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Effects of oral non-protein calorie supplements on nutritional status among maintenance hemodialysis patients with protein-energy wasting: a multi-center randomized controlled trial

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Protein-energy wasting (PEW) is prevalent in maintenance hemodialysis (MHD) patients, and is one of the major risk factors for poor outcomes and death. This study aimed to investigate the effects of non-protein calorie supplements on the nutritional status of MHD patients with PEW. MHD patients with PEW were enrolled in this multi-center, open-label, randomized controlled trial. Then, they were randomly assigned to the intervention group to receive the non-protein calorie supplements containing 280 kcal of energy every day for 6 months or the control group to complete all aspects of the study without receiving supplements. Patients in both groups received dietary counselling from dietitians. Data on nutritional assessments, anthropometric measurements, blood analysis and dietary recall were collected at the baseline and at six months from both groups. Statistical analyses were performed using analysis of covariance (ANCOVA) adjusted for sex and baseline values. Ninety-two MHD patients completed the study. A significant increase in the subjective global assessment (SGA) score was found in the intervention group compared with the control group (4.88 ± 1.41 *vs.* 4.40 ± 1.16, $p = 0.044$). The ratio of PEW patients (diagnosed with SGA ≤5) in the intervention group (61.2%) was also significantly lower than that in the control group (83.7%) ($p < 0.001$). Moreover, significant improvements in body mass index (20.81 ± 2.46 kg m^{-2} *vs.* 19.51 ± 2.60 kg m^{-2}, $p < 0.001$), nutrition risk screening 2002 (2.45 ± 1.40 *vs.* 3.12 ± 1.37, $p = 0.038$), mid-upper arm circumference (23.30 ± 2.78 cm *vs.* 21.75 ± 2.87 cm, $p = 0.001$), and mid-arm muscle circumference (20.51 ± 2.32 cm *vs.* 19.06 ± 2.92 cm, $p = 0.005$) were observed in the intervention group compared with the control group. Patients in the intervention group took in more dietary energy than the control group (26.96 ± 4.75 kcal per kg body weight per day *vs.* 24.33 ± 2.68 kcal per kg body weight per day, $p < 0.001$). In conclusion, non-protein calorie supplements may improve the nutritional status of MHD patients with PEW.

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Introduction

Protein-energy wasting (PEW) is a condition of impaired catabolism due to metabolic and nutritional disturbances in chronic diseases. Lean body mass loss and fat loss, representing protein or energy depletion, could be utilized to characterize PEW.[1] PEW is prevalent in patients on maintenance hemodialysis (MHD) with incidences ranging from 18% to 75%.[2] PEW is associated with poor quality of life and increased risks of morbidity and mortality.[3] Many factors contribute to elevated PEW risks among MHD patients, including comorbidities, insufficient physical activity, gut microbiota dysbiosis, inadequate energy and protein intake owing to anorexia, nutrient loss in dialysate, and an increased net breakdown of protein and fat due to inflammation, acidosis, and endocrine disorders.[4] Insufficient dietary energy and protein intake are the major causes of PEW. The National Kidney Foundation recommends that dietary intake of 1.0–1.2 g kg^{-1} day^{-1} of protein and 25–35 kcal kg^{-1} day^{-1} of energy are necessary to maintain nutritional status.[5] If dietary counselling alone fails to achieve

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sufficient nutrient intake, oral nutritional supplementation is recommended as the optimum choice of nutritional intervention for MHD patients with PEW.[6,7]

