©Operative Dentistry, 2018, **43-1**, 22-30

A Clinical Study on the Effect of Injection Sites on Efficacy of Anesthesia and Pulpal Blood Flow in Carious Teeth

QH Zheng • QC Hong • L Zhang • L Ye • DM Huang

Clinical Relevance

Infiltration anesthesia over the midpoint of the line connecting the root apexes of two adjacent teeth causes less reduction of pulpal blood flow.

SUMMARY

This randomized clinical trial evaluated the efficiency of maxillary infiltration anesthesia in carious teeth at two different injection sites and their impact on the laser Doppler recordings of pulpal blood flow (PBF) during a caries excavation procedure. The null hypothesis tested was that there are no differences in the efficiency of anesthesia and PBF reduction between maxillary infiltrations at the two injection sites. One hundred twenty patients were divided into three groups according to the degree of carious lesion of their maxillary left central incisors (moderate caries, deep caries, or no caries). Forty patients in each group randomly received infiltrations over the root apex of maxillary left central incisors (site X) or over the midpoint of the line connecting the root apexes of both maxillary left central and lateral incisors (site Y) using 0.9 mL 2% lidocaine with 1:100,000 adrenaline. Teeth were pulp tested at five-minute intervals after injection except for the period of cavity cutting, which was done 12 minutes after injection. The PBF changes after injection were monitored by laser Doppler flowmetry. The observation period in this study was 60 minutes. Success of anesthesia was defined as no or mild pain on cavity cutting by visual

Qinghua Zheng, DDS, PhD, State Key Laboratory of Oral Diseases, National Clinical Research Center for Oral Diseases, West China School of Stomatology, Sichuan University, Chengdu, Sichuan Province, China

Qingchun Hong, State Key Laboratory of Oral Diseases, National Clinical Research Center for Oral Diseases, West China School of Stomatology, Sichuan University, Chengdu, Sichuan Province, China

Lan Zhang, State Key Laboratory of Oral Diseases, National Clinical Research Center for Oral Diseases, West China School of Stomatology, Sichuan University, Chengdu, Sichuan Province, China

Ling Ye, State Key Laboratory of Oral Diseases, National Clinical Research Center for Oral Diseases, West China School of Stomatology, Sichuan University, Chengdu, Sichuan Province, China

*Dingming Huang, PhD, State Key Laboratory of Oral Diseases, National Clinical Research Center for Oral Diseases, West China Hospital of Stomatology, Sichuan University, Chengdu, Sichuan Province, China

*Corresponding author: 14# 3rd Section, Renmin South Road, Chengdu 86610041, Sichuan Province, China; e-mail: dingminghuang@163.com

DOI: 10.2341/16-371-C

analog scale recordings. Deep caries group showed significantly higher baseline PBF ($p<0.05$). All groups showed 100% success of anesthesia and similar duration time ($p>0.05$). Subgroups that had the injection at site Y showed significantly less reduction of PBF ($p<0.05$). Cavity-cutting procedures increased the amplitude of the PBF around the lowest value after injection. Independent of the cavity depth, carious anterior teeth anesthetized by infiltration further from the apex had significantly less reduction on the pulpal blood flow compared with teeth anesthetized by infiltration at the apex.

INTRODUCTION

An intact pulpal blood flow (PBF) is critical for maintaining the health of the dental pulp.[1] Because the dental pulp is enclosed in a low-compliance environment surrounded by enamel and dentin and lacks of collateral circulation, it is more vulnerable and does not easily tolerate injury.[1] Under the long-term accumulation of noxious stimuli, even a small rise of pulpal pressure can significantly affect the local circulation.[2,3] The reduction of PBF ensuing from an increase in pulpal pressure fails to provide sufficient oxygen and nutrients for pulpal cells and has the compounding effect of reducing the clearance of large molecular weight toxins or waste products, thus causing irreversible pulpal pathosis.[4,5]

Maxillary infiltration is a common method for pain control in dentistry, which provides effective pulpal anesthesia in more than 60% of the cases.[6-13] Epinephrine added to anesthetics benefits the duration and quality of pulp anesthesia, which mainly depends on its vasoconstrictor properties on blood vessels in close proximity to the injection site.[14] Despite its positive effect on anesthesia, the vasoconstriction effect was considered to have adverse effects on the pulp status of the teeth, particularly if the pulp is inflamed preoperatively.[14] Many studies have assessed the effects of local anesthetics with vasoconstrictors on pulpal circulation.[14-16] They confirmed that epinephrine in local anesthetics does reduce PBF, regardless of whether it is administered by infiltration or nerve block. However, it remains unclear how to minimize the side effect on PBF reduction and simultaneously provide promising effects of anesthesia.

