Title

A Comparison of Local Anesthetics for Intravenous Catheter Insertion in Hospitalized Pediatric Patients

Journal

Journal of Infusion Nursing, 44(6)

ISSN

1533-1458

Authors

Lozano, Sally

Sund, Grace

Guimera, Allison

et al.

Publication Date

2021-11-01

DOI

10.1097/nan.0000000000000449

A Comparison of Local Anesthetics for Intravenous Catheter Insertion in Hospitalized Pediatric Patients

A Randomized Controlled Pilot Trial

Sally Lozano, BSN, RN, CPN • Grace Sund, MSN, RN, CPNP, CPHON • Allison Guimera, MD, FAAP • Grace Deukmedjian, MD • Pamela S. Miller, PhD, RN, ACNP, CNS, PHN, EBP (CH)

[AQ00]

ABSTRACT

Peripheral intravenous catheter (PIVC) insertion is one of the most painful procedures pediatric patients undergo during hospitalization. To date, local anesthetics delivered via cream, patch, and needle-free injection have not been rigorously evaluated together. This study aimed to investigate feasibility and potential efficacy of local anesthetics on pain intensity during PIVC insertion in an unblinded, single-center, randomized clinical pilot trial. Between March 2017 and February 2020, 88 hospitalized children aged 12 months to 18 years in an acute pediatric unit at an academic medical center were randomized to 1 of 3 local anesthetics: 1) lidocaine/prilocaine cream, 2) lidocaine/tetracaine patch, and 3) unbuffered lidocaine needle-free injection. Feasibility outcomes were recruitment and protocol adherence. Pain intensity was measured using the Face, Legs, Activity, Cry, Consolability (age $<$8 years) and Verbal Numeric Rating (VNRS) scales (age $\geq$8 years) before, during, and after procedure. Secondary outcomes included catheterization attempts, procedure time, and parent satisfaction. Recruitment rate was acceptable (2.7 patients per month). Protocol adherence was high (92%). Preliminary clinical findings showed no significant difference in pain intensity across treatments. Procedure time to successful insertion differed in the VNRS group, favoring unbuffered lidocaine needle-free injection. Conduct of a definitive, full-scale randomized clinical trial in the hospitalized pediatric population is feasible.

Key words: local anesthetics, pediatrics, peripheral intravenous catheter insertion

Peripheral intravenous catheter (PIVC) insertion is one of the most common procedures performed in the pediatric inpatient setting. PIVC placement has been shown to cause pain and anxiety among pediatric patients,[1] as well as pain and anxiety among caregivers when present.[2] Many techniques have been proposed to decrease pain during this procedure including local anesthetics, behavioral interventions, distraction techniques, and positioning. However, these methods are not consistently used for all PIVC placements, and no gold standard has been established in the pediatric population at a local or national level. Often methods to reduce pain are used

Author Affiliations: *University of California Los Angeles Medical Center, Santa Monica, California (Ms Lozano); University of California Los Angeles Mattel Children's Hospital, Los Angeles, California (Ms Sund); University of California Los Angeles Health, Los Angeles, California (Drs Guimera, Deukmedjian, and Miller).*

Sally Lozano, BSN, RN, CPN, *has worked as a pediatric nurse for 15 years at University of California Los Angeles (UCLA) Medical Center. She was recently promoted to clinical nurse manager in the general pediatric unit. Ms Lozano has extensive experience placing and teaching techniques for successful peripheral intravenous catheter insertions.* **Grace Sund, MSN, RN, CPNP, CPHON,** *is a clinical nurse specialist in pediatrics at UCLA Mattel Children's Hospital and has worked as a pediatric nurse for 19 years. She helped create the nurse-driven protocol for topical anesthetics prior to intravenous insertion for the pediatric population across the health system.* **Allison Guimera, MD, FAAP,** *worked as a pediatric hospitalist at UCLA Health and currently practices outpatient pediatrics with UCLA Health. She is a board-certified pediatrician and a fellow of the American Academy of Pediatrics.* **Grace Deukmedjian, MD,** *is a pediatric hospitalist at UCLA Health. Her expertise is in global health, social justice and equity, medical education, and humanities in medicine.* **Pamela S. Miller, PhD, RN, ACNP, CNS, PHN, EBP (CH),** *is a senior nurse scientist in the Center for Nursing Excellence at UCLA Health, where she directs the research, evidence-based practice, and innovation programs. Her research focuses on symptom science.*

This study was supported by a Sigma Theta Tau International Gamma Tau research grant. The authors have no conflicts of interest to disclose.

[AQ01]

Corresponding Author: *Sally Lozano, BSN, RN, CPN, UCLA Medical Center, Santa Monica, Pediatric Unit, 1250 16th St, Santa Monica, CA 90404 (salozano@mednet.ucla.edu).*

DOI: 10.1097/NAN.0000000000000449

after several PIVC placement attempts have already been made and the pain has already been experienced.

Several studies have compared ice, vapocoolant sprays,[3,4] different topical anesthetics,[5] and newer methods, including needle-free injection systems[6] and iontophoresis.[7] However, few studies investigated the efficacy of needle-free injection systems compared with local anesthetics, and none have directly compared the 3 anesthetic agents investigated here. Furthermore, the majority of these studies have taken place in the emergency department and in the preoperative area, where patient and family anxiety are likely to be high. For example, Soltesz et al[8] conducted a randomized clinical trial investigating the effect of lidocaine/prilocaine cream and lidocaine/tetracaine patches on overall incidence of pain among 200 pediatric patients aged 3 to 13 years, which favored lower pain incidence using lidocaine/tetracaine patches. Jimenez et al[9] randomly assigned 116 pediatric patients ages 7 to 19 years to lidocaine/prilocaine cream and unbuffered lidocaine needle-free injection. Although there was no statistically significant difference in cannulation attempts, unbuffered lidocaine needle-free injection was more effective than lidocaine/prilocaine cream on reducing pain. Both studies were completed in a perioperative setting before procedure/surgery. Studies conducted in the emergency department with small sample sizes included Lunoe et al,[3] who compared unbuffered lidocaine needle-free injection and vapocoolant spray or placebo, and Spanos et al,[10] who compared lidocaine/prilocaine cream and unbuffered lidocaine needle-free injection. In both studies, unbuffered lidocaine needle-free injection was shown to reduce venipuncture pain compared with vapocoolant spray, placebo, and lidocaine/prilocaine cream.

THEORETICAL FRAMEWORK

This study was guided by Gate Control Theory of Pain,[11] which asserts that a gating mechanism in the spinal cord modulates the sensory information transmitted from afferent neurons to the spinal cord. Pain signals are transmitted through a gate or central control. This gate is opened or closed through stimulation of the large nerve fibers (inhibitory; closed gate) and small nerve fibers (excitatory; opened gate). Pain experience and associated behaviors occur when nociceptive information exceeds the threshold for inhibition, thereby opening the gate. Anesthetics attenuate signaling resulting from painful stimuli.

