Bee Venom Treatment for Refractory Postherpetic Neuralgia: A Case Report

Seung Min Lee, KMD,^{1,*} Jinwoong Lim,^{2,*} Jae-Dong Lee, KMD, PhD,¹
Do-Young Choi, KMD, PhD,¹ and Sanghoon Lee, KMD, PhD¹

Abstract

Objective: Bee venom has been reported to have antinociceptive and anti-inflammatory effects in experimental studies. However, questions still remain regarding the clinical use of bee venom. This report describes the successful outcome of bee venom treatment for refractory postherpetic neuralgia.

Patient: A 72-year-old Korean man had severe pain and hypersensitivity in the region where he had developed a herpes zoster rash 2 years earlier. He was treated with antivirals, painkillers, steroids, and analgesic patches, all to no effect.

Intervention: The patient visited the East-West Pain Clinic, Kyung Hee University Medical Center, to receive collaborative treatment. After being evaluated for bee venom compatibility, he was treated with bee venom injections. A 1:30,000 diluted solution of bee venom was injected subcutaneously along the margins of the rash once per week for 4 weeks.

Results: Pain levels were evaluated before every treatment, and by his fifth visit, his pain had decreased from 8 to 2 on a 10-point numerical rating scale. He experienced no adverse effects, and this improvement was maintained at the 3-month, 6-month, and 1-year phone follow-up evaluations.

Conclusion: Bee venom treatment demonstrates the potential to become an effective treatment for postherpetic neuralgia. Further large-sample clinical trials should be conducted to evaluate the overall safety and efficacy of this treatment.

Introduction

POSTHERPETIC NEURALGIA (PHN) IS THE MOST common and debilitating complication brought on by herpes zoster.¹ It affects every aspect of the patient's life, including daily activities, self-care, sleep, and social/family relations, because the symptoms include severe and unremitting pain on the site of the affected nerve, even after the zoster rash has long been healed. With prompt and proper management, the rash normally subsides within a month of its presentation, but PHN is diagnosed in the 10%–18% of patients left with associated symptoms for over 3 months after rash healing. Of those patients, 48% will continue to have symptoms after a year and some, for the rest of their lives.²

Current treatments for PHN vary. Although a systematic review revealed that tricyclic antidepressants, gabapentin, pregabalin, opioids, and lidocaine patches were effective in

reducing PHN-related pain, further efforts for developing better modalities of treatment are necessary because half of all patients with PHN do not respond to any conventional treatments.³ Furthermore, according to a 2011 study,⁴ a mere 16% of primary care physicians and 19% of neurologists ranked themselves as “very confident” that the chosen treatment for PHN would control a patient's pain, while the majority were doubtful that conventional treatments could heal PHN-associated pain. The number of patients with PHN is expected to rise because of an increase in lifespan; considering that the most well-established risk factor for PHN is age,⁵ the development of an effective therapeutic method for PHN becomes even more pressing.

Bee venom has been used since antiquity for its anti-inflammatory and antinociceptive effects.⁶ Treatment is performed by directly administering bee stings or by collecting the venom itself and injecting dilutions into the

Departments of ¹Acupuncture & Moxibustion and ²Korean Medicine, College of Korean Medicine, Kyung Hee University, Seoul, Republic of Korea.

*These authors contributed equally to this work.

sites of pain. Its treatment properties have been well studied in animals and humans. Its bioactive compounds include many peptides, enzymes, and amines and can effectively treat a variety of diseases, including idiopathic Parkinson's disease.⁷⁻¹⁰

In 2007, Janik et al.¹¹ reported the case of a man whose PHN symptoms, refractory to all forms of treatment, were ultimately relieved by an accidental bee sting. This event, combined with prior knowledge of bee venom's analgesic effects, made it a viable candidate for therapeutic applicability. However, the case occurred in an uncontrolled environment and was not reproducible because of "dosing" issues: The optimal therapeutic dose of venom is not specifically known. The following describes the case of a 72-year-old man whose PHN pain was successfully resolved after four sessions of bee venom treatment, administered under medical supervision.

Case Report

The patient was a man of slight but muscular build, 161 cm in height, and weighing 55 kg. While performing routine tasks at his farm, he started feeling severe unilateral pain on the left side of his chest. He described his pain as continuous, burning, cutting, and sharp, as if somebody were stabbing him with a handful of needles. After immediately driving himself to the nearest hospital, he was admitted for further medical check-up. Two days later, a rash appeared directly on the site of pain. Acute herpes zoster was diagnosed on the basis of the characteristic rash and symptoms, and no further testing was performed. The patient spent 7 days in the hospital, after which the rash disappeared, leaving only the excruciating pain.

