Comparison of Morphine- and Hydromorphone-Containing Patient-Controlled Epidural Analgesia Solutions in Pediatric Postoperative Patients

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OBJECTIVE The use of patient-controlled epidural analgesia (PCEA) in pediatric patients has been shown to be safe and effective in managing postoperative pain in children. However, the optimal opioid to use in the epidural regimen remains undetermined. Morphine, hydromorphone, and fentanyl have been the agents most often used, but comparison of effectiveness across studies is difficult. The goal of this study was to compare postoperative pain scores in patients receiving PCEA solutions that contained either ropivacaine plus morphine or ropivacaine plus hydromorphone.

METHODS Retrospective chart review was used at a single center to identify pediatric patients between the ages of 5 and 17 years who used a morphine- or hydromorphone-containing PCEA solution postoperatively during an 18-month period. Maximum pain scores were recorded during 2 consecutive 24-hour periods postoperatively. The primary outcome was the number of patients who had a maximum pain score of ≤ 4 on postoperative day zero and postoperative day 1.

RESULTS Forty-six patients met the inclusion criteria and were analyzed. Patients prescribed morphine-containing PCEAs had a significantly higher incidence of maximal pain scores ≤ 4 in the 48 hours immediately after surgery compared with those patients prescribed hydromorphone-containing PCEAs ($p = 0.03$). Ropivacaine dosing in the epidural solution did not have a significant effect on pain scores and was not statistically different between opioid groups. Pediatric patients were able to effectively use the PCEA on-demand dose, with patients having pain scores > 4 demanding significantly more on-demand doses from the PCEA than those patients with pain scores ≤ 4 ($p \leq 0.002$). No serious adverse events were reported.

CONCLUSIONS Morphine-containing PCEAs may have an advantage in controlling postoperative pain in pediatric patients compared with hydromorphone-containing PCEAs. However, the heterogeneous nature of the procedures performed and the small sample size limit the generalizability of this study.

ABBREVIATIONS CEA, continuous epidural analgesia; PACU, postanesthesia care unit; PCA, intravenous patient-controlled analgesia; PCEA, patient-controlled epidural analgesia; POD, postoperative day

KEYWORDS epidural; hydromorphone; morphine; pain; pediatric patients

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Introduction

The use of epidural analgesia containing a combination of an opioid and a local anesthetic postoperatively to control pain has been reported previously as a safe and effective option in the pediatric population.^{1–3} Patient-controlled epidural analgesia (PCEA) is one strategy that can be used for epidural pain control, which gives the patient an on-demand dose available via a button in addition to a continuous basal infusion. This approach mimics the more commonly used intravenous patient-controlled analgesia (PCA) that is widely used for pain control in a multitude of adult and pediatric settings. Literature has shown that PCEA can provide effective analgesia with a lower total dose of opioid and local anesthetic compared with simple continuous epidural analgesia (CEA).^{4,5} Most of the available literature

on PCEA use in the pediatric population concerns the safety and efficacy of a single opioid or investigates if pediatric patients are able to appropriately manage a PCEA. Birmingham et al² demonstrated that pediatric patients as young as 5 years can successfully manage their own PCEA, which is similar to findings for intravenous PCAs. Which opioid agent is used in the PCEA is largely institution and provider dependent, because there is little literature evaluating the comparative efficacy of different opioids in PCEA solutions. The goal of this investigation was to evaluate the effect of opioid choice and dosing parameters on postoperative pain scores.

