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CASE REPORT

Serial Ultrasound-guided Stellate Ganglion Block using Bupivacaine, Dexamethasone, and Methylcobalamin to Treat Complex Regional Pain Syndrome type II

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Background

Stellate ganglion block (SGB) has been widely used as a therapeutic approach for refractory complex regional pain syndrome (CRPS), but clinical outcome varies, long-term pain-relieving effect is unknown, and most studies employed local anesthesia per se. We would like to address if the combination of bupivacaine (Bupi), dexamethasone (Dex), and methylcobalamin (MeCbl) can provide a clinically meaningful reduction of pain intensity and quality, as well as improving patient's sleep and functional qualities in a sustainable fashion.

Case presentation

We performed a monthly serial SGB to a painful CRPS type II patient using Bupi and Dex in the first 2 months, then added MeCbl into the regimen until the fifth month onward. We measured weekly baseline pain intensity using baseline and evoked NRS, pain quality and affective using McGill Short-Form Questionnaire (SF-MPQ), sleep quality using Pittsburgh Sleep Quality Index (PSQI), and functional activities using Pain Disability Index (PDI) questionnaire during pre-procedure until the end of the fourth week post procedure. All spectra of pain assessments were also compared between pre- and post-addition of MeCbl and tested using independent t test analysis. Repeated SGBs were safely performed in the absence of significant adverse effects. A dramatic reduction of all spectra of pain measurements, comprising baseline (-62,5%), evoked (-60%) NRS, SF-MPQ (-39.4%), PSQI (-53.3%), and PDI (-56.9%) was observed immediately after procedure. The addition of MeCbl was able to further reduce the baseline (mean reduction 1.38 [-12.5%]; 95% CI 0.53 – 2.22; p=0.003), evoked (mean reduction 1.17 [-20%]; 95% CI -0.16 – 2.50; p=0.048) NRS, SF-MPQ (mean reduction 3.38 [-24.2%]; 95% CI 0.70 – 6.05; p=0.016), PSQI (mean reduction 1.29 [-13.4%]; 95% CI -0.22 – 2.8; 0.089), and PDI (mean reduction 9.75 [-26.2%]; 6.96 – 12.54; p<0.0001), compared to the first week of first injection. Clinical improvements were stable and sustainable until the end of observation period.

Conclusions

Monthly serial US-guided SGB with Bupi, Dex, and MeCbl were proven to be safe, clinically effective, and sustainable to ameliorate baseline and evoked pain intensity and quality, as well as improving sleep quality and functional activities of a subject with CRPS type II.

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Complex regional pain syndrome (CRPS) is defined as a syndrome of chronic severe pain, motor, sensory, autonomic, and trophic disturbances. International Association for the Study of Pain (IASP) classifies CRPS into two types, type I when there is a trivial or limb injury remote to the affected symptom areas, while type II (also known as causalgia) when there is an overt injury to specific major nerves or branches preceding the symptoms onset.[1] While conservative treatments comprising pharmacological therapy, physical rehabilitation, and occupational therapy remain the first line treatment of CRPS, some patients may not respond well and experience persistent debilitating pain which impairs their sleep and functional quality in general.[2] Stellate ganglion blockade (SGB) can be offered as an alternative procedure in the treatment of CRPS, particularly in those with refractory cases. The underlying mechanism of action is through inhibition of both pre- and post-ganglionic sympathetic nerves, given that sympathetic nervous system (SNS) overactivity may have a role in CRPS.[3] However, SGB outcome varies, and long-term prognosis is unclear, which may be partially explained by the use of local anesthetic injection alone in most studies. We therefore wanted to explore the potential addition of dexamethasone and methylcobalamin as an adjuvant for ultrasound (US)-guided SGB in CRPS type II case. The addition of dexamethasone was to prolong the effect of the local anesthetic agent and we postulated a negative effect on aberrant sympathetic activity.[4–7] Whereas methylcobalamin is an active form of vitamin B12 with well-established evidence of its ameliorating capacity toward various types of neuropathic pain under high therapeutic index, according to multiple observational and clinical studies.[8–10]

CASE PRESENTATION

A 37-year-old male patient presented to the pain clinic, complaining of constant pain in his right arm, wrist, and hand in the past 15 years. At the time of onset, he had been involved in a traffic accident in which he had sustained closed fractures (proximal humerus, radius, and ulnar) and a total right-sided brachial plexus palsy. The patient underwent multiple open reduction and internal fixations of the fractured bones before the fixing plates were removed 9 years later, along with gracilis muscle and intercostal nerve transfer to treat the brachial plexus palsy. Following the last surgery, motor strength began to recover by which he was able to abduct, adduct, flex, extend, pronate, and supinate the proximal arm muscles to a greater extent than the forearm, wrist, and hand muscles. In addition, he also regained partial sensation to coarse touch, pressure, vibration, and proprioception more significantly at the upper than his lower arm.

