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The effect of pH adjustment of 1% lidocaine on the onset of sensory and motor blockade of epidural anesthesia in nonpregnant gynecological patients

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Abstract: Using a double-blind randominzed study protocol, we examined the distribution of sensory blockade and the quality of motor blockade after epidural anesthesia with 1% lidocaine with or without bicarbonate in nonpregnant gynecological patients.

Alkalinization significantly decreased the time to onset of sensory blockade. However, there were no statistically significant differences between the low-pH and high-pH groups with respect to motor blockade or the distribution of sensory blockade.

We conclude that pH-adjusted 1% lidocaine offers the advantage of a more rapid onset of sensory blockade, while motor blockade and the distribution of anesthesia are unaffected by pH change in epidural anesthesia.

Key words: Local anesthetic, Lidocaine, pH-adjustment, Epidural anesthesia, Nonpregnant gynecological patients

Introduction

Clinically, alkalinization of local anesthetic solutions reduces the pain of infiltration [1,2] and offers the advantages of rapid onset and good quality, which reduce the waiting time for surgery when the anesthetic is used for regional blockade [3,4]. However, the effects of the alkalinization are not yet fully understood. Many researchers have compared the onset, quality, and duration of epidural anesthesia using low-pH and high-pH local anesthetics in pregnant patients [5–9]. However, in cesarean section or labor and delivery, motor blockade of epidural anesthesia has not been examined nor described in detail. Furthermore, it has been reported that exposure of isolated nerve fibers from pregnant rabbits to a local anesthetic is associated with more rapid onset of conduction block than in nerves from nonpregnant animals [10]. Recently, Siler and Rosenberg [11] and Capogna et al. [12] investigated motor blockade of epidural anesthesia with 2% lidocaine (increasing the pH from 6.49 to 7.26) and 2% mepivacaine (increasing the pH from 5.85 to 7.30) for arthroscopic knee procedures. We believe that patients with knee joint diseases were not suitable for the evaluation of motor blockade.

In the present study, we compared the onset and quality of sensory and motor blockade of commercially available 1% lidocaine hydrochloride (pH 6.68) with 1% lidocaine hydrochloride to which sodium bicarbonate was added in the ratio of 1 ml per 10 ml of solution (pH 7.40) for epidural anesthesia for nonpregnant gynecological patients.

Materials and methods

Fifty-five ASA physical status 1–2, adult female patients (aged 27–57 years) undergoing elective gynecological surgical procedures were included in this study. Patients were randomized to receive either high-pH lidocaine or low-pH lidocaine according to their ID number in a double-blind manner. This study was approved by our local institutional ethical committee. Patients with a history of motor disease of the lower extremities and patients 30% or more over ideal body weight were excluded from the study. The high-pH solution was prepared, at most, 5–10 min before use by adding 2 ml of sterile 7% sodium bicarbonate (8.4% sodium bicarbonate is not available in Japan) to 20 ml of commercial lidocaine. The low-pH solution was prepared by adding 2 ml of sterile saline to 20 ml of commercial lidocaine. Epinephrine 0.1 mg was freshly added to both solutions. The addition of 2 ml to each solution resulted in a concentration of lidocaine of

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approximately 0.9%. Before beginning the protocol, we confirmed that the addition of 2 ml of 7% sodium bicarbonate to 20 ml of 1% lidocaine ($n = 5$) increased the pH from 6.68 ± 0.01 to 7.40 ± 0.02. The pH of each solution was tested using a digital pH meter (CG822, Schott-Geräte, Germany). Two ml of saline did not affect the pH of 1% lidocaine (pH 6.67 ± 0.02). There was no evidence of precipitation after the addition of bicarbonate or saline and the two solutions of lidocaine appeared identical. Two investigators carried out the work. The solutions were prepared by the first anesthesiologist. The second anesthesiologist, who was unaware which local anesthetic was used, administered the anesthetic and collected the data.

All patients received diazepam 10 mg p.o. as premedication 90 min prior to arrival in the operating room. After placement of an intravenous catheter (Ringer's lactate solution was given at 15 ml/kg/h) and applying a blood pressure cuff, ECG electrodes, precordial stethoscope, and pulse oximeter, epidural anesthesia was administered at the L2–3 level with patients in the right lateral decubitus position. The epidural space was identified via the loss-of-resistance technique. After negative aspiration, a 2-ml test dose of the local anesthetic solution was injected through a Tuohy needle and, if no heart rate increase was observed, a further 8 ml (total volume of 10 ml) were incrementally injected over 30 s. A catheter was then inserted 3–4 cm into the epidural space and the patient turned supine. Intravenous ephedrine and Ringer's lactate solution were given as necessary throughout the procedure to maintain a systolic blood pressure above 100 mmHg.