To the best of the authors' knowledge, no studies have rigorously evaluated the effectiveness of 3 local anesthetics delivered via cream, patch, and needle-free injection in reducing pain as rated using the Face, Legs, Activity, Cry, Consolability (FLACC) scale (objective scores 0–10) and the Verbal Numeric Rating Scale ([VNRS], subjective scores 0–10) during PIVC insertion in hospitalized children. The primary aims of this study investigated feasibility with respect to recruitment and protocol adherence for a full-scale randomized clinical trial and potential efficacy of local anesthetics on pain intensity during PIVC insertion. The local anesthetics included lidocaine/prilocaine cream, lidocaine/tetracaine patch, and unbuffered lidocaine needle-free injection. Secondary aims compared the number of catheterization attempts and success of PIVC placement, duration of PIVC insertion procedure, and parental satisfaction across the 3 treatment groups.

METHODS

Study Design

This grant-funded research study used a prospective, unblinded, single-center, randomized clinical pilot trial design to compare the effect of local anesthetics (lidocaine/prilocaine cream versus lidocaine/tetracaine patch versus unbuffered lidocaine needle-free injection) applied prior to PIVC insertion on pain intensity in hospitalized pediatric patients. The study received approval from the institutional review board, and assent and informed consent were obtained from patients and parents/guardians.

Setting and Sample

The study was conducted in a 25-bed pediatric inpatient unit at an academic-affiliated, public medical center from March 2017 to February 2020. Eligible patients were between the ages of 12 months and 18 years and admitted to the unit. Patients were identified on admission and throughout their hospital stay for an indication of nonurgent initial or replacement PIVC access by clinical and research nurses. *Nonurgent PIVC placement* was defined as PIVC placement that was not needed within 60 minutes. Patients were recruited during dayshift and nightshift on weekdays and weekends when a research nurse was available.

Patients were ineligible for study inclusion if they were under 12 months of age or older than 18 years of age; admitted to another unit; <5 kg; received chemotherapy; were on any antiarrhythmic medications; were on any of the following medications attributing to increased effect or toxicity with one or more local anesthetics: Idelalisib, Fusidic Acid (Systemic), Conivaptan, Mifepristone, Stiripentol, or Vemurafenib[12]; had a known allergy to lidocaine, prilocaine, or tetracaine; had a known allergy or sensitivity to Tegaderm (3M, St. Paul, MN); had damaged, denuded, or broken skin at potential PIVC placement sites (eg, severe rash, burns, chronic skin inflammation); had previous use of local anesthetic in the preceding 24 hours, were on blood thinners (eg, therapeutic heparin, coumadin, lovenox); were diagnosed with blood disorders that increase risk for bleeding (eg, thrombocytopenia, hemophilia, von Willebrand Disease); had a history of methemoglobinemia, glucose-6-phosphate dehydrogenase deficiency, or pseudocholinesterase deficiency; or had previously participated in the study.

Randomization and Intervention

To eliminate selection bias and balance each arm of the study, consented patients were randomly assigned (1:1:1) to receive 1 of 3 local anesthetics before PIVC placement. Simple randomization was performed using a computer random number generator. Allocation concealment to each treatment condition was performed using sequentially numbered, opaque sealed envelopes that were opened after enrollment and prior to the procedure. The allocation sequence was kept in a secure locked room and drawer, which was only accessible to the person responsible for randomization. Nurses, patients, and parents/guardians were not blinded to the study treatments. Once the patient was randomly assigned, procedure nurses alerted the physician to obtain a medication order and followed the corresponding anesthetic administration protocol. Compliance with randomization was confirmed observationally by the research nurse to assure that planned and actual treatment conditions were completed as randomly allocated.

Local Anesthetic Cream Containing Lidocaine/Prilocaine

For the local anesthetic cream treatment group, a 5-g tube of local anesthetic cream containing 2.5% lidocaine/2.5% prilocaine was ordered. Two possible sites were identified for PIVC placement, and 2.5 g of lidocaine/prilocaine cream were placed at each site. The lidocaine/prilocaine cream was covered by an occlusive dressing (Tegaderm) and remained in place for 60 minutes. At the time of PIVC placement, the cream was removed and the peripheral intravenous (PIV) cannulation was performed.

Local Anesthetic Patches Containing Lidocaine and Tetracaine

For the local anesthetic patches treatment group, 2 patches (lidocaine 70 mg/tetracaine 70 mg) were ordered. Two possible sites were identified for PIVC placement, and 1 patch was applied to each of the 2 identified sites. The patch remained in place for 30 minutes. At the time of PIVC placement, the patch was removed and PIVC cannulation was performed.

Needle-Free Injection Containing Unbuffered Lidocaine

For the needle-free injection treatment group, 2 injector devices were ordered. One needle-free device with 0.2 mL of 1% unbuffered lidocaine was applied at one identified site. The device is a needleless injection system that uses air to deliver the lidocaine. The device makes a loud popping sound when the CO_2 cartridge is activated. If the nurse performing the cannulation anticipated the child could be scared or startled by the noise produced, the nurse had the ability to demonstrate the needle-free procedure and sound in the air. The second unbuffered lidocaine needle-free injection was applied at a second identified site only if the first cannulation was unsuccessful.

PIVCs were placed by experienced nursing staff according to established pediatric unit protocol.[13] An appropriately sized PIVC gauge was chosen by the procedure nurse based on the patient's size and vasculature. All of the nurses were trained to the same unit-based protocol to ensure standardization of PIVC insertion and cannulation. Therefore, there was no variation with regard to PIVC insertion practice, other than the randomized local anesthetic products. Research nurses requested that parents remain at the bedside during PIVC placement for assessment, patient comfort, and distraction to standardize the procedure environment. Parents had the ability to decline being present during the procedure. Additionally, developmentally appropriate patients could choose not to have the parent present during the procedure. Parent presence was documented by the nurse performing the procedure.

Measures

FLACC Scale

The FLACC scale was selected as the observational measurement of pain during PIVC insertion, because this pain scale was used as standard of care at the study institution. This scale has been validated for children 0 to 18 years of age.[14,15] As the name indicates, it objectively assesses face, legs, activity, cry, and consolability as pain indicators (behaviors) and quantifies each indicator on a 0 to 2 scale with a total possible score of 0 to 10 (Table 2). Interpretation of scores are as follows: 0 (relaxed and comfortable), 1 to 3 (mild discomfort), 4 to 6 (moderate pain), and 7 to 10 (severe discomfort or pain or both).

Verbal Numeric Rating Scale

Self-report of pain is considered the gold standard for pain assessment in those who possess the cognitive skills to report such pain. Pain intensity was assessed with a 10-point VNRS.[16] The VNRS is a verbally reported number rating of pain on a scale from 0 (no pain) to 10 (worst; most intense pain) without visual cues. This scale has been well established and validated in children from 8 to 18 years with acute pain.[17] The VNRS is also used routinely by nurses to assess acute pain intensity in this pediatric setting. Research nurses assessed subjective pain using the VNRS among patients 8 years or older and developmentally appropriate. Children who are 7 years and younger or who have intellectual disabilities were excluded from this measure because they may lack the cognitive development and verbal skills to adequately communicate about pain.