Because the rash appeared while he was in the hospital, the early use of antivirals and combined treatment modalities probably aided in the remission of the rash. Unfortunately, these treatments had no effect on the pain. The patient describes having spent nights lying in bed, sometimes screaming because of the unbearable aching. For months afterward, he visited several major hospitals in South Korea and was diagnosed with chronic postherpetic neuralgia and continued treatment with antivirals, painkillers, steroids, and analgesic patches, which only slightly helped to alleviate the pain.

Two years after the first rash appeared, the patient continued to rate his pain an 8 out of 10, describing it as less severe but still characteristically numb, sore, and hypersensitive. Clinical tests revealed extreme sensitivity to touch, when a light brush of cloth was enough to aggravate the pain. The symptoms greatly reduced the patient's quality of life, and his only relief from pain was through physical distraction, when he was well enough to be active.

He visited Kyung Hee University Medical Center to receive East-West collaborative treatment in March 2010. He was once again prescribed analgesics, lidocaine patches, and antidepressants. However, after considering his poor response to pharmacologic treatments over the past 2 years, the doctor recommended him for complementary and alternative medicine treatments. After undergoing several evaluations that validated him for bee venom therapy, he provided informed consent and received diluted bee venom treatments.

The therapeutic methods were as follows: bee venom (Daehan Pure Bee Venom, Changyoung, Korea) was diluted in distilled water (Daihan Pharm, Seoul, Korea) to a concentration of 1:30,000 and subcutaneously administered along the margins of the rash. A volume of 0.1 mL was injected into each site with a 30-gauge insulin syringe (Hwajin Medical Co., Cheonan, Korea) at a depth of 0.5–1.0 cm, and the total injected volume did not exceed 1 mL. Bee venom treatment was administered once per week over 4 weeks.

Immediately after the first treatment, the patient's average pain rating decreased from 8 to 4 on a 10-point numerical rating scale. The rating decreased to 2 on his fourth visit and remained there until the fifth week. On this fifth visit, he reported that he could no longer feel the pain, which had reduced to an endurable tingly and itchy sensation. In addition to this pain reduction, his level of functioning was improved to the point at which he could not feel the numbness when he was at work. Being satisfied with this outcome, he terminated treatment. No adverse effects were observed during the treatment period, except for a tolerable itchiness at the site of injection for 2 days following treatment.

Discussion

PHN reduces the patient's quality of life¹² and is extremely variable in nature, characterized by constant throbbing/burning of fluctuating severity; intermittent, sudden, sharp, shooting pain and unbearable itchiness; and mechanical or thermal allodynia (pain produced by non-noxious stimuli), experienced by 90% of patients. The pain is often so intense that patients spend days and nights without sleep.

To prevent PHN, the initial stage of acute herpes zoster should be controlled. The first line of treatment is the herpes zoster vaccine, but it is not yet widely available or discussed in PHN treatment guidelines.¹³ Receiving antiviral agents within 72 hours of onset has also proven effective in reducing the duration and probability of developing PHN.¹⁴ If the patient develops PHN, the next set of options for primary care physicians include tricyclic antidepressants, anticonvulsants, topical capsaicin, and local anesthetics.¹⁵ Many patients, however, do not respond to any of these treatments; this has led to myriad cases and randomized, controlled trials investigating new methods for controlling the pervasive pain of PHN, including botulinum toxin, methylprednisolone, aspirin in ointment/cream form, topical capsaicin, and peppermint oil.¹⁶

The mechanism of PHN is not yet fully understood, although it is speculated that, as a result of herpes zoster reactivation, a variety of neurologic pathways are damaged. This suggests that the best treatment approach uses multiple therapies with different mechanisms of action and is tailored to the individual's set of side effects and responses.¹⁷

This case report investigates a new type of therapy, making it relevant for several reasons. First, it differs from other case reports because it has further developed and reproduced a therapeutic method that was observed a few years earlier.¹¹ Despite the increasing number of bee venom studies on animals, there are few clinical reports of bee venom treatments conducted on humans. This case measured exact doses of bee venom, controlling the patient's treatment sessions as much as possible in order to lay a foundation for future large-scale experiments that could help delineate the

exact mechanism of bee venom treatment, as well as specify which types of patients would be best suited for this treatment. Second, the patient's pain was significantly reduced within the first month, an outcome maintained at the 3-, 6-, and 12-month follow-ups. Few other reports on successful PHN treatments have demonstrated such rapid and sustained improvement. Although the natural resolution of PHN could be a confounder in this case, the fact that the patient had unchanging symptoms for more than 2 years before treatment makes such confounding unlikely.

Although the main scale of pain measurement in patients with PHN is the numerical rating scale, or visual analogue scale, further quality-of-life measurements would have been helpful in analyzing changes in related symptoms because pain perception is so subjective.¹⁸ It is possible that the outcome could have been improved had the bee venom been injected into remote PHN-related acupuncture points as well. Further research should be conducted to elucidate the optimal modality of bee venom treatment.

