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Intrawound Liposomal Bupivacaine in Pediatric Chiari Decompression: A Retrospective Study

Melissa A. LoPresti, MD†; B. Nathan Harrell, MSM, PA-C†; Eric Goethe, MD*†; Samuel McClugage, MD*†; Karla Wyatt, MD, MS‡§; Sandi K. Lam, MD, MBA¶‖*

Introduction: Intrawound liposomal bupivacaine is a long-acting local anesthetic used to decrease postoperative pain in various procedures. Although it is used in posterior cervical and suboccipital approaches in the adult population, it is currently off-label for pediatrics. This quality improvement (QI) project examines intrawound liposomal bupivacaine for pediatric Chiari decompression and evaluates its role in postoperative opioid consumption.**Methods:** We retrospectively analyzed all patients 0–18 years old of age who underwent Chiari decompression from January 2017 to July 2019 at our tertiary care hospital. Demographic and clinical data regarding postoperative opioid use, subjective and objective pain control, length of stay, discharge medications, and comorbid conditions were collected. **Results:** We included 30 patients in this study: 19 females and 11 males. Of these, 6 received an intrawound injection of liposomal bupivacaine. **Patients** treated with liposomal bupivacaine require fewer opioids while admitted. There was no apparent difference in pain control immediately postoperatively, pain control at clinical follow-up, or inpatient length of stay between each group. Patients who received liposomal bupivacaine did not require opioid analgesics at the time of discharge from the hospital. **Conclusion:** The use of intrawound liposomal bupivacaine may decrease inpatient and outpatient postoperative opioid consumption amongst pediatric patients following Chiari decompression while providing adequate pain control. We investigate liposomal bupivacaine perioperative blockade in this QI project as a viable option for opioid-sparing pain control in the postoperative setting for the pediatric population. Future investigation via clinical trials and more extensive prospective studies may glean further insights into efficacy. *(Pediatr Qual Saf 2021;6:e397; doi: 10.1097/pq9.0000000000000397; Published online May 5, 2021.)*

INTRODUCTION

Chiari malformations are a group of anatomical configurations of the cerebellum and brain stem, causing herniation of these structures through the foramen magnum, leading to obstructive hydrocephalus, pain, and neurologic deficits.[1,2] Treatment most commonly involves decompression surgery of the posterior fossa, which can be associated with extensive neck dissection, C1 laminectomy, and expansile duraplasty. Due to significant neck musculature inserting on the suboccipital skull and axial cervical spine, new or worsening nociceptive pain is often described following Chiari decompression surgery.[1] Pain medication is often employed in the postoperative period; however, opioid-sparing pain regimens may preserve the postoperative neurologic examination's integrity, allowing for close monitoring of these patients postoperatively while reducing narcotics use.

Liposomal bupivacaine is a local anesthetic preparation that permits slow, extended-release of bupivacaine liposomes to the effector site over nearly 96 hours. Its use has gained much popularity over the last 5 years. Although only approved by the US Food and Drug Administration (FDA) for interscalene and transverse abdominis plane blocks and local infiltration in adult patients, several studies have explored the effect of intrawound liposomal bupivacaine in children, although its efficacy remains unclear.[3–6] Madhavarapu et al[6] investigated its use in Chiari decompression and found no difference in morphine equivalents in the first 48 hours postoperatively. However, 2 recent studies by Day et al[4,5] demonstrated a significant reduction

*From the *Department of Neurosurgery, Baylor College of Medicine, Houston, Tex.; †Division of Pediatric Neurosurgery, Texas Children's Hospital, Houston, Tex.; ‡Department of Anesthesiology, Perioperative and Pain Medicine, Texas Children's Hospital, Houston, Tex.; §Department of Anesthesiology, Baylor College of Medicine, Houston, Tex.; ¶Division of Pediatric Neurosurgery, Ann and Robert H Lurie Children's Hospital of Chicago, Chicago, Ill.; and ‖ Department of Neurosurgery, Northwestern University Feinberg School of Medicine, Chicago, Ill.*

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**Corresponding author. Address: Sandi K. Lam, MD, MBA, Division of Pediatric Neurosurgery, Ann and Robert H Lurie Children's Hospital of Chicago; Department of Neurosurgery, Northwestern University Feinberg School of Medicine, 225 E Chicago Ave Box 28, Chicago, IL 60611*
PH: 312-227-4220; Fax: 312-227-9679
Email: slam@luriechildrens.org; sandilam@gmail.com

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in postoperative pain scores and opioid consumption following perioperative liposomal bupivacaine.

