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The Safety and Effectiveness of Patient-Controlled Analgesia in Outpatient Children and Young Adults with Cancer: A Retrospective Study

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Abstract

Background—Patient-controlled analgesia (PCA) is safe and effective in hospitalized children; however, data regarding its use for outpatients are limited. The aims of the study are to determine the safety of outpatient PCA and to compare the standard and proxy PCA groups.

Methods—All patients receiving outpatient PCA over 54 months were included in this retrospective study. Data regarding age, sex, diagnosis, PCA initiation/discontinuation circumstances, patient vs. proxy-authorized PCA type, opioid doses, pain scores, and complications were collected. Nonparametric tests (Wilcoxon-Mann-Whitney test for comparing two groups or Kruskal-Wallis rank sum test for comparing more than two groups) were used to compare duration of PCA use, opioid doses, pain scores, and circumstances of initiation and discontinuation of outpatient PCA.

Results—Forty-five patients used 69 outpatient PCAs. The complication rate was 0.36%. The starting mean MED (mg/kg/day) was 1.67 when initiation was for an outpatient and 4.04 for those

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Competing Interests

The authors declare that they have no competing interests

Authors' Contributions

DLA conceived of the study, participated in its design and coordination, and helped to draft the manuscript.

KZ participated in its design, coordination, and data collection and helped to draft the manuscript.

LGF participated in its design, coordination, and data collection and helped to draft the manuscript.

DP participated in the design of the study and performed the statistical analysis.

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discharged from the hospital with PCA; this difference was not statistically significant ($p=0.13$). The analysis of mean opioid doses in relationship to the circumstances for the discontinuation of the outpatient PCA revealed a significantly higher dose (mg/kg/day) in the group of patients who died (19.54) than in the group with a change of status to inpatient or transfer to another hospital or hospice (3.70) and in the group in which PCA was discontinued because pain management no longer required a PCA (1.19). The mean opioid daily doses and pain scores were significantly higher at the end of life ($p<0.0001$).

Conclusion—Outpatient PCA use for children and young adults with cancer is safe.

Keywords

Patient-controlled analgesia; pain; opioids; pediatric oncology; outpatient

Background

Patient-controlled analgesia (PCA) is a convenient method of delivering opioid analgesia by allowing patients to self-administer a bolus dose, sometimes in combination with a continuous infusion for optimal management of pain. The use of PCA is well-established for acute postoperative pain management and other indications in the inpatient setting for adults and children. Its use is valuable for pediatric cancer patients to relieve severe pain and provide better quality of life. [1–3] PCA by proxy is authorized opioid boosting by someone other than the patient, such as a health care provider or a parent for pediatric patients; this practice is safe [4–6] and is associated with high satisfaction and good compliance. [7]

While extensive literature describes the use of PCA in the inpatient setting, little has been published describing its use for chronic pain management in the outpatient setting in adults, [8–12] and even fewer studies have included children in the study group [13] or examined the use of PCA in the outpatient setting for pain control in dying children. [1]

The safety and effectiveness of outpatient PCA in pediatric oncology patients either self-administered or by proxy, have not been described in the literature. The primary and the secondary aims of this study were to determine the safety of outpatient PCA in children and young adults with chronic cancer pain and to compare the standard and proxy PCA groups regarding duration of use of PCA and incidence and type of complications. Additionally, we describe the patient demographic characteristics, oncology diagnoses, opioid doses, and pain scores. Based on our clinical experience, the hypothesis was that the use of PCA in outpatient population is a safe practice, in both standard and proxy groups.