A recent case study postulated two types of pain-generating mechanisms in PHN. One type involves nontraumatized, pathologically sensitized, primary afferent nociceptors that produce symptoms such as spontaneous pain, mechanical allodynia, and heat hyperalgesia. The second type involves severe to partial nerve injury and degeneration, producing pain and mechanical allodynia, along with impaired heat pain perception.¹⁹ With these mechanisms in mind, future research conducted on patients with PHN should focus on heat sensation and extent of nerve injury in order to uncover whether different types of nerve injuries respond differently to the same therapy.

Conclusion

Bee venom treatment demonstrates the potential to become an effective treatment for postherpetic neuralgia. Further large-sample clinical trials should be conducted to evaluate the overall safety and efficacy of this treatment.

Acknowledgments

This work was supported by grants from the National Research Foundation funded by the Korean government (no. 2011-0028968) and from the Undergraduate Research Program, funded by the College of Korean Medicine at Kyung Hee University.

Disclosure Statement

No competing financial interests exist.

References

- Weinke T, Edte A, Schmitt S. Impact of herpes zoster and postherpetic neuralgia on patients' quality of life: a patient-reported outcomes survey. *J Public Health* 2010;18:367–374.
- Gershon AA. Epidemiology and management of postherpetic neuralgia. *Semin Dermatol* 1996;15:8–13.
- Dubinsky RM, Kabbani H, El-Chami Z, Boutwell C, Ali H. Quality Standards Subcommittee of the American Academy of Neurology. Practice parameter: Treatment of postherpetic neuralgia: an evidence-based report of the quality standards

- subcommittee of the American Academy of Neurology. *Neurology* 2004;63:959–965.
- Glauser T, Salinas G, Nevins H, et al. Communication gaps between physicians and patients with postherpetic neuralgia: results from a national study on practice patterns. *J Pain Res* 2011;4:407–415.
- Johnson RW, Wasner G, Saddier P, Baron R. Postherpetic neuralgia: epidemiology, pathophysiology and management. *Expert Rev Neurother* 2007;7:1581–1595.
- Yin CS, Koh HG. The first documental record on bee venom therapy in Oriental medicine: 2 prescriptions of bee venom in the ancient Mawangdui books of Oriental medicine. *J Kor Acu Mox Soc*. 1998;15:143–147.
- Lee JD, Park HJ, Chae YB, Lim S. An overview of bee venom acupuncture in the treatment of arthritis. *Evid Based Complementary Alternat Med*. 2005;2:79–84.
- Shin BC, Kong JC, Park TY, et al. Bee venom acupuncture for chronic low back pain: a randomized, sham-controlled, triple-blind clinical trial. *Eur J Int Med* 2012;4:e271–e280.
- Lee MS, Pittler M, Shin BC, Kong JC. Bee venom acupuncture for musculoskeletal pain: a review. *J Pain* 2008;9:289–297.
- Cho SY, Shim SR, Rhee HY, et al. Effectiveness of acupuncture and bee venom acupuncture in idiopathic Parkinson's disease. *Parkinsonism Related Disord* 2012;18:948–952.
- Janik J, Wania-Galicia L, Kalauokalani D. Bee stings—a remedy for postherpetic neuralgia: a case report. *Reg Anes Pain Med* 2007;32:533–535.
- Young MK, Wood M, Jean-Noel N. Postherpetic neuralgia in older adults—culture, quality of life, and the use of alternative/complementary therapies. *Holist Nurs Pract* 2007;21:124–134.
- Harpaz R, Ortega-Sanchez IR, Seward JF. Advisory Committee on Immunization Practices (ACIP) Centers for Disease Control and Prevention (CDC). Prevention of herpes zoster: Recommendations of the advisory committee on immunization practices (ACIP). *MMWR Recomm Rep* 2008;57(RR-5):1–30.
- Nalamachu S, Morley-Forster P. Diagnosing and managing postherpetic neuralgia. *Drugs Aging* 2012;29:863–869.
- Argoff CE. Review of current guidelines on the care of postherpetic neuralgia. *Postgrad Med* 2011;123:134–142.
- Davies SJ, Harding LM, Baranowski AP. A novel treatment of postherpetic neuralgia using peppermint oil. *Clin J Pain* 2002;18:200–202.
- Whitley RJ, Volpi A, McKendrick M, et al. Management of herpes zoster and post-herpetic neuralgia now and in the future. *J Clin Vir* 2010;48(Suppl 1):S20–28.
- Wood MJ. How should we measure pain in herpes zoster: *Neurology* 1995;45(Suppl 8):S61–62.
- Baron R. Post-herpetic neuralgia case study: optimizing pain control. *Eur J Neurol* 2004;11(Suppl 1):3–11.

Address correspondence to:

Sanghoon Lee, KMD, PhD

Department of Acupuncture & Moxibustion

College of Korean Medicine, Kyung Hee University

#1 Hoegi-dong, Dongdaemun-gu

Seoul 130-702

Republic of Korea

E-mail: shlee777@gmail.com