Based on the promising use of intrawound liposomal bupivacaine in adults and small pediatric studies, we aimed to conduct a quality improvement (QI) project to explore its use in pediatric patients undergoing posterior fossa decompression and C1 laminectomy for Chiari decompression at our institution. We hypothesize that intrawound liposomal bupivacaine provides postoperative pain control, reduces postoperative opioid consumption, and reduces hospital length of stay (LOS). We hope that this project may serve as the groundwork for future, more in-depth analyses of this pain management modality's efficacy in children undergoing Chiari decompressions.

METHODS

We retrospectively examined electronic medical records (EMRs) for patients 0–18 years of age, who underwent elective, outpatient surgery for Chiari decompression at our institution between January 2017 and July 2019. Demographic data included age at the time of surgery, sex, race/ethnicity, and clinical data included Chiari Malformation type, presence of syrinx, hydrocephalus, spina bifida, and additional comorbidities. We excluded patients with chronic pain states, those receiving outpatient opioid medications preoperatively, patients whose surgeons categorically did not employ narcotics postoperatively, and those undergoing Chiari decompression as an inpatient or other nonelective surgery.

We stratified patients into 2 groups: (1) those who received intrawound liposomal bupivacaine and (2) those who did not receive intrawound liposomal bupivacaine. As intrawound liposomal bupivacaine use in pediatrics for this indication is off-label, individual administration was approved by the institutional pharmacy by appeal from our pediatric neuroanesthesia team on a case by case basis. We defined administration of intrawound liposomal bupivacaine as an infusion of the drug within the peri-intrawound tissue, anatomically aimed to inject in targeted areas including over bilateral occipital nerves and bilateral cervical 1, 2, 3 rami at the level of the fascia. Liposomal bupivacaine dose was calculated based on weight-based dosing for each patient.

We explored outcome measures assessing pain control, including intraoperative opioid use measured by morphine equivalents administered intraoperatively, inpatient opioid consumption dichotomously, and measured by intravenous morphine equivalents postoperatively, subjective postoperative pain control, and postoperative pain regimen. We assessed the postoperative pain regimen by calculating the total number of intravenous morphine equivalents administered throughout the hospital stay. We measured postoperative pain control by subjective measures, dichotomized as adequate or inadequate pain control as documented in the progress notes by patient reports daily, as well as with more objective measures including visual analog pain scale (VAS) and the Face, Legs, Activity, Cry, Consolability (FLACC) scale documented in electronic medical records with the administration of postoperative pain medications. The VAS typically ranges from 0 to 10 or 0 to 100, with higher numbers signifying more pain.[7] The FLACC scale is an objective behavioral score used to assess pain in nonverbal children. The facial expression, leg movement, activity, cry, and consolability variables are assigned a score from 0 to 2, with overall scores ranging from 0 to 10. Higher numbers correspond with worse pain.[8] We grouped by scores <4, 4–8, and >8 to serve as a proxy for good, moderate, and poor pain control, respectively, as small, incremental score differences may lack clinical significance.[7] We reviewed the EMR to track the postoperative opioid type, dose, and amount received each day after surgery while inpatient and outpatient pain regimen by prescription opioid use at discharge. Additional outcomes examined included LOS and subjective (adequate vs. inadequate) pain control at the 2-week postoperative visit. We obtained local Institutional Board Review approval for this retrospective review.

