ORIGINAL RESEARCH

Intradialytic Protein Supplementation Reduces Inflammation and Improves Physical Function in Maintenance Hemodialysis Patients

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Objective: Protein malnutrition is both a cause and consequence of inflammation and related comorbidities for maintenance hemodialysis (MHD) patients. This study sought to determine if oral supplementation with soy or whey protein during dialysis treatment reduces inflammation and improves physical function and body composition in MHD patients.

Design: The design used in the study was randomized controlled trial, and the setting used was hemodialysis clinics in Champaign and Chicago, Illinois.

Subjects: Patients who received treatment ≥3 days/week, were ages ≥30 years did not have congestive heart failure or chronic obstructive pulmonary disease, and were receiving dialysis treatment for ≥3 months were eligible for inclusion.

Intervention: Patients were randomized to oral supplementation with a whey protein, soy protein, or placebo beverage. Patients (WHEY, $n = 11$; SOY, $n = 12$; CON, $n = 15$) consumed their assigned beverage before every dialysis session for 6 months.

Main Outcome Measures: Body composition was measured by dual-energy x-ray absorptiometry, physical function by gait speed and shuttle walk test, and markers of inflammation (C-reactive protein and interleukin 6) using commercially available enzyme-linked immunosorbent assay kits before and after the 6-month intervention. Dietary intake was assessed by 24-hour dietary recalls.

Results: Six months of whey or soy supplementation significantly reduced predialysis interleukin 6 levels ($P < .05$ for both), whereas there was a trend for a reduction in C-reactive protein when both protein groups were combined ($P = .062$). Gait speed and shuttle walk test performance also significantly improved in the protein groups ($P < .05$ for both). No changes in body composition were observed. However, alkaline phosphatase, a marker of bone turnover, was significantly reduced in the protein groups.

Conclusions: Intradialytic protein supplementation during a 6-month intervention reduced inflammation and improved physical function and represents an affordable intervention to improve the health of MHD patients.

Introduction

PROTEIN–ENERGY WASTING IS common in maintenance hemodialysis (MHD) patients, with a reported incidence of 18% to 75%.[1–4] Protein–energy wasting is associated with a loss of lean mass and functional declines[5] that reduce physical activity levels and exacerbate comorbidities. The mechanism for these losses is complex but includes many chronic abnormalities, such as chronic inflammation, that alter the balance between anabolism and catabolism (reviewed in studies by Mak et al.[6] and Raj et al.[7]). In addition, an acute peak in protein catabolism both during and immediately after dialysis treatment[8,9] contributes to lean mass losses that may range from 1 to 3 kg/year.[5]

Intradialytic protein supplementation has the potential to be a low cost and easily delivered intervention that may be beneficial specifically in preventing the acute losses of lean mass that occur during and immediately after the dialysis procedure.[10–12] The source of protein is an important factor that may influence the outcome of such an intervention. Whey protein may have greater influences on body composition and physical performance due primarily to its higher leucine content.[13] Soy protein, although potentially less anabolic than whey,[14] may reduce inflammation through the activity of its isoflavone compounds.[15] This reduction in inflammation may further reduce the progression of other comorbid conditions. However, the effect of intradialytic protein source has not been examined in MHD patients.

Therefore, the purpose of this study was to test the efficacy of 6 months of intradialytic oral protein supplementation, with either whey or soy protein, on MHD comorbidities, including measures of body composition, bone health, physical performance, and clinically relevant

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plasma markers. We hypothesized that protein supplementation, regardless of source, would improve functional outcomes by increasing substrate availability to improve protein turnover. However, we hypothesized that soy protein would have greater anti-inflammatory effects given its high concentration of isoflavones.

Subjects and Methods

Subjects

MHD patients at the Champaign Urbana Dialysis Center (Champaign, IL) and the Oak Park Dialysis Clinic (Oak Park, IL) were recruited. Patients who received hemodialysis (HD) treatment ≥3 days/week, were ages ≥30 years, did not have uncompensated congestive heart failure or chronic obstructive pulmonary disease, and were receiving dialysis treatment for ≥3 months were enrolled. Consent was obtained from each participant, and all protocols were approved by the University of Illinois Institutional Review Board and were in accordance with the Declaration of Helsinki.

