

Title:

**Intervention trial to improve nutritional status in frail elders using a digestive enzyme drug**

Authors:

Hiroshi Shibata, MD, PhD 1)

Shuichiro Watanabe, MD, PhD 2)

Shu Kumagai 2)

Nami Kobayashi 3)

1) Obirin University

2) Department of Community Health, Tokyo Metropolitan Institute of Gerontology

3) Department of Social welfare, Tokyo Metropolitan Institute of Gerontology

Correspondence to:

Shuichiro Watanabe, MD, PhD

Department of Community Health, Tokyo Metropolitan Institute of Gerontology, 35-2 Sakae-cho, Itabashi, Tokyo 173-0015, JAPAN

Phone: +81-3-3964-3241 ext.3123 / Fax.: +81-3-3579-4776

E-mail: swan@tmig.or.jp

Running title:

IMPROVE NUTRITIONAL STATUS IN THE FRAIL ELDERLY

Key words: frail elderly, intervention trial, nutrition, digestive enzyme

## **Abstract**

Frail institutionalized elderly people have a high prevalence of nutritional risk factors, undernutrition, weight loss, and nutrition-related morbidity and excess mortality. Little information is available on effective means to intervene in this setting. The purpose of the present study was to clarify the usefulness of a digestive enzyme drug for the frail institutionalized elderly. A 25-wk intervention trial was performed in 36 frail elderly people (10 men, 26 women). Subjects were assigned to digestive enzyme drug intervention group (n=19) and control group (n=17). Of 36 subjects, 13 of the intervention group and 11 of the control group underwent follow-up examination. Serum albumin and HDL-cholesterol levels increased significantly in the intervention group, while in the control group, the changes were not significant. Serum aspartate aminotransferase increased significantly in the intervention group, while in the control group, the change was not significant. There were no significant changes in the other variables in either group. The results of this study imply that the digestive enzyme drug is a practical means to improve nutritional status among the frail institutionalized elderly.

## **Introduction**

Nutritional status is strongly related to diseases 1-3), physical function 4,5), life satisfaction 6), and life expectancy 3,7-11) in the elderly. Overnutrition is the risk factor for ischemic heart disease for the middle aged, while undernutrition is the apparent risk factor for infectious diseases and even for ischemic heart disease in the elderly 1).

There are two types of undernutrition: one is from protein-energy undernutrition, and the other is from chronic insufficiency of dietary fiber, calcium, and iron. Undernutrition in the elderly results mainly from protein-energy undernutrition 12,13). The prevalence of undernutrition in the United State is higher than that in Japan, and is related to demographic factors, socio-economic factors, and loss of physical function. One cause of undernutrition of the Japanese elderly is the traditional idea that meat eating carries a stigma, such as 'fish is good and meat is not good for the elderly', since Buddhism entered Japan long ago 14). Nutrition education is the most useful tool to extinguish this superstition 15).

Frail institutionalized elderly people tend to undernutrition though meals are served every day. This is because of chronic diseases, leaving meals 16,17), and loss of chewing ability 18,19).

We proposed the hypothesis that a digestive enzyme drug would improve overall nutritional status of the frail institutionalized elderly. Several studies have reported the usefulness of a digestive enzyme drug for postgastrectomy patients 20) and for postpancreatectomy dogs 21). It has been suggested that the digestive enzyme drug is useful for the elderly 22), but there is no substantiated research on the utility for the elderly.

## Subjects and Methods

One hundred residents, aged 65 or older living in a nursing home in a suburb of Tokyo, were recruited for the study. Of 100 residents, 93 residents except those who stayed outside facilities or hospitalized individuals were divided randomly into 2 groups, matched with sex, age, activities of daily living, and body mass index (BMI) (Table 1). After signing informed consent forms by the subjects and their proxies, which had been approved by the ethics committee of the Tokyo Metropolitan Institute of Gerontology (No.1997-21), 36 residents took part in the survey (Table 2).

