Radiofrequency Thermocoagulation of Bilateral Thoracic Splanchnic Nerves for the Management of Abdominal Cancer Pain

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Abstract:

Background: Abdominal cancers are aggressive with high mortality that causes severe abdominal pain and affects quality of life seriously. The disease is often resistant to analgesics, opioid and adjuvants but better response to neurolysis and pain management in the context of palliative care should be an early part of the overall therapeutic plan.

Objective: To evaluate the efficacy and safety of radiofrequency thermocoagulation (TRF) of bilateral thoracic (Th) splanchnic nerves at the level of Th10 and Th11 in the management of upper abdominal cancer pain.

Methods: It included 30 patients suffering from abdominal pain due to upper abdominal cancers for whom bilateral thoracic splanchnic nerves block (SNB) was performed by radiofrequency thermocoagulation at two level of Th10 and Th11. Visual Analog Scale (VAS) [0-10], 24 hrs oral morphine consumption, functional improvement (success rate) and complications were assessed and recorded before and after the block for 3 months follow up period.

Results: The VAS scores and MST (Morphine sulphate tablets) doses showed significant reduction with TRF from the 1st day postprocedural up to the end of follow up with good success rate. No major complication was recorded.

Conclusion: Radiofrequency thermocoagulation of both splanchnic nerves at level of Th10 and Th11 may offer a safe and effective technique for pain management in patients suffer from upper abdominal cancer.

Trial registry: It was registered at www.clinicaltrials.gov at no.: NCT0306312.

Keywords: Splanchnic nerves, radiofrequency thermocoagulation, upper abdominal cancers, pain.

Introduction:

The prevalence of cancer pain with gastrointestinal malignancies is 59% which is often resistant to analgesics but better response to neurolysis (1). The majority of nociceptive impulses from the upper abdominal viscera pass through the splanchnic nerves and celiac plexus. Thus, the blockade or ablation of thoracic splanchnic nerves and celiac ganglia plays a major role in the pain management of most upper abdominal malignancies, particularly pancreatic malignancies (2). Thoracic splanchnic nerves composed of preganglionic fibers, arising from the anterolateral horn of the spinal cord bilaterally, together with the T5-T12 ventral spinal roots. The greater splanchnic nerve (GSN) arises from ganglia 5–9 and occasionally 10, the lesser splanchnic nerve (LSN) from ganglia 10 and 11 and the least splanchnic nerve (lSN) from ganglion 12 (3).

Radiofrequency thermocoagulation (TRF) is a minimally invasive technique that is performed under local anesthesia and fluoroscopic guidance. It is a target-selective technique, mostly indicated for the management of nociceptive chronic pain that is resistant to conservative therapy like low back pain. TRF can be a safe and useful adjunctive treatment for unresponsive visceral cancer pain. In this patient, ablative therapy eliminated the need for pain medications and was accompanied by dramatic reduction in pain with improvement of quality of life (4).

TRF of splanchnic nerves at level of Th11 & Th12 was reported to be a more predictable, effective and safe technique for the management of pancreatic cancer pain, but the evidence is still limited and there is no studies were done to prove its efficacy when blocking splanchnic nerves at level of Th10 & Th11 in the management of other abdominal cancer pain (5), (6).

Patients and methods:

After obtaining approval of the local ethics committee of South Egypt Cancer Institute, Assiut University, Assiut, Egypt, and parental written informed consent, the study was conducted on 30 patients, who aged ≥ 18 years and suffer from abdominal pain (visceral pain with VAS ≥ 4) due to upper abdominal cancers in the period from October 2014 to April 2017. Patients with organ failure, coagulation disorders, local infection, sepsis, severe displacement of intra-abdominal structures, pregnant women, documented metastatic lesions, and psychiatric disease were excluded from the study. Data was collected one day before block including age, sex, diagnosis, history, and taken medications.

