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Use of Epidural and Peripheral Nerve Blocks at End of Life in Children and Young Adults with Cancer: The Collaboration between a Pain Service and a Palliative Care Service

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Abstract

Background—Clinicians may avoid continuous pain blocks in pediatric cancer patients at the end of life for fear of complications or of interfering with the desired location of death.

Objectives—To examine the impact of epidural or peripheral nerve catheters on pain control in children and young adults with cancer within the last three months of life.

Methods—We retrospectively reviewed the medical records to assess pain scores, systemic opioid requirements, and impact on death at the preferred location.

Results—Ten patients (4.4 to 21.3 years of age), 9 with solid tumors, 1 with lymphoma, had 14 devices (11 epidural, 3 peripheral nerve catheters) for a range of 3 to 81 days. Twelve of 13 catheters provided improvement by at least one of three criteria: improved mean pain scores at 24 hours (8 of 13) and decreased opioid requirement at 24 hours in 9 cases and at day 5 in 9 cases. Eight patients died in their preferred setting. Six patients had catheters (5 epidural, 1 peripheral) until death, including 2 who died at home. In some cases, typical contraindications for indwelling catheters (spinal metastasis, vertebral fracture, thrombocytopenia, fever) were superseded by palliative care needs. We found no bleeding, infectious, or neurological complications.

Conclusions—Our findings suggest that continuous catheter-delivered pain blockade at the end of life contributes to analgesia, moderates opioid requirements, and usually does not preclude death at the preferred location.

Keywords

pain; cancer; end of life; epidural; peripheral nerve block

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Introduction

Children who die of cancer experience significant suffering during the last month of life; 89% were reported to suffer substantially from at least one symptom, most commonly pain (1). Pain is the most commonly treated symptom at the end of life in children (76%) (1), and approximately 90% of children require regular pain medication during terminal care (2, 3); nevertheless, treatment is reported by parents to be successful in only 27% of cases (1). Pain has been reported more commonly in children with solid tumors (98.4%) than in children with other cancers in the context of palliative care (4). Two studies described in 2000 (1) and 2008 (5) by the same team showed the same proportion of parents reported that their child experienced pain at the end of life (76%) (5); the later study found a decrease from 66% to 47% in the proportion of parents who reported that their child suffered significantly from pain (5).

Systemic opioids are usually administered to children with cancer at the end of life; morphine is the drug most commonly used (60% to 90% of cases) (6). However, rapid and massive opioid dose escalation is often necessary (2, 7). When pain control remains inadequate and/or when adverse effects are intolerable despite adjunctive measures, neuraxial (epidural or intrathecal) infusions (8) or peripheral nerve blocks (9) are used, depending on the anatomic distribution of pain. Pain that is difficult to control despite massive, rapid dose escalation of systemic opioids often has a neuropathic component (8, 9).

Central neuraxial blocks (intrathecal blocks) (10, 11) and continuous peripheral nerve blocks (12) are increasingly used for pain control at the end of life in adults, including those with cancer-related pain. However, there is limited experience with neuraxial and peripheral nerve blocks for the end-of-life treatment of cancer-related pain in children. A review of the literature revealed anecdotal reports and small series describing the use of epidural catheters (8, 13-17), intrathecal catheters (8, 17-20), and peripheral nerve block catheters (9).

Here we describe our experience with continuous neuraxial and peripheral blocks (11 epidural catheters and 3 peripheral nerve blocks) for pain management during the last three months of life in 10 children and young adults with cancer.

Methods

Setting

St. Jude Children's Research Hospital (St. Jude) specializes in treating children with cancer and other catastrophic diseases. The St. Jude Institutional Review Board (IRB) approved this retrospective review of patient records and waived the consent requirement. St. Jude provides specialized pain and palliative care services around the clock. The pain service comprises pediatric anesthesiologists trained in pain management and clinical nurse specialists; the palliative care service comprises pediatric oncologists board certified in hospice and palliative care and a nurse practitioner. A psychologist is available for consultation. The palliative care team works in collaboration with hospice agencies during bi-weekly interdisciplinary care meetings, home visits, and telephone consultations for patients discharged to hospices outside the hospital's service area.