We analyzed data using IBM SPSS 26 (IBM Corp, Armonk, N.Y.). Categorical variables were organized into tables, whereas continuous variables were plotted on time-ordered run charts by date of surgery to allow for the visual representation of data.

RESULTS

We included thirty patients: 19 females and 11 males across varied ethnic backgrounds (Table 1). Twenty-eight patients (93.3%) had Chiari I malformation. One patient (3.3%) had a complex Chiari malformation, and 1 patient (3.3%) had an unspecified Chiari malformation. Six patients (20.0%) received liposomal bupivacaine. Patients receiving liposomal bupivacaine were younger

Table 1. Demographic and Clinical Data

	No Incisional Liposomal Bupivacaine (n = 24)	Incisional Liposomal Bupivacaine (n = 6)
Age, y, mean (SD)	10.1 (5.0)	6.1 (2.2)
Range	2.3–18.6	3.5–10.0
Sex, n (%)		
Female	14 (58.3%)	5 (83.3%)
Male	10 (41.7%)	1 (16.7%)
Ethnicity/race*, n (%)		
White	15 (62.5%)	5 (83.3%)
Hispanic	9 (37.5%)	0
African American	0	0
Asian American	0	0
Other	0	1 (16.7%)
Comorbid Conditions†, n (%)		
Hydrocephalus	3 (12.5%)	1 (16.7%)
Presence of Syrinx	17 (70.8%)	4 (66.7%)
Myelomeningocele	0	0
Other spinal dysraphism	8 (33.3%)	1 (16.7%)
Other‡	16 (66.7%)	4 (66.7%)

*Ethnicity/race were self-reported by patient, parent, and/or guardian.
†Of note, percentages may total greater than 100% as patients may have had more than one comorbid condition.
‡Genetic/developmental disorders, seizures, and central sleep apnea.

than those who did not (6.1 vs. 10.1 y). However, we did not observe any marked difference in the distribution of gender, race, or comorbid conditions between groups.

We observed that intraoperative morphine administration was not different between groups and unchanged across the study period (Fig. 1). Postoperative morphine equivalents administered decreased over time. Patients treated with intrawound liposomal bupivacaine were less likely to require postoperative opioids (79.2% vs. 16.7%) (Table 2). There was no difference between the rates of opioid prescriptions at discharge between the groups. There was no difference in subjective pain control rates on postoperative day 1 or outpatient clinic follow-up between groups. Objective maximum measurements of pain (VAS and FLACC scores) were not different between groups on postoperative days 0, 1 (**see Figure 1,** which describes VAS on postoperative day 0 (left) and 1 (right) over time. On both days there was no significant change in VAS over time and no apparent difference between groups, and **Figure 2,** FLACC score on postoperative day 0 (left) and 1 (right) over time. On postoperative day 0 there was no significant change in FLACC over time or apparent difference between groups. On postoperative day 1 there was a slight overall decrease in FLACC over time but no apparent difference between groups, **Supplemental Digital Content 1**, ***http://links.lww.com/PQ9/A247***), or 2 (Fig. 2). We observed a decrease in LOS over time across both groups; LOS was not different between groups (Fig. 3).

DISCUSSION

In this QI project, we explored our experience using intraoperative intrawound liposomal bupivacaine in pediatric patients undergoing Chiari decompression. We found that patients who received intraoperative liposomal bupivacaine appeared to have a lower postoperative narcotic requirement despite equivalent narcotic administration while in the operating room and similar comorbidity profiles—no patient who received liposomal bupivacaine required narcotic medications at discharge. Although the LOS, rates of subjective and objective postoperative pain control, and short-term follow-up outcomes were similar between groups, these preliminary findings underscore the importance of further exploring this pain management modality in treating children undergoing Chiari decompression.