The clinical impact of oral supplements with and without protein was examined in MHD patients in previous studies.[8–12] Even though some renal-specific protein-containing supplements were found to improve the nutritional status of malnourished MHD patients,[9,13,14] high protein intake could also lead to the accumulation of acidic metabolites, thereby accelerating protein degradation.[7] It was known that sufficient energy intake played an important role in sparing protein,[15] which suggested that energy-only supplementation might be able to alleviate protein deficiency and improve the nutritional status of MHD patients with minimum side effects from excessive protein intake. Our previous study proved that intradialytic parenteral nutrition intervention with high-concentration glucose solution could replenish energy stores and improve the amino acid profile in MHD patients.[16] However, inconsistent results were found in several studies which attempted to determine if energy supplements without protein could produce a beneficial effect on the nutritional status of MHD patients. In 1990, Allman *et al.* clarified that 6-month oral glucose polymer supplementation could increase the body weight, body fat and lean body mass in malnourished MHD patients.[12] However, evaluation of the overall nutritional status of patients was not included in the study.[12] In contrast, Yang *et al.*[17] reported no clinically significant effect of fat-based energy-dense supplements on the nutritional status of MHD patients as measured by phase angle. Although different types of oral supplements were utilized to explore meliorating nutritional conditions in MHD patients, the efficacy of renal-specific non-protein calorie oral supplements on MHD patients with PEW has not been studied. Therefore, in this study, we aimed to investigate the effects of non-protein energy supplements on the nutritional status of MHD patients with PEW.

Materials and methods

Trial design

In this investigator-initiated, multi-center, open-label, randomized controlled trial, we studied the effects of 6-month non-protein calorie supplementation on the nutritional status of MHD patients with PEW. Patients from hemodialysis units in Guangzhou Red Cross Hospital, Dongguan People's Hospital and the Affiliated Hospital of Youjiang Medical University for Nationalities in China were recruited for this study between May 2018 and March 2020.

This study was approved by the Ethics Committee of Guangzhou Red Cross Hospital (2017-029-01). All participants signed the informed consent prior to participation. The trial was registered on the Chinese Clinical Trial Registry (**https://www.chictr.org.cn**, ChiCTR2000041392). This trial was conducted in accordance with the principles of the Declaration of Helsinki.

Participants and procedures

Eligible participants were patients aged 18–80 on regular hemodialysis (3 times per week, 4 h each session) for more than 3 months with a 7-point subjective global assessment (SGA) score ≤5 and without nutritional supplements in the last 3 months. Patients were excluded if they suffered from trauma, surgery, heart failure, peptic ulcer, tuberculosis, liver disease, syphilis or serious infection within the previous 3 months, had a confirmed diagnosis of malignancy, or needed elective surgery.

This study included three visits to the research center. During the initial screening visit, participants were informed of the study procedures, signed informed consent forms and underwent preliminary measurements of height, weight and 7-point SGA. Subsequently, participants enrolled in this study were evenly randomized to either the intervention or the control group. After the screening visit, participants made a testing visit to the research center. The 6-month trial started within 3 days after the testing visit. During the trial, all participants received dietary counselling from dietitians. Participants in the intervention group were treated with the oral non-protein calorie jelly dedicated for MHD patients at a dose of 90 g twice a day for 6 months. Each serving (90 g) of jelly contained 140 kcal of energy, 5.4 g of fat and 22.5 g of carbohydrate. The daily amount of jelly could provide 280 kcal of energy. Participants went to the hemodialysis units 3 times per week, and they were dispensed with 28 servings of jelly every 14 days at the hemodialysis units. Participants in the control group continued to follow their diets. Then, another testing visit was taken after the intervention trial lasted for 6 months. During each testing visit, nutrition risk screening 2002 (NRS2002), 7-point SGA, anthropometric measurements, blood analysis and 24-hour dietary recall were carried out.

Randomization

Randomization was performed using an SPSS software-generated randomization table with the permuted block method (block sizes of 4). Allocation was concealed using sequentially numbered opaque envelopes. Each envelope contained the patient's allocation to either the intervention or the control group. Centers received sealed envelopes and opened them in ascending order. Envelopes were checked regularly to ensure they were intact and were used in the correct order.

