RETROSPECTIVE STUDY COMPARING THE EFFICACY OF EPIDURAL ANALGESIA TO PERINEURAL NERVE CATHETER ANALGESIA FOR POSTOPERATIVE PAIN MANAGEMENT IN PEDIATRIC PATIENTS FOLLOWING A UNILATERAL LOWER LIMB SURGERY

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Abstract

The primary aim of this study was to determine if peripheral nerve catheterization offers a better analgesic alternative than an epidural catheter in pediatric patients who undergo a unilateral lower limb surgery. Postoperative pain management is not only important in promoting comfort to patients in pain but can also promote rehabilitation and optimal healing. Multimodal analgesia is the use of multiple modalities to treat patients' pain; two of these methods include epidural and peripheral catheters. Epidural catheter infusions offer global analgesia from the waist to both of the lower extremities. Epidurals do pose side effect risks that include infection, urinary retention, hypotension, pruritus, nausea/vomiting, headaches, backaches, and respiratory depression. Peripheral nerve infusions can act more locally at a targeted area and deliver carefully dosed anesthetics to nerve fibers that can hinder the sensory function of nerves while preserving the motor function, allowing for earlier rehabilitation. The use of multimodal analgesia as a postoperative pain management plan can still vary greatly from clinician to clinician, so it would be of benefit to determine which subset of patients may benefit from having a catheter infusion as part of their treatment regimen and whether a peripheral infusion is superior to an epidural infusion. This was a retrospective study that looked at 65 pediatric patients, ages 5-15, that received either an epidural infusion ($n = 53$) or a peripheral nerve block infusion ($n = 12$) for a unilateral lower limb operation. Their charts were analyzed to determine pain scores, PCA usage, PRN morphine equivalents, total morphine equivalents, adverse events, length of catheter use, and length of hospital stay, amongst other things. The epidural group was used as the control for the study and the data analysis revealed that the patients that received a peripheral infusion had 43% higher ($p = 0.35$) pain scores, received 98% less ($p = 0.001$) continuous morphine equivalents in their infusions, required 31% less ($p = 0.34$) PRN morphine equivalents, had 68% less ($p = 0.049$) PCA usage rates, received 32% less ($p = 0.39$) total morphine equivalents, had 30% less ($p = 0.45$) adverse effects, and left the hospital 0.54 days earlier ($p = 0.13$) on average when compared to patients that received continuous epidural infusions. The data indicates that although the pains scores were higher for the peripheral infusion patients, these patients required less opioid exposure, which indicates relatively acceptable pain management for the patient and healthcare team while also allowing

for the opportunity to engage in rehabilitation and avoid the global effects of epidural infusions and the associated increased profile risk. The conclusion of this study suggests that continuous peripheral infusions are a valid alternative to epidural infusions for pediatric patients that undergo a unilateral lower limb surgery and that a randomized control trial would be warranted to offer more definitive insight.

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Introduction

Orthopedic surgery is especially painful in the postoperative period. Analgesia can be delivered to allow patients to recover from treatment as comfortably as possible. Two of the methods that are used to deliver this analgesic effect are via an epidural route and by blocking a peripheral nerve. Epidural analgesia consists of a catheter being placed into the epidural space of the spine, through which medications can be infused. Perineural catheterization uses imaging modalities to target the area around nerves where analgesics are delivered.

Of these two methods, epidural analgesia is known to produce many side effects. Outside of the desired analgesic effect, epidurals can induce adverse effects that include infection, urinary retention, hypotension, pruritus, nausea/vomiting, headaches, backaches, and respiratory depression. In a study of 3,152 patients receiving continuous epidural analgesia, the rate of complications was 4.2% in neonates, 1.4% in infants, 0.5% in children aged one through eight, and 0.8% in children over eight years of age[12]. A study that compared the side effects of common analgesic methods of patient-controlled analgesia (PCA), intramuscular analgesia (IM), and epidural analgesia identified that out of more than 100,000 patients, urinary retention occurred in 23% of all patients, with epidural analgesia having the highest incidence at 59% [5]. In a prospective study that followed 2,307 pediatric patients that received continuous perineural analgesia post-operatively after a procedure on a lower extremity, adverse effects were detected in 1.4% of patients, all of which had their adverse effects resolve without therapy or sequelae[8].

