Effects of Bilateral Stellate Ganglion Block on Autonomic Cardiovascular Regulation

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Background: Stellate ganglion block (SGB) is performed for the diagnosis and treatment of sympathetic dependent pain in the head, neck and upper limbs. However, the effects of bilateral SGB on cardiovascular and autonomic regulation remain unknown. The aim of this study was to assess the effects of bilateral SGB on cardiovascular and autonomic function by measuring heart rate variability (HRV), systolic blood pressure variability (SBPV) and spontaneous baroreflex sensitivity (SBRS).

Methods and Results: Twenty healthy volunteers were randomly allocated to receive right or left SGB with 8 ml 1% lidocaine solution; after 20 min, the contralateral side SGB was performed. Changes in the RR interval (RRI), systolic blood pressure (SBP), HRV, SBPV and SBRS were assessed before and after bilateral SGB. The low-frequency (LF, 0.04–0.15 Hz) and high-frequency (HF, 0.15–0.4 Hz) components of HRV and SBRS decreased significantly; however, no significant changes were found in RRI, SBP and the LF and HF components of SBPV after bilateral SGB. In subjects with symptoms of vagal blockade, HRV, SBP and SBRS were significantly affected by bilateral SGB.

Conclusions: Bilateral SGB should be performed cautiously because it can reduce cardiac vagal modulation and BRS, especially for those with symptoms of vagal blockade after bilateral SGB. (Circ J 2009; 73: 1909–1913)

Key Words: Bilateral stellate ganglion block; Heart rate variability; Spontaneous baroreflex sensitivity

The autonomic nervous system is an essential part of the regulatory system involved in maintaining circulatory stability. Cardiac vagal function is an important control mechanism for short-term homeostasis of heart rate (HR) and arterial blood pressure (ABP) in humans.1 Previous reports have shown that autonomic dysfunction, such as low baroreflex sensitivity (BRS) or low HR variability (HRV), is associated with an increased prevalence of cardiac dysrhythmias or sudden cardiac death after myocardial infarction.2–4 Moreover, reduced BRS and HRV have been shown in patients with diabetes mellitus, hypertension or congestive heart failure.5–8

Stellate ganglion block (SGB) is used for the diagnosis and treatment of sympathetic dependent pain and circulatory insufficiency in the head, neck and upper limbs; this is because stellate ganglia are the main sources of sympathetic fibers that distribute to the upper extremities and face.9 However, the effects of SGB on cardiovascular and autonomic regulation remain controversial.10–13 Moreover, the effects of bilateral SGB on cardiovascular and autonomic regulation are unknown.

This study aimed to assess the effects of bilateral SGB on cardiovascular and autonomic function, as measured by HRV, systolic blood pressure variability (SBPV) and spontaneous baroreflex sensitivity (SBRS).

Methods

Subjects
The study involved 20 healthy volunteers (12 men and 8 women) with a mean age of 27.3 years (range, 21–33 years). During preliminary screening, each subject completed a medical history questionnaire and underwent electrocardiogram (ECG) and auscultatory blood pressure assessments. All subjects were normotensive, nondiabetic, had no history of autonomic dysfunction or cardiovascular disease, and were receiving no medication. All female subjects who participated in the study had a negative pregnancy test before initiation of the study. The study was approved by the Institutional Review Board for the Protection of Human Subjects at the Asan Medical Center, University of Ulsan, and all subjects provided written, informed consent. Subjects were instructed to abstain from alcoholic beverages and heavy exercise for at least 24 h, from caffeine for at least 12 h and food for 2 h before the assessments.

Measurements
Subjects were placed in the supine position and a venous
catheter was inserted into the right cephalic vein in case of emergency. A standard ECG was used for noninvasive, continuous measurement of HR (Hewlett-Packard 78352A) and beat-to-beat ABP was estimated directly from the radial artery by tonometry (CBM-7000, Colin). Calibration procedures were performed using the sphygmomanometric cuff of an oscillometric ABP recording device attached to the upper arm before and after intervention. Previous results have indicated a close correlation between tonographic and direct ABP measurements.14–16 Each subject underwent identical assessments before and after each SGB procedure. Beat-to-beat ECG and ABP signals were digitized and collected at a rate of 500 samples/s using an online personal computer interfaced with an analog-to-digital converter (DI-720U, Dataq instruments). Offline analysis was performed using signal processing software (CODAS, Dataq instruments; DADiSP, DSP Development, MATLAB 6.0, MathWorks, Nevrokard).

