Pain Outcomes After Celiac Plexus Block in Children and Young Adults with Cancer

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Purpose: The use of celiac plexus block (CPB) for abdominal pain has been extensively reported in adults. However, pediatric literature is limited to three single case reports and a series of three cases. This study evaluated the effectiveness of CPB in children and young adults (aged 8–20 years) with abdominal malignancies.

Methods: Pain outcomes after CPB were evaluated in four children and young adults with cancer. Mean daily pain score (PS, 0–10) and morphine consumption (intravenous morphine equivalent daily [MED], mg/kg/day) before and after CPB were used to assess effectiveness.

Results: Mean daily PS reduced after CPB in all patients. In one patient, this reduction was sustained up to 6 months of follow-up, and analgesics were discontinued 1 week after CPB. The other three patients had limited survival (6, 16, and 37 days) after CPB. One patient had a PS of 0 over the last few days of life, but the MED was escalated from 0.74 before the block to 5.4 mg/kg/day at the end of life. In the other two patients, MED was lower during the first week after CPB than that before CPB (4.55 vs. 1.59 and 2.88 vs. 1.51 mg/kg/day, respectively). As these two patients had disease progression during their last days of life, the MED was increased to 4.75 and 263.9 mg/kg/day, respectively.

Conclusions: Our results suggest that CPB may contribute to reducing PS and MED. We observed the use of CPB rather late in the disease trajectory.

Keywords: celiac plexus block, pain management, cancer, palliative care, pediatrics

Introduction

CELIAC PLEXUS BLOCK (CPB) is an invasive technique used for visceral upper abdominal pain,¹ most commonly reported for pancreatic cancer, and also described for pancreatitis, cirrhosis, inflammatory bowel disease, and cancers of the colon, liver, stomach, intestine, gallbladder, ovary, esophagus, lung, and appendix.^{2,3} CPB has also been employed more broadly for refractory hypertension and postoperative pain.^{4–6} Studies have supported earlier use, such as at the time of attempted surgical resection in pancreatic cancer, regardless of preexistent pain, or before aggressive opioid dose escalation.^{7–9} One study found improved CPB efficacy for pain duration of less than 2 months versus greater than 2 months.⁹

The majority of published CPB literature is concentrated on the adult population. Analgesic outcomes of adult patients with cancer-related visceral pain (most commonly pancreatic cancer) receiving CPB have been compared in 14 publica-

tions analyzed in a systematic review by Mercadante et al.¹ Compared with analgesics or saline, CPB improved analgesia and/or decreased opioid consumption and decreased opioid-induced adverse effects.¹ These beneficial effects have been shown to persist for at least 1–4 months.^{1,7}

CPB use outside of the adult population has been limited, based on a lack of recognition of appropriate indication or a perceived risk of invasive procedures in children.¹⁰ The entirety of the pediatric CPB literature is limited to four patients.^{4,11,12}

The first case of using neurolytic CPB in a pediatric patient was reported by Tanelian and Cousins³ in a 4-year-old boy with inflammatory bowel disease. Literature reporting the use of CPB in children with cancer includes a case of a 3-year-old boy with unresectable hepatoblastoma,¹¹ a 7-year-old child with neuroblastoma,¹² and in a series of three children receiving CPB to control abdominal pain, one patient had metastatic adrenocortical carcinoma.¹³ Pain control improved after CPB in these reports, as measured by decreased

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pain intensity and/or reduction of opioid medication,^{11,12} and by family members qualitatively reporting improvement in pain.¹³ Indications for CPB unique to the adolescent-young adult (AYA) population are less common, but case reports do exist.^{4,14,15}

To address the gap in the literature, we reviewed our single institution experience of four children and AYA with intra-abdominal malignancies receiving palliative treatment for refractory pain, with focus on pain outcome measures.