Opioid administration offers pain management for post-operative patients but also presents with significant risks. Several studies have showed that when continuous peripheral nerve blocks are used for post-operative pain relief, opioid consumption is reduced and the overall pain management is improved[1, 4, 6, 10]. A study that reviewed nineteen articles and 603 patients showed that perineural catheters provided superior analgesia to opioids for all catheter locations and time periods[10]. Another study that looked at fifty patients that had a total knee arthroplasty and compared the effectiveness of either continuous perineural analgesia or intravenous delivery of opioids determined that those patients that received continuous perineural analgesia had less patient-controlled opioids (29.1% vs 84.5%), and had a significantly less length of stay in the hospital (3.6 vs 4.2 days), and better knee flexion and motility[4]. This reduction in opioid-dependent pain management in the post-operative phase was also seen in a study that looked at 198 patients that had a lower limb amputation. Of the patients that received a perineural catheter, there was a 40% decrease in opioid consumption when compared to patients that received other traditional methods of analgesia[1]. The ability to decrease the exposure of post-operative patients to opioids is one that will reduce the adverse effects of opioids, including the potential risk of addiction. In a retrospective study that looked at 1,285 outpatient patients that had received a perineural catheter, 75.4% of patients required either no opioids or oral opioids only on an "as needed" basis[6].

The benefits of perineural analgesia relative to epidural analgesia improve patient satisfaction[7]. Perineural analgesia has also been shown to accelerate the process of discharge from an in-patient setting after an operation because of overall better pain management. Upon discharge, a perineural catheter also allows for accessible delivery for infusions and can be easily managed by home-care or at an outpatient setting[7]. Perineural infusions also offer the benefit of providing complete anesthesia to the entire surgical site without having unnecessary, widespread effects on the entire limb. This is possible because imaging modalities allow for insertion of the catheter to be targeted distally for precise delivery of infusions. This advantage allows for motility and sensation to be as widespread or as limited as intended[3]. In a study that reviewed 45 randomized control trials (2710 participants) from 47 publications, single and continuous femoral nerve blocks were compared with different modalities of analgesia, including epidural anesthesia, in patients that received total knee replacements. Patients that received a continuous peripheral nerve block had less need for opioids, less nausea and vomiting, less pain on movement and during rest, and evidently greater patient satisfaction[2]. Another studying compared patient-controlled analgesia with morphine, patient-controlled epidural analgesia (PCEA), and a continuous nerve block showed that perineural analgesia required the least amount of opioids, a significantly lesser chance of technical problems when compared to PCEA, the least incidence of side effects, and a significantly higher satisfaction score[11].

Epidural analgesia has long been considered as the "gold standard" for post-operative pain management, and especially for lower extremity operations. Research indicates that the best post-operative pain management treatments for procedures can be those that are localized at specific sites instead of the more widespread effects of epidural analgesia[9]. It is worthwhile to examine whether perineural nerve catheter analgesia or epidural analgesia serve as a better method in the treatment of managing pain in pediatric patients who undergo a unilateral lower limb surgery.

Materials and Methods

This study was a retrospective study that looked at 65 overall patients (epidural: n = 52, continuous peripheral nerve block: n = 13) between the ages of 5-15 years who underwent a unilateral lower limb surgery at Phoenix Children's Hospital for 24 months from 2014 to 2016. The primary aim of this study was to examine the efficacy of peripheral nerve infusion compared to epidural catheterization.

Inclusion criteria included: 5-15 years of age, underwent a unilateral lower limb surgery at Phoenix Children's Hospital, required an epidural or peripheral nerve catheter

Exclusion criteria included: history of chronic pain, any previous surgery on extremity, previous surgery on surgical extremity, mental delay or non-verbal or migration of catheter before proper removal

Patients were identified via PCH's Got Data request system by searching all patients who underwent a unilateral lower limb surgery in the last 24 months from the study start date and were reviewed for eligibility before data collection was conducted.

