ORIGINAL RESEARCH

Role of Neurolytic Celiac plexus block in palliative cancer care: A Prospective Non-randomized comparative study

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Abstract
Background: Neurolytic celiac plexus block (NCPB) is used for managing the refractory abdominal pain that originates from the upper abdominal viscera. It involves Injecting a neurolytic medication around the celiac artery destroying the function of the celiac plexus, interrupting the pain pathway and thus reducing the intensity of cancer pain.
Materials and methods: This prospective non-randomized study was conducted by the Department of Anesthesia, SKIMS, J&K in collaboration with the Department of Radiodiagnosis and the artment of medical oncology. Patients with pancreatic head and Gall bladder cancer with clinically mptomatic pain who met the inclusion/exclusion criteria were finally selected for the study. Out of the selected patients, two groups were made, one who received the Intervention (NCPB) and another group who received conservative pain management (Oral Morphine, Fentanyl transdermal patch and NSAIDs) Out of 64 patients selected, 29 were treated by NCPB and 35 were treated by conservative management. These patients were followed up on the 15th, 30th, 60th and 90th day to record the Visual analog pain scores (VAS) and any complications related to the procedure.
Results: VAS scores in the intervention decreases group from (9.09±0.53) to (3.09 ± 0.52) on the 15th day to 3.10±0.67 on the 30th day to 3.27±1.00 on the 60th day and 3.90±0.83 at 90th day. VAS scores also decrease in the conservative group from 9.6±0.59 to 6.60±0.47 on the 15th day to 6.95±0.99 on the 30th day to 6.5±1.29 on the 60th day and from 7.45±1.42 at 90th day**.** However, the p-values obtained at all observation points (15th, 30th60th and 90th day) indicate a statistically significant difference between the two groups on the measure of pain. This suggests more pain relief in the intervention group. Both groups show a significant change (p-value <0.05) compared to baseline, but the maximum pain alleviation was noted in the first 15 days in both groups which was maintained after 90 days. The intervention group showed a steep fall (- 6 points) in VAS as compared to a gradual decrease (-3 points) in the conservative group at the 15th-day follow-up, concluding that conservative treatment has a slower effect on pain relief compared with the early response after celiac plexus block.
Conclusion: NCPB provides early and significant pain improvement in pancreatic head and gall bladder cancer pain in comparison to conservative management.
Keywords: Neurolytic Celiac plexus block, Palliative care, Pancreatic cancer, Gall bladder cancer

INTRODUCTION

Cancer pain management has evolved in the last three decades with new less invasive techniques coming up. Neurolytic celiac plexus block (NCPB) is one of those procedures used for managing the refractory abdominal pain that originates from the upper abdominal viscera. The term celiac plexus refers to a network of nerve fibres located in the retroperitoneum, along the anterolateral wall of the aorta and special visceral afferent fibers relay through the splanchnic nerves and celiac plexus.

Imaging-guided celiac plexus block and neurolysis are invaluable therapeutic options for and have been widely used since their introduction by Kappis et al. in 1914 (1). Celiac plexus block and neurolysis slightly differ in terms of duration of action where Celiac plexus block refers to temporary disruption of pain transmission via the celiac plexus using steroids or local anesthetics and celiac plexus neurolysis block, refers to permanent destruction of the celiac plexus with ethanol or phenol.

The celiac plexus is composed of a dense network of interconnecting presynaptic sympathetic nerve fibres

derived mainly from the greater (T5–T9), lesser (T10–T11), and least (T12) splanchnic nerves. It is anterior to the crura of the diaphragm, over the anterolateral wall of the aorta bilaterally, and just caudal to the level of the origin of the celiac artery. It can be located anywhere from the T12–L1 disk space to the middle of the L2 vertebral body. The celiac plexus supplies sympathetic, parasympathetic, and visceral sensory afferent fibres to the pancreas, liver, biliary tract, gallbladder, renal pelvis and ureter, spleen, mesentery, and bowel proximal to the transverse colon (2,3). Injecting a neurolytic medication around the celiac artery destroys the function of the celiac plexus, and interrupts the pain pathway (4). The interruption of nociceptive pathways through neurolysis of the sympathetic plexus could reduce the intensity of cancer pain by 70–90% (5,6). Haaga and colleagues first used the CT in guiding neurolytic celiac plexus block, since then, CT has superseded fluoroscopy or endoscopic USG (Ultrasound) guided celiac plexus block as the preferred technique, with its proven safety record (7,8). With multidetector CT guidance, needle placement into the region of the celiac plexus and the location of the needle near vital anatomic structures, such as the pancreas, aorta, celiac artery, and SMA, may be directly visualized. Broadly the neurolysis procedure can be dived into anterior and posterior approaches. The posterior paravertebral approach is the most frequently performed for neurolysis. With this approach, the neurolytic agent is injected into the intercrural space by placing needles on each side by way of a posterior paravertebral route.

