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 a 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 declines5 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 treatment8,9 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
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.

**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. 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:

**Table 1. Composition of the Study Beverages**

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

*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.

**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. 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.

**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.
bone densitometer (software version 11.2; Bedford, MA). Mineral-free lean mass was calculated as total lean mass minus bone mineral content. The body composition differential was calculated as follows: (mineral free lean mass final — mineral free lean mass baseline) — (fat mass final — fat mass baseline), where a loss in lean or a gain in fat mass will result in a negative number. All scans were analyzed and quality controlled by the same 2 technicians blinded to treatment status. Precision for dual x-ray absorptiometry measurements of interest is approximately 1.0% to 2.0% in our laboratory.

### Statistical Analysis

All data are presented as the mean ± standard error of the mean, unless otherwise indicated. For analyses without significant differences between protein sources, data from WHEY and SOY were combined to consider the effects of protein supplementation regardless of source (indicated as PRO). Differences in baseline characteristics for continuous variables were analyzed with a one-way analysis of variance. A chi-square test was used to analyze baseline differences between groups with regards to gender, diabetes, and smoking status. Because this was a pilot study, information on patient medications was collected but was not controlled for or included in any analysis.

The monthly blood measurements (7 total time points) collected as part of routine dialysis care (e.g., albumin, creatinine, phosphorus, potassium, and so forth) and provided by an independent laboratory were analyzed using mixed effects linear modeling, controlling for baseline values, gender, age, diabetes status, and smoking status. Correlation analyses were also performed to assess the relationship between selected variables of interest. For all statistical tests, significance was considered as \( P < .05 \).

### Results

#### Patients

Forty-six MHD patients underwent baseline testing for the chronic supplementation study. One participant died during the study (unrelated to study protocol), 2 participants dropped out due to gastrointestinal distress, 1 participant transferred to another clinic, 3 participants withdrew for unknown reasons, and 1 participant withdrew after receiving a kidney transplant. In total, 38 participants completed the 6-month intervention (WHEY, \( n = 11 \); SOY, \( n = 12 \); CON, \( n = 15 \)). At baseline, the 3 groups did not differ significantly regarding age, body mass index, waist circumference, or any clinical laboratory values (Table 2). The etiology of renal failure was hypertension (\( n = 20 \)), type 2 diabetes mellitus (\( n = 10 \)), polycystic kidney disease (\( n = 3 \)), type 1 diabetes mellitus (\( n = 2 \)), nephritis (\( n = 2 \)), and unknown (\( n = 1 \)).

#### Dietary Recall

No differences in calorie or macronutrient intake were observed at baseline. After 6 months of protein supplementation, there was a trend for an increase in relative protein intake (gram per kilogram body weight per day) in PRO compared with CON (\( P = .08 \)).

#### Blood Analysis

There was a significant time by treatment interaction for IL-6 levels among the 3 groups (\( P = .036 \), Fig. 1), with both the WHEY and SOY groups decreasing compared with the control group. There was a trend for an interaction effect for CRP levels when the protein groups were combined (\( P = .062 \), Fig. 2). Moreover, the ΔCRP levels were significantly correlated with the ΔIL-6 levels (\( r = 0.689, P < .001 \)).

For standard blood measures assessed monthly at the dialysis clinic as part of routine care (Table 3), a significant time by treatment interaction was determined for the

<table>
<thead>
<tr>
<th>Table 2. Study Participant Characteristics at Baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variable</td>
</tr>
<tr>
<td>------------------------------------------------</td>
</tr>
<tr>
<td>Gender (male), %</td>
</tr>
<tr>
<td>Age (y)</td>
</tr>
<tr>
<td>Diabetic (yes), %</td>
</tr>
<tr>
<td>Smoker (yes), %</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
</tr>
<tr>
<td>Waist, female (cm)</td>
</tr>
<tr>
<td>Waist, male (cm)</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
</tr>
<tr>
<td>Calcium (mg/dL)</td>
</tr>
<tr>
<td>Phosphorus (mg/dL)</td>
</tr>
<tr>
<td>Potassium (mEq/L)</td>
</tr>
<tr>
<td>Bicarbonate (mEq/L)</td>
</tr>
<tr>
<td>BUN-to-creatinine</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
</tr>
</tbody>
</table>

BMI, body mass index; BUN, blood urea nitrogen.

