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Original Article

Effects of soy or whey protein on weight reduction in patients with obesity: An exploratory, three-arm, placebo-controlled, double-blind, randomized clinical trial

Michiko Takahashi [a, b, *], Takumi Imai [c], Tomoko Yamada [a, b], Naokazu Muramae [d], Kai Yoshimura [e], Yuji Mitomo [c], Hironori Bando [a], Kenji Sugawara [e], Shun-Ichiro Asahara [e], Yushi Hirota [e], Yoshikazu Tamori [e, f], Yutaka Takahashi [g], Wataru Ogawa [e]

[a] *Division of Diabetes and Endocrinology, Department of Internal Medicine, Kobe University Hospital, 7-5-2 Kusunoki-cho, Chuo-ku, Kobe 650-0017, Japan*
[b] *Department of Nutrition, Kobe University Hospital, 7-5-2 Kusunoki-cho, Chuo-ku, Kobe 650-0017, Japan*
[c] *Clinical and Translational Research Center, Kobe University Hospital, 7-5-2 Kusunoki-cho, Chuo-ku, Kobe 650-0017, Japan*
[d] *Muramae Diabetes Clinic, 2-6-9 Kokubo, Akashi 673-0005, Japan*
[e] *Division of Diabetes and Endocrinology, Department of Internal Medicine, Kobe University Graduate School of Medicine, 7-5-1 Kusunoki-cho, Chuo-ku, Kobe 650-0017, Japan*
[f] *Division of Creative Health Promotion, Department of Social/Community Medicine and Health Science, Kobe University Graduate School of Medicine, 7-5-1 Kusunoki-cho, Chuo-ku, Kobe 650-0017, Japan*
[g] *Department of Diabetes and Endocrinology, Nara Medical University, 840 Shijo-cho, Kashihara, Nara 634-8522, Japan*

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SUMMARY

Background & aim: Although weight loss programs including diet and exercise targeting patients with obesity are essential, the percentage of patients who successfully achieve weight loss is less than 10%. One cause of failure to achieve weight loss is a strong sense of hunger, which is difficult to sustain. Additionally, it is important to prevent a decrease in muscle mass. Various protein supplements have been used to overcome these problems. However, there is insufficient evidence to support this theory. This study aimed to evaluate the effect of soy or whey protein beverages in conjunction with general dietary and exercise therapies on weight loss.

Methods: This placebo-controlled, double-blind, randomized clinical trial was conducted at Kobe University Hospital. Patients with

* Corresponding author. Division of Diabetes and Endocrinology, Department of Internal Medicine, Kobe University Hospital, 7-5-2, Kusunoki, Chuo, Kobe 650-0017, Japan.
E-mail address: okazaki@med.kobe-u.ac.jp (M. Takahashi).

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obesity and at least one obesity-related complication were enrolled. Three arms of soy, whey protein, or a placebo were supplemented once a day for 12 weeks, in addition to the general guidance on dietary and exercise therapies in a weight loss program. Energy intake during the trial was calculated using the Food Frequency Questionnaire. The primary outcome was percentage change in body weight from baseline to 12 weeks.

Results: Between March 2021 and April 2022, 44 patients were enrolled. No significant differences were observed in body weight, waist circumference, body composition parameters, resting energy expenditure, blood pressure, or metabolic indicators. However, the energy, protein, and lipid intakes calculated from the prescribed nutritional intake in the weight loss program were significantly lower in the soy protein group (control group vs. soy group; total energy [kcal] -121.0 ± 416.6 vs. -340.0 ± 487.0, respectively $P = 0.016$; protein [g] 8.5 ± 11.9 vs. -5.1 ± 14.7, $P = 0.023$; lipid [g] -5.1 ± 16.1 vs. -19.8 ± 18.2, $P = 0.018$).

Conclusions: No significant weight loss was observed in the soy or whey protein group. However, in the soy protein group, it was possible to maintain a lower energy intake, and protein and lipid intakes decreased in post-hoc analysis. Although further investigation is necessary, extending the administration period may result in significant weight loss.

Clinical trial registration: Japan Registry of Clinical Trials (identifier: jRCTs051200103).

Introduction

Obesity is on the rise worldwide, presenting an urgent public health challenge; it not only worsens life prognosis due to an increased risk of several diseases [1] but also leads to decline in the quality of life due to conditions such as osteoarthritis [2] and depression [3]. Although many complications can improve with weight loss [4], the mechanism underlying human weight maintenance is robust, and effective methods have not been firmly established.

