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Study on the Effects of a Novel Low-Protein Enteral Nutrition Formula on Patients with Chronic Kidney Disease

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Abstract:

Objective: To explore the effects of a novel low-protein enteral nutrition formula on the nutritional status of patients with stage 3–4 chronic kidney disease (CKD) under personalized dietary guidance. *Methods:* Sixty outpatient follow-up patients at West China Hospital, Sichuan University, were randomly divided into an experimental group and a control group. Both groups received personalized dietary guidance and were administered either the novel low-protein enteral nutrition formula or a formula food for special medical purposes (FSMP). Follow-ups were conducted at baseline (day 0), day 45, and day 90 of the intervention. Based on the intention-to-treat analysis principle, generalized estimating equations were used to analyze intergroup differences, time-related trends, and interaction effects of the nutritional formulas. The stability of the results was further verified using a per-protocol analysis. *Results:* There were no significant intergroup differences in nutritional adequacy, clinical efficacy, or anthropometric indicators ($P > 0.05$). During the intervention, both groups showed significant reductions in protein ($\chi^2 = 17.680$, $P < 0.001$) and sodium ($\chi^2 = 21.427$, $P < 0.001$) intake while maintaining stable energy intake. Additionally, total protein ($\chi^2 = 18.075$, $P < 0.001$), calcium ($\chi^2 = 9.438$, $P = 0.009$), phosphorus ($\chi^2 = 13.866$, $P = 0.001$), and uric acid ($\chi^2 = 9.005$, $P = 0.011$) levels fluctuated within normal ranges. Per-protocol analysis results were largely consistent with intention-to-treat analysis results, except for significant differences in trends of mid-arm muscle circumference ($\chi^2 = 6.435$, $P = 0.040$) and intergroup comparisons of energy ratio ($\chi^2 = 4.478$, $P = 0.034$). *Conclusion:* The novel low-protein enteral nutrition formula is non-inferior to FSMP in improving nutritional status and slowing disease progression in CKD patients. The use of enteral nutrition formulas under dietary guidance supports clinical nutrition management in CKD patients.

Keywords:

Chronic kidney disease
Dietary guidance
Low-protein diet
Enteral nutrition formula
Food for special medical purposes

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1. Introduction

Chronic kidney disease (CKD) is a condition characterized by structural and functional kidney impairment lasting for more than three months due to various causes [1]. Studies have shown that the global prevalence of CKD is approximately 13.4%, with a prevalence of about 10.8% in China. The prevalence has been increasing annually, making CKD a significant public health issue [2,3]. Nutritional status is a key prognostic factor for CKD patients. As the disease progresses, renal function declines, and the prevalence of malnutrition increases. Malnutrition accelerates the decline in renal function, raises the risk of cardiovascular complications and hospitalizations, and diminishes the quality of life, creating a vicious cycle [4-6].

Nutritional intervention is a fundamental treatment for CKD patients. Scientific and appropriate nutritional support is critical for improving their nutritional status, enhancing quality of life, and reducing mortality [7,8]. While low-protein diets (LPD) have been shown to protect kidney function and slow disease progression, adherence to LPD is often poor. Protein-energy wasting (PEW) malnutrition is common among CKD patients, with a prevalence of 11%–54%, increasing with disease progression [9-13]. Current clinical practice guidelines recommend oral nutritional supplementation for patients unable to meet dietary requirements through regular intake. Enteral nutrition formulas are utilized to help patients increase energy intake while reducing protein consumption, which plays an important role in maintaining or improving nutritional status and slowing disease progression [14,15].

To regulate enteral nutrition formulas, national authorities have introduced food for special medical purposes (FSMP). These are specially formulated products designed to meet the unique nutritional or dietary needs of individuals with restricted food intake, digestive or absorption disorders, metabolic imbalances, or specific disease states. FSMP serves as an essential tool in nutritional therapy [16,17]. However, FSMP awareness among the general population in China is low, and its market penetration is limited. As of February 2023, only 101 FSMP products and components have been approved by the National Medical Products Administration, with none specifically formulated as a full-nutrition FSMP for CKD. Additionally, there are fewer than 20 commonly available nephrology nutrition products, leaving CKD patients with limited options, which hampers effective nutritional management [18,19].

