# Original Article Efficacy of continuous lumbar sympathetic nerve block for cold allodynia in patients with lumbar disc herniation

Hong-Jin Zhang<sup>1,2</sup>, Bai-Shan Wu<sup>1</sup>, Liang-Liang He<sup>1</sup>, Jia-Xiang Ni<sup>1</sup>

<sup>1</sup>Department of Pain Management, Xuanwu Hospital, Capital Medical University, Xicheng Zone, Beijing 100053, China; <sup>2</sup>Department of Pain Management, The Second People's Hospital of Lianyungang, No.161 Xingfu Street, Haizhou District, Lianyungang, Jiangsu 222023, China

Received November 21, 2015; Accepted April 8, 2016; Epub June 15, 2016; Published June 30, 2016

**Abstract:** Cold allodynia is a complaint in patients with lumbar disc herniation (LDH), and significantly impairs their quality of life. We treated cold allodynia with continuous lumbar sympathetic nerve block (CLSNB) with patient-controlled analgesia (PCA) and determined the therapeutic outcome in long-term follow-up. Eight patients with a median age of 52.0 years were enrolled between September 2013 and August 2014. These patients had long-term cold allodynia in their affected lower extremity, and did not respond to established treatments. CLSNB was finally performed. The patients were followed up for at least 24 weeks. The average cold allodynia score on the visual analog scale (VAS) declined significantly from 7.1 before treatment to 1.6 at discharge, 1.8 at 1 week after discharge, 3.2 at 4 weeks, 4.0 at 8 weeks, and 4.6 at 24 weeks (*P*<0.05). All patients obtained immediate continuous cold relief during hospitalization. Seven of 8 patients had satisfactory pain relief at 1 week after discharge, 6 of 8 at 4 weeks, 5 of 8 at 8 weeks, 4 of 8 at 12 weeks, and 4 of 8 at 24 weeks. There were no reported complications. CLSNB is an effective and safe technique in treating cold allodynia in patients with LDH, and can provide long-term benefit.

Keywords: Continuous lumbar sympathetic nerve block, cold allodynia, lumbar disc herniation

### Introduction

Cold allodynia is a common symptom in a variety of diseases, and is characterized by pain with normally innocuous cold stimulation and an avoidance response in a cold environment [1-3]. It is a complaint in patients with lumbar disc herniation (LDH), and significantly impairs their quality of life.

Previous studies reported improvement in cold allodynia in patients with discogenic visceral pain or complex regional pain syndrome (CRPS) using continuous lumbar sympathetic nerve block (CLSNB) [4, 5]. However, there are no reports on the efficacy of CLSNB in treating cold allodynia in patients with LDH. The purpose of this study was to evaluate the efficacy of CLSNB in treating cold allodynia in the lower extremity in patients with LDH during 24 weeks of follow-up.

## Methods

### Patients

Eight patients with LDH who had clinical symptoms and physical findings suggestive or indica-

tive of cold allodynia in their affected lower extremity were selected as participants in this study. There was no history of cold allodynia in the lower extremity prior to development of LDH. Despite a variety of treatments, the cold allodynia remained unimproved. Exclusion criteria were spondylolisthesis, diabetes mellitus, vascular diseases, injuries, inflammatory arthritis in the lower extremity, and cognitive impairment. This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics Committee of the Xuan Wu Hospital, Capital Medical University. Written informed consent was obtained from all participants.

### CLSNB

Patients who agreed to treatment underwent percutaneous CLSNB using a posterolateral approach with an 18-gauge needle. Under computed tomography (CT) guidance, the needle was inserted into the paravertebral sympathetic trunk at the level of the L4 vertebral body. A 20-gauge catheter was inserted into the paravertebral sympathetic trunk through the needle (**Figure 1A**). CT was used to reconfirm catheter

# Lumbar sympathetic nerve block on cold alodynia

Patient	Age (years)	Sex	Symptomlocation	Symptom duration _ (years)	Level of disc herniation (MRI)	
					Posterior	Anterior
1	46	F	Right leg	2	L3-4/L4-5/L5-S1	/
2	56	Μ	Left leg	1	L4-5/L5-S1	/
3	49	Μ	Right/Left leg	2	L3-4/L4-5	L4-5
4	44	М	Right/Left leg	3	L4-5/L5-S1	L4-5
5	57	F	Right leg	0.5	L4-5	L2-3
6	50	F	Right leg	5	L2-3/L3-4/L4-5/L5-S1	L4-5
7	49	F	Right/Left leg	1	L4-5/L5-S1	L5-S1
8	65	F	Right/Left leg	10	L4-5/L5-S1	L2-3
Average	52	/	/	3.1	/	/

