#### Nutrition 32 (2016) 806-810

Contents lists available at ScienceDirect

### Nutrition

journal homepage: www.nutritionjrnl.com

#### Applied nutritional investigation

# Nutrition-dependent eicosapentaenoic acid deficiency in care house residents

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#### ARTICLE INFO

Article history: Received 22 October 2015 Accepted 30 January 2016

Keywords: Cardiac function EPA administration Fish consumption Group home Older adults Supraventricular arrhythmias

#### ABSTRACT

*Objective:* We have identified that vital prognosis of adults in a group home (GH) in their mid-80s is associated with lower eicosapentaenoic acid (EPA) levels. We investigated the cause of EPA deficiency in residents in a GH and the effect of EPA treatment on cardiac function and nutritional function in 130 older adults.

*Methods:* We compared blood chemistry data among three age- and sex-matched groups—outpatient clinic (OPC) attendees (n = 54, 87 ± 5 y old), GH residents (n = 40, 85 ± 8 y old), and older adults in a geriatric welfare home for the elderly (GWHE) (n = 36, 87 ± 6 y old)—using nonparametric test. Furthermore, we investigated the sequential changes in blood chemistry and cardiac function at 4 to 12 mo after the initiation of EPA administration (1800 mg/d).

*Results*: Non-parametric test revealed that the EPA/arachidonic acid ratio as well as EPA levels were lower in the GH and GWHE residents than in the OPC attendees (OPC:  $0.56 \pm 0.3$ , GH:  $0.23 \pm 0.12$ , GWHE:  $0.31 \pm 0.1$ ). Fish consumption was lower in the GH and GWHE group than in the OPC group. Repeated measured analyses using analysis of variance revealed that EPA administration increased serum EPA levels ( $54.0 \pm 29.0$  to  $210.5 \pm 50.6 \mu$ g/mL, P < 0.001); decreased arachidonic acid, docosahexaenoic acid, triacylglycerol, and LDL cholesterol levels at  $4.5 \pm 3.4$  mo after administration; and reduced the severity of supraventricular arrhythmias on ambulatory electrocardiogram at  $12.5 \pm 4.5$  mo (P < 0.05).

*Conclusion:* EPA deficiency in GH residents could be related to the nutritional characteristics of older adults in care facilities. EPA treatment induced changes in various lipids and reduced the severity of supraventricular arrhythmias.

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#### Introduction

A group home (GH), or assisted care facility for older adults, is an approach in Japan in which medical, nursing, and nutritional care is administered to care for older adults [1–3]. We have recently identified that vital prognoses of older adults in their mid-80s are modified considerably by cardiac and nutritional factors, including lower eicosapentaenoic acid (EPA), especially in GH residents. A study investigating the association between mortality and clinical parameters over 5 y in 111 older adults revealed that vital prognosis in GH residents was dramatically improved by EPA administration (study is under review).

The cause of EPA deficiency in adults in GHs has not been elucidated, nor has the effect of EPA treatment on sequential changes in cardiac and nutritional function been fully reported. To elucidate the cause of EPA deficiency in adults in GHs, we compared blood chemistry data, especially unsaturated fatty acid levels, among the older adults from outpatient clinics (OPC), GHs, and geriatric welfare homes for the elderly (GWHE) in a cross-







We thank all of the research participants and Dr. K. Kitajima (Fureai Machida Hospital), Mr. Yoshinaka (Group Home Ayunosato Sagami), and Ms. Terakado (Group Home Konan). This work was partly supported by Grants-in-Aid for Scientific Research from The Japan Society for the Promotion of Science and The Research Funding for Longevity Sciences (22-5 and 25-6) from the National Center for Geriatrics and Gerontology (NCGG), Japan.

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sectional study. We also investigated the effect of EPA treatment on sequential changes in cardiac and nutritional function in a prospective study.