Although weight loss programs including diet and exercise targeting patients with obesity are essential, the percentage of those who successfully achieve weight loss is less than 10%. One cause of failure to achieve weight loss is a strong sense of hunger, which is difficult to sustain. Even if temporary weight loss is achieved, stagnation in weight reduction can occur due to loss of muscle mass and decrease in basal metabolism [5,6]. To overcome these challenges, we hypothesized that formulating a diet that minimizes feelings of hunger while suppressing the reduction of muscle mass to prevent a decline in basal metabolism, is crucial for achieving effective weight loss. Various protein supplements have been used to overcome these problems; however, the evidence is insufficient. Among the five major proteins, we selected whey as an animal source and soy as a plant source, considering their high biological value: the ratio of protein retained in the body to the absorbed protein and high content of branched-chain amino acids [7]. Increased proportion of protein in the total energy intake is expected to reduce hunger and increase satiety [8]. A high-protein diet accounting for 30% of the energy intake during energy restriction can lead to a decrease in the percentage of muscle loss, compared with diets with less than 20% protein [9]. Additionally, a higher proportion of protein in the diet can lead to reduced hunger and increased satisfaction [10]. High protein intake may affect kidney function, warranting caution, particularly in patients at high risk of renal impairment. Therefore, we designed a 12-week program during which soy and whey proteins were administered to comparatively assess their effects on body weight and evaluate their safety regarding renal function in an exploratory manner. We

conducted a trial to investigate the effectiveness of weight loss through the consumption of a high-protein diet containing protein beverages.

Materials & methods

Trial design

This exploratory, three-arm, placebo-controlled, double-blind, randomized clinical trial was conducted at Kobe University Hospital, Japan. The study protocol was approved by the Kobe University Clinical Research Ethics Committee and registered with the Japan Registry of Clinical Trials (Identifier: jRCTs051200103). The trial was carried out in full compliance with the Declaration of Helsinki, and it adhered to the ethical guidelines and human research regulations of Japan.

Participants

This trial included participants with obesity based on the following criteria: (1) BMI $\geq$30 kg/m^2 or BMI $\geq$25 kg/m^2, with diabetes or dyslipidemia; (2) age $\geq$18 years at the time of obtaining consent, with no sex restriction; (3) for those diagnosed with diabetes, participation required dietary/exercise therapy or stable treatment, with HbA1c below 8.0% (maintained for at least 30 days); and (4) voluntary, written consent for clinical study participation. Exclusion criteria encompassed patients who: (1) participated in other trials, (2) had soy or whey protein allergies, (3) exhibited severe renal failure (chronic kidney disease stage G3 or above), (4) had severe liver impairment with hepatic encephalopathy, (5) received obesity treatment within the 30 days before consent, (6) had weight fluctuation of $\geq$5 kg in the 30 days before consent, (7) underwent or planned obesity surgery or weight-loss device treatment during the study (with exceptions), (8) had uncontrolled thyroid disease (TSH >10.0 mIU/L or <0.4 mIU/L), (9) were pregnant, breastfeeding, desired pregnancy during the study, or couldn't accept effective contraception, (10) had a heart pacemaker, and (11) were considered unsuitable by investigators.

Dietary and exercise therapy guidance

Daily energy intake was set at 25 kcal/kg $\times$ IBW for individuals with a BMI of 25 to $\leq$35 kg/m^2 and 20–25 kcal/kg $\times$ IBW for those with a BMI $\geq$35 kg/m^2, designed based on the Japan Society for the Study of Obesity "Obesity Treatment Guidelines 2022" [11]. The amount of protein intake was initiated at approximately 0.1% of the initial body weight and did not exceed 30% of the total energy intake. The amount of lipid intake was set at 20%, and the amount of carbohydrate intake was set at 50%, as guided by a registered dietitian. Exercise therapy guidance involved explaining a program created by a physical therapist and designed to be safely implemented by patients with obesity. Participants were instructed to execute the program independently.

Dietary assessment

A dietary survey was conducted using a food frequency questionnaire based on food groups (FFQg). The FFQg consists of total 34 questions and elicits information on the average intake per week of 29 food groups and 10 kinds of cookery in commonly used units or portion sizes. The FFQg was externally validated by comparison with weighed dietary records for 7 continuous days of 66 study participants aged 19–60 years [12]. We used standardized software for population-based surveys and nutrition counseling in Japan (EIYO-KUN ver. 9, developed by Shikoku University Nutrition Database; KENPA-KUSHA, Tokyo, Japan) to calculate nutrient and food group intake.

