J Anesth (1996) 10:39–43

Journal of
Anesthesia

Effects of osmotic pressure on intrathecal and epidural lidocaine anesthesia

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Abstract: Lidocaine (1%), either in plain distilled water or in 10% dextrose, was intrathecally or epidurally administered to urethane–chloralose anesthetized cats. Electrical stimulation was applied to the gracile tract at a cervical level, and the resultant antidromic compound action potentials were recorded from the sural nerve. Lidocaine dissolved in plain distilled water was more effective than lidocaine dissolved in 10% dextrose solution in suppressing the compound action potentials. Lidocaine-free plain distilled water or dextrose solution caused partial suppression of the compound action potentials. The suppression was more marked following plain distilled water application than following application of 5% or 10% dextrose.

Key words: Lidocaine, Intrathecal anesthesia, Epidural anesthesia, Osmotic pressure

Introduction

Lund and Cameron [1] reported that tetracaine seems to be more effective as a spinal anesthetic when administered in plain water than when administered in 10% dextrose. It is known that subcutaneous injection of water produces local anesthesia [2]. Halsted [3] used plain water instead of cocaine in skin incision, and asserted that the skin can be completely anesthetized to any extent by cutaneous injection of water. A large sodium loss will block conduction of nerve impulses [4], and sodium depletion is known to enhance local anesthetic conduction blockade [5]. Hence leaching out sodium and other electrolytes from the perifibrillar neural tissue may be partly responsible for the local anesthetic action of water. However, lowering the sodium concentration in the cerebrospinal fluid does not appear to account for the difference in the spinal anesthetic effects between two different solutions of tetracaine [1]. Although Lund and Cameron [1] did not measure sodium concentration, sodium depletion would have been similar with both solutions. Fink et al. [6] compared the effects of lidocaine in hypo-osmotic sucrose with those in iso-osmotic sucrose on the compound action potentials of sheathed vagus nerves of rabbit in vitro. They showed that osmotic swelling plus electrolyte depletion, but not electrolyte depletion alone, markedly intensified conduction blockade by lidocaine. The present study was undertaken to elaborate these previous findings in vivo.

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Received for publication on March 6, 1995; accepted on September 12, 1995

Materials and methods

Experiments were carried out on 21 adult cats weighing 2.8–3.8 kg. General anesthesia was induced with ketamine hydrochloride (20 mg·kg^{-1}, intramuscularly), and the right cephalic vein was cannulated for drug administration, as was the right femoral artery for continuous monitoring of blood pressure. Anesthesia was maintained with an i.v. dose (3.5 ml·kg^{-1}) of urethane–chloralose solution (urethane 125 mg·ml^{-1} and chloralose 10 mg·ml^{-1}) supplemented as required. A thermistor probe was placed in the esophagus and the body temperature was maintained at 37 ± 0.5°C by an electric heating pad under the abdomen and an infrared lamp.

The animal's head was rigidly fixed in a stereotaxic instrument. Spinal segments C_2 through C_4 were exposed by laminectomy for the placement of a stimulating electrode, and were kept in a pool filled with warm liquid paraffin. In the experiments in which a test solution was intrathecally applied, another laminectomy was carried out at the level of 5th and 6th lumbar vertebrae for the application. The left sural nerve was dis-

sected free from the surrounding tissues and mounted (in a liquid paraffin pool) on a bipolar platinum electrode for recording. Another pair of platinum stimulating electrodes was applied to the sciatic nerve in the midthigh region.

The fasciculus gracilis was monopolarly stimulated with single pulses of 0.1 ms duration, using a platinum ball electrode placed on the dorsal surface of the exposed cervical cord (Fig. 1). The averaged antidromic compound action potentials evoked by 100 stimulations at 5 times threshold and at 20 Hz were used for analysis. To monitor the stability of the recording condition, antidromic compound action potentials evoked by stimulation of the sciatic nerve were recorded at frequent intervals. The size of the averaged compound action potentials was measured with a computer using a data-collection and processing program QP-110J (Nihon Kohden, Tokyo, Japan).

In the experiments in which a test solution was intrathecally applied, a small hole about 1 mm in diameter was made in the dura mater covering the cauda equina. A polyethylene tube was inserted into the subarachnoid space through this hole until the tip of the tube reached the 7th lumbar dorsal root. After insertion, the hole was sealed with aron alpha (Toagousei, Osaka, Japan).