The patient was positioned in the prone position with a pillow under the lower abdomen to minimize lumbar lordosis and allow easier palpation of the spinous process. First, Th10 and Th11 vertebrae were identified and aligned cephalocaudally under fluoroscopy. Then the C-arm was moved to a 10–15° oblique position, this minimizes the chance of pneumothorax. The landmarked entry point was at the junction of the rib and vertebra, 3–4 cm paravertebral. Skin and subcutaneous tissue were infiltrated with lidociane 2% under strictly aseptic technique after sterile preparation and drapping of the patient's back. To relax the patient, sedatives could be used on an as-needed basis especially during thermal lesion time by low dose fentanyl, midazolam 0.2 mg/kg and propofol 0.5 mg/kg shots. With ASA (American society of anesthesia) standard monitoring and under fluoroscopic guidance, a 10 cm 20-G curved RF needle with an active tip of 10 mm was positioned and advanced under tunnel vision.

Once the correct position at Th10 was ensured in oblique (end on appearance of the needle) (fig1), postero-anterior (needle tip was in touch with the lateral border of the vertebra)**,** and lateral view (the active tip at the junction between the anterior and middle third of the vertebral body) (fig 2), a 10 cm electrode was introduced through the RF-needle. Prior to the lesioning, a sensory (at 50Hz, up to 1V) and motor (at 2 Hz, up to 2V) test stimulation was performed to verify the location. A satisfactory patient response on sensory stimulation was an epigastric discomfort. If no contraction of the intercostals muscles was observed, the motor stimulation was satisfactory. Then the steps were repeated at level Th11.With assurance of correct responses on both test stimulations and after repeation of the same steps on the other side at Th10 & Th11 levels, 4 lesions were made simultaneously, with settings parameter for 90 seconds at 85°C temperature. Then another lesion was given after rotation of needles 180 degree. Immediately before the generation of every lesion, dexamethasone 4 mg and lidociane 2% were injected to reduce the postoperative edema and discomfort and burning pain during lesion.

All patients were closely observed and compared for post-injection complications and signs of technical success like as hypotension, diarrhea, and colicky pain which means good sympathetic block and unopposed parasympathetic activity. The patients were discharged from the hospital after a total period of 6 hours with obtaining a normal hemodynamics, chest radiograph and pulse oxyimetery. All patients were advised to stay the night close to medical centers, to avoid the risk of pneumothorax being misdiagnosed.

Assessment parameters were:

-Demographic data (age and gender).
-Visual analogue scale VAS [0-10] (straight line with the left end 0 representing no pain but right one 10 representing the worst pain) (7).
-Functional improvement of the blocks or clinical implication of VAS and success rates was reported at the end of 2nd week after blocks as this period is the time of maximum reduction of VAS values (8) as follow:

- ✓ Failed with no improvement block: block which failed to reduce pre-procedural measured VAS more than 25%
- ✓ Mild or fair block: block which lowers the pre-procedural measured VAS by 25 - 50%.

- ✓ Moderate or good block: block which causes reduction of the pre-procedural measured VAS by 50 – 75%.
- ✓ Excellent block: block which causes reduction of pre-procedural measured VAS by more than 75%.

-Total opioid consumption per day at equianalgesic dose of oral morphine (MST) in mg (according to Janssen pharmaceutics, Inc, clinical managrah, 1n 1991).

-Complications that occurred during and after the block were also recorded.

All assessment parameter for follow up were recorded before and after intervention in the same day (D1), after one week (W1), 2nd weeks (W2), and then every month for 3 months (W4, W8, W12).

Statistical methods:

All analyses were done using SPSS® (Statistical Package for Social Sciences) software, version 22.0, Chicago, IL, USA. Categorical variables were expressed as frequencies with percentages. Chi-square test was used for testing proportion independence and Fisher Exact tests if expected number of observations in 25% and more of the cells is less than 5. Mean and standard deviation described quantitative data and median with range for ordinal data. Student t test compared means. Freidman test compared medians of more than 2 dependent or repeated measures and pairwise comparisons were done with Wilcoxon signed test. P value was always 2 tailed and was set significant if ≤ 0.05 level.

