Original Article

The effect of stellate ganglion block on sleeping in patients with intractable insomnia: cases report with successful treatment outcome

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Abstract: Insomnia presents to primary care clinicians as problems in sleep onset, sleep maintenance, non-restorative sleep or a combination of these symptoms. To our knowledge, no previous reports have considered the effect of stellate ganglion block on insomnia. We herein report three patients with intractable insomnia, which improved by stellate ganglion blockade with repeated administrations of 10 ml of 1% lidocaine (4 courses for Case 1, and 3 courses for Case 2 and 3). The severity of insomnia was assessed with the insomnia severity index scores. More significant improvements in sleep onset and sleep maintenance occurred throughout the followed up period. We conclude that SGB with repeated administrations improves sleep induction and quality in patients with insomnia. A large sample clinical study are needed to validate the efficacy of stellate ganglion blockade in patients with insomnia and therefore can also to explain these finding as a suitable hypnotic of potential mechanisms.

Keywords: Insomnia, stellate ganglion block, insomnia severity index scores

Introduction

Insomnia is thought as a disease of hyper-arousal, which is defined as difficulty initiating or maintaining sleep, or sleep that is non-restorative with poor quality, with negative daytime consequences [1]. Autonomic nervous system (ANS) activity has been suggested to influence the perception of the time needed to fall asleep, assessed by morning questionnaires [2, 3]. The treatment of patients with insomnia mainly includes both nonpharmacological and pharmacological approaches. However, to our best knowledge, stellate ganglion block (SGB) is one of the most commonly used treatment in pain clinics, and has been described as involving peripheral vasodilation, resulting from the neural inhibition in the ganglion’s sphere of innervation [4]. SGB studies of patients with breast cancer have shown that SGB is an effective treatment with acceptable morbidity for some survivors with therapy-resistant vasomotor symptoms and/or sleep disturbances [5]. Here, we report our findings on the use of SGB for the treatment of poor sleep quality and herein describe three patients with intractable insomnia whose validated clinical scales acutely decreased and finally get a good night’s sleep with 8 to 11 weeks of SGB therapy, and 3 to 12 months of follow-up after treatment.

Subjects and methods

The study was conducted at the third affiliated hospital of Anhui Medical University, Hefei, Anhui, China, after approval was obtained from the local ethics committee (NO. HFYY-20150016) on 15 March 2015 and written informed consent from each patient or their family members. Three patients with intractable insomnia were observed, with full response to staged SGB therapy, confirmed by follow-up SGB findings and by obvious improvement with an validated clinical scales.

Case reports

Case 1: A 34-year-old chinese woman with a history of intractable insomnia since 5 years
Stellate ganglion block for insomnia treatment

Table 1. The effect of SGB on self-reported measures of sleep scale scores (ISI) at different time points in patients with insomnia

<table>
<thead>
<tr>
<th>Patient</th>
<th>Prior treatment</th>
<th>Period of treatment (days)</th>
<th>Follow-up period (mouths)</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>16</td>
<td>35</td>
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<tr>
<td>Case 1</td>
<td>23</td>
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<td>16</td>
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<tr>
<td>Case 2</td>
<td>21</td>
<td>20</td>
<td>10</td>
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<tr>
<td>Case 3</td>
<td>21</td>
<td>18</td>
<td>11</td>
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ISI: insomnia severity index. The insomnia severity index (ISI). The insomnia index is a 7-item scale, with each item rated on a 5-point Likert-scale. Summation of the 7-items provides a score ranging from 0 to 28, where 0 to 7 indicates no significant insomnia, 8 to 14 indicates sub-threshold insomnia, 15 to 21 indicates moderate insomnia, and 22 to 28 indicates severe insomnia.

Case 1: A 26-year-old woman presented to neurology clinic for a follow-up visit. Her chief complaint at follow-up visit was the severe fatigue during the day and poor sleep at night. After starting a job as a operating-room nurse, a slowly progressive insomnia had emerged 8 years previously, at the age of 26 years. She had two failed marriages because of her sterility. She also had serious mysophobia that always complaining about the health of any person, including her parents. She lives with her parents. She had trouble in falling asleep because of ruminative thoughts and anxiety, and awaked multiple times at night because of convulsions. She estimated that it took her approximately 2 hours to fall asleep on most nights. She denied any positive medical, psychiatric or family history. Her neurologic evaluation were negative. There was no history of birth injury, nor head trauma history. The routine awake electroencephalogram (EEG) and brain MRI examination were unremarkable. 6 years ago, she was treated with a chinese medicine doctor for 1 year, but was not helpful. She then consulted a neurologist, and received a pharmacological clonazepam therapy at bedtime, followed by the addition of 10 mg zolpidem. At her 3 months follow-up visit, she reported her insomnia minimally improved mainly by prolong sleep time. Nevertheless, when she stopped drugs therapy on her own, and remained a sleep deprivation at night.