The baseline survey was carried out in July 1998. In the survey, serum albumin, total cholesterol, HDL cholesterol, iron, blood urea nitrogen, zinc, Vitamin E, uric acid, aspartate aminotransferase, alanine aminotransferase, hemoglobin A1c, hemoglobin, hematocrit, red blood cell count, white blood cell count, body weight, and amount of the remains of daily meals were determined. The staff of the facility determined the remains of daily meals.

The intervention group received the marketed digestive enzyme drug (Biodias, Amano Pharmaceutical Co., Ltd.; biodiastase 45mg, lipase AP12 10mg, newlase 30mg) 3 times/day after meals for 6 months. The follow-up survey was conducted in January 1999. Comparisons of continuous variables between the baseline variables and the follow-up variables were performed with paired t-test.

## Results

Out of the 93 residents identified as eligible and who were asked to participate in the baseline survey, 36 received the baseline survey. There were no significant differences in sex and age between the 2 groups at the baseline survey (Table 1, 2). Among the subjects, 6 (31.6%) of the intervention group and 6 (35.3%) of the control group were regarded as independent in basic activities of daily living. In regard to feeding ability, 9 (47.4%) of the intervention group and 8 (47.1%) of the control group were independent, and 5 (26.3%) of the intervention group and 4 (23.5%) of the control group were fully dependent.

As shown in Table 3, 13 of the intervention group and 11 of the control group underwent follow-up examination. Among the determined variables, there was no difference in amount of the remains of daily meals between groups. There was also no significant change in body weight in either group (Table 4).

Means and SDs for the blood component variables at the baseline and the follow-up are provided in Table 5. Serum albumin level increased significantly in the intervention group, while in the control group, the change was not significant. There were no significant changes in serum total cholesterol levels in either group. Serum HDL-cholesterol level increased significantly in the intervention group, while in the control group, the change was not significant. Aspartate aminotransferase increased significantly in the intervention group, while in the control group, the change was not significant.

There were no significant changes in the other variables in either group.

## **Discussion**

One convenient method for evaluating nutritional status is to evaluate the body build. The result of our former study has clarified that BMI for the elderly had a U-shaped relationship with all-cause mortality in both sexes 9). Other studies showed that serum total cholesterol for the elderly also had a U-shaped relationship with all-cause mortality. The previous study showed that for the 70 years old elderly, lowest relative risk for mortality was at TC between 190 and 219 mg/dL for men, and at TC between 220 and 249 mg/dL for women. The TC levels in the present study were considered lower than the optimal level. Low cholesterol levels were also associated with decline of physical function and depressive symptoms for the elderly 5,6). In the present study, changes in body weight and TC in the intervention group were desirable, though there were no statistically significant differences.

***In the present study, HDL-cholesterol level increased significantly in the intervention group.*** It has been well known that high HDL-cholesterol level is the preventive factor for ischemic heart disease. Further, Shibata et al demonstrated that high HDL-cholesterol level was related both to decreased all causes mortality and cancer mortality in the elderly 3). The results of our study suggested that the digestive enzyme drug would improve life expectancy of the frail institutionalized elderly.

More than cholesterol, serum albumin has been related to physical health in the elderly. Among the elderly, significant negative association was found between serum albumin level and mortality 9,10). Low albumin level was also regarded as a risk factor for declining basic activities of daily living 24). It seems that serum cholesterol level relates to an emotional quality of life and higher functional competence, and serum albumin level relates to the basic physical function 24). It was thought that the digestive enzyme drug improved nutritional status of the elderly, ***because the serum albumin levels increased significantly in the intervention group.*** in the light of the fact that serum albumin in the elderly declines with aging in general. Though there was no significant difference in the control group, there was a tendency to increased albumin level. This might be due to the intervention effect and seasonal variation.

In conclusion, the results of this study imply that the digestive enzyme drug is practical for improving nutritional status among the frail institutionalized elderly, as the digestive enzyme drug is convenient and cost-saving with few side effects.

## **Acknowledgements**

The authors are grateful to residents and staff members of the Taikoro Care Center.

