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**Short Communication**

**Epinephrine in Local Anesthetic Cancels Increase in Tongue Mucosal Blood Flow after Stellate Ganglion Block in Rabbit**

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**Abstract**

The goal of this study was to compare oral mucosal blood flow and duration of anesthetic action after stellate ganglion block (SGB) using lidocaine, with or without epinephrine, and discuss the effect of epinephrine on SGB. Duration of anesthetic action was defined as elapsed time from finish of injection to recovery of common carotid blood flow (CCBF) to within  $\pm 5\%$  of respective control value. Male Japan White rabbits were anesthetized with isoflurane and mechanically ventilated. Common carotid blood flow and tongue mucosal tissue blood flow (TMBF) were measured with an ultrasound flowmeter and laser Doppler flowmeter, respectively. End-tidal partial pressure of carbon dioxide (ETCO<sub>2</sub>) and hemodynamic variables were continuously monitored, including heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP). For SGB, the tip of the needle was placed on the left transverse process of the cervical vertebra, 1–2 mm caudal to the cricoid cartilage. Either 0.1 ml of 1% lidocaine (Group L) or 1% lidocaine containing 10  $\mu\text{g/ml}$  epinephrine (Group LE) was injected for SGB. There were no differences in values at immediately before SGB and at the time when maximal change in CCBF was observed after SGB for ETCO<sub>2</sub>, HR, SBP, DBP or MAP in either group. CCBF showed a significant increase in Group L after SGB. In contrast, CCBF only showed a slight increase in Group LE. TMBF showed a significant increase in Group L after SGB, but not in Group LE. No differences in time required for maximal effect were observed between the two groups. In contrast, duration of anesthetic action in Group LE was significantly longer than that in Group L. Addition of epinephrine to local anesthetic solutions is not suitable for SGB, as it may not facilitate an increase in tissue blood flow, which is the primary objective of SGB.

**Key words:** Stellate ganglion block—Epinephrine—Common carotid blood flow—Tongue mucosal tissue blood flow—Rabbit

**Introduction**

Stellate ganglion block (SGB) inhibits nerve conduction via sympathetic preganglionic

fibers to the superior and middle cervical ganglions and postganglionic fibers of the stellate ganglion. Tissue blood flow in head, face, neck and upper limbs is increased by

its sympatholytic effects<sup>5</sup>). Local anesthetic solutions are used for SGB. It was reported that duration of action and vasodilation were enhanced after SGB by 0.5% mepivacaine combined with clonidine, an agonist of  $\alpha_2$ -adrenergic receptor<sup>3</sup>).

In dental local anesthesia, duration of action is extended by the addition of epinephrine to local anesthetic solutions. This is a result of its vasoconstricting effect through activation of  $\alpha$ -adrenergic receptors<sup>9</sup>). Therefore, it was hypothesized that duration might be enhanced by addition of epinephrine to local anesthetic solutions in SGB. However, it is also possible that tissue blood flow may decrease as a result of the vasoconstricting effects of epinephrine.

Therefore, in this paper, we compare oral mucosal blood flow and duration of action after SGB using lidocaine with or without epinephrine, and discuss the effect of epinephrine on SGB.

## Materials and Methods

### 1. Animals

We utilized male Japan White rabbits (2.2–2.7 kg). Rabbits were purchased from Sankyo Labo Company (Tokyo). This study was performed according to “The Guidelines for the Treatment of Experimental Animals in Tokyo Dental College”. All animals were allowed food and water *ad libitum* until the morning of the experiment.