Dental caries is the main cause of irreversible pulpal inflammation. Restorative dentistry plays an important role in active caries control, which itself may cause significant irritation to the dental pulp.[1] Besides, the effects of pulpal insults are considered cumulative. With each succeeding irritation, the pulp has a diminished capacity to remain vital.[1] Apart from the well-known chemical irritants like restorative materials, physical irritations during cavity preparation such as from heat, desiccation, or vibration are reported factors that may adversely affect the dental pulp.[3,17-19] However, most of the studies were conducted on human or experimental animal teeth with normal pulp, which may not reveal the true effects of these procedures on teeth with carious lesions that are already causing inflammation of the pulp. Moreover, reduced PBF and its underlying effect by a local anesthetic with vasoconstrictors were not considered.

Because the pulp tissue cannot be directly inspected, indirect methods like thermal and electric pulp tests were frequently used to evaluate the pulp vitality. The cold test is a more reliable test (sensitivity and specificity) to prove the vitality of the tooth and the success for anesthesia as found by Petersson and others.[20]

It is generally accepted that assessment of the blood supply within the dental pulp (pulp vitality) is the earliest indicator and may be the only available true indicator of the actual state of pulpal health.[21,22] However, thermal and electric pulp tests actually assess the condition of the nerves within the dental pulp rather than the pulp blood supply. Laser Doppler flowmetry (LDF) is reportedly able to assess changes of blood flow within the dental pulp noninvasively.[23] It is considered the most accurate method for diagnosing the state of pulpal health and came closest to serving as a gold standard.[22,24]

To date, no study has assessed the effect of infiltration anesthesia and following cavity cutting on the PBF of carious teeth. The aims of the present study were to (1) evaluate the anesthesia effect at two injection sites for carious maxillary left central incisors using 2% lidocaine with 1:100,000 adrenaline and (2) monitor the dynamic PBF changes induced by the injection and following cavity cutting by LDF. We compared two injection target sites in this study: site X was centered over the root apex of the carious maxillary left central incisors and site Y was over the midpoint of the line connecting the root apexes of both maxillary left central and lateral incisors. The null hypothesis tested was that there are no differences in the efficiency of anesthesia and PBF reduction between maxillary infiltrations at the two injection sites.

METHODS AND MATERIALS

Subjects

All patients were informed about the purpose and procedures used in the study, and they gave their written informed consent to the protocol approved by the Sichuan University Committee for Research on Human Subjects (WCHSIRB-D-2015-104R1).

Eighty participants with unrestored carious maxillary left central incisors and 40 participants with healthy maxillary left central incisors were included in this study, for a total of 120 subjects (66 men and 54 women; age, 18 to 39 years). All subjects were randomly selected from the pool of patients referred to the Department of Conservative Dentistry, West China Hospital of Somatology, from November 2015, until the number of subjects achieved the requirement of this study.

Tooth responsiveness to external stimuli was evaluated by conventional electrical and thermal tests. Radiographs were taken to ensure that the pulp chamber was visible and the periapical status of the tooth was normal. The extent of caries was determined by radiographic combined with clinical examination. Criteria for exclusion were as follows: caries lesion offended the cervical area of the tooth crown or caused pulp exposure, gingivitis, or periodontitis; a history of spontaneous pain of teeth; a history of recent trauma or orthodontic treatment; active sites of pathology in the area of injection; allergic to anesthesia; a significant medical history or medication that might influence anesthesia and PBF; a history of smoking or drinking; and being pregnant or breastfeeding.

Participants were divided into three groups according to the degree of caries lesion. The moderate caries group included participants with moderate caries lesions limited to the shallow dentin layer (n=40). The deep caries group was participants with deep caries lesions to the inner dentin layer (n=40). The no caries group was participants with healthy intact maxillary left central incisors (n=40). Each subject was randomly assigned to infiltration at one of the examined sites.

Laser Doppler Flowmetry

PBF was measured using a LDF (moorVMS-LDF1-HP, Moor, Axminster, England) with light delivered at a wavelength of 785 nm produced by a 2.5-mW laser and a type CP3 probe (Moor) with a cross-sectional diameter of 1.6 mm. Before each data collection session, the LDF was calibrated using a motility standard liquid consisting of a low concentration of polystyrene microspheres in water undergoing thermal motion (Moor Motility Standard, Moor).

