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Redistribution of tissue blood flow after stellate ganglion block in the rabbit

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Running head: Tissue blood flow and stellate ganglion block
Abstract

**Background and Objectives:** The goal of this study was to compare tissue blood flow at various sites before and after stellate ganglion block (SGB), and discuss the redistribution of tissue blood flow after SGB.

**Methods:** We utilized 16 male Japan White rabbits. For SGB, the tip of the 26-gauge needle was placed on the left transverse process of the cervical vertebra, 1-2 mm caudal to the cricoid cartilage. Either 0.2 ml of 1 % lidocaine (Lidocaine group) or normal saline solution (Saline group) was injected. In Lidocaine group, data were recorded immediately before SGB and at the time when the maximal change in common carotid artery blood flow (CCBF) was observed after SGB. In Saline group, data were recorded immediately before SGB and 3 minutes after SGB. Observed variables were blood pressure, heart rate, CCBF, tongue mucosal blood flow (TMBF), mandibular bone marrow blood flow (BBF), masseter muscle blood flow (MBF), quadriceps muscle blood flow (QBF), liver blood flow (LBF) and renal blood flow (RBF).

**Results:** CCBF, TMBF, BBF and MBF on the block side were increased whereas BBF and MBF on the non-block side, QBF, LBF and RBF were decreased after SGB in Lidocaine group.

**Conclusion:** These results indicate that lower limb and visceral blood flow as well as blood
flow on the non-block side are redistributed to the block side after SGB. In addition, redistribution from peripheral tissue may have more important role than that of visceral blood flow after SGB.

**Key Words:** Stellate ganglion block - Redistribution of tissue blood flow - Face - Lower limb - Viscera
**Introduction**

Stellate ganglion block (SGB) increases regional tissue blood flow in head, face, neck and upper limb depending on its sympatholytic effects. SGB is useful for the treatment of several disorders such as orofacial pain including postherpetic neuralgia.

It has been reported that an increase in regional tissue blood flow on the block side is attributable to the redistribution of that on the non-block side. Cerebral blood flow, and common carotid arterial blood flow (CCBF) and brachial arterial and venous blood flow were increased after SGB whereas those on the non-block side were decreased. Meanwhile, there is a report that facial skin blood flow was bilaterally increased after SGB. In addition, blood flow of celiac artery, which is not innervated by the cervical sympathetic fibers, was increased after SGB. It is assumed that there should be a region where tissue blood flow decreases to balance with increased blood flow on the block side after SGB because circulating blood volume is constant. This blood flow decrease might result in inadequate tissue oxygenation at these sites. However, the change of tissue blood flow distribution before and after SGB remains unknown.

In this study, therefore, we compared tissue blood flow before and after SGB, and discussed the redistribution of tissue blood flow after SGB. Targeted variables included CCBF,
tongue mucosal blood flow (TMBF), mandibular bone marrow blood flow (BBF), masseter muscle blood flow (MBF), quadriceps muscle blood flow (QBF), liver blood flow (LBF) and renal blood flow (RBF).
Methods

Sixteen male Japan White rabbits (2.2-2.7kg) were utilized. 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. The animals were randomly allocated in two groups: Lidocaine group (n=8) and Saline group (n=8).

Anesthesia was induced by inhalation of 4.0% isoflurane in oxygen delivered using a mask. Before skin incisions for each of the experimental procedures, appropriate doses of lidocaine were injected into the surgical field. A #20 Fr non-cuffed pediatric tracheal tube was inserted into the trachea through tracheostomy. The left auricular marginal vein and right femoral artery were cannulated with 22- and 20-gauge Teflon indwelling catheters, respectively. After intravenous acetated Ringer’s solution was started at 10 ml/kg/hr, the animals were paralyzed with 14 mcg/kg/min rocuronium bromide (Eslax, Schering-Plough, Tokyo) and mechanically ventilated. End-tidal partial pressure of carbon dioxide (ETCO2) was maintained at about 35mmHg. 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. 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. 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 to prevent blood flow disturbance in the tongue mucosa. Systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), HR, CCBF and TMBF were continuously recorded on a polygraph (Series360 NEC; Sanei, Tokyo).