### 2. Experimental design

Anesthesia was induced by inhalation of 4.0% isoflurane (ISO) in oxygen delivered via a mask. Before skin incisions were made for each of the experimental procedures, appropriate doses of lidocaine were injected into the surgical field. A #20 Fr non-cuffed pediatric endotracheal tube was inserted into the trachea through tracheostomy. The left auricular marginal vein and right femoral artery were cannulated with 22- and 24-gauge Teflon indwelling catheters. After intravenous lactated Ringer’s solution was started

at 10 ml/kg/hr, the animals were paralyzed with 1 mg/kg alcuronium chloride (Dialferin, Roche, Tokyo) and mechanically ventilated. Femoral artery blood pressure was continuously monitored with a pressure transducer (P231D; Gould, Oxnard, California). Heart rate (HR) was recorded by a tachograph triggered by blood pressure wave. Common carotid blood flow (CCBF) was measured with an ultrasound flowmeter (T108; Transonic, Ithaca, NY). A flow probe (type 3SB) was applied to the isolated left common carotid artery. Tongue mucosal tissue blood flow (TMBF) was measured with a laser Doppler flowmeter (ALF21; Unique Medical, Tokyo). A contact-type probe (type C; Unique Medical) for TMBF measurement was placed at the anterior third of the left dorsal surface of the tongue. Care was taken to minimize the contact pressure of the probe so as to prevent blood flow disturbance in the tongue mucosa. TMBF was expressed as a percentage of control values. After completion of experimental preparations, the end-tidal ISO concentration was reduced to 0.7% and maintained at that level for more than 60 min to stabilize the animal’s hemodynamic and respiratory parameters. End-tidal partial pressure of carbon dioxide (ETCO<sub>2</sub>) was kept constant throughout the experiment. ISO concentration was continuously monitored with an anesthetic gas monitor (Capnmac; Datex, Helsinki). Body temperature was continuously monitored with a rectal probe and maintained between 39.0 and 39.5°C with the aid of a heating lamp. The observed parameters were continuously recorded with a polygraph (Series360 NEC; Sanei, Tokyo).

For SGB, the tip of the needle was placed on the left transverse process of the cervical vertebra, 1–2 mm caudal to the cricoid cartilage. A 26-gauge needle connected to a 1 ml disposable syringe was used. After confirming contact of the tip of the needle with the left transverse process, 0.1 ml of 1% lidocaine was injected (Group L) and changes in CCBF and TMBF were observed. More than 60 min was allowed for the observed parameters to completely recover. After that, 0.1 ml of 1%

Table 1 Changes in  $\text{ETCO}_2$ , heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP)

	Group L		Group LE	
	Pre	Post	Pre	Post
$\text{ETCO}_2$ (mmHg)	41.0 ± 5.4	41.6 ± 5.8	41.7 ± 6.0	41.0 ± 6.3
HR (bpm)	271.6 ± 32.9	276.9 ± 32.8	264.3 ± 35.5	268.1 ± 31.7
SBP (mmHg)	119.1 ± 12.9	123.7 ± 18.2	121.9 ± 14.9	124.4 ± 14.3
DBP (mmHg)	61.6 ± 15.6	64.9 ± 13.3	68.6 ± 16.5	69.9 ± 12.3
MAP (mmHg)	81.9 ± 14.6	85.6 ± 11.8	78.9 ± 19.3	81.1 ± 17.1

Pre: immediately before SGB

Post: at time when maximal change in CCBF was observed after SGB

Data are expressed as mean ± SD. (n=7)

lidocaine containing 10  $\mu\text{g}/\text{ml}$  epinephrine was injected in a similar manner (Group LE) and changes in CCBF and TMBF were again observed. The solution volume of 0.1 ml was determined based on our preliminary study.

Data were recorded immediately before SGB (Pre) and at the time when maximal change in CCBF was observed after SGB (Post). Elapsed time from finish of injection to Post was defined as time for maximal effect. Duration of action was defined as elapsed time from finish of injection to time when CCBF recovered to within  $\pm 5\%$  of the respective control value. In this study, TMBF was expressed as a percentage of the respective control value.

### 3. Statistical analysis

Data were expressed as the mean  $\pm$  SD. A one-way analysis of variance for repeated measurements followed by the Student-Newman-Keuls test for multiple comparisons were used in this study. Time for maximum effect and duration of action were compared by the Student *t*-test for paired samples. *p*-values of less than 0.05 were considered statistically significant.

### Results

There were no differences between Pre and Post values for  $\text{ETCO}_2$ , HR, systolic blood

pressure (SBP), diastolic blood pressure (DBP) or mean arterial pressure (MAP) in either group. There were also no differences between the two groups in their respective Pre or Post values (Table 1).

