

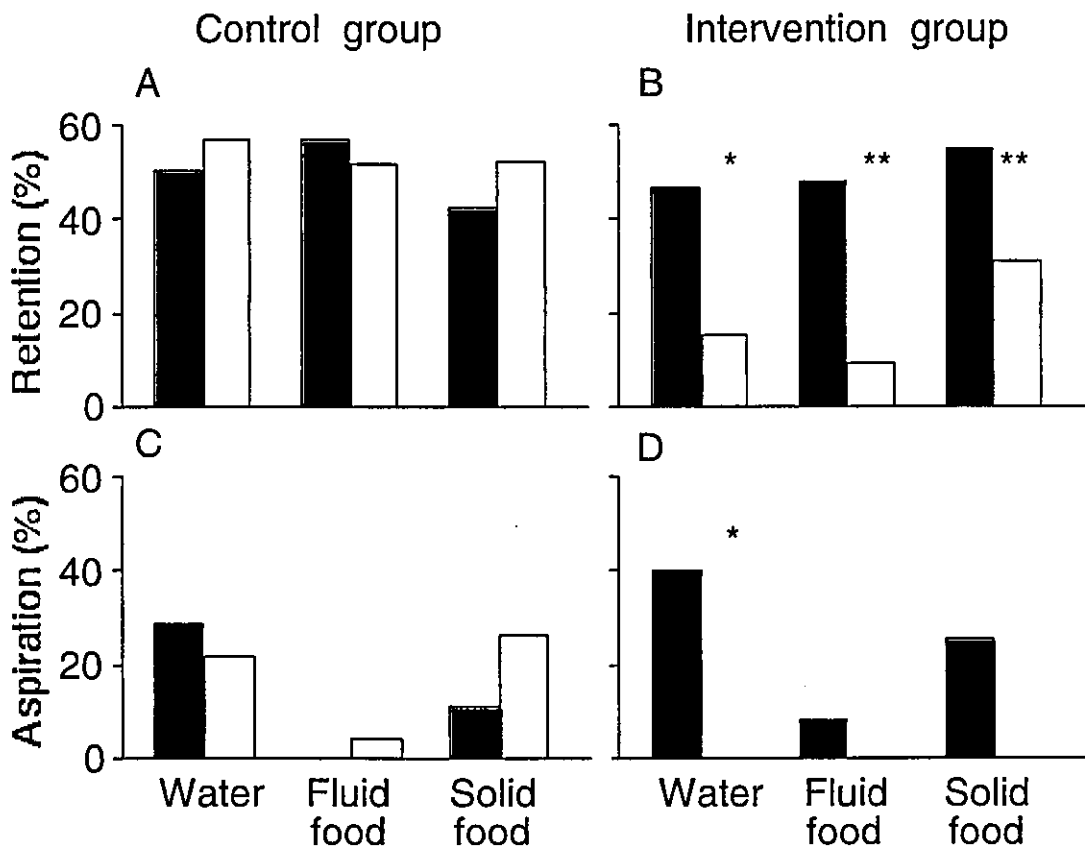
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3. Seki T, Kurusu M, Tanji H et al. Acupuncture and swallowing reflex in post-stroke patients. *J Am Geriatr Soc* 2003;51: 726-727.
4. Seki T, Kurusu M, Arai H et al. Acupuncture for gait disorders in the elderly. *J Am Geriatr Soc* 2004; 52: 643-644.

## FIGURE LEGEND

**Figure 1:** The rate of pharyngeal retention (A, B) and aspiration (C, D) in the control and intervention group at baseline (closed column) and after four weeks (open column).

\* and \*\* show significant decreases after four weeks compared with baseline by the Wilcoxon signed rank test,  $P < 0.05$  and  $P < 0.01$ , respectively.



--Letter to the Editor--

**Acupuncture for Dysphagia in Poststroke Patients**  
**: A Videofluoroscopic Study**

Takashi Seki MD PhD<sup>1</sup>, Hideo Hayashi BSc<sup>2</sup>, Shizuru Yamada MD<sup>2</sup>, Koh Iwasaki MD, PhD<sup>1</sup>, Kenji Toba MD, PhD<sup>3</sup>, Hiroyuki Arai MD, PhD<sup>1</sup>, Hidetada Sasaki MD, PhD<sup>4</sup>

<sup>1</sup>Department of Geriatric and Complementary Medicine  
Center for Asian Traditional Medicine Research, Tohoku University  
Graduate School of Medicine

<sup>2</sup> Health Service Facilities for the Elderly, Mahoroba-no-Sato

<sup>3</sup>Department of Geriatric Medicine, Kyorin University School of Medicine

<sup>4</sup>Department of Geriatric and Respiratory Medicine, Tohoku University  
Graduate School of Medicine

Corresponding Author:

Dr. Takashi Seki, MD, PhD

Associate Professor,

Department of Geriatric and Complementary Medicine, Center for Asian  
Traditional Medicine Research, Tohoku University Graduate School of  
Medicine, 1-1 Seiryomachi, Aoba-ku, Sendai, Miyagi 980-8574, JAPAN

Tel: +81-22-717-7182 Fax :+81-22-717-7186

E-mail : t-seki@geriat.med.tohoku.ac.jp

Acupuncture for Dysphagia in Poststroke Patients

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Severe dysphagia predisposes to medical complications such as aspiration pneumonia in poststroke patients.<sup>1</sup> Existing modalities for treating dysphagia are generally ineffective.<sup>2</sup> We recently reported that acupuncture on two acupoints (Zusanli ST36 and Taixi K3) restored the swallowing reflex<sup>3</sup> and gait disorders<sup>4</sup> in poststroke patients. In this study, we performed a videofluoroscopic study (VFSS) to determine if acupuncture also improves dysphagia and aspiration.

