

While addition of epinephrine 1:200,000 to local anesthetic solutions is not yet routine during caudal anesthesia, the detection of intravascular injection would be facilitated by the resulting abrupt increases in heart rate. The role of epinephrine in the detection of intraosseous local anesthetic injection has not been studied. However, because drug uptake from the marrow space is relatively rapid,<sup>1</sup> the use of epinephrine in local anesthetic solutions may be of use in the detection of intraosseous needle position. The use of epinephrine in our case might have alerted us of an intraosseous insertion.

Marrow punctures during caudal anesthesia have been reported in both normal adults and infants.<sup>2</sup> The likelihood of accidental intraosseous injection of local anesthetics may be increased in patients with predisposing conditions, and we have described such a case in a patient with ankylosing spondylitis. The presence of AS may increase the risk of intraosseous puncture due to the marked osteoporosis found in many such patients. Although inclusion of epinephrine in local anesthetic test doses may increase the likelihood of detecting intraosseous needle placement, there is presently no scientific evidence to

prove this. Because convulsions in patients with ankylosing spondylitis may cause severe trauma, this author now believes that caudal anesthesia is contraindicated for these patients. For patients in whom caudal anesthesia is to be performed, failure to aspirate bone marrow should be considered an unreliable test for intraosseous needle position. The routine inclusion of epinephrine in local anesthetic solutions may be an important way to detect intraosseous injection and may therefore decrease the risk of local anesthetic toxicity in all patients receiving caudal anesthesia.

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## Acceleration of Epinephrine Absorption by Lidocaine

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To obtain optimal local hemostasis in patients undergoing surgery, cutaneous infiltration of a dilute solution of epinephrine often is performed. Use of epinephrine with an inhaled anesthetic such as halothane is known to cause cardiac dysrhythmias. Limiting the dose of epinephrine<sup>1</sup> and use of dextran for suppression of the absorption of epinephrine<sup>2</sup> has helped to make this a safe practice. Also, Johnstone *et al.*<sup>3</sup> suggested that lidocaine

used together with epinephrine might reduce the incidence of cardiac dysrhythmias.

A small amount of epinephrine can be added to anesthetic solutions to prolong the analgesia and reduce the potential danger of systemic toxic reactions. Although the suppressive action of epinephrine on absorption of a locally administered anesthetic has been demonstrated,<sup>4–6</sup> the effect of the local anesthetic on the absorption of the epinephrine has not been studied. We, therefore, measured the plasma level of epinephrine following its injection.

## MATERIALS AND METHODS

After obtaining approval of the Committee for the Protection of Human Subjects and informed consent, we studied 40 ASA I and II adult patients who were scheduled for elective craniotomy. Halothane 4% in 100% oxygen or halothane 2.5% mixed with 50% nitrous oxide in oxygen was inhaled via a semiclosed system for 10 min

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TABLE 1. Physical Status of the Studied Patients (mean  $\pm$  SD)

Group	Number	Age (yr)	Body Weight (kg)	Male/Female
E	8	52 $\pm$ 12	52 $\pm$ 4	3/5
LE	9	52 $\pm$ 7	61 $\pm$ 8	5/4
ED	11	46 $\pm$ 11	55 $\pm$ 9	7/4
LED	12	58 $\pm$ 13	54 $\pm$ 12	5/7

and orotracheal intubation performed without using a muscle relaxant. The patients were ventilated mechanically to keep the  $P_{aCO_2}$  at 30–35 mmHg. During the 30 min usually required for positioning and preoperative preparation, anesthesia was maintained with 2–2.5% halothane in 100% oxygen or 1–1.5% halothane mixed with 50% nitrous oxide in oxygen. The ECG and the arterial pressure waves from an indwelling catheter were displayed continuously on an oscilloscope and simultaneously recorded during the study.

The patients were divided into four groups, and four different solutions were prepared for cutaneous injection: 1) 1:200,000 epinephrine in normal saline solution (E,

$n = 8$ ); 2) 1:200,000 epinephrine with 0.5% lidocaine in normal saline solution (LE,  $n = 9$ ); 3) 1:200,000 epinephrine with 10% low-molecular-weight dextran in saline solution (ED,  $n = 11$ ); and 4) 1:200,000 epinephrine with 0.5% lidocaine and 10% low-molecular-weight dextran in saline solution (LED,  $n = 12$ ). After the patients were positioned for surgery, one of the four solutions was injected at 0.5 ml/kg into the scalp by an anesthesiologist over a period of 5–6 min. Half of the solution first was deposited beneath the aponeurosis, followed by infiltration of the remaining half into the subcutaneous tissue.