The patient electronic medical record was accessed for the enrolled patients and the gender, age, height, diagnosis, surgery information (date of surgery, length of surgery, type of surgery, amount of morphine given), epidural information (placement, medication, length of use), daily morphine usage (all opioids were converted to morphine equivalent), need for analgesic rescue (PCA or other adjunct pain therapies) and adverse events (infection, pruritus, nausea/vomiting, urinary retention, constipation, escalation of care, overdose or compartment syndrome) were gathered.

Outcomes that were assessed included opioid consumption (normalized to patient weight and morphine equivalents), pain scores, need for analgesic rescue, length of stay, time to ambulation and the incidence of adverse events. The epidural exposure group was used as the control group.

Wilson Rank Sum was used to compare continuous variable. Fisher's Exact was used to compare categorical variables. Linear Mixed Model was used to ascertain differences in morphine outcomes over time between epidural and perineural block adjusting for age, gender, height, weight, longitudinal time points, length of stay, intraoperative morphine, and length of anesthesia. Generalized Estimating Equation was used to ascertain the likelihood of adverse events over time between epidural and perineural block catheterization adjusting for age, gender, height, weight, longitudinal time points, length of stay, intraoperative morphine, and length of anesthesia.

Results

The demographics of the patients enrolled in the study include 52 patients that received an epidural infusion and 13 patients that received a continuous peripheral block for a total of 65 patients. Patients of both groups were roughly equal in for both the epidural and peripheral block groups, respectively, for the age (11.1 v. 11.0, p = 0.72), height (144.4 v. 143.4, p =0.54), and weight (43.7 v. 46.7, p = 0.63).

Differences amongst the epidural vs peripheral block groups, respectively, appeared in the length of stay (4.69 v. 4.15 days, p = 0.13), intraoperative morphine (8.63 v. 7.57, p = 0.89), and length of anesthesia (296.8 v. 338.2 min, 0.82).

Of note, 2 (4.08%) of the patients that received a continuous epidural infusion also received a single peripheral nerve block shot (not a continuous infusion) as part of their plan for pain management.

Length of epidural use was 41.5 hours when compared to the peripheral group, 44.3 hours.

Of the patients that received an epidural, 1 (1.92%) had to have the epidural infusion restarted after it was discontinued. In comparison, 1 (7.69%) patient in the peripheral group also had to have the peripheral continuous infusion restarted after it was originally discontinued.

The continuous peripheral nerve block group of patients experienced pain scores that were on average 43% (1.43 [0.33, 1.47], p = 0.35) higher than those of the epidural group. However, the continuous peripheral nerve block group received 98% less (0.02 [0.68, 0.91], p = 0.001) continuous morphine, and 93% less (0.07 [0.03, 012], p < 0.001) continuous clonidine in their infusions when compared to the epidural group.

The continuous peripheral nerve block group also had a PRN morphine requirement that was 31% less (0.69 [0.33, 1.47], p = 0.34) in comparison to the epidural group as well a 68% lower (0.32 [0.11, 0.99], p = 0.049) PCA demand delivery of morphine equivalents.

The continuous peripheral nerve block group received 32% less (0.68 [0.28, 1.67], $p = 0.34$) total morphine equivalents, and when adjusted for weight, received 24% (0.76 [0.36, 1.58], $p = 0.47$) less total morphine equivalents.

The continuous peripheral nerve block group of patients experienced adverse effects at an odds ratio of 0.70 (0.28, 1.74; $p = 0.45$) when compared to the epidural group.

Demographics

Variables	Overall N=65	Epidural N=52	Peripheral Block N=13	P-value
Age, years (mean, SD)	11.1 (3.05)	11.1 (3.17)	11.0 (2.61)	0.72
Sex (male, %)	29 (44.6)	22 (42.3)	7 (53.9)	0.54
Height, cm (mean, SD)	144.2 (20.4)	144.4 (20.9)	143.4 (19.1)	0.81
Weight, kg (mean, SD)	44.3 (22.8)	43.7 (22.9)	46.7 (22.6)	0.63
Length of Stay, days (mean, SD)	1.58 (1.81)	4.69 (1.77)	4.15 (1.95)	0.13
Intra-operative Morphine (mean, SD)	8.41 (6.91)	8.63 (7.32)	7.57 (5.16)	0.89
Length of Anesthesia, min (mean, SD)	305.1 (115.8)	296.8 (112.9)	338.2 (125.6)	0.82
Nerve Block (yes, %)	15 (24.2)	2 (4.08)	13 (100.0)	<0.001
Length of Epidural Use, hours (mean, SD)	41.5 (10.9)	41.5 (10.9)	N/A	N/A
Epidural Restarted (yes, %)	1 (2.00)	1 (1.92)	N/A	N/A
Length of PNC use, hours (mean, SD)	44.3 (15.1)	N/A	44.3 (15.1)	N/A
PNC restarted (yes, %)	1 (7.14)	N/A	1 (7.69)	N/A