In the experiments in which a test solution was epidurally applied, a small hole about 1 mm in diameter was made in the ligamentum flava just caudal to the 5th lumbar lamina. A polyethylene tube was inserted into the epidural space through this hole until the tip of the tube reached the 7th lumbar dorsal root. After insertion, the hole was sealed with aron alpha.

In both intrathecal and epidural experiments, a test solution was injected into the subarachnoid or epidural space through the polyethylene tube using a syringe (1 mL) in 30 s. The dead space in the tube was 0.1 mL. The second injection was usually performed at least 3 h after the first injection. The order of injections was randomly chosen. More than two injections were never given.

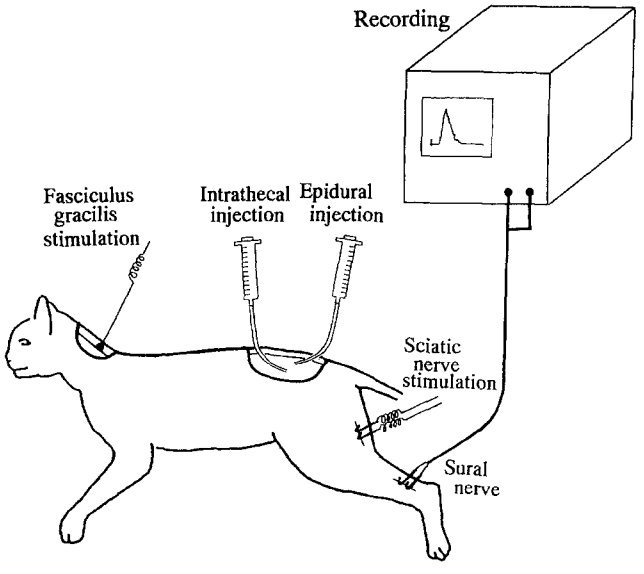

Fig. 1. Experimental methods

During recording, the animal was paralyzed with pancuronium bromide ($4\,mg \cdot kg^{-1} \cdot h^{-1}$) and artificially ventilated. The endtidal CO_2 was monitored and maintained between 3.5% and 4.5%.

Mean values were presented as mean ± standard error (SEM). Data were analyzed for significant differences using the paired *T*-test. When *P* values were <0.05, differences were considered significant. The half-time of recovery was measured from the peak time of suppression.

Results

Effects of intrathecal lidocaine

In six cats, 0.5 ml of 1% lidocaine, either in plain distilled water ($68\,mosm \cdot L^{-1}$; pH 5.68; specific gravity 1.003) or in 10% dextrose ($722\,mosm \cdot L^{-1}$; pH 5.62; specific gravity 1.048), was intrathecally applied to the lumbosacral cord, and the resultant changes in the antidromic compound action potentials were studied. An example is illustrated in Fig. 2. In this figure, changes in the antidromic compound action potentials following intrathecal application of 1% lidocaine in plain distilled water is shown in Fig. 2a, while those in 10% dextrose are shown in Fig. 2b. In the control records, shown in Fig. 2a and Fig 2b, the latency of the compound action potentials was 8.5 ms, and the duration of the potentials was 14.3 ms. Following the application of 1% lidocaine in plain distilled water, the potentials were almost completely suppressed at 10 min after application. The potentials then gradually returned to the control level. Following the application of 1% lidocaine in 10% dextrose, the degree of the maximum suppression at 10 min after application was 65.3%. The potentials then gradually returned to the control level.

The mean time courses of changes in the size of the compound action potentials following intrathecal application of 1% lidocaine in plain distilled water or in 10% dextrose are illustrated in Fig. 2c. Following the application of 1% lidocaine in plain distilled water, the degree of maximum suppression at 10 min after application was 96.2% ± 1.5%. Following the application of 1% lidocaine in 10% dextrose, the degree of maximum suppression at 10 min after application was 56.4% ± 7.8%. The difference in the degree of suppression between these two solutions was statistically significant ($P = 0.0028$). The half-times of recovery were 26 min and 11 min, respectively.