Parent Satisfaction Survey

Parents were asked to complete a self-administered, 5-item survey to assess pain perception, treatment satisfaction, and treatment preference. Research nurses asked parents to rate their child's pain intensity during the procedure using the VNRS. Additionally, parents were asked about their satisfaction with the treatment. Satisfaction was rated

using a 5-point Likert scale (0 = very dissatisfied to 5 = very satisfied). The addition of the parental pain score was value added to this study because their perception of pain can impact the overall satisfaction of their child's overall hospital experience. Hospital-wide patient satisfaction surveys are sent to all discharged patients, and parents often fill this out on behalf of their child. It has been reported that the patient experience with PIVC insertions can impact the overall view of the hospital experience.[18]

Number of Attempts to Successful PIVC Placement. Number of PIVC attempts was defined as the number of times in which the cannula was inserted to achieve successful cannulation and placement.

Duration of PIVC Insertion Procedure. The duration of PIVC insertion procedure (procedure time) was defined as the amount of time starting from the application of the tourniquet to successful PIV cannulation and dressing placement.

Staff Education

Staff education about the study and local anesthetics was implemented as a standardized process on the unit. Three months prior to study initiation, 10-minute group in-services, facilitated by a trained research investigator, who is a board-certified pediatric nurse, were provided to nurses on the unit about how to administer each topical anesthetic. Over the course of the study, twice-daily huddles during dayshift and nightshift were provided to reinforce in-service education and periodic reminders. An educational flyer was developed and placed at each nursing station as a visual reminder.

DATA COLLECTION

All data were collected by trained research nurses and recorded on standardized case report and procedure forms. Research nurses abstracted data on baseline patient demographic and clinical characteristic from the electronic medical record, including age, gender, primary diagnosis, use of pain medications other than acetaminophen or nonsteroidal anti-inflammatories, and presence of child life. Procedural information was recorded to include start-and-stop procedure times (duration), randomly assigned anesthetic group, and number of PIVC attempts. Safety was assessed and documented for any adverse events or complications, which included irritation, allergic reactions, excessive pain, patient anxiety, and unforeseen difficulty with PIVC placement. Research nurses were educated on how to use the FLACC scale and VNRS for assessment of pain intensity and collected data immediately before (pre; time 1), during (intermediate; time 2), and immediately after (post; time 3) the first PIV cannulation attempt. For the second PIVC cannulation attempt, pain intensity assessments were performed and documented immediately before (pre; time 4), during (intermediate; time 5), and immediately after (post; time 6). These pain assessments were standard of practice on the pediatric unit. One research nurse was present to assess or document pain intensity during PIVC cannulation but did not perform the procedure.

OUTCOMES

The primary outcome was feasibility of recruitment and protocol adherence. Feasibility was assessed based on the following: recruitment (number of eligible patients offered participation and consented; recruitment rate [number of patients consented per month] percentage of recruitment target achieved; and timeframe of recruitment period) and protocol adherence (number of protocol deviations; number of patients who completed the intervention). A definitive randomized clinical trial was deemed feasible when the following predetermined criteria for success were met: >2 patients per month recruitment rate and 80% adherence to the study protocol.

The second primary outcome was pain intensity as measured by the FLACC scale and the VNRS. Secondary outcomes included parent satisfaction, number of attempts to successful PIVC placement, and duration of PIVC insertion procedure (procedure time).

Statistical Analysis

Descriptive statistics were used to describe the demographic and clinical characteristics of the sample. Continuous variables were reported using means and standard deviations, whereas categorical variables were reported using counts and percentages. Discrete differences between randomized treatment groups were evaluated using χ^2 and ANOVA tests. The independent variable was treatment condition and the dependent variable was pain intensity score. A linear mixed-effects regression model with restricted maximum likelihood estimation and random intercept for patients was used to estimate the longitudinal effect of treatment conditions on pain intensity over time. The parsimonious model was adjusted for covariates, including treatment-by-time interaction, age, gender, venipuncture site, and years of nursing experience as fixed effects. Time (preprocedure, intermediate, and postprocedure) was treated as continuous. First and second cannulation attempt data were included in the analyses. Postestimation margins analyses were performed to compute predicted pain scores. Separate analyses were performed according to the pain intensity scale, because current evidence does not suggest a strong correlation between FLACC and VNRS to support combined modeling. Agreement between observers was analyzed using simple and weighted κ statistics. All analyses used the intention-to-treat principle. All data were entered into a REDCap database. Statistical analysis was conducted using Stata 14.2 (StataCorp, College Station, TX).

Sample size was determined for the second primary aim (pain intensity), assuming 2-sided α of 0.05 and power

(1-β) of 0.80. Power analysis indicated that 98 observations (measurements) in each FLACC and VNRS group (33 observations [10 patients] within each treatment condition) would be needed to detect a small effect size (0.25) in an intention-to-treat analysis. The calculated sample size was inflated by 10% to allow for possible attrition in follow-up, which yielded a total of 108 observations (36 observations [12 patients] within each treatment condition). The number of observations per patient would be determined by the number of cannulation attempts. We anticipated a minimum of 3 observations per patient, which would be equivalent to 1 cannulation attempt.

RESULTS

Sample Characteristics

A total of 114 patients were screened for eligibility, and 88 patients were enrolled and randomly assigned (32 in the lidocaine/prilocaine cream group, 28 in the lidocaine/tetracaine patches group, and 28 in the unbuffered lidocaine needle-free injection group). Demographic and clinical characteristics by group and treatment are shown in Table 1. All patients were included in the analyses. Treatment groups were comparable on key baseline variables, with the exception of 72% of patients in the VNRS group who received lidocaine/prilocaine cream and had a higher history of previous venipuncture compared with their counterparts. Among the 88 patients, the mean age was 9.48 ± 5.29 years, 52 (60%) were ~~men~~, and 45 (51%) were Hispanic/Latino. The most common admitting diagnoses were broadly categorized as orthopedic (45%), followed by respiratory (13%), gastrointestinal (13%), and eating disorders (9%).

Feasibility Outcomes

Recruitment

A total of 114 patients were screened for eligibility. There were no exclusions related to eligibility criteria, which was noteworthy given the restrictive nature of the exclusion criteria. Seventeen patients were screened but not consented for reasons that included lack of time because of stat laboratory samples (n = 1, 6%), no longer required a PIVC (n = 1, 6%), insufficient time to commit to the study due to sleepy patient (n = 1, 6%), parent/guardian unavailable for in-person consent (n = 5, 29%), and general lack of interest (n = 9, 53%). Eighty eight (77%) of 114 eligible patients consented, were randomly assigned, and subsequently completed participation. Recruitment of the desired sample size was achieved at 100%. The feasibility objective was met; however, the recruitment rate was slower than the projected 1-year recruitment period, and took 35 months. An overall mean recruitment rate of 2.7 patients per month were enrolled over the course of the trial. Recruitment was variable depending on the availability of the research nurse, who also performed administrative and clinical responsibilities, as well as patient census on the unit.