Methods

Retrospective chart review was used to identify pa-

tients who underwent a planned surgical intervention during an 18-month period between June 2015 and December 2016 and used a PCEA postoperatively for pain control. Inclusion criteria were use of a PCEA with both a basal rate and an on-demand dose for at least 48 hours postoperatively, morphine or hydromorphone as the opioid in the PCEA, and patient age between 5 and 17 years. Exclusion criteria were defined as <48 hours of PCEA use postoperatively, patient admission not preplanned, the surgical intervention not preplanned, use of a PCEA without an opioid, use of a continuous epidural without an on-demand dose (CEA), or age greater than 17 or less than 5 years. Data collected included demographic data, medical condition that necessitated the surgical intervention, type of procedure performed, spinal level of epidural placement, duration of epidural use, concentration of ropivacaine and opioid in the epidural solution, PCEA dosing parameters, whether or not the dosing parameters were adjusted after initiation of infusion, type of dosing adjustment done, length of hospital stay, type of pain assessment, maximum pain scores on postoperative days (PODs) 0 to 1, number of PCEA bolus dose demands per day, number of PCEA bolus dose deliveries per day, the need for naloxone for pruritus, and the use of scheduled acetaminophen postoperatively concomitantly with the PCEA. All dosing parameters, such as hourly rate and bolus dosing, were ordered by the medical provider in terms of milliliters of PCEA solution. This information was converted into weight-based dosing for purposes of comparing data. POD 0 was defined as the first 24 hours postoperatively after leaving the postanesthesia care unit (PACU). POD 1 was defined as the second postoperative 24-hour period after leaving the PACU. Scheduled acetaminophen was defined as oral, rectal, or intravenous acetaminophen ordered on an every 6-hour or every 4-hour schedule with at least 3 doses given, with the first dose given within 12 hours of surgery. Length of stay was measured from the time the patient was admitted to the general nursing unit to account for differences in procedure length, time spent in the PACU, and any time spent in the hospital prior to the procedure. This review was approved by the Institutional Review Board and was exempt from obtaining patient consent due its retrospective nature.

The primary outcome was the percentage of patients in each opioid group with pain scores ≤ 4 on POD 0 and POD 1 (0–48 hours after completion of procedure). Pain scores of ≤ 4 were considered as adequate pain control. Pain scores were determined by the bedside nurse using the Face, Legs, Activity, Cry, Consolability (FLACC) pain scale or the Verbal Numerical Rating Scale as appropriate for age.^{6,7} The choice of which pain scale to use was at the discretion of the bedside nurse. Both of these scales were recorded as a 0 to 10 numeric score in the electronic medical record by the bedside nurse with each completed pain assessment. Data for pain

Table 1. Most Common Exclusion Criteria

Exclusion Criteria	No. of Exclusions
Age <5 yr or >17 yr	38
Epidural used for <48 hr	21
Not a planned admission	12
Fentanyl-containing PCEA	1
Other	9

PCEA, patient controlled epidural analgesia

scores were collected beginning at the time of admission to the general nursing unit. Pain scores recorded in the PACU were not collected. Secondary outcomes included an analysis of the percentage of patients with pain scores ≤ 4 on POD 0 and POD 1 independent of each other, the impact of opioid dosing on pain scores, the impact of ropivacaine dosing on pain scores regardless of opioid choice, and appropriate use of the on-demand bolus dose.

Statistical analysis of demographic and PCEA data was completed using χ^2 analysis or Fisher exact test for categorical variables and Wilcoxon rank sum test or Student *t*-test for continuous variables. An α level of 0.05 for all statistical tests was used.

Results

Chart review identified a total of 127 patients in the electronic medical record who used a ropivacaine with opioid-containing PCEA in the 18-month review period. A total of 85 patients were excluded based on the exclusion criteria previously defined. Details related to exclusions can be found in Table 1. A total of 46 patients met criteria for analysis. Morphine-containing PCEAs were documented in 25 eligible patients, and hydromorphone-containing PCEAs were documented in 21 eligible patients. A total of 5 morphine patients and 4 hydromorphone patients had their on-demand dose controlled by a parent or RN. The youngest patients controlling their own on-demand doses were 7 years old. No patient was transitioned from one opioid to the other. Demographic data can be found in Table 2. There were no significant differences between the 2 opioid groups in baseline characteristics. All epidural catheters were placed in the operating suite, and the PCEA solution was initiated in the operating room or, occasionally, in the PACU. Placement of the epidural catheter ranged from the T4 to L4 level. The exact thoracic or lumbar level of placement was not recorded in 1 patient. The most common procedure performed was the Nuss procedure for pectus excavatum (21 of 46 patients). This procedure accounted for 36% and 57% of the morphine and hydromorphone PCEA uses, respectively. The next most common procedures were exploratory laparotomies, followed by various abdominal mass and cyst excisions. The primary outcome mea-

Table 2. Baseline Patient Population Characteristics

Characteristics	Morphine (n = 25)	Hydromorphone (n = 21)	p value
Age, yr, mean (range)	12.9 (6–17)	13 (5–16)	0.94
Weight, kg, mean (range)	48.7 (17–70)	51.1 (13–75)	0.62
Female, %	44	42.8	0.94
Thoracic epidurals, %	70.8	76.2	0.68
Duration of use, hr, mean $\pm$ SD	82.16 $\pm$ 22.95	85.3 $\pm$ 22.4	0.59
Patients undergoing Nuss procedure, %	36	57	0.15
Patients with PCEA dosing adjustment made, %	32	42.8	0.45
Patients with scheduled acetaminophen started postoperatively, %	56	43	0.37