Methods

This retrospective study included four patients treated with CPB for severe cancer-related abdominal pain and was approved by the Institutional Review Board. The study included the first 2 years of experience with CPB in our institution, from June 2015 to June 2017. Patients were identified by the primary oncologist who referred the patients for CPB (S.M.F.) and the interventional radiologists (H.P., R.G.) who performed the procedures. Data on demographics, diagnoses, pain outcomes, CPB technique, and medications were collected from institutional medical records. Demographic data included age, gender, race, and weight. Data on quantitative pain outcomes were collected in two categories: (1) pain intensity based on an 11 point 0–10 numeric rating scale and reported as mean daily pain score (PS); and (2) opioid consumption reported as daily intravenous (IV) morphine equivalents daily (MED, mg/kg/day). Pain intensity data were collected from nursing documentation as all the PS documented for the abdomen and lower back and reported as mean PS over 24 hours. Our institutional standard requires nursing documentation of PS every 4 hours on the regular floor. For data collection of PS during outpatient visits, the mean PS was collected from the pain service notes. Opioid consumption included oral (PO) doses as short-acting and long-acting formulations and IV doses as scheduled doses or as patient-controlled analgesia (PCA), and was collected from the medication administration records and reported as cumulative doses over 24 hours. Conversions to IV morphine equivalents were based on opioid equianalgesic potency, using the following analgesic potency relationships: IV hydromorphone: morphine, 5:1; PO:IV morphine, 1:3; and PO oxycodone:PO morphine, 2:1. Opioid doses taken *pro re nata* were not included, as the precise quantity used in the outpatient setting could not be determined.

Adjuvant medications for pain including gabapentin, methadone, ketamine, muscle relaxants, steroids, and nonsteroidal anti-inflammatory drugs were noted but not reported as specific doses. Medications used for anxiety were also noted.

Pain outcome measures (PS and MED) were collected during the week before CPB and every day during the first week after CPB and then approximately every month up to 6 months. The time interval between diagnosis and CPB and between CPB and date of death were noted, if applicable.

Data on CPB technique, equipment, and medications and their doses used were collected from procedure operative reports and supplemented by narrative from the interventional radiologists (H.P., R.G.). Postprocedure adverse events were noted.

Procedural methods

The CPBs were given to hospitalized patients with advanced intra-abdominal malignancies who were receiving

palliative treatment. Before the procedure, patients were kept nil per os for at least 8 hours, and anticoagulants were temporarily discontinued to minimize the risk of bleeding. All CPB procedures were performed under general anesthesia with propofol or inhalational agents at the discretion of the anesthesiologist.

After induction of anesthesia, the CPBs were performed in the prone position by using the unilateral posterior paravertebral approach. Preoperative cross-sectional images of patients were reviewed in detail to determine patient position, computed tomography (CT) approach, needle entry site, needle path, and injection site for the neurolytic agent. For one patient in whom the tumor was nearly completely encasing the celiac and superior mesenteric arteries, weight-based IV iodinated contrast was injected and preplanning limited CT scan of the abdomen was performed at the level of the celiac artery to identify level of the aorta at the origin of the celiac artery. In the other patients, preplanning non-contrast CT of the upper abdomen was performed. The CT images were obtained by using a 256-row multidetector CT scanner (256 slice, Revolution CT; GE Healthcare). The appropriate trajectory for needle entry point was decided, and the site was marked on the skin before starting each procedure. Skin at the point of needle entry was cleaned with an antiseptic solution, and a sterile field was prepared.

In the first two patients, a 22-gauge China needle (Cook Medical) was used. In the subsequent two patients, a 21-gauge co-axial Pakter curved needle set (Cook Medical) was used. The choice of needle was operator dependent. The needle was inserted through the marked site and advanced toward the celiac plexus region under CT fluoroscopic guidance. The needle was advanced alongside the vertebral bodies into the antecrural space, taking care to avoid the ribs, lungs, pleura, transverse processes, vertebral bodies, kidneys, and major vascular structures. When the needle tip was accurately placed beside the aorta at the site of the celiac artery origin or in-between the celiac trunk and the superior mesenteric artery level, negative aspiration was used to ensure that the needle tip was extravascular. Next, 1 mL of 1:10 normal saline-diluted iodixanol 270 mg/mL (Visipaque™ 270; GE Healthcare) contrast was injected and CT fluoroscopic images were obtained. After confirming that the needle tip was in the appropriate para-aortic fat plane (Fig. 1), a prepared mixture of neurolytic agent was slowly injected under CT fluoroscopic guidance. The mixture comprised ethanol (98%), bupivacaine (0.5%), and iodinated contrast (iodixanol 270 mg/mL) in a 6:3:1 ratio. The maximum total dose of ethanol (98%) was 1 mg/kg, up to 50 mg. The endpoint of the procedure was either complete injection of the maximum dose or acceptable distribution of contrast material in the retroperitoneal space around the celiac and superior mesentery artery origins, based on CT scan images. The distribution appeared hyperdense on CT images (Fig. 2).