Protocol Adherence

Among randomly assigned participants, retention and intervention adherence (completion per protocol) were reported at 91% (n = 88/97). There were 9 patient cases (9%) of 97 randomly assigned patients with protocol deviations. Reasons for protocol deviations were patient delayed because of magnetic resonance imaging prior to PIVC placement (n = 1, 11%), patient received deep PIVC by ultrasound (n = 1, 11%), vein no longer viable for second cannulation attempt using local anesthetic cream (n = 1, 11%), PIVC no longer needed (n = 2, 22%), needle-free injection out of stock (n = 2, 22%), and local anesthetic patch removed by patient (n = 2, 22%). The data included a sufficient number of observations per patient in the FLACC group (114 observations, 29 patients, mean = 3.9, minimum = 3, maximum = 6) and the VNRS group (190 observations, 46 patients, mean = 4.1, minimum = 2, maximum = 6). The research nurse observed each PIVC procedure nurse for quality assurance and consistency with the study protocol and unit-based practice; compliance was met at 100%.

Effect of Local Anesthetic Treatments on Pain Intensity

In the adjusted linear mixed-effects analysis of pain intensity using FLACC pain scores, the overall model was significant (Wald χ^2= 28.65, *df* = 11, *P* = .003). The main effects of treatment group (lidocaine/prilocaine cream, lidocaine/tetracaine patches, and unbuffered lidocaine needle-free injection) and time were not significantly different. The analyses revealed no significant treatment group-by-time interaction (χ^2 = 2.98, *df* = 2, *P* = .23). Figure 2 and [AQ03] Table 2 show predicted marginal FLACC pain scores as a function of treatment and time. Parent perception of the child's pain before, during, and after the procedure (using the VNRS of 0–10) showed no significant difference across treatment conditions for either the FLACC or VNRS group (data not shown). No treatment-related adverse events were observed.

In the adjusted linear mixed-effects analysis of pain intensity using VNRS pain scores, the overall model was significant (Wald χ^2 = 48.87, *df* = 12, *P* < .0001). There were no significant main effects for treatment group or time. The interaction between treatment and time was not significantly different (χ^2 = 5.00, *df* = 2, *P* = .08) A graphical and tabular representation of the model with predicted marginal VNRS pain scores is presented in Figure 3 and Table 2, respectively. Parent perception of the child's pain before, during, and after the procedure (using the VNRS of 0–10) was not significantly different across treatment conditions for either the FLACC or VNRS group (data not shown). There were no observed treatment-related adverse events.

TABLE 1

[AQ02] **Sample Characteristics by Group and Treatment Condition**

	FLACC GROUP			VNRS Group		
	Lidocaine/ prilocaine cream n = 14	Lidocaine/ tetracaine patch n = 10	Unbuffered lidocaine needle-free injection n = 9	Lidocaine/ prilocaine cream n = 18	Lidocaine/ tetracaine patch n = 18	Unbuffered lidocaine needle-free injection n = 19
Age, mean ± SD, y	3.57 ± 2.50	3.90 ± 3.25	4.23 ± 3.82	12.22 ± 3.49	12.82 ± 2.79	13.68 ± 2.31
Gender, n (%)[b]						
Male	9 (64)	8 (80)	6 (67)	12 (67)	9 (53)	8 (42)
Female	5 (36)	2 (20)	3 (33)	6 (33)	8 (47)	11 (58)
Race/ethnicity, n (%)[b]						
White	1 (7)	3 (30)	3 (33)	7 (38)	4 (23)	12 (63)
Hispanic/Latino	10 (72)	6 (60)	5 (56)	8 (44)	9 (53)	7 (37)
Black	1 (7)	1 (10)	0 (0)	1 (6)	2 (12)	0 (0)
Asian	1 (7)	0 (0)	1 (11)	1 (6)	2 (12)	0 (0)
Hawaiian/Pacific Islander	1 (7)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Unknown	0 (0)	0 (0)	0 (0)	1 (6)	0 (0)	0 (0)
Admission diagnosis, n (%)[b]						
Respiratory	2 (14)	3 (30)	2 (22)	2 (11)	1 (6)	1 (5)
Gastrointestinal	0 (0)	0 (0)	0 (0)	3 (16)	4 (23)	4 (22)
Cardiac	0 (0)	0 (0)	0 (0)	0 (0)	1 (6)	0 (0)
Orthopedic	9 (64)	5 (50)	3 (34)	7 (39)	10 (59)	6 (32)
Neurology	0 (0)	0 (0)	1 (11)	0 (0)	0 (0)	0 (0)
Infectious Disease, n (%)	1 (7)	0 (0)	1 (11)	0 (0)	0 (0)	0 (0)
Hematology/oncology	2 (15)	0 (0)	1 (11)	2 (11)	0 (0)	0 (0)
Eating disorder	0 (0)	0 (0)	0 (0)	2 (11)	1 (6)	5 (26)
Dermatology	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	0 (0)
Fluids/electrolytes	0 (0)	0 (0)	0 (0)	1 (6)	0 (0)	1 (5)
Head and neck	0 (0)	1 (10)	1 (11)	1 (6)	0 (0)	1 (5)
Nephrology	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (5)
Previous venipuncture[b]	6 (43)	5 (50)	5 (56)	13 (72)	3 (18)	11 (58)

[AQ04] Abbreviations: FLACC, Face, Legs, Activity, Cry, Consolability; VNRS, Verbal Numeric Rating Scale.

Parent-Reported Satisfaction With Treatments

Parental reporting of overall satisfaction was similar among all 3 treatments for FLACC scores (F [2, 25] = 0.80, P = .46; lidocaine/prilocaine cream, 2.54 ± 0.97; lidocaine/tetracaine patches, 3.17 ± 1.17; and unbuffered lidocaine needle-free injection, 2.83 ± 0.98) and VNRS scores (F [2, 44] = 0.77, P = .47; lidocaine/prilocaine cream, 3.25 ± 0.97; lidocaine/tetracaine patches, 2.71 ± 1.27; and unbuffered lidocaine needle-free injection, 3.06 ± 1.11).

Successful PIVC Placement

Procedure characteristics are reported in Table 3. The number of successful first-attempt PIVC cannulations was not significantly different across treatments in the FLACC (χ^2 = 2.95, df = 2, P = 0.23) or VNRS (χ^2 = 0.47, df = 2, P = 0.79) groups.

Duration of IV Cannulation

Average procedure times (duration) for PIVC placement were similar among all 3 treatments in the FLACC group (F [2, 23] = 0.35, P = 0.71). However, in the VNRS group, the duration of PIVC placement was shorter for those who received unbuffered lidocaine needle-free injection (F [2, 30] = 3.81, P = 0.04) compared with lidocaine/prilocaine cream and lidocaine/tetracaine patches (Table 3).

