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Original Research

Soy milk powder supplemented with phytosterol esters reduced serum cholesterol level in hypercholesterolemia independently of lipoprotein E genotype: a random clinical placebo-controlled trial

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ABSTRACT

Phytosterols (PSs) are reported to lower the serum total cholesterol and low-density lipoprotein cholesterol concentrations enriched in some fatty foods, such as margarine. However, these high-fat foods are not very suitable for older people. Soy milk is the favorite food for elderly people in China; therefore, we hypothesized that the consumption of soy milk powder supplemented with PSs would decrease the serum cholesterol levels in older Chinese people independent of the genotypes of apolipoprotein E (ApoE). Mild to moderate hyperlipidemic patients (n = 170) were recruited from different communities and treated with placebo soy milk powder or 3.4 g PS esters–enriched soy milk powder (2.0 g/d free PS in 30 g soy milk powder). The fasting serum lipid profiles at the baseline and after 3 and 6 months of intervention were measured. The ApoE genotype was also determined. After 3 months of PS intervention, the serum lipid profile was not changed significantly in either group. The serum total cholesterol, low-density lipoprotein cholesterol, and non– high-density lipoprotein cholesterol levels decreased by 9.3%, 11.4%, and 12.6%, respectively, in the PS group at the end of the intervention (6 months) compared with the control group, whereas the serum high-density lipoprotein cholesterol and triglyceride levels were not affected significantly. In the PS group, both the ApoE3 and ApoE4 carriers had a similar response to PS consumption. These findings suggested that PS-fortified soy milk powder was effective in lowering the serum cholesterol levels in older Chinese volunteers with mild to moderate hypercholesterolemia in both the ApoE3 and ApoE4 carriers.

Abbreviations: BMI, body mass index; LDLC, low-density lipoprotein cholesterol; HDLC, high-density lipoprotein cholesterol; PS, phytosterol; TC, total cholesterol; TG, triglyceride.

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1. Introduction

Plant sterols and stanols (PS), also called phytosterols or phytostanols, are natural, nonnutritive compounds that abound in seeds and oils. In a recent meta-analysis by Ras et al [1], the human clinical studies, which were related to the lowering effect of PS on the low-density lipoprotein cholesterol (LDLC), have shown that PS intake of 1.6 g/d decreased LDLC levels by an average of 8.5%. The effectiveness of PS on lowering blood cholesterol has been observed in children [2], individuals with familial hypercholesterolemia [3], statin users [4], men [5], and women [6]. The epidemiologic investigation showed that the average daily PS intake from a normal diet is about 200 to 400 mg/d in Sweden [7], Belgium [8], and Spain [9]. The dietary PS intake of elderly women on a Chinese diet varies in different cities. It was reported [10] that the dietary PS intake in Urumchi was much higher (550.4 mg/d) than that in Beijing (340.3 mg/d) and Hefei (313.5 mg/d). Although it is believed that the cholesterol-lowering dose of PS is 0.6 to 3.3 g/d [11], some studies found that there was an inverse relationship between the dietary PS intake and the serum cholesterol levels, even if the daily PS intake was less than 0.6 mg [12].

In previous studies, PS was always supplemented into margarine [13], low-fat spread [14], yogurt [15], buttermilk drink [16], and other fatty foods. However, these foods are less popular with older Chinese people. Soy and its products are favorite foods among the elderly Chinese population, but it is not known whether or not PS in soy products is effective for cholesterol lowering in China. Some researchers have reported that the intake of soy drinks supplemented with PS decreased the serum cholesterol level in Thailand [17], Canada [18], and Germany [19], but these studies had small sample sizes. The apolipoprotein E (ApoE) genotype was also reported to affect the serum lipid concentrations in people of different ethnicities [20].

We hypothesized that PS consumed in soy milk would decrease the serum cholesterol levels in older Chinese people independent of the ApoE genotypes. The objective of the present study was to investigate if the long-term consumption of soy milk fortified with PS esters (30 g/d with 2.0 g PS) was effective for cholesterol lowering in older Chinese people with hypercholesterolemia. Hence, this random clinical placebo-controlled trial was designed. In addition, we also examined the effects of the ApoE genotype on the efficacy of PS on cholesterol lowering.

2. Methods and materials

2.1. Participants

Subjects with mild to moderate hypercholesterolemia were recruited from the San-li-tun Community Health Service Center, Zuo-jia-zhuang Community Health Service Center, and Wang-si-ying Community Health Service Center, Beijing, China. The inclusion criteria were as follows: (1) men and women aged 55 to 65 years, (2) body mass index (BMI) between 18.5 and 28 kg/m^2, and (3) fasting serum total cholesterol (TC) of 5.18 to 7.0 mmol/L. The exclusion criteria were as follows: (1) use of medication that could significantly affect the lipid profile, (2) obesity (BMI > 28.0 kg/m^2), (3) history of cardiovascular diseases and other chronic diseases (eg, diabetes, liver or kidney disorders, or cancer), (4) hypersensitivity to soy proteins, and (5) use of fish oil or other dietary supplements likely to affect the lipid profile.

The research was conducted according to the Declaration of Helsinki and was approved by the Ethics Committee for Clinical Research in the Health Care Area of Capital Medical University (Approval No. 2012sy35). All of the subjects signed the informed consent document once they learned of the purpose, procedures, risks, and benefits of this study.

2.2. Design

This study was a double-blind, randomized-controlled trial. The sample size calculation was based on the formula as follows: $N = 2(Z\alpha + Z\beta)2\sigma^2/d^2$. To obtain a power of 90% with an α error of .05 (bilateral hypothesis), 78 individuals were required in each group. Based on the assumed rate of loss to follow-up, 170 individuals were recruited. The subjects (Figure) were randomly assigned to the control group or PS group according to the baseline serum TC levels. For this study, 68 and 69 volunteers completed the intervention in the control group and PS group, respectively. The experimental period was from February 2014 to November 2014. The follow-up duration was 6 months. Once the consent letter was signed, the subjects were scheduled for the baseline visit. All of the subjects were randomized to the control group or PS group. Information on dietary intake, medical history, demographics, and physical examination was obtained, and the soy milk powder was dispensed. (Subsequent deliveries were 1 month later.)

2.3. Test soy milk powder

The packaging of the soy milk powder (with or without PS esters) was the same in appearance other than the date of manufacture. The soy milk powder contained 2.0 g plant sterol (recommended dose of the American Heart Association, 1.5-3.0 g). Both the supplemented product and the placebo had the same characteristics (ie, composition, external appearance, and taste), except that the placebo contained no sterol esters. (The composition of the placebo and soy milk supplemented with PS esters is shown in Table 1.) All participants consumed the soy milk powder every day with no change of their usual diets and lifestyle, and any newly prescribed lipid-lowering therapies were recorded.

2.4. Blood sampling and laboratory analyses

Serum was sampled at the baseline and after 3 and 6 months of intervention, and dietary intake data were obtained at the baseline and after 6 months of intervention. The fasting serum TC, high-density lipoprotein cholesterol (HDLC), LDLC, and triglyceride (TG) were measured at the baseline and after 3 and 6 months of intervention using commercial kits (Ying-Ke-Xin-Chuang Science and Technology Ltd, Xia-Men, China) on an automatic biochemical analyzer (Olympus, Japan, AU400). Non-HDLC concentration was calculated as follows: non-HDLC = TC − HDLC.