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Original Article

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Preliminary Experience With a Continuous Lidocaine Infusion as an Analgesia Adjunct for Acute Pain Management Following Surgery in Pediatric Patients

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Abstract

Background: Lidocaine is a local anesthetic of the amide class that has been used for various therapeutic interventions. Its potential analgesic effects have been reported in anecdotal reports and larger clinical trials.

Methods: We retrospectively reviewed our 24-month experience with the use of lidocaine outside of the intensive care unit (ICU) setting as an adjunct to acute pain management following major surgical procedures in children and adolescents.

Results: The study cohort included 168 patients (mean age 13.8 years). The majority of patients (N = 142) underwent a posterior spinal fusion for treatment of scoliosis (idiopathic or neuromuscular). Thirty-one patients received a bolus dose followed by an infusion starting at 0.2 to 2 mg/kg/h (average dose 0.97 mg/kg/h). Most patients (86.3%) received a continuous lidocaine infusion for 1 - 3 days at an average dose of 1 mg/kg/h. Lidocaine was infused for a total of 503 days in the study cohort of 168 patients. Despite that these were major surgical procedures, pain scores were generally acceptable. The lidocaine infusion was discontinued or decreased in eight patients due to concerns of adverse effects. Adverse effects were noted in 38 days of the 503 days of infusion (7.6%). A total of 29 patients (17.3%) experienced at least one adverse effect. The majority of these were related to the central nervous system (CNS) including blurred vision, dizziness, drowsiness/difficult to arouse, delirium, hallucinations, agitation, and confusion.

Conclusions: We present the largest study to date outlining the use of lidocaine as an adjunct to acute pain management in children and adolescents. These preliminary data suggest that with enhanced clinical observation for signs of potential toxicity and increased clinical monitoring of vital signs, the lidocaine infusion can be administered on the inpatient ward without routine serum concentration monitoring. The current cohort and other studies in pediatric patients provide a background for prospective studies to evaluate dosing regimens, optimal patient populations, and analgesic efficacy.

Keywords: Lidocaine infusion; Multimodal analgesia; Acute pain; Postoperative analgesia

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Introduction

Although the mainstay for the treatment of acute post-surgical pain has been opioids, their use can result in adverse effects including opioid-induced respiratory depression, sedation, nausea, vomiting, constipation, postoperative ileus, and pruritus [1-3]. Recent strategies for the management of severe postoperative pain have focused on a multimodal approach using non-opioid adjunctive agents to improve analgesia while decreasing opioid needs and limiting opioid-related adverse effects. The need to develop these initiatives for the treatment of acute pain has been further supported by the increasing concern regarding opioid abuse and diversion [4].

Lidocaine is a local anesthetic of the amide class that has been used primarily for the treatment of arrhythmias, neuraxial anesthesia, and superficial infiltration for cutaneous analgesia. Shortly after its release for clinical use in 1948, its potential analgesic effects were noted, anecdotal reports were published, and larger clinical trials demonstrated its efficacy in both acute and chronic pain of various etiologies [5]. More recently, several prospective trials in adults have demonstrated its effects on acute post-surgical pain with improvement in pain scores and decreased opioid needs in addition to its anti-hyperalgesic and anti-inflammatory effects [6, 7]. However, there remains limited information regarding its use in pediatric-aged patients. Part of this may be related to restriction of its use to the

intensive care unit (ICU) setting in many pediatric hospitals. We present our protocol for the continuous intravenous infusion of lidocaine on the inpatient ward as an adjunct for pain management in the perioperative setting following major surgical procedures in pediatric-aged patients. Additionally, we retrospectively review our initial 15 months of experience with the use of lidocaine in this clinical setting.