According to Magnetic Resonance Imaging findings, 32 poststroke patients ( $84 \pm 9$  (mean  $\pm$  SD) years, Female/Male 20/12) with episodes of choking while taking food or drinking liquid were selected randomly at an elderly care facility and participated in this study under written informed consent. Participants were randomly assigned into two groups. We practiced acupuncture on the intervention group (18 patients;  $77 \pm 9$  (mean  $\pm$  SD) years, F/M 10/8) three times a week for four weeks with usual care. Four disposable stainless steel fine needles (diameter 0.16 mm, length 40 mm; SEIRIN, Shizuoka, Japan) were inserted in two acupoints (ST36 and K3) bilaterally and kept at a 10 mm depth for 15 minutes without any extra stimulation such as electrical or manual. Fourteen other patients were assigned to the control group ( $79 \pm 5$  (mean  $\pm$  SD) years, F/M 10/4) and

received usual care without acupuncture. VFSS was performed at the base line and four weeks later in both groups. The interval of VFSS was 5 minutes with a random order of three different kinds of food. The patients were asked to swallow 5 mL of water, 5 mL of fluid food (liquidized food) and one piece of solid food (approximately 5ml of a cookie). The water and food were blended with barium (Enemastar Enema Powder, FUSHIMI Pharmaceutical, Marugame, Japan). In each swallowing, VFSS was performed in a lateral projection with the patient in a sedentary position using a fluoroscopy unit (Prestige II, GEMedical Systems, Tokyo, Japan) connected to a DVD-HDD recorder (RD-XS30, TOSHIBA, Tokyo, Japan). Images were obtained at 30 frames per second and reviewed frame by frame with image processing software (Premier 6.0, Adobe Systems, Tokyo, Japan) by a radiologist who did not know if the patient had been treated with acupuncture. Pharyngeal retention was defined as pharyngeal residue of material in the valleculae and in the piriform sinuses after swallowing. Tracheobronchial post-deglutitive aspiration was defined as penetration of material below the level of the vocal folds. VFSS frames from the instruction of swallowing to the time that the material passed the entrance of the esophagus were observed. Body temperature was measured at 2:00 p.m. every day. The

total number of days of fever above 37.8 degrees was counted for four weeks.

The swallowing times at baseline from the instruction of swallowing to the time of passing the entrance of the esophagus were  $1.7 \pm 1.0$ ,  $8.7 \pm 13.2$  and  $10.4 \pm 7.0$  (mean  $\pm$  SD) sec with water, fluid food and solid food, respectively in the intervention group and  $1.9 \pm 0.6$ ,  $4.5 \pm 3.7$ ,  $9.7 \pm 7.6$  sec in the control group. After four weeks the average times were  $1.1 \pm 0.3$  ( $P < .05$ ),  $5.0 \pm 4.8$  ( $P < .05$ ),  $11.8 \pm 9.3$  sec, respectively, in the intervention group and  $2.1 \pm 0.9$ ,  $5.4 \pm 5.4$ ,  $10.1 \pm 6.9$  sec, respectively, in the control group. In the intervention group the swallowing time of water and fluid food were shortened significantly after four weeks.

Figure 1 shows the percentage of pharyngeal retention and aspiration in the two groups. In the intervention group, there were significant decreases of retention, but in the control group there was no significant change. In the intervention group, aspiration at the baseline was observed in 40%, 8% and 25% of the patients with water, liquid and solid foods, respectively, but no aspiration was observed after four weeks. Aspiration did not change in the control group after four weeks. High fever over 37.8 degrees was observed in 28 of 394 days of the control group but only in four days of 356 days of the intervention

group. Fever-up days of the intervention group was significantly lower than that of the control group ( $P < .01$ ). The combination of these acupoints was selected according to the traditional theory of Chinese medicine, and is novel and safe, easy to use. These data show the significant effect of the acupuncture treatment on pharyngeal retention and aspiration. The present study suggests that this acupuncture therapy is a new way to prevent aspiration and aspiration pneumonia in poststroke patients.



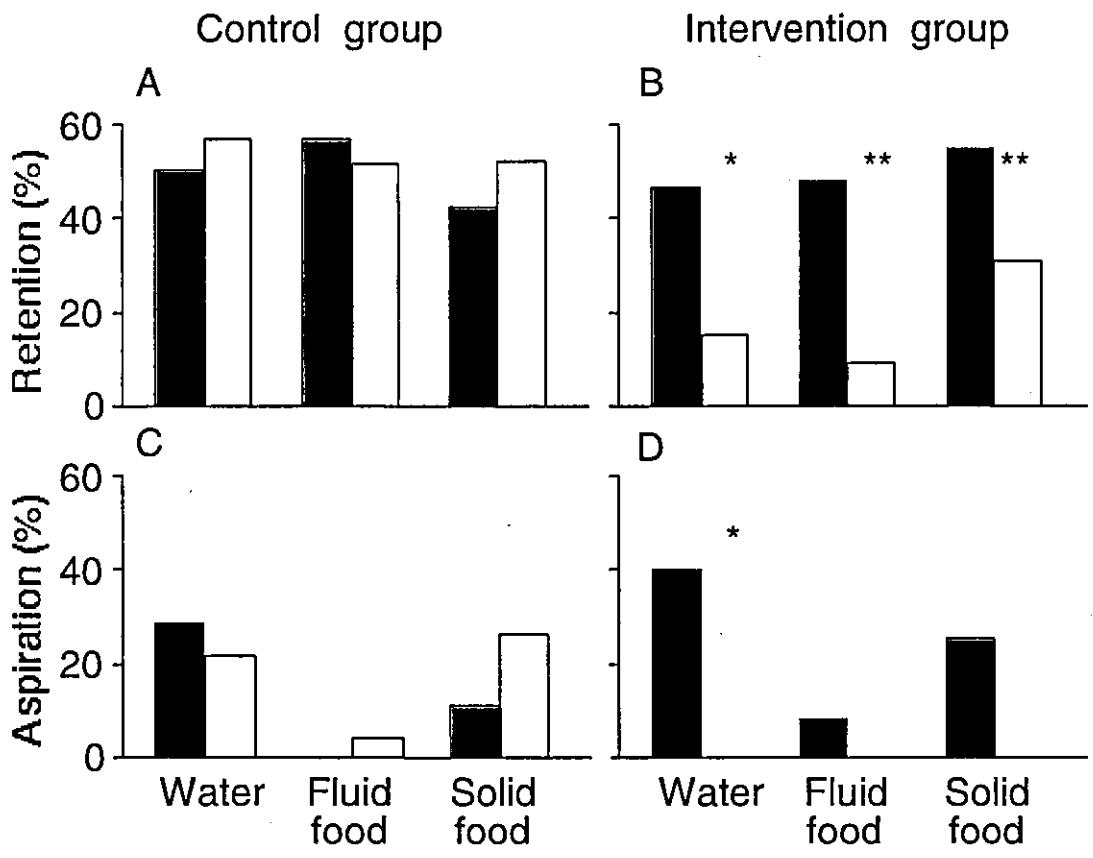
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## LETTERS TO THE EDITOR