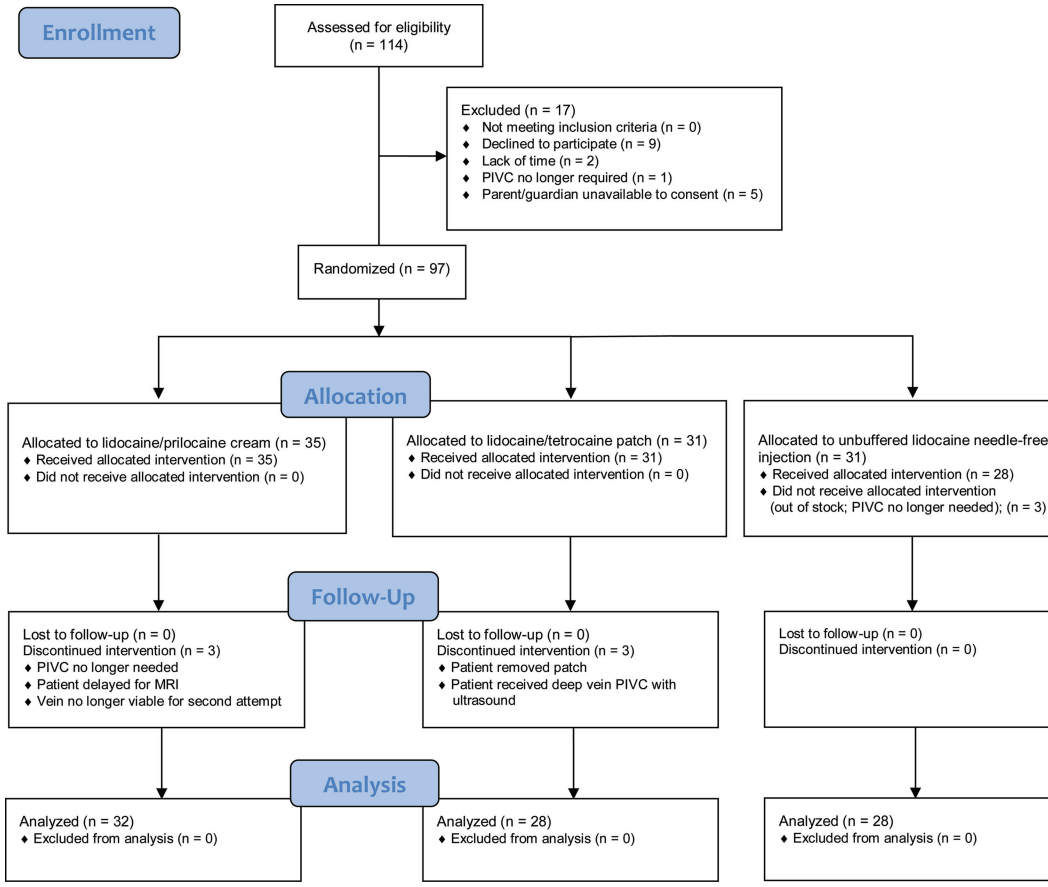

Figure 1 Flow diagram.

DISCUSSION

To the authors' knowledge, this is the first clinical trial to evaluate the feasibility and effectiveness of lidocaine/prilocaine cream, lidocaine/tetracaine patch, and unbuffered lidocaine needle-free injection on pain intensity in an understudied population that includes hospitalized pediatric patients ages 12 months to 7 years. Given the paucity of research in the hospitalized pediatric population, it was imperative to generate feasibility and preliminary evidence to support best practices in decreasing pain during PIVC insertion. The main findings of this study revealed the following:

1. Feasibility was demonstrated with good patient recruitment and high protocol adherence.
2. The lidocaine/prilocaine cream, lidocaine/tetracaine patch, and unbuffered lidocaine needle-free injection treatments had similar effects on pain intensity during PIVC.
3. The number of successful attempts did not differ across the 3 treatments.
4. Procedure time (duration) to successful PIVC differed in the VNRS group in favor of unbuffered lidocaine needle-free injection but did not differ among those in the FLACC group.
5. Parent-reported satisfaction and perception of pain did not differ across the 3 treatments.

In terms of feasibility, this study was designed to be pragmatic and conducted under "real-world conditions" with the potential for scalability. Consistent with previous research,[19,20] findings revealed a critical "lesson learned" relating to effective recruitment, which warrants careful consideration for future clinical trials. As previously described earlier in this article, the recruitment period was longer than anticipated, and potential participants were recruited from a small pool of hospitalized pediatric patients. The research team offers salient recommendations to build on this experience through recruitment optimizations. Research nurses served as the recruitment team for the trial while concurrently supporting clinical and administrative responsibilities on the unit. Their availability around the clock (eg, days, nights, weekdays, and weekends) was a strength but was variable, depending on when they were scheduled to work on the unit. Potential patients were likely missed for recruitment, despite expanding the number of trained research nurses who had strong relationships with the clinical team and patients. In retrospect, the provision of dedicated recruitment staff will be key to facilitate recruitment activities by 1) increasing the recruitment rate to reach a sufficiently powered sample size; 2) reducing the recruitment period; and 3) lowering the burden of recruitment activities for busy nurses with patient care priorities. Additionally, marked, and at times,

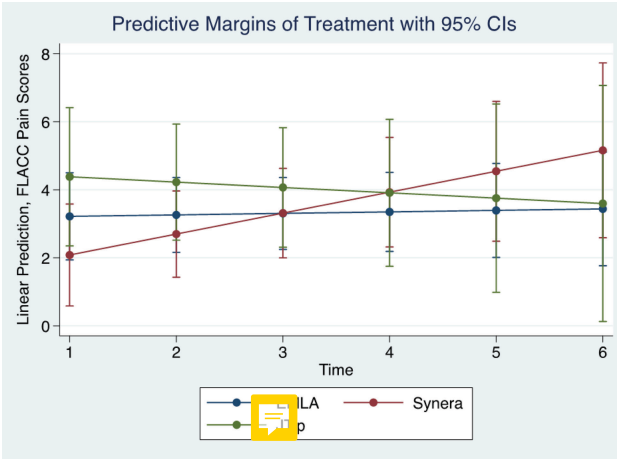

Figure 2 Estimated margins plot showing predicted FLACC pain scores with 95% CIs over time by treatment condition. Note: Estimated margins plot showing predicted FLACC pain scores with 95% CI over time by treatment. Predictive margins are the predicted average pain score among patients in the sample. The CI provides, with 95% certainty, a range of values that contains the true pain score for this pediatric population. First cannulation attempt: Time 1 = Pre (immediately before treatment), Time 2 = Intermediate (during procedure), Time 3 = Post (immediately after procedure); second cannulation attempt: Time 4 = Pre (immediately before treatment), Time 5 = Intermediate (during procedure), Time 6 = Post (immediately after procedure). *Abbreviations: CIs, confidence intervals; FLACC, Face, Legs, Activity, Cry, Consolability.*

unpredictable, temporal, or seasonal variation impacted the unit census, particularly during the winter, spring, and summer months. Therefore, setting realistic incremental recruitment targets and expectations should be considered with trial planning. Eligibility criteria was not a limiting factor in recruitment. Furthermore, local anesthetic treatment preferences did not appear to impact recruitment, because all 3 treatments were administered as part of routine care on the unit. Adherence to the study protocol was high, and no safety issues were reported.

