Reducing the Discomfort of Lidocaine Administration through pH Buffering[1]

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PURPOSE: A prospective, double-blind study was undertaken to evaluate the effect of using a buffered lidocaine solution on the perception of pain experienced by a patient during its intradermal injection.
PATIENTS AND METHODS: One hundred fifty patients undergoing diagnostic angiographic and interventional procedures at the authors' institution were randomly assigned to receive a 1-mL aliquot of one of three lidocaine solutions: plain 1% lidocaine, 1% lidocaine diluted with normal saline in a 10:1 ratio, and 1% lidocaine diluted with 8.4% sodium bicarbonate in a 10:1 ratio. The lidocaine solutions were administered intradermally over 10–15 seconds. A numerical value was placed on the patient's perception of pain, separate from that associated with the 25-gauge needle insertion, with use of a linear visual analog scale.
RESULTS: Mean pain scores were as follows: for the 1% lidocaine solution, 2.83 ± 2.60; for 1% lidocaine plus normal saline solution, 2.89 ± 2.34; and for 1% lidocaine plus sodium bicarbonate solution, 1.37 ± 1.73 (P = .0018).
CONCLUSION: Buffering lidocaine significantly decreased the discomfort associated with its administration as a local anesthetic.

LIDOCAINE is frequently used in the angiography and interventional radiology suite. It is a local anesthetic of the amide class and is a weak organic base consisting of uncharged and charged fractions when in solution (1). It is believed that only the uncharged or nonionized form of the local anesthetic is capable of diffusing through interstitial tissues, the perineural tissues, and the nerve membrane (1,2). Once within the nerve axoplasm, the nonionized molecule recalibrates into its ionized and nonionized portions, according to the axoplasmal pH. The ionized form attaches itself within the sodium channel of the nerve, blocking neurotransmission (3).

Most commercially available preparations of lidocaine are marketed in an acidic form (pH = 6.2). At this pH, the local anesthetic is more soluble and has a shelf life of 3–4 years (4). If the pH of the anesthetic solution is adjusted closer to its pKa of 7.9, an increasing percentage of the product will be in its uncharged, nonionized form. When the pH of the lidocaine solution is below 6, less than 1% of the lidocaine is in its uncharged form, whereas at a pH of 7, 11% is uncharged (5). Unfortunately, most amides are chemically unstable in the uncharged form, being subject to photodegradation, aldehyde formation, and other denaturing reactions (6).

The administration of lidocaine as a local anesthetic causes a characteristic burning discomfort. A few studies with a small number of volunteers have suggested that the discomfort of intradermal lidocaine administration can be reduced through pH buffering (7–9). The purpose of this study was to determine whether a buffered lidocaine solution can decrease the perception of pain associated with its intradermal injection in a large cohort of patients undergoing a variety of diagnostic and interventional radiology procedures.

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Table 1
Summary of Pain Scores for All Patients

Group	No. of Patients	Type of Procedure		Mean Age (y)	Mean Pain Score ± SD	*P* Value*
		Angio	NVI			
Plain solution (lidocaine alone)	50	37	13	52	2.83 ± 2.60	. . .
Control solution (lidocaine + saline)	50	23	27	50	2.89 ± 2.34	NS
Buffered solution (lidocaine + $NaHCO_3$)	50	27	23	51	1.37 ± 1.73	.0018

Note.—Angio = angiographic, NS = not significant, NVI = nonvascular diagnostic or interventional procedures, SD = standard deviation.
* Versus plain lidocaine.

PATIENTS AND METHODS

One hundred fifty patients (15 years of age or older) undergoing diagnostic angiography or nonvascular diagnostic or interventional radiology procedures were enrolled into this randomized, prospective, double-blind study according to a protocol approved by the institution's Human Investigations Committee. A special investigational consent to participate in the study was obtained from each patient. Patients were excluded from the study if they had a history of an allergic or adverse reaction to lidocaine, had received prior sedation, had an altered mental status, were uncooperative or unable to comprehend the nature of the study and/or the linear visual analog scale, had severe trauma, and/or were diabetic. The physician administering the local anesthetic and the patient were blinded to the type of lidocaine solution that was administered. The lidocaine solutions (Abbott Laboratories, Abbott Park, Ill) were as follows: 1% lidocaine (plain lidocaine solution); 10 mL of 1% lidocaine diluted with 1 mL of normal saline (control lidocaine solution); 10 mL of 1% lidocaine diluted with 1 mL of 8.4% sodium bicarbonate (buffered lidocaine solution). The lidocaine solution was prepared by the technologist immediately prior to initiation of the procedure. To minimize confusion, only one type of lidocaine solution was used per day. The lidocaine solution chosen for each day was randomly determined by the chief technologist