Arterial blood for analysis of the epinephrine concentration was obtained six times, *i.e.*, before injection, and 1, 5, 10, 20, and 30 min after completion of the injection. The sampled blood was treated with ethylene-diamine-tetra-acetic acid (EDTA) and centrifuged immediately. The plasma was stored in a freezer at  $-25^\circ\text{C}$  and analyzed within 3 days. Epinephrine was measured by the method reported previously.<sup>2</sup> The limit of sensitivity of the method was 0.01 ng/ml.

The results were expressed as the mean  $\pm$  SD. Comparison of variables between groups was made with the use of the unpaired Student's *t* test. *P* values of less than 0.05 were considered significant.

## RESULTS

Physical status of the four groups of the patients is shown in table 1. They were comparable with respect to age, body weight, and sex distribution. None of the patients developed serious circulatory complications such as ventricular dysrhythmias or hypertensive episodes due to the use of epinephrine in this study.

The control value of plasma epinephrine was below 0.01 ng/ml in 36 out of 40 cases. In the four remaining cases, two in each of Group ED and LED, the value was 0.01 ng/ml. The peak plasma epinephrine levels produced by the injection of epinephrine are shown in figure 1. In 33 out of 40 cases, the plasma concentration of epinephrine peaked 5 min after completion of the injection. In the seven remaining cases, one in Groups LED and two in each of Groups E, LE and ED, the concentration of epinephrine peaked at 1 min. No relationship was found between the age or body weight and the plasma epinephrine level. By mixing lidocaine with the epinephrine, the peak levels of plasma epinephrine were significantly ( $P < 0.005$ ) increased both in normal saline solution and in 10% low-molecular-weight dextran solution (fig. 1). The time course of the plasma epinephrine concentration of Groups E and LE is shown in figure 2, and of Groups ED and LED in figure 3. The difference in the plasma level of epinephrine between Groups E and LE was significant

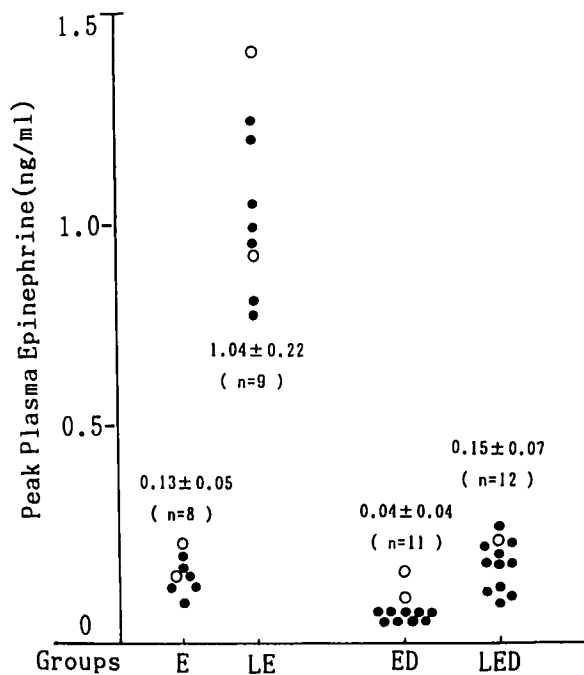


FIG. 1. The peak plasma epinephrine levels following epinephrine injection. Each circle represents one patient. The concentration of plasma epinephrine peaked 5 min after completion of the injection in 33 out of 40 cases. The empty circles represent the seven cases in which the plasma epinephrine level peaked 1 min after completion of the injection. The difference in the values between Groups E and LE and between Groups ED and LED are significant ( $P < 0.005$ ).

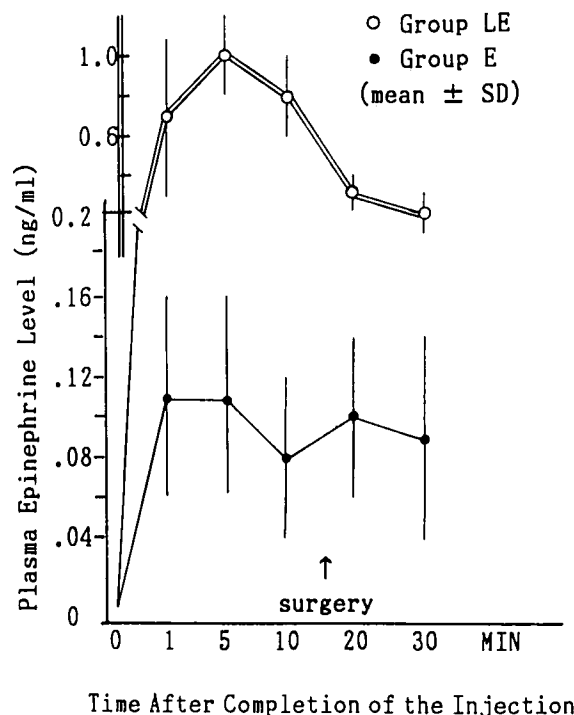


FIG. 2. The time course of plasma epinephrine level after the injection of epinephrine in Group E and LED. The difference in the plasma level of epinephrine between Groups E and LE is significant ( $P < 0.005$ ) throughout the study, except the control value at zero min.