Randomization/blinding

After checking for eligibility and enrollment to the study, participants were randomly allocated to soy protein, whey protein, and placebo groups at a ratio of 1:1:1 using stratified permuted block

randomization (block size of 3 or 6) based on the strata by BMI ($\geq$35 kg/m^2, <35 kg/m^2). To preserve blinding, the allocation and correspondence tables between the allocation and drug numbers were independently managed, separately from the investigators and attending physicians. The assignment groups were disclosed only after the completion of data collection, finalization of case-handling outcomes, and data locking, except in emergencies.

Interventions and follow-up

The protein beverage examined in this study was custom-formulated for research purposes and is not commercially available as a consumer product. It was developed by combining commercially available food ingredients to ensure suitability for human consumption. The composition included 15 g of soy or whey protein, 3 g of HMB Ca, 7.5 billion Bifidobacterium, 6.5 g of PHGG, and multivitamins. The placebo was prepared by replacing protein with dextrin. The nutritional value of each beverage is summarized in Supplementary Table 1. The beverage was dissolved in water, soymilk, or regular milk, and consumed once a day without a specific prescribed administration time. Participants were orally administered the assigned investigational drug once daily for 12 weeks, starting from the day following registration.

Nutritional and exercise counseling sessions were conducted for all participants every four weeks. The study participants were instructed to maintain a daily weight diary that included their dietary records. Body measurements, blood tests, and other evaluations were performed at the start of the study and at 4, 8, and 12 weeks. Concurrent use of anti-obesity drugs, protein beverages, or supplements designed for weight loss was prohibited. In cases of abnormal digestive symptoms, allergic reactions, or renal function deterioration, intake was reduced or discontinued.

Outcomes

The primary efficacy outcome measure was the percentage change in body weight from baseline to 12 weeks. Secondary efficacy outcome measures included the percentage changes in waist circumference, muscle mass, body fat, basal metabolic rate, blood pressure, and metabolic parameters. Additionally, this study explored the changes in dietary habit parameters using a FFQg. Safety was assessed based on the incidence of renal impairment or other adverse events related to the trial intervention.

Sample size

Based on the setting of this trial and a previous study [13] that investigated the weight loss effects of a whey protein-based formula diet in patients with type 2 diabetes and obesity, we anticipated a difference of 3% in weight loss rate, with a conservative standard deviation of approximately 2%. With a one-sided significance level of 2.5% and a power of 90%, the required sample size was calculated as 12 participants per group to test the null hypothesis that there is no weight loss, compared with the placebo group. Considering the potential dropouts, we set the total sample size to 45 (15 participants in each group).

Statistical analysis methods

Considering the objectives of this trial, the analyses targeted participants who adhered to the trial protocol to assess efficacy, rather than the intention-to-treat population typically used for practical effectiveness assessments. The safety analysis set included all participants who were randomized and received the trial intervention.

The primary analysis involved comparisons between the soy protein and placebo groups, and between the whey protein and placebo groups. The percentage change in body weight from baseline to12 weeks was analyzed using analysis of covariance, incorporating BMI category, which was used as a stratification factor in the randomization. To control alpha errors resulting from multiple comparisons, a one-sided alpha level of 0.125 was set for both comparisons. Secondary outcomes and parameters

related to dietary and exercise habits were analyzed using analysis of covariance, incorporating baseline values. Changes from baseline were estimated with 95% confidence intervals (95% Cis) along with the corresponding two-sided *P*-values. Statistical analyses were performed using the R 4.3.1 software (R Core Team, 2023).

Results

Forty-four patients were enrolled between March 2021 and April 2022, with 14, 15, and 15 allocated to the soy protein, whey protein, and placebo groups, respectively (safety analysis set). After excluding two patients deemed ineligible after enrollment, three who withdrew, one lost to follow-up due to an infectious disease, and one with insufficient trial intervention intake, the analyses included 11, 12, and 14 eligible patients in the soy protein, whey protein, and placebo groups, respectively. Fig. 1 shows the patient selection flowchart. The demographic and baseline clinical characteristics of the patients are shown in Table 1. The mean age of the participants was approximately 50 years, and more than half were female. The mean baseline BMI values in the soy protein, whey protein, and placebo groups were 36, 37, and 38 kg/m^2, respectively.

