Localization of ^{14}C-Labeled 2% Lidocaine Hydrochloride after Intraosseous Anesthesia in the Rabbit

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Abstract

Objective: The purpose of this study was to investigate the tissue distribution of lidocaine hydrochloride in mandibular bone marrow after intraosseous anesthesia (IOA) in rabbits. **Methods:** We used macroautoradiography to examine the tissue distribution of a ^{14}C-labeled 2% lidocaine hydrochloride solution containing 1:80,000 epinephrine (^{14}C-lidocaine). Under general anesthesia, ^{14}C-lidocaine was injected intraosseously or paraperiosteally. After IOA, animals were divided into three groups and observed at 1 (IOA-1), 5 (IOA-5), and 10 minutes (IOA-10) after injection. After infiltration anesthesia (IA), animals were observed at 1 minute after injection. **Results:** The accumulation of ^{14}C-lidocaine was observed around the injection site in both the IA and the IOA groups. Paraperiosteally injected ^{14}C-lidocaine diffused to the surrounding tissues such as the lip, whereas IOA showed concentrated accumulation around the root apex throughout the experiment. The distribution area was significantly smaller in the IOA-1 group than in the IA group. The distribution area in the IOA-5 group was larger than those in the IOA-1 and IOA-10 groups. **Conclusions:** The accumulation of ^{14}C-lidocaine injected by IOA in rabbits was concentrated around the root apex. These results may explain the rapid onset time of IOA. *(J Endod 2011;37:1376–1379)*

Key Words

Alveolar bone, intraosseous anesthesia, lidocaine, macroautoradiography, radioisotope, tissue distribution

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Local anesthesia is essential for pain control during dental treatment. Currently, infiltration anesthesia (IA) is the most common procedure. However, an anesthetic effect in the mandibular molars is frequently insufficient after IA only (1, 2). In these cases, supplemental techniques such as intraosseous anesthesia (IOA), intraligamental anesthesia, and/or block anesthesia are combined with IA. In general, IOA is used as either a primary injection technique or a supplemental injection technique. Of those, IOA is often used as a supplemental technique after a failed inferior alveolar nerve block, and this technique provides fast and sufficient anesthesia even in the mandibular molars (3–6). In a rabbit study, the onset time, which was defined as the elapsed time until the electromyogram of the digastric muscle disappeared after the injection, was reported less than 1 minute after primary IOA (7). In human studies, it is also reported that the onset time after primary IOA was quite rapid (8–15). The anesthetic area and duration of anesthesia after supplemental IOA were sufficient for the treatment even in the tooth with pulpitis (3–6). Primary IOA also has advantages of minimal anesthetic effects beyond the intended site compared with an alveolar nerve block (13–15). Many studies have investigated the clinical findings such as the onset or duration and anesthetic efficacy after local anesthetics (8–12, 15). However, there are few studies that investigated the tissue distribution of an anesthetic solution after local anesthesia (16–19). Yamazaki et al (16) reported the diffusion process of ^{14}C-labeled 2% lidocaine hydrochloride in rabbit oral tissue after IA. However, there has been no study on the tissue distribution of a local anesthetic solution in the bone marrow administered as IOA. Therefore, we used macroautoradiography to investigate how anesthetic solution administered by primary IOA diffusion in the oral tissues.

Materials and Methods

This study was conducted in compliance with the Guidelines for the Treatment of Experimental Animals at Tokyo Dental College in accordance with the guidelines of the Japanese government (approval no. 222502). Thirty-six male Japan White rabbits, 10 to 12 weeks old, weighing between 2.5 and 3.0 kg, were used in this study. The rabbits were anesthetized with 3% isoflurane. Tracheotomy was performed under local anesthesia, and then an 18- to 20-French size pediatric endotracheal tube was inserted into the trachea and fixed. A venous indwelling catheter was inserted into the left auricular marginal vein as a route for fluid infusion and drug administration. Anesthesia was maintained by an intermittent intravenous injection of sodium thiopental (Ravonal; Mitsubishi Tanabe Pharma Corporation, Kyoto, Japan).