PCEA, patient-controlled epidural analgesia

sure of maximum pain scores ≤ 4 on POD 0 and POD 1 was achieved in 12 of 25 morphine patients and 3 of 21 hydromorphone patients ($p = 0.03$; Table 3). When broken down by individual postoperative day, 15 of 25 morphine patients had a maximum pain score of ≤ 4 on POD 0 compared with 6 of 21 hydromorphone patients ($p = 0.03$). On POD 1, 14 of 25 morphine patients and 7 of 21 hydromorphone patients had a maximum pain score of ≤ 4 ($p = 0.12$).

PCEA basal flow rates were between 0.06 and 0.38 mL/kg/hr. There was no significant difference in the weight-based flow rates in patients with adequate vs. inadequate pain control on either POD individually or during the entire 48-hour study period. Details for morphine and hydromorphone PCEA opioid usage can be found in Table 4. The total amount of opioid delivered, on a mcg/kg basis, POD 0 and POD 1 was not statistically different between patients with pain scores of ≤ 4 or > 4 for either opioid group. There were also no statistically significant differences in the percent of total daily opioid delivered by the on-demand bolus between morphine and hydromorphone groups on POD 0 or POD 1. Total numbers of demands and deliveries were also not statically different between the 2 opioid groups on either POD.

All PCEAs contained either 0.1% or 0.2% ropivacaine. Across all patients, ropivacaine was administered at an average basal rate of 0.2 mg/kg/hr (range, 0.09–0.38 mg/kg/hr), which falls within our institutional recommendations of a maximum dose of 0.4 mg/kg/hr. Neither the basal dose of ropivacaine (mg/kg/hr) nor the total daily amount of ropivacaine delivered (mg/kg/day) was significantly different between opioid groups or between patient groups with pain values of > 4 or ≤ 4 on either postoperative day (all $p > 0.6$).

Table 5 shows PCEA bolus demands and deliveries compared with maximal pain scores irrespective of opioid. Bolus dose volumes were between 0.5 and 5 mL per bolus. The number of allowed boluses per hour ranged from 1 to 3. The median lockout interval between boluses was 30 minutes (range, 15–60 minutes). There were significantly more demands and deliveries in the patients with inadequate pain control on both PODs. These numbers remained significantly different when the 9 patients who had a parent- or nurse-controlled on-demand dose were removed from the data analysis.

Naloxone was initiated by the bedside nurse in 10 morphine patients and 14 hydromorphone patients for symptoms of pruritus ($p = 0.06$). At our institution, the bedside RN may start a low- dose naloxone infusion when he or she deems it necessary for signs of pruritus. Scheduled acetaminophen was used in 50% of patients (14 morphine and 9 hydromorphone patients). However, because of the small number of patients, an appropriate multivariate analysis of the effect of acetaminophen and the choice of opioid on pain scores was not possible.

At least 1 episode of emesis was seen in 22 patients within the 48-hour study period. However, several patients had a nasogastric sump tube in place, which may have prevented emesis episodes from being clinically recognized, and thus an accurate analysis of emesis between the 2 opioid groups was not possible with the retrospective data available. There were no serious adverse effects reported related to epidural use during the 18-month study period.

Discussion

Although only a total of 15 of 46 patients between the 2 opioid groups in this study achieved the primary

Table 3. Patients With Maximum Pain Scores ≤ 4

Postoperative Day	Morphine (n = 25)	Hydromorphone (n = 21)	p value
0, n (%)	15 (60)	6 (29)	0.03
1, n (%)	14 (56)	7 (33)	0.12
0 and 1, n (%)	12 (48)	3 (14)	0.03

Table 4. Morphine and Hydromorphone PCEA Opioid Delivery

Opioid Delivery	Morphine, Mean (Range)			Hydromorphone, Mean (Range)		
	POD 0	POD 1	p value	POD 0	POD 1	p value
Opioid delivered by basal rate, mcg/kg/day	65.5 (49–82.3)	64 (43–74.5)	0.19	24.8 (16.4–30.8)	24.8 (16.4–30.8)	0.94
Opioid delivered by on-demand bolus doses, mcg/kg/day	6.9 (3.1–10.8)	7.1 (3.7–10.7)	0.34	2.8 (1.4–4.4)	2.8 (1.2–4.4)	0.35
Total daily dose delivered by on-demand bolus, %	10 (4.8–13.4)	10 (5.3–17.2)	0.28	9.4 (5.3–20)	10 (5–21)	0.83