For the primary efficacy outcome, the percentage changes in body weight from baseline to the 12 weeks were −2.55% (SD 3.24%), −2.69% (SD 3.49%), and −1.34% (SD 2.92%) in the placebo, soy protein, and whey protein groups, respectively. The difference between the soy protein and placebo groups was −0.17% (95% CI −2.70% to 2.44%, one-sided $P = 0.447$), and that between the whey protein and placebo groups was +1.23% (95% CI −1.33% to 3.78%, one-sided $P = 0.168$). Thus, the anticipated body weight loss was not achieved with the custom-formulated protein beverage. When the subjects were stratified by BMI of 35, there were no changes in body weight (data not shown).

The results of the other efficacy and safety outcomes are presented in Tables 2–4. No notable differences were observed in abdominal circumference, muscle mass, body fat, resting energy expenditure, or respiratory quotient (Table 2). The same was observed for blood pressure, glucose metabolism, and lipid metabolism (Table 3). Fig. 2 illustrates the time courses for body weight and abdominal circumference in each group.

In the safety evaluation, no dose reduction or discontinuation of the trial intervention occurred due to abnormal digestive symptoms, allergic reactions, or renal function deterioration. In addition, no renal impairment or other adverse events related to the trial intervention were observed (Table 4). The World Health Organization (WHO) recommends protein intake within the range of ideal body weight × 2.0 g, and when the requirement exceeds 2.1 g, individual health conditions should be

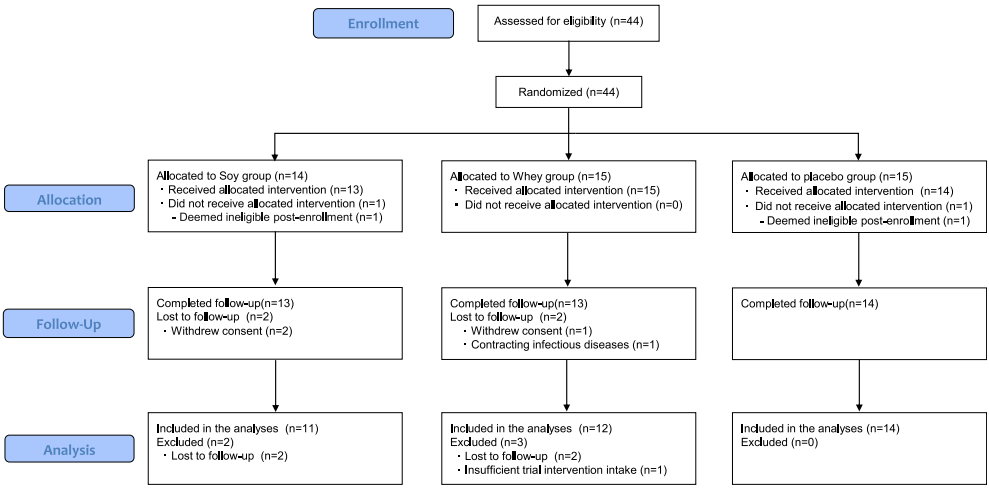

Fig. 1. Patient flow diagram.

Table 1
Patient characteristics.

Characteristic	Placebo (N = 14) mean ± SD or N (%)	Soy protein (N = 11) mean ± SD or N (%)	Whey protein (N = 12) mean ± SD or N (%)
Age (year)	47.07 ± 14.78	46.18 ± 10.38	50.33 ± 7.10
Sex			
Male	6 (42%)	4 (36%)	4 (33%)
Female	8 (57%)	7 (63%)	8 (66%)
BMI (kg/m^2)	38.35 ± 9.08	35.57 ± 7.16	36.54 ± 6.55
Presence of comorbidity			
Diabetes	11 (78%)	11 (100%)	7 (58%)
Dyslipidemia	6 (42%)	9 (81%)	9 (75%)
Hypertension	9 (64%)	5 (45%)	4 (33%)
Hyperuricemia	2 (14%)	4 (36%)	2 (16%)
Coronary artery disease	0 (0%)	0 (0%)	0 (0%)
Cerebrovascular disorders	0 (0%)	0 (0%)	1 (8%)
Non-alcoholic fatty liver disease	5 (35%)	5 (45%)	5 (41%)
Menstrual irregularities/Infertility	0 (0%)	0 (0%)	2 (16%)
Obstructive sleep apnea	6 (42%)	2 (18%)	4 (33%)
Musculoskeletal disorders	1 (7%)	2 (18%)	3 (25%)
Obesity-related kidney disease	0 (0%)	0 (0%)	0 (0%)

Abbreviations: SD, standard deviation; BMI, body mass index.

Table 2
Body composition and metabolic parameters.