Two years ago, after consultation with an anesthesiologist, this case was accepted for the SGB therapy. Her ISI scores was 23 out of 28, indicating severe insomnia (sub-threshold insomnia is < 14) (Table 1).

Case 2: A laid-off 43-year-old chinese man with a history of sleep disorder since 2012 who presented with a lesser degree of executive dysfunction and significant sleep-onset insomnia occurring on a nightly basis. He lives with her wife, who accompanied his to the appointment. His wife described that he was constantly walking back and forth in the home at night in order to be able to get his asleep. He had a 9-year history of heavy drinking, and he often became unconscious by heavy drinking after starting a job as a public employees at 25 years old. He had to stop drinking because of severe hypertension with symptoms of forgetfulness since 9 years ago, and then he received standard antihypertension drugs therapy. His hypertension was basically under control when he comes to help since 3 years ago. They describe a 4-years history of insidious and slowly sleep deprivation with symptoms of so hot-tempered, excitable, and endorsed mild snoring on most night as well as poor quality sleep, difficulty falling asleep several times per week, and frequent nighttime awakenings. He showed no remarkable abnormal findings on neurological examinations, including the spinal cord reflex and motor function. His oxygen saturation on waking was normal. His body mass index (BMI) was 24 kg/m², with a neck circumference of 37 cm. He had normal upper airway anatomy with a modified Mallampati II airway. All of his laboratory tests including routing blood and biochemical tests were normal, brain MRI examination was unremarkable.

Clonazepam treatment at bedtime was chosen before 2 years, which promptly improved his symptoms within 2 weeks of therapy, other than poor sleep quality.

One and a half years ago, after consultation with an anesthesiologist, this case was accepted for the SGB therapy. His ISI scores was 21 out of 28, indicating moderate insomnia (Table 1).

Case 3: A 29-year-old chinese woman was admitted to the outpatient clinic with severe insomnia. Her chief complaint was difficulty in falling asleep, repetitive sleep fragmentation
and awakening, and short duration of night sleep (3-5 hours/night) for the previous 8 months period. Her elder sister (a pediatrician) describes that she would typically have great difficulty in sleeping for 2 to 3 nights consecutively, and then there would usually be 1 night of 5 to 6 hours of sleep, and followed by another days of insomnia for 2 to 3 nights consecutively. She was a company salesaman, and her elder sister thought that her insomnia was interfering markedly with Company work performance as well as with most other aspects of her daily life. She used to tried to treat insomnia with sleep restriction in daytime for improved the sleep quality of night, after her 4-weeks of hard work, but she reported her sleep quality (including the total time spent in bad, sleep latency and early awaking) have not resulted in a significant improvement in insomnia. She denied any substance abuse, such as caffeine, nicotine or alcohol. She was seen by a Chinese medicine doctor who prescribed her Herbal decoction at bedtime to help her sleeping, which remains very light and unsatisfactory sleep with frequently awaking at nights and early morning awakenings. Her elder sister was apprehensive because her clinical interviewing revealed no presence of any symptoms, nor the evidence of significantly psychopathology other than insomnia. All of her routing blood and biochemical tests were well within the normal range.

Until 1 year and a half ago, consultation with a anesthesiologist, and this case be accepted for SGB therapy. Her ISI scores was 21 out of 28, indicating moderate insomnia (Table 1).

Study procedures and manipulation

SGB was performed for each patient based on the modified technique of Janik [6]. All the SGB manipulations were performed on the left-sided or right-sided alternatively by two trained anesthesiologists who have passed the special training examination, and before the initial treatment appointment, the anesthesiologist gave the patient a brief introduction outlining the duration and the course of treatment, as well as the possible complications. The anesthesiologist also reassured the patient that a temporary Horner syndrome (miosis, ptosis, anhydrosis) would be proof of a correctly carried out SGB. The primarily therapy provided according to SGB treatment guidelines, which the anterior paratracheal approach at C₆ using surface landmarks, the transverse process of C₆ joins the lateral margin of vertebral body is uniformly broad in the cephalad-caudad dimension and lies medial to the vertebral artery, representing a simple alternate target for SGB.