The development of novel low-protein nutrition formulas to enhance the effectiveness of nutritional therapy, delay CKD progression, and reduce the associated life expectancy loss and economic burden is an urgent issue that demands attention [20,21]. Therefore, this study focuses on patients with CKD stages 3–4 and employs a novel low-protein enteral nutrition formula developed in earlier research. The study aims to evaluate the effectiveness of using enteral nutrition formulas under personalized dietary guidance in maintaining or improving the nutritional status of CKD stage 3–4 patients, thereby promoting the development of CKD-specific FSMP.

2. Participants and methods

2.1. Study participants

The study participants were CKD follow-up patients from an outpatient follow-up clinic at a tertiary hospital in Sichuan Province. Inclusion criteria were as follows: aged 18–70 years, able to consume food orally, with good gastrointestinal function, and a confirmed diagnosis of CKD stages 3–4. Exclusion criteria included: (1) patients with nephrotic syndrome, diabetes, those undergoing dialysis, or kidney transplantation; (2) those requiring tube feeding, enterostomy, or parenteral nutrition; (3) pregnant or lactating women; and (4) other conditions deemed unsuitable for participation by the researchers.

The study was approved by the Ethics Committee of West China Hospital, Sichuan University (Approval No. 2021(1194)), and was registered with the clinical trial number ChiCTR2300070604. All participants signed informed consent forms.

2.2. Study content

2.2.1. Study design

This study was a single-center, randomized controlled trial. The aim was to investigate the effects of a novel low-protein enteral nutrition formula versus a full-nutrition FSMP on the nutritional status and disease progression of CKD stage 3–4 patients under personalized dietary guidance. Follow-ups were conducted at 0, 45,

and 90 days of the intervention to evaluate changes in dietary intake, nutritional status, and disease progression.

2.2.2. Intervention

Patients were randomized into an experimental group and a control group using a random number table. The experimental group received the novel low-protein enteral nutrition formula under personalized dietary guidance, while the control group received the full-nutrition FSMP under the same guidance. At each follow-up, nutritionists developed individualized meal plans tailored to the patient's condition. The dietary energy intake ranged from 30–35 kcal/(kg·d), with protein intake ranging from 0.6–0.8 g/(kg·d). Both groups consumed 400 kcal from the nutritional formulas daily [14,15].

The experimental group consumed 95 g of the novel low-protein enteral nutrition formula daily (providing approximately 10 g of protein), while the control group consumed 90 g of the full-nutrition FSMP daily (providing approximately 15 g of protein). Details are shown in **Table 1**.

The novel low-protein enteral nutrition formula used in this study was developed and produced collaboratively by the Sericulture and Agricultural Product Processing Research Institute of the Guangdong Academy of Agricultural Sciences and other teams, specifically designed to meet the low-protein, low-sodium dietary needs of CKD patients.

Table 1. Nutritional composition of the new low-protein nutritional preparation and the total nutrition food for special medical purposes (FSMP)

Nutritional components	New low-protein enteral nutritional preparation (per 100 g)	Total nutrition FSMP (per 100 g)
Energy (kJ)	1,812	1,913
Protein (g)	10.0	18.5
Fat (g)	15.0	17.5
Carbohydrates (g)	61.2	53.2
Na (mg)	330	460
K (mg)	500	685
P (mg)	220	220
Ca (mg)	310	430

2.2.3. Clinical laboratory tests

On the day of follow-up, fasting venous blood samples were collected from patients to test relevant indicators. Laboratory indicators included:

(1) Nutritional adequacy indicators: hemoglobin (Hb, g/L), total protein (TP, g/L), serum albumin (ALB, g/L), and prealbumin (PAB, mg/L).