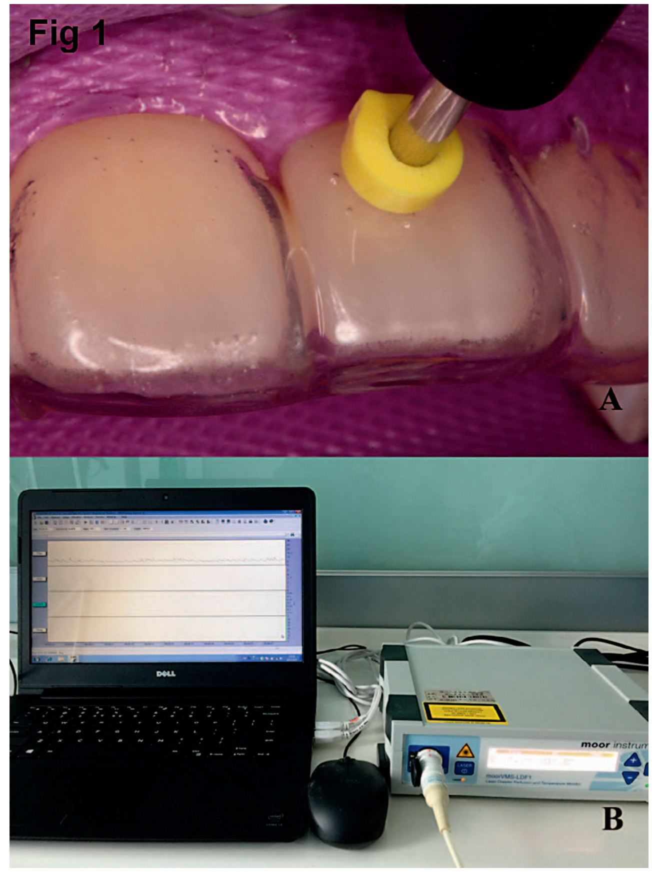


Figure 1. *Photographs showing the recording of laser Doppler. (A): View of the placement of rubber dam, acrylic guard, and application of the LDF tester. (B): Setup for the recording of the laser Doppler.*

Customized acrylic resin splints were used to secure the probe in the appropriate positions. Channels were drilled through the splint to allow for the insertion of the optical probe for pulpal recordings. The probe was placed perpendicular on the labial enamel surface of the tooth crown approximately 3 mm from the gingival margin, over the central long axis of the crown (Fig. 1). An opaque, heavy-gauge rubber dam was placed, and the participant was allowed to rest in a supine position in the dental chair for 15 minutes prior to LDF measurement. Heart rate and blood pressure were taken throughout the measurement sessions. The PBF was expressed in perfusion units (PUs), monitored, and subsequently analyzed using data processing software (Moor VMS-PC) (Figure 1). All measurements were performed by the same operator under standardized environmental conditions at a constant room temperature. The operator only

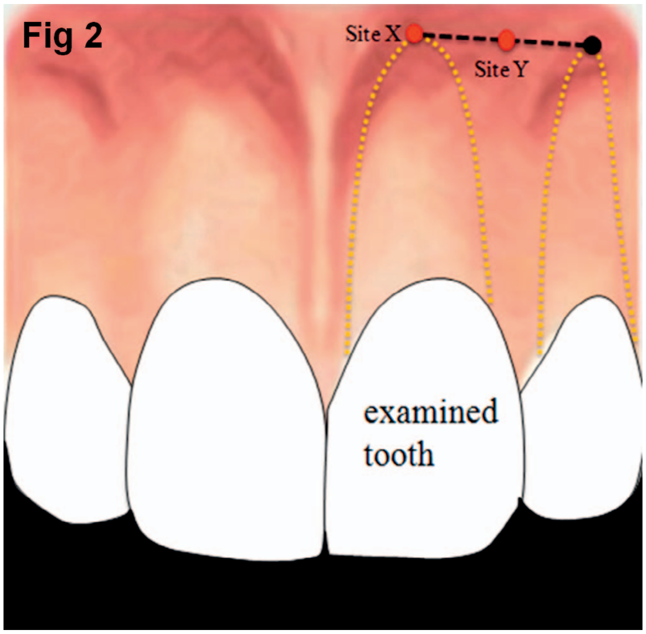


Figure 2. *Schematic diagram of injection sites.*

recorded the PU values and did not know the aim and design of the study.

Experimental Procedures

An electric pulp tester (Analytic Technology, Redmond, WA, USA) was used to record pulpal sensitivity of the subjects in each group in machine units before the experiment to determine the baseline response. The contralateral maxillary canine was used as a control to ensure that the pulp tester was operating properly and that the volunteers were responding appropriately during the study. The current rate was set at 25 seconds to increase from no output (0) to the maximum output (80). All the preinjection and postinjection pulp tests were performed by the same trained person who was blinded to the anesthetic target site administered.

After the measurement of the baseline response using the electric pulp tester, the rubber dam and splint were put on, and the LDF measurement was made to obtain the baseline PU value of the subjects. The rubber dam and splint were then removed, and the participants in each group randomly had buccal infiltration at one of the two sites using 0.9 mL 2% lidocaine hydrochloride with 1:100,000 adrenaline. Site X was centered over the root apex of the maxillary left central incisor, the common recommended site (n=20), and site Y was centered over the midpoint of the line connecting the root apexes of both maxillary left central and lateral incisors (n=20) (Figure 2).The randomization process involved selection of one from among 40 sealed envelopes for each group by the operator immediately before the anesthesia, and this revealed to the operator the target sites to inject. The participants did not know the site of injection. All administration was done quantitatively with a 31-gauge needle (CK-JECT, CK Dental Ind Co, Bucheon, Korea) placed in the submucosa over the estimated position by a computer-controlled local anesthetic delivery system at default mode (KM-7500, KMG Co, Busan, Korea). Criterion for pulpal anesthesia was no response from the subject at the maximum output (80 reading) of the pulp tester. The onset of anesthesia was defined as the time from the end of injection to the first of two consecutive 80 readings. The duration of pulpal anesthesia was defined as the time from the onset of pulpal anesthesia to the time recorded before two positive responses to the pulp tester were obtained.[9]