Study outcomes

The primary outcome was the 7-point SGA score. The secondary outcome included serum albumin, BMI and handgrip strength. The other composite nutritional indices, anthropometric measurements, laboratory measurements and dietary intake were also assessed. These outcome measurements were determined at the baseline and at the end of the 6-month trial.

Composite nutritional indices

The 7-point SGA and NRS2002 were used as nutritional screening and assessment tools at the baseline and at the sixth

month of the study. The score of the 7-point SGA[18] ranges from 1 to 7, among which a score of 6 to 7 indicates normal nutritional status, 3 to 5 indicates mild to moderate malnutrition, and 1 to 2 indicates severe malnutrition. Patients with a 7-point SGA score ≤5 were diagnosed as PEW. The NRS2002 scoring system is calculated by adding the score of three parts together, with a total score range from 0 to 7. A total NRS2002 score ≥3 was considered to be nutritionally at risk for patients.[19]

Anthropometrics

Anthropometric measurements including weight, height, body mass index (BMI), handgrip strength, triceps skinfold thickness (TSF), mid-upper arm circumference (MAC) and mid-arm muscle circumference (MAMC) were measured after the hemodialysis sessions. Handgrip strength, TSF, and MAC were assessed on the non-fistula side using the grip dynamometer (Fabrication Enterprises Inc., 12-0072, USA), the skinfold caliper (Guangdong Xiangshanweihua Corporation Ltd, EH101, China), and non-stretchable tape, respectively. MAMC was calculated using the following equation:[20]

$$\mathrm{MAMC\ (cm)} = \mathrm{MAC\ (cm)} - [\mathrm{TSF\ (cm)} \times \pi].$$

Laboratory measurements

Blood samples were collected before hemodialysis sessions. Samples were centrifuged, and the supernatants were stored at −80 °C until further use. Routine laboratory methods were applied to obtain data on the concentrations of bicarbonate, creatinine, calcium, phosphorus, calcium-phosphorus product, blood urea nitrogen (BUN), interleukin-6 (IL-6), total cholesterol (TCHOL), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), very low-density lipoprotein cholesterol (VLDL-C), alanine aminotransferase (ALT), aspartate aminotransferase (AST), hemoglobin, prealbumin, triglyceride, albumin, transferrin, homocysteine, high-sensitivity c-reactive protein (HsCRP), ferritin, intact parathyroid hormone (iPTH), and folic acid.

Dietary intake

Food and beverage consumption was estimated using 24-hour dietary recall[21] questionnaires through face-to-face interviews for three days. Energy and protein intakes were calculated according to *China Food Composition*.[22]

Statistical analysis

Sample size calculation was performed with the PASS 15.0.5 software based on results from a previous study[23] that reported a 0.7 increase in SGA following oral nutritional supplementation for 6 months. To detect a difference in group means of 0.7 with a standard deviation of 0.90, a power of 80% and a type-I error rate of 1% (two sided), the target sample size was 41 subjects per group. Assuming a drop-out rate of 20%, 52 enrolled patients were required in each group.

The normality of the distribution of variables was analyzed using the Kolmogorov–Smirnov test. Differences in non-normal distributed demographic variables between two groups at the baseline were evaluated using a Wilcoxon rank-sum test. Differences in continuous variables between groups at 6 months were analyzed using analysis of covariance (ANCOVA) adjusted for sex and baseline values. The chi-squared test was used to test the differences in categorical variables. Demographic measurements at the baseline were expressed as medians (first quartile and third quartile) for non-normal distributed continuous variables and percentages for categorical variables. Study outcomes including composite nutritional indices, anthropometric measurements, laboratory measurements and dietary intake were expressed as mean ± standard deviation. Statistical analyses were performed using SPSS version 23.0 for Windows (IBM Corp., Armonk, NY, USA). Statistically significant differences were defined as $p < 0.05$.