During the immediate postprocedure period, patients were placed on bed rest for at least 12 hours. Cardiorespiratory status, including blood pressure, heart rate, and other vital signs was regularly monitored. Adequate fluid replacement in the form of IV fluids was given as needed. In the immediate postprocedure period and postprocedure day 1, a focused neurologic evaluation was performed to check for neurologic complications.

FIG. 1. CT fluoroscopic image of needle tip in the para-aortic fat plane. CT, computed tomography.

Results

The patients were 8 (patient #3), 14 (patient #2), 19 (patient #4), and 20 years old (patient #1), with diagnoses of rhabdomyosarcoma, hepatoblastoma, primitive neuroectodermal tumor, and rhabdomyosarcoma, respectively. Table 1 compares pain outcome measures after CPB for our patients and those from previous pediatric studies. Table 2 shows pain outcomes after CPB for the four patients in our study. Compared with PS before CPB, mean daily PS reduced 1 week after CPB for all four patients in our study. The mean daily PS of the entire group before CPB and in the week after CPB was 4.55 (range 2.6–8.6) and 0.5 (range 0–2), respectively. One patient (#2) was weaned off opioid pain medications 1 week after CPB and has remained off scheduled opioids for 6 months. This patient received a liver transplant and survived. The other three patients had a limited survival of 6, 16, and 37 days after CPB. The patient (#4) who survived 6 days after CPB had a PS of 0 over the last 3 days of life, but the MED was increased from 0.74 before CPB to 5.4 mg/kg/day at the end of life. In patients who survived 16

FIG. 2. CT fluoroscopic image of the acceptable distribution of contrast material in the retroperitoneal space around the celiac and superior mesentery artery origins. The distribution appears hyperdense (white) on CT images.

(#3) and 37 (#1) days after CPB, MED was reduced during the first week after CPB, from 4.55 to 1.59 and from 2.88 to 1.51 mg/kg/day, respectively. As these two patients had disease progression at numerous sites outside the abdomen in their last days of life, the MED was escalated to 4.75 and 263.9 mg/kg/day, respectively (Table 2).

Table 3 details the technique, equipment, and medications used for CPB. All CPBs were CT-guided ablative blocks with absolute alcohol, in addition to the local anesthetic, using 20–50 mL of absolute ethanol divided para-aortic bilaterally by using the unilateral posterior paravertebral antecrural approach. In two patients (#3 and #4), the 21-/25-gauge coaxial curved needle set, a novel equipment that facilitates the deposition of ablative medication at two locations through a single needle placement, was used. Adjuvant pain medications included gabapentin, methadone, ketamine, muscle relaxants, steroids, and nonsteroidal anti-inflammatory drugs (Table 3). Medications for anxiety included benzodiazepines and haloperidol (Table 3).

All patients had normal vital signs during and immediately after the procedure. Except for transient diarrhea for 1 day in one patient, no other adverse events were noted.

Discussion

Few pediatric studies have reported the use of CPB for severe visceral abdominal pain related to malignancy. Berde et al.¹¹ noted an improved quality of life and decrease in pain medications after CPB for a pediatric patient with hepatoblastoma and that CPB provided excellent pain relief without the sedation and respiratory depression associated with systemic opioids.

