Concentration- and pH-dependent Effects of Local Anesthetics on Onset of Epidural Anesthesia

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This study was undertaken to determine the effect of concentration of pH-adjusted local anesthetics on the onset time of anesthesia.

Lidocaine (0.9% and 1.8%) and bupivacaine (0.25% and 0.5%) were used. In the 0.9 percent lidocaine and 0.25 percent bupivacaine groups, the onset time of analgesia was shortened by about 100 and 200 seconds, when pH was adjusted to 7.4 and 7.0, respectively ($P < 0.05$ and $P < 0.01$). In the 1.8 percent lidocaine and 0.5 percent bupivacaine groups, however, pH adjustment exerted no significant effect on the onset time.

Alkalinization of low-concentration local anesthetics shortened the onset time, whereas that of high-concentration did not shorten. (Key words: epidural anesthesia, onset, pH-adjustment, lidocaine, bupivacaine)

(Fukuda T, Sato S, Naito H: Concentration- and pH-dependent effects of local anesthetic on onset of epidural anesthesia. J Anesth 4: 327–330, 1990)

It is controversial how pH of local anesthetics affects the onset time of neural blockade. Some groups reported rapid onset of neural blockade such as epidural and brachial plexus anesthesia in patients receiving local anesthetics alkalinized with sodium bicarbonate[1–5]. Other groups, however, failed to demonstrate any significant difference in the onset time of neural blockade between the pH-adjusted group and the non-pH-adjusted group[6–8].

We speculated that a combination of two factors, the magnitude of pH increase and the concentration of local anesthetics affected the onset time. Thus, we examined the effects of alkalinization on the onset time using local anesthetics of different concentration.

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Methods

This investigation was carried out in 180 (ASA physical status 1–2) patients who were scheduled to have elective surgery. Patients with arterial disease, large abdominal tumors or parturient women were excluded. The patients were divided into eight groups for administration of local anesthetics of various pH and concentration (table 1). GL and GB represent the lidocaine group and bupivacaine group, respectively. Age, height and weight of the patients in each group are shown in table 2.

All the patients were premedicated with 5 to 10 mg of oral diazepam approximately 90 min before anesthesia. After patients were positioned in the right lateral decubitus, epidural puncture was performed mainly at the first lumbar vertebral space (17 gauge Tuohy needle) using the balloon method. The bevel of the needle was directed cranially. Fifteen ml of each solution of local anesthetics was injected at a rate of about

Table 1. pH and concentration of the local anesthetics used

Group	Chemicals		concentration	pH (mean ± SD)
GL-1	1.0% lidocaine	20 ml	0.9%	6.70 ± 0.05
	normal saline	2 ml		
	1:1,000 epinephrine	0.1 ml		
GL-2	1.0% lidocaine	20 ml	0.9%	7.41 ± 0.04
	7.0% sodium bicarbonate	2 ml		
	1:1,000 epinephrine	0.1 ml		
GL-3	2.0% lidocaine	20 ml	1.8%	6.74 ± 0.05
	normal saline	2 ml		
	1:1,000 epinephrine	0.1 ml		
GL-4	2.0% lidocaine	20 ml	1.8%	7.34 ± 0.01
	7.0% sodium bicarbonate	2 ml		
	1:1,000 epinephrine	0.1 ml		
GB-1	0.25% bupivacaine	20 ml	0.25%	5.91 ± 0.04
GB-2	0.25% bupivacaine	20 ml	0.25%	7.09 ± 0.03
	7.0% sodium bicarbonate	0.1 ml		
GB-3	0.5% bupivacaine	20 ml	0.5%	5.83 ± 0.06
GB-4	0.5% bupivacaine	20 ml	0.5%	6.86 ± 0.03
	7.0% sodium bicarbonate	0.1 ml		

GL: Lidocaine group, GB: Bupivacaine group

Table 2. Age, height and weight of patients

Group	n	Age (yr)	Height (cm)	Weight (kg)
GL-1	20	53.8 ± 16.0	156.7 ± 8.1	53.1 ± 12.6
GL-2	20	53.7 ± 13.0	157.7 ± 8.4	57.2 ± 11.5
GL-3	20	56.2 ± 11.6	157.7 ± 7.1	58.1 ± 7.1
GL-4	20	56.8 ± 10.7	156.6 ± 7.0	56.6 ± 7.5
GB-1	30	55.6 ± 13.7	156.2 ± 7.9	55.5 ± 11.3
GB-2	30	56.8 ± 12.1	154.7 ± 7.2	55.2 ± 10.4
GB-3	20	59.1 ± 16.1	155.2 ± 10.4	56.2 ± 11.6
GB-4	20	60.3 ± 12.6	154.7 ± 6.7	53.4 ± 8.5

mean ± SD

1 ml·sec^{-1}. Every solution was prepared just before use. No precipitate was observed macroscopically in any solution. An epidural catheter was then inserted and the patients were quickly put in the supine position.

The onset of analgesia was checked by pin-pricking the skin of the inguinal region (LI) every 15–20 seconds.

All statistical analyses were done by Student's t-test (two-tailed). Significance was recognized at $P < 0.05$.