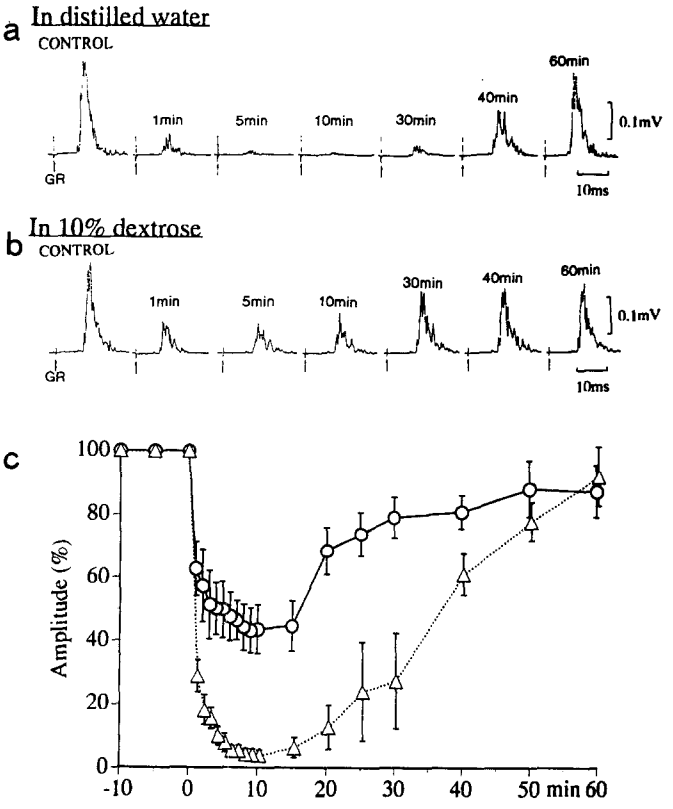

Fig. 2. Changes in antidromic compound action potentials following intrathecal application of 1% lidocaine in plain distilled water and in 10% dextrose. **a** Sample records in an experiment with 1% lidocaine in plain distilled water. Time after application is indicated in each record. **b** Sample records in an experiment with 1% lidocaine in 10% dextrose. **c** Mean time courses of suppression of antidromic compound action potentials following intrathecal application of 1% lidocaine in plain distilled water and in 10% dextrose. The size of antidromic compound action potentials prior to administration served as a control. *Open triangles*, in distilled water; *Open circles*, in 10% dextrose

Effects of epidural lidocaine

In five cats, 0.5 ml of 1% lidocaine in plain distilled water or in 10% dextrose was applied to the epidural space. The results are summarized in Fig. 3. The degree of maximum suppression was 51.8% ± 7.6% following the application of 1% lidocaine in plain distilled water, while it was 28.8% ± 5.7% following the application of 1% lidocaine in 10% dextrose. The difference in the degree of suppression between these two solutions was statistically significant ($P = 0.0421$).

Effects of plain distilled water and of dextrose solution

In ten cats, the effects of intrathecal application of lidocaine-free plain distilled water (pH 6.71), lidocaine-free 5% dextrose solution (pH 4.20), or lidocaine-free 10% dextrose solution (pH 3.90) were studied. The results are summarized in Fig. 4. Following application of

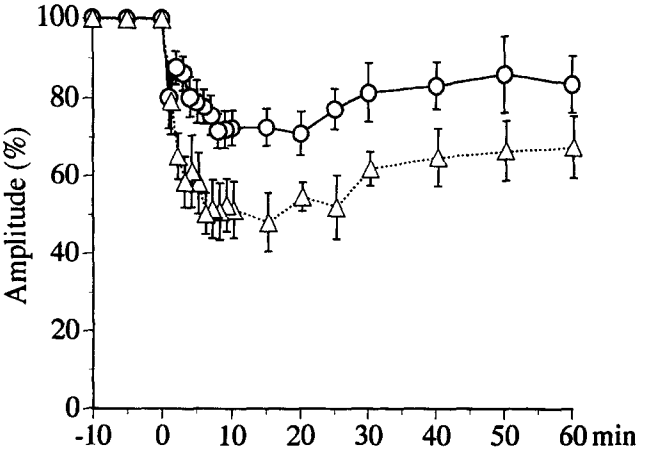

Fig. 3. Mean time courses of suppression of antidromic compound action potentials following epidural application of 1% lidocaine in plain distilled water and in 10% dextrose. *Open triangles*, in distilled water; *open circles*, in 10% dextrose

0.5 ml plain distilled water or dextrose solution, the antidromic compound action potentials were suppressed. The degree of maximum suppression was 40.1% ± 7.6%, 12.8% ± 3.6%, and 19.0% ± 7.3% following distilled water, 5% dextrose, and 10% dextrose application, respectively. The difference in degree of maximal suppression between plain distilled water and dextrose solutions (5% and 10%) was statistically significant ($P = 0.0179$ and $P = 0.0290$, respectively); plain distilled water was more effective than either dextrose solution. However, the difference between the two different solutions of dextrose was insignificant ($P = 0.5159$).