Results

Baseline characteristics

A total of 104 eligible participants were recruited and assigned to the control group (n = 52) and the intervention group (n = 52), but 12 participants did not complete the study. Thus, 92 participants were integrated in the data analysis including 43 patients in the control group and 49 patients in the intervention group (Fig. 1). No significant difference was observed between the two groups in age or etiology of end-stage renal disease (ESRD) at the baseline ($p > 0.05$). Sex distribution between groups was found to be slightly different, but the differences were not statistically significant ($p = 0.060$) (Table 1).

Nutritional scores and anthropometric measurements

As shown in Table 2, a significant increase in the SGA score and a decrease in the ratio of PEW patients (diagnosed with SGA ≤ 5) were found in the intervention group compared with the control group ($p < 0.05$). The NRS2002 score in the intervention group was significantly lower than that in the control group ($p < 0.05$). As for the anthropometric measurements, BMI, MAC, and MAMC were significantly higher in the intervention group compared with the control ($p < 0.05$).

Laboratory measurements

Table 3 illustrates that the blood measurements were not significantly different between the two groups ($p > 0.05$). Results suggested that bicarbonate was higher in the intervention group compared with the control, but the difference was not statistically significant ($p = 0.082$).

Nutrient intake

As can be seen from Table 4, the intervention group showed an increase in energy intake ($p < 0.001$) but not protein intake ($p > 0.05$) compared with the control during the trial.

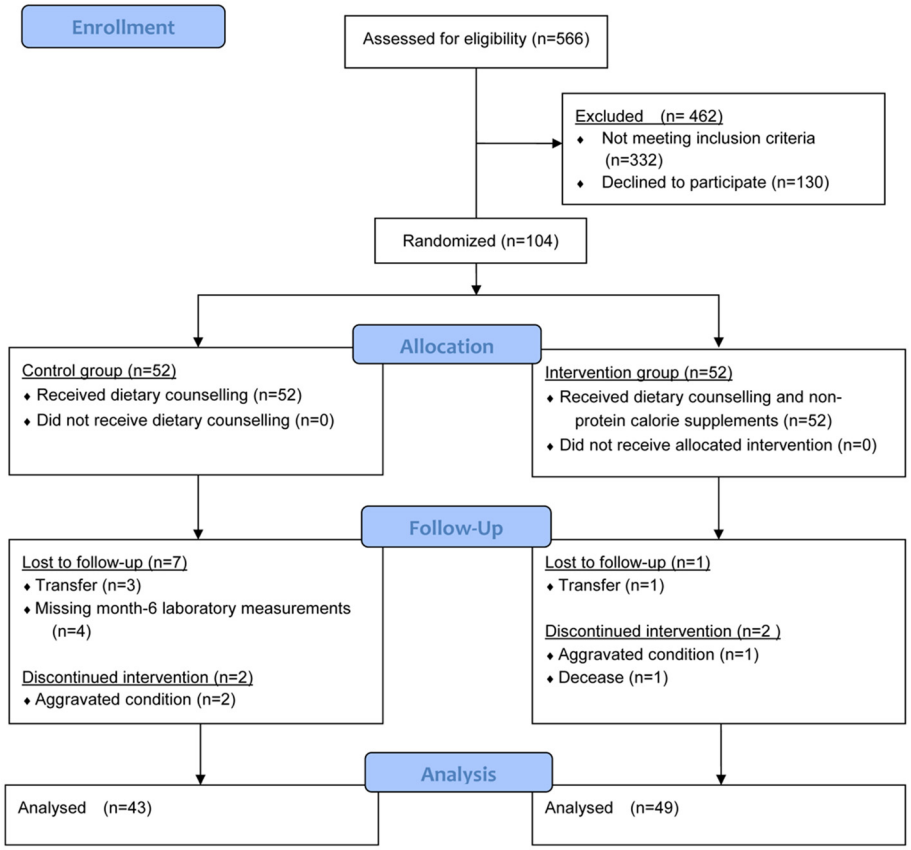

Fig. 1 Enrollment, randomization and follow-up of participants in the study.