### EFFECTS OF PHYSICAL EXERCISE ON PLASMA CONCENTRATIONS OF SEX HORMONES IN ELDERLY WOMEN WITH DEMENTIA

*To the Editor:* Physical exercise may slow the functional decline in elderly people and has been associated with a low incidence of dementia.<sup>1</sup> Physical activities have shown favorable effects on cognitive function as well as on neuropsychiatric symptoms and behavioral disturbance in demented subjects,<sup>1,2</sup> the mechanism of which is currently unknown. Because low plasma levels of sex hormones have been implicated in dementia,<sup>3</sup> it is reasonable to hypothesize that physical exercise could elevate plasma sex hormone levels. Here, we report a preliminary study in which daily physical exercise for 3 months increased the plasma levels of sex hormones, including dehydroepiandrosterone (DHEA) and testosterone, in elderly women with dementia. Thirteen women (aged 74–91, mean age  $\pm$  standard deviation  $84 \pm 5$ ) living in group homes for the elderly (small-scale facilities providing communal living) located in Nagano Prefecture, Japan, were enrolled. They were diagnosed as having Alzheimer's disease according to the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*, but did not have malnutrition, malignancy, or endocrine disease. Blood sampling and functional assessment were performed at baseline, at the end of a 3-month exercise program, and at the end of a 3-month follow-up period, during which the subjects returned to ordinary sedentary living. The exercise program consisted of stretching and mild resistance training using a chair and a 0.5-kg weight. The exercise was performed as a group, with training for 30 minutes daily under the instruction of a physical therapist twice a week and by other caregiver staff five times a week. Care other than exercise was comparable throughout the study. Fasting blood samples were collected early in the morning before exercise. A commercial laboratory determined plasma levels of estradiol, testosterone, DHEA, DHEA sulfate, and sex hormone-binding globulin, in addition to blood cell counts and blood chemical parameters.

Basic activities of daily living (ADLs) were assessed using the Barthel Index and cognitive function using the Mini-Mental State Examination.

At baseline, the subjects showed moderate cognitive impairment and dependency and relatively low sex hormone levels (Table 1). After 3 months of exercise, significant increases were found in plasma levels of testosterone of 18%, estradiol of 38%, and DHEA of 37%, all of which returned to the baseline levels 3 months after cessation of the exercise program. A similar alteration was found in plasma DHEA sulfate level, but the increase by exercise was not statistically significant (mean  $\pm$  standard error  $452 \pm 62$  ng/mL at baseline,  $508 \pm 72$  ng/mL after exercise, and  $464 \pm 77$  ng/mL after discontinuation. Sex hormone-binding globulin, albumin, and other blood parameters did not change throughout the study (Table 1 and data not shown). Despite the increases in sex hormones after the exercise program, neither Barthel Index nor Mini-Mental State Examination scores changed significantly during the study.

Previous studies<sup>4,5</sup> have shown stimulatory effects of endurance or resistance exercise on circulating hormones in healthy postmenopausal women; metabolic alterations and increased blood flow of endocrine organs via nitric oxide and cyclic adenosine monophosphate production may play a causal role, but hormonal responses in frail or demented women have not been examined. In the present study, plasma levels of estradiol, testosterone, and DHEA were higher after 3 months of physical exercise in elderly women with dementia, whereas cognitive function and basic ADLs did not improve. Given the protective effect of exercise and sex hormones on cognitive impairment, a control sedentary group should be included to examine whether this exercise program might delay cognitive decline. Nevertheless, the finding that exercise can increase plasma sex hormone levels in demented women provides a mechanistic insight into the effect of exercise or physical activities on cognitive impairment. The results of this preliminary study need to be confirmed using larger randomized, controlled trials with longer follow-up periods.

Table 1. Effects of Daily Physical Exercise on Plasma Concentrations of Sex Hormones in Elderly Women with Dementia (N = 13)

Measurement	Baseline	Exercise (3 Months)	Discontinuation (3 Months)
	Mean $\pm$ Standard Error of the Mean		
Testosterone, ng/dL	51.4 $\pm$ 3.3	60.8 $\pm$ 3.3 <sup>†</sup>	47.9 $\pm$ 3.9
Estradiol, pg/mL	15.2 $\pm$ 1.2	21.0 $\pm$ 1.2 <sup>†</sup>	19.4 $\pm$ 2.9
Dehydroepiandrosterone, ng/mL	1.84 $\pm$ 0.29	2.52 $\pm$ 0.41*	1.95 $\pm$ 0.27
Sex hormone binding globulin, nmol/L	75.0 $\pm$ 6.1	69.1 $\pm$ 8.1	68.3 $\pm$ 8.3
Barthel Index	75.0 $\pm$ 5.4	70.0 $\pm$ 7.1	66.5 $\pm$ 9.4
Mini-Mental State Examination score	13.9 $\pm$ 1.9	13.8 $\pm$ 2.0	12.4 $\pm$ 2.5

P < .05; <sup>†</sup>.01 versus baseline using paired t test.