Data are presented as mean ± standard error of the mean. Gender, diabetes status, and smoking status were assessed using chi-square analysis. All other variables were analyzed using one-way analysis of variance.
neutrophil-to-lymphocyte ratio, a marker of systemic inflammation; this ratio improved in SOY per month \((-0.14 \pm 0.07)\) compared with an increase for WHEY \((0.12 \pm 0.08)\) and CON \((0.08 \pm 0.07)\) \((P = .02)\). In addition, a significant time by treatment interaction was determined for alkaline phosphatase (ALP), a marker of bone turnover; ALP increased at a significantly greater rate throughout the intervention period in CON compared with PRO \((5.12 \pm 2.60\) vs. \(-1.55 \pm 1.99\) in U/L, \(P = .04)\). No other significant differences in standard clinic blood variables were observed.

**Physical Function**

For gait speed, the time by treatment interaction effect was significant \((P = .048)\) when all 3 groups were analyzed, indicating improved gait speed for both WHEY \((0.84 \pm 0.27\) to \(0.91 \pm 0.26\)) and SOY \((0.86 \pm 0.23\) to \(0.97 \pm 0.22\)) and a decline in CON \((0.86 \pm 0.29\) to \(0.83 \pm 0.28\)). For the shuttle walk test, there was a trend for a time by treatment interaction effect when the protein groups were combined \((F = 3.63, P = .065)\). Shuttle walk test time was significantly improved (longer time on the course) for the WHEY \((+31.6 \pm 11.5\) seconds, \(P < .05)\) and combined PRO
the 2-group analysis (PRO and CON). For both analyses, the same control group with the same values was used.

Routine care at the clinic. The period from blood sample collected monthly during the study and assessed by the renal-specific Spectra Laboratory (Rockleigh, NJ) as part of (P = 0.006 ± 0.01).

Composition

Anthropometrics, BMD, and Body Composition

No significant time by treatment effects for anthropometric measurements, bone density, or body composition were observed (Table 4). However, the change in ALP was inversely related to both the change in whole body BMD (r = −0.555, P < .01) and hip BMD (r = −0.668; P = .001).

Discussion

In this study, we demonstrated improvements in chronic inflammation, physical function, and markers of bone turnover after 6 months of intradialytic protein supplementation. These data support the use of intradialytic protein supplementation as a low-cost intervention to improve dialysis-related comorbidities in MHD patients.

We found that oral administration of 27 g of protein at the start of dialysis treatment attenuated inflammation in MHD patients. We were able to demonstrate a significant improvement in IL-6 and a trend for an improvement in CRP in the groups consuming protein for 6 months compared with the group consuming the placebo. Furthermore, we found a reduction in the neutrophil-to-lymphocyte ratio, a commonly used clinical measure of inflammation, in the SOY group. Overall, these data suggest an improvement in the inflammatory profile of the patients receiving protein compared with the control.

IL-6 as a marker of inflammation may be particularly important to this population, as elevations in IL-6 are associated with particularly poor outcomes in MHD patients and contribute to the development and progression of many comorbidities. However, IL-6 is also sensitive to changes in energy state, and these data raise the possibility that worsening nutritional status, caused in part by the loss of amino acids into the dialysate, may contribute to the acute rise in inflammation demonstrated to occur during hemodialysis treatment. This acute rise in inflammation, if experienced during every treatment, may consequently contribute to the chronic elevation in inflammation experienced by MHD patients reflected by elevated circulating levels of CRP, IL-6, and tumor necrosis factor alpha. Simply providing substrate may be adequate to attenuate inflammation, and future studies are needed to determine the mechanism for the reduction in IL-6 demonstrated in this study. With regards to CRP, Fanti et al. previously demonstrated a negative association between the change in plasma isoflavones and CRP levels after 8 weeks of soy protein supplementation in MHD patients; these isoflavones and other bioactive compounds in the protein may contribute to the attenuation of this inflammatory response in the present study.

Serum albumin levels are often used as a marker of nutritional status. However, inflammatory cytokines can influence albumin in MHD patients, making it difficult to separate the effects of inflammation and malnutrition on this negative acute phase protein. Indeed, we found albumin levels to be