Staats and Kost-Byerly¹² reported CPB in a 7-year-old girl with metastatic neuroblastoma who showed decreased pain scores on the faces scale and the visual analog scale; reduced opioid requirement; and less adverse effects of pruritus, nausea, and vomiting. The patient experienced pain in the left shoulder, a relatively common transient side effect of celiac plexus neurolysis in adults. One month later, the patient's pain was under control and she was able to spend a week at Disney World. However, in subsequent weeks, the patient's opioid requirement increased and she died at home 11 weeks after CPB.

Goldschneider et al.¹³ reported the use of a new radiologic technique called three-dimensional rotational angiography for performing retrocrural CPB in three children and young adults: a 5-year-old boy with chronic pancreatitis, whose mother reported that he had 3–4 weeks of moderate relief after CPB; a 19-year-old man with metastatic adrenocortical carcinoma, who experienced good analgesia for 3 weeks; and a 5-year-old boy with mitochondrial disorder, whose mother reported considerable reduction in his pain and greater participation in usual activities.

Our study is the first to report quantitative pain outcomes by using an approach of serial timepoint evaluations of pain outcomes (PS and MED) before and after CPB and, despite the small sample size, represents the largest case series to date in children and AYA with cancer suggesting that CPB can reduce pain intensity and/or opioid consumption in children and young adults with cancer.

We found considerable reduction in MED in three of four patients (patients 1–3) within 1 week of CPB. Patient 4

TABLE 1. STUDIES ON CELIAC PLEXUS BLOCK IN CHILDREN AND YOUNG ADULTS

Author (year)	Patient characteristics	CPB data	Pain outcome measures		
			Pain score	Opioid use	Other
Tanelian and Cousins (1998) ³ N=1	4 y/o M (weight not given) Inflammatory bowel disease	Block 1: Fluoro-guided neurolytic CPB with alcohol Block 2: CT-Guided neurolytic CPB with alcohol	Not reduced	Not reduced	NA
Berde et al. (1990) ¹¹ N=1	3 y/o M (11 kg) Hepatoblastoma	CT-guided neurolytic CPB with alcohol	Reduced	IV morphine decreased from 79 to 7 mg/kg/day over 10 days	Clonidine patch
Staats and Kost-Byerly (1995) ¹² N=1	7 y/o F (18 kg) Metastatic neuroblastoma	Fluoro-guided neurolytic CPB with alcohol	Reduced	Reduced	Decreased opioid-related adverse effects (e.g., pruritus, enuresis)
Goldschneider et al. (2007) ¹³ N=3	5 y/o M (22 kg) Acute chronic pancreatitis	Bilateral retrocrural 3-dimensional rotational angiography CPB technique with local anesthetic and steroid	Reduced	Discharged without any analgesic medications 1 week later	
	19 y/o M (weight not given) Metastatic adrenocortical Carcinoma		A 3- to 4-week moderate relief as per mother's report	NA	NA
	5 y/o M (weight not given) Mitochondrial Disorder		Good relief for 3 weeks	NA	NA
			Significant reduction in pain over 3 weeks as per mother's report	NA	NA
	20 y/o M (66.1 kg) Rhabdomyosarcoma 14 y/o M (34.8 kg) Hepatoblastoma	CT-guided neurolytic CPB with alcohol CT-guided neurolytic CPB with alcohol	Reduction for 3 weeks Increase before death Decrease in duration of follow-up (6 months) PS=0	Reduction for 3 weeks Increase before death No use of opioids after 6 days after CPB	Ketamine infusion Gabapentin Methadone
Current study N=4	8 y/o F (18.3 kg) Rhabdomyosarcoma	CT-guided neurolytic CPB with alcohol	Decrease for the first week Increase at time of death (day 16)	Decrease for the first week	Methadone
	19 y/o M (59.1 kg) Primitive neuroectodermal tumor	CT-guided neurolytic CPB with alcohol	Decrease for 6 days until death (day 6)	Increase at time of death (day 16) Increase	Methadone

CPB, celiac plexus block; CT, computed tomography; F, female; IV, intravenous; M, male; N/A, not applicable; PS, pain score; y/o, years old.