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*Masahiro Akishita, MD*  
*Shizuru Yamada, MD*  
*Hiroshi Nishiyama, MD*  
*Kazuki Sonohara, MD*  
*Ryuhei Nakai, MD*  
*Kenji Toba, MD*

*Department of Geriatric Medicine*  
*Kyorin University School of Medicine*  
*Tokyo, Japan*

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LETTER TO THE EDITOR

# Successful aging with constant physical training

Tomoko Yamazaki, Masahiro Akishita, Kumiko Kobayashi, Ayako Machida and Kenji Toba

*Department of Geriatric Medicine, Kyorin University School of Medicine, Mitaka, Tokyo Japan*

Dear Editor,

On 22 May 2003, the press reported that Yuichiro Miura, the 70-year-old Japanese adventure skier, became the oldest person to reach the peak of Mt. Everest. He, being well known internationally as the man who skied down Mt. Everest in 1970, also skied down Mont Blanc this year with his son and his 99-year-old-father, indicating that his family represents a case of successful aging. In April 2003, we had a chance to perform a checkup on Mr Yuichiro Miura, and we here report, with his informed consent, his age-related changes.

He does not have any specific history of illness, and has been a professional adventure skier for more than 40 years. He has constantly performed hard physical training to maintain his muscle strength and alertness. Specifically, his daily training consisted of walking around and climbing the nearest mountains with a 12-kilogram weight on, in addition to skiing in winter. He has taken regular food, and has not paid special attention to his diet. He has never smoked but drinks two bottles of beer four times per week. Body mass index was 27.9 kg/m<sup>2</sup> with waist/hip circumference ratio of 0.93. Blood pressure was 119/89 mmHg. Physical examination and laboratory tests indicated no abnormal findings except for a slightly low plasma HDL-cholesterol level of 39 mg/dL. Unsurprisingly, he showed excellent physical performance measures; e.g. timed up-and-go test of 6.3 s and one-leg standing time with eyes open of more than 10 s. Non-invasive mea-

surements of subclinical atherosclerosis showed that endothelium-dependent flow-mediated dilatation of the brachial artery was 6.7% and brachial-ankle pulse wave velocity was 1279 cm/s, which both corresponded to the average values in middle-aged healthy controls.<sup>1,2</sup> Abdominal CT (Fig. 1) revealed that the areas of visceral and subcutaneous fat were 97 cm<sup>2</sup> and 141 cm<sup>2</sup>, respectively, indicating that subcutaneous fat was predominant, but calcification was found in the abdominal aorta.

Overall, he was obviously healthy and had outstanding physical function and vascular function that was young for his age, although some aspects of aging such as aortic calcification were found. Given the preventive effect of physical training on aging,<sup>3</sup> the influence may differ according to organ and function. The present case suggests that even a superman cannot avoid aging.

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Correspondence: Kenji Toba, MD, PhD, Department of Geriatric Medicine, Kyorin University School of Medicine, 6-20-2 Shinkawa, Mitaka, Tokyo 181-8611, Japan. Email: toba@kyorin-u.ac.jp