After the administration, PU value was recorded for 12 minutes to evaluate the PBF change during the time from the end of injection to the beginning of cavity cutting. Pulp sensitivity was recorded at five and 10 minutes after injection. If the teeth showed response at the maximum output, one more pulp electrical test was done five minutes later.

Cavity cutting began on the moderate and deep caries groups 12 minutes after injection. Each two minutes, drilling was followed by four minutes recording of the PU value. The drilling session was repeated three times to ensure the complete excavation of carious lesions. All the drillings were done by the same experienced doctor. Teeth in the no caries group remained undrilled. The PBF was then monitored continuously, and pulp sensitivity was recorded at five-minute intervals until the end of the observation time.

Participants were instructed to definitively rate any pain felt during the cavity cutting using the Heft-Parker Visual Analog Scale (VAS)[25] on a 170-mm marked line. The VAS was divided into four categories: no pain (0 mm), mild pain (1-54 mm), moderate pain (55-113 mm), and severe pain (114-170 mm). A designated doctor not involved with the clinical phase of the study collected and analyzed the VAS forms. The success of the maxillary infiltration was defined as the ability to clean the carious lesion of the tooth without pain (VAS score of 0) or with mild pain (VAS score of ≤54 mm). After the study ended, the cavities were restored following routine procedures.

Table 1: *Duration of anesthesia and mean pain ratings after cavity cutting in each group (mean±SD)*

Injection target sites	Participants					
	Moderate caries group		Deep caries group		No caries group	
	X	Y	X	Y	X	Y
Duration of anesthesia (min)	53.2±7.4	47.9±5.1	51.9±6.8	46.2±5.7	52.6±7.0	47.0±5.3
Mean pain ratings	14.6±6.7	15.0±5.9	15.1±7.1	17.4±7.3	—	—

Statistical Analysis

Assuming a 70% anesthetic success rate and a nondirectional α risk of 0.05, a total sample size of 110 subjects and almost 18 subjects for each of the six subgroups would be required to show a difference in anesthetic success of a 30% decrease with a power of 0.90. The effects of the degree of caries and the injection sites on the results and their interaction were analyzed using analysis of variance for factorial design. Comparisons between and within groups for the duration of anesthesia, baseline PU value, and the percentage of fluctuation amplitude (percentage of fluctuation amplitude of PU value to baseline PU value) during drilling were analyzed using Tukey's test. The data of percentage reduction of the PU value (percentage of maximal reduction of PU value to baseline PU value) within 12 minutes after injection was analyzed using the Games-Howell test. $p<0.05$ was considered significant.

RESULTS

All the subjects had successful anesthesia. None of the subjects showed response to the electric pulp tester at five minutes after injection. The mean durations of anesthesia are presented in Table 1, and no statistical differences were found between the groups.

The baseline PBF values, the mean percentage reduction of PBF within 12 minutes after injection, and the mean percentage fluctuate amplitude of PBF during cavity cutting in each group are listed in Table 2. The deep caries group has a higher baseline PBF than the other groups ($p<0.05$). The subgroups with injection at site Y showed a lower percentage reduction of PBF than those injected at site X ($p<0.05$). The degree of caries showed no obvious effect on the PBF change and had no interaction with the injection sites ($p>0.05$). None of the subjects returned to baseline PBF by the end of the observation time.

Subjects who had the same treatments showed a similar trend of PBF change within 60 minutes after injection. The decrease in PBF is illustrated in Figure 3. During the first 12 minutes after injection, the reduction of PBF seemed to be more abrupt in the subgroups with injection at site X than at site Y (Figure 4). Obvious fluctuations of PBF were found during cavity cutting in all study groups (Figure 5). The percentage fluctuation amplitude of PBF during the cavity-cutting procedures presented no statistical differences among the groups ($p>0.05$). No obvious fluctuation of PBF was found in the group with healthy maxillary left incisors (no cavity cutting).

DISCUSSION

We used the 80 reading (maximum output) of the electric pulp test as a criterion for pulpal anesthesia based on the studies of Drevenet and others[26] and Certosimo and Archer.[27] Petersson and others[20] reported that the probability of a sensitive reaction representing a vital pulp was 90% with the cold test using ethyl chloride and 84% with the electrical test. Due to the lack of ethyl chloride in the clinical department during the period of our study, we used the electrical test instead of the cold test.