STUDY DESIGN

This Prospective study was conducted by the Department of Anaesthesia, (Sher I Kashmir Institute of Medical Sciences) SKIMS, J&K in collaboration with the Department of Radiodiagnosis and the Department of medical oncology. Institutional ethics committee approval and informed consent were taken from the patients.

Sample Size estimation was done using G-POWER software (v3.0.1.0; Franz Faul Keil University, Keil, Germany). It was estimated that the minimum number of patients required should be 27, Provided 80%. Power, the effect size of 0.4 and 5% significance.

Patients referred from medical oncology were enrolled for the study.Those who fulfilled. the inclusion & exclusion criteria were finally selected for the intervention group.

Inclusion Criteria

1. Histologically or Radiologically proven Gall bladder or pancreatic head malignancy
2. Pain measured more than 4 out of 10 on a numeric scale(Visual analogue scale).

Exclusion Criteria

1. Bleeding diathesis /Coagulopathy
2. Known allergy to local anaesthetics.
3. History of aortic aneurysm
4. A moribund patient who cannot lie prone for several minutes
5. Prior Contrast-enhanced CT showing the eccentric origin or variable anatomy of the celiac axis.
6. Patient with distant metastasis.
7. A patient who refuses to give consent for the procedure

Intervention (NCPB) was performed in the first group and post-procedure these patients were kept off the pain medications and were prescribed pain medications only if the pain does not subside or reoccur. The second group received the conservative treatment which includes Morphine tablets (20- 40 mg BD), Fentanyl transdermal patch and NSAIDS.

Our intervention arm had 29 Patients and the conservative arm have 35patients.

MATERIALS USED FOR CELIAC PLEXUS BLOCK

Equipment/Materials that were used during the study-

1. Computed tomography unit (Siemens, Somatom Sensation 16 slice)
2. 22 or 23 G Chiba needle (by COOK, 15 cm length), 5 cc Luer loc syringes
3. Local anaesthetic (a long-acting agent, Bupivacaine) and Iodinated contrast agent (Omniopaque 300)
4. Ethanol (60 % solution)
5. Sedatives (midazolam and fentanyl)

PROCEDURE

The patient was prepared in the ward in the morning on the day of the procedure and baseline (preop) Visual analog scores(VAS) were recorded just before the procedure. Intravenous infusion of Ringer'slactate solution was started 2-*3* h before the block to reduce the risk of post-procedure hypotension. The patient was positioned prone on the CT table with cushions placed under the abdomen to make the region of interest in the spine prominent. Under CT guidance, we plan the entry of approx. 5 to 8 cm away from the midline below the twelfth rib, between the Celiac axis and superior mesenteric artery origin (SMA). The entry site was painted using povidone Iodine and Local infiltration with *1%* lidocaine (5-10 ml) was done. 22 or 23 G Chiba Needle was advanced slowly under CT guidance and final position (Anterior to the diaphragmatic crura in para midline location, just lateral to aorta between Celiac axis and SMA origin) A bilateral transcranial preaortaic celiac plexus block was performed by 5mllignocaine mixed with 5 ml iodinated contrast on each side, in the first step. Then 20 ml of 60% ethanol solution was injected on either side (Final volume of 30 ml) in the next step. The first step helps in confirming the needle tip location and reducing the pain caused by the ethanol. Sedatives were not routinely used during the procedure, only some patients were premedicated with the above-

mentioned sedatives.Patient blood pressure, heart rate, and oxygensaturation was monitored during the procedure, After the procedure, the patients were shifted to the recovery room where they were kept prone for another half hour and not allowed to walk for another 4-5 hours to reduce the risk of hypotension. Post-op VAS scores were recorded after 24 hours. Further, follow-up (done on Day 14th, Day30th, Day 60th, and Day 90th after the procedure) was made by a separate doctor telephonically with the patient or by personal contact with the patient during the follow-up. The intensity of pain was evaluated by a VAS scale in which 0 meant 'no pain' and 10 meant ‹the worst possible pain.

