Title

Unilateral stellate ganglion block produces bidirectional changes in tissue oxygen tension of the mental nerve in rabbits.

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Journal


URL

http://hdl.handle.net/10130/2536
Abstract

Purpose: The purpose of this study was to investigate the changes in tissue oxygen tension of the mental nerve (PO$_2$) in both sides before and after unilateral stellate ganglion block (SGB).

Materials and Methods: We used nine male Japan White rabbits. Anesthesia was maintained by continuous infusion of propofol under mechanical ventilation with room air. For SGB, the tip of the 26-gauge needle was placed on the left transverse process of the cervical vertebra. Zero point two milliliter of 1 % lidocaine solution was injected. Data were recorded immediately before SGB and at the time when the maximal change in PO$_2$ was observed after SGB. Observed variables were heart rate, blood pressure, common carotid arterial blood flow (CCBF), tongue mucosal blood flow (TMBF), left PO$_2$ (L-PO$_2$) and right PO$_2$ (R-PO$_2$).

Results: PO$_2$ showed maximal changes 7.9 ± 2.0 min after SGB. No changes were observed in heart rate and blood pressure after SGB. CCBF, TMBF and L-PO$_2$ were increased by 106.4 ± 39.8 %, 36.2 ± 35.2 % and 38.7 ± 19.8 % after SGB, respectively. In contrast, R-PO$_2$ was reduced by 29.8 ± 7.4 % after SGB.

Conclusion: These results suggest that unilateral SGB produces bidirectional changes in tissue oxygen tension of the mental nerve. SGB reduces tissue oxygen tension of the mental nerve on the contralateral side.
Introduction

Stellate ganglion block (SGB) increases tissue blood flow in head, face, neck and upper limb based on its sympatholytic effects.¹ SGB has been applied for several kinds of disorders including traumatic trigeminal neuropathy,²,³ postherpetic neuralgia⁴, facial nerve paralysis,⁵ or progressive facial hemiatrophy.⁶,⁷

Some studies have reported that an increase in tissue blood flow on the ipsilateral side is attributable to the redistribution of that from the contralateral side.⁸,⁹ Recently, Terakawa et al.¹⁰ have showed that SGB increases mandibular bone marrow blood flow and masseter muscle blood flow on the ipsilateral side, while SGB reduces those on the contralateral side through redistribution mechanisms. It is therefore suggested that tissue blood flow in the mental nerve on the contralateral side also reduces after SGB. If nerve tissue blood flow reduces, consequential reduction in oxygen supply to nerve tissue, which might be followed by possible disturbances of nerve functions, may occur. However, it is difficult to directly measure tissue blood flow of the mental nerve because nutrient vessels are quite small and most of them are on the surface of the nerve. Since there is a positive correlation between tissue blood flow and tissue oxygen tension (PO₂) and changes in PO₂ reflect changes in tissue blood flow,¹¹ PO₂ may be a good index of tissue blood flow in the mental nerve.
The purpose of this study was therefore to investigate the changes in PO₂ of the mental nerve in both sides before and after unilateral SGB.
Materials and Methods

This study was performed according to The Guidelines for the Treatment of Experimental Animals of the Tokyo Dental College. Nine male Japanese White rabbits (2.5kg) were studied (Sankyo Labo, Tokyo, Japan). All animals were allowed food and water *ad libitum* until the morning of the experiment.

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 1% lidocaine solution (Xylocaine®, Dentsply, Tokyo, Japan) 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⁻¹·hr⁻¹, muscle relaxation was achieved with 14 μg·kg⁻¹·min⁻¹ rocuronium bromide (Eslax; Schering-Plough, Tokyo, Japan). The lungs were mechanically ventilated to maintain end-tidal partial pressure of carbon dioxide (ETCO₂) at approximately 35mmHg. ETCO₂ was continuously monitored with an anesthetic gas monitor (Capnmac; Datex, Helsinki, Finland). Femoral artery blood pressure was continuously monitored with a pressure transducer (P231D; Gould, Oxnard, California, USA). Heart rate (HR) was counted
from pressure pulse wave. A flow probe (type 3SB) of an ultrasound flowmeter (TS420; Transonic, Ithaca, NY, USA) was placed at the isolated left common carotid artery to measure common carotid arterial blood flow (CCBF). Tongue mucosal blood flow (TMBF) was measured with a laser Doppler flowmeter (ALF21; Unique Medical, Tokyo, Japan). 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. To expose bilateral mental nerves, skin incisions along both left and right lower margins of the mandible were performed without local anesthesia to prevent tissue blood flow change by lidocaine. A polarographic needle electrode (IPS-020; Inter medical, Aichi, Japan) was inserted into each of the left and right isolated mental nerves and fixed to measure both left PO₂ (L-PO₂) and right PO₂ (R-PO₂), respectively. PO₂ was measured with a PO₂ monitor (PO₂-100DW; Inter Medical, Aichi, Japan). Systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), HR, CCBF, TMBF, L-PO₂ and R-PO₂ were continuously recorded on a polygraph (Polygraph series360; NEC San-ei, Tokyo, Japan).

