Efficacy of Neurotropin in Fibromyalgia: A Case Report

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ABSTRACT

Fibromyalgia is a refractory disorder that often necessitates long-term treatment. A 45-year-old woman has suffered from a stiff neck for 27 years and severe widespread pain for 4 years. Her visual analog scale (VAS), global-VAS, self-rating depression scale (SDS), and face scale were 48, 38, 42, and 15, respectively. She met the American College of Rheumatology 1990 criteria for the classification of fibromyalgia. Four tablets of Neurotropin (NT) per day alone were administered, and her pain was gradually alleviated over 3 weeks. Her heavy sensation of the body and morning stiffness had almost disappeared 5 months later. Her VAS was 40 after 6 months, but the subjective pain decreased to half that at the initial visit. Her global-VAS, SDS, and face scale were 0, 35, and 8, respectively. No adverse effects were observed. NT, a nonprotein extract from the inflamed skin of rabbits inoculated with vaccinia virus, is a commonly prescribed analgesic drug for chronic pain in Japan. One of the advantages of NT is its few and slight adverse effects. Because NT does not suppress the synthesis of prostaglandin, NT does not cause digestive ulcers. Recent studies suggest that the analgesic mechanism of NT is due to the activation of a descending pain inhibitory system in the brain. Two open studies have shown the efficacy of NT for fibromyalgia. In order to determine whether NT is effective for fibromyalgia, a rigid clinical study, such as a double-blinded, placebo-controlled study, is needed.

Key Words. Fibromyalgia; Neurotropin; Complex Regional Pain Syndrome; Adverse Effects

Introduction

Fibromyalgia is a chronic widespread pain disorder that has been associated with fatigue, sleep disturbance, and other symptoms. Approximately 2% of the population is thought to suffer from fibromyalgia [1,2]. Fibromyalgia is a refractory disorder, and it often necessitates long-term treatment. Therefore, treatments with slight to little adverse effects would be valuable. Neurotropin (NT; Nippon Zoki Pharmaceutical Co., Ltd, Osaka, Japan) has been widely used to treat chronic pain in Japan. Here, we present a fibromyalgia patient who responded to NT.

Case Report

A 45-year-old female office clerk who suffered from severe widespread pain visited our hospital. She had always suffered from a stiff neck since taking a job at age 18. Using a personal computer deteriorated her symptom. She had had lumbago and pain of the right thigh since April 2001. She visited four orthopedic hospitals. Frequent X-ray examinations, magnetic resonance imaging, blood examination, and physical examinations did not reveal any abnormalities. She was diagnosed as...
having no abnormalities or osteoarthritis of the spine. Cervical traction, pelvic traction, nonsteroidal anti-inflammatory drugs (NSAID), massage therapy, and acupuncture were ineffective. At the first visit, symmetric tendon jerk was within normal limits. Her visual analog scale (VAS), global-VAS, self-rating depression scale (SDS), and face scale were 48, 38, 42, and 15, respectively. The patient was barely able to work because of severe pain and fatigue during and after work. She had a history of widespread pain for more than 3 months, but her tender points were less than 11 at the initial visit. However, her tender points were 12 after 1 month, and she met the American College of Rheumatology 1990 criteria for the classification of fibromyalgia [3]. Four tablets of NT per day alone were administered, and her pain was gradually alleviated over 3 weeks. Her heavy sensation of the body almost disappeared 4 months later. Her morning stiffness almost disappeared 5 months later. Her VAS was 40 after 6 months, but her subjective pain decreased to half that at the initial visit. Her global-VAS, SDS, and face scale were 0, 35, and 8, respectively. No adverse effects were observed.