STATISTICAL ANALYSIS

The recorded data was compiled and entered in a spreadsheet (Microsoft Excel) and then exported to the data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). The age and sex distribution of the patients between the groups were calculated by the t-test and the chi-squared test, respectively. The differences in the VAS scores were statistically compared by the t-test, and differences were considered significant when $P < 0.05$.

RESULTS

No significant differences were observed between the two groups about age, gender. All patients experienced effective pain relief after the celiac plexus block regardless of the time of pain duration, severity, or pain medication.Three patients (1 in the intervention group, and 2 in the conservative management group) died of cancer and could not be followed for 90 days, so 28 patients from group 1 and 33 patients from group 2 is being part of the final statistical analysis. Data regarding the VAS results are shown in Table 1and Fig. 1. After CT-guided NCPB, all patients in group 1had effective pain relief, as shown by changes in their VASscore (9.09 ± 0.53 before treatment, decreasing to 3.09 ± 0.53after treatment, and 3.9 ± 0.83 at day 90, $P < 0.05$).

VAS scores of those in group 1 weresignificantly lower than those in group 2 ($P < 0.05$) even atdays 60, and 90.

PAIN STATUS

Table 1: Comparison of Pain scores between both the groups at different timelines

Timeline	Intervention Group (mean±sd)	Conservative Group (mean±sd)	p-values
Baseline VAS	9.09±0.53	9.6±0.59	**More than 0.05**
Day 15th VAS	3.09±0.52	6.60±0.47	**<0.05**
Day 30th VAS	3.10±0.67	6.95±0.99	**<0.05**
Day 60th VAS	3.27±1.00	6.5±1.29	**<0.05**
Day 90th VAS	3.90±0.83	7.45±1.42	**<0.05**

p<0.05 are significant at 0.05 level of significance (group 2 versus group 1, unpaired t-test)

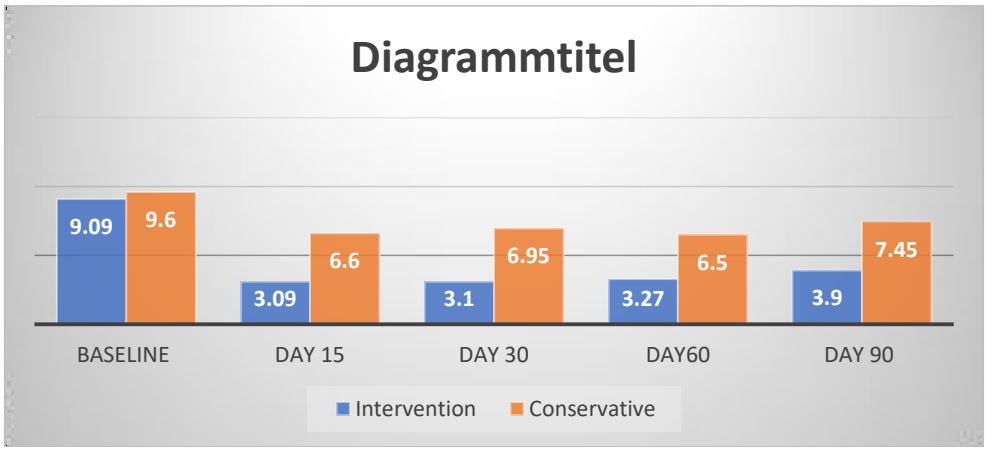

Figure 1: Comparison of Pain scores between both the groups at different timelines

Table and Figure :1 show a comparison of pain scores between both groups. At baseline, there is no statistically significant difference between the two groups on the measure of pain. The p-values obtained on Day 15th, Day 30th, Day 60th and Day 90th indicate a statistically significant difference between the two groups on the measure of pain. This shows better pain alleviation by Celiac axis block than conservative management and the maximum pain alleviation of is in the first 1 month.

