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A Retrospective Comparison of Liposomal Bupivacaine and Bupivacaine HCl for Preincision Scalp Block in Pediatric Patients Undergoing Craniofacial Surgery at Arkansas Children's Hospital

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OBJECTIVE

The objective of this study was to compare the effect of LB and bupivacaine HCl on opioid consumption (in morphine milligram equivalents [MMEs]) and hospital length of stay (LOS) among pediatric patients who underwent craniofacial surgery

CONCLUSIONS

1. Preincision scalp blocks with LB versus bupivacaine HCl significantly reduced postsurgical opioid consumption and LOS for pediatric patients receiving craniofacial surgery
   - LB was associated with an over 3-fold higher cumulative opioid-free rate on days 1-3 after surgery
2. Overall, this study found that preincision scalp blocks with LB were effective in reducing postoperative opioid consumption and hospitalization in pediatric patients undergoing craniofacial surgery
   - A future prospective trial is warranted to support these findings

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INTRODUCTION

- Although opioids may be included in pain management protocols for pediatric craniofacial surgery, opioid use in pediatric patients can cause complications such as nausea, vomiting, and respiratory depression[1,2]
  - Scalp nerve blocks can reduce postoperative pain and opioid consumption for craniofacial surgery[3]
- Liposomal bupivacaine (LB) is an extended-release formulation of bupivacaine
  - Use of LB has been found to result in decreased postoperative pain and opioid consumption relative to short-acting local anesthetics (eg, bupivacaine hydrochloride [HCl]) in other patient populations when administered via local infiltration or via specific nerve blocks[4,5]; however, data are limited regarding LB use for scalp blocks in pediatric patients

METHODS

STUDY DESIGN

- This was a retrospective cohort study that used electronic medical records of pediatric patients who underwent craniofacial surgery (cranioplasty, cranial vault remodeling, or craniosynostosis repair) from August 2019 through August 2023 at Arkansas Children's Hospital and received LB or bupivacaine HCl administered via preincision scalp block
  - Exclusion criteria included known allergy or hypersensitivity to bupivacaine, endoscopically assisted craniofacial procedures, and postoperative mechanical ventilation
- The study was approved by the University of Arkansas for Medical Sciences Institutional Review Board (protocol number: 276304); because this was a medical chart review, waivers of the informed consent process and Health Insurance Portability and Accountability Act were granted by the institutional review board

OUTCOMES

- The outcomes of the study included postoperative opioid consumption (measured by mg/kg MMEs) determined for each 24-hour period through postoperative day 4 and hospital LOS (defined as the number of days after surgery to discharge)
  - Subgroup analyses examining cumulative opioid consumption stratified by sex, age, and surgery type were also performed between the LB and bupivacaine HCl groups

STATISTICAL ANALYSIS

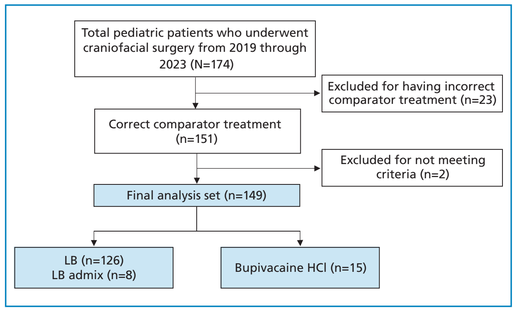
- Descriptive analyses included *t* tests or Wilcoxon rank sum tests for continuous data and chi-squared tests or Fisher's exact tests for categorical data
- Multivariable regression models adjusted for age, sex, and weight were used to estimate the least squares mean (LSM) for each treatment group
- A 2-sided *P* value <0.05 was considered significant

RESULTS

PARTICIPANT CHARACTERISTICS

- Of 174 pediatric patients who underwent craniofacial surgery during the study period, 149 met all eligibility criteria and were included in the final analysis (Figure 1)
  - 134 received LB (126 LB alone, 8 LB admixed with bupivacaine HCl) and 15 received bupivacaine HCl
  - 25 total patients were excluded (23 for having incorrect comparator treatment and 2 for not meeting the inclusion criteria [1 underwent a noncraniofacial procedure, 1 was >18 years of age at the time of procedure])
- The mean age (range, 3.8-4.2 years) and sex (range, 32%-33% female) were similar between groups (Table 1)
  - Most participants who received LB were between 1 and 5 years old (89/134; 66%); most participants underwent cranial vault reconstruction (~80%) and the rest underwent split bone cranioplasty (~20%)
  - Figure 2 shows the LB dose stratified by age group; among the 15 participants who received bupivacaine HCl, the mean dose was 23.3 mg and ranged from 12.5 to 45.0 mg

Figure 1. Sample population for retrospective analysis.