Discussion

In the latter half of the 1940s, Yaoi studied the efficacy of the purified vaccine lymph in autonomic imbalance and allergy in Tokyo University. Kinoshita, who had been engaged in the study of mesenchymal tissue reaction in Osaka University, had studied inflammatory tissue reaction in rabbits inoculated with the purified vaccine lymph. He speculated that the efficacy was not from the activity of the virus itself, but due to biological components produced by the virus in inflammatory tissues. Vaccinia virus causes strong inflammation. A study by Nippon Zoki Pharmaceutical Co., Ltd, with an extract from the inflamed skin of rabbits inoculated with vaccinia virus, was based on Kinoshita’s speculation. It was found that the nonprotein extract from the inflamed skin of rabbits had an antiallergic and sedative effect. NT has been marketed since 1951 and was initially mainly used as an allergy medicine, but it was found that it had an analgesic effect, especially for chronic pain. Nowadays, NT, a nonprotein extract from the inflamed skin of rabbits inoculated with vaccinia virus, is a commonly prescribed analgesic drug for chronic pain in Japan. It is administered in China, too. NT consists of multiple components. Its components and analgesic components in NT are not clear. A deficit of descending pain inhibitory systems has been suggested to contribute to fibromyalgia [4]. Recent studies suggest that its analgesic mechanism is due to the activation of a descending pain inhibitory system in brain [5,6]. Suzuki et al. reported that effect of NT probably involved the supraspinal site of action and the sequential activation of spinal noradrenaline neurons as one of its mechanisms of action [7]. The analgesic mechanism of antidepressants is an activation of a descending pain inhibitory system at the dorsal horn of the spinal cord.

One of the advantages of NT is its few and slight adverse effects [8]. NT does not cause an addiction after administration for more than 1 year. Because it does not suppress the synthesis of prostaglandin, NT does not cause digestive ulcer [9,10]. In rats, NT decreases NSAID-induced ulcers [11] and prevents certain kinds of stress-induced ulcers [12]. Because antidepressants often cause thirst, antidepressants sometimes aggravate burning mouth syndrome. However, NT does not cause thirst, and it does not aggravate burning mouth syndrome. The concomitant administration of NT and antidepressants rarely causes adverse effects. Because medication for chronic pain often requires an extended period, its few and/or slight adverse effects are of tremendous advantage.

NT has often been administered to treat complex regional pain syndrome (CRPS), postherpetic neuralgia, subacute myelo-optico-neuropathy, osteoarthritis, scapulohumeral periarthritis, and chronic low back pain in Japan. We experienced a patient with chronic fatigue syndrome who had been treated for more than a year with NT [13]. NT has been used in National Institutes of Health in a clinical study of CRPS (protocol number: 00-D-0200). Muneshige et al. reported that NT was clinically effective for CRPS in an open study [14]. NT was more effective than placebo in chronic constriction injury model, which is thought to be an animal model of CRPS [15].

Strong evidence suggests that amitriptyline and cyclobenzaprine are effective for fibromyalgia [16,17]. Because cyclobenzaprine cannot be prescribed in Japan, we have prescribed amitriptyline as a first-line drug. The other first-line drug is NT and the second-line drugs are milnacipran, dextromethorphan, and pramipexole in our department. In terms of adverse effects, NT is obviously superior to amitriptyline.

Nishioka et al. administered NT, ranging from 2 to 8 tablets per day (mean 3.3 tablets per day),
to 67 patients with fibromyalgia, and reported that NT was effective for 41 patients (61.2%) after an average of 8.9 months (range 3–15 months) of administration [18]. Their diagnostic criteria may differ from the criteria for the classification of fibromyalgia established by the American College of Rheumatology [3]. Nagaoka et al. administered four NT tablets per day for 12 weeks to 30 patients who had suffered from fibromyalgia for an average of 6 years [19]. A significant improvement was observed in the VAS, global-VAS, and face scale. Of the 30 patients, the improvement rates of 6 (20%) and 9 (30%) were more than 50% and more than 30%, respectively.

Four NT tablets per day were administered in this patient. Muneshige et al. reported that 6 or 8 NT tablets per day were more effective for CRPS than 4 NT tablets per day [14]. Nagaoka et al. reported that a patient, who did not respond to 4 NT tablets per day, responded to 6 NT tablets per day and the VAS improved more than 50% [19]. New adverse effects rarely occur if the dose of NT is increased from 4 to 8 tablets per day. Just 4 NT tablets per day are usually able to be administered because of the Japanese medical system; however, 8 NT tablets per day are preferable from the viewpoint of effects and adverse effects.

NT may be effective for patients with fibromyalgia. However, this case study and two open studies [18,19] do not conclude that NT is effective for fibromyalgia. In order to determine that NT is effective for fibromyalgia, a rigorous clinical study, such as a double-blind, placebo-controlled study, is needed.

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References

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