Table 1 Characteristics of the participants at the baseline

Variables	Control (n = 43)	Intervention (n = 49)	p
Age, years	62 (54, 74)	60 (53, 68)	0.243
Sex (male), n (%)	17 (39.5)	29 (59.1)	0.060
Etiology of ESRD, n (%)			0.466
Chronic glomerulonephritis	19 (44.19)	22 (44.9)	
Diabetic nephropathy	8 (18.6)	14 (28.57)	
Unknown causes	10 (23.26)	6 (12.24)	
Other causes	6 (13.95)	7 (14.29)	

Discussion

MHD patients tend to have poor nutritional status caused by multiple factors including anorexia, chronic kidney disease, comorbidities, and hemodialysis therapy itself. Anorexia, following inadequate energy and protein intake, plays a critical role in the pathophysiology of PEW, leading to increased mortality in MHD patients.[1] Oral nutritional supplements are considered to be crucial for MHD patients with existing PEW conditions, especially when dietary counselling alone is not efficient. In the current study, MHD patients with PEW were treated with oral non-protein calorie supplements containing 280 kcal of energy every day for 6 months as their nutritional status was assessed. After the intervention, the SGA score and the ratio of MHD patients with PEW diagnosed by SGA in the intervention group were significantly improved compared with the control. Another key fact to remember, a significant improvement in NRS2002, BMI, MAMC, and MAC was observed in participants with the provision of oral non-protein calorie supplements.

Most of the available literature on oral nutritional supplementation in MHD patients has focused on the efficacy of protein-energy supplements. Although oral protein-energy supplements were demonstrated to be effective in improving the SGA scores, serum albumin, and anthropometric measurements in MHD patients,[9,10,24] high protein intake could also result in the accumulation of acidic metabolites.[7] There is a relatively small body of literature that is concerned with the efficacy of non-protein calorie supplements in MHD patients. In accordance with the present results, Allman *et al.*[12] concluded that the addition of glucose polymer to the diet could increase the weight of MHD patients with low BMI. Nonetheless, contrary to our expectation, Yang *et al.*[17] evaluated the efficacy of three-month administration of an oral energy-dense protein-free nutritional supplement (300 kcal, fat-based) among 240 MHD patients with low energy intake, and no significant effect was recognized on the nutritional status, which is conflicting with the current study. This incon-

Table 2 Nutritional score and anthropometric measurements of the participants (mean ± SD)

	Control (n = 43)		Intervention (n = 49)		
Variables	Baseline	6 months	Baseline	6 months	p
SGA	3.81 ± 1.24	4.40 ± 1.16	3.61 ± 1.17	4.88 ± 1.41	0.044
SGA ≤ 5, n (%)	43 (100)	26 (83.72)	49 (100)	30 (61.22)	<0.001
NRS2002	3.47 ± 1.05	3.12 ± 1.37	3.39 ± 0.95	2.45 ± 1.40	0.038
BMI, kg m^{-2}	19.66 ± 2.46	19.51 ± 2.60	19.97 ± 2.68	20.81 ± 2.46	<0.001
Handgrip strength, kg	15.07 ± 7.66	16.09 ± 7.43	16.40 ± 6.67	18.92 ± 7.06	0.095
MAC, cm	23.16 ± 3.32	21.75 ± 2.87	23.24 ± 3.67	23.30 ± 2.78	0.001
TSF, mm	8.07 ± 4.03	8.58 ± 3.37	7.85 ± 5.44	8.89 ± 4.15	0.874
MAMC, cm	20.62 ± 2.83	19.06 ± 2.92	20.78 ± 3.38	20.51 ± 2.32	0.005

The ratio of patients with SGA ≤ 5 was analyzed using the chi-squared test. Statistical analyses for SGA, NRS2002, BMI, handgrip strength, MAC, TSF, and MAMC were performed using analysis of covariance (ANCOVA) adjusted for sex and baseline values. BMI, body mass index; NRS2002, nutrition risk screening 2002; SGA, subjective global assessment; MAC, mid-arm circumference; TSF, triceps skinfold; and MAMC, mid-arm muscle circumference.