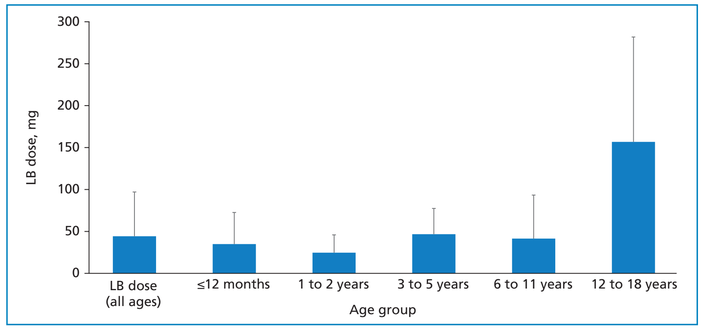
HCl, hydrochloride; LB, liposomal bupivacaine.

Table 1. Baseline Participant Characteristics in the LB and Bupivacaine HCl Groups

	LB (n=134)	Bupivacaine HCl (n=15)	*P* value[a]
Age, mean (SD), y	4.25 (3.3)	3.83 (3.2)	0.64
Age group, n (%)			
≤2 y	54 (40.3)	9 (60.0)	0.17
3 to 18 y	80 (59.7)	6 (40.0)	
Sex, n (%)			
Female	43 (32.1)	5 (33.3)	1.00
Male	91 (67.9)	10 (66.7)	
Weight, mean (SD), kg	20.12 (14.4)	18.25 (11.4)	0.56
Procedure, n (%)			
Vault	107 (79.9)	12 (80.0)	1.00
Cranioplasty	27 (20.1)	3 (20.0)	
Year of procedure, n (%)			
2019	0 (0.0)	5 (33.3)	<0.0001
2020	24 (17.9)	9 (60.0)	
2021	35 (26.1)	1 (6.7)	
2022	34 (25.4)	0 (0.0)	
2023	41 (30.6)	0 (0.0)	

[a]*P* values for between-group comparisons were calculated using *t* tests with the Satterthwaite method for continuous variables and Fisher's exact test for categorical variables. HCl, hydrochloride; LB, liposomal bupivacaine; SD, standard deviation.

Figure 2. Mean LB administration dose stratified by age group.

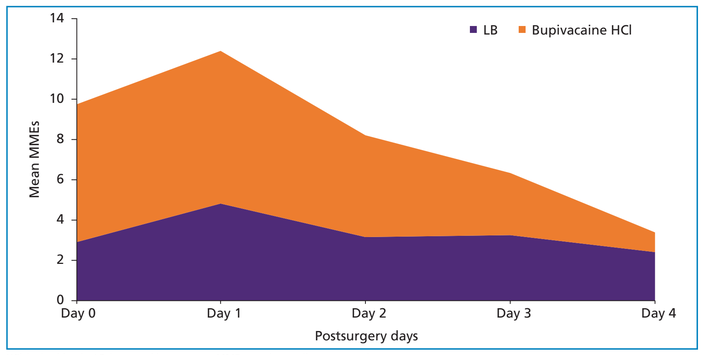


Error bars are the standard deviation. LB, liposomal bupivacaine.

OPIOID OUTCOMES

- Univariate analyses indicated that there was a significant reduction in cumulative opioid consumption in the LB versus bupivacaine HCl groups through postsurgery day 3 (mean [SD] cumulative MMEs, 12.56 [14.8] vs 22.16 [18.7]; *P*=0.01)
- When data were analyzed via multivariable regression, the LB group had a significant 44% reduction in cumulative opioid consumption through postsurgery day 3 versus the bupivacaine HCl group (LSM [95% confidence interval (CI)] cumulative MMEs, 8.30 [6.18-11.14] vs 14.74 [9.75-22.29]; *P*=0.002)
  - Similar differences in opioid consumption were observed when assessing days 0-4 post surgery
- A smooth plot of mean opioid consumption over time by treatment group is shown in Figure 3

Figure 3. Smooth plot of mean opioid consumption (in MMEs) in the LB and bupivacaine HCl groups for each postsurgery day.



HCl, hydrochloride; LB, liposomal bupivacaine; MME, morphine milligram equivalent.