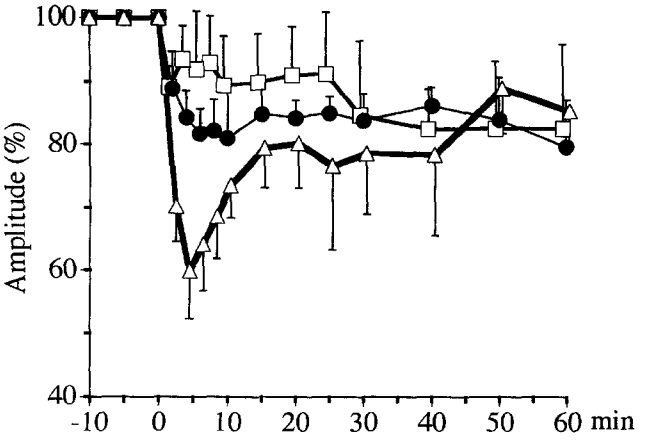

Fig. 4. Mean time courses of changes in antidromic compound action potentials following intrathecal application of lidocaine-free plain distilled water, lidocaine-free 5% dextrose, and lidocaine-free 10% dextrose. *Open triangles*, distilled water; *Open squares*, 5% dextrose; *Solid circles*, 10% dextrose

Discussion

In the present study, we have introduced a new method to test the intrathecal and epidural blocking actions of local anesthetics on primary afferent fibers in vivo. The fasciculus gracilis comprises several different classes of fibers (Fig. 5).

1. The stem axons of dorsal root fibers that first emit local segmental and descending collaterals at the level of entry and then project through the fasciculus gracilis to terminate within the nucleus gracilis.
2. Ascending axons of dorsal root origin that enter the fasciculus gracilis but leave it at some higher segmental level.

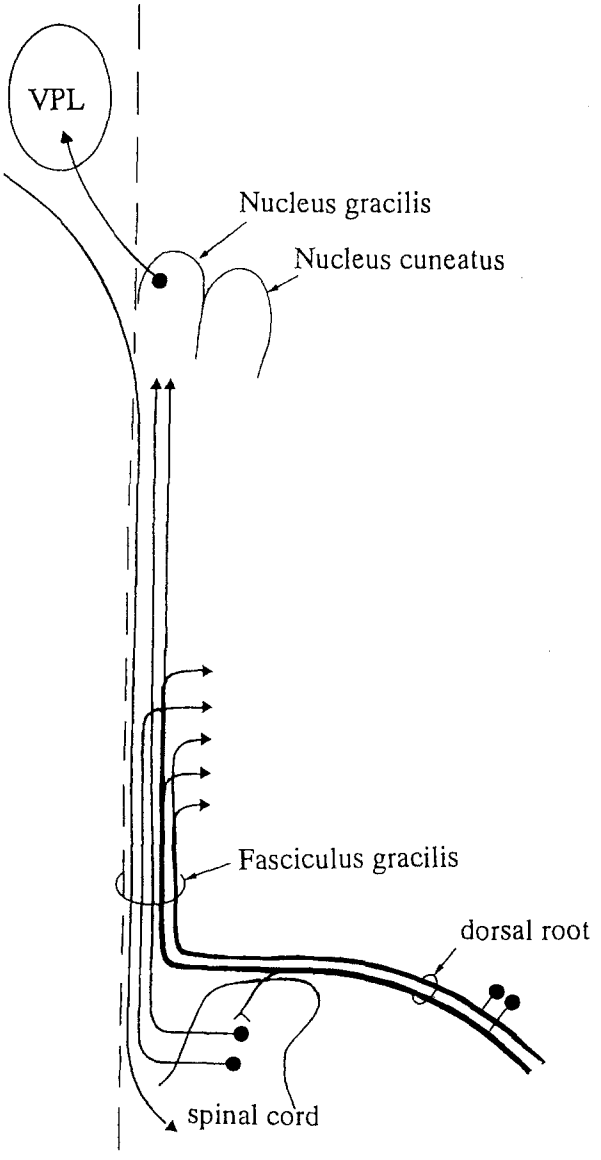

Fig. 5. Highly simplified representation of ascending fibers in the fasciculus gracilis referred to in the text

3. Axons of intraspinal neurons which project through the fasciculus gracilis to terminate within the nucleus gracilis.
4. Intersegmental propriospinal axons.
5. Descending axons from the brain.

