CHEST

Comparison of Two Lidocaine Administration Techniques on Perceived Pain From Bedside Procedures

A Randomized Clinical Trial

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BACKGROUND: Lidocaine is used to alleviate procedural pain but paradoxically increases pain during injection. Pain perception can be modulated by non-noxious stimuli such as temperature or touch according to the gate control theory of pain. We postulated that lidocaine dripped onto the skin prior to injection would cool or add the sensation of touch at the skin surface to reduce pain perception from the procedure.

METHODS: A randomized clinical trial of patients referred to the procedure service from February 2011 through March 2015 was conducted. All patients received 1% subcutaneous lidocaine injection. Patients randomized to the intervention group had approximately 1 to 2 ml of lidocaine squirted onto the skin surface prior to subcutaneous lidocaine injection. Patients were blinded to the details of the intervention and were surveyed by a blinded investigator to document the primary outcome (severity of pain from the procedure) using a visual analog scale.

RESULTS: A total of 481 patients provided consent and were randomized to treatment. There was a significant improvement in the primary outcome of procedural pain (control, 16.6 $\pm$ 24.8 mm vs 12.2 $\pm$ 19.4 mm; $P = .03$) with the intervention group as assessed by using the visual analog scale score. Pain scores were primarily improved for peripherally inserted central catheters (control, 18.8 $\pm$ 25.6 mm vs 12.2 $\pm$ 18.2 mm; $P = .02$) upon subgroup analysis.

CONCLUSIONS: Bedside procedures are exceedingly common. Data regarding the severity of procedural pain and strategies to mitigate it are important for the informed consent process and patient satisfaction. Overall, pain reported from common bedside procedures is low, but pain can be further reduced with the addition of lidocaine onto the skin surface to modulate pain perception.

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ABBREVIATIONS: PICC = peripherally inserted central catheter; VAS = visual analog scale

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More than five million bedside procedures are performed annually in the United States.[1] Lidocaine by subcutaneous injection is the most commonly administered local anesthetic; during the consent process, patients commonly ask about procedural pain. Although local anesthetic is intended to alleviate the pain of the procedure, it paradoxically increases pain with the injection of the local anesthetic itself.[2,3] Because provider efforts toward effective pain control have been associated with improved patient outcomes,[4] it is important to develop strategies to minimize all elements of procedure-associated pain.

Previous studies have investigated ways to reduce pain by manipulating the properties of the local anesthetic such as warming or pH buffering with sodium bicarbonate, or by altering the rate of administration of lidocaine.[5-8] Although these techniques have shown decreased pain perception, they require specialized formulations of lidocaine to be prepared at frequent intervals[7] and thus are difficult to implement practically at the bedside. In 1965, Melzack and Wall proposed the gate control theory of pain,[9] which suggests that pain transmission from peripheral afferent nerves to the CNS is modulated by a gating system in the dorsal horn of the spinal cord. Specifically, the afferent pain-receptive nerves that signal acute pain signals (A-delta fibers and C fibers) can be blocked by non-noxious stimuli such as light touch (A-beta fibers) or temperature. This modulation occurs by activation of inhibitory interneurons within the substantia gelatinosa in lamina II of the spinal cord dorsal horn.[10,11] The resulting inhibition prevents the ascending transmission of pain sensation through the second-order fibers carried from the spinal cord within the lateral spinothalamic tract.[12] A non-noxious stimulus such as cold temperature[13] or light touch might block or interfere with the transmission of pain signals. Indeed, studies have shown that vibration[14] and cooling[15] can reduce pain associated with procedures, thus showing proof-of-concept that nerve activation by non-noxious stimuli can reduce pain transmission by "gating," or inhibiting, pain signals. Although these interventions are effective, they also require specialized devices,[14,15] thus limiting their practical use.