### Protocol

The subjects were encouraged to stay relaxed throughout the testing. After 20 min of rest, baseline values of HR, ABP and end-tidal CO$_2$ (ETCO$_2$) were recorded continuously for 5 min with controlled frequency breathing (15 breaths/min, or 0.25 Hz). Each subject synchronized their breathing with a computer-controlled voice that signaled the beginning and end of each inspiration and expiration, at an inspiratory–expiratory ratio of 1:1. During paced breathing, the subjects were instructed to keep their eyes open and not to force their breathing, to prevent hyperventilation. After baseline values of HR, ABP and ETCO$_2$ were recorded, patients were randomly assigned to the right (n=10) and left SGB (n=10) groups, and SGB procedures were performed. After 20 min of unilateral SGB, contralateral-side SGB was performed if there was no dyspnea. After 20 min of bilateral SGB, HR, ABP and ETCO$_2$ values were recorded.

### Stellate Ganglion Blockade

SGB was performed with 8 ml of 1% lidocaine solution using a 24-gauge needle and a paratracheal anterior approach aimed at the transverse process C6. All SGB procedures were performed by the same anesthesiologist. The efficacy of blockade was confirmed by the appearance of Horner’s sign and changes in skin temperature on the ipsilateral upper extremity.

### Data Management

The RR interval (RRI) was calculated from the time difference between marks placed on the peaks of the R waves. Systolic blood pressure (SBP) was calculated from the maximum and minimum of the beat-to-beat pressure waveform.

Frequency-domain analysis of variability was performed on beat-to-beat RRI and beat-to-beat SBP measurements using a power spectrum analysis technique based on the Welch periodogram averaging algorithm. Briefly, to obtain equidistant time intervals, a 300-s time series of beat-to-beat RRI and arterial pressure free from ectopic beats was interpolated at 5 Hz. Each time series was divided into 5 equal segments of 100 s each, overlapping by 50 s, following which each was detrended, Hanning filtered and fast Fourier transformed to its frequency representation of HRV, SBPV. This method yields a frequency resolution of 0.01 Hz. The resulting five periodograms were averaged to produce the estimated spectrum. The areas under power spectra in the low-frequency (LF) and high-frequency (HF) regions (defined as 0.04–0.15 and 0.15–0.40 Hz, respectively) were integrated and used for statistical comparisons.

To evaluate the effects of SGB on the baroreflex functions, the transfer function gain, phase and coherence (the squared coherence function) between SBP and RRI were estimated using the cross-spectral method.17,18 A coherence function greater than 0.5 (range, 0–1), indicates that the transfer function gain and phase function are statistically reliable estimates between the 2 signals. A negative phase indicates that changes in input (SBP) precede changes in output (RRI), whereas a positive phase indicates the converse. It has been proposed that, if the coherence is greater than 0.5 and the phase shift is negative, the transfer function gain can be used as an index of SBRS. We separately calculated the transfer function gain between HRV and SBPV as an index of BRS in the LF and HF regions, where coherence is greater than 0.5.

### Statistical Analysis

All data are presented as mean ± SD. The effects of SGB were assessed using the Student’s paired t-test or Wilcoxon signed rank test. The distributions of the HF and LF components of HRV were skewed, so the data were analyzed after a natural logarithmic transformation. Pearson product–moment correlation analysis was used to assess significant correlations between the variables. P<0.05 was considered statistically significant.

### Results

All patients developed Horner’s sign and changes in skin temperature on the ipsilateral upper extremities within 10 min of injection of the local anesthetic. However, one volunteer (a woman aged 30 years) experienced mild dyspnea and severe dizziness after undergoing bilateral SGB. Therefore, she was excluded from further assessment, even though she recovered completely after 20 min.

There were no significant changes in RRI or SBP after bilateral SGB (Table 1). The LF and HF components of HRV decreased significantly; from 5.9±0.8 to 5.4±1.0 natural logarithm (Ln) ms$^2$ for the LF component (P=0.018), and from 6.0±0.8 to 5.3±1.1 Ln ms$^2$ (P=0.014) for the HF component (Figure). The LF and HF components of SBRS also decreased significantly after bilateral SGB (SBRS_LF: 17.7±8.1 to 11.5±5.0 ms/mmHg, P=0.006; SBRS_HF: 24.1±15.1 to 8.3±7.3 ms/mmHg, P=0.007).