Results:

Regarding demographic data, the mean (standered deviation SD) of patients age was 58.30 (15.00) with minimum and maximum age of 25 and 82 years respectively (table2). Also there were no significant difference between patients sex (table1).There was significant reduction ($P < 0.001$) (table 4 & figure 3) of VAS median (range) was observed 30 min after the block and during first day 3(2-5) when compared to the baseline 7(4-8) and it stay significant in until the end of the follow-up period after 3 months 2.5(0-4). The maximum decline by 85.71% occurred after one week. The baseline median MST consumption (Range) was 25 (10 – 650) and it significantly reduced ($P < 0.001$) (table 5 & figure 4) from D1 10 (0 – 180) till the end of the follow up period 5 (0 – 50). The maximum reduction of oral opioid consumption median (range) started after end of the 2nd week post-procedural 0 (0 - 45 mg), by 99.0% according to median value.

Regarding functional improvement of the block and clinical implication on VAS. There were 12 patients (40.0%) showed complete pain relief (VAS= 0 – 1) and they stopped the MST and shifted to NSAIDs and Acetaminophen on demand. There were 10 of these 12 patients showed excellent block (33.4%), and presented as follow: 5 patients with cancer pancreas, 2 gall bladder carcinoma, 1 hepatic focal lesion, 1 hepatocelullar carcinoma, and 1 cancer esophagus. There were 11 patients (36.6 %) showed good block (two of them stopped the MST, one with cancer pancreas and the other one is suprarenal carcinoma), 5 of patients who showed good results presented with cancer pancreas, 3 hepatocelullar carcinoma, 1 hepatic focal lesion, 1 gall bladder mass, and 1 suprarenal carcinoma. There were 6 patients (20.0%) showed mild block, 1 patient for each of cases with cancer stomach, duodenal mass, right colon cancer , HFL, HCC, and gall bladder mass. There were 3 patients (10.0%) showed failed block, 1 patient presented with hepatic focal lesion, 1 cancer stomach, and 1 retroperitoneal mass. It was observed that all the patients presented with pancreatic cancer were in zone of excellent (5 patients of total 10), and good (the other 5) blocks and they did not give failed results at all.

The recorded complications (table 3) were abdominal colic observed in 10 cases (33.3%), diarrhea in 11 cases (36.6%), hypotension in 8cases (26.6 %), injection pain in 9 cases (30.0 %), and backache in 3 cases (10.0 %). No major complications were recorded (e.g.; pneumothorax, chylothorax or paraplegia which more serious one).

Discussion:

Pain is one of the most common presenting symptoms in a cancer patient. It occurs in 30% to 50% of patients with active therapy and 60% to 90% of patients with advanced disease. Cancer patients with pain report significantly lower levels of performance status than those without pain with higher levels of perceived disability and a lower degree of activity. The experience of cancer pain may also result in disruption to family (9). Opioids remain the mainstay of cancer pain management, but due to long-term consequences of side effects and evidence suggesting that chronic use of high doses of opioids may have a negative effect on immunity, thus the analgesic techniques that lower opioid consumption should have positive effects on patient's outcomes (10).

Abdominal and pelvic visceral pain is conveyed by sensory afferents that travel with the sympathetic and parasympathetic system. Recently, the thoracic splanchnic nerves block has gained renewed interest

because they exist in a less variable anatomical relationship with surrounding structures, as they lie in a small triangular space with well-defined landmarks and boundaries. Thus, they are a perfect target for interrupting these pain signals because they are contained in a narrow compartment, which is defined medially by the vertebral bodies, laterally by the pleura, ventrally by the posterior mediastinum, and dorsally by the pleura attachment to the vertebra. This compartment is limited caudally by the crura of the diaphragm (3) and is therefore easier to reach offering advantages over the more used conventional celiac plexus block. Thus, the potential for more accurate needle placement reduces the risk of iatrogenic damage to other structures. On the other hand, chemical neurolysis is the only possible method of celiac plexus neurolysis as it has large size with wide distributing area which cannot be covered by RF lesion and needs for larger amount of alcohol for neurolysis with more incidence of toxicity and other related complications of alcohol spread. In addition it does not always lead to adequate pain control, possibly due to degeneration and fibrosis of nerves, ganglia and nerve-adjacent tissues from the injected chemical substances. Also the difficult technique if there is large multiple lymph nodes or ascitis (2).