Time zero was defined as the end of injection. Measurements of sensory analgesia and motor blockade were taken at 5-min intervals for 15 min. Sensory levels were assessed using the sensation to pinprick method, and motor function was assessed using the Bromage scale [13]: (1) able to bend knees and flex thighs; (2) able to bend knees and move feet only; (3) unable to move knees but able to move feet; and (4) unable to move feet.

After the study period, general anesthesia was induced in all patients with thiamylal sodium 5 $mg \cdot kg^{-1}$, and tracheal intubation was facilitated with the administration of vecuronium using approximately 0.2 $mg \cdot kg^{-1}$. Subsequently, anesthesia was maintained with nitrous oxide 33% in oxygen, together with supplemental isoflurane 0–0.5%, and epidural anesthesia. Ventilation was mechanically controlled to maintain end-tidal CO_2 at 5.0%–5.5% and rectal temperature was monitored.

Data were expressed as mean ± standard deviation (SD). Statistical analysis was performed using Student's *t*-test for quantitative parametric data, the Mann-Whitney U-test for quantitative nonparametric data, and chi-square test for qualitative nonparametric data.

Results

The patients in both the high-pH group and the low-pH group were comparable with regard to age, height, and weight (Table 1). The dermatomal spread and corresponding number of segments manifesting sensory blockade and the degree of motor blockade are presented in Table 2. The differences in mean total number of sensory blocked segments on the right side at 5 min (7.8 *vs* 12.4 segments) and the lowest segmental level of the sensory blockade on the left side at 10 min (S2 *vs* S4) were statistically significant ($P < 0.05$). Although the total number of sensory blocked segments at 5 min and 10 min were slightly higher in the high-pH group, these differences did not reach statistical significance. Adjustment of the pH show no significant effect on the motor blockade. A total of three patients achieved grade 3 motor blockade, with one in the high-pH group and two in the low-pH group. This difference was not statistically significant. There were no side effects in either group during the study.

Discussion

The results of this study demonstrated that increasing the pH of 1% lidocaine from 6.7 to 7.4 accelerated the onset of epidural analgesia, while neither the spread of sensory blockade nor the degree of motor blockade were significantly affected by increasing pH. Bromage et al. [14] reported that grade 3 or 4 motor blockade was achieved by 37% of patients in their 2% lidocaine group, but no patients in the 1% lidocaine group achieved more than grade 2 motor blockade. The group which received 1% lidocaine with bicarbonate in our study (pH-adjusted group) exhibited a lower intensity of motor blockade than the non-pH-adjusted 2% lidocaine group. The effect of epinephrine, which enhances the intensity of epidural blockade, may be decreased in the high-pH condition [15]. Adjustment of the pH showed no significant effect on the motor blockade in our study. Since there is a buffer effect in the

Table 1. Patient characteristics

	Low-pH group	High-pH group
Number of patients	25	30
Age (years)	39 ± 9	41 ± 8
Height (cm)	157 ± 5	156 ± 5
Weight (kg)	53 ± 6	52 ± 5

Values are expressed as mean ± SD.

Table 2. Sensory analgesia and motor blockade

		Low-pH group					High-pH group				
Sensory analgesia[a]			(dermatomal spread)					(dermatomal spread)			
5-min	Right	7.8 ± 6.7	(T8–L5)				12.4 ± 7.1*	(T7–S1)			
	Left	7.1 ± 6.3	(T9–L5)				10.1 ± 7.4	(T8–S2)			
10-min	Right	15.8 ± 3.9	(T6–S4)				16.1 ± 4.5	(T6–S4)			
	Left	13.0 ± 4.9	(T7–S2)				15.3 ± 4.4	(T7–S4*)			
15-min	Right	17.8 ± 3.2	(T5–S5)				17.6 ± 3.7	(T5–S5)			
	Left	16.7 ± 2.9	(T6–S4)				16.7 ± 3.8	(T6–S5)			
Motor blockade[b]		Bromage scale	1	2	3	4	Bromage scale	1	2	3	4
5-min	Right		0	25	0	0		0	30	0	0
	Left		0	25	0	0		0	30	0	0
10-min	Right		0	25	0	0		0	30	0	0
	Left		0	25	0	0		0	30	0	0
15-min	Right		0	23	2	0		0	29	1	0
	Left		0	25	0	0		0	30	0	0

mean ± SD.
* $P < 0.05$ vs low-pH group.
[a] Number of blocked segments.
[b] Number of blocked patients.

tissues, the effect of pH adjustment may be lost at the segment that is most distant from the injection site. The maximum level of sensory blockade was not significantly affected by increasing pH.