Table 1. Demographics of the enrolled patients

Differences in morphine

Outcomes	Epidural vs Peripheral Block Ln (Beta (95% CI)	Epidural vs Peripheral Block exp(Beta (95% CI)	P-value[1]
Pain Score	0.36 (-1.11, 0.39)	1.43 (0.33, 1.47)	0.35
POD continuous Morphine	-4.18 (-0.39, -0.09)	0.02 (0.68, 0.91)	0.001
POD continuous Clonidine	-2.71 (-3.35, -2.08)	0.07 (0.03, 0.12)	<0.001
POD PRN Morphine	-0.36 (-1.12, 0.39)	0.69 (0.33, 1.47)	0.34
POD Total	-0.38 (-1.27, 0.51)	0.68 (0.28, 1.67)	0.39
POD mg/kg Total	-0.28 (-1.03, 0.46)	0.76 (0.36, 1.58)	0.47
POD PCA	-1.11 (-2.23, -0.004)	0.32 (0.11, 0.99)	0.049
	Epidural vs Peripheral Block OR (95% CI)		P-value[2]
Adverse Events	0.70 (0.28, 1.74)	N/A	0.45

Table 2. Epidural (control) group vs. Peripheral continuous infusions

Table 3 shows how the data points changed over time for the 65 enrolled patients. The pain scores for the entire patient cohort showed a subtle decrease of 0.5% (0.995 [0.97, 1.02], p = 0.70). Continuous clonidine saw a 105% increase (2.05 [1.08, 3.86], p = 0.025) in infusions over time while continuous morphine had a 14% decrease (0.86 [0.68, 1.09, p = 0.23).

PRN morphine saw a 10% decrease (0.90 [0.83, 0.90], p = 0.024) over time while PCA usage was also most prevalent in the early post-operative period as there was a 72% decrease (0.28 [0.18, 0.44], p < 0.001) over time. Total morphine equivalent delivery to patients decreased by 14% (0.86 [0.78, 0.95], p = 0.004) over times as well as a 7% decrease (0.93 [0.87, 1.01), p = 0.09) in total morphine equivalents adjusted for weight.

Patient adverse events were also most prevalent earlier on in the post-operative period as there was a 19% decrease (0.81 [0.68, 0.96], p = 0.018) in events over time.

Change over time

Outcomes	Over Time Overall		P-value
	Ln (Beta (95% CI)[1]	exp(Beta (95% CI)	
Pain Score	-0.005 (-0.03, 0.02)	0.995 (0.97, 1.02)	0.70
POD continuous Morphine	-0.15 (-0.39, 0.09)	0.86 (0.68, 1.09)	0.23
POD continuous Clonidine P-value	0.72 (0.08, 1.35)	2.05 (1.08, 3.86)	0.025
POD PRN Morphine P-value	-0.10 (-0.19, -0.10)	0.90 (0.83, 0.90)	0.024
POD Total P-value	-0.15 (-0.25, -0.048)	0.86 (0.78, 0.95)	0.004
POD mg/kg Total P-value	-0.07 (-0.14, 0.007)	0.93 (0.87, 1.01)	0.09
POD PCA P-value	-1.25 (-1.70, -0.81)	0.28 (0.18, 0.44)	<0.001
	OR (95% CI)[2]		
Adverse Events P-value	0.81 (0.68, 0.96)	N/A	0.018

Table 3. Change in time for enrolled patients

Discussion

Both of the groups each had similar breakdowns in demographics in regards to age, sex, height, and weight. Patients in the peripheral group had operations that were on average approximately forty minutes longer (p = 0.82) and received less morphine equivalents intraoperatively (7.57 v. 8.63 [p = 0.89]) when compared to the epidural infusion group. However, the peripheral infusion group had a shorter length of stay in the hospital (4.15v. 4.69 [p = 0.13]), which suggests that these patients had a less eventful recovery and were able to progress more quickly to warrant safe discharges after undergoing procedures that were similarly invasive.