Patients and data collection

We surveyed the pain and palliative care services databases for patients who had epidural and/or peripheral nerve block catheters for pain control at the end of life, between May 2008 and October 2009. End of life was defined as three months preceding death. The following data were collected: age, primary diagnosis, location of pain, type of pain (nociceptive, neuropathic, visceral), adjuvant medications for pain control (opioids, anticonvulsants, tricyclic antidepressants, methadone, ketamine, steroids and nonsteroidal anti-inflammatory drugs), type of catheter (epidural or nerve block, tunneled or not tunneled), duration of catheter placement (days), medications infused via catheter (local anesthetic, opioid, clonidine), changes in rates and concentrations, reason for catheter removal, and time between catheter placement and death.

Analgesic efficacy was assessed by comparing mean pain intensity scores (0-to-10 pain scale) for 24 hours before and after catheter placement and by comparing doses of intravenous opioids via patient-controlled analgesia (PCA) pump for 24 hours before, 24 hours after, and on the fifth day after catheter placement. According to institutional policy, pain assessments are performed at least every four hours while awake and one hour after any pain intervention, using age-appropriate pain assessment tools: the Wong-Baker FACES pain scale (21) and the numerical rating scale (22) for patients ages 4 to 7 and older than 7, respectively. Parenteral opioid doses were calculated as mean intravenous morphine equivalent dose (mg/kg/day) on the basis of opioid equianalgesic potency. The ratios used were: fentanyl to morphine, 100:1; hydromorphone to morphine, 5:1; and sufentanil to morphine, 1000:1.

We investigated whether patients had relative contraindications to catheter placement: thrombocytopenia, neutropenia, fever, local wound at the site, and vertebral or spinal pathology (metastases, fractures).

By examining the palliative care service notes, we determined the preferred location of death, whether it was met, outpatient status with the catheters in situ, and the temporal relationship between catheter placement and completion of the physician orders for scope of treatment (POST). The POST form establishes orders for cardiopulmonary resuscitation (CPR) or for “do not attempt resuscitation” (DNAR) and defines the scope of medical interventions (comfort measures, limited additional interventions, or full treatment).

Written informed consent is obtained before placement of epidural or peripheral nerve blocks using the standardized consent for anesthesia approved at our institution, which includes the benefits and risks (bleeding, infection, and neurological complications).

Results

Between May 2008 and October 2009, 11 epidural and 3 nerve block catheters were used for pain management at the end of life in 10 children and young adults with cancer. During this time, the pain service and the palliative care service provided 207 and 102 consultations, respectively. Twenty-seven patients received consultations from both services, representing 26.5% of palliative care consults and 13% of pain consults.

Table 1 summarizes the clinical characteristics of the patients and the interventions for pain management. Patients ranged in age from 4.4 to 21.3 years. Nine had solid tumors, most commonly osteosarcoma, neuroblastoma, and rhabdomyosarcoma. Epidural and nerve block catheters were used for 4 to 57 days and 3 to 81 days, respectively. At death, six patients had catheters in place (5 epidural, 1 nerve block). Six patients were discharged to hospice care and 2 died at home with catheters in situ.

The analysis of the type of pain determined that 6 of 10 patients experienced mixed nociceptive and neuropathic pain, treated with gabapentin; additionally, amitriptyline, methadone and ketamine were used in one patient each. Four patients received benzodiazepines for anxiety or nausea.

Twelve of 13 evaluable blocks provided improved pain control; specifically, the criteria for improved pain control were met in 8 cases for pain score reduction at day 1, in 9 cases for reduction of the opioid requirement at day 1, and in 9 cases for reduction of opioid requirement at day 5. One epidural catheter was not evaluated for pain control (case 10.2) because it replaced a preexistent catheter removed for an MRI evaluation. Three of 4 catheters removed for device-related failure (occlusion, broken catheter, leak) were replaced as soon as feasible.

Table 2 presents comorbidities that conventionally limit placement of epidural and nerve block catheters. Despite thrombocytopenia and/or other contraindications in 6 patients, we found no bleeding, infectious, or neurological complications.

Eight patients died in their preferred setting (Table 1). Use of catheters precluded death at the preferred location in only 2 patients: one patient's hospice could not manage epidural catheters in the home setting; another patient lacked home support of any kind and died while hospitalized for comfort care. Eight of 10 patients in this series were described as "being comfortable at the time of death" and "not suffering" by the palliative care service notes.