Methods

Patients

St. Jude Children's Research Hospital specializes in treating catastrophic childhood diseases. The St. Jude institutional review board approved this study and waived consent. We collected the following data from the medical records of all outpatients at our pediatric oncology institution who used PCA between October 2006 and April 2011: age, sex, diagnosis, PCA initiation/discontinuation circumstances, patient vs. proxy-authorized PCA

type, opioid dose, pain scores, and complications. An outpatient PCA was defined as either a new PCA order for an outpatient or a PCA for an inpatient who was discharged from the hospital to outpatient status. PCA days were defined as days during which PCA was in place for an outpatient. Of these, data evaluation days were defined as days of outpatient clinic visits during which a pain evaluation was completed and sometimes adjustments to the PCA settings were made. The data evaluation days generated information regarding pain scores and opioid dose and settings (infusion, bolus, and time between boluses), changes in the settings, and data regarding opioid-related respiratory or neurological complications. For consistency, we identified the first ordered opioid per PCA for analysis of the type of opioid. Total opioid daily doses were calculated and weight-adjusted and presented as morphine equivalent daily (MED) based on equianalgesic potency. The ratios used for equianalgesic potency were fentanyl to morphine 100:1 and hydromorphone to morphine 5:1. Pain scores were collected as documented during outpatient clinic visits and calculated as mean daily scores. Pain intensity was assessed by using the Faces, Legs, Activity, Cry, Consolability scale, [14] the Wong-Baker FACES scale, [15] or the numerical rating scale, [16] depending on the patient's age and developmental status, according to our institutional standard of care.

The duration of PCA use as outpatient was calculated for each PCA, from the initiation of the outpatient PCA to either the change of location of care, the discontinuation of the PCA, or death. If patients received PCA treatment as outpatients more than once during the review period, each time was recorded separately. The circumstances for outpatient PCA initiation were noted in the two categories defined: either a new PCA order for an outpatient or a PCA for an inpatient who was discharged from the hospital to outpatient status. The discontinuation of outpatient PCA was recorded in one of three categories of circumstances: 1) change of location of care, including change from outpatient to inpatient status or transfer to hospice or to another institution; 2) discontinuation of outpatient PCA and replacement with an oral opioid regimen; or 3) patient death. The authorized PCA users—the patient (standard) or parent (proxy)—were noted at the initiation of the PCA and reported each day for its duration.

Data for adverse events were obtained from the pain management service quality improvement database and were reviewed for accuracy by comparison with the medical records. The quality improvement database contains data indicating respiratory or neurological complications noted during evaluations in outpatient visits. Whether the change was significant enough to represent a complication was left to the clinical judgment of the caregiver making the chart notations. A respiratory complication included, but was not limited to, any record of decrease in respiratory rate and amplitude or pulse-oximetry values. Neurological complications included, but were not limited to, any record of confusion, difficulty in arousing the patient, major personality change, hallucinations, or seizures.

Standard PCA and PCA by proxy

Standard PCA and PCA by proxy were defined based on the individual who administered the bolus doses, the patient or an authorized user (parent or another family member), respectively; health care providers were not authorized proxy users for outpatients. The drugs, doses, and equipment used for standard or proxy PCA and for inpatients or

outpatients were identical. The standard starting doses of opioid bolus, which are available on the hospital's intranet site, are: morphine, 0.02 mg/kg; hydromorphone, 0.004 mg/kg; and fentanyl, 0.5 mcg/kg, with a 15-minute lockout interval for all three. When a background infusion is indicated, the recommended starting hourly dose is equivalent to the bolus dose. Any physician or advanced practice nurse can order a PCA without consultation from our institution's pain service. The portable CADD-Prizm Variable Infusion Profile Ambulatory Infusion Pump, Model 6101 (Smiths Medical MD Inc., St. Paul, MN) was consistently used.

Statistical Analyses

Nonparametric tests (Wilcoxon-Mann-Whitney test for comparing two groups or Kruskal-Wallis rank sum test for comparing more than two groups) were used to compare duration of PCA use, opioid doses, pain scores, and circumstances of initiation and discontinuation of outpatient PCA.