Previous studies with alkalinized agents in epidural or brachial plexus block have yielded conflicting results. Increasing pH accelerates the transport of local anesthetics through the cell membrane, so it may improve the onset and distribution of sensory blockade. However, this effect may be dependent on whether the block at which the local anesthetics was injected was distant from or proximal to the nerve tissue. Capogna et al. [12] found a faster onset of grade 3 motor blockade using 2% mepivacaine (increasing the pH from 5.85 to 7.30) in epidural anesthesia (15 min in the pH-adjusted group and 24 min in the non-pH-adjusted group), but the motor blockade was achieved by almost the same number of patients (62% of the pH-adjusted group and 60% of the non-pH-adjusted group). Quinlan et al. [16] reported that alkalinization of 1.25% mepivacaine (increasing the pH from 5.55 to 7.30) significantly shortened the time to onset of paralysis in an axillary block. The 5-min interval between measurements in our study might have missed a slight, but significant difference in the onset of motor blockade.

Benhamou et al. [7] reported that epidural block using 0.5% bupivacaine (increasing the pH from 5.38 to 6.87) and 0.5% bupivacaine with 1:200 000 epinephrine (increasing the pH from 4.80 to 6.68) did not result in a more rapid onset of motor blockade. Siler and Rosenberg [11] found no effect in regard to the time to maximum motor blockade and degree of motor blockade using 2% lidocaine to which sodium bicarbonate was added in the ratio of 1 ml per 10 ml of solution (increasing the pH from 6.49 to 7.26) for epidural anesthesia in outpatient arthroscopic knee procedures. There are several factors that may account for these contradictory results regarding the ability of alkalinization to accelerate the onset of motor blockade. Stevens et al. [17] reported that the advantage of increasing the pH of local anesthetics might be slight and obscured at higher concentrations due to the increased mass of the drug present. They also suggested the possibility that differences in testing procedures and patient populations might result in a greater difference in outcome than the pH adjustment itself.

DiFazio et al. [4] reported that pH-adjusted lidocaine increased the speed of onset of analgesia in epidural anesthesia. Other authors have also reported that alkalinization of bupivacaine results in a more rapid onset of sensory analgesia [5,18]. These results are similar to our findings.

We reported that high-pH 1% lidocaine significantly increased the speed of onset of sympathetic blockade ($P < 0.01$) and sensory blockade ($P < 0.05$) by measuring the rise of toe skin temperature and pin-prick pain [19]. The effect of pH-adjustment in the toe skin temperature change was larger than that in sensory change. Sympathetic fibers may be influenced by alkalinization of local anesthetics more than somatosensory fibers. On the other hand, Gissen et al. [20] reported that the time needed for a large fiber block to equal a small fiber block was 88 min in acid solution (pH 6.6–6.8) and 26 min in neutral solution (pH 7.2–7.4) in the isolated rabbit nurve. Therefore, it is possible that the effects of alkalinization of local anesthetics depends on the size of the fiber and various other conditions.

Since the Bromage score is not quantitative, further investigation is necessary to evaluate the precise degree of motor blockade. Furthermore, Bromage et al. [14]

reported that the latency of complete spread of epidural analgesia for 1%–5% lidocaine with epinephrine was about 15 min (from 13 min to 18 min). However, the latency of a complete motor blockade has not yet been clearly defined. In this study, there was no statistically significant effect on the onset of motor blockade, as a result of raising the pH of the lidocaine prior to epidural injection. However, if we had examined the motor blockade after more than 15 min, we might have obtained different results.

We selected patients strictly for this study and our results did not conflict with those reported by others. The possibility exists that the pH-adjustment method has a limited acceleration effect on anesthesia. We conclude that high-pH 1% lidocaine (pH 7.4) offers the advantage of a more rapid onset of sensory blockade, but the distribution of anesthesia and motor blockade are unaffected by pH change in epidural anesthesia.

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