In this series, no patients continued to receive cancer-directed therapy. Nine of the 10 patients had a POST document indicating DNAR. Six of these 9 patients were to receive comfort care only and 3 were to receive limited additional interventions. The POST form was completed within 48 hours of the first catheter placement in 4 cases.

Discussion

This retrospective study is the first to investigate the analgesic efficacy of epidural and peripheral nerve blocks, their effect on death at the preferred site, and their relation to decisions to limit medical interventions at the end of life in patients with pediatric cancer. The results suggest that a strong collaboration between the pain and palliative care services has unique benefits for pain management at the end of life in pediatric oncology. Our experience of coordinated dual consultations from the pain service and the palliative care service for complex pediatric oncology patients in the context of end of life is a novel approach.

Little has been published about the use of continuous blocks in children with cancer at the end of life; therefore, it is difficult to draw conclusions about this practice. Three single case reports describe epidural catheter use for caudal administration of intermittent doses of morphine (14), cervical opioid administration (15), and continuous lumbar infusion of morphine, bupivacaine and clonidine (17). In addition, three small case series describe epidural catheter use in 9 patients (of 11 with epidural or intrathecal catheters) (8), 7 patients (16), and 10 patients (of 25, some with non-cancer pain) (13). Two case reports (17, 18) and two small series (n= 5 and 5) (8, 19) describe the use of intrathecal catheters for pain control in pediatric cancer patients at the end of life; another small series describes intrathecal catheters in 3 children with cancer who were not at the end of life (20). There is only one report describing the use of peripheral continuous nerve block for pain control in pediatric cancer; it describes a catheter-delivered interscalene brachial plexus block in a child with progressive osteosarcoma (9).

Our findings indicate that continuous epidural and peripheral nerve blocks can reduce pain scores and intravenous opioid requirements and should be interpreted in the context of disease progression at the end of life, (i.e. progression of pain at the initial site, additional sources of pain not addressed by existing catheters) and/or development of opioid tolerance. Additionally, the joint medical decisions by the Palliative Care and the Pain Services to recommend the replacement of 3 of 4 catheters with device failure as well as the continued presence of blocks until death in 6 patients are indicators of perceived medical benefit from these devices.

Epidural and nerve block catheters can provide extended analgesia; tunneled epidural catheters have been reported to function in pediatric patients for as long as 240 days (13); in one patient in our series, a nerve block remained in place for 81 days.

The medical indications for catheter-delivered analgesia at the end of life in patients with pediatric cancer are complex and multifactorial, including inadequate analgesia with systemic opioids and adjuvants, the need for rapid and massive dose-escalation of systemic opioids, and uncontrollable side effects of systemic opioid (12). Additional considerations may include reduction of somnolence to facilitate interaction with family members and discussion of the goals of comfort and symptom control, DNAR status, and the preferred location of end-of-life care and death.

In our series and others (12), the contraindications for placement of invasive catheters were superseded by the priority to relieve suffering at the end of life. The benefits of pain control are greater than the risks associated with invasive catheter placement when comfort is the primary goal. The most significant risks to consider are bleeding, infection and neurological deficits, since thrombocytopenia and/or low white cell count are frequent in the context of end of life. Platelet counts < 100 x 10⁶/L are generally considered a contraindication for epidural catheter placement. Despite thrombocytopenia, fever and local wound at the catheter site, vertebral or spinal metastases or fractures in 6 patients in this series, no bleeding, infection or neurological adverse events were recorded.

The decisions for epidural vs. peripheral nerve block were based on the location of pain: for abdominal and/or back pain, a thoracic or lumbar epidural was chosen, whereas for extremity pain, a peripheral nerve block or a plexus block was indicated. The type of block had to be changed from a lumbar plexus to an epidural catheter in one patient with poorly controlled phantom limb pain post hemipelvectomy. Intrathecal catheters were not preferred to epidural catheters due to the short life expectancy in the majority of the patients in our series.

The standard technique used at our institution for nerve block placement is via electrical nerve stimulation; in this series, ultrasound was used to complement the technique. Epidural catheter placement is rarely facilitated by fluoroscopy at our institution.