<table>
<thead>
<tr>
<th>Variable</th>
<th>Normal Range</th>
<th>WHEY</th>
<th>SOY</th>
<th>CON</th>
<th>P-value</th>
<th>PRO</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin (mg/dL)</td>
<td>3.5-5.2</td>
<td>0.008±0.02</td>
<td>0.004±0.01</td>
<td>0.002±0.01</td>
<td>.95</td>
<td>0.006±0.01</td>
<td>.81</td>
</tr>
<tr>
<td>ALP (U/L)</td>
<td>40.0-129.0</td>
<td>−1.70±3.1</td>
<td>−1.45±2.72</td>
<td>5.12±2.60</td>
<td>.14</td>
<td>−1.55±1.99</td>
<td>.04</td>
</tr>
<tr>
<td>Bicarbonate (mEq/L)</td>
<td>22.0-29.0</td>
<td>0.13±0.21</td>
<td>−0.33±0.21</td>
<td>−0.26±0.16</td>
<td>.26</td>
<td>−0.11±0.15</td>
<td>.54</td>
</tr>
<tr>
<td>BUN (mg/dL)</td>
<td>6.0-19.0</td>
<td>−1.68±1.0</td>
<td>0.07±0.93</td>
<td>−0.18±0.84</td>
<td>.39</td>
<td>−0.74±0.69</td>
<td>.61</td>
</tr>
<tr>
<td>BUN-to-creatinine</td>
<td>10-20:1</td>
<td>0.04±0.09</td>
<td>0.04±0.10</td>
<td>−0.08±0.09</td>
<td>.12</td>
<td>−0.10±0.07</td>
<td>.86</td>
</tr>
<tr>
<td>Calcium (mg/dL)</td>
<td>8.4-10.2</td>
<td>−0.01±0.01</td>
<td>0.03±0.09</td>
<td>−0.001±0.08</td>
<td>.95</td>
<td>0.01±0.07</td>
<td>.91</td>
</tr>
<tr>
<td>Creatinine (g/dL)</td>
<td>0.5-1.2 (M), 0.4-1.1 (F)</td>
<td>−0.42±0.48</td>
<td>−0.75±0.44</td>
<td>0.01±0.41</td>
<td>.44</td>
<td>−0.60±0.32</td>
<td>.24</td>
</tr>
<tr>
<td>Ca × P</td>
<td>0.0-54.0</td>
<td>−1.18±0.83</td>
<td>0.61±0.73</td>
<td>0.42±0.73</td>
<td>.23</td>
<td>−0.16±0.56</td>
<td>.53</td>
</tr>
<tr>
<td>Iron (μg/dL)</td>
<td>45-160 (M), 30-160 (F)</td>
<td>0.21±2.31</td>
<td>1.98±2.12</td>
<td>4.04±1.91</td>
<td>.44</td>
<td>1.17±1.55</td>
<td>.24</td>
</tr>
<tr>
<td>Ferritin (ng/mL)</td>
<td>22-322 (M), 10-291 (F)</td>
<td>−15.7±29.0</td>
<td>29.2±22.1</td>
<td>39.1±21.1</td>
<td>.31</td>
<td>11.9±17.6</td>
<td>.34</td>
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<tr>
<td>Hemoglobin (g/dL)</td>
<td>14-18 (M), 12-16 (F)</td>
<td>−0.12±0.09</td>
<td>0.01±0.08</td>
<td>0.07±0.07</td>
<td>.25</td>
<td>−0.05±0.06</td>
<td>.22</td>
</tr>
<tr>
<td>iPTH (pg/mL)</td>
<td>42-52 (M), 37-47 (F)</td>
<td>−0.43±0.28</td>
<td>−0.02±0.26</td>
<td>0.27±0.24</td>
<td>.16</td>
<td>−0.21±0.19</td>
<td>.11</td>
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<tr>
<td>Potassium (mEq/L)</td>
<td>3.5-5.1</td>
<td>−0.08±0.05</td>
<td>0.07±0.04</td>
<td>−0.001±0.04</td>
<td>.07</td>
<td>0.002±0.03</td>
<td>.94</td>
</tr>
<tr>
<td>Phosphorus (mg/dL)</td>
<td>2.6-4.5</td>
<td>−0.20±0.08</td>
<td>0.03±0.07</td>
<td>0.02±0.07</td>
<td>.06</td>
<td>−0.07±0.05</td>
<td>.28</td>
</tr>
<tr>
<td>Neutrophil-to-lymphocyte</td>
<td>N/A</td>
<td>0.12±0.08</td>
<td>−0.14±0.07</td>
<td>0.08±0.07</td>
<td>.018</td>
<td>−0.03±0.05</td>
<td>.20</td>
</tr>
</tbody>
</table>

ALP, alkaline phosphatase; BUN, blood urea nitrogen; Ca × P, calcium phosphorus product; F, female; iPTH, intact parathyroid hormone; M, male. Data are presented as the mean ± standard error of the mean. The values represent the mean change per month over the 6-month intervention period from blood sample collected monthly during the study and assessed by the renal-specific Spectra Laboratory (Rockleigh, NJ) as part of routine care at the clinic. The P value indicates a significant time × treatment interaction for either the 3-group analysis (WHEY, SOY, and CON) or the 2-group analysis (PRO and CON). For both analyses, the same control group with the same values was used.