The aim of the present study was to investigate whether a simple technique of letting room temperature lidocaine drip onto the surface of the skin just prior to its injection would decrease pain perception. The perception of wetness on the skin integrates sensory afferents of cooling and mechanosensation.[16] We postulated that activation of afferent nerves with the relative sensation of coolness and wetness from contact with room temperature lidocaine would subsequently activate inhibitory interneurons and decrease propagation of pain sensations due to the gating effects of cooling[10,17,18] and light touch.[9] To our knowledge, no previous studies have examined whether simply stimulating peripheral nerve fibers with room temperature lidocaine placed onto the surface of the skin is sufficient to modulate the pain perception of common bedside procedures.

Patients and Methods

Design

We conducted a randomized controlled trial in which patients and research investigators, but not operators, were blinded to treatment assignment. The institutional review board at the University of Chicago Medical Center approved the protocol (#10-621). All patients provided written informed consent for participation in the trial.

Setting and Participants

This single-center study was conducted at a quaternary university medical center from February 2011 through March 2015. Attending physicians in the section of Pulmonary/Critical Care were the operators who evaluated consecutive adult patients referred to the University of Chicago Medical Center's Procedure Service for a planned medical bedside procedure that required local lidocaine injection for analgesia. These bedside procedures included peripherally inserted central catheters (PICCs), central venous catheters, thoracentesis, paracentesis, and lumbar puncture. Patients were excluded if they lacked the decisional capacity to consent and/or lacked the ability to answer questions based on the pain scales.

Randomization and Interventions

During the informed consent process, patients were informed according to a script that they will receive one of several lidocaine administration techniques. No details regarding the various techniques were provided. After informed consent was obtained, patients were randomized to two groups prior to the bedside procedure. Both groups were given 1% lidocaine without epinephrine, which is referred to as "1% lidocaine" going forward. Patients randomized to the control group received 1% lidocaine subcutaneous injection alone by a standard approach using a 25-gauge needle that was attached to a lidocaine syringe. As per usual care, the needle punctured the patient's skin, and lidocaine was then injected through the needle. Patients randomized to the intervention group had approximately 1 to 2 mL of 1% lidocaine dripped onto the surface of the skin immediately prior to subcutaneous injection of the 1% lidocaine. The subcutaneous lidocaine injection portion of the procedure in the intervention group was identical to the control group. All proceduralists were instructed to avoid negative words such as "pain, sting, burn, or hurt" during the procedure and instead use neutral words such as "pressure, sensation, or numb."

Patients were randomly assigned in a 1:1 ratio to the control or intervention groups. A computer-generated, permuted block randomization scheme with varying block sizes was used to allocate patients to each group. Each assignment was designated in a consecutively numbered, sealed, opaque envelope. Of note, all patients received lidocaine subcutaneous injection as indicated for the medical procedure, with no limits on the amount of lidocaine to be administered. The only difference was that the intervention group received 1 to 2 mL of lidocaine squirted onto the surface of the skin via the needle/syringe apparatus prior to the needle touching the skin. Patients were blinded to treatment allocation at the time of the procedure and during completion of the follow-up pain questionnaire.

The study controlled for injection-related variables known to affect pain perception. For instance, lidocaine was stored and administered at room temperature. Injections were given with the initial syringe position at approximately 30 degrees to the skin and the bevel of a 25-gauge needle pointing upward. In all cases (intervention and control groups), the rate of injection was approximately 1 mL per 15 s.

Follow-Up Procedures and Monitoring

An investigator who was not present for the procedure and blinded to the patients' group assignments (intervention vs control) gathered data regarding patients' perceptions of pain from the lidocaine subcutaneous injection and pain from the procedure (excluding lidocaine injection). Data on perceived pain were collected by using a 100-mm visual analog scale (VAS),[19] which is a standard measuring tool for pain. Investigators used a standard script to explain the survey and ensured that patients wore visual/hearing aids to ensure accurate comprehension of the tool and recording of the VAS score. Patients were given a sealed disclosure envelope after completion of the pain survey revealing their treatment allocation.

Outcomes

The primary end point was the procedure pain perception as measured by using the VAS. Secondary end points included a priori subgroup analyses of pain perceived according to procedure type (eg, PICC, central venous catheter, thoracentesis, lumbar puncture, paracentesis).