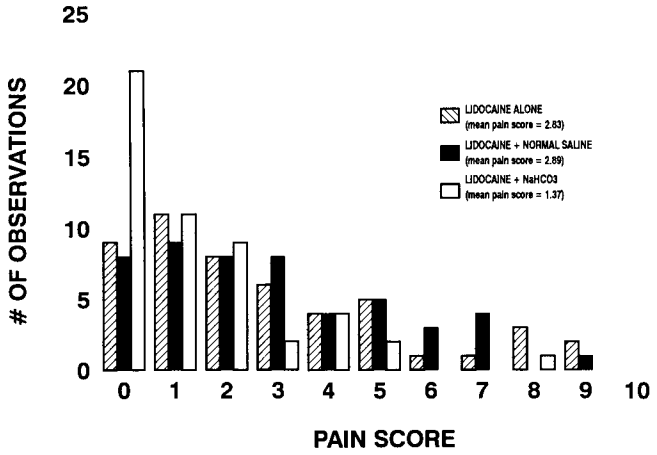

Figure. Histographic comparison of pain scores (according to the linear visual analog scale) associated with the intradermal administration of each respective lidocaine solution.

until 50 patients were entered into each subgroup of the study. The pH of the lidocaine solution was measured as a baseline with a Beckman 3560 pH meter (Beckman Instruments, Irvine, Calif). Each lidocaine solution was visually inspected for the formation of a precipitate.

A 1-mL aliquot of one of the three lidocaine solutions was administered intradermally over 10–15 seconds into each patient with use of a 25-gauge needle by a physician (resident, fellow, or attending) in a double-blind fashion. The pain separate from the insertion of the 25-gauge needle was graded during infiltration of the lidocaine solution. The patients were asked to place a numerical value to the pain sensation from 0 to 10, by using a linear visual analog scale, where 0 represented no pain, 5 represented moderate pain, and 10 represented extremely severe pain. The linear visual analog scale enabled subjects to assign a numerical value corresponding to their perception of pain associated with the infiltration of the lidocaine solution. This device has been used as a reproducible means to assign different descriptive levels of pain along a graphic scale from one extreme sensation to another (10).

The quantification of pain by each patient using the linear visual analog scale was pooled into one of three groups: plain lidocaine, control lidocaine, and buffered lidocaine solutions. Statistical analysis of the data was performed by using an unpaired nonparametric Mann-Whitney rank

Table 2
Pain Score versus Type of Intervention

Group	No. of Patients	Mean Age (y)	Mean Pain Score ± SD	*P* Value*
Patients Undergoing Angiography				
Plain solution	37	59	2.54 ± 2.47	. . .
Control solution	23	60	2.28 ± 2.58	NS
Buffered solution	27	58	1.04 ± 1.40	.0089
Patients Undergoing Nonvascular Procedures				
Plain solution	13	31	3.65 ± 2.90	. . .
Control solution	27	42	3.41 ± 2.02	NS
Buffered solution	23	43	1.76 ± 2.00	.0310

Note.—NS = not significant, SD = standard deviation.
* Versus plain lidocaine.

Table 3
Pain Score versus Patient Age

Group	No. of Patients	Mean Pain Score ± SD	*P* Value*
Patients 40 Years Old or Younger			
Plain solution	12	4.00±2.82	. . .
Control solution	16	3.75±2.67	NS
Buffered solution	17	2.03±2.44	.0417
Patients Older than 40 Years			
Plain solution	38	2.46±2.45	. . .
Control solution	34	2.49±2.09	NS
Buffered solution	33	1.03±1.11	.0325

Note.—NS = not significant, SD = standard deviation. *Versus plain lidocaine.

sum test and a two-tailed unpaired Student *t* test (11); $P < .05$ was considered statistically significant.

RESULTS

Fifty patients were entered into each subgroup, for a total of 150 patients. The pH of each lidocaine solution was as follows: plain lidocaine solution pH, 6.2; control lidocaine solution pH, 6.2; and buffered lidocaine solution pH, 7.2.

The 50 patients receiving the plain 1% lidocaine solution had a mean age of 52 years, with a range of 16–86 years. They underwent 37 angiographic and 13 nonvascular diagnostic or interventional procedures. The 50 patients who received the control lidocaine solution had a mean age of 50 years, with a range of 15–85 years. They underwent 23 angiographic and 27 nonvascular diagnostic or interventional procedures. The third group of 50 patients received the buffered lidocaine solution. They had a mean age of 51 years, with an age range of 16–78 years, and underwent 27 angiographic and 23 nonvascular diagnostic or interventional procedures (Table 1).

The mean pain scores for each group were as follows: 1% lidocaine (plain) solution, 2.83 ± 2.60; 1% lidocaine plus normal saline (control) solution, 2.89 ± 2.34 (2.83 vs 2.89; P = not significant); 1% lidocaine plus sodium bicarbonate (buffered) solution, 1.37 ± 1.73. When the mean pain scores for the plain lidocaine solution and buffered lidocaine solution are compared (2.83 vs 1.37), there is a significant difference ($P = .0018$) (Table 1). The histogram of pain scores demonstrates that 21 of the 50 patients who received the buffered lidocaine solution had no pain (pain score = 0) (Figure).