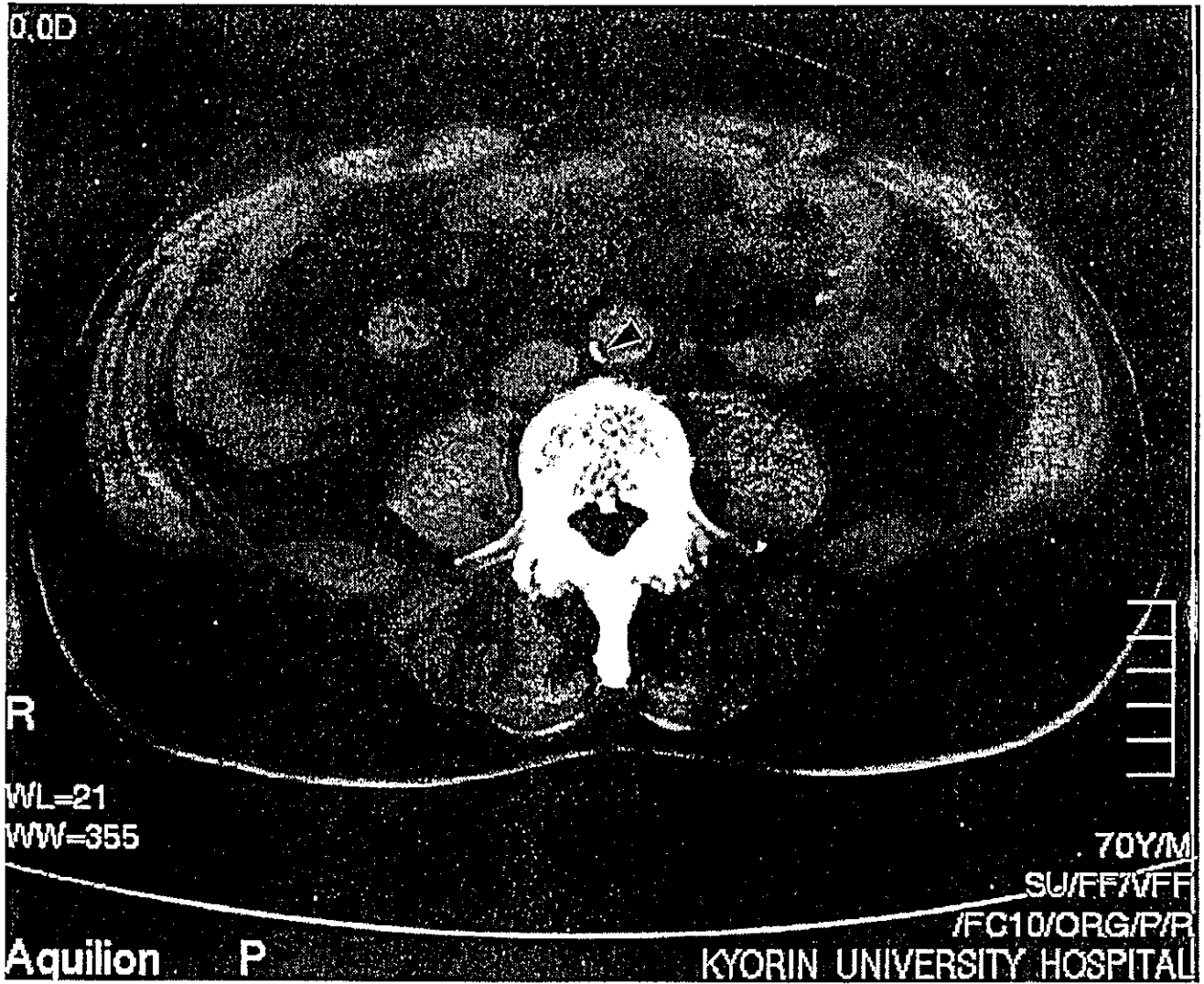


Figure 1 Abdominal plain computed tomographic image at the umbilical level showing that subcutaneous fat is predominant. The arrowhead indicates calcification of the abdominal aorta.

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### CORRELATION BETWEEN PULSE WAVE VELOCITY AND COGNITIVE FUNCTION IN NONVASCULAR DEMENTIA

To *The Editor*: We read with interest the paper by Shimoda et al.<sup>1</sup> showing that pulse wave velocity (PWV), an indicator of arterial stiffness, was higher in patients with vascular dementia than in patients with Alzheimer's disease and nondemented control subjects. Vascular factors such as smoking, hypertension, diabetes mellitus, and apolipoprotein E  $\epsilon 4$  allele have also been implicated in the development of nonvascular dementia, including Alzheimer's disease,<sup>2</sup> but there has been no quantitative study of the relationship between the stage of arteriosclerosis and the severity of nonvascular dementia. In this study, PWV was measured in patients with mild to moderate nonvascular dementia, and greater arterial stiffness was associated with cognitive impairment.

Patients who were referred to the Memory Clinic of our department were enrolled. Patients with definite vascular dementia such as poststroke patients and patients with multiple cerebral infarcts were excluded. Twenty-seven subjects (12 men and 15 women, mean age  $\pm$  standard deviation =  $76 \pm 7$ ) were analyzed, including 14 patients with Alzheimer's disease diagnosed using the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*, and others with mild cognitive impairment. PWV was measured using the automated device Form PWV/ABI (Colin Co. Ltd, Komaki, Japan), and two measurements, heart-brachial (hb) PWV and brachial-ankle (ba) PWV, were analyzed.<sup>3</sup> Cognitive function was assessed using the Hasegawa Dementia Scale Revised (HDSR;  $20 \pm 7$  points out of 30). Basic activities of daily living (ADLs), instrumental ADLs, mood, and volition were also measured using the Barthel index, Lawton-Brody instrumental ADLs, Geriatric Depression Scale, and Vitality Index,<sup>4</sup> respectively.

In the analysis including all the subjects, HDSR correlated with hbPWV ( $r = -0.450$ ,  $P < .05$ ) (Figure 1) and baPWV ( $r = -0.433$ ,  $P < .05$ ), whereas other indices of the comprehensive geriatric assessment did not correlate with hbPWV or baPWV. Multiple regression analysis using HDSR as a dependent variable and hbPWV, age, sex, mean blood pressure, and use of antihypertensive agents as independent variables showed that hbPWV ( $\beta = -0.535$ ,  $P < .05$ ) was a significant determinant of HDSR. Analysis using systolic blood pressure instead of mean blood pressure

showed a comparable result, but analysis using baPWV instead of hbPWV did not reach statistical significance.

Subjects were excluded because they had obvious vascular factors ( $n = 9$ ), extensive white-matter lesions on brain magnetic resonance imaging scans ( $n = 5$ ), or a history of hypertension ( $n = 8$ ) as determined by the use of antihypertensive agents or blood pressure of 140/90 mmHg or higher. These subjects showed higher hbPWV than the other 18 subjects ( $665 \pm 139$  vs  $561 \pm 98$  cm/s,  $P < .05$ ) and lower HDSR score ( $15.6 \pm 5.4$  vs  $21.9 \pm 6.7$ ,  $P < .05$ ), whereas age was not significantly different ( $79 \pm 9$  vs  $76 \pm 7$ ,  $P = .29$ ). Then, the correlation between PWV and cognitive function was analyzed in the 18 subjects without vascular factors. In simple regression analysis, HDSR correlated with hbPWV ( $r = -0.615$ ,  $P < .01$ ) (Figure 1) and baPWV ( $r = -0.618$ ,  $P < .01$ ). Multiple regression analysis using HDSR as a dependent variable and hbPWV, age, sex, and mean blood pressure as independent variables revealed that hbPWV ( $\beta = -0.700$ ,  $P < .05$ ) was independently related to HDSR.