Table 3 Serum biochemical measurements of the participants (mean ± SD)

	Control (n = 43)		Intervention (n = 49)		
Variables	Baseline	6 months	Baseline	6 months	p
Kt/v	1.34 ± 0.29	1.39 ± 0.34	1.35 ± 0.38	1.37 ± 0.39	0.364
Bicarbonate, mmol L^{-1}	20.71 ± 4.03	21.41 ± 3.22	21.04 ± 3.68	22.53 ± 3.86	0.082
BUN, mmol L^{-1}	24.56 ± 10.41	24.45 ± 8.1	27.4 ± 7.11	25.55 ± 7.36	0.817
Creatinine, μmol L^{-1}	864.07 ± 307.48	905.84 ± 304.94	1074.96 ± 274.08	1022.82 ± 300.78	0.488
Calcium, mol L^{-1}	2.18 ± 0.23	2.16 ± 0.33	2.23 ± 0.27	2.21 ± 0.25	0.733
Phosphorus, mol L^{-1}	1.94 ± 0.64	1.99 ± 0.65	2.12 ± 0.58	2.18 ± 0.63	0.400
Calcium-phosphorus product	55.09 ± 22.62	53.54 ± 18.76	57.68 ± 16.5	59.56 ± 19.15	0.209
Hemoglobin, g L^{-1}	111.84 ± 18.73	110.47 ± 17.69	104.94 ± 24.13	105.14 ± 20.70	0.187
IL-6, pg mL^{-1}	14.18 ± 14.14	10.56 ± 9.87	8.50 ± 7.97	9.58 ± 8.41	0.863
TCHOL, mmol L^{-1}	4.51 ± 1.40	4.09 ± 1.10	4.02 ± 1.11	3.9 ± 1.23	0.805
HDL-C, mmol L^{-1}	1.26 ± 0.35	1.22 ± 0.33	1.15 ± 0.33	1.18 ± 0.41	0.218
LDL-C, mmol L^{-1}	2.43 ± 0.96	2.37 ± 0.91	2.21 ± 0.72	2.20 ± 0.89	0.725
VLDL-C, mmol L^{-1}	0.67 ± 0.44	0.72 ± 0.32	0.55 ± 0.35	0.56 ± 0.27	0.122
ALT, U L^{-1}	20.71 ± 28.1	13.43 ± 12.58	10.59 ± 6.65	11.65 ± 7.38	0.947
AST, U L^{-1}	22.33 ± 19.58	16.99 ± 11.12	15.29 ± 9.21	13.85 ± 6.07	0.693
Prealbumin, mg L^{-1}	308.47 ± 81.08	313.31 ± 79.2	327.50 ± 94.84	322.64 ± 98.86	0.650
Triglyceride, mmol L^{-1}	1.50 ± 1.00	1.72 ± 1.33	1.62 ± 1.01	1.87 ± 1.39	0.655
Albumin, g L^{-1}	36.96 ± 4.61	36.32 ± 3.34	36.77 ± 3.88	37.19 ± 3.72	0.121
Transferrin, g L^{-1}	1.63 ± 0.34	1.64 ± 0.50	1.64 ± 0.40	1.64 ± 0.35	0.715
HsCRP, mg L^{-1}	4.89 ± 6.37	5.23 ± 6.85	9.02 ± 15.63	11.13 ± 18.32	0.355
Homocysteine, μmol L^{-1}	26.11 ± 6.91	23.82 ± 11.98	29.92 ± 13.52	28.82 ± 13.53	0.871
Ferritin, μg L^{-1}	713.63 ± 553.23	780.98 ± 567.01	733.80 ± 552.60	801.75 ± 509.46	0.132
iPTH, pg mL^{-1}	131.98 ± 217.93	133.51 ± 259.01	150.61 ± 256.44	193.57 ± 298.72	0.265
Folic acid, nmol L^{-1}	15.51 ± 6.70	12.96 ± 8.44	14.91 ± 6.80	12.16 ± 8.03	0.225