We found that 5% of the pain service consultations at a pediatric oncology specialty hospital were provided for patients with complex pain problems in the context of end-of-life for epidural or nerve block catheters placement. The use of epidural or nerve block catheters is often limited to hospitalized patients under close monitoring (10, 23); however, interdisciplinary collaboration can make home care feasible for patients with pain refractory to systemic opioids. Our institutional policies for epidural and nerve block catheters are developed for acute care settings; nevertheless, at the end of life, the standards of management and monitoring may be changed (no vital signs, limited blood draws, etc).

Based on our collaborative experience between the pain and the palliative care services, we recommend the development of partnerships between pediatric oncology programs, pain and palliative care services, and hospice agencies. Such collaborations may facilitate early evaluation and decision to use blocks as earlier interventions at the end-of-life, to benefit the patients.

The limitations of this study are those inherent to retrospective studies. In addition, our comparison of opioid doses before and after catheter placement excluded the use of sustained-release oral or transdermal opioids. We analyzed PCA-delivered opioids exclusively because it is the “titratable” component of a pain management regimen and therefore reflects the change in opioid need; catheter placements did not alter the remainder of the pain treatments. At our pediatric institution, children continue to be treated even after they exceed the age of 18 years, due to the need for continuity of care under the circumstances of long term cancer treatment; therefore, we included young adults and children in our review.

Conclusion

Continuous catheter-delivered pain blockade provided improved pain control and lowered opioid requirements with few complications in this series of young cancer patients near the end of life. The coordinated efforts of the primary oncology service, the institution's pain and palliative care services, and the hospice agency allowed the continuation of catheter analgesia without precluding death at the preferred location in most cases. While we present our collaborative experience retrospectively, prospective studies to investigate the analgesic

efficacy and the safety of continuous neuraxial and peripheral nerve blocks in children at the end of life are necessary to further advance knowledge in the field.

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Table 1

Continuous Pain Blockade in 10 Young Patients with End-Stage Cancer

Case #	1	2	3.1	3.2	3.3	4	5	6	7.1	7.2	8	9	10.1	10.2
Age (years)	16.5	18.4	21.3			6.8	20.9	13.2	18.1		4.4	8.3	18.2	
Primary diagnosis	Clear cell sarcoma	Osteosarcoma	Osteosarcoma			Neuroblastoma	Ewing sarcoma (with spinal metastases)	Burkitt's lymphoma	Rhabdomyosarcoma		Neuroblastoma	Rhabdomyo-sarcoma	Osteosarcoma	
Site of pain	Back	Leg	Phantom limb pain, post-hemipelvectomy			Abdomen	Leg, back	Axilla wound	Abdomen	Abdomen	Abdomen	Abdomen	Back, hip	
Type of pain	N/NP	N/NP	N/NP			N/NP/V	N	N	N/V		N	N	N/NP	
Pain control regimen at block placement	Op, Gbp, TCA, NSAID, Bz	Op, Gbp, NSAID	Op, Gbp, Me, CS			Op, Gbp, K	Op, CS	Op	Op, Bz		Op, Bz	Op	Op, Gbp, NSAID, Bz	
Device type (location)	Epidural (T7-8)	NB (Femoral)	NB (Lumbar Plexus)	Epidural (L3-4)	Epidural (L3-4)	Epidural (T9-10)	Epidural (T9-10)	NB (Interscalene)	Epidural (L2-3)	Epidural (T12-L1)	Epidural (T9-10)	Epidural (T10-11)	Epiduraly (L3-4)	Epidural (L2-3)
Tunneled	y	y	y	y	y	y	y	y	n	n	y	y	y	y
Anesthetic agent(s) at insertion	Bupivacaine/fentanyl	Ropivacaine	Bupivacaine	Bupivacaine/hydromorphone/clonidine	Bupivacaine/hydromorphone/clonidine	Bupivacaine/fentanyl/clonidine	Bupivacaine/hydromorphone/clonidine	Ropivacaine	Bupivacaine/fentanyl/clonidine	Bupivacaine/fentanyl/clonidine	Bupivacaine/hydromorphone	Ropivacaine/hydromorphone/clonidine	Bupivacaine/fentanyl/clonidine	Bupivacaine/hydromorphone
Anesthetic agent(s) at day 5	No change	Ropivacaine/clonidine	n/a	No change	No change	Bupivacaine/hydromorphone/clonidine	No change	No change	n/a	Bupivacaine/fentanyl	No change	Bupivacaine/hydromorphone/clonidine	Bupivacaine/hydromorphone	No change
Concentration at * insertion (day 5)	0.125/3 (No change)	0.2 (0.2/0.4)	0.2 (n/a)	0.2/10/0.4 (No change)	0.2/10/0.4 (No change)	0.125/3/0.4 (0.1/10/0.4)	0.1/10/0.4 (0.1/6/0.4)	0.2 (No change)	0.125/5/0.4 (n/a)	0.2/10/0.4 (0.2/5)	0.125/10 (No change)	0.125/10/0.4 (No change)	0.1/3/0.4 (0.125/10)	0.125/10 (No change)
Rate at insertion (day 5) (ml/hr)	8 (8)	10 (12)	12 (n/a)	12 (12)	15 (15)	6 (9)	10 (14)	8 (12)	13 (n/a)	10 (9)	5 (5)	6 (8)	10 (12, 3ml boost/hour)	12, 3ml boost/hour (18, 3ml boost/hour)
Change in mean pain score at 24h	0	↓(-5.5)	↓(-2.5)	↓(-6.2)	0.4	0	↓(-2.5)	↓(-2.7)	0	1.3	↓(-5.5)	↓(-0.3)	↓(-9)	n/a [‡]
Change in PCA requirement at 24h [‡]	0	↓(-0.57)	↓(-0.16)	↓(-0.52)	↓(-2.28)	0.13	0.96	↓(-0.24)	↓(-1.43)	0.73	↓(-1.4)	↓(-0.7)	↓(-0.05)	
Change in PCA requirement at 5d [‡]	↓(-1.87)	↓(-0.71)	1.09	↓(-0.14)	↓(-1.09)	↓(-0.02)	6.13	↓(-0.1)	↓(-0.98)	0.15	↓(-0.38)	↓(-0.73)	0	
Device duration/ patient lifespan (days)	57/57	81/81	3/33	11/31	12/19	35/35	20/20	35/94	4/10	7/7	11/11	23/47	8/57	14/50
Outpatient with device	y	y	n	y	y	n	y	n	n	n	n	y	y	n

