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Efficacy of alkalinized lidocaine for reducing pain on intravenous and epidural catheterization

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Abstract
Purpose. To investigate whether increasing the pH of lidocaine could reduce the pain caused by its skin infiltration as well as that caused by intravenous and epidural needle insertion.
Methods. A randomized, double-blind trial was undertaken in patients who were allocated to receive topical anesthesia with either plain (plain group; $n = 25$) or alkalinized lidocaine (alkalinized group; $n = 25$). An alkalinized lidocaine solution was prepared by adding 8.4% sodium bicarbonate to a plain 1% lidocaine solution at a ratio of 1:10. Pain was assessed using the verbal analog scale (VAS).
Results. In the alkalinized group, the VAS scores on skin infiltration in the hand (2.5 ± 1.4) and the back (2.7 ± 1.4) were significantly lower than the respective scores in the plain group (3.5 ± 1.4, and 4.9 ± 1.9). Although the VAS score on intravenous needle insertion did not differ between the two groups, the VAS score on epidural needle insertion was significantly lower in the alkalinized group (1.3 ± 1.0) than in the plain group (3.6 ± 1.3).
Conclusions. Alkalinization of lidocaine was effective in attenuating pain on skin infiltration and on epidural needle insertion.

Key words Cannulation · Epidural anesthesia · Lidocaine · pH

Introduction

Patients scheduled for surgery suffer pain associated with various anesthetic procedures. For example, intravenous (IV) cannulation is necessary for anesthesia and is a source of pain. Epidural anesthesia provides excellent intra- and postoperative analgesia. However, the insertion of an epidural needle frequently causes pain and anxiety in patients. Local anesthetics, although effective in reducing pain on needle insertion, may themselves produce pain on injection.

Increasing the pH of the local anesthetic solution has been reported to improve the quality of regional blockade [1,2] and to reduce pain on skin infiltration and needle insertion on the hand and the forearm [3–8]. However, it is uncertain whether alkalinization of local anesthetic solution effectively reduces pain on the back during large-bore epidural needle insertion. In the present study, therefore, we evaluated the efficacy of alkalinized lidocaine in reducing pain caused by IV and epidural needle insertion, as well as that caused by skin infiltration.

Patients and methods

This study was approved by our ethics committee, and informed consent was obtained from each patient. Fifty adult patients, of American Society of Anesthiologists (ASA) physical status 1 or 2, who were undergoing elective surgery under epidural anesthesia, were the subjects in this study. Each patient was instructed in the evaluation of pain using the verbal analog scale (VAS; score 0, no pain to score 10, the worst possible pain). The patients were randomly allocated, in a double-blind manner, to receive topical anesthesia either with a plain lidocaine solution (plain group; $n = 25$) or with an alkalinized lidocaine solution (alkalinized group; $n = 25$). The topical preparations were made either by adding 8.4% sodium bicarbonate solution to a commercially available 1% lidocaine solution at a ratio of 1:10, or by adding preservative-free sterile water, at a ratio of 1:10. The pH values were measured with a pH meter (M-8; Horiba, Kyoto, Japan) at a temperature of about 25°C.

In the operating room, the dorsum of the left hand was cleaned with 70% isopropyl alcohol and allowed to dry. Using a 1-ml syringe with a 26-gauge needle, 0.2 ml of either the plain or the alkalinized lidocaine solution

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was injected intradermally over the vessel, and an 18-gauge IV catheter was inserted 30 s later. The patients were blinded to these procedures. They were then turned to the lateral position for the placement of an epidural catheter. After the skin had been swabbed with iodine, plain or alkalinized lidocaine was infiltrated to the back, 0.5 ml intradermally and 1 ml subcutaneously, using a 5-ml syringe with a 25-gauge needle. Thirty s later, a 16-gauge Tuohy needle was inserted into the epidural space at the site of local infiltration, using the hanging drop method and the median approach.

All procedures were performed by the same investigator, who was blinded to the patient group. The VAS was used for the evaluation of pain associated with intradermal injections in the hand and the back, as well as for the evaluation of pain associated with the IV and epidural needle insertions. The VAS was administered to patients just after the needle had penetrated their skin. Values for results were expressed as means ± SDs. Statistical analysis was performed using analysis of variance or the Mann-Whitney *U*-test. A *P* value of less than 0.05 was considered significant.

Results

The two groups were comparable in regard to sex, age, weight, and height distribution (Table 1). The pH values of the plain and the alkalinized lidocaine solutions were 6.35 ± 0.01 and 7.29 ± 0.06, respectively.

Table 2 shows the mean VAS scores for intradermal injections on the hand and the back, and for the IV and epidural needle insertions. The patients in the alkalinized group showed significantly lower VAS scores than the plain group during intradermal anesthesia in both the hand and the back. VAS scores during IV needle insertion were similar in the two groups, whereas the VAS scores during epidural needle insertion were significantly lower in the alkalinized group than in the plain group.