In contrast to several trials involving children,[8,9,21] this trial showed no substantial difference in pain intensity scores across 3 treatment conditions. These results may reflect a limited sample size, imbalance within the FLACC group (although addressed through statistical modeling), and variation in the pain intensity scales used to assess treatment effectiveness. Previous studies reported lower pain scores with each treatment condition included in the present study. For example, in a randomized controlled trial of 150 children aged 8 to 18 years and undergoing PIVC placement, significantly lower pain scores were found in the lidocaine/prilocaine cream group compared with the unbuffered lidocaine needle-free injection group using the visual analog scale (VAS) but noted that pain scores were generally low in both treatment groups.[21] Conversely, Jimenez et al[9] compared local anesthetic cream containing lidocaine/prilocaine cream and unbuffered lidocaine needle-free injection in a randomized controlled trial using VAS pain scores among children 7 to 19 years of age and showed significantly lower pain scores with unbuffered lidocaine needle-free injection. However, using a 4-point pain score, lidocaine/tetracaine patches were associated with lower pain scores compared with lidocaine/prilocaine cream in a randomized trial of 200 children aged 3 to 13 years.[8]

The results of the present study were consistent with previous research that found no difference in first-attempt PIVC placement success[3] or number of attempts.[9] Other studies supported the premise that PIVC access can be

TABLE 2

Predicted FLACC and VNRS Pain Scores With 95% Confidence Intervals Over Time by Treatment Condition

	FLACC Group			VNRS Group		
	Lidocaine/ prilocaine cream (n = 14)	Lidocaine/ tetracaine patch (n = 10)	Unbuffered lidocaine needle-free injection (n = 9)	Lidocaine/ prilocaine cream (n = 18)	Lidocaine/ tetracaine patch (n = 18)	Unbuffered lidocaine needle-free injection (n = 19)
First cannulation attempt[a,b]						
Time 1	3.22 (1.94–4.50)	2.08 (0.58–3.58)	4.38 (2.35–6.41)	1.02 (–0.09 to 2.13)	1.65 (0.67–2.64)	1.67 (0.67–2.67)
Time 2	3.26 (2.15–4.36)	2.70 (1.43–3.96)	4.22 (2.52–5.93)	1.35 (0.51–2.19)	2.21 (1.46–2.96)	1.58 (0.83–2.32)
Time 3	3.30 (2.25–4.36)	3.31 (2.00–4.62)	4.07 (2.31–5.82)	1.67 (0.94–2.42)	2.77 (2.07–3.46)	1.48 (0.81–2.15)
Second cannulation attempt[a,c]						
Time 4	3.35 (2.19–4.51)	3.93 (2.32–5.54)	3.91 (1.75–6.07)	2.01 (1.14–2.87)	3.33 (2.47–4.19)	1.39 (0.57–2.21)
Time 5	3.39 (2.01–4.77)	4.54 (2.49–6.60)	3.75 (0.99–6.52)	2.34 (1.19–3.48)	3.89 (2.73–5.04)	1.29 (0.18–2.40)
Time 6	3.44 (1.77–5.11)	5.16 (2.59–7.73)	3.60 (0.13–7.07)	2.67 (1.17–4.16)	4.45 (2.93–5.96)	1.20 (–0.26 to 2.66)

Abbreviations: FLACC, Face, Legs, Activity, Cry, Consolability; VNRS, Verbal Numeric Rating Scale.
[a]Data reported as predicted pain scores (95% CI).
[b]First cannulation attempt: Time 1 = Pre (immediately before treatment), Time 2 = Intermediate (during procedure), Time 3 = Post (immediately after procedure).
[c]Second cannulation attempt: Time 4 = Pre (immediately before treatment), Time 5 = Intermediate (during procedure), Time 6 = Post (immediately after procedure).

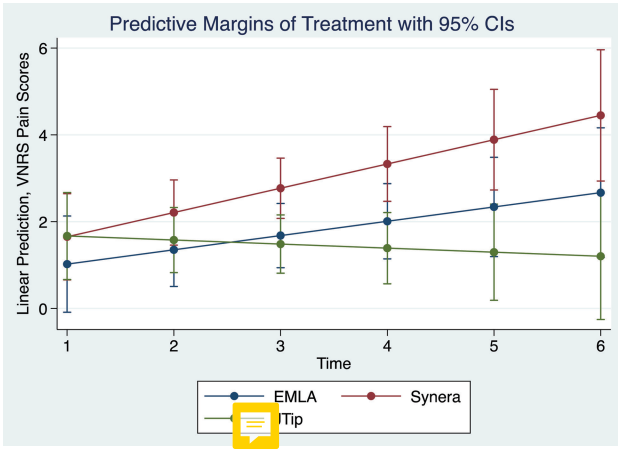

Figure 3 Estimated margins plot showing predicted VNRS pain scores with 95% CIs over time by treatment condition. Note: Estimated margins plot showing predicted VNRS pain scores with 95% CI over time by treatment. Predictive margins are the predicted average pain score among patients in the sample while controlling other variables at the mean. The CI provides, with 95% certainty, a range of values that contains the true pain score for this pediatric population. First cannulation attempt: Time 1 = Pre (immediately before treatment), Time 2 = Intermediate (during procedure), Time 3 = Post (immediately after procedure); second cannulation attempt: Time 4 = Pre (immediately before treatment), Time 5 = Intermediate (during procedure), Time 6 = Post (immediately after procedure). *Abbreviations: CIs, confidence intervals; VNRS, Verbal Numeric Rating Scale.*

challenging and may require on average 2 attempts over 28 minutes,[22] even for the most experienced personnel.[23]

LIMITATIONS

Although this study provided many strengths, including randomization and repeated measures, there are several limitations. First, this study included a small convenience sample in 1 pediatric unit, which may limit generalizability. Second, nurses and patients/parents/guardians were not blinded to the treatment methods used given the nature of the study and special vulnerable population of pediatric patients, which may limit internal validity. Third, recruitment rates varied because of seasonal (temporal) changes and resulted in periods of low patient census that hampered recruitment. Fourth, for practical reasons, simple randomization was used in this study, but it is acknowledged that the protocol should be modified to apply a more restrictive randomization scheme using blocks in a full-scale randomized clinical trial to achieve balanced groups. Fifth, as a methodologic limitation, this study compared 3 active treatments and did not use a control condition. Consideration for selecting a control or inactive comparator condition was complex and based on current practice, patient risk assessment, and the clinical setting. All 3 local anesthetics were established usual care treatments on the study unit, and implementing an inactive treatment raised ethical concerns for this vulnerable population. Sixth, there were only 12 nurses trained to observe. This would limit the availability of always having a research nurse present to conduct the study. Seventh, as a strength, the pain scales administered in the study were standard of practice on the pediatric unit. However, FLACC scores may be limited by observational bias that reflects pain behavior confounded by anxiety and distress.[24] Although several studies have described both overreporting[25,26] and underreporting[27,28] of pain in children, a parent may still be the best proxy for assessing subjective pain because they know their child best. Lastly, the findings highlight the need in the future for replication in a larger sample to include unmeasured personal and environmental factors that may confound or influence pain (eg, body temperature, circadian effect).