The present study demonstrated that subjects with extensive white-matter lesions or a history of hypertension had higher PWV than others, consistent with a previous report,<sup>1</sup> even though subjects with typical vascular dementia were excluded. Multivariate analysis and analysis using the subjects without obvious vascular factors showed that arterial stiffness as measured using PWV was independently related to cognitive function. These results suggest that arteriosclerosis, even in a subclinical state, plays a role in cognitive impairment and that PWV serves as a useful tool to assess the vascular contribution in subjects with mild to moderate nonvascular dementia. Recent papers have shown that PWV can predict the future occurrence of cardiovascular disease.<sup>5</sup> Furthermore, a new paradigm—vascular cognitive impairment—in which vascular factors play a variety of roles in the pathogenesis of dementia has been proposed.<sup>2</sup> It is necessary to perform a large-scale study to confirm our preliminary results and a prospective

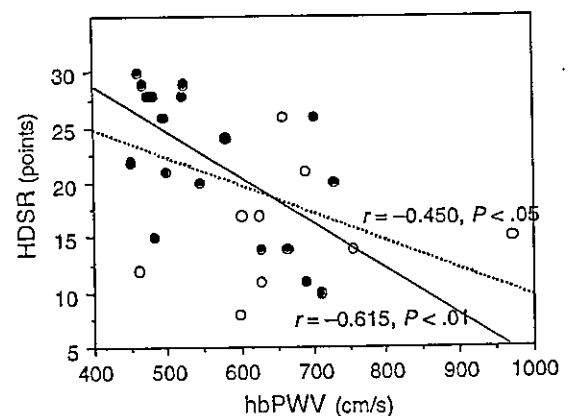


Figure 1. Correlation between heart-brachial pulse wave velocity (hbPWV) and Hasegawa Dementia Scale Revised (HDSR) in subjects with (open circles,  $n = 9$ ) and without (closed circles,  $n = 18$ ) vascular factors such as extensive white-matter lesions and history of hypertension. Dotted line and solid line indicate regression lines in all the subjects and the subjects without vascular factors, respectively.



longitudinal study to examine whether high PWV could be a risk factor for cognitive impairment.

Kumiko Nagai, MT  
Masahiro Akishita, MD  
Ayako Machida, CSLP  
Kazuki Sonohara, MD  
Mitsuo Ohni, MD  
Kenji Toba, MD  
Department of Geriatric Medicine  
Kyorin University School of Medicine  
Tokyo, Japan

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## GERIATRIC TRAINING IN PROBLEM-BASED LEARNING: AN ASIAN PERSPECTIVE

*To the Editor:* Problem-based learning (PBL) is gradually becoming popular in medical schools in Asian countries.<sup>1</sup> It is an integrated, student-centered educational approach, which uses problems (triggers) as the key units for stimulating and structuring relevant student learning. Such learning is largely dependent on the quality of the problems<sup>2</sup> and the areas tested in PBL.<sup>3</sup> Aligning PBL activities with subsequent student assessment often proves to be difficult, because it is different from the assessment conducted in the traditional curriculum. A study was conducted to analyze the PBL problems and examination questions used in the School of Medical Sciences, Universiti Sains Malaysia (USM) to examine the demographic characteristics of the people featured and the level of acuity of case scenarios presented.

All PBL problems ( $n = 51$ ) used in Phase II (Years 2 and 3) of USM PBL curriculum, 95 modified essay questions (MEQ), and 169 objective-structured clinical examination (OSCE) questions (in which age and presenting illness were mentioned) of five academic sessions (1998–2003) were analyzed. The findings revealed that problems and examination questions mostly included acute and rapidly resolving illnesses in young people and underemphasized elderly people (aged  $\geq 60$ ) with chronic, irreversible diseases. Only nine (17%) problems and 34 examination questions (MEQ 19%, OSCE 10%) featured older people. Moreover, those problems and questions mainly involved the early elderly (aged 60–74). Only one problem and one MEQ featured advanced elderly (aged  $\geq 70$ ). In the problems and questions, where the presenting illness was mentioned, it was of one month's duration in 78% of

problems, 69% of MEQs, and 41% of OSCEs. Conversely, only in 4% of problems, 8% of MEQs, and 22% of OSCEs, was the presenting complaint of more than 1 year's duration. In 41 PBL problems, the outcome was mentioned; this occurred within 1 year in 11%, within 1 month in 28%, and within 1 week in 61%.

Adequate exposure to geriatric-related issues is provided to the students in the different phases of the USM curriculum. As the PBL is the main teaching-learning strategy in Phase 2 that facilitates the integration of basic and clinical sciences, such emphasis may contribute to the development of negative attitudes among the students toward elderly patients and people with chronic diseases, as mentioned in other studies.<sup>4,5</sup> Studies also showed that this type of emphasis might also deter students from careers that focus on the elderly<sup>6</sup> and chronically sick.<sup>7</sup> This has wider implications when there is a clear demographic trend toward a rapid increase of the elderly population in Malaysia and worldwide.<sup>8</sup> According to United Nations estimates, the population of elderly in the world will reach 1.2 billion by 2025, the majority of whom will be in developing countries.<sup>9</sup> This is also important because health care is shifting away from the diagnosis and management of acute diseases toward caring for increasingly elderly people with chronic illnesses.<sup>8</sup>

As a subject, geriatric medicine is not well established in the schools of Asian countries. The World Health Organization<sup>8</sup> strongly advocated including relevant aging- and geriatric-related issues in the medical curriculum. Medical schools should provide opportunities for their students to be exposed to older patients with adequate positive experiences in hospital, community, and long-term care settings. Some problems of the PBL segment and examination questions could be designed to focus exclusively on the elderly with chronic diseases.<sup>10</sup> Curriculum planners should regularly analyze the demographic and pedagogical characteristics of problems and examination questions to determine whether aging- and geriatric-related content is adequately covered in PBL curriculum. Emphasis given to such content significantly improves attitudes and knowledge of students toward the elderly.<sup>4</sup> Reorientation of medical education is necessary to promote more concern among physicians about the needs of the elderly and people who are chronically ill.