Many studies comparing between chemical neurolytic CPB and bilateral SNB as: Ozyalçin et al., compared CPB (19 patients) and bilateral SNB (20 patients) in body and tail located pancreatic cancer, Shwita et al., assessed the effectiveness upon a 6 months follow up for 60 patients with upper GIT tumors, and Marra et al., performed SNB under guidance of computed tomography. All of these studies reported that the VAS values and opioid consumption in the SNB decreased more than CPB with more improvement of quality of life and patient satisfaction in SNB. Although, all scores decreased significantly in both groups and all deteriorated over the time (11), (12), (13). Those results confirm previously published experience and support the use of SNB instead of CPB (14), (15), (16), (17). A multicenter randomized control trial of 65 patients with pancreatic and upper abdominal cancer found that no difference in pain relief or opioid consumption between patients who underwent medical management versus celiac plexus neurolysis or thoracic splanchnicectomy (18).

The first percutaneous approach to SNB was described by Kappis in 1914 (19). The first splanchnectomy for intractable pancreatic pain was performed in 1942 by Mallet- Guy (20). In a series of 215 patients by the same author, 89% of patients treated obtained prolonged pain relief (21). Splanchnic nerve interruption can be performed at open operation (22), thorascopically (23) or percutaneously (24). Traditionally, chemical neurolysis of SNB with 10 mL of absolute 100% alcohol or 6–10% phenol has been performed and they produce a block that lasts 3 – 6 months (16). However, they may cause inflammation and necrosis wherever they spread into the surrounding tissues. This can cause denervation of nerve roots and secondarily produce persistent pain, parathesia, paraplegia and/or neuritis. Another result could be damage to important blood vessels such as adamkiewicz's arteries, even if the needle is placed correctly. One can hypothesize that the technique which could be safer and reliable if the needle tip itself produce neurolysis; radiofrequency (RF) lesion could produce that point (4).

In our study, the SNB was done by retrocrural approach by fluoroscopy using TRF at new levels of Th10 & Th11 (which was not in agreement with what was first described by Raj et al, who performed SNB at levels of Th11 & Th12). The lesion was done at 85°C for 90 seconds. The temperature was higher and the duration was longer than what was done in the study by Raj et al., (80°C for 60 sec) (25). Another lesion was done after rotation of needles 180 degrees to complete the ablation.

The advantage of level of Th10 is that level represents the site of intersplanchnic connections between GSN and LSN which was observed by Naidoo et al., (26), also it is the site of intermediate splanchnic ganglion which is usually found in the lower part of the course of the GSN at the interval between GSN and LSN (27). So the block of SN at this level may help in ablation of the two most major supplying nerves and intermediate splanchnic ganglion.

The common known cause of limitation of use of the higher level of Th10 for TRF of SNB and also do it bilaterally in the same session is the fear from occurrence of pneumothorax as Th10 level is more close to lungs and pleura (28). So to reduce the risk of pneumothorax, we moved the C-arm to a 15° oblique position not more than that to ensure close approximation of the needle to paravertebral space and this was recommended by Puylaert et al., (29). This made the final entry point at junction between rib and vertebra at the distance of 3–4 cm paravertabrally which is away from lung. However, clinical experience with the technique, as well as adequate information delivered to the patients regarding overnight stay close to a medical center

and examination by medical personnel before leave, was essential in avoiding such complications in this study.

In our study, the median of VAS, opioid consumption (MST) were reduced from first day of block and the reduction stayed significant until the end of the follow-up period after 3 months. There were slight increase in score values observed after 3 months due to the progression of the disease but the scores were still significantly lower than the basal values. There were 12 patients (40.0%) showed complete pain relief (VAS= 0 – 1) and they stopped MST. This good results till the end of our study, may be due to many reasons as: we blocked the splanchnic nerves at higher level of Th10, used curved needles in tangential manner and large sized electrodes with long active tip (20 G → Lesion with a radius of 2 mm), the most high temperature and longest duration of lesion known in clinical use, with another lesion after rotation of RF needle 180 degree and lidociane with dexamethasone were injected immediately before the lesion. All of the above was done at two levels bilaterally in one session as GSN ends in celiac gland at both sides and interventional cancer pain management must be multi-station. Also lesions of splanchnic nerves which in contact with vertebral body bones (of high electrical resistance) may be large in size or regular in shape as heat generated may be not washed rapidly by blood or CSF increasing local tissue temperature rise and lesion size which may help in effective pain relief (25).

