THE PAIN RELIEF EFFECT OF THE SILICONE TUBE COVERING THE PROXIMAL NERVE STUMP


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1. Introduction
When the peripheral nerve is cut, deafferentation pain or localized pain accompanying tissue injury occur in the acute stage. Then, they may be shifted to neuropathic pain such as phantom limb pain or painful neuroma which last morbidly. Lundborg et al published many reports on prevention and treatment of neuroma using tube. They described that the proximal nerve stump (PNS) inserted into the tube grows by several millimeters, did not form neuroma but formed the cone-shaped structure and neurophysiological characteristics of painful neuroma were not observed. However, pathophysiological mechanism of pain relief effect by tube remains unclear.

Recently, it was found that nerve growth factor (NGF) was involved in onset of persistent acute pain. As the action mechanism, it is considered that not only NGF itself acts as algesic substance, but also it has action to increase neuro transmitter substances relating to pain in the dorsal root ganglion (DRG). As the receptor of NGF, there are TrkA, high-affinity receptor and p75, low-affinity receptor. NGF binding to TrkA is taken into the nociceptive fibers and transferred to the cell body of the DRG via retrograde axonal transport, and regulates gene expression related to pain.

In the proximal stump of the sciatic nerve of the rat, development of neurotrophic factors such as NGF or BDNF are observed. From the human neuroma also, an increase in NGF and TrkA are observed. Furthermore, in neuroma, infiltration of inflammatory cells such as macrophages or mast cells was observed. Macrophage regulates NGF synthesis of Schwann cell and mast cell binds to NGF and releases algesic substance, suggesting relation with neuropathic pain by means of NGF.

In the present study, to elucidate the pain relief action of covering the nerve stump, we observed autotomy as the index of pain. Additionally, to elucidate the pathophysiological pain relief mechanism of ST, we examined the changes of NGF and TrkA expression in the DRG and PNS, and evaluated the changes inflammatory cells in the PNS.

2. Materials and Methods
We produced the ST group in which the proximal stump of the rat sciatic nerve was introduced into the ST and the control group was no tube. Then we observed autotomy as the index of pain, and evaluated expression of NGF and TrkA in the DRG and the PNS. Additionally, in order to observe the inflammatory cell infiltration in the PNS, immunohistochemistry using S-100 antibody and ED-1 antibody and Toluidine blue stain were performed.

3. Results
The score of autotomy in the ST group was significantly lower than that in the control group between 3days and 2weeks (Fig 1). Although an increase in NGF-immunoreactivity (IR) and TrkA-IR in the PNS were significantly inhibited in the ST group (Fig 2 A, B), there were no differences in the DRG. An increase in the number of macrophages and mast cells and lymphocytes in the PNS was significantly inhibited in the ST group (Fig 2 C, D).

4. Discussion and Conclusion
Based on the observation of autotomy, it was considered that pain relief effect of the ST occurs primarily in the early stage after nerve transection and retards the shift from acute pain to neuropathic pain. As the mechanism, the action of blocking infiltration of NGF as algesic substance. Schwann cell, macrophage, and lymphocyte which promote an increase in NGF synthesis, and furthermore mast cell which binds to NGF and releases algesic agents into the PNS was considered.

Reference

Fig. 1 Time course of autotomy. Autotomy scores indicate mean values of each group at each follow-up period (mean ± SEM). The ST group is indicated by closed circle and the control group by open circle (n = 10/group). *P<0.05 compared with the control rats.

Fig. 2 Photomicrographs showing the NGF-IR in the PNS in the control group (A) and in the ST group (B) at 1 week after surgery. In the control group, NGF-IR were scattered in the disarrayed nerve fibers or in the cells among nerve fibers. In the ST group, an increase in NGF-IR was inhibited when compared with the control group. Photomicrographs showing the ED-1-IR in the PNS in the control group (C) and in the ST group (D) at 1 week after surgery. In the control group, there were several macrophages indicating ED-1-IR among disarrayed nerve fibers. In the ST group, an increase in macrophages was inhibited when compared with in the control group. Scale bar, 100 µm in (A, B). Scale bar, 50 µm in (C, D).

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