The following complications were recorded: Orthostatic hypotension in 4 patients, diarrhoea in 2 patients, and local entry site pain in the 4 patients. However, all these were transient and were well tolerated.(Table 2).

TABLE: 2 Types of complications

TYPES OF COMPLICATIONS	NUMBER
Orthostatic Hypotension	4
Diarrhoea	2
Constipation	0
Local site pain	4
Drunkenness syndrome	0
Vascular injury	0

Table: 2 shows that Complications are secondary to celiac plexus block.

DISCUSSION

Pancreatic or Gall bladder cancers often lead to intractable abdominal pain, and the standard approach to pain management is based on the three-step ladder of the World Health Organization (WHO), beginning with non-opioid analgesics (nonsteroidal anti-inflammatory drugs or acetaminophen), followed by weak opioids, and finally, strong opioids as necessary [9] Percutaneous NCPB has been proven to have long-lasting benefits in 70%–90% of patients with various upper abdominal cancers, regardless of the technique employed (10). Ischia et al. used this in patients with pancreatic cancer with considerable success. (11,12) while some authors have also employed this procedure in chronic pancreatitis pain. (13) The major benefit of celiac plexus block in cancer care is the reduced rate of analgesic consumption and lower incidence of drug-related adverse effects. Rykowski et al. (17) in their study have shown more pain relief in pancreatic head cancers than the cancers of the pancreatic body and tail region. This may be due to multi-factorial pain origin in the body and tail cancers (like the involvement of peritoneal, retroperitoneal and somatic structures etc.). Therefore we didn't include the pancreatic body and tail cancer patients. Ischia et al. in their study showed that better pain relief was seen in patients with a shorter time of onset of pain to neurolytic block, thus the duration of the procedure also becomes critical in the outcome. In our study, the time from diagnosis to the celiac plexus block was *7 to**10*** weeks (mean, 45days). However, we could not confirm these findings in our study as the mean time to procedure was more in our study because most of the patients were treated pharmacologically before being referred for the intervention, so there is a slight delay in the intervention compared to the study. (11) Our results show a clear improvement in the pain status of the patients. There is a decrease in VAS scores in the intervention group from (9.09±0.53) to (3.09 ± 0.52) on the 15^{th} day to 3.10±0.67 on the 30^{th} day 3.27±1.00 at 60^{th} day and 3.90±0.83 at 90^{th} day. VAS scores also decrease in the conservative group from 9.6±0.59 to 6.60±0.47 on the 15^{th} day to 6.95±0.99 on the 30^{th} day to 6.5±1.29 on the 60^{th} day and from 7.45±1.42 at 90^{th} day **(Table 1).** However, the p-values obtained at all observation points (15^{th}, $30^{th}60^{th}$ and 90^{th} day) indicate a statistically significant difference between the two groups on the measure of pain. This suggests more pain relief in the intervention group. Both groups show a significant change (p-value <0.05) compared to baseline, but the maximum pain alleviation was noted in the first 15 days in both groups which was maintained after 90 days. The intervention group showed a steep fall (- 6 points) in VAS as compared to a gradual decrease (-3 points) in the conservative group at the 15^{th}-day follow-up, concluding that conservative treatment has a slower effect on pain relief compared with the early response after celiac plexus block. NCPB is considered a safe procedure but sometimes serious complications can occur like celiac axis and SMA injury. The complications rate was considerably high (10 out of 28) but all the complications were transient and well tolerated. Postprocedural hypotension can be avoided by fluid loading doe and by maintaining the post-procedure supine posture for a few hours. Local site pain was also relieved in few days after the procedure without any extra treatment. Although all precautions were taken to make the study methodologically strong, however, still some of the limitations could not be avoided. Randomization was not done, as it could raise ethical issues. To reduce bias, the doctor recording postoperative pain scores and other parameters was blinded to group allocation. Following are the strengths of our study: 1. This is a dual-arm study comparing the procedure with conservative management. 2. Follow up of patients were done for 3 months, to find the long-term effect and complications of the procedure 3. No significant patient dropout rates during the follow-up. In conclusion, NCPB has emerged as an effective and virtually complication-free technique in palliative care armamentarium for intractable cancer pain.

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