceive for most people and doesn't need clear vision, paper & pen **[17]**.

Patients included in this study showed significant decrease in their NRS score and opioid consumption. All patients exhibited a decrease in their NRS scores at all measured time points from 1 st day till 3 months post CPN. Prior block NRS score was 9.1 ±0.85. One day after CPN, pain severity decreased markedly to 1.3 ±0.71. Three months later, pain severity still decreased significantly to 2.3± 1.02. This decrease in pain severity after CPN resulted in a high significant statistical difference p-value <0.001. That is similar to Bhatnagar et al. (2012) results who reported that the VAS score prior to CPN was 9.10±0.85. One day after CPN, VAS score markedly decreased to 1.2 ± 1.02. 2 months after CPN, pain scores had decreased to 2.10±0.79 (p<0.001).

Carlson et al., (2001) stated that the use of CT fluoroscopy for the guidance of interventional radiologic procedures markedly decreased patient radiation dose and total procedure time compared with use of conventional CT guidance. The median calculated patient absorbed dose per procedure and the median procedure time with CT fluoroscopy were 94% less and 32% less, respectively, than those measurements with conventional CT scanning (p<.05).

In our study the patient radiation exposure dose with CT fluoroscopy was 93% less than exposure dose with conventional CT as we found that the average DLP of total CTF dose in our study was 48.2mGy X cm Compared to study done by Joemai et al., **[14]** which reported an average DLP of 681 mGy X cm for biopsies and drainages while the procedures were completed at full dose parameters **[14]**.

Conclusion:

CT fluoroscopy guidance for CPN provides high success rates in alleviating pain in HCC cancer patients as it allows accurate localization of the needle, accurate demonstration of anatomical structures and also reduce patient radiation dose & is less time consuming for sever ill patients. CPN should be considered earlier for controlling HCC related abdomen pain and not to be reserved as a last plan when everything else fails.

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تقييم فعالية وآمان التنظير الإشعاعى بالآشعة المقطعية فى تدمير الضفيرة العصبية البطنية فى حالات آورام الكبد

يعانى الكثير من مرضى آورام الكبد الخبيثة من آلام شديدة وغير محتملة. وتخفيف هذه الآلام يعتبر من آصعب ما يواجه المريض والطبيب المعالج.

يعتبر إنحلال شبكة الآعصاب الجوف باطنية آحد طرق علاح آلالام المصاحبة لآورام الكبد. ويتم تنفيذ هذه التقنية بآكثر من طريقة ولقد تفوق إستخدام التنظير الإشعاعى بالآشعة المقطعية كمرشد على غيره من الآجهزة من حيث الدقة والآمان حيث يوفر جهاز الآشعة المقطعية.

الهدف من البحث هو تقييم تحلل شبكة الآعصاب الجوف باطنية بإستخدام التنظير الإشعاعى بالآشعة المقطعية كطريقة فعالة لعلاج آلام البطن الناتجة عن آورام الكبد المتقدمه.

هذه الدراسة تم إجراؤها على ثلاثين مريض يعانون من آلام شديدة بالبطن نتيجة لوجود آورام كبد سرطانية غير مستجيبة للمسكنات الدوائية آو حدوث مضاعفات نتيجة إستخدام المسكنات.

خطوات البحث:

- تحديد طبيعة الآلم الموجود فى البطن درجة قياسية بالنسبة إلى مقياس التناظرية الرقمى.
- وضع المريض على منضدة الآشعة المقطعية ثم آخذ صورة بالآشعة المقطعية للمنطقة محل الإهتمام لتحديد مكان شبكة الآعصاب الجوف باطنية وتحديد مسار إبرة الحقن من الجلد وحتى العقدة العصبية وإستخدام إرشاد التنظير الإشعاعى بالآشعة المقطعية وصولاً إلى شبكة الآعصاب الجوف باطنية على جانب واحد آو على جانبى الشريان الجوف باطنى ومن ثم حقن ١٥–٣٠ مليليتر من الكحول الإيثيلى (تركيز ٩٠٪).
- تم إستخدام مقياس التناظرية الرقمى لتحديد درجة قياس الآلم: فوراً بعد إنتهاء الحقن، ثم بعد يوم، وبعد إسبوع ثم شهر و٣ آشهر من الحقن.
- تسجيل التغيرات التى طرآت على جرعات المسكنات ومقارنتها بما كانت عليه قبل الحقن.

وبعد التحليل الإحصائى قد خلصت النتائج إلى نجاح كبير على المستوى التقتنى بنسبة ١٠٠٪ من حالات البحث كما آدى إلى تقليل جرعات المسكنات التى يتناولها هؤلاء المرضى يومياً ويقلل من آثارها الجانبية.