Md. Anwarul Azim Majumder, PhD  
Ahmed Fuad Ab. Rahim, MHPEd  
Department of Medical Education  
Sayeeda Rahman, MPharm, MBA  
Department of Pharmacology  
School of Medical Sciences  
Universiti Sains Malaysia  
Kelantan, Malaysia

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ORIGINAL ARTICLE

# Improvement of inappropriate prescribing and adverse drug withdrawal events after admission to long-term care facilities

Yumikó Mita,<sup>1</sup> Masahiro Akishita,<sup>1</sup> Katsuaki Tanaka,<sup>1</sup> Shizuru Yamada,<sup>1</sup> Ryuhei Nakai,<sup>2</sup> Eigo Tanaka,<sup>3</sup> Tetsuro Nakamura<sup>4</sup> and Kenji Toba<sup>1</sup>

<sup>1</sup>Department of Geriatric Medicine, Kyorin University School of Medicine, <sup>3</sup>Mizukusaki-En and <sup>4</sup>Research Institute of Aging Science, Tokyo, and <sup>2</sup>Department of Neurology, Fukuoka University School of Medicine, Fukuoka, Japan

**Background:** The objectives of this study were to determine whether medications, particularly inappropriate prescribing, would be reduced after admission to long-term care facilities, and whether adverse drug withdrawal events (ADWEs) would occur in relation to discontinuation of medications.

**Methods:** The study consists of a retrospective survey using medical chart review in five health service facilities for the elderly in Japan. All the patients who were admitted to the facilities between January 2001 and December 2002 ( $N = 627$ ) were participants in the study. Medications taken on admission, at 1 month and 3 months after admission, and events (significant worsening of the disease status, accidents, new symptoms and signs, and other acute events) during a 3-month period were recorded. Inappropriate prescribing was determined using Beers' criteria with some modification. ADWEs were determined using the Naranjo causality algorithm.

**Results:** On admission, the patients were taking  $3.5 \pm 2.5$  (mean  $\pm$  SD) drugs. One month later, the number of prescribed drugs was decreased by 17% ( $P < 0.01$  vs on admission), but did not show an additional reduction 3 months later. Inappropriate prescribing was found in 10% of the patients taking drugs on admission, but the number of inappropriately prescribed medications was reduced by 33% after 1 month. Of 105 events recorded, only five (2% of the patients with drug reduction) were considered ADWEs; three cases of confusion, a case of depression, and a case of hyperglycemia, following discontinuation of psychotropic drugs, antidepressants and a sulfonylurea, respectively.

**Conclusion:** Adverse drug withdrawal events were not frequent despite the significant reduction of medications after admission to long-term care facilities. This might be because the rate of reduction was relatively high for inappropriately prescribed medications.

**Keywords:** adverse drug reaction, long-term care, medical expense, medical injury, pharmacotherapy.

## Introduction

Adverse drug reactions in elderly people increase with age,<sup>1-3</sup> with most being attributable to medication errors that are preventable.<sup>3,4</sup> Age-dependent changes in pharmacokinetics and pharmacodynamics, polypharmacy and non-compliance related to patients' functional

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Correspondence, Masahiro Akishita, MD, PhD, Department of Geriatric Medicine, Kyorin University School of Medicine, 6-20-2 Shinkawa, Mitaka, Tokyo 181-8611, Japan. Email: akishita-ky@umin.ac.jp

decline may play a role.<sup>1,3</sup> In particular, polypharmacy resulting from multiple pathology in elderly people is a critical problem leading to adverse drug reactions.<sup>1-3</sup> To prevent polypharmacy, review of prescriptions is essential according to evidence-based medicine and criteria for inappropriate prescribing.<sup>5,6</sup> In fact, inappropriate use of medication in elderly people has been reported to be as frequent as 16% to 25%.<sup>7-9</sup>

Conversely, discontinuation of medications to improve polypharmacy or inappropriate prescribing may induce adverse drug withdrawal events (ADWEs),<sup>10</sup> although the net effect on adverse drug reactions can be favorable in elderly outpatients.<sup>11</sup> Fixed payment insurance systems restrict medication use, possibly leading to a reduction of inappropriate prescribing and/or an increase of ADWEs. In health service facilities for the elderly in Japan, where functional training and nursing/personal care are provided under long-term care insurance,<sup>12</sup> a fixed payment system including prescribing of medication is applied. Accordingly, it is hypothesized that prescribed drugs, particularly inappropriate prescribing, would be reduced after admission to the facilities, and that ADWEs would occur in relation to discontinuation of medications. To test this hypothesis, we performed a retrospective chart review of a total of 627 patients in five health service facilities for the elderly, and found that prescribed drugs can be reduced with few ADWEs in such a frail elderly population with chronic diseases.

## Methods

### Sample and data collection

The data were derived from five health service facilities for the elderly (Mahoroba-no-Sato, Nagano; Moeuno-Sato, Nagano; Himawari-En, Fukuoka; Millennium-Sakuradai, Tokyo; Mizukusaki-En, Tokyo) in Japan. Institutional medical charts were reviewed for all the patients admitted between January 2001 and December 2002. Diagnoses of each patient were not recorded because they were unclear from the institutional charts, but Alzheimer's disease, cerebrovascular disease and osteoporosis were the main causes of disability in each institution. The average basic activities of daily living, as measured by the Barthel index, were 70–80 points out of 100 points according to the institutions. Medications that the patients were taking on admission and prescribed drugs 1 month and 3 months after admission were recorded. Similarly, all the events (significant worsening of the disease status, accidents, new symptoms and signs, and other acute events) during a 3-month period were recorded. The institutions that managed the patients before admission were categorized as acute care hospitals, outpatient clinics (home), sanitarium-type wards, special nursing homes for the

elderly and health service facilities for the elderly. Patients with voluntary discharge within 3 months excluding cases of death or transfer to another hospital were excluded, and a total of 627 patients were analyzed. The director of each institution gave written approval to the participation in this study. The study protocol was approved by the committee on ethics and the institutional review board of Kyorin University School of Medicine.

### Analysis

Inappropriately prescribed medications were determined using an updated version of the list developed by Beers with some modification.<sup>5</sup> Basically, we followed the list by Sloane *et al.* in which several drugs were excluded from Beers' list in consultation with Dr Beers,<sup>5,9</sup> reflecting changes in pharmacotherapy, but we included digoxin at more than 0.125 mg/day and oral iron at more than 325 mg/day in the list because these dosages were recorded in the medical chart. In this study, diagnosis-related inappropriate prescribing was excluded,<sup>3</sup> as in the study by Sloane *et al.* because the institutional chart did not include all the diagnoses of the patients.<sup>9</sup>

All the events were reviewed by a consultant geriatrician, and ADWEs were determined using the Naranjo causality algorithm.<sup>13</sup> Because detailed information, such as the effect of re-administration was lacking in most cases, a probability scale  $\geq 1$  (possible, probable or definite) was considered to indicate an ADWE.