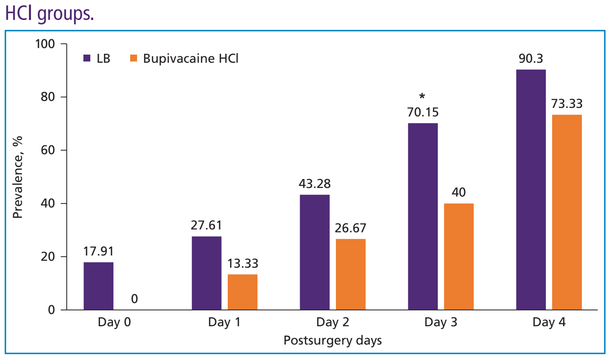
- Subgroup analyses of cumulative opioid consumption from 0 to 3 days after surgery were generally consistent with the overall analysis (Table 2)
  - Compared with participants who received bupivacaine HCl, participants who received LB consumed fewer opioids in all age subgroups (except 3 to 5 years of age, where there was only 1 participant in the bupivacaine HCl group); females receiving LB consumed significantly fewer opioids than females receiving bupivacaine HCl
  - There was significantly lower opioid consumption (in MMEs) observed with LB versus bupivacaine HCl within the cranioplasty subgroup
- A larger proportion of participants who received LB (23.9%) achieved cumulative opioid-free status from days 1 to 3 versus those receiving bupivacaine HCl (6.7%; *P*=0.19)
  - When accounting for covariates, the likelihood of achieving opioid-free status was numerically higher for participants who received LB versus those who received bupivacaine HCl (mean likelihood, 0.44 [95% CI, 0.35-0.54] vs 0.28 [95% CI, 0.15-0.45]; *P*=0.08)
  - Opioid-free status on each day of the postoperative period is shown in Figure 4

Table 2. Subgroup Analyses of Cumulative Opioid Consumption Between the LB and Bupivacaine HCl Groups on Days 0-3 Post Surgery

	LB (n=134)	Bupivacaine HCl (n=15)	*P* value[a]
Age subgroup			
≤12 months			0.55
n	11	2	
Mean (SD), MMEs	5.5 (3.8)	7.4 (5.0)	
Median (minimum, maximum), MMEs	5.40 (0.0, 10.4)	7.36 (3.8, 10.9)	
1 to 2 years			0.03
n	43	7	
Mean (SD), MMEs	9.8 (7.5)	16.2 (7.1)	
Median (minimum, maximum), MMEs	7.62 (0.0, 34.0)	14.07 (7.1, 25.3)	
3 to 5 years			0.19
n	46	1	
Mean (SD), MMEs	12.5 (11.1)	1.4	
Median (minimum, maximum), MMEs	8.14 (0.1, 46.7)	1.43 (1.4, 1.4)	
6 to 11 years			0.01
n	26	5	
Mean (SD), MMEs	14.6 (17.4)	40.5 (21.1)	
Median (minimum, maximum), MMEs	10.37 (0.0, 61.4)	38.28 (15.2, 73.3)	
12 to 18 years			
n	8	NA	
Mean (SD), MMEs	31.2 (37.5)	NA	
Median (minimum, maximum), MMEs	15.50 (0.0, 105.0)	NA	
Sex subgroup			
Female			0.02
n	43	5	
Mean (SD), MMEs	10.9 (13.2)	27.3 (26.3)	
Median (minimum, maximum), MMEs	7.90 (0.0, 66.6)	14.07 (10.9, 73.3)	
Male			0.12
n	91	10	
Mean (SD), MMEs	13.4 (15.5)	19.6 (14.7)	
Median (minimum, maximum), MMEs	8.10 (0.0, 105.0)	17.48 (1.4, 42.8)	
Surgery subgroup			
Cranioplasty			0.01
n	27	3	
Mean (SD), MMEs	8.6 (12.2)	42.2 (29.3)	
Median (minimum, maximum), MMEs	4.74 (0.0, 61.4)	38.28 (15.2, 73.3)	
Vault reconstruction			0.14
n	107	12	
Mean (SD), MMEs	13.6 (15.3)	17.1 (12.4)	
Median (minimum, maximum), MMEs	9.04 (0.0, 105.0)	13.60 (1.4, 42.8)	

[a]*P* values were calculated using a 2-sided Wilcoxon rank sum (Mann-Whitney U) test. HCl, hydrochloride; LB, liposomal bupivacaine; MME, morphine milligram equivalent; NA, not applicable; SD, standard deviation.

Figure 4. Opioid-free rate comparisons between the LB and bupivacaine HCl groups.



P values were calculated using Fisher's exact test; asterisk indicates *P* value for comparison was below the prespecified significance value of *P*<0.05. HCl, hydrochloride; LB, liposomal bupivacaine.

SAFETY

- No adverse events or complications were recorded for participants who received LB before craniofacial surgery

LOS OUTCOMES

- In univariate analysis, participants receiving LB had a significant 1-day reduction in LOS versus those receiving bupivacaine HCl (3 days [minimum 1 day, maximum 28 days] vs 4 days [minimum 2 days, maximum 11 days]; *P*<0.001)
- When data were analyzed via multivariable regression, participants receiving LB had significantly shorter hospitalization LOS compared with the bupivacaine HCl group (LSM [95% CI] LOS, 2.2 [1.6-3.1] vs 3.2 [2.2-4.9] days; *P*=0.03)