After the skin incision along both left and right lower margins of the mandible without local anesthesia, the periosteum of the mandibular body was exposed. The periosteum was detached to expose the surface of the mandibular body on both sides. Two small holes (approximately 1 mm in diameter, one in the left side and the other in the right side) perforating into the bone marrow through the cortical bone were drilled with a round bar (ISO 008, Morita, Japan). Needle probes of a hydrogen clearance tissue blood flowmeter (UHE-100, Unique Medical, Japan) were inserted 3 mm deep into the left and right bone marrow to measure both left BBF (L-BBF) and right BBF (R-BBF), respectively. In addition, the fascia of the masseter muscle was detached to expose the masseter muscle on both sides. Two needle
probes of the hydrogen clearance tissue blood flowmeter were inserted 3mm deep into the left and right masseter muscle to measure left MBF (L-MBF) and right MBF (R-MBF), respectively. Then, after the skin incision along the left femoral region without local anesthesia, the quadriceps muscle was exposed. A needle probe of the hydrogen clearance tissue blood flowmeter was inserted 5mm deep into the center of the left quadriceps muscle to measure QBF. Furthermore, after midline laparotomy, two needle probes of the hydrogen clearance tissue blood flowmeter were inserted 5mm and 2mm deep into the right lobe of the liver just below xiphoid process of the sternum and the left renal cortex to measure LBF and RBF, respectively.

After completion of experimental preparations, isoflurane inhalation was discontinued. Then, inhalation of sevoflurane was started at 1.8% of end-tidal concentration and maintained at that level for more than 60 min to stabilize the hemodynamic and respiratory parameters. Sevoflurane 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.

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, either 0.2 ml of 1 % lidocaine (Lidocaine group) or 0.2 ml of normal saline solution (Saline group) was injected. In Lidocaine group, data were recorded immediately before SGB (Pre) and at the time when the maximal change in CCBF was observed after SGB (Post). In Saline group, data were recorded immediately before SGB (Pre) and 3 minutes after SGB (Post).

In this study, data were expressed as the mean ± standard deviation. The paired t-test was used for within-group comparisons and the unpaired t-test for between-group comparisons. P values less than 0.05 were considered statistically significant. All blood flow data in Lidocaine group were expressed as a percentage of the respective Pre value.
Results

Time for the maximal effect was 2.6 ± 0.2 min in Lidocaine group. There were no differences in respective Pre values between two groups. In Saline group, there were no differences between Pre and Post values for all observed variables. In contrast, in Lidocaine group, significant changes from Pre to Post values were observed in CCBF, TMBF, BBF, MBF, QBF, LBF and RBF. In addition, there were significant differences in respective Post values between two groups. (Table 1)

In Lidocaine group, Post values for CCBF, TMBF, L-BBF and L-MBF were significantly increased by 138%, 75%, 60% and 40% in comparison with Pre values, respectively. In contrast, Post values for R-BBF, R-MBF, QBF, LBF and RBF were significantly decreased by 40%, 38%, 34%, 9% and 13% in comparison with Pre values, respectively. (Fig. 1)
Discussion

This study showed that CCBF, TMBF, L-BBF and L-MBF were increased whereas R-BBF, R-MBF, QBF, LBF and RBF were decreased in Lidocaine group after SGB.

Stellate ganglion was confirmed by exposing cervical sympathetic nerve trunk in our preliminary study. When SGB was performed based on these results, CCBF was increased immediately after SGB in a reproducible manner. Consequently, SGB was performed by the technique written in the method session in this study.

In a previous study, minimum alveolar concentration (MAC) of sevoflurane is 1.5 to 1.8 times as high as that of isoflurane. Therefore, isoflurane was used for induction of anesthesia and experimental preparations in this study because isoflurane was able to induce anesthesia more smoothly than sevoflurane. Anesthesia was maintained with 1.8% sevoflurane throughout experiment. This concentration was equal to almost 0.5 MAC of sevoflurane in the rabbit. Sevoflurane has less sympatholytic effects than isoflurane and these effects occur at the level higher than 0.75 MAC of sevoflurane. Therefore, sevoflurane might minimally modify the sympatholytic effects of SGB.

In our pilot study, infusion rate of rocuronium bromide which provided stable muscular relaxation was 14 mcg/kg/min during inhalation of 1.8% sevoflurane. In addition,
based on a previous study\textsuperscript{8} and the results of our pilot study, Post values in Saline group were recorded 3 minutes after SGB. This was almost equal to the time for the maximal change in CCBF in Lidocaine group. Blood flow in the internal carotid artery (ICA) was increased after SGB with 2\% lidocaine.\textsuperscript{14} In cases of facial palsy, CCBF and blood flow of the facial nerve were increased after SGB with 1\% mepivacaine.\textsuperscript{15} CCBF and TMBF were significantly increased after SGB with 1\% lidocaine.\textsuperscript{8} Based on these reports, it is suggested that the significant increase in CCBF in this study was caused by the effect of SGB.