Statistical Analysis

Continuous data, specifically results on the VAS, were described with either mean ± SD or median (interquartile range). The data were compared by using either the two-sided *t* test or the Wilcoxon rank sum test, depending on the distribution of the data. Categorical data were described as proportions and were compared by using χ^2 testing.

The dependent variable (VAS score of procedure) was subjected to multivariable analysis with the following independent variables: age, sex, race, procedure performed, success/failure of procedure, number of attempts, duration of procedure, and use of systemic sedatives (defined as benzodiazepines) or systemic analgesics (defined as opioids and nonsteroidal medications). With nine independent variables included in the linear regression model and a Cohen's f^2 effect size of 0.1 (ie, "moderate") anticipated, a power of 0.9, and alpha = 0.05, we estimated a need for 207 patients in each group. Conservatively anticipating 15% incomplete data, we targeted 240 patients in each group, or a total of 480 patients.

Results

A total of 481 eligible patients were referred to the procedure service during the study period (Fig 1). There was no significant difference between the two groups in terms of age, race, sex, smoking history, chronic pain conditions, and use of in-hospital pain medications (Table 1). There was no difference in time from procedure completion to collection of pain scores between groups (control 15 min [5-70.2 min] vs intervention 15 min [5-45 min]; $P = .36$) In the study period, a total of 283 PICC lines (59%), 31 central lines (6%), 63 thoracenteses (13%), 41 paracenteses (9%), and 63 lumbar punctures (13%) were completed. There was a slightly higher proportion of paracenteses performed in the intervention group (11% vs 6%; $P = .04$) (Table 2). No difference was recorded in the number of procedure attempts between groups; as expected, there was a statistically significant difference in the amount of lidocaine used in the intervention group due to use of lidocaine on the skin surface (4.7 ± 2.5 mL vs 5.7 ± 3.1 mL; $P = .0001$).

Primary and Secondary Outcomes

For all of the procedures, the mean VAS score for pain perception from the procedure was 16.6 ± 24.8 mm in the control group and 12.2 ± 19.4 mm in the intervention group ($P = .03$) (Table 3), indicating a statistically significant reduction in pain. With regard to each of the individual procedures analyzed separately, patients undergoing PICC placement had a statistically significant reduction in pain from the procedure (18.8 ± 25.6 mm vs 12.2 ± 18.2 mm; $P = .02$). There was no difference in any other specific procedure analyzed separately by using the VAS (Table 3).

On multivariate linear regression analysis of VAS scores for procedural pain, the addition of lidocaine to the skin surface prior to subcutaneous injection (intervention) was also significantly associated with a decrease in reported pain from the procedure. Other independent predictors, including female sex, in-hospital analgesic use, number of attempts, and central line insertion, had a statistically significant association with increased pain scores (Table 4).

Discussion

A simple intervention of dripping lidocaine on the skin surface prior to subcutaneous injection led to a 26% relative reduction in procedural pain. Lidocaine dripped onto the skin from the syringe is water soluble and has no direct anesthetic effect; rather, we hypothesize that it is the room temperature solution on the skin (a cooler temperature than the skin body temperature) that generates sensory nerve traffic within