Outcome	Group	Value at baseline	% Change from baseline to 12 weeks	Difference in % change[a]	
		Mean (SD)	Mean (SD)	Mean estimate (95% CI)	*P* value[b]
Body weight (kg)	Placebo	97.55 (25.14)	−2.55 (3.24)	Ref.	
	Soy	97.68 (23.57)	−2.69 (3.49)	−0.17 (−2.79 to 2.44)	0.894
	Whey	98.40 (19.52)	−1.34 (2.92)	1.23 (−1.33 to 3.78)	0.336
Abdominal circumference (cm)	Placebo	117.14 (16.98)	−5.86 (3.88)	Ref.	
	Soy	110.92 (17.41)	−4.67 (4.60)	0.52 (−2.71 to 3.75)	0.747
	Whey	115.12 (15.58)	−3.16 (4.28)	2.48 (−0.64 to 5.60)	0.115
Muscle mass[c] (kg)	Placebo	50.59 (9.05)	0.56 (2.83)	Ref.	
	Soy	53.32 (11.15)	−1.65 (3.52)	−2.20 (−4.83 to 0.42)	0.097
	Whey	50.46 (8.50)	0.26 (3.09)	−0.30 (−2.85 to 2.24)	0.810
Body fat[c] (kg)	Placebo	43.86 (17.85)	−6.30 (7.68)	Ref.	
	Soy	41.34 (15.91)	−3.80 (7.03)	2.32 (−3.13 to 7.76)	0.393
	Whey	45.12 (12.90)	−3.19 (4.60)	3.21 (−2.10 to 8.51)	0.228
Resting energy expenditure (kcal)	Placebo	1956.23 (288.15)	−2.66 (9.24)	Ref.	
	Soy	2011.18 (263.66)	0.45 (13.14)	3.75 (−7.89 to 15.39)	0.516
	Whey	1977.67 (307.22)	−5.64 (18.57)	−2.74 (−14.08 to 8.60)	0.626
Respiratory quotient	Placebo	0.80 (0.06)	0.87 (9.88)	Ref.	
	Soy	0.86 (0.11)	0.87 (8.48)	3.24 (−3.12 to 9.61)	0.308
	Whey	0.81 (0.10)	4.45 (9.30)	4.08 (−1.96 to 10.12)	0.179

Abbreviations: SD, standard deviation; CI, confidence interval.
[a] For body weight, adjusted by body mass index (stratification variable for randomization); otherwise, adjusted by the baseline value.
[b] Two-sided *P* value.
[c] Obtained by bioelectrical impedance analysis.

assessed. In this study, the protein beverage administration exceeded the ideal body weight × 2.0 g range in some cases. However, regarding safety confirmation, there were no issues with renal and hepatic functions.

We examined the differences between the recommended nutritional intake, set individually as dietary habit parameters and the actual nutrient intake as a guide. The findings are summarized in

Table 3
Blood pressure and laboratory parameters.

Outcome	Group	Value at baseline	Change from baseline to 12 weeks	Difference in % change[a]	
		Mean (SD)	Mean (SD)	Mean estimate (95% CI)	*P* value[b]
Systolic blood pressure (mmHg)	Placebo	126.14 (13.46)	−7.71 (10.10)	Ref.	
	Soy	130.18 (13.93)	−14.36 (18.78)	−4.80 (−15.82 to 6.21)	0.381
	Whey	118.33 (11.28)	−0.83 (14.10)	3.31 (−7.71 to 14.34)	0.545
Diastolic blood pressure (mmHg)	Placebo	80.71 (10.19)	−0.86 (7.13)	Ref.	
	Soy	80.73 (9.73)	−2.00 (11.35)	−1.14 (−7.80 to 5.53)	0.731
	Whey	80.33 (10.65)	−3.33 (10.46)	−2.68 (−9.18 to 3.83)	0.409
HbA1c (%)	Placebo	6.06 (0.59)	−0.14 (0.20)	Ref.	
	Soy	6.03 (0.68)	−0.24 (0.43)	−0.10 (−0.33 to 0.12)	0.355
	Whey	6.25 (0.58)	−0.15 (0.36)	0.06 (−0.16 to 0.28)	0.611
Glucose (mg/dL)	Placebo	102.57 (14.22)	−2.00 (7.04)	Ref.	
	Soy	102.55 (9.38)	−6.45 (9.50)	−4.46 (−13.50 to 4.58)	0.322
	Whey	101.33 (4.83)	3.50 (16.23)	5.08 (−3.76 to 13.92)	0.251
Triglycerides (mg/dL)	Placebo	131.07 (80.52)	−21.64 (35.72)	Ref.	
	Soy	159.18 (93.49)	2.27 (41.58)	25.37 (−6.71 to 57.44)	0.117
	Whey	110.58 (34.28)	1.00 (37.96)	21.59 (−9.55 to 52.73)	0.168
HDL-C (mg/dL)	Placebo	56.21 (12.99)	1.21 (5.06)	Ref.	
	Soy	53.82 (17.77)	−2.36 (7.09)	−3.95 (−8.80 to 0.89)	0.106
	Whey	60.83 (9.97)	−3.83 (6.53)	−4.32 (−9.09 to 0.44)	0.074
LDL-C (mg/dL)	Placebo	120.71 (28.42)	2.71 (19.25)	Ref.	
	Soy	125.45 (27.25)	−0.55 (25.34)	−2.44 (−18.25 to 13.37)	0.755
	Whey	128.75 (28.81)	−6.58 (12.73)	−7.91 (−23.42 to 7.60)	0.307
Uric acid (mg/dL)	Placebo	6.44 (1.59)	0.11 (0.75)	Ref.	
	Soy	5.67 (1.09)	0.71 (0.71)	0.42 (−0.15 to 1.00)	0.141
	Whey	5.13 (1.08)	0.39 (0.73)	−0.02 (−0.61 to 0.57)	0.947