(2) Clinical efficacy indicators: glucose (GLU, mmol/L), triglyceride (TG, mmol/L), total cholesterol (TC, mmol/L), urea (mmol/L), creatinine (CREA, μmol/L), estimated glomerular filtration rate (eGFR, mL/min·1.73m²), uric acid (UA, μmol/L), sodium (Na, mmol/L), potassium (K, mmol/L), calcium (Ca, mmol/L), and phosphorus (P, mmol/L).

2.2.4. Physical measurements

A portable grip strength dynamometer was used to measure the grip strength (kg) of the participant's right hand. Participants were asked to keep their hands naturally down, and the measurement was taken twice during each follow-up, recording the maximum value.

Arm circumference (AC, cm) was measured using a soft measuring tape at the midpoint of the upper right arm, with the participant's arms naturally down. Triceps skinfold thickness (TSF, mm) was measured using a skinfold caliper on the back of the upper right arm, at a point 2 cm above the midpoint between the acromion and olecranon.

Arm muscle circumference (AMC, cm) was calculated as AMC = AC - 0.314 × TSF.

Body weight and height were measured using a weighing scale and a stadiometer, and body mass index (BMI, kg/m²) was calculated as BMI = weight / height².

2.2.5. Dietary survey

A 24-hour dietary recall method was used to record the participants' food intake. Daily energy intake (DEI, kcal/(kg·d)) and daily protein intake (DPI, g/(kg·d)) were used to represent energy and protein consumption.

The adequacy of energy and protein intake was assessed using the energy ratio (ER) and protein ratio (PR), calculated as actual intake/recommended intake. Values ≥ 1.00 indicated sufficient or excessive intake, while values < 1.00 suggested insufficient intake. Protein-

energy contribution ratios and sodium salt intake were recorded at each follow-up.

2.3. Statistical methods

Statistical analysis was performed based on the intention-to-treat (ITT) principle. Quantitative data were expressed as the mean ± standard deviation (SD), while categorical data were reported as counts (proportions). Quantitative data were analyzed for group differences using an independent Student's *t*-test. Categorical data were analyzed using the χ^2 test or Fisher's exact test.

A generalized estimating equation (GEE) was used to analyze group differences, time trends, and interactions for different nutritional interventions. For GEE analysis:

(1) Linear models were applied for continuous variables.

(2) Binary logistic models were used for categorical variables.

(3) The working correlation matrix was set as an unstructured correlation.

To further validate the stability of the results, a per-protocol (PP) analysis was conducted as a sensitivity analysis.

All statistical analyses were performed using IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY, USA). All tests were two-sided, with a significance level of $\alpha = 0.05$.

3. Results

3.1. Baseline characteristics of included patients

A total of 60 patients were enrolled in the study. Eight patients were lost to follow-up, leaving 52 patients who completed the study, with a loss-to-follow-up rate of 13.33%, as shown in **Figure 1**. The average age of the 52 patients was 46.44 ± 9.486 years, with 21 males (40.38%). Among the participants, 42 patients (80.77%) were in CKD stage 3. There were no significant differences in age, gender, or disease stage between the two groups (see **Table 2**).

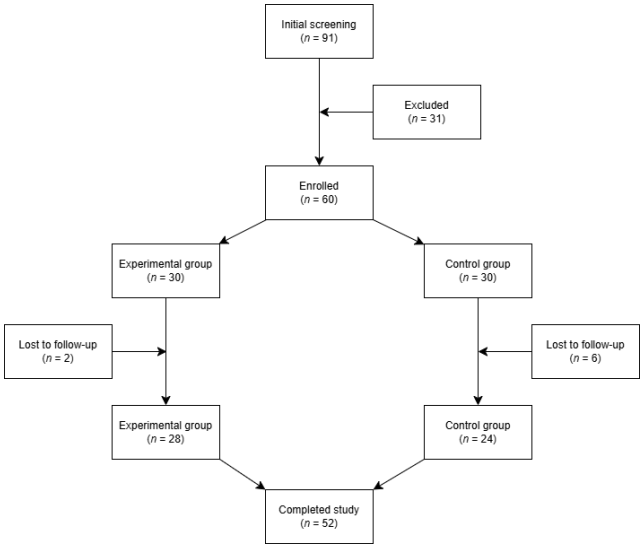

Figure 1. Flowchart of patient inclusion and exclusion

Table 2. Basic information of patients in both groups [(mean ± SD), *n* (%)]