^{14}C was used as a labeled radioisotope (RI) because it had an appropriate half-life long enough for this study, and it was commercially available for labeled lidocaine. The experimental local anesthetic solution consisted of ^{14}C-labeled 2% lidocaine hydrochloride (American Radiolabeled Chemicals Inc, St. Louis, MO) containing 1:80,000 epinephrine (^{14}C-lidocaine). The concentration of radioactivity was 37.2 kBq/mL.

The ^{14}C-lidocaine was injected by IOA or IA. In the IOA groups, the tip of the needle was placed in the vicinity of the root apex of the lower right incisor. The X-tip system (Dentsply International Inc, York, PA) was used for IOA. The diameter of the guide sleeve was 0.64 mm. The length of the guide sleeve and drill were modified to 4 and 6 mm, respectively. The X-tip was inserted through the lateral compact bone near the inferior border of the mandible through the skin by using a slow-speed handpiece at 20,000 rpm. The ^{14}C-lidocaine was injected through the guide sleeve of the X-tip by using

a 1-mL syringe with a 27-G needle. The injection volume was 0.03 mL. In eight rabbits, a dental cone-beam computed tomography scan was used immediately after an insertion of the guide sleeve to confirm that the tip of the needle was within the mandible. In the IA group, ^{14}C-lidocaine was injected into the vestibular fornix corresponding to the right incisor. The injection needle was inserted to a depth of 5 mm in an apical direction from the mucous membrane side. A volume of 0.04 mL was injected using a microsyringe with a 30-G needle. After the IOA with ^{14}C-lidocaine, animals were divided into three groups. Observation was preformed at 1 (IOA-1 group, n = 9), 5 (IOA-5 group, n = 9), and 10 minutes (IOA-10 group, n = 9) after injection. These time periods were determined based on the previous study (17). After the IA injection with ^{14}C-lidocaine, observation was performed at 1 minute after injection (IA group, n = 9). Each rabbit received one anesthesia in this study.

After the elapse of each observation time, animals were sacrificed with an overdose of sodium thiopental. The animals were rapidly frozen with liquid nitrogen, and then the maxilla and mandible were excised in one piece. These samples were embedded in 8% carboxymethylcellulose paste, frozen with acetone, cooled in dry ice, and prepared as specimen blocks. Sections of 50-μm thickness were prepared using an autocryotome from the specimen blocks. Sections were made parallel to the plane perpendicular to the guide sleeve direction. This plane was almost parallel to the plane that includes the long axis of the incisor. The sections were dried in a freezer at −20°C for about 10 days. Then, the section was contacted with an imaging plate for 90 minutes in an imaging cassette. Accumulation images were acquired with a Bioimaging Analyzer System (BAS; Fuji Film, Tokyo, Japan). BAS is a device that visualizes radioisotopic information on the imaging plate. Specimens were scanned, and anatomic imaging data were obtained. Finally, two imaging data were superimposed, and the position of the image showing accumulation was determined (Fig. 1*A*).

Images obtained from the BAS were analyzed with image analysis software (ImageJ 1.42q; National Institutes of Health, Bethesda, MD). A circular region of interest with a diameter of 45 pixels (pixel size = 200 μm) was set at the center of the local anesthetic injection site. The volume of the ^{14}C-lidocaine was quantified by determining the amount of radioactivity within the circle, calculated as density × pixel count, and the volume was compared with that at the control site. Because a radiation dosage obtained from the BAS was in proportion to pixels, the RI level, and the volume of ^{14}C-lidocaine, the radiation dosage obtained from the BAS was considered as volume of the ^{14}C-lidocaine because pixels and RI level were constant in this study (Fig. 1*A*a and *A*b). To investigate the time course change in diffusion area after IOA, regions of ^{14}C accumulation in images obtained were selected, and the area of local anesthetic distribution (pixel count) was calculated.