SD, standard deviation; CI, confidence interval; HbA1c, glycated hemoglobin; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.
[a] For body weight, adjusted by body mass index (stratification variable for randomization); otherwise, adjusted by the baseline value.
[b] Two-sided *P* value.

Table 4
Renal function and liver function parameters.

Outcome	Group	Value at baseline	Change from baseline to 12 weeks	Difference in % change[a]	
		Mean (SD)	Mean (SD)	Mean estimate (95% CI)	*P* value[b]
Creatinine (mg/dL)	Placebo	0.73 (0.22)	0.01 (0.06)	Ref.	
	Soy	0.63 (0.08)	0.04 (0.05)	0.03 (−0.02 to 0.07)	0.217
	Whey	0.67 (0.12)	−0.02 (0.04)	−0.03 (−0.07 to 0.01)	0.099
eGFR (mL/min/1.73 m^2)	Placebo	82.36 (19.52)	−2.35 (7.74)	Ref.	
	Soy	90.99 (16.15)	−6.35 (6.68)	−3.10 (−8.94 to 2.74)	0.288
	Whey	82.49 (14.51)	3.18 (6.63)	5.55 (−0.03 to 11.12)	0.051
Urine protein (g/gCr)	Placebo	0.05 (0.06)	−0.01 (0.03)	Ref.	
	Soy	0.09 (0.09)	−0.07 (0.10)	−0.04 (−0.07 to 0.00)	0.029
	Whey	0.05 (0.04)	0.00 (0.03)	0.01 (−0.02 to 0.04)	0.583
AST (U/L)	Placebo	24.14 (8.58)	−2.71 (4.95)	Ref.	
	Soy	23.73 (14.61)	−2.36 (10.10)	0.10 (−2.63 to 2.84)	0.94
	Whey	27.17 (13.34)	−4.25 (8.73)	0.27 (−2.41 to 2.96)	0.837
ALT (U/L)	Placebo	31.57 (20.20)	−7.93 (13.20)	Ref.	
	Soy	36.18 (28.68)	−7.82 (19.18)	2.88 (−1.69 to 7.45)	0.209
	Whey	38.08 (31.12)	−10.08 (18.57)	1.76 (−2.72 to 6.23)	0.43
γ-GTP (U/L)	Placebo	44.50 (42.63)	−11.29 (39.86)	Ref.	
	Soy	30.18 (17.23)	−5.82 (13.61)	−5.61 (−16.61 to 5.39)	0.307
	Whey	27.50 (13.55)	−0.42 (5.33)	−2.28 (−13.13 to 8.57)	0.672

Abbreviations: SD, standard deviation; CI, confidence interval.
[a] Adjusted by baseline value.
[b] Two-sided *P* value.