In concordance with our results, the study of Papadopoulos et al., in which they used same lesion setting parameters of TRF for SNB but at levels of Th11 & Th12 bilaterally in 30 patients presented with end stage pancreatic cancers, Pain scores and consumption of fentanyl was significantly reduced during the first 4 postoperative months compared to baseline values in all patients. At 5 months, a slight increase in opioid consumption, but there were no statistical significance compared with baseline values (6).

In Garcea et al., study which on line with us, 10 patients with non-malignant chronic pancreatic pain examined for the efficacy of the TRF for SNB which was done by 3 lesions at level of T12 bilaterally; each lesion was produced at 80º C for 60 s, all patients experienced a decrease of their pain scores and all were weaned of opioid following TRF and this was found to be statistically significant (4).

In agreement with us, the study of Verhaegh and his colleagues in which the percutaneous TRF of splanchnic nerves in 11 patients with chronic pancreatitis was done at T11 & T12 level with 2 lesions were done with lesion for 60 seconds at 80°C and in the case of bilateral pain, the procedure was repeated on the opposite side. The mean of numerical rating scale (NRS) of the whole group decreased significantly, all patients showed reduced (4 cases) or stopped (4 cases) analgesic drugs postprocedural. The 3 non-responders continued their usual doses of analgesics (8).

In studies that discussed success rates of TRF, one of the earliest and largest studies performed by Raj et al., using TRF for SNB in 107 patients with abdominal pain of malignant and non-malignant origin, The series reported that 40% of patients showed excellent block (defined as a reduction in pain by using a VAS of 50 – 75%) and revealed good block in 55 – 70% of patients, with only a 15% of patients showed poor results (pain reduction of less than 10%)(28). This was consistent with our results. Also the study of Verhaegh et al., results agreed with ours as an excellent block (> 75% reduction in pain score) was obtained in 6 (33%) patients. A good (> 50% reduction) was obtained in 14 (78%) patients. 2 patients were completely pain-free (NRS = 0) (8).

It seems that the patients with pancreatic cancer were the most responding type of patient to TRF in this study and this result were in agreement with other studies which were done on chronic pancreatic diseased patients (4), (6), (8).

Reasons for failure of RF ablation are poor electrical connections (cable damage is commonest), poor needle placements, temperature selected is too low and finally misdiagnosis (5). All of the above hazards were taken into our consideration while conducting this study which led to increased success rate. De Leon-Casasola had explained the cause of failed block; as that pain associated with cancer may be somatic, visceral, or neuropathic type. Approximately 50% of cancer patients experience a combination of pain types at same time of diagnosis. Also, most patients referred to cancer-related symptoms management have at least 2 anatomically distinct pain sites; more than 40% have 4 or more sites (30).

Regarding complications of the blocks in our study, diarrhea, hypotension, and abdominal colic were observed in 36.6%, 26.6% and 33.3% of patients respectively. Injection pain was observed in 30.0 % due to burning effect of thermocoagulation, this could be overcomed by injection of LA agent, steroid and small dose of sedating drugs. Backache was observed in 10.0 % as it was related to 4 needles

insertion and it was managed by non-steroidal analgesia if persisted. Most of complications were transient (lasting < 7 days), and resolved spontaneously without treatment and did not affect the acceptance and efficacy of the technique. Hypotension was treated by intravenous fluids. No major complications were recorded (e.g.; pneumothorax or paraplegia).

The complications in the studies of TRF for SNB were not different from our complications as: in Papadopoulos et al., included temporary diarrhea in 11 patients and temporary intestinal colic in 5 patients (6), in Garcea et al., study also only self-resolving diarrhea was reported (4), and in Verhaegh et al., only temporal hypoesthesia of the flank was reported (8).

Conclusion:

Our results suggest that bilateral thoracic splanchnic nerve radiofrequency thermocoagulation at double level of Th10 & Th11 in the same session significantly reduced abdominal cancer pain, reduced consumption of oral opioids and give good functional improvement. It may offer a minimally invasive, safe, and effective technique for the management of all types of abdominal cancer pain rather than pancreatic cancer pain. Expertise with the technique and adequate information delivery to patients are essential for minimizing the risk of perioperative pneumothorax.