Materials and Methods

The study cohort included patients ≤ 21 years of age who received a postoperative lidocaine infusion as an adjunct to pain management. The 15-month study period included August 1, 2020 through October 31, 2021. The start date for the study was chosen as it was the date of initiation of an institutional policy and procedure for the administration of lidocaine infusion as an adjunct to perioperative pain management on the inpatient ward (outside of the pediatric ICU setting). Information regarding the development of this protocol and its requirements is outlined below. Patients receiving a therapeutic lidocaine infusion for control of perioperative arrhythmias were excluded. Patients were identified and the patient list created from records from the Acute Pain Service, pharmacy database, and the EPIC Data Warehouse. For each patient, demographic data were collected including age, gender, weight, height, race, ethnicity, surgical procedure, and comorbid conditions. Perioperative information and data regarding the lidocaine infusion included the surgical procedure, whether a bolus of intravenous lidocaine was administered intraoperatively and its dose, and the initial infusion rate (mg/kg/h) administered in the operating room (OR). Adjustments to the lidocaine infusion rate during the intraoperative period and in the post-anesthesia care unit (PACU) were noted. Information was retrieved regarding pain and analgesia; data collected included pain scores, analgesic agents administered (opioids and adjunctive agents), and the dose and frequency of pain medications. Postoperative information gathered about the lidocaine infusion included the infusion rate (mg/kg/h), adjustments to the infusion rate including the new infusion rate, reasons for stopping the lidocaine infusion, and total duration (in days) of lidocaine therapy. Lidocaine and analgesia efficacy included objective data of pain scores using the r-FLACC (face, legs, activity, cry, consolability), Wong-Baker pain rating scales (FACES), or numeric rating pain scales (NRS) depending on the patient's age and cognitive state. Additional subjective data regarding efficacy were obtained from reviewing the daily progress notes. Pain scores were documented prior to (if applicable), during, and after initiation of lidocaine therapy. Adverse events were also recorded each day for patients while on the lidocaine infusion including the need to stop the lidocaine infusion or decrease the infusion rate. End organ function (renal and hepatic) was assessed by reviewing available laboratory values including complete blood count, renal, and hepatic function tests. Baseline and subsequent electrocardiogram (ECG) data were reviewed. Lidocaine levels were not routinely obtained as part of the protocol (see below).

Lidocaine protocol

Prior to the start of this initiative, a standardized lidocaine policy and protocol was created for the hospital which outlined the use of a lidocaine infusion on the inpatient ward as an adjunct to pain management for acute or chronic pain related to surgical or medical conditions. Mandatory education was provided to inpatient nursing staff prior to caring for these patients after surgery through the hospital online learning system. This education provided information about the use of lidocaine for analgesia, dosing, adverse effects, patient monitoring, and documentation requirements in the electronic medical record (EMR). After completion of the module the nurse completed a post-test to receive credit for completing the module. Information about the use of lidocaine for analgesia was also added to the hospital's pain management intranet website. The use of the lidocaine infusion started on the inpatient ward for Hematology & Oncology patients and was then expanded to other inpatient wards approximately 6 months later. The lidocaine infusion for analgesia on patients on the inpatient wards was managed by a consultation to either the acute pain service or the palliative care service. As part of the protocol, a baseline ECG within 30 days was obtained and if no arrhythmias were noted, the patient was not placed on an ECG monitor during the infusion on the inpatient ward. For patients who received an intraoperative lidocaine infusion, the intraoperative ECG was used instead of a standard 12-lead ECG. During the postoperative infusion, all patients were placed on continuous oxygen saturation monitoring during the infusion. Blood pressure, heart rate, respiratory rate, sedation, and level of consciousness were monitored at initiation of the infusion, every 30 min for 1 h, hourly for 2 h and then every 4 h during the remainder of the infusion. The presence of any symptoms of central nervous system (CNS) toxicity was documented every 30 min × 2 and then every hour during the infusion. Pain scores were monitored per hospital protocol. An order set was created in the EMR system to include all the necessary dosing and monitoring information from the lidocaine for analgesia protocol. Dosing for acute pain management included a lidocaine infusion initiated at 1 mg/kg/h intraoperatively and continued postoperatively on the inpatient ward. A bolus dose of 1 mg/kg was optional prior to starting the infusion. Per institutional policy, the maximum lidocaine infusion rate was 3 mg/kg/h or 200 mg/h. For obese patients, ideal body weight was used for dosing.