All the subjects had successful infiltration, regardless of the injection site and degree of caries, which

Table 2: *Baseline PBF, percentage reduction and percentage fluctuation amplitude of PBF in each group (mean±SD)[a]*

Injection target sites	Participants					
	Moderate caries group		Deep caries group		No caries group	
	X	Y	X	Y	X	Y
Baseline PBF	5.79±0.90[b]	5.75±0.81[b]	9.91±0.85[a]	10.09±1.18[a]	5.98±0.86[b]	6.02±0.86[b]
Maximal reduction of PBF to baseline PBF (%)	57±6[a]	39±8[b]	58±5[a]	32±10[b]	57±5[a]	36±7[b]
Fluctuation amplitude of PBF to baseline PBF (%)	13±3	14±2	14±1	12±2	—	—

[a] *In each row, statistical groups are designated by superscript letters (p<0.05).*

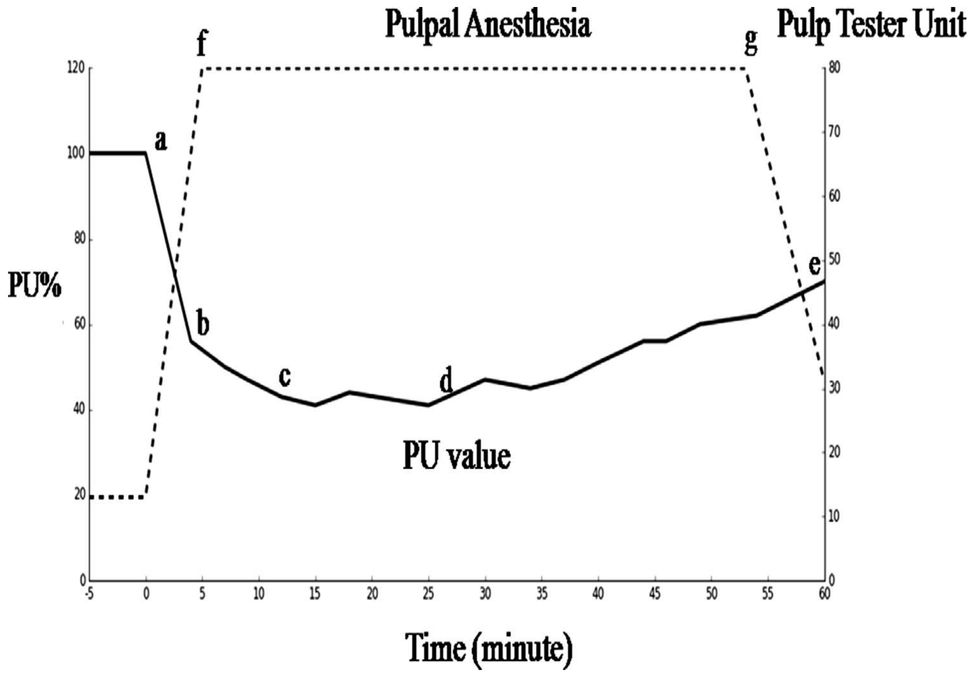


Figure 3. *Dynamic changes of PBF and tooth response to electric pulp tester of one subject's injection at site X in moderate caries group 60 minutes after injection. PU%, the percentage of the real-time PU value to the baseline PU value; a, complement of injection; c, beginning of cavity cutting; ab curve, stage of PBF abruptly reduced after injection; bc curve, phase that PBF slowly declines; d, complement of cavity cutting; e, the percentage PU value at 60 minutes after injection; fg segment, tooth showed no response at 80 reading of the pulp tester.*

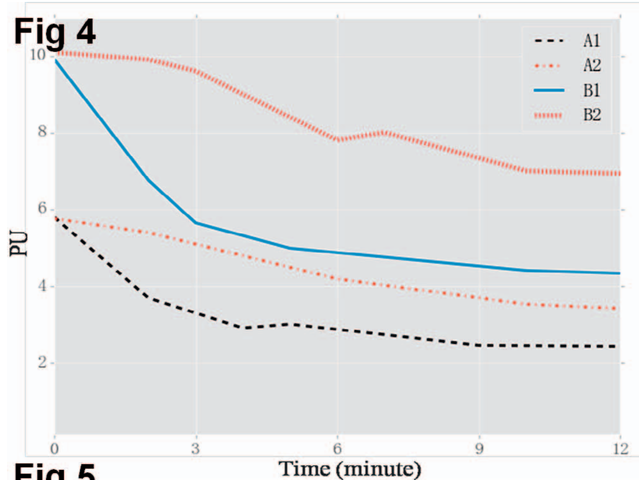
means that no obvious pain was reported during the cavity-cutting procedure. The reported success rate of infiltration anesthesia for healthy maxillary central incisors ranged from 72% to 100%.[12,13,28,29] These variations may be partly due to the different kind and dosage of the anesthetic agents, as well as the population and operator difference.[8]

The information about the onset and duration of infiltration is important for clinic treatment. Kämmerer and others[28] reported that the mean onset of infiltration for maxillary central incisors using 4% articaine with varying dosages of epinephrine was 4.2 to 5.3 minutes. For PBF evaluation, we performed the electric pulp test at five and 10 minutes after the injection instead of evaluating the timely onset of the anesthesia. We found that five minutes was enough for the left maxillary central incisors in all groups to show no response to a reading of 80. It is difficult to compare our study with that of Kämmerer and others[28] because of the different kinds of anesthetics. The present results were close to those found in research on maxillary lateral incisors with a similar study design.[8,9] Whether there are differences in the anesthesia effects between the central and lateral incisors needs further investigation.