Persistent postoperative pain is a common concern in neurosurgery, specifically in spine surgery. Inadequate acute pain control increases LOS, limits participation in postoperative therapy services and wound healing, and increases the risk of chronic pain.[9–11] The number of opioid prescriptions in the United States has quadrupled between 1999 and 2010, with a concomitant rise in overdose-related deaths.[12,13] This highlights the ever-concerning opioid crisis, to which children are not immune: 3.6% of children 12–17 years of age reported misusing prescription opioids in 2016.[13] High school-age children who use opioids are more likely to misuse them as adults.[13] With early exposure to these medications in the postoperative period, children are at a greater risk. Thus, it is essential to identify pain management strategies that minimize inpatient and outpatient opioid use.

There are several reasons opioids are not a satisfactory frontline treatment for postoperative pain management. Postoperative respiratory depression, which can occur due to compression or manipulation of the brainstem and lower cranial nerves, can be magnified by respiratory depression that can occur even in children prescribed appropriate weight-based opioids.[17–20] Additionally, sedation due to narcotics may obscure neurological examination vital to patient monitoring postoperatively.[21]

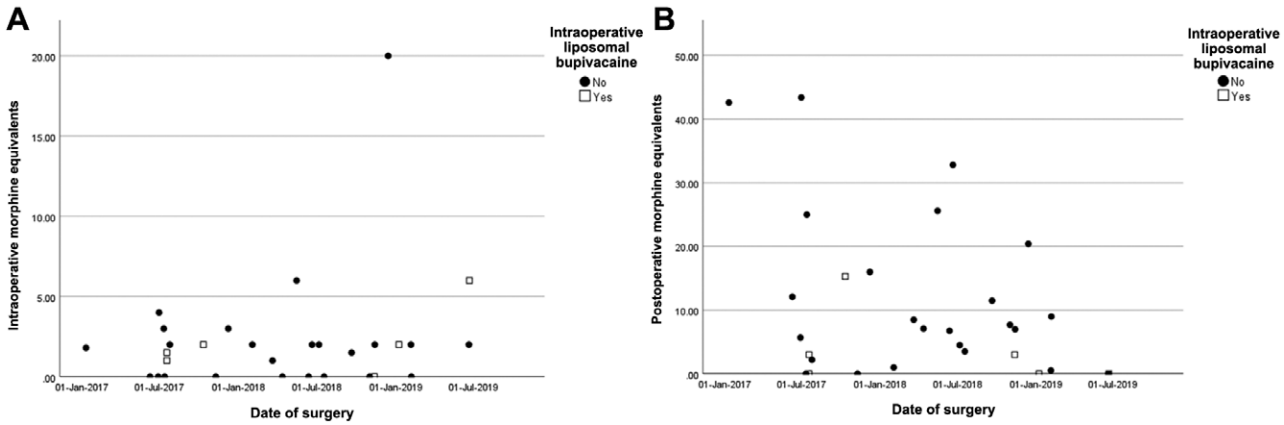

Fig. 1. Intraoperative morphine equivalents administered over time. A, Intraoperative morphine equivalents administered over time. Intraoperative morphine use remained relatively consistent and low over time and did not vary between groups. B, Postoperative morphine equivalents administered over time, highlighting both the efforts of our surgeons to minimize postoperative narcotics and their increased proficiency with other forms of analgesia. The number of postoperative morphine equivalents received decreased over time, with only 2 patients operated upon after July 2018, receiving more than 10 equivalents throughout their hospital stay. Additionally, postoperative morphine equivalents appeared lower in patients who received intraoperative liposomal bupivacaine.