Statistical analysis and data presentation

Data were collected through research electronic data capture (REDCap) and analysis was performed using IBM SPSS 28.0.0 and R 4.3.1. To gain a comprehensive understanding of the data, exploratory data analysis (EDA) was conducted. The statistical analysis was conducted with a focus on the descriptive statistics. For continuous variables, the mean and range were reported, as well as the median and interquartile range (IQR). Categorical variables were presented using counts and percentages. To identify significant variations in the variables,

Table 1. Patient Characteristics of the Study Cohort (N = 168)

Variable	N (%)	Mean (range)	Median (IQR)
Age (years)		13.8 (1, 21)	14 (12, 16)
Gender			
Male	65 (38.7%)		
Female	103 (61.3%)		
Race			
White	137 (81.5%)		
Black	16 (9.5%)		
Asian	5 (3.0%)		
Mixed race	10 (6.0%)		
Weight (kg)		51.1 (6.9, 141.3)	48.7 (36.8, 61.4)
Height (cm)		152.1 (58.2, 181.4)	156.3 (146.4, 163.5)
ASA physical class			
I	21 (12.5%)		
II	79 (47.0%)		
III	63 (37.5%)		
IV	5 (3.0%)		

IQR: interquartile range; ASA: American society of anesthesiologists.

both parametric and non-parametric tests were employed based on the distribution of each variable. The threshold for establishing significance was set at 0.05.

This retrospective study was approved by the Institutional Review Board of Nationwide Children's Hospital. As this was a retrospective study using de-identified data, the need for written informed consent was waived. The study was conducted in accordance with the guidelines of the Declaration of Helsinki.

Results

The demographic data are outlined in Table 1. The study cohort includes 168 patients, ranging in age from 1 to 21 years with a mean age of 13.8 years. The patients ranged in weight from 6.9 to 141.3 kg with a mean weight of 51.1 kg. Intraoperative data including anesthetic and surgical information as well as lidocaine dosing parameters are outlined in Table 2. The majority of patients (N = 142) underwent a posterior spinal fusion for treatment of scoliosis (idiopathic or neuromuscular). A total of 148 of the cohort of 168 patients (88.1%) had the lidocaine infusion started intraoperatively. Of these patients, 31 received a bolus dose of lidocaine prior to starting the infusion. The bolus dose varied from 30 to 100 mg with an average dose of approximately 1 mg/kg. This was followed by an infusion starting at 0.2 to 2 mg/kg/h (average dose of 0.97 mg/kg/h). The infusion was continued intraoperatively during the surgical procedure for an average of 329 min (range from 110 to 627 min). No significant adverse effects which could be attributed to lidocaine were noted intraoperatively. There was no difference in pain scores when comparing those who received a lidocaine infusion intraoperatively and those who did not (P-value = 0.408).

Postoperatively, the majority of patients (86.3%) received a continuous lidocaine infusion for 1 - 3 days at an average dose of 1 mg/kg/h. The infusion was started at 2 mg/kg/h in one patient and 1.5 mg/kg/h in one patient while 14 patients had the infusion started at less than 1 mg/kg/h. In the remaining patients, lidocaine infusions were continued from 4 up to 12 days. Lidocaine was infused for a total of 503 days in the study cohort of 168 patients. The lidocaine infusion was discontinued or decreased in eight patients due to concerns of adverse effects (see below). The infusion was increased in two patients due to pain. A Spearman's rank-order correlation was conducted to assess the relationship between the amount of lidocaine administered and the length of hospital stay. The results indicated a weak, negative correlation with statistical significance (r = -0.237, P-value = 0.004). As the amount of lidocaine administered increased, the length of hospital stay tended to decrease. In addition to lidocaine and an opioid infusion, intraoperative and postoperative analgesic adjuncts included dexmedetomidine in three patients and ketamine in one patient. Pain was well controlled during the first 7 postoperative days from these major surgical procedures (Table 3).