The mean duration of anesthesia of each group was greater than 45 minutes but limited to one hour, and no differences were found at the two injection sites. There are controversies regarding the duration of infiltration anesthesia for maxillary central incisors using 2% lidocaine with 1:100,000 epinephrine. Similar to our study, Lawaty and others[29] reported that anesthesia of short duration (less than one hour) occurred in 42% of the subjects. In contrast, Pitt and others[13] reported that the duration of anesthesia exceeded 80 minutes in all of the maxillary central incisors. Adding the dose of anesthetics was considered helpful for prolonging the duration of anesthesia.[7] In our pilot study, anesthesia using 1.8 mL 2% lidocaine with 1:100,000 epinephrine can provide a longer duration of anesthesia. However, considering the possible side effects induced by prolonged vasoconstriction,[2,14] 45 minutes was adequate for short dental operative procedures to minimize injury to the pulp.

The baseline PBF of the subjects in the deep caries group was much higher than the other groups, which indicated that there may be primary pulpal congestion in teeth with deep caries, although these subjects showed normal responses to the thermal and electrical tests. The increase in baseline PBF seemed to have no obvious effect on the success rate, onset, and duration of infiltration for maxillary central incisors in the present study, yet the long-term side effects on these teeth should be monitored.

A significant reduction in PBF occurred after the injection in all subjects, as reported by other studies.[13,14,30,31] Pitt and others[13] reported a prom-



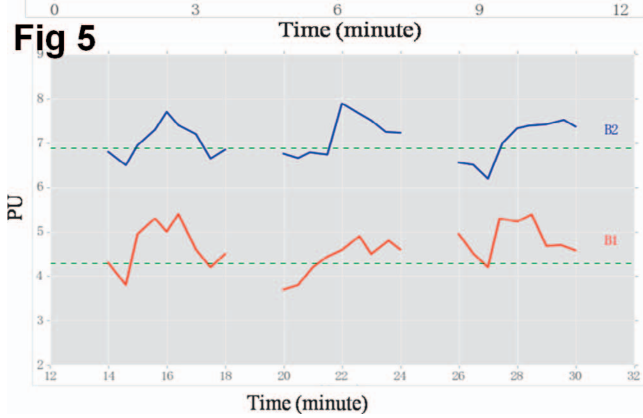


Figure 4. *Curve of the mean PBF change within 12 minutes after injection in four study groups. A1, moderate caries group with injection at site X; A2, moderate caries group with injection at site Y; B1, deep caries group with injection at site X; B2, deep caries group with injection at site Y.*

Figure 5. *An illustration of fluctuation of PU values after each cavity-cutting section of one subject for each subgroup in the deep caries group. The horizontal dotted line represents the mean PU value at the beginning of cavity cutting. B1, deep caries group with injection at site X; B2, deep caries group with injection at site Y.*

inent reduction (31%) of PBF in maxillary central incisors when 1 mL 2% lidocaine with 1:80,000 adrenalin was administered. Ahn and others[14] found a 73% reduction of PBF in the maxillary premolars after infiltration using 2% lidocaine with 1:100,000 epinephrine. The variations in PBF reduction between each study were partly attributed to the tooth position, dosage of vasoconstrictor, and population. Our results showed that reduction of PBF in subgroups injected at site Y was significantly less than those injected at site X. It is difficult to compare this result with other studies because none of the previous studies determined the effect of injection sites. Site X subgroups showed a 3- to 4-minute linear decrease of PBF soon after injection followed by a gradual reduction. Most studies reported that PBF after injection showed a rapid decrease and a gradual return toward the baseline value.[13,31] However, site Y subgroups exhibited a more moderate change of PBF, which was not reported in previous studies. The results mentioned above suggest that site Y may induce less effect on the PBF of the ill tooth, which may benefit pulp health. Despite the reduction speed of PBF, the PBF became comparatively stable at the time the cavity cutting procedure began in this study.