POD, postoperative day

outcome, only maximum daily pain scores were being evaluated in this study, and therefore it does not necessarily reflect the overall success of PCEA as a pain control strategy. A patient with a single moment of pain scoring >4 could have been effectively managed by a push of the on-demand button but would still have failed to meet criteria for the primary outcome. A search of the literature only identified 2 studies that directly compare hydromorphone to morphine epidurals in postoperative patients, and these studies used CEA instead of PCEA.^{8,9} Chaplan et al⁸ examined adult patients after major surgical procedures and found hydromorphone and morphine to be equivalent in controlling pain. Goodarzi⁹ published a study of pediatric patients after orthopedic procedures and concluded that morphine, hydromorphone, and fentanyl to have equivalent pain control; however, that study used a 3-fold higher rate of morphine infusion compared with the dosing reported in this study. Both studies noted an increased incidence of side effects with morphine; however, the differences in opioid doses and patient populations between these published studies and this investigation make direct comparison challenging. A meta-analysis of adult and pediatric epidural opioid analgesia, not specific to PCEAs in the postoperative setting, was also unable to draw any conclusions as to the most efficacious opioid to use.¹⁰

Ropivacaine dosing had no apparent effect on maximum pain scores. This is likely due to the homogenous nature of the dosing reported in this study between the 2 opioid groups. The data on the number of demand and delivery doses in patients with well controlled compared with inadequately controlled pain reaffirms that pediatric patients can appropriately use an on-demand epidural bolus dose.

Although data pertaining to side effects other than pruritus were unable to be adequately collected in

this retrospective study, there were a large number of patients switched from PCEA therapy to PCA therapy in the first 48 hours postoperatively and thus excluded from analysis, which may be concerning for poor efficacy or intolerable side effects. Unfortunately, it was difficult to determine with certainty in every case if the change in delivery routes was made because of issues with the epidural site, lack of adequate pain control, side effects, and/or patient/caregiver preference.

The largest limitation to this study was the heterogeneous nature of the procedures performed. The population of available patients was not large enough to control for this variable in this investigation, and different procedures can result in vastly different amounts of pain in the initial postoperative period. Another limitation was that this study only looked at maximal pain scores in two 24-hour periods. It is possible that some patients with pain scores of 5 or greater had reasonably well controlled pain at rest and experienced isolated periods of pain with attempts to move or reposition the patient. Urinary retention is a common side effect of epidural analgesia; however, due to the retrospective nature of this investigation and the heterogeneous patient population, a standardized collection of urine output data was not possible. Finally, this was a retrospective single-center study with a small cohort of patients available for examination.

Conclusion

This retrospective study showed that ropivacaine + morphine PCEAs may have a superior ability to control pain compared with ropivacaine + hydromorphone PCEAs in the initial 48-hour postoperative period, with the largest benefit of morphine compared with hydromorphone seen in the initial 24 hours after surgery. Epidural ropivacaine dosing does not appear to

Table 5. Patient-Controlled Epidural Analgesia Patient-Initiated Bolus Dose Demands and Deliveries

	Postoperative Day 0, Median (25%–75% IQR)			Postoperative Day 1 (25%–75% IQR)		
	Max Pain Score ≤4	Max Pain Score >4	p value	Max Pain Score ≤4	Max Pain Score >4	p value
Deliveries	5 (4–9)	12 (8–16)	<0.001	7 (2–9)	13 (9–20)	<0.001
Demands	7 (4–10)	18 (10–29)	<0.001	7 (2–13)	20 (14–35)	0.002

influence pain scores. The ability of patients aged 5 to 17 years to effectively manage a PCEA on-demand button was demonstrated in this study and supports earlier research on this topic. Unfortunately, the small sample size and heterogeneity of the surgical procedures performed limit the strength of this study. A larger study controlling for the operative procedure performed with more granular pain score reporting is warranted to further investigate the differences in effectiveness of morphine and hydromorphone PCEAs postoperatively in pediatric patients.

ARTICLE INFORMATION

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