Item	Experimental group (*n* = 28)	Control group (*n* = 28)	t / χ^2 value	*P* value
Age (years)	46.11 ± 9.66	46.83 ± 9.48	-0.273	0.786
Gender			0.154	0.695
Male	12 (42.86)	9 (37.50)		
Female	16 (57.14)	15 (62.50)		
Disease stage				
CKD stage 3	23 (82.14)	19 (79.17)	- *	1.000
CKD stage 4	5 (17.86)	5 (20.33)		

Note: *Fisher's exact test was used.

3.2. Safety and tolerance of enteral nutritional preparations

Throughout the study, no serious adverse reactions were observed in either group. In the experimental group, no patients reported symptoms such as abdominal pain, bloating, nausea, vomiting, diarrhea, or constipation. In the control group, two cases of abdominal pain were reported: one due to an acute appendicitis infection in the late intervention phase, and the other resolved after adjusting the method of using the enteral nutritional preparation. These findings indicate that both enteral

nutritional preparations exhibited good safety and tolerability.

3.3. Nutritional status

No statistically significant differences were observed between the two groups in Hb, TP, ALB, or PAB levels ($P > 0.05$). However, TP levels showed a declining trend over time in both groups ($\chi^2 = 18.075$, $P < 0.001$). Details are presented in **Table 3**.

3.4. Clinical conditions

There were no statistically significant differences between the two groups in GLU, TG, TC, CREA, urea, UA, eGFR, Na, K, Ca, or P ($P > 0.05$). However, both groups showed an upward trend over time for CREA ($\chi^2 = 24.530$, $P < 0.001$), UA ($\chi^2 = 9.005$, $P = 0.011$), Ca ($\chi^2 = 9.438$, $P = 0.009$), and P ($\chi^2 = 13.866$, $P = 0.001$), while eGFR ($\chi^2 = 24.407$, $P < 0.001$) exhibited a downward trend over time. See **Table 4**.

3.5. Anthropometric measurements

No differences were observed between the two groups in terms of weight, BMI, TSF, AC, AMC, or grip strength. There were also no time-related trends in these parameters ($P > 0.05$). See **Table 5**.

3.6. Dietary intake

There were no statistically significant differences between the experimental and control groups in terms of energy, protein, or salt intake ($P > 0.05$). However, as the intervention progressed, protein ($\chi^2 = 17.680$, $P < 0.001$) and salt ($\chi^2 = 21.427$, $P < 0.001$) intake decreased significantly in both groups. See **Table 6**.

3.7. Stability analysis

Per-protocol (PP) analysis indicated that with the progression of the intervention:

(1) TP ($\chi^2 = 15.066$, $P = 0.000$), eGFR ($\chi^2 = 21.416$, $P < 0.001$), and AMC ($\chi^2 = 6.435$, $P = 0.040$) decreased.

(2) Protein ($\chi^2 = 17.699$, $P < 0.001$) and sodium salt ($\chi^2 = 21.235$, $P < 0.001$) intake also decreased.

(3) CREA ($\chi^2 = 18.803$, $P < 0.001$), UA ($\chi^2 = 9.212$, $P = 0.010$), Ca ($\chi^2 = 12.022$, $P = 0.002$), and P ($\chi^2 = 12.793$, $P = 0.002$) increased.

(4) The ER in the experimental group was lower than in the control group ($\chi^2 = 4.478$, $P = 0.034$).

Other indicators showed no significant differences ($P > 0.05$).