#### Materials and methods

#### Subjects

Using a cross-sectional study to investigate EPA deficiency and its causes in a GH, we recruited 54 elderly patients who regularly visited the OPC ( $87 \pm 5 \text{ y}$  old), 40 older adults living in a group home ( $85 \pm 8 \text{ y}$  old), and 36 older adults living in a GWHE ( $87 \pm 6 \text{ y}$  old). Between January 2010 and December 2014, the OPC patients were recruited from the Department of Cardiology at the city hospital (Fureai Machida Hospital, Tokyo, Japan), and the residents of two GHs and one GWHE were recruited from one of the three facilities in Kanagawa prefecture. The same physician treated all 130 enrolled patients from the OPC of our city hospital, the GH, and the GWHE. In a GH, five to nine residents live together and receive support by two to three caregivers, as if in their own home. Residents have a private room and share a living room, dining room, and kitchen. Outside doctors can visit the residents. In contrast, a GWHE is a large care facility consisting of approximately 100 residents with one doctor assigned to the GWHE.

In a prospective observational study, we evaluated the effects of EPA on cardiac and nutritional function by investigating the sequential changes after EPA administration therapy in both OPC patients and GH residents.

#### Protocol

We examined blood chemistry data in all 130 participants for grouped comparison. The measured items were listed below (see the measurement of variables section). To determine the nutritional and medical differences between the OPC patients and GH residents and the similarity of GH residents to those in a GWHE, we compared these values among the OPC, GH, and GWHE patients or residents. To elucidate the cause of EPA deficiency, we also compared fish consumption (fried fish and non-fried fish) among the three groups. The questionnaire about fish consumption (which asked about frequency, not quantity, in a 1 mo period) was given to the subjects, their family, or their caregivers who knew the food menu and quantity of meals of the subjects. In other words, family members or caregivers responded to the questionnaire instead of the older adults with dementia. However, quantity of food intake was not included in this study. We analyzed the correlation between fish consumption and plasma EPA levels in 123 of the 130 subjects using Spearman correlation test.

To prospectively elucidate the effect of EPA treatment, 20 to 32 subjects out of the 94 subjects from OPC or GH were selected, and we performed three analyses of blood chemistry data and cardiac parameters, such as cardiothoracic ratio and supraventricular and ventricular arrhythmia. Once before initiation (pre), Epadel was administered at 1800 mg/d divided into two doses, (Mochida Pharmaceutical Co., Ltd. Tokyo Japan) and twice after EPA administration (post 1: the first at  $4.5 \pm 3.4$  mo after the initiation of Epadel; post 2: the second assessment at  $12.5 \pm 4.5$  mo after the initiation of Epadel).

#### Measurement of variables

#### General parameters, blood chemistry and cardiac function data

The general parameters measured were body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure, and cognitive function, evaluated using the Mini-Mental State Examination (MMSE) divided into three levels (MMSE score 24-30: 1, MMSE score 10-23: 2, MMSE score 0-9: 3). Activities of daily living (ADLs) were evaluated using the Barthel index. Serum unsaturated fatty acids (EPA, docosahexaenoic acid [DHA], and arachidonic acid [AA]) were analyzed by gas chromatography. Lipids (low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and triacylglycerol) were measured by enzymatic methods. Glycosylated hemoglobin (HbA1 c) value was measured by latex agglutination immunoassay and ion-exchange high-performance liquid chromatography. Hemoglobin value was measured by the sodium lauryl sulfatehemoglobin method. Serum total protein levels were measured by the Biuret method. Serum albumin levels were measured by the bromocresol green or purple method. N-terminal pro-brain natriuretic peptide was measured by electro-chemiluminescence immunoassay. Renal function was measured by the urease ultraviolet method or the enzymatic method. Liver function parameters were determined by the Japan Society of Clinical Chemistry transferable method, according to the manufacturer's instructions.

Cardiothoracic ratio was examined on chest X-ray with the subject supine or in a standing position. The severity of supraventricular and ventricular arrhythmias was examined on an ambulatory electrocardiogram. We defined the severity of supraventricular arrhythmias by six categories: 1 = no arrhythmia, 2 = supraventricular extrasystole (single or couplet), 3 = 3 to 29 supraventricular tachycardia,  $4 = \geq 30$  supraventricular tachycardia, 5 = paroxysmal atrial

807

fibrillation, and 6 = sustained atrial fibrillation. The severity of ventricular arrhythmias was defined as follows:1 = no arrhythmia, 2 = a single arrhythmia, 3 = two premature ventricular contractions (PVCs), 4 = 3 to 29 PVCs, 5 =  $\geq$ 30 PVCs, and 6 = ventricular fibrillation.