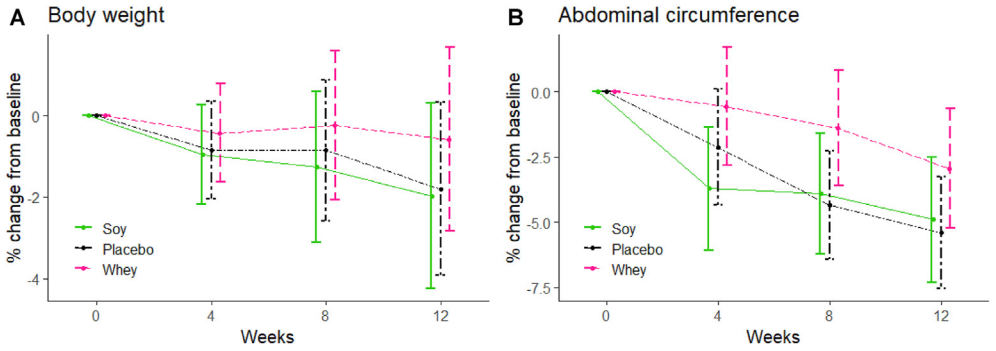

Fig. 2. Temporal changes in mean body weight and abdominal circumference. A: Temporal changes in the mean body weight. B: Temporal changes in mean abdominal circumference.

Table 5
Dietary habits parameters (excess or insufficient from the indicated amount).

Outcome	Group	Value at baseline	Change from baseline to 12 weeks	Difference in change[a]	
		Mean (SD)	Mean (SD)	Mean estimate (95% CI)	*P* value[b]
Caloric intake (kcal)	Placebo	413.15 (375.60)	−121.00 (416.64)	Ref.	
	Soy	221.82 (446.55)	−339.73 (486.93)	−373.21 (−671.44 to −74.98)	0.016
	Whey	374.50 (730.66)	−325.42 (724.47)	−235.63 (−523.92 to 52.66)	0.106
Protein intake (g)	Placebo	−18.59 (23.01)	8.54 (11.85)	Ref.	
	Soy	−21.75 (19.20)	−5.11 (14.65)	−15.25 (−28.24 to −2.26)	0.023
	Whey	−29.32 (28.80)	11.54 (28.30)	−2.43 (−15.33 to 10.48)	0.704
Lipid intake (g)	Placebo	34.06 (12.03)	−5.14 (16.11)	Ref.	
	Soy	30.76 (22.69)	−19.80 (18.22)	−16.88 (−30.65 to −3.10)	0.018
	Whey	39.52 (30.90)	−10.73 (30.27)	−1.93 (−15.44 to 11.57)	0.772

Abbreviations: SD, standard deviation; CI, confidence interval.
[a] Adjusted by baseline value.
[b] Two-sided *P* value.

Table 5 and Fig. 3. In the soy protein group, the actual energy intake was significantly below the recommended amount after 12 weeks, demonstrating a notable decrease, compared with that in the placebo group (Fig. 3A). Both protein and lipid intakes also showed significant reductions in the soy protein group (Fig. 3B, C) compared with the placebo group.

Discussion

Aims

This study investigated whether introducing a high-protein diet with soy or whey protein supplementation to prevent decrease in muscle mass and subsequent reduction in basal metabolism is associated with weight loss, and whether combining it with exercise therapy could achieve ideal weight loss without compromising muscle mass, by minimizing feelings of hunger.

Main findings

Participants consumed a protein beverage daily for 12 weeks and attended weight loss-related outpatient visits and nutritional counseling every 4 weeks to confirm dietary goals and receive