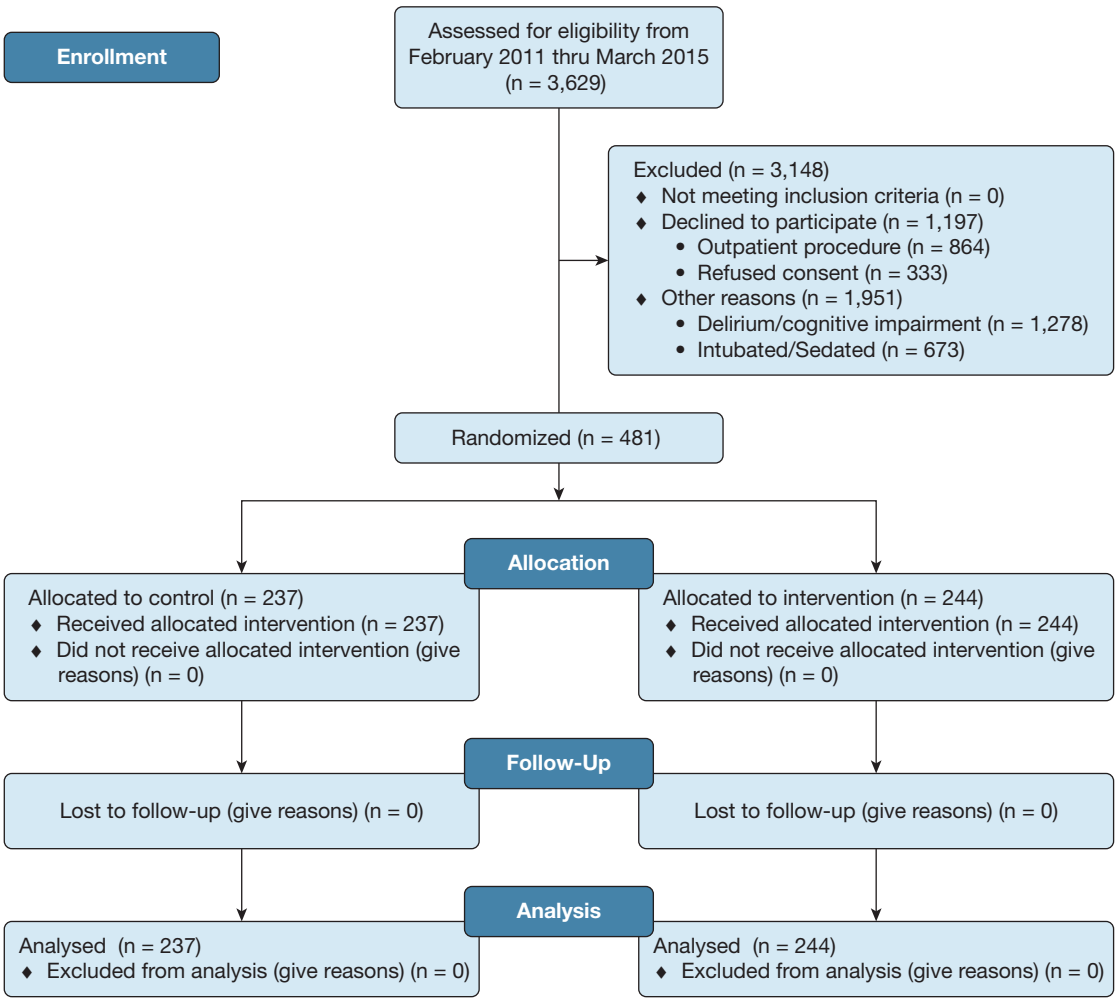

Figure 1 – *Patient flow through enrollment.*

the spinal cord dorsal horn that can "gate" or inhibit the noxious signal from the lidocaine injection.[10,13,18,20,21] In effect, the temperature and mechanosensation coded in the sensory perception of wetness[16] was immediately prior to the pain signal transmitted with the lidocaine injection. This timing of sensory stimulation was critical for gating/inhibiting the pain signal transmission at the dorsal horn of the spinal cord.

Improving pain control for common bedside procedures can affect patient outcomes in a number of ways. Previous studies have shown an association between increased body movement and higher pain ratings during subcutaneous lidocaine injection.[22] Therefore, optimizing procedural analgesia may be important for improving safety and comfort for these bedside procedures. In addition, there is an established link between pain control and patient satisfaction,[23] a metric that is playing an increasingly prominent role in measures of hospital quality and reimbursement models.[24] Finally, previous research examining epidural steroid injections for lower back pain revealed an association between pain scores for local lidocaine injection just prior to the procedure and back pain scores at 1 and 3 months.[25] This finding suggests that local anesthesia administration may influence pain perception well beyond the duration of the actual procedure.