Two CCBF values at Pre in Groups L and LE were similar. CCBF was significantly increased from Pre ( $39.6 \pm 15.5 \text{ ml}/\text{min}$ ) to Post ( $60.3 \pm 24.0 \text{ ml}/\text{min}$ ) in Group L. In contrast, CCBF showed a slight increase from Pre ( $36.7 \pm 11.3 \text{ ml}/\text{min}$ ) to Post ( $45.3 \pm 10.7 \text{ ml}/\text{min}$ ) in Group LE (Fig. 1). TMBF showed a significant increase to  $121.6 \pm 13.9\%$  of the control values after SGB in Group L. However, in Group LE, TMBF showed no change ( $100.8 \pm 13.9\%$ ) after SGB (Fig. 2).

Time for maximal effect was  $2.7 \pm 1.5 \text{ min}$  in Group L and  $4.6 \pm 2.9 \text{ min}$  in Group LE. Duration of anesthetic action was  $22.0 \pm 10.5 \text{ min}$  in Group L and  $33.5 \pm 14.9 \text{ min}$  in Group LE. Duration of anesthetic action in Group LE was significantly longer than that in Group L (Table 2).

### Discussion

In this study, CCBF and TMBF showed a significant increase in Group L, whereas they showed no increase in Group LE.

An increase in CCBF is caused by an increase in cardiac output (CO). Increases in CO are produced by afterload (total

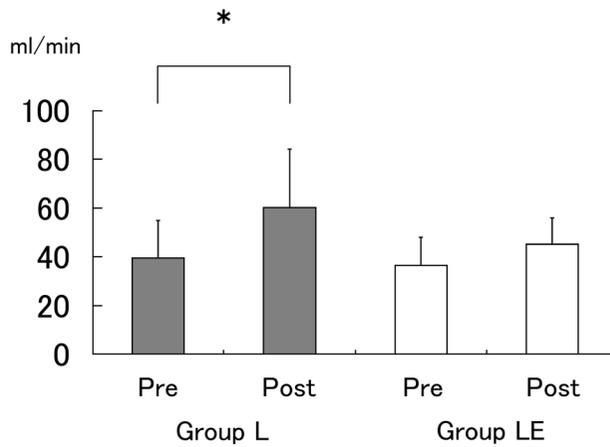


Fig. 1 Changes in common carotid blood flow (CCBF) in Groups L and LE. Data are expressed as mean  $\pm$  SD. (n=7) Asterisk indicates significant difference ( $p < 0.05$ ) from Pre. Pre and Post are same as in Table 1.

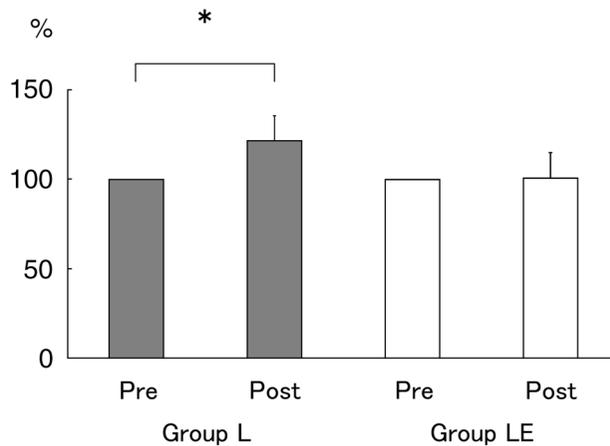


Fig. 2 Changes in tongue mucosal tissue blood flow (TMBF) in Groups L and LE. TMBF was expressed as percentage of respective control value. Data are expressed as mean  $\pm$  SD. (n=7) Asterisk indicates significant difference ( $p < 0.05$ ) from Pre. Pre and Post are same as in Table 1.