Table 2. Treatment and Outcome Data

	No Incisional Liposomal Bupivacaine (n = 24)	Incisional Liposomal Bupivacaine (n = 6)
Intraoperative morphine equivalents, mean (SD)	2.3 (4.1)	2.1 (2.1)
Range	0–20.0	0–6.0
Postoperative morphine equivalents, mean (SD)	12.2 (13.0)	3.6 (5.9)
Range	0–43.4	0–15.3
Postoperative opioid use, n (%)		
No opioid use after POD 0	5 (20.8%)	5 (83.3%)
Postoperative opioid use on POD 1	10 (41.7%)	0
Postoperative opioid use on POD 2+	9 (37.5%)	1 (16.7%)
Subjective postoperative pain control, n (%)		
Postoperative day 1	15 (62.5%)	5 (83.3%)
Follow-up visit	20 (83.3%)	5 (83.3%)
Maximum postoperative day 0 visual analog scale score, n (%)		
<4	2 (16.7%)	0
4–8	8 (66.7%)	1 (100.0%)
>8	2 (16.7%)	0
Maximum postoperative day 1 visual analog scale score, n (%)		
<4	2 (14.3%)	0
4–8	7 (50.0%)	1 (100.0%)
>8	5 (35.7%)	0
Maximum postoperative day 2 visual analog scale score, n (%)		
<4	5 (41.7%)	2 (100.0%)
4–8	6 (50.0%)	0
>8	1 (8.3%)	0
Maximum postoperative day 0 FLACC score, n (%)		
<4	14 (73.7%)	2 (33.3%)
4–8	4 (21.1%)	3 (50.0%)
>8	1 (5.3%)	1 (16.7%)
Maximum postoperative day 1 FLACC score, n (%)		
<4	15 (75.0%)	4 (66.6%)
4–8	5 (25.0%)	2 (33.3%)
>8	0	0
Maximum postoperative day 2 FLACC score, n (%)		
<4	19 (90.5%)	5 (100.0%)
4-8	2 (9.5%)	0
>8	0	0
Mean LOS, d (SD)	3.4 (1.2)	2.5 (1.0)
Range	2–7	1–4
Postoperative pain regimen, n (%)		
OTC pain medications*	14 (58.3%)	6 (100.0%)
Muscle relaxants	6 (25.0%)	0
Opioids	4 (16.7%)	0

*OTC pain meds included oral acetaminophen and ibuprofen.
OTC, over the counter; POD, postoperative day.

Although the use of nonnarcotics may mitigate these pitfalls, they are not without risk as well. There is some evidence that liposomal bupivacaine, when administered intravenously, can exert cardiotoxic effects refractory to the intralipid rescue traditionally given for cases of toxicity from other local anesthetics; this is a risk that must be accounted for in deciding between postoperative analgesic modalities.

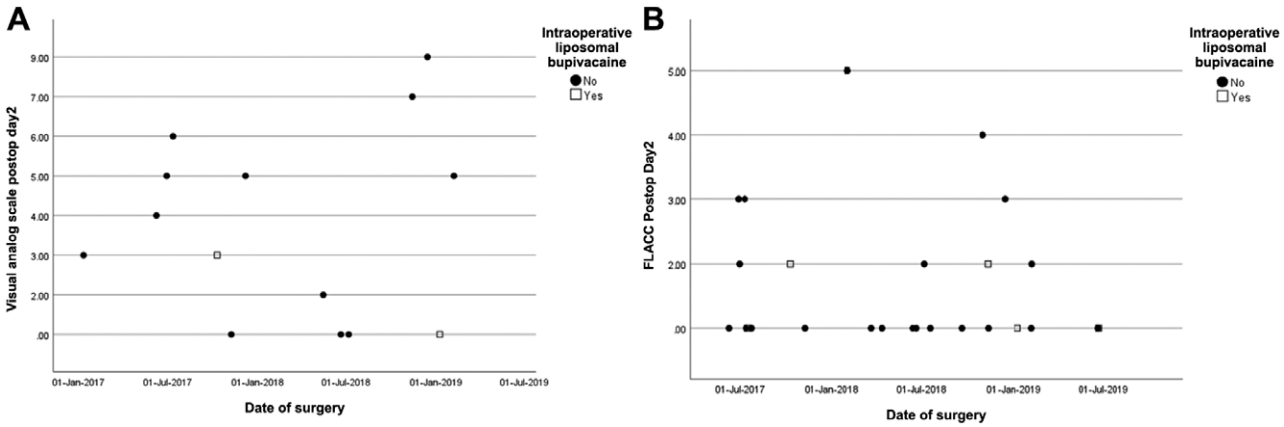

Fig. 2. VAS (A) and FLACC score (B) on postoperative day 2 over time. VAS (A) and FLACC score (B) on postoperative day 2 over time. There was no significant change in VAS over time, but patients who received liposomal bupivacaine tended to have lower scores than those who did not. There was no change in FLACC over time, but patients who received liposomal bupivacaine tended to have lower scores than those who did not.