Following completion of preparations for the experiments, inhalation of isoflurane was discontinued. Then, anesthesia was maintained by continuous infusion of propofol at rate
of 12 mg·kg⁻¹·hr⁻¹ under mechanical ventilation with room air. 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 baseline measurements were obtained when hemodynamic and respiratory stability was established one hour or more after completion of surgical preparation.

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, 0.2 mL of 1 % lidocaine was injected. Data were recorded immediately before SGB and at the time when the maximal change in PO2 was observed after SGB.

In this study, data were presented as mean ± SD. The Wilcoxon t-test was used for comparisons between respective values before and after SGB. The Mann-Whitney U-test was used for comparisons between L-PO2 and R-PO2 values. P values less than 0.05 were considered statistically significant. Tissue blood flow and PO2 data were expressed as a percentage of the respective value before SGB.
Results

PO$_2$ showed maximal changes 7.9 ± 2.0 min after SGB. No changes were observed in HR, SBP, DBP and MAP after SGB. There were no differences in PO$_2$ values on both sides before SGB. CCBF, TMBF, L-PO$_2$ and R-PO$_2$ showed significant changes after SGB (Table 1). CCBF, TMBF and L-PO$_2$ were increased by 106.4 ± 39.8%, 36.2 ± 35.2% and 38.7 ± 19.8% after SGB, respectively. In contrast, R-PO$_2$ was reduced by 29.8 ± 7.4% after SGB (Fig. 1).
Discussion

SGB has been widely used for the treatment of nerve dysfunctions such as trigeminal neuropathy or facial nerve paralysis because SGB increases tissue blood flow based on its sympatholytic effects. SGB is also able to improve sympathetically maintained pain including complex regional pain syndrome or postherpetic neuralgia. In addition, it is reported that SGB is effective to prevent the development of progressive facial hemiatrophy caused by a putative mechanism of local sympathetic hyperactivity. Thus, SGB may be available for several disorders on the ipsilateral side attributable to nerve dysfunctions. However, little is known about the effects of SGB on the contralateral side.

Unilateral SGB produces bidirectional changes in tissue oxygen tension of the mental nerve. SGB reduces tissue oxygen tension of the mental nerve on the contralateral side. It is reported that tissue blood flow in the masseter muscle on the ipsilateral side and contralateral side were increased by about 40% and reduced by about 38%, respectively, after SGB. Changes in PO2 observed in this study were similar with those in tissue blood flow in the masseter muscle. It is therefore suggested that tissue blood flow in the mental nerve may increase on the ipsilateral side and reduce on the contralateral side.

In this study, SGB was performed by the same technique with that in previous
studies.\textsuperscript{10-12} In those studies, CCBF and TMBF were increased immediately after SGB with 1% lidocaine solution.\textsuperscript{10-12} The time for the maximal change in CCBF was approximately 2.6 minutes.\textsuperscript{10} In this study, time for the maximal change in PO\textsubscript{2} was 7.9 ± 2.0 min. It is therefore suggested that there is time-lag for maximal PO\textsubscript{2} changes during tissue blood flow change after SGB.

We used isoflurane for induction of anesthesia and experimental preparations. Isoflurane was able to induce anesthesia more smoothly than sevoflurane,\textsuperscript{10-13} and was able to give a sufficient anesthesia under surgical preparations in rabbit experiments. Anesthesia was maintained with propofol and room air throughout the experiment. Tissue oxygen tension should increase under 100% oxygen in comparison with room air. Because PO\textsubscript{2} changes after SGB may be smaller under such a condition, misunderstanding of the results might happen. Continuous infusion of propofol at a rate of 12 mg·kg\textsuperscript{-1}·hr\textsuperscript{-1} is based on the blood concentration of propofol at Cp\textsubscript{50} skin incision.\textsuperscript{14,15} Stable muscle relaxation was achieved with 14 μg·kg\textsuperscript{-1}·min\textsuperscript{-1} rocuronium bromide in rabbit experiments.\textsuperscript{10,11,16} To expose bilateral mental nerves, skin incisions were performed without local anesthesia to prevent tissue blood flow change by lidocaine. These surgical procedures themselves might influence tissue blood flow though similarly on each side. However, these procedures were essential to precisely place the
needle electrodes at the mental nerves.