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		No	%
	males	17	56.6
	les	13	43.4
	al	30	100.0

Table (1) Demographic data of patients included in this study

	an	ndered deviation	lue
(Years)	30	15.00	
gth of hospital stay (Hours)	0	3.50	

Table (2) Of Age and length of hospital stay

Table (3) shows the complications

Complications	No	%
c	20	66.6
	10	33.3
al	30	100.0
rhea	19	63.3
	11	36.6
al	30	100.0
otension	22	73.3
	8	26.6
al	30	100.0
ction pain	21	70.0
	9	30.0
al	30	100.0
kache	27	90.0
	3	10.0
al	30	100.0

	Median	Range
VAS before	7.00	4 – 8
VAS Day1	3.00	2 – 5
VAS week1	1.50	0 – 4
VAS week2	1.75	0 – 3
VAS week4	1.50	0 – 3
VAS week8	2.00	0 – 3
VAS week12	2.50	0 – 4
alue for time effect	**< 0.001***	

Table (4) Comparison of VAS scores over study period

VAS : Visual analogue scale

	Median	Range
Morphine EAD before	25.00	10 – 650
MEAD Day1	10.00	0 – 180
MEAD Week1	0.00	0 – 75
MEAD Week2	0.00	0 – 45
MEAD Week4	0.00	0 – 45
MEAD Week8	0.00	0 – 45
MEAD Week12	5.00	0 – 50
value for time effect	**< 0.001**	

Table (5) Comparison of Morphine EAD over study period

MEAD: Morphine Effective Analgesic Dose

Fig (1) in oblique view showing end on appearance of needles at level of T10

Fig (2) in lateral view showing needle tip at junction of anterior 1\3 and posterior2\3 at T10

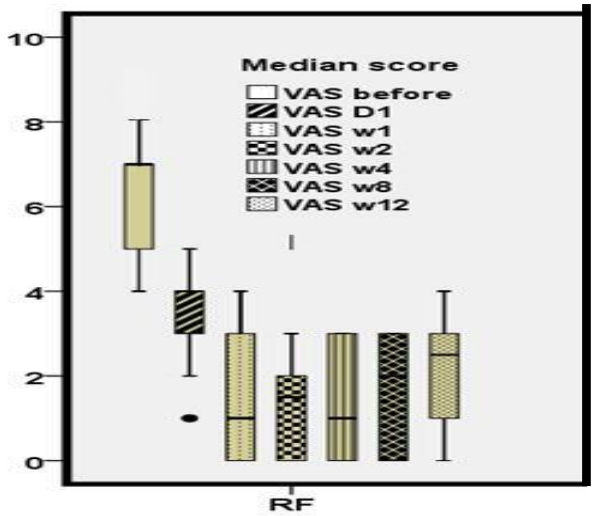

Figure (3) Comparison of VAS (Visual analogue scale) score over study period

D1: 1st Day
W1: 1st Week
W2: 2nd Week
W4: 4th Week
W8: 8th Week
W12: 12th Week

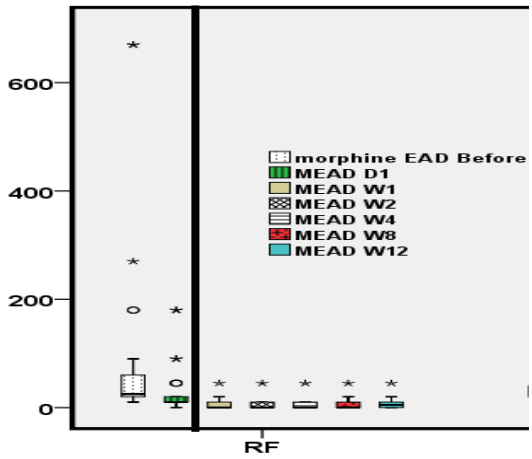

Figure (4) Comparison of Median Morphine Effective Analgesic Dose (MEAD) over study period

D1: 1st Day
W1: 1st Week
W2: 2nd Week
W4: 4th Week
W8: 8th Week
W12: 12th Week