The duration of PCA use was compared between the groups of standard PCA and PCA by proxy. The opioid doses and pain scores were compared at 2 time points; at the initiation and at the discontinuation of all outpatient PCAs. The comparisons were made between 2 groups at the initiation of the outpatient PCA (a group of new PCA orders for outpatients and a group of PCA for inpatient who were discharged from the hospital to outpatient status) and between 3 groups at the time of discontinuation of the outpatient PCA, based on the following circumstances: 1) change of location of care, including change from outpatient to inpatient status or transfer to hospice or to another institution; 2) discontinuation of outpatient PCA and replacement with an oral opioid regimen; or 3) patient death. All statistical analyses were performed with SAS release 9.2 software (Cary, NC).

Results

Patients

Forty-five outpatients received 69 PCAs over 1,110 PCA days; of these, 281 were data collection days. The mean age at the time of initiation (SD) was 13.0 years (6.34). Patient demographic characteristics and diagnoses are described in Table 1.

Standard vs. Proxy PCA

Of 69 PCAs, 56 (81.2%) were standard, and 13 (18.8%) were parent proxy, and of 1,110 PCA days, 956 (86.1%) were standard and 154 (13.9%) were parent proxy PCA days. The parent proxy group included parent boosting only in 6 PCAs and parent and patient boosting in 5. Two patients switched from standard PCA to both patient and parent proxy due to the addition of parents as proxy users; we included these patients in both groups. We observed a lower age (years) (mean±SD) at the onset of the PCA in the parent proxy group in 11 patients (7.5±7.1), compared with the standard PCA group in 36 patients (14.8±5.0) (p=0.003). The mean duration of PCA use was 17.5 days for standard and 9.3 days for parent proxy PCA (p=0.36) (Table 2).

Opioids and Circumstances for Initiation and Discontinuation of PCA

Hydromorphone was used in 29 (48%) outpatient PCAs, morphine in 24 (34.8%), and fentanyl in 16 (23.2%). Hydromorphone was used significantly fewer times for outpatient PCA by proxy (2) than for standard PCA by the patient (27) ($p=0.05$). Morphine was used in 16 standard and 8 proxy PCAs. Fentanyl was used in 12 standard and 4 proxy PCAs. On 252 of 1,110 PCA days (22.7%), PCA settings (infusion, boost, or time between boosts) were adjusted. Dose titrations were made on 12.9% (143 of 1,110) PCA days; the duration of an outpatient PCA was a mean ($\pm$ SD) of 16.1 ($\pm$ 18.7) days. Opioid rotations were made 8 times in 6 of 69 PCAs (2 PCAs had opioid rotations twice). The circumstances for initiation and discontinuation are presented in Table 3.

Complications

We found 4 of 1,110 PCA days with complications (0.36%) in 3 patients (1 respiratory and 3 neurological). The distribution of complications observed in standard and parent proxy groups is described in Table 4. No patient experienced respiratory and neurological complications concurrently.

Opioid Doses and Pain Scores

Mean pain scores and mean opioid doses as MED at the time of outpatient PCA initiation and discontinuation are reported, as well as specific circumstances for initiation and discontinuation (Table 3).

The starting MED (mg/kg/day) was 1.67 when initiation was for an outpatient and 4.04 for those discharged from the hospital with PCA; this difference was not statistically significant ($p=0.13$). The analysis of mean opioid doses in relationship to the circumstances for the discontinuation of the outpatient PCA revealed a significantly higher dose (mg/kg/day) in the group of patients who died (19.54) than in the group with a change of status to inpatient or transfer to another hospital or hospice (3.70) and in the group in which PCA was discontinued because pain management no longer required a PCA (1.19) (Table 3).

The differences between mean pain scores at the time of initiation of outpatient PCA in the groups of patients discharged from inpatient status versus the group having a new outpatient PCA started were not statistically significant (3.2 versus 3.43, $p=0.71$). In contrast, the mean pain scores were significantly higher ($p<0.0001$) in the group of patients who died (4.29) than in the group who changed the outpatient status through admission (3.80) and the group who discontinued the outpatient PCA due to a change in the requirement of pain management (1.83) (Table 3).