Results

1) Lidocaine Group (GL 1–4)

Results are shown in table 3. The onset time in GL-2 was significantly shorter than that in GL-1, but there was no significant difference between GL-3 and GL-4.

2) Bupivacaine Group (GB 1–4)

Results are shown in table 3. The onset time in GB-2 was significantly shorter than that in GB-1, but there was no significant

Table 3. Onset time of analgesia at L1 (sec)

GL-1	387.3 ± 126.3	GB-1	635.1 ± 150.9
GL-2	289.3 ± 127.7*	GB-2	442.0 ± 190.0**
GL-3	246.5 ± 99.0	GB-3	356.3 ± 113.6
GL-4	264.2 ± 125.4	GB-4	353.0 ± 156.4

*$P < 0.05$ vs GL-1, **$P < 0.01$ vs GB-1 (mean ± SD)

difference between GB-3 and GB-4.

Neither systemic toxicity of the local anesthetics nor localized nerve damage was observed clinically in all the groups during and after this examination.

Discussion

Many recent clinical studies on the effects of pH-adjustment of local anesthetics have been performed to shorten the onset time of anesthesia. These reports, however, showed inconsistent results[1–8]. This discrepancy seems to have been caused by the fact that many factors, such as the magnitude of pH change, the sort and concentration of local anesthetics, and the type of block, affected the results of each study. In general, the past reports indicate that the onset time of local anesthesia can be reduced by the large changes in pH and/or low concentration. We can easily speculate that changes in pH play an important role. However, there have been few reports to compare the effects of pH-adjustment on the onset time of local anesthetics of different concentration.

In the present study, we examined the effects of pH-adjustment on the onset time of epidural anesthesia with lidocaine (0.9% and 1.8%) and bupivacaine (0.25% and 0.5%). In the 0.9 percent lidocaine and 0.25 percent bupivacaine groups, pH-adjustment reduced the onset time significantly ($P < 0.05$ and $P < 0.01$ respectively). In 1.8 percent lidocaine and 0.5 percent bupivacaine groups, however, pH-adjustment exerted no significant effect on the onset time. It is well known, uncharged base traverses the lipophilic nerve sheath easily and then the positively charged cation binds to the axonal membrane to block conduction[9]. The concentration of diffusible anesthetic base governs the induction time. In other words, the greater concentration of anesthetic base brings the shorter latency[10–12]. The pKa of the drug and the tissue pH determine the relative amount of each agent present in the basic or protonated form[9,13], and the concentration of the drug determines the absolute amount of each agent.

There were no significant effects by pH adjustment in groups administered local anesthetics of higher concentration. It was probably due to the following two mechanisms. Firstly, there may be a ceiling point of base concentration to determine the onset time of local anesthesia. In the 1.8 percent lidocaine and 0.5 percent bupivacaine groups, base in the drugs might be above the ceiling point to determine a particular onset time. Consequently, pH adjustment might not exert any significant effect. Secondly, there is an upper limit in base solubility of local anesthetics and the solubility limit decreases with the temperature[14]. In high-concentration local anesthetic groups, the amount of base exceeds the solubility limit at body temperature, and therefore, pH-adjustment may exert no effect on the onset time.

Hilgier reported that alkalinization of 0.5 percent bupivacaine from 3.9 to 6.4 induced quicker onset of brachial plexus block[1]. Bedder et al., however, reported that alkalinization of bupivacaine 0.5 percent solution from 5.5 to 7.1 did not give any clinical advantage in brachial plexus blockade[7]. Magnitude of pH change in the study of Hilgier was larger than that in the study of Bedder et al. Also, base in the study of Bedder et al. possibly exceeded the ceiling point. These two may explain the discrepancy of their reports.

DiFazio et al.[2] investigated the onset time

of epidural anesthesia using local anesthetics of the same concentration alkalized in two different magnitudes. They increased pH of 1.5 percent lidocaine from 4.55 to 7.20 and from 6.35 to 7.20, and reported that the onset time in both groups was significantly shortened compared with that in non-pH-adjusted group. Their technique to determine analgesia and total dose of drug was different from ours. In addition to effects of pH-increase and concentration of local anesthetics, these factors practically may effect on the onset time of analgesia.

McMorland et al.[3,6] used local anesthetics of different concentrations alkalized by the same degree, and investigated the onset time of epidural anesthesia in the same manner as in our study. They reported shortened onset time in both groups in which the pH of 0.25 percent bupivacaine was elevated from 5.65 to 7.26 and the pH of 0.5 percent bupivacaine was elevated from 5.49 to 7.04. The larger pH change in their study than in ours may have accounted for the difference in the results.

We judged the initial onset of epidural anesthesia by pin-prick method performed at L1 area. Spread of epidural analgesia is affected by some factors such as injection speed of analgesic solutions and patient's conditions (height, age, arteriosclerosis)[13]. At it was impossible to make the same conditions, we selected L1 area for assessment of the onset which was hardly correlated with the segmental spread of anesthesia.

In conclusion, this study demonstrated that raising the pH of low-concentration local anesthetic shortened the onset time. However, raising the pH of high-concentration did not cause any changes.

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