Cavity cutting was considered to have adverse effects on the PBF of the teeth.[32-34] In the present study, the PBF of the subjects experiencing cavity cutting exhibited prominent fluctuations after every two minutes of drilling, whereas the teeth without drilling showed no obvious variation in the amplitude of PBF. No statistically relevant differences were found in the percentage of fluctuation amplitude of PBF to baseline PBF between each study group, which suggests that cavity-cutting procedures may independently affect the PBF. Whether the accumulation effect of the reduction of PBF after anesthesia and the repeated fluctuation in PBF after dentin cutting found in our study has short- or long-term effects on the pulp status of teeth still needs further investigation.

By the end of the observation period in this study, none of the teeth returned to its baseline PBF, which was similar to the results reported by Ahn and others[14] and Pitt and others.[13] Although blood flow measurements were not continued past 60 minutes, a rebound hyperemic effect may be expected.

Assessments of PBF using laser Doppler may be highly susceptible to environmental and technique-related factors, including characteristics of the laser beam, probe position, tooth type, and nonpulpal signals obtained from nearby tissue.[24,35] In this study, the combination of the splint and rubber dam ensures the greatest possible accurate repositioning of the probe and isolation of the periodontal signal. Besides, maxillary central incisors were reported as having no significant interindividual differences on PBF characteristics[36]; the interindividual controls in our study leads to a convincing result.

CONCLUSION

With the limitations of this present study, we concluded that, independent of cavity depth, carious anterior teeth anesthetized by infiltration further from the apex had significantly less reduction on the pulpal blood flow compared with teeth anesthetized by infiltration at the apex, which may be beneficial for the prognosis of teeth with suspicious pulp congestion.

Acknowledgments

This study was supported by the National Natural Science Foundation of China (11402154) and Innovation Team of Sichuan Province (2015TD0011).

Regulatory Statement

This study was conducted in accordance with all the provisions of the local human subjects oversight committee guidelines and policies of Sichuan University Committee for Research on Human Subjects. The approval code for this study is WCHSIRB-D-2015-104R1.

Conflict of Interest

The authors of this manuscript certify that they have no proprietary, financial, or other personal interest of any nature or kind in any product, service, and/or company that is presented in this article.

(Accepted 7 March 2017)

REFERENCES

1. Fouad AF LL (2016) Pulpal reaction to caries and dental procedures In: Cohen SBR (ed) *Pathways of The Pulp* **11th edition** Elsevier Inc, St. Louis, Mo, 573-598.
2. Kim S (1985) Regulation of pulpal blood flow *Journal of Dental Research* **64(Special Number 3)** 590-596.
3. Kim S (1990) Neurovascular interactions in the dental pulp in health and inflammation *Journal of Endodontics* **16(2)** 48-53.
4. Pashley DH (1979) The influence of dentin permeability and pulpal blood flow on pulpal solute concentrations *Journal of Endodontics* **5(12)** 355-361.
5. Caviedes-Bucheli J, Munoz HR, Azuero-Holguin MM, & Ulate E (2008) Neuropeptides in dental pulp: The silent protagonists *Journal of Endodontics* **34(7)** 773-788.
6. Gross R, McCartney M, Reader A, & Beck M (2007) A prospective, randomized, double-blind comparison of bupivacaine and lidocaine for maxillary infiltrations *Journal of Endodontics* **33(9)** 1021-1024.
7. Mikesell A, Drum M, Reader A, & Beck M (2008) Anesthetic efficacy of 1.8 mL and 3.6 mL of 2% lidocaine with 1:100,000 epinephrine for maxillary infiltrations *Journal of Endodontics* **34(2)** 121-125.
8. Evans G, Nusstein J, Drum M, Reader A, & Beck M (2008) A prospective, randomized, double-blind comparison of articaine and lidocaine for maxillary infiltrations *Journal of Endodontics* **34(4)** 389-393.
9. Mason R, Drum M, Reader A, Nusstein J, & Beck M (2009) A prospective, randomized, double-blind comparison of 2% lidocaine with 1:100,000 and 1:50,000 epinephrine and 3% mepivacaine for maxillary infiltrations *Journal of Endodontics* **35(9)** 1173-117.
10. Katz S, Drum M, Reader A, Nusstein J, & Beck M (2010) A prospective, randomized, double-blind comparison of 2% lidocaine with 1:100,000 epinephrine, 4% prilocaine with 1:200,000 epinephrine, and 4% prilocaine for maxillary infiltrations *Anesthesia Progress* **57(2)** 45-51.
11. Younkin K, Reader A, Drum M, Nusstein J, & Beck M (2014) Anesthetic efficacy of a combination of 0.5 M mannitol plus 36.8 mg of lidocaine with 18.4 mug epinephrine in maxillary infiltration: a prospective, randomized, single-blind study *Anesthesia Progress* **61(2)** 63-68.
12. Parirokh M, Sadeghi AS, Nakhaee N, Pardakhty A, Abbott PV, & Yosefi MH (2012) Effect of topical anesthesia on pain during infiltration injection and success of anesthesia for maxillary central incisors *Journal of Endodontics* **38(12)** 1553-1556.
13. Pitt Ford TR (1993) Action of adrenaline on the effect of dental local anaesthetic solutions *Endodontics & Dental Traumatology* **9(1)** 31-35.
14. Ahn J, & Pogrel MA (1998) The effects of 2% lidocaine with 1:100,000 epinephrine on pulpal and gingival blood flow *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics* **85(2)** 197-202.
15. Chng HS, Pitt Ford TR, & McDonald F (1996) Effects of prilocaine local anaesthetic solutions on pulpal blood flow in maxillary canines *Endodontics & Dental Traumatology* **12(2)** 89-95.
16. Kim S, Edwall L, Trowbridge H, & Chien S 1984 Effects of local anesthetics on pulpal blood flow in dogs *Journal of Dental Research* **63(5)** 650-652.
17. Cox CF, White KC, Ramus DL, Farmer JB, & Snuggs HM (1992) Reparative dentin: Factors affecting its deposition *Quintessence International* **23(4)** 257-270.
18. Byers MR, Narhi MV, & Mecifi KB (1988) Acute and chronic reactions of dental sensory nerve fibers to cavities and desiccation in rat molars. *Anatomical Record* **221(4)** 872-883.
19. Nyborg H, & Brannstrom M (1968) Pulp reaction to heat. *Journal of Prosthetic Dentistry* **19(6)** 605-612.
20. Petersson K, Söderström C, Kiani-Anaraki M, & Lévy G (1999) Evaluation of the ability of thermal and electrical tests to register pulp vitality *Endodontics & Dental Traumatology* **15(3)** 127-131.
21. Baumgardner KR, Walton RE, Osborne JW, & Born JL (1996) Induced hypoxia in rat pulp and periapex demonstrated by 3H-misonidazole retention *Journal of Dental Research* **75(10)** 1753-1760.
22. Alghaithy RA, & Qualtrough AJ (2017) Pulp sensibility and vitality tests for diagnosing pulpal health in permanent teeth: A critical review *International Endodontic Journal* **50(2)** 135-142.
23. Gazelius B, Olgart L, & Edwall B (1988) Restored vitality in luxated teeth assessed by laser Doppler flowmeter *Endodontics & Dental Traumatology* **4(6)** 265-268.
24. Jafarzadeh H (2009) Laser Doppler flowmetry in endodontics: A review *International Endodontic Journal* **42(6)** 476-490.
25. Heft MW, Parker SR (1984) An experimental basis for revising the graphic rating scale for pain *Pain* **19(2)** 153-161.
26. Dreven LJ, Reader A, Beck M, Meyers WJ, & Weaver J (1987) An evaluation of an electric pulp tester as a