During the postoperative infusion, no clinically significant adverse hemodynamic, neurologic or respiratory effects that required an escalation of care or pharmacologic intervention were noted. Adverse effects, which may or may not have been related to the lidocaine infusion, were noted in 38 days of the 503 days of infusion (7.6%). A total of 29 patients (17.3%) experienced at least one adverse effect (Table 4). The majority of these adverse effects were related to the CNS includ-

Table 2. Anesthesia and Surgical Times With Lidocaine Infusion Information

Variable	N (%)	Mean (range)	Median (IQR)
Surgical procedure			
Posterior spinal fusion	142 (84.5%)		
Other	26 (15.5%)		
Total anesthesia time (min)		409.70 (76, 946)	400 (345.5, 469.5)
Total surgery time (min)		288.54 (13, 800)	281.5 (229.0, 343.8)
Lidocaine infusion used intraoperatively	148 (88.1%)		
Number patients who received lidocaine bolus	31 (18.5%)		
Amount of lidocaine bolus (mg)		53.5 (30, 100)	50 (40, 60)
Intraoperative starting dose rate (mg/kg/h)		0.97 (0.5, 2)	
Total lidocaine infusion time during procedure (min)		329 (110, 627)	327 (264, 382)
Lidocaine infusion used postoperatively	168 (100%)		
Infusion rate (mg/kg/h)		1 (0, 2)	1 (1, 1)
Number of postoperative infusion days			
One	5 (2.98%)		
Two	43 (25.60%)		
Three	97 (57.74%)		
Four	14 (8.33%)		
Five	2 (1.19%)		
Six	3 (1.79%)		
Seven	1 (0.60%)		
Eight	1 (0.60%)		
Ten	1 (0.60%)		
Twelve	1 (0.60%)		

IQR: interquartile range.

ing blurred vision, dizziness, drowsiness/difficult to arouse, delirium, hallucinations, agitation, and confusion. During the study period, there was an inadvertent programming error with an intraoperative infusion pump which resulted in a lidocaine overdose. The programming error was noted during the hand-off from the OR to the PACU. The lidocaine infusion was discontinued and the patient admitted to the pediatric ICU overnight for monitoring. These patient data were not included in this study cohort because they did not receive a postoperative lidocaine infusion.

Discussion

Lidocaine is a local anesthetic agent of the amide class that was originally synthesized in the 1940s. It is tertiary amine and a class Ib anti-arrhythmic agent on the Vaughan-Williams classification that is used primarily in clinical practice to treat

Table 3. Postoperative Pain Scores 0 - 10

Postoperative day	N	Pain score (mean, range)	Pain score (median, IQR
Day 1	164	2.3 (0, 10)	2.0 (0.5, 3.8)
Day 2	165	2.2 (0, 7.5)	1.9 (0.9, 3.3)
Day 3	155	2.1 (0, 8)	1.9 (0.6, 3.3)
Day 4	83	2.0 (0, 9.5)	1.5 (0, 3.20)
Day 5	36	1.4 (0, 4.5)	1.1 (0.3, 2.4)
Day 6	11	0.7 (0, 5.3)	0 (0, 0.5)
Day 7	6	1.2 (0, 5)	0.4 (0, 2.5)

IQR: interquartile range.

Table 4. Type of Adverse Event[a]

Type of adverse event	N	Percentage[b]
Blurred vision, dizziness, drowsiness/difficult to arouse	13	8.1%
Delirium, hallucinations, agitation, confusion	10	6.2%
Nausea	9	5.6%
Hypotension	7	4.3%
Pruritus	7	4.3%
Headache	2	1.2%
Bradycardia	2	1.2%
Myoclonus/muscle spasms	2	1.2%
Hypertension	1	0.6%
Breathing difficulties	1	0.6%
Circumoral numbness	1	0.6%
Bradypnea	1	0.6%
Edema	1	0.6%
Head bobbing	1	0.6%
Constipation	1	0.6%
High pain scores	1	0.6%
Sore throat	1	0.6%
Total	61	-

[a]Some patients experienced more than one adverse event. [b]The study cohort included 168 patients.

ventricular arrhythmias [8, 9]. In addition to its anti-arrhythmic effects, it has been shown to inhibit nociception through several mechanisms including a reduction in the inflammatory cascade with a depression of the release of inflammatory cytokines and complement, reducing peripheral and central pain sensitization and wind-up [6, 10, 11].