Statistical analyses were performed using analysis of covariance (ANCOVA) adjusted for sex and baseline values. BUN, blood urea nitrogen; IL-6, interleukin-6; TCHOL, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; VLDL-C, very low-density lipoprotein cholesterol; ALT, alanine aminotransferase; AST, aspartate aminotransferase; HsCRP, high-sensitivity C-reactive protein; and iPTH, intact parathyroid hormone.

sistency may be due to the fact that the participants were not selected based on the nutritional status in Yang *et al.*'s study, while the present study targeted MHD patients diagnosed with PEW. Another possible explanation for this discrepancy might be that our study was thought to have a longer duration compared with Yang *et al.*'s study.

Nutritional supplementation was considered to increase energy intake and improve the nutritional status of patients as inadequate energy intake was the main contributor to PEW in MHD patients.[4,25] It is worthy to note that in this study, the SGA score of patients in the intervention group was significantly higher compared with the control at the end of the trial, suggesting that the oral non-protein calorie supplements had a positive influence on the nutritional status of MHD patients. One unanticipated finding was that the SGA scores in the control group were significantly higher compared with the baseline as well. It might be suggested that a certain amount of dietary counselling and surveillance might provide a moderate effect on the nutritional status to some extent.[26] Given the fact that 60% of chronic kidney disease (CKD) patients did not

Table 4 Nutrient intake of the participants (mean ± SD)

	Control (n = 43)		Intervention (n = 49)		
Variables	Baseline	6 months	Baseline	6 months	p
Energy, kcal per kg BW per d	23.58 ± 3.07	24.33 ± 2.68	22.13 ± 3.99	26.96 ± 4.75	<0.001
Protein, g per kg BW per d	1.03 ± 0.24	1.04 ± 0.24	0.98 ± 0.20	1.08 ± 0.26	0.070

Statistical analyses were performed using analysis of covariance (ANCOVA) adjusted for sex and baseline values. BW, body weight.

adhere well to dietary recommendations due to a lack of advice from trained dietitians,[27] CKD patients might profit from regular dietitian visits.

The difference in BMI and other elements of anthropometry had attracted attention additionally. Low BMI was a strong predictor of higher mortality,[28] while high BMI showed a protective effect in MHD patients.[29]It could not be ignored that BMI in MHD patients was found to be significantly lower than in age- and sex-comparative people from the general population and from non-ESRD patients.[30,31] In this study, increased BMI was observed in the intervention group. The results corroborated the findings of the previous work of Allman *et al.*, which revealed that oral non-protein supplements could increase body weight in malnourished MHD patients.[12] We also were interested in changes in MAC and MAMC after the trial since they are reliable indicators of muscle mass. Studies already showed that muscle loss was commonly observed in MHD patients with PEW due to catabolic conditions.[5,32] Accelerated muscle loss was related to worse quality of life, depression and a higher risk of hospitalization and death in CKD patients,[33] and it is therefore important to alleviate muscle loss. In the present study, MAC and MAMC of participants in the intervention group were higher than those in the control group after the six-month trial, indicating that the non-protein calorie supplements could improve the muscle loss of MHD patients with PEW.[3] A possible explanation for this might be that the protein-sparing effect of non-protein energy supplementation contributed to preserving the muscle mass of the MHD patients.[34]