### Table 1. Effects of Bilateral SGB on Autonomic and Baroreflex Sensitivity

<table>
<thead>
<tr>
<th></th>
<th>Baseline (n=19)</th>
<th>Bilateral SGB</th>
<th>P-value</th>
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</thead>
<tbody>
<tr>
<td>RRI, ms</td>
<td>835.6±101.2</td>
<td>808.8±82.7</td>
<td>0.175</td>
</tr>
<tr>
<td>SBP, mmHg</td>
<td>118.7±19.2</td>
<td>126.6±18.4</td>
<td>0.069</td>
</tr>
<tr>
<td>HRV_Lf, Ln ms$^2$</td>
<td>5.9±0.8</td>
<td>5.4±1.0*</td>
<td>0.018</td>
</tr>
<tr>
<td>HRV_Hf, Ln ms$^2$</td>
<td>6.0±0.8</td>
<td>5.3±1.1*</td>
<td>0.014</td>
</tr>
<tr>
<td>SBPV_Lf, mmHg$^2$</td>
<td>2.4±2.1</td>
<td>3.0±3.4</td>
<td>0.51</td>
</tr>
<tr>
<td>SBPV_Hf, mmHg$^2$</td>
<td>1.3±1.2</td>
<td>1.2±1.1</td>
<td>0.46</td>
</tr>
<tr>
<td>SBRS_Lf, ms/mmHg</td>
<td>17.7±8.1</td>
<td>11.5±5.0*</td>
<td>0.006</td>
</tr>
<tr>
<td>SBRS_Hf, ms/mmHg</td>
<td>24.1±15.1</td>
<td>16.6±7.3*</td>
<td>0.045</td>
</tr>
</tbody>
</table>

All values are shown as mean±SD. *P<0.05 compared with baseline.

SGB, stellate ganglion block; RRI, RR interval; SBP, systolic blood pressure; HRV, heart rate variability; LF, low frequency; HF, high frequency; SBPV, systolic blood pressure variability; SBRS, spontaneous baroreflex sensitivity.
Effects of Bilateral Stellate Ganglion Block

16.6±7.3 ms/mmHg, P=0.045; **Figure, Table 1**.

We found that some subjects experienced symptoms of hoarseness and foreign body sensation due to vagal blockade. Hence, the patients were divided into two groups based on whether they experienced vagal blockade symptoms or not. In the group without symptoms (n=11), HRV, SBPV and SBRs were not affected by bilateral SGB (**Table 2**). However, in the group with symptoms (n=8), the LF and HF components of HRV decreased significantly after bilateral SGB, from 6.1±0.7 to 5.0±1.0 ln ms² (P<0.01) for the LF

**Table 2. Effects of Bilateral SGB on Autonomic and Baroreflex Sensitivity in the Subjects Without Symptoms of Vagal Blockade**

<table>
<thead>
<tr>
<th></th>
<th>Baseline (n=11)</th>
<th>Bilateral SGB</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RRI, ms</td>
<td>802±78.5</td>
<td>811.6±96.8</td>
<td>0.440</td>
</tr>
<tr>
<td>SBP, mmHg</td>
<td>128±17.8</td>
<td>132±21.2</td>
<td>0.597</td>
</tr>
<tr>
<td>HRV, Ln ms²</td>
<td>5.8±0.8</td>
<td>5.7±1.0</td>
<td>0.884</td>
</tr>
<tr>
<td>SBPV, Ln ms²</td>
<td>5.8±0.9</td>
<td>6.6±1.0</td>
<td>0.593</td>
</tr>
<tr>
<td>SBRS, ms/mmHg</td>
<td>2.8±2.1</td>
<td>4.3±3.9</td>
<td>0.089</td>
</tr>
</tbody>
</table>

**Table 3. Effects of Bilateral SGB on Autonomic and Baroreflex Sensitivity in the Subjects With Symptoms of Vagal Blockade**

<table>
<thead>
<tr>
<th></th>
<th>Baseline (n=8)</th>
<th>Bilateral SGB</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RRI, ms</td>
<td>881.6±115.6</td>
<td>804.9±64.4</td>
<td>0.074</td>
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<tr>
<td>SBP, mmHg</td>
<td>104.9±10.7</td>
<td>118±10.3*</td>
<td>0.003</td>
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<tr>
<td>HRV, Ln ms²</td>
<td>6.1±0.7</td>
<td>5.0±1.0*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SBPV, Ln ms²</td>
<td>6.3±0.6</td>
<td>4.9±1.2*</td>
<td>0.003</td>
</tr>
<tr>
<td>SBRS, ms/mmHg</td>
<td>1.8±2.0</td>
<td>1.3±1.2</td>
<td>0.318</td>
</tr>
<tr>
<td>SBRS, ms/mmHg</td>
<td>22.9±9.5</td>
<td>11.7±4.3*</td>
<td>0.02</td>
</tr>
</tbody>
</table>

All values are shown as mean±SD. Abbreviations see in Table 1.
component, and from 6.3±0.6 to 4.9±1.2 Ln ms² (P=0.003) for the HF component. Moreover, the LF and HF components of SBRs also decreased significantly (SBRs_LF: 22.9±9.5 to 11.7±4.3 ms/mmHg, P=0.02, SBRs_HF: 33.1±17.5 to 15.2±6.8 ms/mmHg, P=0.008); however, there were no significant changes in the LF and HF components of SBPV (Table 3).