peripheral resistance) reduction, HR increase, cardiac contractility increase and preload (venous return) increase. In this study, no increase in HR was seen in Group L. In addition, cardiac contractility and venous return should not increase after SGB because of its sympatholytic effect. Therefore, it is suggested that the significant increase in CCBF seen here was due to CO increase

through afterload reduction (vasodilatation). ISO increased coronary blood flow<sup>1)</sup>, whereas it did not increase aortic blood flow<sup>2)</sup>. On the other hand, blood flow in the internal carotid artery (ICA) showed an increase after SGB with 2% lidocaine<sup>4)</sup>. In addition, in cases of facial palsy, CCBF and blood flow of the facial nerve showed an increase after SGB with 1% mepivacaine<sup>6,7)</sup>. Based on these findings, it

Table 2 Time for maximal effect and duration of anesthetic action

	Group L	Group LE
Time for maximal effect (min)	2.7 ± 1.5	4.6 ± 2.9
Duration of anesthetic action (min)	22.0 ± 10.5	33.5 ± 14.9*

\*:  $p < 0.05$ , compared with value obtained from Group L.

\*: Data are expressed as mean ± SD. (n=7)

is suggested that the significant increase in CCBF seen here was due to the effect of SGB in Group L.

Changes in CCBF are dependent on changes in blood flow in both ICA and external carotid artery (ECA). ICA blood flow should minimally change due to the autoregulatory mechanisms of cerebral blood flow. In contrast, ECA blood flow may change depending on degree of stimulation of  $\alpha$ - and  $\beta$ -adrenergic receptors, which innervate blood vessels of skin, mucosa ( $\alpha$ -adrenergic receptors dominant) and skeletal muscles ( $\beta$ -adrenergic receptors dominant)<sup>9</sup>. It is known that  $\alpha$ -adrenergic receptors are dominant in the vasculature of the head and neck region<sup>9</sup>. It is, therefore, suggested that CCBF in Group LE showed no increase due to no afterload reduction by the  $\alpha$ -adrenergic stimulating effects of epinephrine.

It is suggested that the increase in TMBF seen in Group L was a result of afterload reduction due to the sympatholytic effects of SGB, as  $\alpha$ -adrenergic receptors are dominant in tongue mucosa. In contrast, the constriction of the tongue mucosa blood vessels seen in Group LE may have been brought about by the  $\alpha$ -adrenergic stimulatory effect of epinephrine, resulting in cancellation of vasodilatation after SGB, with no subsequent increase in TMBF. It is possible that blood flow after SGB redistributes to the blood vessels in the skeletal muscles in which  $\beta$ -adrenergic receptors are dominant.

In this study,  $\text{ETCO}_2$ , HR, SB, DBP and MAP in both Groups L and LE showed no change after SGB. Therefore, changes in these variables may have only a minimal effect on CCBF and TMBF. Although time for

maximal effect showed no difference between the two groups, duration of anesthetic action was significantly longer in Group LE. This result is similar to that for the effect of epinephrine contained in local anesthetic solutions used in routine dental practice<sup>8</sup>.

Based on the above results, it is suggested that addition of epinephrine during SGB may extend duration of anesthetic action, but with no increase in TMBF. This may be due to cancellation of the vasodilatory effects of SGB by epinephrine. Therefore, it is suggested that the addition of epinephrine to local anesthetic solutions may not be suitable for SGB, especially in the treatment of skin and mucosal lesions. Because CO and muscular blood flow of head and neck region were not measured in this study, redistribution of blood flow remains to be clarified in further research.

In this study, 1% lidocaine was used in Group L because 1% lidocaine is a common local anesthetic for SGB in a clinical setting. In contrast, in Group LE, 1% lidocaine containing 10  $\mu\text{g}/\text{ml}$  epinephrine was used because it is commercially available as a 1% lidocaine solution. TMBF was expressed as a percentage of the control value in this study. Laser Doppler flowmetry shows blood flow data per 100 g of tissue. This is unrealistic for rabbit's tongue mucosa, and the reliability of the absolute values may be in question. Therefore, TMBF was expressed as a percentage of the control values.

In conclusion, it is suggested that the addition of epinephrine to local anesthetic solutions is not suitable for SGB as it may not facilitate an increase in tissue blood flow, which is the primary objective of SGB.

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