Maintaining Weight and Nutritional Status with Ninjinyoueito in Elderly Patients with Chronic Wasting Diseases

Yumi Nakagawa,\textsuperscript{1} Katsunori Kagohashi,\textsuperscript{2} Ayako Shioya,\textsuperscript{3} Kensuke Kinoshita,\textsuperscript{4} Hiroshi Tsuji,\textsuperscript{5} *Hiroaki Satoh\textsuperscript{2}

\textit{Divisions of\textsuperscript{1} Pharmacy, \textsuperscript{2}Respiratory Medicine and \textsuperscript{3}Neurology, Mito Medical Center, University of Tsukuba-Mito Kyodo General Hospital, Mito, Japan; \textsuperscript{4}Division of General Medicine, Kasama City Hospital, Kasama, Japan; \textsuperscript{5}Department of Neurology, University of Tsukuba, Tsukuba, Japan}

*Corresponding Author’s e-mail: hirosato@md.tsukuba.ac.jp

Abstract

\textbf{Objectives}: To obtain information on the nutritional maintenance effects of Ninjinyoueito (NYT) in elderly patients with chronic wasting disease, a retrospective study was conducted. \textbf{Methods}: we investigated changes in bodyweight and serum levels of total protein and albumin in patients who received NYT for more than 6 months for chronic wasting diseases in our hospital from April 2009 and October 2019. \textbf{Results}: During the study period, 11 patients (median age: 75 years) had NYT for 6 months or more. The median administration period of NYT was 14 months. The bodyweight, serum total protein, and albumin at the time of last observation were not
statistically different from those at the time of the start of NYT administration (p=0.1755, p=0.7659, p=0.5498, respectively). **Conclusions:** Our study suggested the possibility of maintaining nutritional condition by NYT in elderly patients with chronic wasting disease of various etiologies. More evidence will be required to confirm our results.

**Keywords:** body weight; nutritional status; ninjinyoueito; elderly patients; chronic wasting diseases

**Introduction**

Several Japanese traditional herbal medicines (Kampo medicines in Japanese) have favorable nutritional effects in patients with chronic wasting diseases. ¹ Among Kampo medicines, Hozai in Japanese is a drug that supplements what is physically and mentally lacking.¹ Ninjinyoueito (NYT) is one of the Hozai and has been used for improving disturbances and imbalances in the homeostatic condition of the body.² ³ This Kampo medicine is comprised of twelve herbs including ginseng, which is one of the most famous herbal medicines and is used to treat various symptoms in patients with chronic wasting diseases.⁴ It is hypothesized that the NYT might be a candidate drug for a treatment for the frailty symptoms observed in the elderly.⁵

A retrospective study was conducted in order to obtain information on the nutritional maintenance effects of NYT in elderly patients with chronic wasting disease. For the purpose of obtaining information for exploring the nutritional status-maintaining effects of NYT in elderly patients with chronic wasting disease, a retrospective study was conducted. For this purpose, we investigated changes in bodyweight, serum levels of total protein and albumin in all the patients who received NYT for more than 6 months for chronic wasting diseases in our hospital.
Methods

Medical records of all of the patients who had NYT for more than 6 months for chronic wasting diseases in our hospital from April 2009 and October 2019 were reviewed. Bodyweight, serum levels of total protein and albumin in these patients were evaluated at the times of start and termination of NYT prescription. NYT (2.5g: Kracie Pharmaceutical, Ltd., Tokyo, Japan or 3.0g: Tsumura Pharmaceutical Ltd., Tokyo, Japan) was given orally three times per day. To rule out possible effects on bodyweight, serum protein, and albumin levels, patients treated with continuous administration of corticosteroids, and those with serum protein transfusion during the study period were excluded in this study.

Due to a small number of patients who took NYT for a long time period, comparisons of bodyweight, serum levels of total protein, and albumin levels before and after NYT administration for each patient were performed in this study instead of a background-matched property case-control study. We used Wilcoxon rank-sum test, a non-parametric test of paired samples.

This study was approved by the Institutional Review Board in our institute (No. 15-26). Comprehensive written informed consent was obtained from each patient.