IMPLICATIONS FOR NURSING PRACTICE

This study sought to address 4 important gaps in knowledge and contribute to the body of biomedical literature. First, previous studies have been conducted in the emergency department and perioperative setting. To the best of our knowledge, this was the first prospective pediatric study conducted on the inpatient unit, where response to physiologic pain control may be very different. The challenges and considerations for PIVC placement on the inpatient pediatric unit are multifactorial, which requires the balance of acute clinical patient needs, timing of necessary interventions such as medications or PIVC hydration, developmental stage, and effectiveness and timing of local anesthetic pharmacokinetics. Second, this study compared 3 anesthetics that, based on the previous trial outcomes,[8,9] were most likely to be effective in a pediatric inpatient population: lidocaine/prilocaine cream, lidocaine/tetracaine patches, and unbuffered lidocaine needle-free injection. To our knowledge, no clinical trial has compared the effectiveness of these 3 anesthetics on pain and other clinical outcomes. Third, previous studies on needle-free injection used buffered lidocaine during their clinical trials.[3,9,21] In the time since those trials were conducted, a new pharmacy regulation now requires time limits to administer lidocaine once it is drawn up. Thus, most hospital institutions have changed their needle-free injection preparations to use unbuffered lidocaine. There is no difference in time to effectiveness with buffered compared with unbuffered lidocaine. When lidocaine is unbuffered, it excludes bicarbonate from the preparation, therefore causing some discomfort when administered. Nurses must fill the needle-free injector with the appropriate amount of lidocaine. To date, there are no published studies using unbuffered lidocaine administration through the needle-free injection device. Last, there is a paucity of studies examining the effect of anesthetics on pain among patients <7 years of age in the inpatient setting.[3,8]

Taken together, these findings suggest that, given the importance of reducing PIVC placement pain, all 3 treatments may be used in pediatric patients undergoing a PIVC cannulation procedure. In nonurgent cases, lidocaine/prilocaine

TABLE 3

Procedure Characteristics by Group and Treatment Condition

	FLACC Group				VNRS Group			
	Lidocaine/ prilocaine cream n = 14	Lidocaine/ tetracaine patch n = 10	Unbuffered lidocaine needle-free injection n = 9	*P* value	Lidocaine/ prilocaine cream n = 18	Lidocaine/ tetracaine patch n = 18	Unbuffered lidocaine needle-free injection n = 19	*P* value
First attempt								
Procedure time, mean ± SD, min	2.75 ± 1.98	3.86 ± 2.97	2.88 ± 3.23	.71	5.75 ± 4.27	2.00 ± 2.41	2.18 ± 3.06	.04
Successful cannulation, n (%)	8 (57)	7 (78)	8 (89)	.23	7 (47)	9 (53)	10 (59)	.79
Second attempt								
Procedure time, mean ± SD, min	2.67 ± 1.53	2.50 ± 2.12	1.00 ± 0.00	.73	4.67 ± 4.03	4.43 ± 2.94	2.25 ± 2.63	.50
Successful cannulation	3 (60)	2 (100)	1 (100)	.45	2 (33)	6 (85)	2 (33)	.09
Cannulation site				.61				.45
Hand	7 (50)	6 (60)	2 (25)		6 (46)	9 (53)	10 (56)	
Wrist	1 (7)	1 (10)	2 (25)		0 (0)	5 (29)	1 (6)	
Forearm	1 (7)	1 (10)	0 (0)		0 (0)	3 (18)	1 (6)	
Antecubital fossa	5 (36)	2 (20)	4 (50)		7 (54)	4 (23)	5 (28)	
Upper arm	0 (0)	0 (0)	0 (0)		0 (0)	0 (0)	1 (6)	
Catheter Size				.10				.25
20-gauge	0 (0)	0 (0)	0 (0)		1 (6)	0 (0)	0 (0)	
22-gauge	10 (71)	9 (90)	4 (44)		13 (81)	18 (100)	16 (84)	
24-gauge	4 (29)	1 (10)	5 (56)		2 (13)	0 (0)	3 (16)	
Assistive tools								
Accuvein	7 (50)	6 (60)	4 (44)	.77	8 (44)	8 (47)	11 (65)	.43
Ultrasound	0 (0)	1 (10)	1 (11)	.45	1 (6)	0 (0)	1 (6)	.61
Child life	5 (36)	4 (40)	4 (44)	.92	0 (0)	1 (6)	0 (0)	.34
Distraction or toys	9 (64)	8 (80)	7 (78)	.64	6 (33)	2 (12)	4 (22)	.31
Nurse experience, mean ± SD, y								
First attempt	7.89 ± 6.40	8.50 ± 8.37	5.43 ± 6.60	.67	6.58 ± 4.91	6.64 ± 8.19	7.24 ± 5.40	.94
Second attempt	11.92 ± 7.47	15.00 ± 7.07	11.00 ± 0.00	.86	11.25 ± 7.45	16.33 ± 9.91	5.67 ± 3.71	.07

Abbreviations: FLACC, Face, Legs, Activity, Cry, Consolability; ~~G, gauge;~~ VNRS, Verbal Numeric Rating Scale.

cream may be applied, which has up to a 60-minute wait time. Both lidocaine/tetracaine patches and unbuffered lidocaine needle-free injections are also suitable alternatives, particularly when a procedure delay is not possible.

Although all 3 anesthetics have been administered by the research and procedure nurses prior to this study, the unbuffered lidocaine needle-free injection was the least common. Qualitatively, nurses reportedly found the z-track method, which is the preferred method for needle-free injection, to be difficult to achieve during the study. The popping sound may elicit anxiety reactions for nurses if they have not previously used the device. Most nurses agreed that lidocaine/tetracaine patches were easy to apply and enhanced visualization of the vein prior to catheterization. The lidocaine/prilocaine cream prevented the patient from flinching according to several nurses performing the PIVC insertion.

CONCLUSION

Pain is a pervasive issue among pediatric patients who undergo PIVC insertion. Pain control during pediatric PIVC

placement in the inpatient setting may be achieved with local anesthetics. Conduct of a definitive, full-scale randomized clinical trial in the hospitalized pediatric population is feasible with protocol modifications to enhance recruitment and methodology. Although preliminary, there was no significant difference among lidocaine/prilocaine cream, lidocaine/tetracaine patch, and unbuffered lidocaine needle-free injection on pain intensity over time. Future research efforts should be directed toward a larger, multicenter trial comparing similar treatments to confirm the results of this study. Findings may inform recommendations for best practices in the management of pain during PIVC insertion.

ACKNOWLEDGMENTS

The authors extend great appreciation to the patients and parents/guardians who participated in this study. The authors would also like to thank the following individuals who assisted with study procedures: Krystle Britton, Jillian Cuevo, Sharon Doggett, Hannah Marshall, Adrienne Puglisi, Azucena Sandoval, Diane Tamondong, Krizia Torres, and Vincent Yalung.