Since multiple anatomic sites were used for the injection of the lidocaine solution, the data were analyzed based on the type of procedure (Table 2). All of the angiograms were obtained from the transfemoral approach. Plain 1% lidocaine was used in 37 patients prior to angiography, with a mean pain score of 2.54 ± 2.47. Buffered lidocaine was administered to 27 patients prior to angiography, with a mean pain score of 1.04 ± 1.40 (2.54 vs 1.04; $P = .0089$). In preparation for the nonvascular diagnostic or interventional procedures, 13 patients received plain 1% lidocaine, with a mean pain score of 3.65 ± 2.90. Twenty-three patients were given buffered lidocaine before the procedure, with a mean pain score of 1.76 ± 2.00 ($P = .0310$). When patient populations are compared, the 87 patients undergoing angiography were significantly older (mean age, 59 years) than the 63 patients undergoing nonvascular procedures (mean age, 40 years) ($P < .0001$).

When the data are divided for patients 40 years of age or younger and those older than 40 years, use of buffered lidocaine is still associated with a significant reduction in pain perception compared with the plain lido-

caine solution. For patients 40 years of age or younger, $P = .0417$; for patients older than 40 years, $P = .0325$ (Table 3).

There were no obvious clinical consequences or complications related to buffering the lidocaine solution. Although it was not objectively assessed, there was no apparent subjective difference in the effectiveness or duration of action of each solution. There was no visible precipitation within the buffered lidocaine solution.

DISCUSSION

This prospective, randomized, double-blind study of 150 patients demonstrates a significant reduction in the perception of pain associated with the administration of a buffered 1% lidocaine solution regardless of the age of the patient or the anatomic location of skin infiltration. This has been attributed to the adjustment of the pH of the local anesthetic solution toward a more physiologic range of 7.0–7.4. By raising the pH of a commercially available lidocaine solution from 6.2 to 7.2, there is a 10-fold reduction in the hydrogen ion concentration in the solution (7). Reducing the concentration of hydrogen ion within the solution apparently decreases the local irritation on its administration. It has also been suggested that the uncharged, nonionized form of lidocaine disburses much more rapidly through the interstitial tissues resulting in almost instantaneous nerve blockage (5,6,8). It is clear that the reduction of pain associated with the infiltration of a buffered anesthetic solution is not due to a dilutional or volume effect, since our control lidocaine solution containing normal saline was just as painful on infiltration as the plain 1% lidocaine solution and a 1-mL volume was administered in all the patients.

Buffering the lidocaine solution to a pH of 7.0–7.4 does not adversely affect the degree and duration of local analgesia. Indeed, the onset of analgesia appears more rapid with the buffered solution (5,6). A number of studies on nerve preparations, major nerve block, and regional nerve block have shown that the duration of the anesthetic effect is unchanged by buffering the local anesthetic (2,5,12,13). Subjectively, we did not appreciate a difference in the analgesic effect among the three lidocaine solutions.

Alkalinization of the lidocaine solution can be easily accomplished by adding 1 mL of an 8.4% $NaHCO_3$ solution to a syringe containing 10 mL of a 1% lidocaine solution. This gives 11 mL of a buffered lidocaine solution with a pH of 7.2. As previously reported, buffering a lidocaine solution to this pH results in no visible precipitation (7,8). The 8.4% $NaHCO_3$ solution comes in a 50-mL vial (Abbott Laboratories) and costs approximately $0.50 per vial. Once opened, any unused portion of the 50-mL vial is discarded at the end of the day. Since the $NaHCO_3$ solution is inexpensive and easy to use, we have not found it necessary to neutralize a multidose vial of lidocaine. Despite this, one study has demonstrated that a solution of lidocaine containing epinephrine buffered to a pH of 7.0–7.3 and stored at room temperature for 1 week was just as effective as a freshly made buffered solution at producing analgesia, while continuing to be less painful on intradermal injection (14). These authors recommend that the alkalinized anesthetic be discarded within 1 week of preparation, primarily because epinephrine appears to degrade in buffered solutions at a rate of 25% per week (15).

Other local anesthetics are also prepared in an acidic solution (5,8, 14). One such agent, bupivacaine (Sensorcaine; Astra Pharmaceuticals, Westborough, Mass), is a local anesthetic of the amide group, with a pKa of 8.1 (6). This agent has a longer duration of action compared with lidocaine. We frequently use it with nonvascular interventional procedures. One study has demonstrated that by buffering the bupivacaine solution, a more rapid onset and a longer duration of action can be expected (16).

Our current study validates prior reports (7,8,9) that buffering lidocaine (10 mL of 1% lidocaine mixed with 1 mL of 8.4% sodium bicarbonate) significantly decreases the discomfort of its intradermal administration. Indeed, many patients in this study indicated that the buffered anesthetic solution was painless on its infiltration. Because it is easy, relatively inexpensive, and safe to do, buffering the lidocaine solution should be routinely performed prior to its administration as a local anesthetic.

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