An increase in CCBF is dependent on an increase in cardiac output (CO). Increase in CO is supplied by an afterload (total peripheral resistance) reduction and increases in HR, cardiac contractility and/or preload (venous return). In this study, no change in HR was observed. In addition, cardiac contractility and venous return should not increase after SGB because of its sympatholytic effect. Therefore, it is suggested that significant increase in CCBF was attributable to CO increase through afterload reduction (vasodilatation). Although afterload decrease may induce hypotension, blood pressure was unchanged after SGB in this study. Tissue blood flow in the block side was increased because peripheral vascular resistance at head, neck and upper limb was decreased after SGB. In contrast, it was speculated that peripheral vascular resistance in other sites was increased because tissue blood flow in the non-block side
and lower limb were decreased. Therefore, total peripheral resistance might minimally change in this study. As a result, blood pressure should be unchanged throughout the experiment. This means that afterload decrease observed in this study was a regional phenomenon based on the effect of SGB.

Although changes in CCBF result from changes in the blood flow in both ICA and external carotid artery (ECA), ICA blood flow under normal condition should minimally change because of the autoregulatory mechanisms of cerebral blood flow. In contrast, ECA blood flow may change depending on the degree of activations of alpha- and beta-adrenergic receptors, which innervate blood vessels of skin and mucosa (alpha-adrenergic receptors dominant) and skeletal muscles (beta-adrenergic receptors dominant). Bone marrow blood flow may change depending on blood pressure. It is suggested that the increases in BBF, MBF and TMBF on the block side in LIDOCaine group resulted from afterload reduction caused by the sympatholytic effects of SGB. In this study, TMBF and L-MBF were significantly increased by 75% and 40% in comparison with respective Pre values in LIDOCaine group. Since alpha-adrenergic receptors dominantly exist in the vasculature in head and neck area, it may be reasonable that the increase in TMBF was more than that in L-MBF in this study.

It has been reported that the increase in blood flow on the block side is caused by
redistribution of that on the non-block side.\textsuperscript{4,5} However, in this study, QBF, LBF and RBF, which are out of the sympatholytic effects of SGB, as well as R-BBF and R-MBF on the non-block side were decreased. Therefore, it is suggested that the increase in blood flow on the block side is redistributed from not only the non-block side but also lower limb and viscera.

The blood flow of quadriceps muscle, well-vascularized liver and renal cortex\textsuperscript{17} were adopted as indicators that were not affected by the sympatholytic effects of SGB in this study. Quadriceps muscle can be a good indicator for the blood flow of muscular tissue like the masseter muscle. Similarly, liver and renal cortex can be good indicators for the blood flow of visceral organ. Biceps brachii muscle blood flow was decreased by 40% whereas liver and renal blood flow were decreased by 25% to 30% during deliberate hypotention with trinitroglycerine.\textsuperscript{18} Hindlimb blood flow was decreased by 60% whereas cerebral blood flow remained unchanged during deliberate hypotention with sodium nitroprusside.\textsuperscript{19} When the circulating blood volume is constant, there is a fundamental mechanism to control tissue blood flow in vital and non-vital organs as needed through the change of the vascular bed.\textsuperscript{20} However, the mechanism of blood flow redistribution is still unclear and to be investigated in future. Therefore, it is suggested that peripheral tissue blood flow decreased in a compensatory fashion to maintain vital organ blood flow. Similar to the previous reports,\textsuperscript{18,19} LBF and RBF
were less decreased in comparison with peripheral MBF, TMBF and QBF in this study. Renal blood flow was decreased by 40% during deliberate hypotention whereas this decrease never reached the critical level.\textsuperscript{21} Additionally, there are no reports of impaired liver function during deliberate hytotention in patients with normal liver function.\textsuperscript{22} In this study, changes in visceral blood flow after SGB might be of no clinical significance because the decrease in LBF and RBF were slight and blood pressure showed no major change. Based on the previous studies and the results of this study, it is suggested that blood flow in peripheral tissue such as lower limb has more important role on the increase in tissue blood flow after SGB in comparison with visceral blood flow.