Table 1. Demographic data

	Plain (n = 25)	Alkalinized (n = 25)
Sex (M/F)	13/12	12/13
Age (years)	53 ± 11	52 ± 10
Weight (kg)	56 ± 9	61 ± 10
Height (cm)	155 ± 6	158 ± 7

Values are means ± SDs. There were no significant differences between the two groups

Discussion

The present study demonstrated that alkalinized lidocaine was effective in attenuating the pain associated with epidural needle insertion. This preparation also caused less pain on skin injection than the plain lidocaine solution.

The pain-reducing effect of sodium bicarbonate may reflect a change in the relative amounts of ionized and nonionized forms of lidocaine. Only the nonionized form of lidocaine can diffuse through interstitial tissues and nerve membranes. The fraction of the nonionized form in commercially available lidocaine is less than 2%. This fraction is increased more than tenfold in buffered lidocaine (pH adjusted to 7.4) [7] and the presence of this greater amount of the nonionized form may enhance the interstitial dispersion and anesthetic efficacy of the local anesthetic.

Although the alkalinized lidocaine attenuated the pain associated with epidural needle insertion, it was not effective in reducing the pain associated with venipuncture. Because the IV catheter was smaller in size than the epidural needle, it caused less pain than the epidural needle when the plain lidocaine was used. Therefore, we could not detect any reduction in pain, partly because of the subjective nature of pain assessment. It is also possible that the volume of lidocaine injected was not sufficient to suppress the pain at venipuncture.

Several studies have attempted to determine whether the alkalinization of local anesthetics decreased pain on skin infiltration (Table 3). McKay et al. [3] first reported that the addition of sodium bicarbonate to lidocaine reduced pain on skin infiltration. This finding was confirmed by the more recent report of Nuttall et al. [4], who demonstrated that alkalinized lidocaine was significantly less painful on injection than most other local anesthetics. Christoph et al. [5], using mepivacaine as well as lidocaine, showed results similar to those of

Table 2. Verbal analogue scores for intradermal anesthesia and needle insertion

	Intradermal anesthesia		Needle insertion	
	Hand	Back	Intravenous	Epidural
Plain group	3.5 ± 1.4	4.9 ± 1.9	2.6 ± 1.2	3.6 ± 1.3
Alkalinized group	2.5 ± 1.4*	2.7 ± 1.4*	2.0 ± 1.4	1.3 ± 1.0*

* $P < 0.05$ versus plain group
Values are means ± SDs

Table 3. Efficacy of alkalinized lidocaine for skin infiltration

Author, year	*n*	Drug used	Volume (ml)	Needle gauge	Assessment	Reductions in pain score	Efficacious
McKay et al. [3] 1987	24	1% Lidocaine	0.3	26	VAS	38 ± 5 to 15 ± 3	Yes
Christoph et al. [5] 1988	25	1% Lidocaine 2% Mepivacaine	0.5	25	VAS	49 ± 4 to 11± 2 52 ± 3 to 10 ± 2	Yes
Martin [6] 1990	100	1% Lidocaine	0.1	NA	VRS	1.1 to 0.6	Yes
Gershon et al. [9] 1991	100	1% Lidocaine	NA	25	VAS	12 to 8	No
Bartfield et al. [7] 1992	24	1% Lidocaine	0.5	27	VAS	NA	Yes
Nuttall et al. [4] 1993	280	1% Lidocaine	0.5	25	VAS	14 ± 3 to 7 ± 1	Yes
Palmon et al. [8] 1998	40	2% Lidocaine	0.25	25 30	VAS	32 ± 2 to 19 ± 2 25 ± 3 to 13 ± 2	Yes

VAS, Visual analogue scale; VRS, verbal rating scale; NA, information not available

Nattall et al. [4]. On the other hand, Gershon et al. [9] found no differences in pain on intradermal injection between plain and alkalinized lidocaine. However, they prepared alkalinized lidocaine by adding sodium bicarbonate solution to lidocaine at a ratio of 1:2, which resulted in a greater dilution and a more alkaline lidocaine solution than the 1:10 mixture used in the present study and most other studies.

The mechanism responsible for the decrease in pain on skin infiltration with alkalinized lidocaine is still unclear. It seems likely that the pH of the solution is an important factor in determining the pain. Adjustment of the pH of a local anesthetic towards the physiologic range may reduce direct tissue irritation [5]. However, there are inconsistencies in the relationship between the pH of local anesthetic solutions and the pain on injection, because procaine and chloroprocaine are more acidic than lidocaine, but less painful on infiltration [10]. Thus, factors other than pH, such as lipid solubility, may play an important role in the pain experienced on injection [10].

In conclusion, increasing the pH of lidocaine by the addition of sodium bicarbonate decreased the pain caused by both its skin infiltration and epidural needle insertion.

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