TABLE 2. PAIN OUTCOMES AFTER CELIAC PLEXUS BLOCK

Patient characteristics	Time from diagnosis to CPB/Survival post CPB (days)	Pain outcomes: IV MED/mean daily PS			
		Preblock IV MED/PS	Within 1-week postblock IV MED/PS	1 week to >1-month postblock IV MED/PS	
#1—20 y/o M Recurrent refractory RMS of the chest wall with abdominal metastases	1484/37	2.88/2.6 d - 5	1.51/0 d + 3	1.01/0 d + 12	1.26/0.67 d + 20
#2—14 y/o M Metastatic hepatoblastoma	49/Alive	0.56/3 d - 1	0.63/0 0.53/0 0.28/0 d + 1 d + 5 d + 6	1.92/3 d + 18	1.8/3.5 d + 19
#3—8 y/o F RMS paraspinal abdominal	1493/16	4.55/4 d - 4	1.59/0 1.99/0 d + 1 d + 5	4.75/6 d + 10	
#4—19 y/o M Progressive, refractory, metastatic adrenal PNET	536/6	0.74/8.6 d - 2	2.94/8 3.82/0 5.63/0 5.4/0 d + 1 d + 3 d + 4 d + 5		263.96/07 d + 36

All further data collection reflected up to 6 months

0 MED

0 PS

d, day; MED, morphine equivalents daily (mg/kg/day); PNET, primitive neuroectodermal tumor; RMS, rhabdomyosarcoma.

showed no reduction in MED, but died 6 days after CPB. The lack of reduction in MED may be due to rapid disease progression at the end of life. Patients 1 and 3 had limited survival after CPB and also a substantial increase in the MED in the final days of life. In the last week of life, their MED exceeded pre-CPB levels. In patients 1 and 4, the MED toward the end of life far exceeded pre-CPB levels. The MED escalation at this time in their disease progression was attributed to rapid pre-terminal disease progression. The benefits of opioid consumption reduction by performance of a CPB are to be considered in terms of reducing the side effects of opioids; nevertheless, our study did not investigate these implications.

Three of four patients had decreased opioid consumption after CPB, and all patients experienced substantial reduction in mean daily PS during the days immediately after CPB. Pain scores were 0 for all patients within 3 days of CPB. In patient 1, pain scores were recorded as 0 until day 18, after which PS and MED began to increase and continued until the patient expired on day 37. In patient 2, pain scores remained 0 until there was definitive cure (liver transplant). In patient 3, pain scores remained 0 until day 10 and the patient died on day 16. In patient 4, pain scores remained 0 and he died on day 6 (though he was sedated with other medications during that time). Subjectively, this patient had a dramatic response to CPB: he was visibly uncomfortable and unable to ambulate in the weeks leading up to CPB. After CPB, he had no pain and could ambulate to and from the bathroom up to and on the day he died.

A previous retrospective study at St. Jude reported that mean MED increased over the last 2 weeks of life for all patients and across age groups and cancer diagnoses.¹⁶ The mean MED increased from 10.7 mg/kg/day 2 weeks before death to 19 mg/kg/day at death, with the highest PS on the day before death. These patients were treated with PCA and did not receive neurolytic blocks as part of pain management. Although this study showed a decrease in mean MED and PS, it was most striking within the first week after CPB. The finding of increased mean MED and PS in patients given CPB at St. Jude is consistent with those from patients treated with PCA alone when considering days just before death.

Benefits of CPB are supported by the observed decrease in opioid consumption and PS in our study. The near absence of side effects or adverse events demonstrated the safety of CPB. One patient experienced diarrhea, which is common with CPB and was self-limited and resolved in a day. Our findings are consistent with the low incidence of adverse outcomes reported in studies of pediatric patients given CPB. Among previous case reports,^{3,11-13} only the study by Staats and Kost-Byerly reported a side effect (transient shoulder pain) of CPB, which was not likely a complication of block correlation as the pain was preexistent.¹² These findings, although limited, suggest that CPB is safe in the pediatric population.