Pain was felt consistently following the accident. Initially he felt aching and cramping at his arm, but after several weeks post-surgery, severe pain subsided and pain quality was described as lancinating, burning, cramping, and numbness in the affected area. The pain was felt continuously and he experienced allodynia (it got worse by touch or skin exposure to clothing or cold air or water). He also complained that the pain increased with exercise/exertion. Pain intensity was equally reported on the right arm, forearm, wrist, and hand, both anterior and posterior.

On physical examination, motor strength was reduced (MRC grade 3, 3, 4-, 4 on the hand, wrist, forearm, and arm flexion and extension, respectively), accompanied significant muscle atrophy and slightly increased tone. The patient held his limb in a shoulder and arm guarding position with flexion contracture. Sensation was impaired to fine touch, vibration, temperature, and proprioception in the whole right arm. Allodynia, hyperalgesia, and paresthesia were all present in the affected region. Baseline and evoke pain NRS were 8/10 and 10/10, respectively and Short-Form McGill Pain Questionnaire (SF-MPQ) score was 33/45. Pain was identified as affecting sleep and impair daily activities with global Pittsburgh Sleep Quality Index (PSQI) and Pain Disability Index (PDI) scores of 15/21 and 65/70, respectively. We diagnosed patient with CRPS type II according to 1994 IASP CRPS diagnostic criteria.[1]

The patient underwent right SGB under US guidance in semi-lateral decubitus positioning. A linear ultrasound probe of 4-13 MHz was used to identify key anatomical landmarks including the C6 cervical nerve root (bounded by the more prominent anterior [Chassaignac] tubercle), longus colli (LC) muscle, longus capitis (LCa) muscle, prevertebral fascia, carotid artery (CA), and internal jugular vein (JV). The area was then scanned caudally to identify the C7 level with its prominent posterior tubercle and vestigial anterior tubercle along with the presence of the vertebral artery in the vicinity. The primary target for SGB was the prevertebral fascia located superior to LC, lateral to CA. A lateral, posterior-to-anterior, transverse approach was used. A 3.5 inch 25-G spinal needle was introduced in-plane to the probe under constant ultrasound monitoring and aseptic procedure.[11] Color flow doppler was activated to

avoid any accidental blood vessel punctures. Upon reaching the target, 2 mL of normal saline was injected for hydrolocation. Upon target confirmation and 3 mL of 0.5% bupivacaine HCl, 10 mg (2 mL) of dexamethasone were administered consecutively (Figure 1). The procedure was repeated monthly for 5 consecutive months, and from the third injection onward, 500 µg (1 mL) of methylcobalamin were also administered. During each procedure, a successful SGB was determined objectively by the presence of Horner's syndrome and increased cutaneous arm temperature immediately after the procedure, that the patient reported as lasting for up to 36 hours post injection (Figure 2).

Subjectively, the patient reported marked reduction of hyperalgesia and allodynia intensity from the first injection, lasting about 3-4 weeks, as well as improved quality and duration of sleep, and increased functional and social activities afterward. Measurable reductions of pain intensity and quality, and significant improvements in sleep quality and functional activities were noted by baseline (-62.5%) and evoked (-60%) NRS, SF-MPQ (-39.4%), PSQI (-53.3%), and PDI (-56.9%) (Figure 3). The addition of methylcobalamin from the third injection procedure onward led to further improvements baseline (-12.5%) and evoked (-20%) NRS, SF-MPQ (-24.2%), PSQI (-13.4%), and PDI (-26.2%). We compared all rating scale values weekly between pre- and post-addition of methylcobalamin (i.e. week 0 of first injection to week 8 vs. week 9 post-third injection to week 20) and obtained a modest-but-significant mean reduction of all measurements, except PSQI as displayed in Table 1.