Another important finding was that the intervention group reported a slightly higher serum bicarbonate after 6 months of treatment, though it was not statistically significant (p = 0.082). Serum bicarbonate was independently associated with adverse renal outcomes and mortality in CKD patients.[35] MHD patients with serum bicarbonate <22 mmol L^{-1} have higher mortality,[36] while those with excess serum bicarbonate might have a higher risk of heart failure.[37] The KDOQI Clinical Practice Guideline for Nutrition in CKD suggests maintaining serum bicarbonate levels at 24–26 mmol L^{-1}.[5] Furthermore, acidosis could lead to PEW by stimulating proteolysis, and correction of acidosis might result in improvement of PEW in MHD patients.[38] In the present study, the changes in bicarbonate were small and were not statistically significant, which may be due to the small sample size. Further research with a larger sample size would be required to investigate the effect non-protein calorie supplements might have on ameliorating acidosis in MHD patients with PEW.

Multiple factors could disclose why non-protein calorie supplements could improve PEW in patients. First, extra intake of non-protein calorie supplements could compensate for additional energy expenditure owing to the catabolic state and the hemodialysis treatments (consuming 200–480 kcal per session). In addition, our previous study demonstrated that intravenous supplementation of glucose promoted the amino acid profile in MHD patients, suggesting that energy supplementation without protein may still facilitate protein synthesis and alleviate protein catabolism in patients with MHD.[16] Indeed, participants in this study who consumed non-protein calorie supplements containing 280 kcal of energy, 10.8 g of fat and 45 g of carbohydrate per day were found to alleviate muscle loss. More importantly, the non-protein calorie supplements with high energy density used in this study are less likely to induce the overloaded volume status in patients with MHD, which is more conducive to nutritional supplementation.

This study had some limitations. Initially, selection bias was unavoidable due to the small sample size, resulting in differences in some parameters between the intervention group and the control group at the baseline, which restricted the generalizability of this study. Moreover, the study was limited by the short duration of the trial period. Further research will have to ascertain the effects of non-protein calorie supplements on PEW with a long-term and large-scale set. Furthermore, the medication record of patients was not collected, which may affect the anthropometric and serum biochemical measurements.

Conclusion

In summary, the provision of non-protein calorie supplements containing 280 kcal of energy per day induced a significant improvement in SGA, NRS2002, BMI, MAC, and MAMC. It is concluded that non-protein calorie supplements could improve the nutritional status of MHD patients with PEW.

Author contributions

Luona Wen: Investigation, methodology, data curation, formal analysis, writing – original draft, and writing – review & editing. Chunrong Tang: Investigation, methodology, data

curation, formal analysis, resources, and writing – review & editing. Yun Liu: Formal analysis and writing – review & editing. Jie Jiang: Investigation, data curation, and resources. Dee Zou: Investigation and validation. Wenxuan Chen: Investigation. Shilin Xu: Investigation. Yuqi Wang: Investigation. Jingxian Qiu: Investigation. Xiaoshi Zhong: Conceptualization, methodology, and resources. Yan Liu: Conceptualization, funding acquisition, methodology, project administration, and writing – review & editing. Rongshao Tan: Conceptualization, funding acquisition, methodology, project administration, supervision, and writing – review & editing. Rongshao Tan had primary responsibility for the final content. All authors read and approved the final manuscript.

Data described in the manuscript will be made available upon request pending application and approval by the corresponding author.

Abbreviations

ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
BMI	Body mass index
BUN	Blood urea nitrogen
CKD	Chronic kidney disease
ESRD	End-stage renal disease
HDL-C	High-density lipoprotein cholesterol
HsCRP	High-sensitivity c-reactive protein
IL-6	Interleukin-6
iPTH	Intact parathyroid hormone
LDL-C	Low-density lipoprotein cholesterol
MAC	Mid-upper arm circumference
MAMC	Mid-arm muscle circumference
MHD	Maintenance hemodialysis
NRS2002	Nutrition risk screening 2002
PEW	Protein-energy wasting
SGA	Subjective global assessment
TCHOL	Total cholesterol
TSF	Triceps skinfold thickness
VLDL-C	Very low-density lipoprotein cholesterol

Conflicts of interest

There are no conflicts of interest to declare.

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