Case #	1	2	3.1	3.2	3.3	4	5	6	7.1	7.2	8	9	10.1	10.2
Reason for removal	Death	Death	Incomplete pain control	Broken, unable to repair	Occlusion	Death	Death	Transitioned to oral medication	Incomplete pain control	Death	Death	Leak	MRI, planned	Leak
Death location (preference/actual)	home/home	home/hospital	home/home			hospital/hospital	home/home	home/home	hospital/hospital		home/hospital	home/home	home/home	

NB= Nerve block, N= Nociceptive pain, NP= Neuropathic pain, V= Visceral pain, Op= Opioid, Gbp= Gabapentin, TCA= Tricyclic Antidepressant, Me= Methodone, K= Ketamine, CS= Corticosteroid (dexamethasone), NSAID= Nonsteriodal antiinflammatory drug, Bz= Benzodiazepine

* Concentration of medications: Bupivacaine (%); fentanyl, hydromorphone, clonidine (mcg/ml)

** Mean pain scores based on all awake pain scores for 24 hour (range 6-16)

[†] Morphine equivalent, mg/kg/day

[‡] Catheter 10.1 was removed for MRI and replaced at same settings

Table 2

Limiting Factors and Contraindications at the Time of Catheter Insertion

Case	Device type	ANC ($\times 10^3/L$)	Platelet count ($\times 10^6/L$)	Other contraindications
1	E	5300	283	T12 fracture, spinal metastases, fever
2	NB	8300	362	
3.1	NB	6300	39	Spinal metastases
3.2	E	nd	94	
3.3	E	4600	26	
4	E	2100	84	
5	E	4100	123	
6	NB	1300	89	Large wound in targeted area
7.1	E	6300	477	
7.2	E	22300	488	
8	E	5800	20	Fever
9	E	5400	241	
10.1	E	4500	76 (trx)	
10.2	E	4800	106 (trx)	

E=epidural; NB=nerve block; ANC=absolute neutrophil count; nd=not done; trx=value after transfusion(s)