Those of the third and fifth classes are rare in the cat [7–9].

In the cat, only 48% of large myelinated fibers in the sural nerve belong to the axons of the first class [10]. In other words, approximately half the large myelinated afferent fibers in the sural nerve enter the long pathway extending the length of the spinal cord to reach the nucleus gracilis. These fibers are almost exclusively rapidly adapting cutaneous afferent fibers [10]. The afferent fibers in the sural nerve which responded to antidromic stimulation of the fasciculus gracilis in the present experiments were primarily of this category.

We recorded compound action potentials from the sural nerve, which is a skin nerve. Hence contamination by motor-evoked responses could be avoided. However, the antidromic compound action potentials recorded in the sural nerve may be contaminated by a dorsal root reflex or by a similar type of reflex generated in the nucleus gracilis [11–14]. However, the reflex component is known to be very sensitive to the frequency of stimulation, and almost completely disappears at frequencies as low as 10 Hz [11–14]. In the present study, the antidromic compound action potentials evoked by five times threshold stimulation at 20 Hz were used for analysis. Hence, contamination by reflex components was unlikely.

There is a sharp decrease in the diameter of the primary afferent fibers as they ascend the fasciculus gracilis, probably due to branching. The decrease is, in turn, associated with a parallel decrease in their conduction velocities. These afferent fibers exhibit some branching upon entering the spinal cord, and then traverse the upper lumbar and lower thoracic segments with little (if any) further decrease in diameter. They do, however, show further decreases in their conduction velocities in the region of, or just caudal to, the cervical enlargement [10]. This results in a temporal dispersion of antidromic latencies in individual fibers in the sural nerve, thus causing an increase in the duration of antidromic compound action potentials. However, the stem fibers influenced by local anesthetic action at the level of the lumbosacral cord are of fairly uniform size.

In the present experiments, we have confirmed that intrathecal or epidural lidocaine is more effective when administered in plain water than when administered in 10% dextrose. In addition, we confirmed that intrathecally applied plain water, 5% dextrose and 10% dextrose cause a partial conduction blockade of nerve

impulses in the primary afferent fibers. Conduction blockade by plain water was more marked than that by 5% or 10% dextrose. Although nerve fibers in the dorsal root are not protected by connective tissues, the effects of water on their excitation may be similar to those in sheathed vagal nerve in vitro [2,6]. Thus, intrathecal and epidural water may block nerve conduction through osmotic swelling as well as through electrolyte depletion.

An additional mechanism responsible for the stronger intrathecal or epidural anesthetic action of lidocaine in plain water may be the difference in baricity between the anesthetic solutions employed. It is widely acknowledged that a solution made hyperbaric by the addition of dextrose spreads in a different manner than one containing no dextrose [15–19]. Lee et al. [17] examined the spread of intrathecal 0.5% amethocaine solutions containing 0%, 1.25%, 2.5%, and 5% dextrose. The plain, isobaric solution produced a block restricted to the legs and perineum, but all three dextrose solutions spread to midthoracic level in the supine position. Brown et al. [15] reported that an amethocaine solution made hyperbaric by adding dextrose produced more widespread blockade than a hypobaric solution in plain distilled water or an isobaric solution in saline. In addition, the mean duration of anesthesia was shorter with the hyperbaric solution. They suggested that the greater spread of the solutions allowed more rapid uptake into the blood stream from the anesthetized nervous tissues [20]. This kind of mechanism may be responsible for the difference in intrathecal anesthetic action between 1% lidocaine in plain distilled water and that in 10% dextrose, in addition to osmotic swelling and electrolyte depletion caused by water. However, whether or not this mechanism works in the epidural anesthesia is uncertain.

In the prone position for anorectal procedures or in the lateral position for hip repairs, spinal anesthesia with a hypobaric solution is often adequate [20]. In the United States, the most common method of formulating a hypobaric solution is to mix a local anesthetic with sterile water [20]. The present data supported the effectiveness of this hypobaric anesthetic solution in blocking conduction of peripheral afferent nerve fiber.

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