REFERENCES

1. Martin HA. The power of topical anesthetics and distraction for peripheral intravenous catheter placement in the pediatric perianesthesia area. *J Perianesth Nurs*. 2018;33(6):880-886. doi:10.1016/j.jopan.2017.08.005
2. Kennedy RM, Luhmann J, Zempsky WT. Clinical implications of unmanaged needle-insertion pain and distress in children. *Pediatrics*. 2008;122(suppl 3):S130-S133. doi:10.1542/peds.2008-1055e
3. Lunoe MM, Drendel AL, Levas MN, et al. A randomized clinical trial of jet-injected lidocaine to reduce venipuncture pain for young children. *Ann Emerg Med*. 2015;66(5):466-474. doi:10.1016/j.annemergmed.2015.04.003
4. Zhu Y, Peng X, Wang S, et al. Vapocoolant spray versus placebo spray/no treatment for reducing pain from intravenous cannulation: a meta-analysis of randomized controlled trials. *Am J Emerg Med*. 2018;36(11):2085-2092. doi:10.1016/j.ajem.2018.03.068
5. Cozzi G, Borrometi F, Benini F, et al. First-time success with needle procedures was higher with a warm lidocaine and tetracaine patch than an eutectic mixture of lidocaine and prilocaine cream. *Acta Paediatr*. 2017;106(5):773-778. doi:10.1111/apa.13764
6. Kelly S, Russell J, Devgon P, Rosen P. Transformation of the peripheral intravenous catheter placement experience in pediatrics. *J Vasc Access*. 2017;18(3):259-263. doi:10.5301/jva.5000652
7. Pershad J, Steinberg SC, Waters TM. Cost-effectiveness analysis of anesthetic agents during peripheral intravenous cannulation in the pediatric emergency department. *Arch Pediatr Adolesc Med*. 2008;162(10):952-961. doi:10.1001/archpedi.162.10.952
8. Soltesz S, Dittrich K, Teschendorf P, Fuss I, Molter G. Topische Anästhesie vor Venenpunktion bei Kindern. Vergleich eines wärmenden Lidocain-Tetracain- mit einem Lidocain-Prilocain-Pflaster [Topical anesthesia before vascular access in children: comparison of a warmth-producing lidocaine-tetracaine patch with a lidocaine-prilocaine patch. [in German]. *Anaesthesist*. 2010;59(6):519-523. doi:10.1007/s00101-010-1727-5
9. Jimenez N, Bradford H, Seidel KD, Sousa M, Lynn AM. A comparison of a needle-free injection system for local anesthesia versus EMLA for intravenous catheter insertion in the pediatric patient. *Anesth Analg*. 2006;102(2):411-414. doi:10.1213/01.ane.0000194293.10549.62
10. Spanos S, Booth R, Koenig H, Sikes K, Gracely E, Kim IK. Jet injection of 1% buffered lidocaine versus topical ELA-Max for anesthesia before peripheral intravenous catheterization in children: a randomized controlled trial. *Pediatr Emerg Care*. 2008;24(8):511-515. doi:10.1097/PEC.0b013e31816a8d5b
11. Melzack R, Wall PD. Pain mechanisms: a new theory. *Science*. 1965;150(3699):971-979. doi:10.1126/science.150.3699.971
12. Taketomo CK, Hodding JH, Kraus DM, eds. *Pediatrics and Neonatal Dosage Handbook: An Extensive Resource for Clinicians Treating Pediatric and Neonatal Patients.* 25th ed. Lexicomp/Wolters Kluwer; 2018.
13. Lippincott Procedures. IV catheter insertion, pediatric. Published 2020. Accessed June 27, 2021. https://procedures.lww.com/lnp/view.do?pId=3469686&hits=catheter,iv,insertion,intravascular,insert,catheters,intravenous,inserting&a=true&ad=false&q=IV%20cATHETER%20INSERTION
14. von Baeyer CL, Spagrud LJ. Systematic review of observational (behavioral) measures of pain for children and adolescents aged 3 to 18 years. *Pain*. 2007;127(1-2):140-150. doi:10.1016/j.pain.2006.08.014
15. Andersen RD, Langius-Eklöf A, Nakstad B, Bernklev T, Jylli L. The measurement properties of pediatric observational pain scales: a systematic review of reviews. *Int J Nurs Stud*. 2017;73:93-101. doi:10.1016/j.ijnurstu.2017.05.010
16. Voepel-Lewis T, Malviya S, Tait AR. Validity of parent ratings as proxy measures of pain in children with cognitive impairment. *Pain Manag Nurs*. 2005;6(4):168-174. doi:10.1016/j.pmn.2005.08.004
17. McCaffery M, Pasero C. Teaching patients to use a numerical pain-rating scale. *Am J Nurs*. 1999;99(12):22.
18. Helm RE. Accepted but unacceptable: peripheral IV catheter failure: 2019 follow-up. *J Infus Nurs*. 2019;42(3):149-150. doi:10.1097/NAN.0000000000000324
19. Varse F, Janani L, Moradi Y, Solaymani-Dodaran M, Baradaran HR, Rimaz S. Challenges in the design, conduct, analysis, and reporting in randomized clinical trial studies: a systematic review. *Med J Islam Repub Iran.* 2019;33:37. doi:10.34171/mjiri.33.37
20. Beasant L, Brigden A, Parslow RM, et al. Treatment preference and recruitment to pediatric RCTs: a systematic review. *Contemp Clin Trials Commun*. 2019;14:100335. doi:10.1016/j.conctc.2019.100335
21. Stoltz P, Manworren RCB. Comparison of children's venipuncture fear and pain: randomized controlled trial of EMLA® and J-Tip Needleless Injection System®. *J Pediatr Nurs*. 2017;37:91-96. doi:10.1016/j.pedn.2017.08.025
22. Larsen P, Eldridge D, Brinkley J, et al. Pediatric peripheral intravenous access: does nursing experience and competence really make a difference? *J Infus Nurs*. 2010;33(4):226-235. doi:10.1097/NAN.0b013e3181e3a0a8
23. Nafiu OO, Burke C, Cowan A, Tutuo N, Maclean S, Tremper KK. Comparing peripheral venous access between obese and normal weight children. *Paediatr Anaesth*. 2010;20(2):172-176. doi:10.1111/j.1460-9592.2009.03198.x
24. Babl FE, Crellin D, Cheng J, Sullivan TP, O'Sullivan R, Hutchinson A. The use of the faces, legs, activity, cry and consolability scale to assess procedural pain and distress in young children. *Pediatr Emerg Care*. 2012;28(12):1281-1296. doi:10.1097/PEC.0b013e3182767d66
25. Chambers CT, Giesbrecht K, Craig KD, Bennett SM, Huntsman E. A comparison of faces scales for the measurement of pediatric pain: children's and parents' ratings. *Pain*. 1999;83(1):25-35. doi:10.1016/s0304-3959(99)00086-x
26. Stein PR. Indices of pain intensity: construct validity among preschoolers. *Pediatr Nurs*. 1995;21(2):119-123.
27. Bellman MH, Paley CE. Pain control in children: parents underestimate children's pain. *BMJ*. 1993;307(6918):1563. doi:10.1136/bmj.307.6918.1563
28. Chambers CT, Craig KD. An intrusive impact of anchors in children's faces pain scales. *Pain*. 1998;78(1):27-37. doi:10.1016/s0304-3959(98)00112-2

AUTHOR QUERIES

TITLE: A Comparison of Local Anesthetics for Intravenous Catheter Insertion in Hospitalized Pediatric Patients: A Randomized Controlled Pilot Trial

AUTHORS: Sally Lozano, Grace Sund, Allison Guimera, Grace Deukmedjian, and Pamela S. Miller

[AQ00]: Please check if authors name are correctly captured for given names (in red) and surnames (in blue) for indexing after publication.

[AQ01]: Please confirm disclosure statement.

[AQ02]: Please check all table content very carefully to ensure accuracy.

[AQ03]: Please cite Figure 1 in body text in numeric order where appropriate

[AQ04]: Please change footnote b to a throughout and define in footnote section if it is needed. Remove if it represents n (%). Check all uses throughout this table.