Overall, the reduction in pain was sustained during the four-week intervals between injections. Pain quality and intensity, as well as sleep and functional quality fluctuated but values remained below baseline prior to next SGB.

DISCUSSION

Our patient was diagnosed with CRPS type II according to 1994 IASP criteria. We included this patient in our study due to several reasons. Firstly, he suffered from florid (full-blown) causalgia with severe neuropathic pain, dysesthesia, vasomotor impairments, and motor dysfunction.[12] Secondly, his baseline pain quality and intensity, as well as sleep and functional activity index were considered moderate-to-severe, consequently and thirdly, because he declined all oral or intravenous therapies through personal choice. However, he accepted to

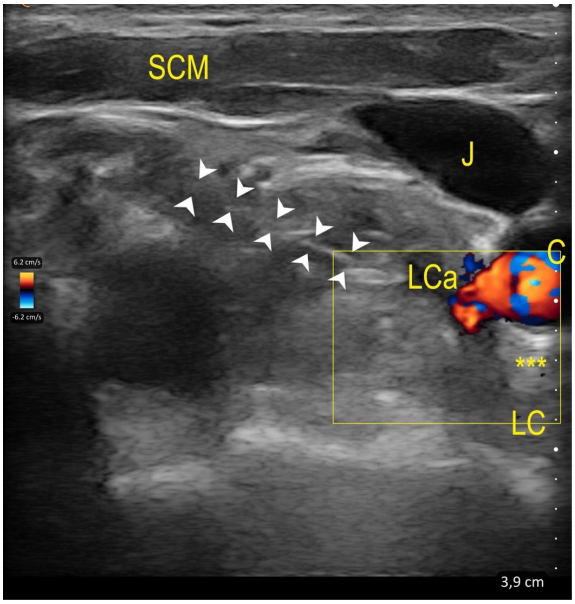

Figure 1 *US-guided SGB block. A lateral, posterior-to-anterior, transverse approach was used, with needle inserted in-plane to the probe with color flow Doppler to address vasculatures and aid in hydrolocalization. C: carotid artery; J: jugular vein; SCM: sternocleidomastoid muscle; LCa: longus capitis muscle; LC: longus colli muscle; Arrowheads: penetrating needle; ***: prevertebral fascia and target for SGB.*

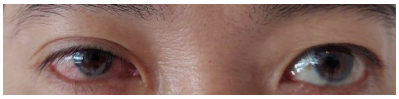

Figure 2 *Horner's syndrome comprising ipsilateral ptosis, with slight enophthalmos and pupillary miosis was noted immediately after injection. Horner's syndrome is an objective sign of successful sympathetic block. Of note, conjuctival injection was observed, indicating unopposed activation of parasympathetic nervous system activity*

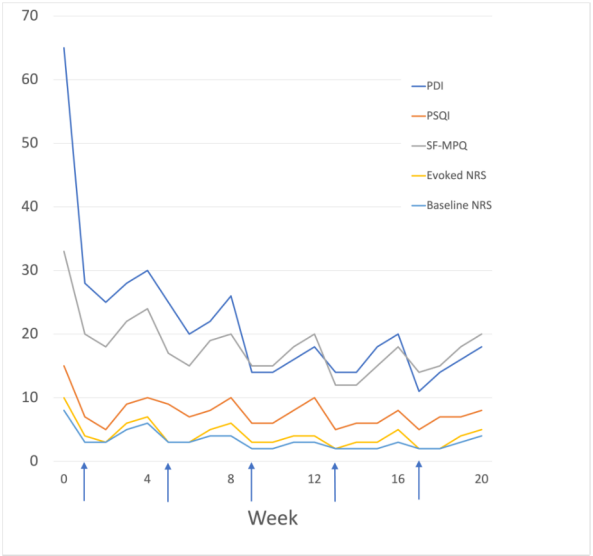

Figure 3 *Pain intensity and quality, as well as sleep and functional capacity measured over time from baseline to week 20 post monthly serial injection. NRS: numerical rating scale; PDI: pain disability index; PSQI: Pittsburgh sleep quality index; SF-MPQ: the short-form McGill pain questionnaire. Arrows denote time of injection.*