## **References**

- 1) Corti MC. et al: Serum albumin and physical function as predictors of coronary heart disease

- mortality and incidence in older persons. *J. Clin. Epidemiol.* 49: 519, 1996.
- 2) Mowe M. and Bohmer T: Nutrition problems among home-living elderly people may lead to disease and hospitalization. *Nutr Rev.* 54: 1 Pt 2, S22-24, 1996.
  - 3) Shibata H. et al.: Relationship of serum lipids to 10-year deaths from all causes and cancer in Japanese urban dwellers aged 40 years and over. *J. Epidemiol.* 5: 87-94, 1995.
  - 4) Kumagai S. et al.: Relationship of dietary patterns to change in functional capacity (intellectual activities) in the community dwelling elderly. *Japanese Journal of Gerontology.* 16: 146-155, 1995.
  - 5) Shibata H. et al.: Health problems in aging populations. *J. Epidemiol.* 6: s71-s78, 1996.
  - 6) Shibata H et al.: Relationship of serum cholesterols and vitamin E to depressive status in the elderly. *J. Epidemiol.* 9: 261-267, 1999.
  - 7) Haga H. et al.: Risk factors for mortality of the aged at old people's homes. *Japanese Journal of Geriatrics.* 18: 425-431, 1981.
  - 8) Shibata H. et al.: Nutrition for the Japanese elderly. *Nutrition and Health.* 8: 165-175, 1992.
  - 9) Shibata H. et al.: Predictors of all-cause mortality between ages 70 and 80: the Koganei Study. *Arch. Gerontol. Geriatr.* 14: 283-297, 1992.
  - 10) Shibata H. et al.: Longitudinal changes of serum albumin in the elderly people living in the community. *Age and ageing.* 20: 417-420, 1992.
  - 11) Frisoni GB. Et al.: Food intake and mortality in the fail elderly. *Journals of gerontology. Series A, Biological Sciences & Medial Sciences.* 50: M203-210, 1995.
  - 12) Gariballa SE: Nutritional support in elderly patients. *J Nutr. Health Aging.* 4: 1, 25-7, 2000.
  - 13) Kumagai S. and Shibata H.: Relationships between undernutrition and diseases in the elderly. *Geriatric Medicine.* 35: 739-744, 1997
  - 14) Oiso T.: History of food and diet in Japan. *Progress in Food & Nutrition Science.* 2: 35-48, 1976.
  - 15) Kumagai S. et al.: An intervention trial to postpone aging in competent elderly: trial of nutritional improvement in the retirement home. *Japanese Journal of Public Health.* 46: 1003-1012, 1999.
  - 16) Kim T. et al.: Comparison of waste composition in a continuing-care retirement community. *Journal of the American Dietetic Association.* 97: 396-400, 1997.
  - 17) Hackes BL. et al.: Tray service generates more food waste in dining areas of a continuing-care retirement community. *Journal of the American Dietetic Association.* 97: 879-882, 1997.
  - 18) Nagai H. et al.: The relationship of chewing ability to nutrient and food intakes in the community elderly. *Japanese Journal of Public Health.* 38: 853-858, 1991.
  - 19) Teraoka K. et al.: Interrelationship between chewing ability, oral condition and dietary attitude among the elderly. *Japanese Journal of Gerontology.* 10: 11-17, 1995.
  - 20) Bar W. and Usbeck W.: Care of patients after gastrectomy. *Zentralblatt fur Chirurgie.* 96: 1181-1188, 1971.

- 21) Yamada S, Mayahara T, Maruyama I, Shibasaki S, Tokuyoshi K, Iso A: Digestant effects of a new digestive enzyme capsule, Excelase, on jejunectomized and pancreato- jejunectomized Beagle dogs. *Folia Pharmacologica Japonica*. 74(1): 49-60, 1978.
- 22) Kataria MS.: A clinical double-blind trial with a broad spectrum digestive enzyme product ("Combizym") in geriatric practice. *British Journal of Clinical Practice*. 23: 15-17, 1969.
- 23) Yukawa H. et al.: Relationship between nutrient intake and bone mineral density in an urban community of healthy elderly women. *Japanese Journal of Public Health*, 45: 968-978, 1998.
- 24) Wu\_AW.: Predicting functional status outcomes in hospitalized patients aged 80 years and older. *J. Am. Geriatr. Soc*, 48: S6-15, 2000.