*P value for 3-group analysis (WHEY, SOY, and CON).

†P value for 2-group analysis (PRO and CON).
related to baseline IL-6 levels. However, despite improvements in inflammation, we did not observe an improvement in albumin levels with nutrition supplementation. This finding may be due to the relatively high albumin levels in patients at the start of this study (≥3.9 g/dL).

Inflammation underlies the development and progression of many comorbid conditions, such as muscle wasting and reduced physical function. We demonstrated beneficial effects of protein supplementation on functional outcomes, such as gait speed and shuttle walk test performance. The shuttle walk test is a measure of physical performance frequently used to assess function in older and diseased individuals instead of more objective measures of aerobic capacity, such as VO2max testing, because functional limitations (e.g., muscle weakness and shortness of breath) prevent these individuals from achieving standard criteria used in assessment of more objective tests.28 We have previously shown that cycling during dialysis treatment also improved these measures,29 further highlighting the importance of the intradialytic therapeutic window. Moreover, deficits in gait speed are also clinically relevant in maintenance dialysis patients because they reflect a phenotype of increasing frailty and predict mortality in the aged and many clinical populations.30,31

We did not observe any significant differences in body composition or BMD after protein supplementation. These results are similar to those of many others that have failed to find an improvement in body composition with nutritional supplementation.32,33 However, others have hypothesized that protein supplementation may improve muscle quality by increasing the turnover of damaged or poorly functioning protein.34 Our data support this hypothesis, as we found improvements in ALP in the groups consuming protein. This finding is clinically significant, as previous research has found ALP to be an independent predictor of mortality in a 3-year cohort of more than 70,000 MHD patients.35 In addition, we demonstrated that ALP levels were inversely associated with several measures related to baseline IL-6 levels.

Table 4. Physical Function, Bone Mineral Density (BMD), and Body Composition Variables Before and After 6 Months of Intervention

<table>
<thead>
<tr>
<th>Variable</th>
<th>WHEY (n = 11) Baseline</th>
<th>6 Mo</th>
<th>SOY (n = 12) Baseline</th>
<th>6 Mo</th>
<th>CON (n = 15) Baseline</th>
<th>6 Mo</th>
<th>3 Group 2 Group P Value for Interaction Effect</th>
</tr>
</thead>
</table>
| Shuttle walk test (s)             | 216 ± 36               | 247 ± 37* | 268 ± 35               | 297 ± 41 | 222 ± 34               | 210 ± 38 | .19  
| Gait speed (m/s)                  | 0.84 ± 0.27            | 0.91 ± 0.26 | 0.86 ± 0.23            | 0.97 ± 0.22 | 0.86 ± 0.28            | 0.89 ± 0.29 | .048 N/A |
| Chair stand (n)                   | 10.5 ± 1.8             | 9.8 ± 2.0 | 8.5 ± 1.2             | 9.4 ± 1.2 | 8.3 ± 1.1             | 8.8 ± 1.1 | .53  
| Arm curl (n)                      | 14.7 ± 2.1             | 14.4 ± 2.2 | 13.2 ± 1.4             | 13.7 ± 1.0 | 14.9 ± 1.7             | 12.8 ± 1.4 | .21  
| Shoulder flexibility (in):        | -4.5 ± 2.1             | -5.0 ± 1.6 | -7.7 ± 1.9             | -5.9 ± 2.0 | -4.3 ± 1.9             | -4.7 ± 1.4 | .47  
| Leg flexibility (in)              | -3.6 ± 1.4             | -3.5 ± 1.4 | -3.9 ± 1.2             | -2.6 ± 1.1 | -2.7 ± 1.2             | -2.2 ± 1.3 | .82  
| Up and Go Test (s)                | 7.3 ± 1.0              | 7.6 ± 1.1 | 7.6 ± 8.5             | 7.3 ± 0.8 | 7.7 ± 0.9             | 8.2 ± 1.1 | .49  
| Max leg flexion torque (ft × lb)  | 37.7 ± 6.4             | 39.5 ± 5.3 | 28.5 ± 7.8             | 30.9 ± 4.1 | 33.0 ± 6.2             | 33.7 ± 4.3 | .95  
| Max leg extension torque (ft × lb)| 91.0 ± 24              | 81.5 ± 16 | 62.9 ± 10             | 72.4 ± 11* | 67.1 ± 16              | 67.4 ± 10 | .17  
| Body weight (kg)                  | 89.8 ± 7.4             | 90.7 ± 7.7 | 91.9 ± 5.6             | 93.4 ± 5.7 | 95.4 ± 6.6             | 95.3 ± 7.0 | .85  
| Whole body BMD (g/cm²)            | 1.12 ± 0.06            | 1.11 ± 0.05 | 1.08 ± 0.04            | 1.03 ± 0.04 | 1.09 ± 0.04            | 1.09 ± 0.04 | .30  
| Lumbar spine BMD (g/cm²)          | 1.20 ± 0.09            | 1.21 ± 0.09 | 1.14 ± 0.04            | 1.06 ± 0.04 | 1.16 ± 0.06            | 1.17 ± 0.06 | .17  
| Hip BMD (g/cm²)                   | 0.97 ± 0.07            | 0.95 ± 0.08 | 0.90 ± 0.06            | 0.84 ± 0.07 | 0.95 ± 0.05            | 0.97 ± 0.05 | .49  
| Whole body lean mass (kg)         | 57.2 ± 3.6             | 57.6 ± 3.8 | 56.7 ± 3.3             | 54.5 ± 4.3 | 59.5 ± 4.2             | 59.1 ± 3.8 | .80  
| Whole body fat (kg)               | 28.9 ± 4.6             | 28.7 ± 4.6 | 30.0 ± 4.7             | 25.5 ± 3.9 | 31.5 ± 4.2             | 33.0 ± 4.3 | .48  
| Whole body fat (%)                | 31.4 ± 2.5             | 31.1 ± 2.5 | 32.3 ± 3.2             | 30.5 ± 3.1 | 32.4 ± 2.7             | 33.0 ± 4.3 | .48  
| Body composition differential (kg) | 0.6 ± 0.8              |              | -0.3 ± 1.4             |              | -2.0 ± 2.0             |              | .50  