Toxicity is manifested as CNS excitation (seizures) and cardiac manifestations (hypotension and cardiac arrest). The potential for life-threatening cardiac toxicity is less with lidocaine than with the other amide local anesthetic agents such as bupivacaine, thereby making successful resuscitation more likely [12-14]. Lidocaine is one of the most commonly used local anesthetic agents with applications for topical anesthesia of the skin and mucous membranes, superficial and deep infiltration to provide analgesia during minor surgical procedures, for regional anesthetic techniques (spinal anesthesia, epidural anesthesia, and peripheral nerve blockade), and as a therapeutic agent to treat cardiac arrhythmias. In addition, it has seen increasing use to treat acute and chronic pain of various etiologies via intravenous use.

The beneficial effects of the perioperative administration of intravenous lidocaine during and following major surgical procedures has been well documented in the adult literature. The majority of this literature pertain to major gastrointestinal procedures, both open and laparoscopic and major orthopedic (spinal) surgery with the demonstration of a reduction in pain scores, decreased opioid use, reduced incidence of postoperative ileus, earlier return of bowel function, decreased incidence of postoperative nausea and vomiting, as well as decreased hospital length of stay [15-19]. Despite significant use and outcome data in adults, the pediatric literature is confined to smaller studies demonstrating the benefit in both the postoperative period as well as for acute and chronic pain of various etiologies [7].

The first reported series regarding the use of a continuous lidocaine infusion as an analgesic adjunct in pediatric-aged patients was published by Wallace and colleagues in 1997 [20]. The open-label study cohort included five patients, 4 - 7 years of age, with neuroblastoma presenting for multiple courses of immunotherapy with anti-GD2 antibody. The patients received either lidocaine (2 mg/kg) or morphine (0.1 mg/kg) over 30 min prior to the start of therapy followed by an infusion of either lidocaine (1 mg/kg/h) or morphine (0.05 - 0.1 mg/kg/h). Breakthrough pain was managed with intravenous morphine and outcomes were evaluated by pain scores and opioid needs. Although overall opioid-consumption was decreased when patients received lidocaine, there was no significant differences in pain scores or breakthrough morphine consumption. Subsequently, various studies have evaluated the efficacy of lidocaine to improve analgesia and decrease opioid use following major abdominal surgery, spinal surgery, laparoscopic appendectomy, and tonsillectomy [7, 21-25]. Although not uniformly successful based on study design and study cohort numbers, in general, the perioperative infusion of lidocaine in children has demonstrated similar results to those reported in adults including decreased opioid use, decreased pain scores, decreased intraoperative anesthetic requirements, earlier return of bowel function, and decreased pro-inflammatory mediators.

As noted previously, when compared to the adult popula-

tion, there remains a paucity of data in pediatric-aged patients. Part of this may relate to concerns of toxicity and adverse effects as well as limited availability to provide a continuous lidocaine infusion outside of the ICU setting. In the pediatric population, lidocaine infusion is used most commonly to treat ventricular arrhythmias, mandating its administration in the ICU setting. As outlined above, given our interest in the use of this potentially valuable adjunct to treat postoperative pain, acute medical pain, and chronic pain, we developed a pathway for its administration on the inpatient ward. As part of the protocol, serum levels were not routinely monitored and continuous ECG monitoring was not required. Enhanced postoperative monitoring included continuous oxygen saturation monitoring (pulse oximetry) as well as monitoring of blood pressure, heart rate, respiratory rate, sedation, and level of consciousness at initiation of the infusion, every 30 min for 1 h, hourly for 2 h and then every 4 h during the remainder of the infusion. Additionally, ongoing assessment is included to evaluate for signs or CNS toxicity.

The current study involved a retrospective review of our initial 168 postoperative patients, ranging in age from 1 to 21 years with a cumulative duration of 503 days of infusion. Given the surgical population with the inclusion of a lidocaine infusion as part of our enhanced recovery after surgery (ERAS) pathway for spinal surgery (posterior spinal fusion), the majority of the patients were adolescents presenting for major orthopedic surgery. Dosing included a bolus dose of 1 mg/kg followed by an infusion of 1 mg/kg/h. Clinically significant adverse effects that required pharmacologic intervention or escalation of care were not noted. The infusion was paused only seven times due to concerns of adverse effects. Although various adverse effects were noted in the study cohort, a direct causal relationship attributed to lidocaine could not be differentiated as these patients were also receiving additional medications and recovering from a major surgical procedure. The majority of the adverse effects were minor and related to the CNS including blurred vision, dizziness, drowsiness/difficult to arouse, delirium, hallucinations, agitation, and confusion. Although neurologic sequelae are the most common serious adverse effect from lidocaine, no seizures were noted and no concerns were noted that mandated obtaining a serum lidocaine level.

