

# Effect of Peripheral Bee Venom Stimulation on Spinal Inflammatory Responses and Central Neuropathic Pain Behaviors in Spinal Cord Injury Model of Rats

Suk-Yun Kang<sup>1</sup>, Dong-Kyu Uh<sup>1</sup>, Dae-Hyun Roh<sup>1</sup>, Seo-Yeon Yoon<sup>1</sup>, Hyoung-Sig Seo<sup>1</sup>, Ji-Young Moon<sup>1</sup>,  
Hyun-Woo Kim<sup>2</sup>, Young-Bae Kwon<sup>3</sup>, Ho-Jae Han<sup>4</sup>, Jang-Hem Lee<sup>1\*</sup>

<sup>1</sup>*Department of Veterinary Physiology, College of Veterinary Medicine and BK21 Program for Veterinary Science, Seoul National University, Seoul,*

<sup>2</sup>*Department of Physiology, College of Medicine and Research Institute for Medical Sciences, Chungnam National University, Daejeon,*

<sup>3</sup>*Department of Pharmacology, Institute for Medical Science, Chonbuk National University Medical School, Jeonju,*

<sup>4</sup>*Biotherapy Human Resources Center, College of Veterinary Medicine, Chonnam National University, Gwangju, South Korea*

**Introduction:** Spinal cord injury (SCI), which results from a direct traumatic damage on the cord itself, has been associated with many clinical complications such as functional disability, autonomic dysreflexia, urinary tract problems and altered sensations (1). Chemical acupuncture with bee venom (BV) has been traditionally used in eastern medicine to treat several inflammatory diseases or chronic pain conditions (2, 3). In the present study, we investigated whether the treatment of BV into Zusanli acupoint suppressed intraspinal inflammatory responses as well as hyperalgesic and allodynic behaviors in SCI model of rats.

**Materials and Methods:** SCI was induced by T13 spinal cord hemisection after laminectomy. SCI surgery produced acute migration of the neutrophils and the dramatic increment of myeloperoxidase (MPO) activity in the spinal cord lesions at 24 hours following hemisection. In addition, the thermal hyperalgesic and mechanical allodynic behaviors were developed in the bilateral hind paws throughout the 28 days of experiment. Subcutaneous injection (0.25 mg/kg) of BV was applied into each ipsilateral or contralateral Zusanli acupoint twice a day for five days.

**Results:** BV stimulation significantly suppressed neutrophils infiltration and the MPO activity at 24 hours after hemisection. Moreover, mechanical allodynia and thermal hyperalgesia were relieved throughout the experimental period. BV injection also showed the facilitated motor function recovery as indicated by the Basso-Beattie-Bresnahan rating score. Finally, spinal glial fibrillary acidic protein (GFAP) expression, a marker for astroglial activation, was also suppressed by BV injection.

**Conclusions:** These results demonstrated that the repetitive application of BV into acupoint not only enhanced functional recovery but also reduced acute-inflammatory response and neuropathic pain behavior after SCI. This study suggests that BV acupuncture can be a potential clinical therapy for management of SCI.

## References

1. Weaver LC, Marsh DR, Gris D, Brown A, Dekaban GA. Autonomic dysreflexia after spinal cord injury: central mechanisms and strategies for prevention. *Prog Brain Res* 2006, **152**, 245-63.
2. Kwon YB, Lee JD, Lee HJ, Han HJ, Mar WC, Kang SK, Beitz AJ, Lee JH. Bee venom injection into an acupuncture point reduces arthritis associated edema and nociceptive responses. *Pain* 2001, **90**, 271-80.
3. Roh DH, Kwon YB, Kim HW, Ham TW, Yoon SY, Kang SY, Han HJ, Lee HJ, Beitz AJ, Lee JH. Acupoint stimulation with diluted bee venom (apipuncture) alleviates thermal hyperalgesia in a rodent neuropathic pain model: involvement of spinal alpha 2-adrenoceptors. *J Pain* 2004, **5**, 297-303.