When compared to continuous epidural infusions, the patients that received peripheral continuous infusions had pain scores that were 43% higher (p = 0.35) on average. However, patients in the peripheral group actually received 98% less (p = 0.001) continuous morphine equivalents in their infusions, required 31% less (p = 0.34) PRN morphine equivalents, had 68% less (p = 0.049) PCA usage rates, and received 32% less (p = 0.39) total morphine equivalents when compared to patients that received continuous epidural infusions. One explanation for this observation is that with a more localized analgesia modality, these patients were able to engage in physical activity and rehabilitation sooner than a patient who received the more global effects of an epidural catheter infusion. One benefit of a peripheral nerve block is that the anesthetic agent that acts on nerve fibers first affects the sensory function and careful dosing can preserve the motor function for patients--enabling earlier rehabilitation.

Also, the patients that received a peripheral nerve block encountered less adverse events than the epidural group, odds ratio of 0.70 (p = 0.45). The side effect profiles of epidural infusions are broad and include systemic effects. In addition, patients of both groups did well once their infusions were stopped, but one patient in each the peripheral and epidural group required to have their infusions restarted, respectively, due to inadequate pain control.

All 65 patients' data was analyzed to determine how outcomes changed over time in the postoperative window. The data analysis was not broken down into subset groups of peripheral vs epidural since there was not enough data to trend the change for the groups separately. The analysis shows that over time the patient's pain scores did not vary to a great degree during their hospital stay and only decreased by 0.5% on average ($p = 0.70$) for interval averages at every 12 hours. However, patients received less total and PRN morphine equivalents over time, 14% ($p = 0.004$) and 10% ($p = 0.024$), respectively. Also, patient usage of PCA pumps decreased by 72% ($p < 0.001$) over time. Although pain scores did not decrease markedly, the significant decreases for total morphine, PRN morphine, and PCA usage indicate that patients were less dependent on pain medications the further the removed from the time of operation.

Limitations of this study include that it was retrospective in design. In addition, the sample size, while offering interesting insights into some of the data involving continuous epidural v. continuous peripheral block infusions, was not large enough (total, n = 65 patients; epidural, n = 52; peripheral, n = 13) to provide significant data findings for most or all of the measured outcomes. Surgeons also may choose one form of multimodal analgesia for specific reasons that are important to consider when analyzing outcomes that were not analyzed in this study (e.g., typical expected patient pain/discomfort postoperatively for various procedures, expected time to ambulation and rehabilitation regiment postoperatively for various procedures). Also, some clinicians may have a philosophy of consistently utilizing multimodal analgesia for postoperative pain management for their patients while other clinicians may choose to offer only a spinal or peripheral block intraoperatively and not send patients to the floor with a running infusion. The use of multimodal analgesia is still very much based off of clinician preference.

Future Directions

A randomized control trial with an adequate sample size would better elucidate the benefits of multimodal analgesia for pediatric patients that undergo unilateral lower limb surgery. A future study can also compare patients that received an infusion, either peripheral or epidural, to those that only received a single shot peripheral or spinal block. Also, randomly assigning patients to treatment groups would account for surgeons' individual preferences, and would also account for variables involving patient demographics.

Conclusions

This study suggests that patients that received a peripheral continuous block in comparison to an epidural infusion experienced less adverse effects, had shorter hospital stays, and had a similar length of catheter use. Also, while they had higher pain scores, they also had significantly less exposure to opioids in via infusions, PCA pumps, scheduled oral pain medications, and as needed pain medications. Continuous peripheral infusions are a valid alternative to epidural infusions for pediatric patients that undergo a unilateral lower limb surgery and should be considered as part of the therapeutic plan for these patients.

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