measure of analgesia in human vital teeth. *Journal of Endodontics* **13(5)** 233-238.

27. Certosimo AJ, & Archer RD (1996) A clinical evaluation of the electric pulp tester as an indicator of local anesthesia *Operative Dentistry* **21(1)** 25-30.
28. Kammerer PW, Seeling J, Alshihri A, & Daublander M (2014) Comparative clinical evaluation of different epinephrine concentrations in 4% articaine for dental local infiltration anesthesia *Clinical Oral Investigations* **18(2)** 415-421.
29. Lawaty I, Drum M, Reader A, & Nusstein J (2010) A prospective, randomized, double-blind comparison of 2% mepivacaine with 1:20,000 levonordefrin versus 2% lidocaine with 1:100,000 epinephrine for maxillary infiltrations *Anesthesia Progress* **57(4)** 139-144.
30. Hashimoto S, Yamashiro M, Fujita K, Yasuda A, & Sunada K (2014) Effects of epinephrine on lidocaine pharmacokinetics and blood volume in the dental pulp *Journal of Endodontics* **40(9)** 1370-1374.
31. Yoon MJ, Lee SJ, Kim E, & Park SH (2012) Doppler ultrasound to detect pulpal blood flow changes during local anaesthesia. *International Endodontic Journal* **45(1)** 83-87.
32. Ottl P, & Lauer HC (1998) Temperature response in the pulpal chamber during ultrahigh-speed tooth preparation with diamond burs of different grit *The Journal of Prosthetic Dentistry* **80(1)** 12-19.
33. Ohmoto K, Taira M, Shintani H, & Yamaki M (1994) Studies on dental high-speed cutting with carbide burs used on bovine dentin. *Journal of Prosthetic Dentistry* **71(3)** 319-323.
34. Zach L (1972) Pulp lability and repair: Effect of restorative procedures *Oral Surgery, Oral Medicine, and Oral Pathology* **33(1)** 111-121.
35. Akpinar KE, Er K, Polat S, & Polat NT (2004) Effect of gingiva on laser Doppler pulpal blood flow measurements *Journal of Endodontics* **30(3)** 138-140.
36. Norer B, Kranewitter R, & Emshoff R (1999) Pulpal blood-flow characteristics of maxillary tooth morphotypes as assessed with laser Doppler flowmetry *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics* **87(1)** 88-92.