( $P < 0.005$ ) throughout the study. The plasma epinephrine levels in Group LED were significantly ( $P < 0.005$ ) higher than that in Group ED by 10 min, but the significance of the difference between the two disappeared after the start of surgery.

### DISCUSSION

Absorption of locally injected epinephrine is retarded by its own vasoconstrictor action. The results of this study demonstrated the potential of lidocaine for accelerating the absorption of epinephrine; this effect may be due to the vasodilating action of lidocaine.<sup>7</sup> This mechanism also might have contributed to the finding that the suppressive

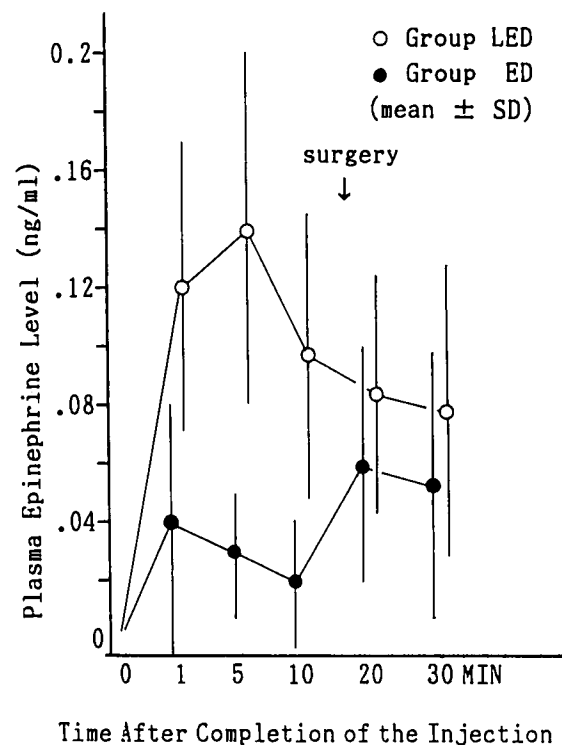


FIG. 3. The time course of plasma epinephrine level after the injection of epinephrine in Groups ED and LED. The plasma epinephrine level in Group LED is significantly ( $P < 0.005$ ) higher than that in Group ED at 1, 5, and 10 min.

action of dextran on the absorption of epinephrine was more prominent in the presence of lidocaine. An increase in the concentration of epinephrine to 1:100,000 did not antagonize the effects of lidocaine (table 2). The causes of this might be similar to those behind the finding that the addition of epinephrine to a lidocaine solution at greater than 1:200,000 did not increase the duration of action of lidocaine.<sup>8</sup>

The results of our study could neither prove nor rule out the existence of an antiarrhythmogenic effect of lidocaine in epinephrine solution as reported by Johnstone *et al.*<sup>3</sup> Changes in the plasma epinephrine level caused by surgery indicate that the antiarrhythmogenic effects of

TABLE 2. The Time Course of Plasma Epinephrine Level (ng/ml) after the Injection of 1:100,000 Epinephrine with 0.5% Lidocaine in Normal Saline Solution, in Two Female Patients

Age (yr)	Body Weight (kg)	Time after Completion of the Injection					
		0 min	1 min	5 min	10 min	20 min	30 min
52	42	0.02	1.44	2.39	1.58	1.05	0.63
46	56	<0.01	0.69	2.40	1.74	0.58	0.28

Amount of the injected epinephrine solution was 0.5 ml/kg. The

study was performed under the same conditions as the other 40 patients.

lidocaine can be expected not only from its direct action on the heart but also from its analgesic effect of blocking surgical stress.<sup>2</sup> Perhaps epinephrine should be given by the surgeon 10 min before the start of surgery to avoid the synergistic effect produced by the combination of exogenous epinephrine and surgical stress.

In conclusion, lidocaine accelerates the transfer of locally injected epinephrine to the blood. This effect of lidocaine can be attenuated by using 10% low-molecular-weight dextran to dilute the epinephrine, instead of normal saline solution.

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