Table 1. Characteristics of patients with cold alodynia in lumbar discherniation

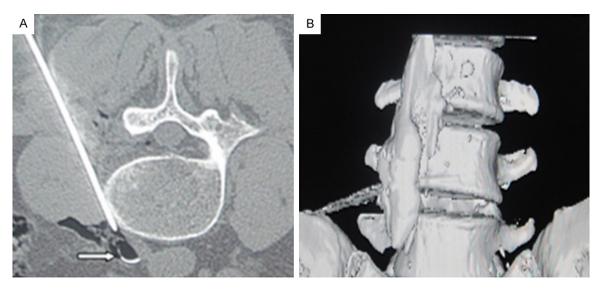


Figure 1. A: CT guided puncture of right lumbar sympathetic trunk (L4). Catheter with steel wire (the arrow) was inserted through needle; B: Contrast medium spread along L4 to L3 and L2 paravertebral sympathetic ganglion.

position by infusion of 4 mL of 1% lidocaine plus 1 mL contrast medium (Omnipaque) (Figure 1B). After 5 min, when the temperature in the affected lower extremity had clearly increased, a subcutaneous tunnel was created to fix the catheter. If no side effects occurred 20 min later, a mixture of 20 mL of 1% lidocaine and 20 mg of methylprednisolone was injected, and the catheter was connected to a patientcontrolled analgesia (PCA) pump containing 0.4% lidocaine and 1 mg/mL methylprednisolone. The basal dose of PCA was 5 mL/h. The pump connector was immersed in 95% alcohol for 20 min before a replacement pump was connected to the catheter. The duration of CLSNB was 3 wk [4].

## Cold pain assessment

All of the patients were assessed for cold pain severity using a visual analog scale (VAS), rang-

ing from 0, indicating no cold or pain, to 10, indicating worst cold or pain. The degree of cold pain was estimated before treatment, on the 1st, 7th, and 14th day during treatment, at discharge, and at 1, 4, 12, and 24 weeks after discharge. Satisfactory cold pain relief was defined as a 50% or more reduction in the VAS score.

### Adverse effects and complications

Postural hypotension, diarrhea, or other complications during the procedure were recorded.

## Statistical analysis

Statistical analyses were performed using Statistical Packages for Social Sciences 14.0 version (SPSS Inc., Chicago, IL, USA). The clinical course was analyzed via one-way analysis of variance (ANOVA) followed by a Tukey posthoc test, and further comparison was estimat-

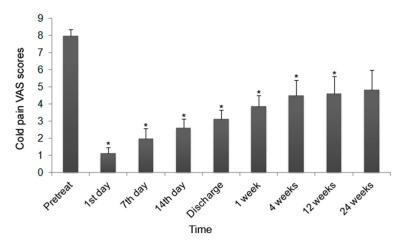
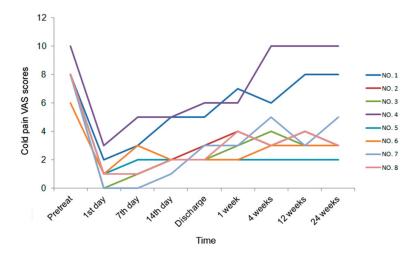


Figure 2. Changes in the average cold pain VAS scores during the follow-up time (compared with pretreatment, \*P<0.05).



**Figure 3.** Individual changes in cold pain VAS scores versus time at pretreatment; 1st day, 7th day, and 14th day during treatment; discharge; and at 1 week, 4, 12, and 24 weeks after discharge.

ed using q test. A *P*<0.05 was regarded as statistically significant.

#### Results

The median age and symptom duration of the 8 patients (three men and five women) were 52 and 3.1 years, respectively. Patient characteristics are shown in **Table 1**. The average VAS score for cold pain declined significantly from 8.0 before treatment to 3.125 at discharge (P<0.05), 3.875 at 1 week after discharge (P<0.05), 4.5 at 4 weeks (P<0.05), 4.62 at 8 weeks (P<0.05), and 4.857 at 24 weeks (**Figure 2**). All patients obtained immediate continuous cold relief during hospitalization. Seven of 8

patients had satisfactory pain relief at 1 week after discharge, 6 of 8 at 4 weeks, 5 of 8 at 8 weeks, 4 of 8 at 12 weeks, and 4 of 8 at 24 weeks (**Figure 3**).