Results

During the study period, 11 patients (6 males and 5 females) who had NYT for 6 months or more were found in our in-hospital database. The median age of them was 75 years (range 56-90 years). All 11 patients had lost appetite, and 8 had general fatigue. Underlying chronic diseases of them were as follows: 4 patients had respiratory diseases
(2 patient with chronic obstructive pulmonary disease, 1 patient with nontuberculous mycobacteriosis, and 1 patient with combined pulmonary fibrosis and emphysema), 4 neurological diseases (2 patient with Parkinson disease and 2 patients with polyneuropathy), and 3 digestive diseases (2 patients with chronic gastritis and 1 patient with gastric ulcer). The median administration period of NYT was 14 months (range: 8-61 months). The bodyweight at the last observation (median: 47.9kg, range: 43.5-70 kg) was not statistically different from the bodyweight at the start of administration (median: 48 kg, range: 42.7-70 kg)(p=0.1755, Wilcoxon rank-sum test). There was no statistical significant difference in serum total protein level between them (median: 7.0, range: 5.7 - 8.2 g/dl vs median: 6.9, range: 5.8 - 7.9g/dl)(p=0.7659). Serum albumin level at the last observation (median: 3.9, range: 2.8 - 4.6g/dl) was not lower than that at the start of administration (median: 3.9, range: 2.4 - 4.6g/dl) (p=0.5498). In male patients, changes in bodyweight, serum levels of total protein and albumin between at the start and end of NYT administration were not statistically significant (all p=0.2763, respectively). In female patients, there also were no changes in these three indicators at the time of two measurements (all p=0.2850, respectively).

Discussion

Among Japanese traditional herbal medicines (Kampo medicines), Hozai is a drug that supplements what is physically and mentally lacking.⁴ Since the 18th century, NYT has been prescribed according to the original text without any changes in our country.⁶ NYT is made up of a combination of several crude herbal medicines; rehmannia root, Japanese angelica root, atractylodes rhizome, poria sclerotium, ginseng, cinnamon bark, polygala root, peony root, citrus unshiu peel, astragalus root, glycyrrhiza and schisandra fruit.⁶ Of these herbal medicines, ginseng is one of the most famous herbal medicines and has been administered to patients with chronic wasting diseases⁴ NYT has been
reported to be effective in anorexia in elderly individuals\textsuperscript{5} and fatigue in patients with cancer in various organs.\textsuperscript{2} The effects of NYT on frailty, cachexia, and sarcopenia in patients with malignant and those with non-malignant diseases have been studied.\textsuperscript{2, 5} However, only a few studies have reported the long-term effects of this Kampo medicine on bodyweight gain in patients with various chronic wasting diseases in English literature.\textsuperscript{2, 5} Considering these backgrounds, we examined the effects of NYT on the maintenance of bodyweight and nutritional status in elderly patients with chronic wasting diseases. Recently, researchers in Kracie Co. Ltd. conducted a post-marketing survey in elderly patients to evaluate the safety and effectiveness of NYT.\textsuperscript{5} In this post-marketing survey, the safety and effectiveness of NYT in 808 elderly patients were evaluated.\textsuperscript{5} Median age of them was 78 years. In their study, bodyweight at both baseline and week 24 were analyzed in 275 (34.0\%) of 808 patients. They reported that the mean bodyweight in 275 patients increased significantly from 49.4 ± 9.0 kg at baseline to 50.0 ± 9.0 kg at week 24 (p < 0.01). There was a significant difference in women (p<0.01), but not in men.\textsuperscript{5} Although bodyweight increased 0.6 kg on average, it was not the result of all the 808 patients, and bodyweight was analyzed using a paired t-test, which is not a non-parametric test.\textsuperscript{5} In addition, serum levels of total protein and albumin were not evaluated in their study.\textsuperscript{5} It was interesting that the mean or median bodyweight was around 50kg in the postmarketing survey\textsuperscript{5} as well as in our study. Regarding the difference in changes of bodyweight in the post-marketing survey and those in our study, it might be due to the difference in background diseases and that the statistical analyzing method must be considered. The characteristics of the traditional Japanese herbal medicine (Kampo) approach is to deal with anorexia due to different pathologies in an integrated manner, rather than comparative analyses by Western medical way of approaches. Therefore, it is meaningful to share information on the treatment results of patients who wish to be treated with herbal medicine. We followed
up patients more than 6 months and confirmed no patients received drugs that might affect the nutrition of the patients after the start of NYT administration. Although this small sized study without a comparative group could not be enough to draw conclusion, the information obtained in this study might help to explore the role of the NYT.

Conclusion
The results obtained in this study suggested the possibility of maintaining nutritional condition by NYT in elderly patients with chronic wasting disease of various etiologies. As there is no control group in our study, future studies should include a control group to enable a solid conclusion to be drawn.

Conflict of Interest
The author declares no conflicts of interest.

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Authors’ Contributions
YN, KK and HS designed the study. KK, YN, AS, KK, HK, HT and HS collected the data. YN, KK, and HS analyzed the data and prepared the manuscript. All authors approved the final version of the article.

References