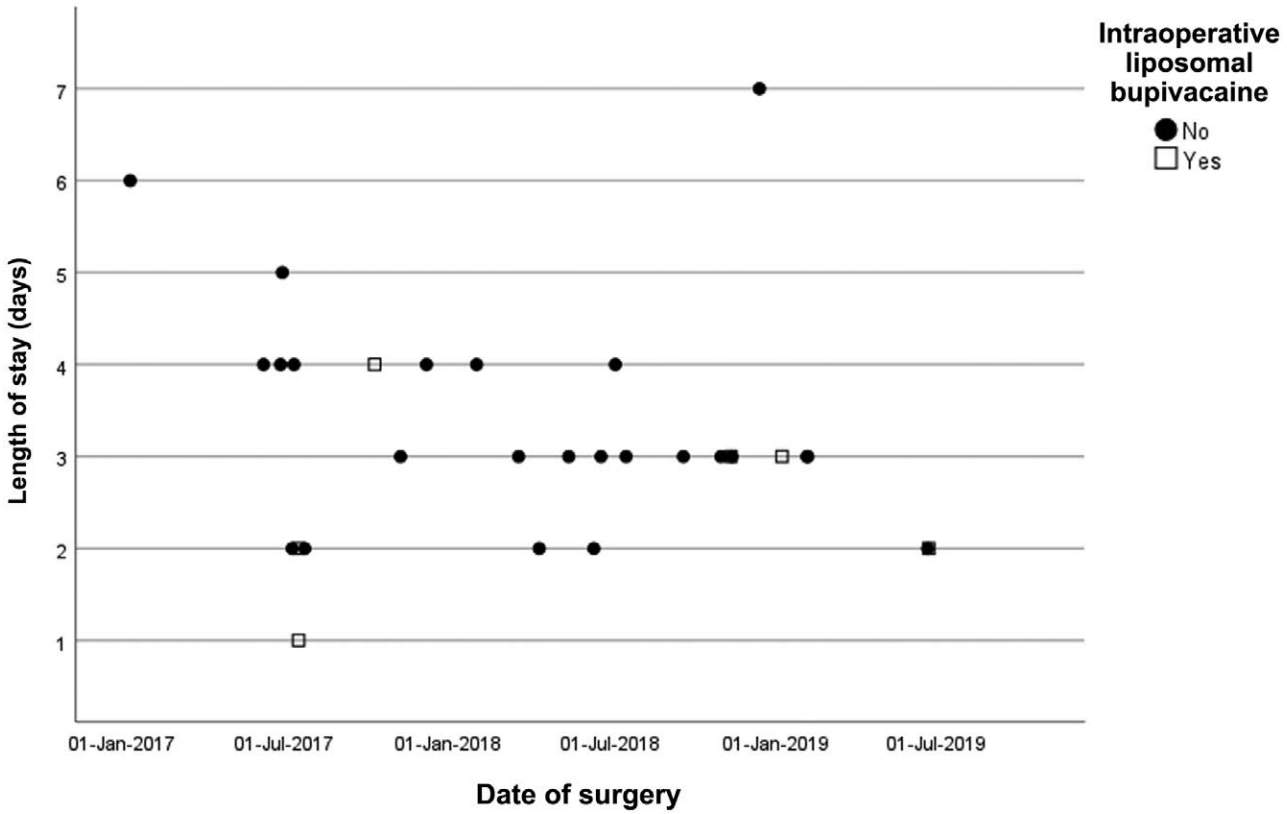

Fig. 3. LOS over time. LOS appeared to decrease over time across all groups and was not significantly different between groups.