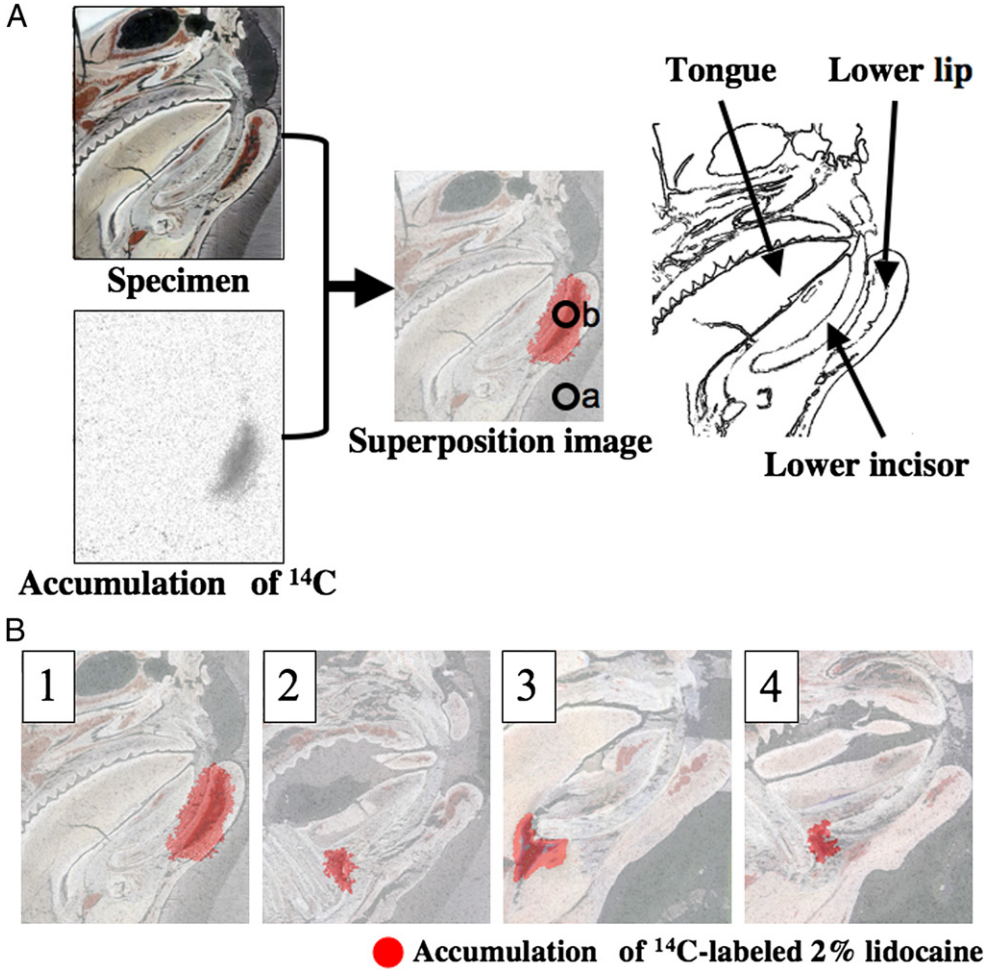

Figure 1. Specimen and accumulation image are superimposed and accumulation area is determined. (*A*) Superposition of the prepared specimen and the accumulation image. Superposition of these two images identifies the location where ^{14}C-lidocaine is present in rabbit oral tissue. a, the measurement area of the volume of ^{14}C-lidocaine (control site); b, the measurement area of the volume of ^{14}C-lidocaine (injection site). (*B*) The distribution area of ^{14}C-lidocaine. 1, 1 minute after IA; 2, 1 minute after IOA; 3, 5 minutes after IOA; 4, 10 minutes after IOA.