Table 1 *Baseline and evoked NRS, SF-MPQ, PSQI, and PDI scores of pre- and post treatment group differences*

Parameters		Mean ± SD	Mean reduction	95% CI	*p* value*
Baseline NRS	Pre-MeCbl	3.88 ± 1.13	1.38	0.53 – 2.22	*0.003*
	Post-MeCbl	2.50 ± 0.67			
Evoked NRS	Pre-MeCbl	4.50 ± 1.77	1.17	-0.16 – 2.50	*0.048*
	Post-MeCbl	3.33 ± 1.07			
SF-MPQ	Pre-MeCbl	19.38 ± 2.83	3.38	0.70 – 6.05	*0.016*
	Post-MeCbl	16.00 ± 2.76			
PSQI	Pre-MeCbl	8.13 ± 1.73	1.29	-0.22 – 2.8	0.089
	Post-MeCbl	6.83 ± 1.47			
PDI	Pre-MeCbl	25.50 ± 3.30	9.75	6.96 – 12.54	*<0.0001*
	Post-MeCbl	15.75 ± 2.63			

**p* value significant at <0.05; mean difference significance was computed with independent t test using SPSS version 23.0.

undergo SGB. We initially consider the sole administration of bupivacaine, but decided to add non-particulate corticosteroid and methylcobalamin. We chose a non-particulate steroid to minimize the risk of arterial embolism. For the same reason, we opted to use ultrasound guidance to better visualize soft tissue structures in the vicinity of prevertebral fascia.

Although the effect of local anesthesia may last for approximately a week, it was postulated that SGB promotes reduced firing of nociceptive fibers of the pathological pain pathways, thus providing analgesia effect that may outlast the local anesthesia's onset of action.[13] The addition of Dex was shown to prolong the clinical effects of bupivacaine toward suppression of aberrant sympathetic activity. In fact, a double-blind RCT involving the addition of 8 mg of dexamethasone to bupivacaine for TAP block was shown to significantly prolong the effect of anesthesia by approximately 41% compared to bupivacaine alone.[14] In our patient we observed significant reductions of pain intensity and quality, and significant improvements in sleep quality and functional activities since the beginning of first injection. We suspect that the significant response may have been partially due to patient's naïve, medication-free state prior to the procedure, which primed him toward a maximized response to the medications used for SGB. The corresponding reduction seemed to be stable and sustainable over the course of four weeks until the onset of subsequent injection.

To our best knowledge, we were the first to clinically administer methylcobalamin via SGB for CRPS type II. Its mechanism of action is pleiotropic, including enhancing nerve myelination, promoting axonal regeneration, protecting the nerve against glutamate-induced neurotoxicity, and inhibiting ectopic spontaneous discharge.[15,16] However, its potential role in SGB is unknown, though it may potentially act as an indirect modulator and enhances nociceptive firing suppression of sympathectomy-simulated environment. Regardless, given the clinically significant favorable effects of MeCbl toward ameliorating CRPS type II's baseline and evoked pain intensity and quality, as well as improving sleep quality and functional activities, its therapeutic use can be prudently justified ad interim, preceding the discovery of its exact mechanism of action.

Even though we achieved clinically observable signs of sympathetic block via Horner's syndrome and increased cutaneous temperature, it was uncertain if total block was achieved by SGB. In addition, there has been a subclassification of CRPS, comprising 1) vasomotor-predominant, 2) neuropathic pain/ dysesthesia-predominant, and 3) florid CRPS[12], by which it is still unknown if SGB will benefit to all of

these subgroups equally. However, given the account of consistent clinical improvements across multiple spectra of measurements, we prudently assume to have achieved the necessary therapeutic goal. The long-term therapeutic effects of SGB using a combination of bupivacaine, dexamethasone, and methylcobalamin, as well as dose regimen and administration interval which exert the longest and most optimal pain amelioration intensity, quality, duration, and its impact toward sleep and functional qualities, need to be addressed in a well-designed and sufficient observational period of clinical trial.

CONCLUSION

Monthly serial US-guided SGB with bupivicaine, dexamethasone, and methylcobalamin were proven to be safe, clinically effective, and sustainable to ameliorate baseline and evoked pain intensity and quality, as well as improving sleep quality and functional activities of a subject with CRPS type II.

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