The data in the text and the tables are expressed as means  $\pm$  SD unless otherwise specified. Changes in the number of prescribed drugs after admission were analyzed using paired *t*-test. Differences between the groups were analyzed using ANOVA followed by Newman-Keuls' test.

## Results

### Number of prescribed drugs

The patients were taking  $3.5 \pm 2.5$  drugs when admitted to the facilities (Table 1). Forty-six patients (7.3%) were not taking any drug, while 50 patients (8.0%) were on eight or more drugs. Women were taking fewer drugs than men. This sex difference seemed independent of age, although a statistically significant difference was found only at 80–89 years of age when the patients were categorized by age groups (Table 1). Interestingly, patients of 80 years or older were taking fewer drugs than those younger than 70 years, in contrast to a previous finding that the number of prescribed drugs increased according to age.<sup>2,14,15</sup>

As shown in Table 2, the mean number of prescribed drugs had decreased by 0.6 (17%) 1 month

**Table 1** Number of drugs taken on admission according to sex and age

	All	Men	Women	P for sex difference
Total	3.5 ± 2.5 (627)	4.2 ± 2.8 (177)	3.3 ± 2.4 (450)	< 0.01
≤ 69 years	4.4 ± 3.1 (36)	4.6 ± 3.5 (19)	4.2 ± 2.6 (17)	0.70
70–79 years	4.0 ± 2.6 (131)	4.6 ± 3.0 (43)	3.7 ± 2.3 (88)	0.08
80–89 years	3.3 ± 2.3* (316)	4.0 ± 2.6 (81)	3.0 ± 2.2 (235)	0.02
≥ 90 years	3.5 ± 2.7* (144)	4.2 ± 2.4 (34)	3.2 ± 2.8 (110)	0.08

\* $P < 0.05$  versus ≤ 69 years by Newman-Keuls' test.

Data are expressed as mean ± SD. Number of subjects is indicated in parentheses.

**Table 2** Changes in number of prescribed drugs after admission to health service facilities for the elderly

	No. of subjects	On admission	After 1 month	After 3 months
Total	627	3.5 ± 2.5	2.9 ± 2.2*	3.0 ± 2.1*
Type of institution before admission				
Acute care hospital	115	4.8 ± 3.3 <sup>†</sup>	4.2 ± 2.9* <sup>†</sup>	4.1 ± 2.7 <sup>†</sup>
Outpatient	200	3.6 ± 2.3	2.8 ± 1.8*	2.9 ± 2.0
Special nursing home	24	3.3 ± 2.1	2.5 ± 1.7*	2.6 ± 1.8*
Sanitarium-type ward	188	3.1 ± 2.3	2.6 ± 1.9*	2.6 ± 1.9*
Health service facility	100	2.6 ± 1.8	2.4 ± 1.6*	2.5 ± 1.7*
Facility				
A	83	4.9 ± 3.4	4.6 ± 3.0	4.6 ± 2.4
B	80	4.2 ± 2.8	3.9 ± 2.4*	4.0 ± 2.5
C	39	4.1 ± 2.7	2.4 ± 1.7*	2.2 ± 1.4*
D	172	3.2 ± 1.9	2.4 ± 1.5*	2.4 ± 1.5*
E	253	3.0 ± 2.2	2.6 ± 1.9*	2.5 ± 1.9
Event				
No	517	3.5 ± 2.5	2.8 ± 2.0*	2.8 ± 2.1*
Yes	104	3.6 ± 2.7	3.4 ± 2.5***	3.7 ± 2.2** <sup>†</sup>

\* $P < 0.01$  versus on admission by paired  $t$ -test; \*\* $P < 0.01$  versus after 1 month by paired  $t$ -test; <sup>†</sup> $P < 0.01$  versus other types of institution by Newman-Keuls' test; \*\*\* $P < 0.05$ ; \*0.01 versus Event (-) by Newman-Keuls' test. Data are expressed as mean ± SD.

after admission ( $P < 0.01$  versus on admission), but did not show an additional reduction 3 months after admission. A significant reduction was seen at 1 month irrespective of the type of institution that had managed the patients before admission, although the number of drugs on admission and the degree of reduction differed between the types of institutions. However, there was a large variation in the reduction of prescribed drugs between the facilities, presumably due to differences in the overall philosophy of the attending physicians and the disease and/or functional status of the patients. Patients with and without events during a 3-month period were analyzed separately (Table 2). They were taking a comparable number of medications on admission. The number of drugs in the patients with events was not significantly decreased at 1 month, and was rather increased at 3 months after admission because in many cases additional drugs were prescribed for treatment of events.

#### Discontinued drugs and inappropriate prescribing

Categorized by therapeutic class, discontinuation was frequent with neuropsychologic (121 cases), gastrointestinal (116 cases) and cardiovascular (94 cases) drugs, followed by metabolic/endocrine drugs (36 cases). Anti-ulcer drugs (44 cases) including H<sub>2</sub> blockers and prostaglandin analogs, antipsychotics (35 cases), antihypertensives (33 cases) including calcium channel blockers,  $\beta$  blockers and angiotensin converting enzyme inhibitors, hypnotics (31 cases), laxatives (31 cases) and non-steroidal anti-inflammatory drugs (22 cases) were frequently withdrawn.

On admission, inappropriate prescribing was seen in 58 patients (10.0% of 581 patients taking drugs). Ticlopidine, digoxin at more than 0.125 mg/day and oxybutynin were prescribed in five or more cases (Table 3). Inappropriately prescribed medications were reduced by 33% 1 month after admission, and did not change