PO₂ but not tissue blood flow in the mental nerve was observed in this study. Common methods to observe tissue blood flow include hydrogen clearance tissue blood flowmetry,¹⁷ microsphere injection technique,¹⁸,¹⁹ thermal diffusion flowmetry²⁰ and laser Doppler flowmetry.²¹ Hydrogen clearance tissue blood flowmetry and microsphere injection technique are able to measure absolute values, but do not allow continuous monitoring of tissue blood flow. In contrast, thermal diffusion flowmetry allows continuous monitoring of tissue blood flow, but does not be able to measure absolute values. However, these methods could not be applied to measure blood flow of the mental nerve in this study because nutrient vessels are quite small and most of them are on the surface of the nerve. Laser Doppler flowmetry is suitable for continuous monitoring of blood flow at tissue surface. However, since the diameter of isolated mental nerve was very small, Laser Doppler flowmetry also could not be applied. Therefore, we monitored PO₂ as an index of tissue blood flow in the mental nerve. PO₂ is continuously measurable¹¹ and the diameter of a needle electrode for PO₂ measurement was only 0.2 mm and minimally invasive to the nerve tissue.

PO₂ reduction in the mental nerve on the contralateral side after SGB may disturb nerve functions including generation and transmission of nerve impulses. These effects might
be of clinical importance in peripheral circulatory disorders such as diabetes mellitus and arteriosclerosis. It is reported that peripheral nerve function is influenced by tissue hypoxia and improving tissue oxygenation by bypass surgery can improve nerve conduction velocity of the peroneal nerve in diabetic patients. In this study, however, the duration of PO₂ reduction was not observed. Both magnitude and duration of PO₂ reduction are important factors affecting nerve functions. Further study is needed to clarify the clinical importance of PO₂ reduction on the contralateral side after SGB on nerve functions.

In conclusion, unilateral SGB produces bidirectional changes in tissue oxygen tension of the mental nerve. SGB reduces tissue oxygen tension of the mental nerve on the contralateral side.
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### Table 1  Changes in heart rate, blood pressure, tissue blood flow and tissue oxygen tension

<table>
<thead>
<tr>
<th></th>
<th>Before SGB</th>
<th>After SGB</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HR (bpm)</strong></td>
<td>284.7 ± 26.0</td>
<td>284.7 ± 26.8</td>
</tr>
<tr>
<td><strong>SBP (mmHg)</strong></td>
<td>140.9 ± 17.0</td>
<td>143.4 ± 16.2</td>
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<tr>
<td><strong>DBP (mmHg)</strong></td>
<td>71.7 ± 13.2</td>
<td>72.2 ± 15.2</td>
</tr>
<tr>
<td><strong>MAP (mmHg)</strong></td>
<td>98.3 ± 12.7</td>
<td>100.7 ± 13.9</td>
</tr>
<tr>
<td><strong>CCBF (mL/min)</strong></td>
<td>24.7 ± 9.4</td>
<td>49.9 ± 18.0 *</td>
</tr>
<tr>
<td><strong>TMBF (mL/min/100g)</strong></td>
<td>24.8 ± 5.6</td>
<td>33.3 ± 8.3 *</td>
</tr>
<tr>
<td><strong>L-PO₂ (mmHg)</strong></td>
<td>21.2 ± 7.3</td>
<td>28.3 ± 6.9 *#</td>
</tr>
<tr>
<td><strong>R-PO₂ (mmHg)</strong></td>
<td>22.2 ± 7.5</td>
<td>15.9 ± 6.6 *#</td>
</tr>
</tbody>
</table>

HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; CCBF, common carotid arterial blood flow; TMBF, tongue mucosal blood flow; PO₂, tissue oxygen tension of the mental nerve; L, left side; R, right side

Values are presented as mean ± SD (n=9)

* p < 0.05 versus “Before SGB”  # p < 0.05 between L-PO₂ and R-PO₂
Figure legend

Fig. 1 Changes in tissue blood flow and tissue oxygen tension. CCBF, TMBF and L-PO$_2$ were increased by 106.4 ± 39.8%, 36.2 ± 35.2% and 38.7 ± 19.8% after SGB, respectively. R-PO$_2$ was reduced by 29.8 ± 7.4% after SGB.

Data were expressed as a percentage of respective values before SGB.

CCBF, common carotid artery blood flow; TMBF, tongue mucosal blood flow; PO$_2$, tissue oxygen tension of mental nerve; L, left side; R, right side

mean ± SD (n=9)