Discussion
We have shown that the LF and HF components of HRV and SBRs decreased significantly after bilateral SGB, but there were no marked changes in the LF and HF components of SBPV, RRI and ABP. In the subjects without symptoms of vagal blockade, HRV, SBPV and SBRs were not affected by bilateral SGB; however, in those with symptoms of vagal blockade, the LF and HF components of HRV and SBRs were significantly affected. We therefore suggest that vagal blockade contributes to decreased cardiac vagal tone and BRS after bilateral SGB.

We have also found that sympathetic neural outflow to the skeletal muscle via the tibial nerve was markedly activated during the head-up tilt test in humans. 

Transfer function analysis has been used extensively to evaluate dynamic baroreflex control of HR, allowing the assessment of baroreflex gain without the use of vasoactive drugs.17 Power spectral analysis of the HRV components allows separate estimation of the sympathetic and parasympathetic effects on the heart and allows quantitative analysis of cardiac sympathovagal tone.18–20

SGB has been widely used to treat sympathetically maintained pain, vascular disease and complex regional pain syndrome involving the face and upper arms.21,22 Also, unilateral SGB may be effective in severe chronic refractory angina and prolonged QT-syndrome, which is an electrophysiological disorder.23–25 One report has also described the use of bilateral cervico-thoracic sympathetic ganglionectomy to treat disabling symptoms due to refractory ventricular tachycardia.26 However, the effects of SGB on cardiovascular regulation remain controversial.10,12,13,28

Our results do not reveal the exact mechanisms underlying changes in cardiovascular and autonomic regulation; however, we presume that these alterations might be due, at least in part, to blockade of arterial and cardiopulmonary baroreceptors by local anesthetic agents. Fujiki et al evaluated the effects of unilateral SGB on autonomic neural control of the heart by transfer function analysis.13 They suggested a right-side predominance of autonomic nerve innervation of the sinus node because pharmacological blockade of the right stellate ganglion reduced both the sympathetic and parasympathetic activities. Koyama et al demonstrated that right SGB might suppress not only cardiac sympathetic activity but also parasympathetic function without significantly affecting blood pressure using the head-up tilt test in humans.9

By contrast, other studies have shown that SGB can affect the peripheral sympathetic nervous system. Fagius et al, demonstrated that unilateral lidocaine blockade of glossopharyngeal and vagal fibers from baroreceptors in the human neck resulted in marked increases in muscle sympathetic nerve activity (MSNA) and blood pressure.29 Ikeda et al also found that sympathetic neural outflow to the skeletal muscle via the tibial nerve was markedly activated during left SGB, indicating blockade of vagal fibers from arterial baroreceptors in the aortic arch by local anesthetics.30 We did not assess the effects of bilateral SGB on MSNA; however, we measured the LF component of SBPV to estimate the peripheral sympathetic vasomotor tone because the LF component of SBPV is closely linked to vascular sympathetic outflow.31–35 In contrast to previous reports, our data showed that the LF component of SBPV did not change after bilateral SGB.29,30 Further investigation is needed to clarify the SGB-induced changes in peripheral sympathetic vasomotor tone.

In our study, there were no significant changes in RRI or SBP after bilateral SGB. In particular, in subjects without symptoms of vagal blockade, HRV, SBPV and SBRs were not affected, indicating that bilateral SGB without vagal blockade did not affect cardiac vagal modulation and BRS. By contrast, in the subjects with symptoms of vagal blockade, HRV, SBRs and SBP changed significantly. These results indicate that suppression of carotid arterial and cardiopulmonary baroreceptors caused by local anesthetics might reduce vagal modulation, which contributes to decreased cardiac vagal tone and BRS after bilateral SGB. Our results also showed an increase in SBP after bilateral SGB. Although we cannot explain the exact mechanism, we speculate that the attenuation of the baroreceptors might result in increase of SBP.

There are some potential limitations of the present study that should be addressed. First, although SGB was performed by a specialist pain clinician, the subjects might have experienced anxiety and pain during the SGB procedure. We therefore measured the RRI, SBPV, SBRs and HRV in the sham group (n=6) who underwent SGB with 0.9% normal saline 8 ml. There were no significant changes in each variable between those who underwent SGB with lidocaine and those who underwent the sham procedure. Second, although the stellate ganglia are the main sources of cardiac efferent sympathetic fibers, the second to the fifth thoracic ganglia can also be sources of cardiac sympathetic fibers.31,36 Therefore, although Horner’s signs were observed after SGB, sympathetic innervation may not be totally interrupted by SGB using 8 ml of 1% lidocaine in each subject. Although the present study has certain limitations, we believe that our results provide insights into the autonomic modulation of human HRV through bilateral SGB.

In conclusion, bilateral SGB should be performed cautiously because it can reduce cardiac vagal modulation and BRS. Therefore, care should be taken in patients with cardiovascular disease, especially for those with symptoms of vagal blockade after bilateral SGB.

Reference