In addition, our investigation is novel and pragmatic. We chose to use lidocaine on the skin surface as opposed to any other liquid solution because this medication is readily available for any procedure that uses lidocaine injection and does not require extra steps such as warming the lidocaine solution or mixing it with sodium bicarbonate. Although other studies have shown that changes to lidocaine can reduce pain with local infiltration, these require manipulations such as warming or buffering, which involve extra time, expense,

TABLE 1] Patient Baseline Characteristics

Characteristic	Control (n = 237)	Intervention (n = 244)
Age, y	56.8 (44.8-65.4)	58.5 (46.4-68.6)
Race		
White, non-Hispanic	123 (52%)	136 (56%)
White, Hispanic	14 (6%)	10 (4%)
African American	94 (39%)	90 (37%)
Asian	3 (1%)	5 (2%)
Other	3 (1%)	3 (1%)
Female	105 (44%)	120 (49%)
Ever smoker	113 (48%)	109 (45%)
Pain conditions		
Diabetic neuropathy	4 (2%)	6 (2%)
Nerve impingement	2 (1%)	2 (1%)
Chronic back pain	20 (8%)	11 (4%)
Chronic joint pain	16 (7%)	11 (4%)
Other pain syndrome	13 (5%)	11 (4%)
Postsurgical pain	10 (4%)	8 (3%)
Hospital medications		
Sedatives	19 (8%)	13 (5%)
Analgesics	127 (54%)	118 (48%)

Data are presented as mean (percentage) unless otherwise indicated.

and equipment not readily available in commercially purchased procedure kits.[5-8] Accordingly, they are not practical for routine use. It is particularly remarkable that our intervention showed a significant reduction in pain compared with very low pain scores in the control group. To our knowledge, no other study has examined simply placing lidocaine onto the skin prior to injection, which is simple, risk free, time efficient, and effective. Although previous research has shown that adjustments to provider technique can reduce pain associated with lidocaine injection,[26] the bulk of these studies have involved more invasive procedures such as spinal injections performed by interventional radiology, with very few studies investigating commonly performed bedside procedures. These data provide valuable insights into the pain associated with common bedside procedures and can be helpful when patients inquire about pain during the informed consent process.

Our findings should be interpreted with several cautions and limitations. Our intervention was associated with a small absolute reduction in pain scores and does not meet the minimally clinically important difference in VAS score of approximately 10 mm.[27] However, given the low VAS scores reported in the control group, to achieve this threshold would require the intervention scores to be in the single digits. Others have interpreted the clinical effect of intervention on pain perception by calculating z scores; this intervention has a z score of 0.23, indicating a small clinical effect.[28] This small clinical effect may be explained by the fact that lidocaine

TABLE 2] Procedure Characteristics

Characteristic	Control (n = 237)	Intervention (n = 244)	*P* Value
Lidocaine amount, mL	4.7 ± 2.5	5.7 ± 3.1	.0001
No. of attempts			
1	199 (84%)	205 (84%)	.99[a]
2	26 (11%)	27 (11%)	
3	8 (3%)	8 (3%)	
4	3 (1%)	4 (2%)	
Types of procedures			
Peripherally inserted central catheter	145 (61%)	138 (56%)	.30
Central lines	12 (5%)	19 (8%)	.22
Thoracentesis	36 (15%)	27 (11%)	.18
Paracentesis	14 (6%)	27 (11%)	.04
Lumbar puncture	30 (13%)	33 (13%)	.78

Data are presented as mean ± SD unless otherwise indicated.
[a]Comparing one attempt vs multiple attempts, χ^2 test.