Discussion

To our knowledge, this is the first study to describe the use of PCA in the outpatient setting in pediatric and young adult oncology patients, with a focus on the characteristics of this population, the opioid regimens used, the unique aspects of PCA by proxy, and the safety and effectiveness of this practice. The use of outpatient opioid PCA to treat cancer pain has been described in several adult studies, [8, 10–12] in a review article of adult studies, [9] and

in one study of combined adult and pediatric patients. [13] Even though the use of PCA in pediatric and young adult patients has not previously been specifically investigated in the outpatient setting, its safety in pediatric inpatients has been established. [2, 4, 7]

The most important finding of our study is the safety of outpatient PCA use for children and young adults. Furthermore, the fact that the complication rates were low in the overall group, as well as in the standard and parent proxy groups, suggests that the operation of outpatient PCA by proxy does not contribute to a higher risk of complications. Our previous research in the use of inpatient PCA in pediatric oncology showed complication rates of 1.41%, 1.25% and 1.48%;[4, 6, 17] our current findings in an outpatient population (complication rate of 0.36%) strengthen this evidence and support the recommendation of outpatient use of PCA by parents for children who are unable to self-boost due to age, developmental status, or end-of-life circumstances. Based on the previously reported complication rates of 1.41% (70/4,972) and 1.25%(93/7,389) with inpatient PCA use, compared to the findings of the current study of 0.36% (4/1,106) with outpatient PCA use, we calculated the odds ratio to reflect the inpatient and outpatient chance of complications. The inpatients had 3.68 times more chance (95% CI 1.36–9.95) to have complication than outpatients. The complication rates that we have reported in both the inpatient (previous publications) and outpatient populations (current study) are low as compared to the data in the literature [4]. During the 4 PCA days with complications (0.36%) in 3 patients (1 respiratory and 3 neurological), no patient experienced respiratory and neurological complications concurrently. No complications were life-threatening; they were transient, easily reversed complication. Three episodes of neurological complications consisted of drowsiness/sedation; two of them occurred in the same patient, on two consecutive outpatient evaluation visits. The episode of respiratory complication consisted of bradypnea without oxygen desaturation. All complication episodes were managed by decreasing the rate of the basal infusion of the PCA. Additionally, one patient who experienced drowsiness/sedation was treated by up-titration of the methylphenidate regimen.

The overall low complication rates in our study can be attributed to a combination of factors. Our patients with cancer diagnoses were generally not opioid naïve and may have received various treatments (chemotherapy, radiotherapy, and surgery) that had previously induced pain and warranted the use of opioids. Furthermore, patients who were discharged with a PCA from inpatient status had acquired experience with the device and were familiar with its use and safety precautions. Patients who started PCA as outpatients were also generally not opioid naïve. Patients and parents receive PCA educational materials and training according to our institutional policy. Parents are often quite involved in the care of their children, and families are housed in close proximity to our hospital, allowing for immediate access to medical care.

Our study also showed trends in opioid doses and pain scores as measures of the effectiveness of outpatient PCA. Our finding of lower mean opioid doses at the start of outpatient PCA in the new PCA as outpatient group versus discharge from inpatient status group reflects the fact that opioid up-titration is a common practice in chronic pain management. Starting doses may be lower than optimal doses, and their adjustment is based

on effectiveness and side-effect profiles, following our institutional guidelines that standardize low opioid starting doses.

The circumstances of discontinuation of outpatient PCA contribute to the differences observed in the opioid doses and pain scores between different categories of circumstances. Outpatients who discontinued PCA completely or switched to an oral opioid had both lower opioid doses and lower pain scores on the last day of PCA administration than the other groups, suggesting adequate analgesic effectiveness. The change of outpatient status (readmission or transfer to another institution or hospice) was not associated with significant changes in mean opioid doses or mean pain scores. This may be related to the fact that the reasons for admission were chemotherapy or treatment of medical complications of cancer, and no admissions were motivated by inadequate pain control. Patients at the end of life, in terminal stages of cancer, had higher pain scores and required larger doses of opioids to adequately manage pain.