Course of treatment

Three patients were prospectively performed by SGB alternatively with right and left which injections with 1% lidocaine of 10 ml was identified as the dose of each injection. The same technique was performed using unilateral of each injection with the same volume of local anesthetisc, with 1 injection per 2 days for a total of 8 injections as 1 course of treatment. For each patient, before the next course of treatment, patient with at least 3 days rest between two courses so that ensuring higher SGB effectiveness in patient. Up to the course of treatment until patient satisfactory. We withheld SGB procedure when the patient’s self-reported measures of sleep quality with ISI scales acutely decreased and finally get a good night’s sleep with the long-term efficacy. Patients were followed up, at least once every 3 months, either via phone calls or through outpatient meeting to ensure that sleep diary was being completed.

Adverse events reported by patients undergoing SGB procedure were recorded as present: (1) intravascular injection; (2) pneumothorax; (3) ipsilateral phrenic nerve block (cause subjective symptoms of dyspnea); (4) involvement of the vagus and recurrent laryngeal nerves (causes hoarseness); (5) possible epidural and intrathecal injections. A patient experiencing symptoms related to these adverse events may require reassurance or get prompt treatment.

Assessment of insomnia

The insomnia severity index (ISI) was used as a questionnaire-based measure of global insomnia severity [7]. It provides a total score assessing subjective severity of insomnia symptoms through 7 components: “difficulty falling asleep”; “Difficulty staying asleep”; “Problems waking up too early”; “How satisfied/dissatisfied are you with your current sleep pattern”; “How noticeable to others do you think your sleep problem is in terms of impairing the quality of your life?”; “How worried/distressed are
you about your current sleep problem?"; "To what extent do you consider your sleep problem to interfere with your daily functioning (e.g., daytime fatigue, mood, ability to function at work/daily chores, concentration, memory, etc.) currently?". Patients who reported one or more aforementioned symptoms were treated with SGB. Responses were coded on a five-point Likert type scale ranging from 0 (not at all) to 4 (very much). The scores of all the components are added to obtain a value between 0 and 28. The cut-off score of > 14 has been reported to be the most accurate point to detect patients with primary insomnia.

Statistical analysis

Data were presented as counts or numbers as appropriate. Statistical analyses were performed with SPSS 13.0 for Windows statistical package (Chicago, IL, USA). The sleep scale scores at different time points were expressed with single value from averaged value using every period of data collection. Incidence data were presented as numbers or percentages, which the effects of SGB were compared between right and left blockade with Chi-square test. Significance was defined as \( p < 0.05 \) (two-sided).

Results

Three patients had the SGB unilateral alternatively with right and left, no patient refused the SGB. Patients’ SGB treatment process and response to SGB in patients are presented in Figure 1. Case 1 received 4 course of treatment during 75 days, Case 2 and Case 3 received 3 course of treatment during 55 days, respectively, and completed the planned follow-up at 3 to 12 months (Figure 1A). A total of 80 blockade were completed in three patients throughout the treatment period, and patients’ response to SGB was associated with the incidence rate of Horner syndrome (right side, 80%; left side, 87.5%). About 10 to 15 minutes after the injection, the patient was associated with an incidence rate of the natural sleepy (right side, 35%; left side, 57.5%) (Figure 1B).

According to the summation of ISI scales provides a score ranging from 0 to 28, which use of the same scores indication as described in our case study. After two successive course of treatment with SGB, three patients’ insomnia and sleep quality had gradually improved from severe or moderate insomnia to sub-threshold insomnia. and after the fourth course of treatment in Case 1, her insomnia were promptly and effective controlled, and Case 2 and Case 3 sleep scales following the third course of treatment also were normalizing with insomnia control. No significant insomnia were assessed in three patients throughout the follow-up with one year (Table 1).

In the pilot cases reported, all three cases presented with a temporary Horner syndrome following the procedure. There were no serious short- or long-lasting adverse events reported apart from Case 1 and Case 2 who presented with a temporary hoarseness at the first SGB treatment.
Discussion