An intrawound local anesthetic is beneficial for a multitude of surgical applications. In the region of surgical exposure for Chiari decompression, we can reach bilateral occipital nerves and bilateral cervical 1, 2, 3 rami at the level above the fascia. Day et al[4,5] demonstrated a significant reduction in postoperative pain scores and opioid consumption following perioperative intrawound liposomal bupivacaine. In one systematic review, intraperitoneal local anesthetic following abdominal surgery in children was shown to reduce perioperative opioid use but did not affect LOS.[14] We observed similar results in our QI project. In the neurosurgical population, the utility of intra-wound local anesthesia varies by procedure type. Cloyd et al[3] demonstrated no statistical significance in postoperative opioid consumption or pain scores following intrawound liposomal bupivacaine in 140 pediatric patients undergoing posterior spinal fusion surgery for scoliosis. However, these patients underwent a median of 11 (range 10–13) levels of fusion—a substantially more extensive procedure involving hardware instrumentation, extensive dissection, and associated surgical tissue injury.[15] Scoliotic deformity correction is reportedly one of the most painful pediatric surgeries, and patients often require several days of intravenous opioids for adequate pain control.[15] The findings from spinal fusion studies, therefore, may not generalize to our patient population. Law-Koune et al[16] demonstrated a significant reduction in postoperative opioid requirements in patients undergoing supratentorial craniotomy who received intrawound bupivacaine or ropivacaine compared to placebo, a finding consistent with our series.

Limitations

This QI project's primary limitations are its retrospective design and small sample size, limiting the level of evidence derived from its findings. Statistically significant relationships are challenging to determine, given this small sample, lack of randomization, and reduced power, precluding our ability to stratify and perform inferential statistical analyses. Directions for future study include further investigation with a larger sample size that allows for comparative statistics. A large prospective study or randomized clinical trial would overcome these limitations and better assess liposomal bupivacaine's impact on postoperative pain control.

Additionally, subjective measures of pain control collected via EMR documentation and objective VAS and FLACC scores documented at the time of medication administration were used to evaluate pain control postoperatively. Due to the retrospective nature of these data, charting and documentation variations may limit the quality of these assessments. Also, despite using validated scales for objective pain score measurement in children of various ages, it is challenging to assess pediatric patients' pain levels accurately. Prospective standardized approaches to evaluate and measure pain may be systematically applied in a future study to gauge this metric uniformly.

Furthermore, opioid-related side effects such as nausea, emesis, pruritis, respiratory depression, and somnolence are essential considerations when weighing the side effect profile and risks/benefits of alternative pain control modalities. However, given that there was no difference in subjective pain control between the two groups, analysis of a better side effect profile or the reduced need for rescue therapy (ie, antiemetics and supplemental oxygen) would further enhance the assessment of efficacy when using intra-wound liposomal bupivacaine. Last, due to the small sample size, we did not stratify the procedure by inclusion or exclusion of expansile duraplasty, which may entail differences in the postoperative course in terms of pain, nausea, and emesis, due to implications regarding implant reactions and cerebrospinal fluid irritation due to surgical blood products.

CONCLUSIONS

In this QI project, we explored the role of intrawound liposomal bupivacaine in children undergoing Chiari decompression surgery. We found that targeted use of intrawound liposomal bupivacaine is safe and appears to be associated with a decreased need for postoperative opioids. Patients receiving intrawound liposomal bupivacaine did not require prescription opioids upon discharge. Our findings support further investigation into the impact of liposomal bupivacaine in postoperative pain management. The future study into the role of liposomal bupivacaine postoperatively in the setting of more extensive, prospective, randomized controlled trials with standardized treatment arms may glean further insights regarding the impact it may have on improving perioperative pain control, reducing opioid consumption, and enabling recovery after surgery.

DISCLOSURE

The authors have no financial interest to declare in relation to the content of this article.

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