In clinical situations, palm skin temperature at the block side was elevated while that at the non-block side was lowered following upper thoracic sympathetic ganglion block.\textsuperscript{23} In addition, when lumbar sympathetic ganglion block was performed to the patients with arteriosclerosis obliterans of lower limbs, blood flow on the non-block side was decreased.\textsuperscript{24} Therefore, it is suggested that blood flow redistribution to the block side from the non-block side and the other parts of the body after unilateral sympathetic ganglion block might cause “steal” phenomenon. Attention should be paid to patients undergoing SGB who have bilateral peripheral circulatory disorder such as arterial sclerosis.
There are some reports focusing on the effect of SGB on coronary hemodynamics. It is reported that SGB has deteriorative effects on the myocardial oxygen supply-demand relationship with normal coronary circulation in the dog. In that study, coronary artery blood flow was measured whereas myocardial oxygen consumption and oxygen extraction ratio were calculated. In addition, myocardial blood flow and tissue oxygen tension were not measured. Therefore, the effect of SGB on coronary hemodynamics still remains controversial and is to be investigated.

In conclusion, it is suggested that lower limb and visceral blood flow as well as the non-block side are redistributed to the block side after SGB. Peripheral tissue blood flow has more important role on the increase in tissue blood flow after SGB than visceral blood flow.
References


8) Terakawa Y, Handa M, Ichinohe T, Kaneko Y: Epinephrine in local anesthetic cancels increase in tongue mucosal blood flow after stellate ganglion block in rabbit. Bull Tokyo Dent


## Tables

### Table 1  Hemodynamic variables and blood flow data

<table>
<thead>
<tr>
<th>Variable</th>
<th>Saline group</th>
<th>Lidocaine group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>268.1 ± 17.7</td>
<td>265.9 ± 17.1</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>119.9 ± 11.7</td>
<td>121.8 ± 10.9</td>
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<tr>
<td>DBP (mmHg)</td>
<td>63.8 ± 10.3</td>
<td>64.4 ± 10.2</td>
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<tr>
<td>MAP (mmHg)</td>
<td>81.3 ± 12.2</td>
<td>80.6 ± 12.9</td>
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<tr>
<td>CCBF (ml/min)</td>
<td>21.8 ± 5.5</td>
<td>21.1 ± 5.7</td>
</tr>
<tr>
<td>TMBF (ml/min/100g)</td>
<td>23.6 ± 4.4</td>
<td>22.9 ± 3.9</td>
</tr>
<tr>
<td>L-BBF (ml/min/100g)</td>
<td>41.3 ± 5.2</td>
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<tr>
<td>R-BBF (ml/min/100g)</td>
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<td>49.9 ± 11.5</td>
</tr>
<tr>
<td>L-MBF (ml/min/100g)</td>
<td>48.9 ± 6.8</td>
<td>47.3 ± 7.0</td>
</tr>
<tr>
<td>R-MBF (ml/min/100g)</td>
<td>47.3 ± 8.6</td>
<td>48.3 ± 9.0</td>
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<tr>
<td>QBF (ml/min/100g)</td>
<td>60.6 ± 14.8</td>
<td>63.7 ± 11.2</td>
</tr>
<tr>
<td>LBF (ml/min/100g)</td>
<td>80.9 ± 10.7</td>
<td>83.7 ± 8.7</td>
</tr>
<tr>
<td>RBF (ml/min/100g)</td>
<td>167.6 ± 19.6</td>
<td>168.7 ± 18.8</td>
</tr>
</tbody>
</table>
HR: heart rate; SBP: systolic blood pressure; DBP: diastolic blood pressure; MAP: mean arterial pressure; CCBF: common carotid artery blood flow; TMBF: tongue mucosal blood flow; BBF: mandibular bone marrow blood flow; MBF: masseter muscle blood flow; QBF: quadriceps muscle blood flow; LBF: liver blood flow; RBF: renal blood flow

L: left side; R: right side

Pre: immediately before SGB

Post: at the time when maximal change in CCBF was observed after SGB (Lidocaine group) or 3 minutes after SGB (Saline group)

mean ± standard deviation (n=8)

*p<0.05 vs Pre

#p<0.05 between two groups
Legends for figures

Fig. 1  Changes in tissue blood flow in the Lidocaine group.

Data were expressed as the percentage of respective Pre value in the Lidocaine group.

CCBF: common carotid artery blood flow; TMBF: tongue mucosal blood flow; BBF: mandibular bone marrow blood flow; MBF: masseter muscle blood flow; QBF: quadriceps muscle blood flow; LBF: liver blood flow; RBF: renal blood flow

L: left side; R: right side

Pre: immediately before SGB

Post: at the time when maximal change in CCBF was observed after SGB (Lidocaine group) or 3 minutes after SGB (Saline group)

mean ± standard deviation (n=8)
Fig. 1