#### Statistical analyses

We used SPSS software (version 23, IBM, Armonk, New York, USA) for all statistical analyses. To compare the clinical data among the subjects from OPC, GH, and GWHE, the chi-square test was used to compare the categorical values and the Kruskal-Wallis test was used to compare ranked or continuous variables. The Spearman correlation coefficients were calculated for fish consumption and plasma EPA levels. Repeated measured analysis using analysis of variance was applied to compare the changes in blood and cardiac parameters caused by EPA treatment in the subacute phase  $(4.5 \pm 3.4 \text{ mo})$ , the chronic phase  $(12.5 \pm 4.5 \text{ mo})$ , and the control values. Some of those variables were evaluated by paired *t* test or Friedman two-way analysis of variance by ranks.

#### Results

Forty GH residents had lower cognitive function, less ADLs, lower SBP, and slightly poorer nutritional function indicated by lower BMI compared with OPC attendees. GH residents also had fewer rates of fried fish consumption than the 54 OPC attendees (Table 1). GWHE residents had a significantly lower rate of non-fried fish consumption. BMI and SBP were not significantly different.

Furthermore, the rates of consuming both fried and non-fried fish were significantly correlated with the plasma EPA levels, but weakly correlated (r = 0.181, P = 0.046, 0.181, and 0.045, respectively) in 123 of 130 subjects in which the fish consumption and blood chemistry were investigated (Fig. 1). DHA was correlated only to non-fried fish consumption (r = 0.198, P = 0.028), and AA was negatively correlated only to fried fish consumption (r = -0.210, P = 0.020).

The non-parametric comparison of blood chemistry among the three groups showed that EPA, EPA/AA, and HbA1 c levels were lower in both the GH and GWHE residents than in the OPC attendees. EPA/AA levels in the GH residents were the lowest among the three groups (OPC:  $0.56 \pm 0.3$ , GH:  $0.23 \pm 0.12$ , GWHE:  $0.31 \pm 0.1$ ). In contrast, AA levels in the GH residents were the highest. High-density lipoprotein cholesterol in GWHE residents was significantly lower than in OPC attendees. In contrast, triacylglycerol in the GWHE residents was the highest

#### Table 1

Characteristics of 54 outpatient clinic attendees, 40 group home residents and 36 geriatric welfare home for the elderly residents

Parameters	OPC (n = 54)	GH (n = 40)	$\begin{array}{l} \text{GWHE} \\ (n=36) \end{array}$	P value
Age, y	87 ± 5	85 ± 8	87 ± 6	0.7
Sex: Male/female, n	18/36	7/33	10/26	0.229
BMI, kg/m <sup>2</sup>	$21.9\pm3.8$	$20.0\pm2.9$	$20.5\pm4.2$	0.043
SBP, mmHg	$132\pm26$	$120\pm19^{\dagger}$	$123 \pm 14$	0.003
DBP, mmHg	$71\pm13$	$72\pm13$	$73\pm10$	0.926
Cognitive function: 1/2/3	31/17/6	$11/14/15^{\dagger}$	NA	0.003
ADL score	$74\pm29$	$50\pm38^{\dagger}$	NA	0.001
Fried fish, month*	$14\pm7$	$10\pm3^{\dagger}$	$16\pm0^{\dagger,\ddagger}$	< 0.001
Non-fried fish, month*	$5\pm 6$	$2\pm1$	0 <sup>†,‡</sup>	< 0.001

ADL, activity of daily living; BMI, body mass index; DBP, diastolic blood pressure; GH, group home; GWHE, geriatric welfare home for the elderly; NA, not available; OPC, outpatient clinic; SBP, systolic blood pressure

Data are presented as the mean  $\pm$  SD

The degree of cognitive function was defined based on the Mini-Mental State Examination score as follows: Level 1, 24 to 30; level 2, 10 to 23; level 3, 0 to 9 \*n = 47 in OPC

Bonferroni multiple-comparisons procedure for comparisons of pairs of means:  $^{\dagger}P < 0.05$  (versus OPC)

 $^{\ddagger}P < 0.05$  i(versus GH)

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