In a similar study, Lemming et al sought to determine the adverse effect profile of lidocaine infusion used for acute pain management in a retrospective review of a total of 51 infusions in 50 patients, ranging in age from 2 to 17 years (median age of 14 years). [23]. The infusions were used as an adjunct to opioids for multimodal postoperative analgesia following major surgical procedures including posterior spinal fusion, nuss procedure for pectus excavatum, and nephrectomy. The starting infusion rate was 13.6 ± 6.5 µg/kg/min (approximately 1 mg/kg/h) with a similar infusion rate during administration (15.2 ± 6.3 µg/kg/min and 14.4 ± 6.2 µg/kg/min at discontinuation). The mean length of therapy was 30.6 ± 22 h. Adverse effects were noted in 12 infusions (24%) and included primarily complaints referable to the CNS such as paresthesias and visual disturbances. The average time to onset of adverse effects following the start of the infusion was 16.2 ± 15.2 h. In response to these adverse effects, the infusions were discontinued in seven patients and decreased in the remaining. No patients experienced toxicity requiring treatment with lipid emulsion.

Specific limitations of the current study include its retrospective nature and the potential to miss adverse effects given the chart review nature of the study and difficulties with data extraction. The potential for missing data especially that related to adverse effects is present as these may not always be accurately charted in medical notes. However, there were a limited number of patients who required pauses in the infusions, none who required escalation of care, and none who required any type of pharmacologic intervention for adverse effects. Additionally, without a control group, we cannot comment on the specific efficacy of the lidocaine infusions as an adjunct to opioid analgesia following major surgical procedures and the impact of the lidocaine infusion on opioid requirements. However, the primary intent of the study was to outline our protocol for the administration of lidocaine on the inpatient ward, evaluate the safety of lidocaine in the doses used, and provide a setting for future prospective trials without the need for ICU admission or continuous ECG monitoring.

In summary, we present the largest study to date outlining the use of lidocaine as an adjunct to acute pain management in pediatric patients. Our study cohort included a total of 503 days of infusions in a total of 168 patients. Our dosing algorithm generally included a bolus dose of 1 mg/kg followed by an infusion of 1 mg/kg/h. With enhanced clinical observation for signs of potential toxicity and increased clinical monitoring of vital signs, the lidocaine infusion was administered on the inpatient ward without the need for routine serum concentration monitoring. Although we used an intraoperative infusion as part of the clinical pathway, our preliminary data did not show a difference in outcomes (pain scores) when compared to patients who had the infusion started postoperatively. In general, the infusion was continued for 1 - 3 days while the patients were receiving intravenous opioids. Although we did not have a control group, our patients had effective pain control with low pain scores (2 - 3/10) following major surgical procedures. There was a positive weak correlation between total dose of lidocaine and decreasing length of hospital stay. Our current cohort and the other studies in pediatric patients support the safety of using this technique on the inpatient ward and provides a background for prospective studies to evaluate dosing regimens, optimal patient populations, and analgesic efficacy.

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None to declare.

Financial Disclosure

None to declare.

Conflict of Interest

None to declare.

Informed Consent

As this was a retrospective study using de-identified data, the need for written informed consent was waived.

Author Contributions

DFC and CR helped with the data collection and analysis, preparation of initial and subsequent drafts, review of final draft; MH helped with the data collection and analysis, data storage and oversight, preparation of initial and subsequent drafts, review of final draft data collection and analysis, preparation of initial and subsequent drafts, review of final draft; SAYK helped with the data collection, primary author for data analysis and presentation, preparation of initial and subsequent drafts, review of final draft; SW helped with protocol development, preparation of initial and subsequent drafts, review of final draft; DM helped with patient care, protocol development, review of final draft; JDT helped with the protocol development, data analysis, preparation of initial and subsequent drafts, and review of final draft.

Data Availability

Any inquiries regarding supporting data availability of this study should be directed to the corresponding author.

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