



The long-term relationship between dietary pantothenic acid (vitamin B₅) intake and C-reactive protein concentration in adults aged 40 years and older

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Abstract *Background and aims:* Low-grade inflammation, represented by minor C-reactive protein (CRP) elevation, has a critical role in the early stages of atherosclerosis, and pantothenic acid (PA) may have an antioxidant effect in inflammatory process. However, the long-term relationship between PA intake and CRP has not yet been studied. The objective of the present study was to evaluate the long-term relationship of PA intake to CRP concentration in healthy adults aged 40 years or older living in a rural area of South Korea.

Methods and Results: A total of 908 subjects (349 men, 559 women) with repeated data on dietary PA intake and CRP concentration were included in the final analysis. To represent the long-term effect of PA intake, both PA intake at the baseline and average PA intake were used as the exposure, and CRP concentration at the third visit and its change from the baseline to the third visit were used as the outcome. After adjustment for potential confounders, a significant inverse relationship between PA intake and CRP concentration at the third visit was observed (P for trend = 0.001, β = −0.07 (P -value = 0.001) for PA_{baseline}; P for trend = <0.0001, β = −0.11 (P -value = 0.0004) for PA_{average} (baseline, 2nd, 3rd)). Higher PA intake was significantly related to lower or attenuated increase in CRP concentration (P for trend = 0.002, β = −0.24 (P -value = 0.002) for PA_{baseline}; P for trend = 0.001, β = −0.35 (P -value = 0.001) for PA_{average} (baseline, 2nd, 3rd)).

Conclusions: In conclusion, dietary PA intake was inversely related to subsequent CRP concentration in both men and women aged 40 years or older in South Korea.

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Introduction

Low-grade inflammation is likely to be involved in the early stages of atherosclerosis [1], which is the major underlying mechanism of cardiovascular disease [2]. Of

several inflammatory markers, a minor elevation of C-reactive protein (CRP) without acute inflammatory events has been regarded as a general marker of low-grade inflammation [3]. CRP is a potent risk indicator for cardiovascular events [4], because it may directly bind oxidized low-density lipoprotein (LDL) cholesterol [5] and promote foam cell formation, the crucial step in the early stages of atherosclerosis [6].

Of various dietary factors, pantothenic acid (PA), also known as pantothenate or vitamin B₅, is an essential

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vitamin and a precursor for coenzyme A (CoA), which has long been recognized as an essential cofactor of biochemical reactions in various organisms [7,8]. Though the direct role of PA in the etiology of atherosclerosis has not been fully elucidated, PA may contribute to inflammatory process through increasing CoA level and promoting glutathione (GSH) synthesis, thereby reducing oxidative stress [9,10].

Despite the potential evidence of the role of PA and its derivatives in the inflammation process, the relationships between CRP concentration and dietary factors have not been thoroughly studied. The studies that have been completed have mostly been cross-sectional studies and have focused on fish [11], dairy products [12], fiber [13], flavonoids [14], and dietary patterns [15] in healthy adults [11–15]. Considering the fact that low-grade inflammation represents a chronic condition that differs from acute inflammation [3], it is necessary to be addressed with long-term perspective with repeated data on CRP concentration. Previously, two studies with longitudinal approaches have reported an inverse relationship between CRP concentration and the alternative healthy eating index (AHEI) [16], as well as CRP concentration and polyunsaturated fatty acids intake [17], but there has been no study on its relationship with PA intake.

The aim of the present study was to investigate the long-term relationship of PA intake to CRP concentration in healthy men and women aged 40 years or older living in a rural area of South Korea.

Methods

Study population

The study population was that of the **C**Ardio**V**ascular disease **A**ssociation **S**tudy in Yangpyeong county (CAVAS_Yangpyeong), located 45 km east of Seoul, the capital of South Korea, as part of the ongoing community-based cohort in the **K**orean **G**enome **E**pidemiology **S**tudy (KoGES), which was initiated to ascertain risk factors for cardiovascular diseases. Subjects were recruited between January 2005 and December 2009, and they were followed at 2–4 year intervals between January 2007 and December 2013. Of the 1427 subjects with complete data on CRP concentration and dietary factors at each visit, we excluded subjects with the following conditions: a history of heart disease, stroke, and/or cancer (physician-diagnosed) ($n = 150$); taking medication for hypertension, diabetes mellitus, and/or dyslipidemia ($n = 330$); or missing values for information about general characteristic components at the baseline visit (alcohol intake ($n = 3$), anthropometric measurements ($n = 2$), education level ($n = 1$), and/or exercise habits ($n = 3$)). There could be implausibly high or low responses in the dietary assessment and total energy intake have been used as a primary criterion to decide the allowable range of dietary intake [24]. We found that in three days 24 h recall data in the subgroup of this study (men 212 and women 327), most subjects (99.3%) reported total energy intake within the

range of 500 to 4000 kcal/d. Therefore, although the criterion was arbitrary, we excluded subjects with implausible dietary intakes (<500 or >4000 kcal/d) ($n = 13$) at each visit. To consider possible cases of acute inflammation and immune activation due to current illness, we further excluded subjects with extreme values of cytokines (defined as having values 10 times higher than the 99th percentile of IL-6 and/or TNF- α [18]) and CRP (defined as having CRP values >10 mg/L [19]) ($n = 60$) both at the baseline and the third visit. Therefore, 908 subjects (349 men, 559 women) were included in the final analysis (Fig. 1). This study was approved by the Institutional Review Board of Hanyang University and was conducted in accordance with the Declaration of Helsinki. All subjects provided written informed consent to participate in this study.

Assessment of dietary pantothenic acid intake

At each visit, food and nutrient intakes were measured using a food frequency questionnaire (FFQ) with 106 food items. Subjects were asked to identify how frequently they consumed the 106 food items during the past year as well as the average amount they consumed. On the FFQ, nine frequency categories ranging from “never or rarely” to “3 times/d” were used to determine the frequency of consumption, and three serving sizes were listed to determine the amount of consumption. For food items with limited seasonal availability, subjects were asked to indicate whether they ate them for 3, 6, 9, or 12 months of the year. The validity and reproducibility of the FFQ have been examined in detail elsewhere [20]. Nutrient intake including PA was calculated using a weighted frequency per day and serving size for each food item. This study used the 2011 nutrient database of the Korea Nutrition Society based on the seventh edition of the Korean Food Composition Table [21].

Biochemical analyses

Blood samples were collected in the morning after at least 8 h of fasting, and all biochemical markers were analyzed on the same day. Serum cytokines (IL-6 and TNF- α) were measured using the multiplex method (Luminex 200, Luminex Corp, USA) and ranged from 0.14 to 400 pg/mL for IL-1 β , 0.11–400 pg/mL for IL-6, and 0.16–400 pg/mL for TNF- α [22]. Serum CRP was assayed by turbidimetric immunoassay for high sensitivity CRP using an ADVIA 1650 Automatic Analyzer (Siemens Medical Sol., NY, USA) with a range from 0.2 to 400 mg/L.

Plasma total cholesterol, triglycerides, glucose, and high-density lipoprotein (HDL) cholesterol concentrations were measured with the ADVIA 1650 Automatic Analyzer. If plasma triglycerides were less than 400 mg/dl, LDL cholesterol was calculated as described by Friedewald et al. [23].

We measured blood pressure in a seated position from the right arm by auscultation using a standard mercury sphygmomanometer and cuff. Two consecutive

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