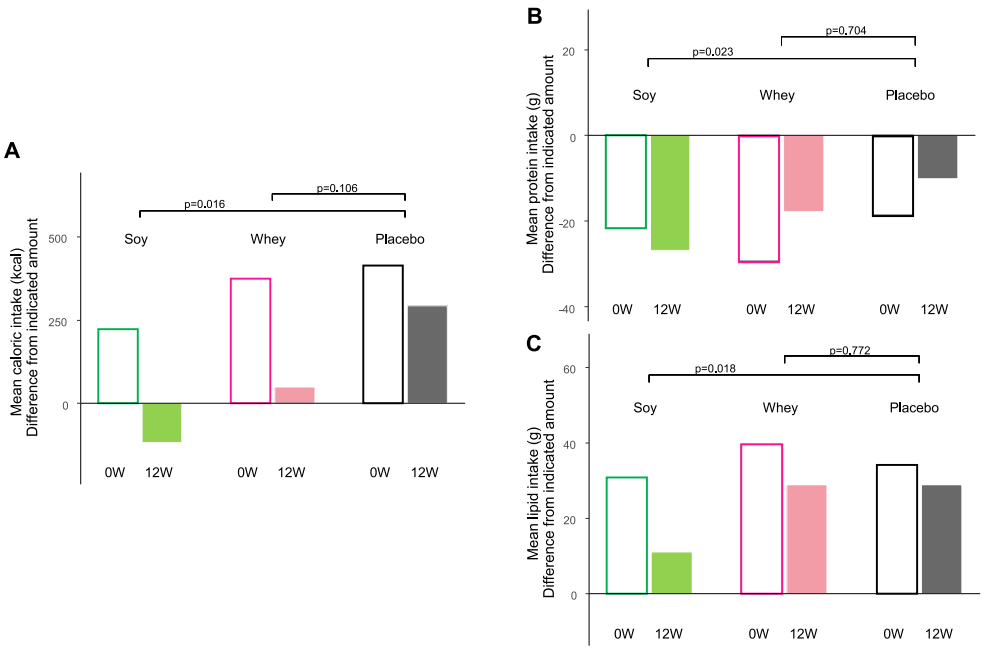

Fig. 3. Changes in dietary habits parameters from baseline to 12 weeks. A: Excess or insufficient calorie intake from the indicated amount. B: Excess or insufficient protein intake from the indicated amount. C: Excess or insufficient lipid from the indicated amount.

guidance on lifestyle habits. The observed weight loss during the intervention (2.2 kg/12 w) was less than anticipated; however, this is comparable to the findings of other weight loss studies that utilized dietary advice and coaching [14].

No significant differences were observed in weight, waist circumference, body composition parameters, resting energy expenditure, blood pressure, or metabolic indicators. However, the energy, protein and lipid intakes calculated from the prescribed nutritional intake in the weight loss program were significantly lower in the soy protein group. Regarding the breakdown of consumed nutrients, the soy protein group showed a significant decrease in protein and lipid quantities. Reports on appetite and protein calorie intake have suggested that consuming a higher proportion of calories from protein (approximately 18%) can help satisfy hunger, leading to increased satisfaction, reduced overall food intake, and 38% decrease in total calorie intake, compared with the free-choice phase [15]. While no significant difference in weight loss rate was observed over the 12-week protein supplementation period in this trial, the soy protein group maintained a lower energy intake than the prescribed amount. In terms of nutrient breakdown, there was a decrease in the intake of proteins and lipids in the soy protein group. Kozuka et al. demonstrated that γ-oryzanol containing brown rice alleviates endoplasmic reticulum stress in the hypothalamus, thereby mitigating preference for animal fats [16]. It has been reported that there is an effect of restoring an unsatisfied brain to a satisfactory state by recovering the decreased expression of dopamine receptors in the brain reward system responsible for recognizing meal satisfaction through an epigenetic mechanism [17]. Our study showed that consumption of soy, a plant protein source, had an effect similar to that reported on γ-oryzanol. Although the molecular biological mechanisms have not been clearly elucidated, it is possible that the mechanisms are similar.

In this study, while no significant difference in body weight was observed over the 12-week intervention period, participants in the soy protein group were able to continue dietary therapy with energy, protein, and lipid intake at or below the levels instructed in the nutritional guide.

Although further investigation is necessary, extending the administration period may result in significant weight loss.

Strengths

The primary strength of this study lies in its double-blind, randomized, controlled trial design. By analyzing the composition of the protein beverages and distinguishing between plant-based (soy) and animal-based (whey) proteins, we observed that the soy protein group may have experienced reduced feelings of hunger and achieved satisfaction earlier. Furthermore, the intake of these protein beverages did not result in any health issues, including kidney or liver impairment, indicating their safety.

Limitations

A limitation of this study is that the dietary intake calculated from the FFQ was based on patient self-reporting, and the actual intake was not objectively verified, which may introduce potential errors. In addition, exercise guidance was provided by a physician during consultations rather than by a specialized physical therapist. Consequently, there were many cases where the guidance was not adequately provided, and it was not possible to standardize the exercise intensity.

Conclusion

No significant weight loss was observed in the soy or whey protein group. However, in the soy protein group, it was possible to maintain a lower energy intake, and protein and lipid intakes decreased in post-hoc analysis. Although further investigation is necessary, extending the administration period may result in significant weight loss.

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None.

Author contributions

Michiko Takahashi: Conceptualization, data curation, funding acquisition, investigation, methodology, project administration, supervision, and writing the original draft.

Takumi Imai: Data curation, formal analysis, methodology, writing-original draft.

Tomoko Yamada, Naokazu Muramae, Kai Yoshimura, Hironori Bando, Kenji Sugawara, Shun-Ichiro Asahara, Yushi Hirota, Yoshikazu Tamori, Yutaka Takahashi, Wataru Ogawa: Writing review & editing.

Yuji Mitomo: Data curation, Formal analysis, Writing review & editing.

Data statement

The data underlying this article will be shared on reasonable request to the corresponding author.

Declaration of competing interest

None.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.nutos.2024.04.005.

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