Table 1. Comparison of eligible subjects on background variables

	Intervention group	Control group
Male (N)	12	12
Female (N)	35	34
Total	47	46
Age (Mean±S.D.)	79.1±9.8	80.4±9.0
BMI (Mean±S.D.) kg/m <sup>2</sup>	19.1±3.5	19.4±3.5

Table 2. Respondents at the baseline survey

	Intervention group	Control group
Male (N)	6	4
Female (N)	13	13
Total	19	17
Age (Mean±S.D.)	77.2±12.1	80.4±7.3

Table 3. Outcomes of subjects in the follow-up, 6 months later

	Intervention group	Control group
Discharge	2	3
Impossible to collect blood	1	0
Discontinue (Dropout)	3	-
Admit	0	3
Follow-up	13 (Male: 4, Female: 9)	11 (Male: 3, Female: 8)
Age * (Mean±S.D.)	76.2±13.7	77.5±5.1

\*: Mean age for the follow-up groups

Table 4. Change in body weight for intervention group and control group

	Group	Baseline	Follow-up	p
Body weight (Kg)	Intervention group	45.2±8.4	45.7±7.9	n.s.
	Control group	41.1±6.0	40.6±5.1	n.s.

Table 5. Changes in blood components for intervention group and control group

Variables	Group	Baseline	Follow-up	p
Albumin (g/sL)	Intervention group	3.98+0.21	4.24+0.26	<0.05
	Control group	3.88+0.45	4.00+0.71	n.s.
Total cholesterol (mg/dL)	Intervention group	180.8+26.5	192.0+40.9	n.s.
	Control group	174.3+40.1	170.8+42.2	n.s.
HDL-cholesterol (mg/dL)	Intervention group	46.5+14.2	53.5+16.6	<0.001
	Control group	53.7+15.8	54.6+17.9	n.s.
Serum iron (mcg/dL)	Intervention group	65.9+35.0	71.2+34.6	n.s.
	Control group	67.5+30.7	64.9+31.3	n.s.
Blood urea nitrogen (mg/dL)	Intervention group	13.4+2.9	14.2+3.3	n.s.
	Control group	16.0+4.1	16.2+3.7	n.s.
Zinc (mcg/dL)	Intervention group	74.1+8.4	76.5+13.9	n.s.
	Control group	74.8+17.3	69.5+15.8	n.s.
Vitamin E (mg/dL)	Intervention group	1.02+0.31	1.01+0.31	n.s.
	Control group	1.12+0.44	1.07+0.50	n.s.
Uric acid (mg/dL)	Intervention group	5.4+1.3	4.7+1.3	n.s.
	Control group	4.8+1.2	4.6+1.0	n.s.
Aspartate aminotransferase (U/L)	Intervention group	19.5+4.1	21.9+5.2	<0.05
	Control group	28.0+12.7	25.7+12.3	n.s.
Alanine aminotransferase (U/L)	Intervention group	13.4+7.0+	16.1+9.6	n.s.
	Control group	23.3+21.6	21.4+18.1	n.s.
Hemoglobin A1c (%)	Intervention group	5.2+0.4	5.2+0.4	n.s.
	Control group	5.3+0.6	5.4+0.8	n.s.
Hemoglobin (g/dL)	Intervention group	12.1+2.0	12.3+2.2	n.s.
	Control group	12.6+1.4	12.2+1.9	n.s.
Hematocrit (%)	Intervention group	37.9+5.7	38.5+6.3	n.s.
	Control group	38.6+5.0	37.8+6.5	n.s.
Red blood cell count (millions/mm <sup>3</sup> )	Intervention group	404+50	409+48	n.s.
	Control group	413+54	402+72	n.s.
White blood cell count (/mm <sup>3</sup> )	Intervention group	5930+825	6000+1543	n.s.
	Control group	5872+1735	6136+1492	n.s.