TABLE 3] Visual Analog Scores With Bedside Procedures

Procedure Pain	Control (n = 237)	Intervention (n = 244)	*P* Value
All procedures, mm	16.6 ± 24.8	12.2 ± 19.4	.03
	Control (n = 145)	Intervention (n = 138)	
Peripherally inserted central catheter, mm	18.8 ± 25.6	12.2 ± 18.2	.02
	Control (n = 12)	Intervention (n = 19)	
Central venous catheter, mm	33 [5-53]	35 [0-46]	.71
	Control (n = 36)	Intervention (n = 27)	
Thoracentesis, mm	2.0 [0-11]	3.5 [0-13]	.41
	Control (n = 14)	Intervention (n = 27)	
Paracentesis, mm	2 [0-13]	0 [0-3]	.3
	Control (n = 30)	Intervention (n = 33)	
Lumbar puncture, mm	3 [0-7]	2 [0-6]	.49

Data are presented as mean ± SD or median and [interquartile range].

is a very effective local anesthetic and was given to both groups. Nonetheless, the improvement in pain scores with a relative reduction in pain of > 25% compared with a control group using a standard, established local anesthetic suggests an important incremental benefit of our intervention over the standard technique. This study reports pain scores that fall well below 30 mm in both groups, which is generally considered to be adequate analgesia.[29] The fact that we were able to demonstrate any difference in pain scores under these circumstances suggests that this intervention has substantial incremental benefit over established and effective procedural analgesia. Furthermore, the pain scores in the control group were comparable to (if not lower than) previously published reports of pain with lidocaine injection[30] or procedural pain from venous access,[31]

TABLE 4] Linear Regression Analysis of Visual Analog Scores Reported for Pain From Procedure

Variable	β Coefficient	95% CI	*P* Value
Intervention	−4.66	−8.48 to −0.85	.02
Age	−0.02	−0.15 to 0.99	.71
Race			
White, non-Hispanic	−0.26	−29.33 to 28.80	.99
White, Hispanic	0.65	−29.49 to 30.80	.97
African American	3.61	−25.56 to 32.78	.81
Asian	2.51	−29.68 to 34.71	.88
Other	19.5	−17.77 to 56.77	.3
Female	3.97	0.14 to 7.81	.04
In-hospital sedatives	−0.06	−7.75 to 7.63	.99
In-hospital analgesics	5.45	1.53 to 9.37	.006
No. of attempts			
1	18.68	−10.51 to 47.88	.21
2	24.73	−4.91 to 54.37	.1
3	26.22	−4.58 to 57.02	.09
4	65.99	33.01 to 98.97	.0001
Procedure			
Peripherally inserted central catheter	5.04	−0.80 to 10.88	.09
Central line	22.13	12.95 to 31.31	.0001
Thoracentesis	0.89	−6.63 to 8.41	.82
Paracentesis	−0.31	−8.56 to 7.94	.94

central venous catheter insertion,[32] paracentesis,[33] or lumbar puncture.[34] Several factors likely contributed to the generally low pain ratings. First, we controlled many of the variables known to reduce pain associated with lidocaine injection, such as bevel position, needle size, and injection rate in both groups. Second, all procedures were performed by an experienced, dedicated procedure team, although the proceduralists were not blinded to the intervention and could have influenced the pain score.

Another limitation is that the majority of procedures in our study were PICC insertions; however, given that about 4.3 million PICCs are placed per year,[35] this intervention can have a substantial impact on this common bedside procedure. We were unable to detect a significant difference in pain perception in all other procedures in the subgroup analysis, but it is likely that these analyses were underpowered. Furthermore, VAS scores reported for pain with central line insertion were higher than with other procedures, suggesting that the site, process, and method of the procedure may contribute to baseline pain scores; these factors may not be readily modifiable with this simple intervention.

It should also be noted that all clinically significant differences in the present study were detected when measuring with the VAS. Comparative studies of validated pain scales have suggested a correlation between greater number of response levels and sensitivity,[36] and studies directly comparing the VAS vs the Faces Pain Scale have found superior responsiveness with the former.[37] Because the control group had such low pain scores to begin with and reductions in the intervention group were small, the design of the VAS was better suited to detect any differences.

Conclusions

The present study found that letting room temperature lidocaine drip onto the surface of the skin just prior to subcutaneous injection resulted in decreased pain from PICC insertion. These findings illustrate that this simple and inexpensive maneuver can reduce pain for patients undergoing such procedures.

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