There was no report of vascular injury or infection. There were no serious complications such as nerve damage resulting in paralysis. No patients reported postural hypotension, diarrhea, or other complications during the procedure. No patient reported worse pain after the procedure. There were no issues with postoperative instability during follow-up, but surveillance flexion-extension X-rays were not performed.

#### Discussion

The symptoms of cold allodynia in the lower extremity were clearly improved with CLSNB in patients with LDH in this study. The transient receptor potential (TRP) protein family plays an important role in cold sensation [6, 7]. In particular, the TRP melastatin 8 (TRPM8) and (TRPA1) ion channels are important in cold allodynia [8-11]. Inflammatory reactions and nerve injury can stimulate

ion channels and lead to cold pain [12]. Cold allodynia is associated with lumbar sympathetic nerves. It was reported that the lumbar sympathetic nerves could play a role in cold sensation by changing the expression of TRPA1 [13]. The TRPA1 receptor was involved in cold allodynia in a mouse model of sympathetically maintained neuropathic pain [14]. However, it was unclear how this affected the sympathetic nerves. Tang suspected that anterior herniation of the lumbar disc could induce sympathetic inflammation [4].

In our 8 patients, the symptoms of cold allodynia did not improve despite nerve blocks, radiofrequency, or decompression surgery. However, anterior herniation of the lumbar disc was found in 7 of 8 patients in this study.

CLSNB was effective in improving the symptoms of sympathetically maintained pain (SMP) through modulation of the function of sympathetic nerves, and therapeutic value was identified in previous studies [4, 5, 15]. Initially, lumbar sympathetic nerve block was able to provide transient relief in SMP by altering the excitation of the sympathetic nerves [16-18], but the therapeutic efficacy returned when the sympathetic block subsided [19]. Lumbar sympathectomy could improve the symptoms of cold hypersensitivity in neuropathic pain [20, 21]. It could cause further sensitivity to catecholamines with complete denervation, which could lead to a high incidence of refractory cases. In contrast, up to 24 weeks of relief of cold allodynia was seen in patients with LDH after receiving CLSNB with lidocaine and methylprednisolone in our study.

There are limitations in this study. First, the number of patients was small, but preliminary clinical data was provided for further research. Second, a randomized, controlled clinical trial was not conducted due to ethical issues. Third, whether methylprednisolone played an important role in treating cold allodynia in patients with LDH was uncertain. However, there has been no evidence that methylprednisolone could improve the symptoms of cold allodynia in patients with LDH in previous literature.

In conclusion, CLSNB is an effective and safe technique in treating cold allodynia in patients with LDH, and can provide long-term benefit.

## Disclosure of conflict of interest

None.

Address correspondence to: Jia-Xiang Ni, Department of Pain Management, Xuanwu Hospital, Capital Medical University, Xicheng Zone, Beijing 100053, China. Tel: +86 10 83198160; Fax: +86 10 63175890; E-mail: jiaxiangnidoc@163.com

## References

- [1] Kim SO and Kim HJ. Berberine ameliorates cold and mechanical allodynia in a rat model of diabetic neuropathy. J Med Food 2013; 16: 511-517.
- [2] Reinersmann A, Maier C, Schwenkreis P and Lenz M. Complex regional pain syndrome:

more than a peripheral disease. Pain Manag 2013; 3: 495-502.