Our study showed consistent efficacy despite using variable CPB techniques. The CPB was performed in four patients by two interventional radiologists (R.G. and H.P.), and the technique details varied. Previous studies in children describe a "two-needle" approach to the celiac plexus by using different imaging modalities. In our study, a single-needle/single-injection technique was used for patients 1 and 2 and a coaxial curved needle set was used for patients 3 and 4. The coaxial needle set, which allows for multiple medication administration sites through a single needle technique, has not been previously

TABLE 3. CELIAC PLEXUS BLOCK TECHNIQUE AND ADJUVANT PAIN MEDICATIONS

<i>Patient characteristics</i>	<i>Weight (kg)</i>	<i>CPB technique (CT guided)</i>	<i>Adjuvant pain medications</i>	<i>Other</i>
#1 20 y/o M Recurrent refractory RMS of the chest wall with abdominal metastases	66.1	10 mL contrast 15 mL bupivacaine 0.5% (75 mg) 20 mL absolute alcohol 20-g needle Left posterior abdominal wall, advanced adjacent to the abdominal aorta	Ketamine infusion Hydromorphone PCA	Lorazepam infusion Haloperidol
#2 14 y/o M Metastatic hepatoblastoma	34.8	Contrast (dose not specified) 10 mL bupivacaine 0.5% (50 mg) 30 mL absolute alcohol 22-g needle Posterior approach; in the antecrural space	Acetaminophen Gabapentin Oxycodone Methadone Ketorolac	
#3 8 y/o F RMS paraspinal abdominal	18.3	2 mL contrast 20 mL absolute alcohol 10 mL bupivacaine 0.5% (50 mg) 21-gauge/25-gauge coaxial curved needle set Periaortic and paraaortic; around and in between celiac and superior mesenteric artery	Morphine PCA Methadone	
#4 19 y/o M Progressive refractory metastatic adrenal primary neuroectodermal tumor	59.1	5 mL iodine contrast 25 mL bupivacaine 0.5% (100 mg) 50 mL absolute alcohol 21-gauge/25-gauge coaxial curved needle set Paravertebral approach; around the celiac artery from right	Hydromorphone PCA Methadone Kadian Cyclobenzaprine Dexamethasone	Clonazepam Haloperidol

PCA, patient-controlled analgesia.

described. In our experience, this technique combines the benefit of multisite injectate administration with the safety of a single needle stick. Also, the curved shape of the coaxial needle set allows easier navigation around the vertebral body into the retrocrural space.

Further procedural variability arose from the alcohol dose injected, which varied by the interventional radiologist's preference. The injected alcohol dose varied from 20 mL (patients 1 and 3) to 50 mL (patient 4) and had no immediate relationship with patient weight. This is explained by the rationale that the endpoint of injection is either bilateral distribution of the injectate at sites of bilateral celiac plexus regions or reaching the 1 mL/kg alcohol dose limit. In patient 4, before the dose limit was reached, the injectate was appropriately distributed in the bilateral celiac plexus regions and further injection was not deemed necessary. For the other three patients, the maximum weight-based dose of alcohol 98% (1 mL/kg) was injected. Despite this dose variability, visual distribution of injectate in the bilateral celiac plexus regions was confirmed for all patients and pain outcomes suggest that all 4 blocks were successful.

In view of the procedural variability noted in this review, the authors recommend that a standard procedural approach is desirable, including the needle approach technique and the dose of local anesthetic and chemoablative agent. The procedural variability, the small sample size, and the retrospective design are notable limitations of our study. Furthermore, based on our observation that in three of our four patients the CPB were performed late in the disease trajectory, we would rec-

ommend that the performance of the CPB be considered earlier in the course of the oncological disease. An additional limitation pertains to the lack of dose regimen data for the adjuvant pain medications.

Conclusion

Our results suggest that CPB may contribute to reducing PS and MED. Early incorporation of this modality in the course of cancer therapy may be beneficial, but additional analgesic measures are likely required at the end of life. Findings from this retrospective case series can be applied to develop prospective observational studies of pain outcomes after CPB for visceral pain related to intra-abdominal malignancies.

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Author Disclosure Statement

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