In this report of three cases, we were able to support that SGB is feasible and safe methods for the treatment of poor sleep quality in patients with intractable insomnia. The second supporting evidence was that onset asleep after SGB can provide a logical response pattern because the significant predictor of treatment effect in conjunction with a directly attributed to physiological response indicates more likely to influence outcome of long-term and lasting insomnia. The mechanism of action of SGB is not completely understood, but this hypnotic effects is likely due to several reasons: (1) The result was consistent with previous studies that showed SGB inhibition of sympathetic nervous activities and could regulated autonomic nervous system equilibrium [8]; (2) SGB effectiveness may involve a far more complicated mechanism of action than a transient increase in blood flow, such as with SGB reducing the concentration in brain both nerve growth factor (NGF) and norepinephrine (NR) and deactivating intracerebral pathologic states, which may be induced fall asleep associated with the core body temperature and metabolisms [9, 10]; (3) The action for SGB is based on correction of melatonin (N-acetyl-5-methoxytryptamine) rhythm disorder resulting from increased sympathetic nerve tone [4], and the melatonin could exhibits both hypnotic and chronobiotic properties, and improves sleep induction and quality in cancer patients with insomnia [11, 12].

The data presented in Table 1 suggest that ISI scale scores in patients with intractable insomnia were reduced after SGB with repeated administrations, and for each time point, after 2 course of treatment were significantly decrease for each ISI scale scores compared to prior treatment. Note that these reductions in ISI scores were associated with relatively number of SGB treatment, and that the reduction in Case 1, who received 4 course of treatment, was proportionally more than in Case 2 and 3 received 3 course of treatment. The clinical history or severe insomnia status could have potentially opted the prolonged effect in the determination of continuous SGB treatment. However, this explanation were only made at roughly quantitative estimation to the before and after treatment effects.

Better understanding of sympathetic neuroanatomy via anatomical labeling techniques was start to support explanations of the extensive effects of SGB for treatment of hot flashes, posttraumatic stress disorder, and neuropathic pain as well as including systemic diseases of the immune and endocrine systems [13-15]. It would be of major clinical relevance to evaluate the prolonged efficacy of SGB treatment, which mainly due to the course of mapping the sympathetic nervous system to related regions of the cerebral cortex. Westerhaus and Loewy used pseudorabies virus injections of the SGB produced extensive transneuronal labeling in the basolateral, medial amygdala, infralimbic, insular, and ventromedial temporal cortical regions [16]. The pattern of the tomography of regional cerebral blood flow suggest that a functional CNS abnormalities associated with insomnia during the non-rapid-eye-movement (NREM) sleep cycle may be due to a consistent pattern of hypoperfusion across all 8 pre-selected regions of interest, with particular deactivation in the basal ganglia [17, 18]. To the best of our knowledge, the present study showed that SGB can lead to a significant increase in the diameter, perimeter, and cross-sectional area of the middle cerebral artery (MCA) and the basilar artery (BA), and improve the gross anatomical appearance of these arteries [19]. SGB, which has a good vaso-dilatation profile as involving CNS by repeatedly blocking the sympathetic out flow to certain regions, may be an explaining in patients who have insomnia. However, the possibility of a longer effect is increased when a series of blocks are performed as compared with a single event.

Our reported was limited by only three investigated cases and the results of three cases do not seem to prove any clinical practice benefit from choosing SGB for patients with insomnia, hence it can only provided useful information. Also, although there are a wide clinical indications for SGB in diseases of the head, neck, and upper extremity, but most of the evidence has been insufficient to substantiate the assertions. Furthermore, this cases reported was performed at a single center, and not taking into account the most commonly reported sleep problems including: sexual distinction, age, especially the standardized instrument with subjective sleep quality for assessment of...
pathophysiology of insomnia as well as we should also mention the daily sleep diaries in each patient. Lastly, although rare, some potential adverse events and complication can occur with any peripheral nerve block, including local anesthetic toxicity as a result of intravascular injection should be guarded against by careful aspiration and incremental injection; exaggerated medial needle direction may result in pneumothorax; involvement of the vagus and recurrent laryngeal nerves (causes hoarseness) is rarely significant and is usually self-limited; and epidural and intrathecal injections can occur with any peripheral nerve block, but it is uncommon or theoretically possible. A finding emphasizing the importance of inserting the needle in a caudad direction. However, a successfully performed SGB with the help of ultrasound have been reported by Kapral et al [20].

We conclude that the results of three cases report are expected to provide clinical evidence for the effectiveness of SGB with repeated administrations as a nonpharmacological hypnosis, which mainly due to improves sleep induction and quality in patients with insomnia. However, further prospective with large sample clinical studies should be performed to evaluate the hypnotic efficacy of SGB in patients with insomnia and therefore can also to explain these finding as a suitable hypnotic of potential mechanisms.

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Disclosure of conflict of interest

None.

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References

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[14] Bellesi M, Tononi G, Cirelli C, Serra PA. Region-specific dissociation between cortical nora-