- [3] Linglu D, Yuxiang L, Yaqiong X, Ru Z, Lin M, Shaoju J, Juan D, Tao S and Jianqiang Y. Antinociceptive effect of matrine on vincristine-induced neuropathic pain model in mice. Neurol Sci 2014; 35: 815-821.
- [4] Tang YZ, Shannon ML, Lai GH, Li XY, Li N and Ni JX. Anterior herniation of lumbar disc induces persistent visceral pain: discogenic visceral pain. Chin Med J (Engl) 2013; 126: 4691-4695.
- [5] Tang YZ, Ni JX and An JX. Complex regional pain syndrome type I following disc TRODE radiofrequency treated with continuous lumbar sympathetic trunk block using patient-controlled analgesia. Pain Med 2013; 14:309-310.
- [6] Mckemy DD, Neuhausser WM and Julius D. Identification of a cold receptor reveals a general role for TRP channels in thermal sensation. Nature 2002; 416: 52-58.
- [7] Dhaka A, Viswanath V and Patapoutian A. Trp ion channels and temperature sensation. Annu Rev Neurosci 2006; 29: 135-161.
- [8] Mckemy DD. How cold is it? TRPM8 and TRPA1 in the molecular logic of cold sensation. Mol Pain 2005; 1: 16.
- [9] Caspani O, Zurborg S, Labuz D and Heppenstall PA. The contribution of TRPM8 and TRPA1 channels to cold hypersensitivity and neuropathic pain. PLoS One 2009; 4: e7383.
- [10] Kato Y, Tateai Y, Ohkubo M, Saito Y, Amagai SY, Kimura YS, Iimura N, Okada M, Matsumoto A, Mano Y, Hirosawa I, Ohuchi K, Tajima M, Asahi M, Kotaki H and Yamada H. Gosha-jinki-gan reduced oxaliplatin-induced hypersensitivity to cold sensation and its effect would be related to suppression of the expression of TRPM8 and TRPA1 in rats. Anticancer Drugs 2014; 25: 39-43.
- [11] Namer B, Kleggetveit IP, Handwerker H, Schmelz M and Jorum E. Role of TRPM8 and TRPA1 for cold allodynia in patients with cold injury. Pain 2008; 139: 63-72.
- [12] Obata K, Katsura H, Mizushima T, Yamanaka H, Kobayashi K, Dai Y, Fukuoka T, Tokunaga A, Tominaga M and Noguchi K. TRPA1 induced in sensory neurons contributes to cold hyperalgesia after inflammation and nerve injury. J Clin Invest 2005; 115: 2393-2401.
- [13] Smith MP, Beacham D, Ensor E and Koltzenburg M. Cold-sensitive, menthol-insensitive neurons in the murine sympathetic nervous system. Neuroreport 2004; 15: 1399-1403.
- [14] PinheiroFde V, Villarinho JG, Silva CR, Oliveira SM, PinheiroKde V, Petri D, Rossato MF, Guerra GP, Trevisan G, Antonello Rubin M, Geppetti P, Ferreira J and André E. The involvement of the TRPA1 receptor in a mouse model of sympa-

thetically maintained neuropathic pain. Eur J Pharmacol 2015; 747: 105-113.

- [15] Chelly JE, Casati A, Al-Samsam T, Coupe K, Criswell A and Tucker J. Continuous lumbar plexus block for acute postoperative pain management after open reduction and internal fixation of acetabular fractures. J Orthop Trauma 2003; 17: 362-367.
- [16] Meier PM, Zurakowski D, Berde CB and Sethna NF. Lumbar sympathetic blockade in children with complex regional pain syndromes: a double blind placebo-controlled crossover trial. Anesthesiology 2009; 111: 372-380.
- [17] Abramov R. Lumbar sympathetic treatment in the management of lower limb pain. Curr Pain Headache Rep 2014; 18: 403.
- [18] Woo JH, Park HS, Kim SC and Kim YH. The effect of lumbar sympathetic ganglion block on gynecologic cancer-related lymphedema. Pain Physician 2013; 16:345-352.

- [19] Zhao C, Chen L, Tao YX, Tall JM, Borzan J, Ringkamp M, Meyer RA and Raja SN. Lumbar sympathectomy attenuates cold hypersensitivity but not mechanical allodynia and hyperalgesia in rats with spared nerve injury. J Pain 2007; 8: 931-37.
- [20] Ringkamp M, Eschenfelder S, Grethel EJ, Häbler HJ, Meyer RA, Jänig W and Raja SN. Lumbar sympathectomy failed to reverse mechanical allodynia- and hyperalgesia-like behavior in rats with L5 spinal nerve injury. Pain 1999; 79: 143-153.
- [21] Lee KS, Su YF, Lieu AS, Chuang CL, Hwang SL, Howng SL and Lin CL. The outcome of percutaneous computed tomography-guided chemical lumbar sympathectomy for patients with causalgia after lumbar discectomy. Surg Neurol 2008; 69: 274-279.