Group Assignment

Participants were randomly assigned to 27 g whey protein (WHEY; True Nutrition, Vista, CA), 27 g soy protein (SOY; Solae, Gibson City, IL), or a noncaloric placebo powder (CON; 2 g Crystal Light, Kraft Foods, Northfield, IL), all mixed with 4 oz of water (Table 1). The amount of protein was chosen to represent a supplemental dose that was not intended to replace any protein consumed as part of the normal diet. Participants were blinded to group assignment, and beverages were provided in a nontransparent container. The beverage was consumed within 15 minutes of the start of dialysis treatment under direct supervision by the research staff. Compliance was tracked, and a level of 75% compliance was established for remaining in the study. At baseline and immediately after the 6-month intervention, all patients underwent the testing described in the following on a nondialysis day (18-24 h after a dialysis treatment). Data were analyzed by blinded study personnel who did not participate in administration of the beverage.

Table 1. Composition of the Study Beverages

Per Serving	Whey Isolate (30 g)	Soy Isolate (32 g)*	Crystal Light (2 g)
Total fat (g)	0	0.9	0
Saturated fat (g)	0	0.3	0
Cholesterol (mg)	0	0	0
Sodium (mg)	53	373	35
Carbohydrates (g)	0	0	0
Protein (g)	27	27	0
Leucine (g)	3.3	2.1	0
Vitamin A	0 mg	<2%	0 mg
Vitamin C	0 mg	<2%	0 mg
Calcium (mg)	151	23	0
Iron (mg)	0	4.5	0
Phosphorus (mg)	72.6	244	0
Potassium (mg)	194	182	0†
Isoflavones (mg)	0	40	0

*A higher total gram amount of the soy isolate was given to supply the same amount of protein as the whey protein isolate.

†Crystal Light contains low amounts of potassium (as potassium sulfate and acesulfame potassium) but the amounts are not listed on the label.

Diet Recall

Dietary recalls for a dialysis and nondialysis day were collected by trained study personnel using the United States Department of Agriculture 5-pass method.[16] Diet recalls were reviewed by a registered dietitian and analyzed for nutrition composition using Nutritionist Pro Version 5.2.0 (Axxya, Stafford, TX).

Blood Analysis

Plasma was collected before an HD session and stored at −80°C until analysis. Circulating levels of interleukin 6 (IL-6) and C-reactive protein (CRP) were measured before and after the intervention in duplicate using commercially available enzyme-linked immunosorbent assay kits (IL-6: R&D Biosystems, Minneapolis, MN; CRP: Alpco Diagnostics, Salem, NH). In addition, blood draws were collected monthly by the HD clinics as part of routine care, and a standard blood panel was independently analyzed using these collected samples (Spectra Laboratories, Rockleigh, NJ).

Physical Function

Normal gait speed was determined as the average walking speed (meter per second) recorded over a 10-m course. The measurement was taken in triplicate and averaged. After the measurement of gait speed, participants underwent a validated shuttle walk test to assess physical performance as previously described.[17] In short, this test involved walking back and forth over a 10-m course to successively faster time constraints until the participant was no longer able to complete the course in the allotted time. Participants also underwent a battery of functional tests, including both sit-to-stand and up-and-go tests, to assess functional fitness.[18]

Quadriceps and hamstring strength was assessed using isokinetic dynamometry (Biodex System 3 Pro dynamometer; Biodex Corp., Shirley, NY) at a rate of 60° per second. Two sets of 6 repetitions were performed with a 3-minute rest period between sets, and the highest peak torque was used for analysis.

Anthropometrics, Bone Mineral Density, and Body Composition

Barefoot standing height was measured to the nearest 0.1 cm with a stadiometer, and body weight was measured on a balance scale with shoes and superfluous outer garments removed. All measurements were taken in duplicate and averaged. Bone mineral density (BMD) and whole-body soft tissue composition were measured by dual x-ray absorptiometry using a Hologic QDR 4500A