Three-group analysis included WHEY, SOY, and CON; 2-group analysis included PRO and CON; P values were calculated using repeated-measured ANOVA. Because only the gait speed repeated-measures ANOVA interaction term was significant, significant changes determined by paired-samples t tests measuring changes from baseline to final testing are also reported for all other measures (indicated by *, P < .05). All data are reported as the mean ± standard error of the mean.

* A longer time indicates better performance.
† A faster time indicates better performance.
‡ A negative score indicates poorer performance for both flexibility tests.
§ A faster time indicates a better performance.
Indicates mineral-free lean mass.
Body composition differential = (mineral-free lean mass final − mineral-free lean mass baseline) − (fat mass final − fat mass baseline), where a loss in lean or a gain in fat will give a negative number (analyzed by one-way analysis of variance [ANOVA]).
demonstrated improvements in albumin, subjective global assessment score, quality of life, and mortality after 3 to 12 months of intradialytic nutritional support. In addition, Daud et al. observed an attenuation in the rise of inflammation after 6 months of intradialytic protein and omega-3 supplementation. However, the present study is the first study to observe improvements in inflammation and physical function after intradialytic nutritional support in MHD patients with an average serum albumin ≥3.9 g/dL.

This study was limited by the relatively short intervention period. Longer, larger studies are needed to assess more completely the effects of intradialytic protein supplementation on inflammation, physical function, bone, and body composition and to detect any possible differences among types of protein. Additionally, studies are needed to investigate the effects of supplementation on other comorbid conditions, specifically, the significantly elevated rates of cardiovascular disease present in the population. The strength of this study was that we observed reductions in inflammation and improvements in physical function using a simple, low-cost, easy to implement nutritional supplement. It is also worth noting that providing intradialytic nutrition is a controversial topic among health care professionals. Despite the reported benefits of improved nutritional status and reduced mortality, concerns have been raised related to hemodynamic stability. Clinic staff should consider these concerns when making decisions about implementing intradialytic nutrition programs.

In summary, we found intradialytic whey or soy protein supplementation was associated with attenuated inflammation and improved physical performance. We also found lower ALP in patients receiving protein that was inversely related with several measures of bone density. Moreover, these changes were observed in patients with an average albumin ≥3.9 g/dL who do not meet the traditional criteria for malnutrition and without a significant change in these plasma albumin levels. Intradialytic protein supplementation induced modest favorable changes in functional outcomes and could represent a low-cost therapeutic treatment strategy for this critically ill population. Moreover, a review of policies regarding food intake during dialysis is warranted to fully consider this important therapeutic window.

Practical Applications

In this study, we demonstrated improvements in chronic inflammation after intradialytic protein supplementation in MHD patients. In addition, we observed improvements in physical function and markers of bone turnover after 6 months of intradialytic protein supplementation. Taken together, these data support the use of intradialytic protein supplementation as a low-cost intervention to improve dialysis related comorbidities in these patients.

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