This study showed an outpatient population with equal distribution across age groups and lower ages in the parent proxy group than the standard PCA group, suggesting the need for parental use of boluses for younger children. At our institution, PCA by proxy is selected for patients less than 5 years old, those with impaired cognitive ability, and those with concurrent neuromuscular impairment that limits the ability to self-administer PCA, including weakness or sedation around end-of-life circumstances. We provide parents an educational program that incorporates written material and an instructional video on safe PCA administration, including emphasis on boosting only when the patient is awake and indicates verbally or non-verbally that pain is present. Required documentation includes physician orders for parent proxy boosting and providing the education on PCA by proxy.

A limitation of our study is its retrospective design. Data collection relied on medical record review, and the documentation may have been limited. Our patient population included patients with various stages of cancer, from early diagnosis to end-of-life palliative care, with a wide age range from young children to young adults. Our findings should not be extrapolated to the general pediatric population due to the uniqueness of our outpatient families being housed in hospital-provided facilities close to the hospital, which gives them relatively fast access to medical care compared with other institutions.

In conclusion, our study of pediatric and young adult patients with cancer showed that PCA with or without proxy appears to be safe in the outpatient setting. This retrospective study serves as preliminary evidence for the safety and effectiveness of outpatient PCA. Further studies are needed to evaluate this pain management strategy in other pediatric patient populations.

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Table 1

Demographic Characteristics and Diagnoses for Outpatients Using PCA

Sex	n=45 (%)
Male	26 (57.8)
Female	19 (42.2)
Age @ first PCA onset	n=45 (%)
<6	6 (13.3)
6–12	14 (31.1)
13–17	12 (26.7)
18	13 (28.9)
Primary diagnosis	n=45 (%)
Solid tumor	27 (60.0)
Brain tumor	4 (8.9)
Leukemia or lymphoma	14 (31.1)

PCA: patient-controlled analgesia

Table 2
Opioid Doses, Pain Scores, and Circumstances of Initiation and Discontinuation of Outpatient PCA

	Opioid Dose (mg/kg/day) [†] p=0.13				Pain Score p=0.70			
	Number of PCAs (data evaluation days)				Number of PCAs (data evaluation days)			
	69 (278)	Mean ± SD	Median	Range	69 (244)	Mean ± SD	Median	Range
Initiation of PCA	53 (219)	4.0 ± 7.1	1.5	0 – 48.3	191	3.2 ± 3.4	3	0 – 10
Inpatient discharged with PCA	16 (59)	1.7 ± 1.3	1.5	0 – 6.7	53	3.4 ± 3.6	3	0 – 10
PCA new order as outpatient								
	Opioid Dose (mg/kg/day) p<0.0001 *				Pain Score p<0.0001 *			
	Number of PCAs (data evaluation days)				Number of PCAs (data evaluation days)			
Discontinuation of PCA	69 (278)	Mean ± SD	Median	Range	69 (244)	Mean ± SD	Median	Range
Change of outpatient location of care	48 (194)	3.7 ± 4.9	1.6	0 – 29.2	167	3.8 ± 3.5	3	0 – 10
Discontinuation of PCA as outpatient	19 (75)	1.2 ± 1.0	0.9	0 – 5.0	70	1.8 ± 2.9	0	0 – 10
PCA used at end-of-life	2 (9)	19.5 ± 21.6	2.9	1.3 – 48.3	7	4.3 ± 2.8	4	0 – 8

* Kruskal-Wallis test

[†] Opioid dose calculated based on basal infusion rate
PCA: patient-controlled analgesia

Table 3

Complications During Use of Outpatient PCA

PCA type	No Complications		Respiratory Complications		Neurological Complications		Overall Complications ^I	
	n	(%)	n	(%)	n	(%)	n	(%)
Standard PCA days	953	(99.7)	1	(0.1)	2	(0.2)	3	(0.3)
Parent proxy days	153	(99.4)	0	(0)	1	(0.6)	1	(0.6)
Total PCA days	1,106	(99.6)	1	(0.1)	3	(0.3)	4	(0.4)

^I No patient had 2 complications concurrently.

PCA: patient-controlled analgesia