The results of the PP analysis were consistent with those of the ITT analysis, except for the significant time trend in AMC ($\chi^2 = 6.435$, $P = 0.040$) and the inter-group comparison of ER ($\chi^2 = 4.478$, $P = 0.034$). This indicates that the study results are stable and the conclusions are reliable.

4. Discussion

Nutritional status is a critical factor affecting the progression of CKD. Timely assessment and improvement of patients' nutritional status are of significant importance for delaying disease progression, enhancing quality of life, and reducing mortality [7]. This study compared the application effects of two enteral nutrition formulas in patients with CKD stages 3–4 and found that the new low-protein enteral nutrition formula was not inferior to the full-nutritional FSMP in terms of safety, tolerability, improving nutritional status, and maintaining clinical condition. Furthermore, the study highlighted the crucial role of dietary guidance in the clinical management of CKD patients.

4.1. Safety and gastrointestinal tolerability of enteral nutrition formulas

FSMPs are regulated by the National Market Supervision Administration, with their commercial and nutritional value established on the premise of no harm to human health [22-24]. In clinical practice, CKD patients may experience side effects such as appetite loss, nausea, vomiting, and diarrhea due to medications such as hormones and immunosuppressants, leading to insufficient protein and energy intake, malnutrition, and impaired treatment outcomes [25,26]. Therefore, the use of enteral nutrition formulas with good gastrointestinal tolerability can effectively help patients maintain adequate nutrient intake, alleviate discomfort, and improve clinical prognosis. In this study, no adverse reactions were observed in the intervention group. While the control group reported two cases of abdominal pain, one was attributed to acute appendicitis in the later intervention stages, and the other improved after adjusting

Table 3. Nutrition status of patients in both groups (mean ± SD)

Indicator	Experimental group			Control group			Wald χ^2 (between groups)	*P* (between groups)	Wald χ^2 (time)	*P* (time)	Wald χ^2 (interaction)	*P* (interaction)
	0 d	45 d	90 d	0 d	45 d	90 d						
Hb (g/L)	133.07 ± 17.38	134.10 ± 18.79	134.70 ± 19.70	128.40 ± 22.09	128.23 ± 20.20	127.93 ± 19.83	1.407	0.236	0.310	0.856	0.823	0.663
TP (g/L)	73.64 ± 3.60	71.91 ± 3.77	73.15 ± 4.23	72.24 ± 3.47	70.67 ± 4.72	71.03 ± 5.05	2.871	0.090	18.075	< 0.001	1.617	0.445
ALB (g/L)	45.83 ± 2.85	45.17 ± 3.42	45.91 ± 3.19	45.80 ± 2.63	45.15 ± 3.03	45.14 ± 3.52	0.152	0.696	5.288	0.071	1.500	0.472
PAB (mg/L)	319.50 ± 44.88	320.27 ± 53.81	331.00 ± 51.58	335.20 ± 64.81	336.63 ± 64.05	341.07 ± 67.66	0.991	0.319	5.861	0.053	0.806	0.668

Table 4. Clinical information of patients in both groups (mean ± SD)

Indicator	Experimental group			Control group			Wald χ^2 (between groups)	*P* (between groups)	Wald χ^2 (time)	*P* (time)	Wald χ^2 (interaction)	*P* (interaction)
	0 d	45 d	90 d	0 d	45 d	90 d						
GLU (mmol/L)	5.06 ± 0.38	4.91 ± 0.39	4.93 ± 0.38	5.12 ± 0.59	5.08 ± 0.52	4.98 ± 0.55	0.805	0.370	5.188	0.075	2.662	0.264
TG (mmol/L)	1.47 ± 0.76	1.58 ± 0.83	1.60 ± 0.65	1.24 ± 0.63	1.28 ± 0.43	1.28 ± 0.44	3.690	0.055	2.503	0.286	0.570	0.752
TC (mmol/L)	4.60 ± 1.11	4.44 ± 0.86	4.57 ± 0.70	4.45 ± 0.89	4.36 ± 0.97	4.31 ± 0.97	0.577	0.447	3.029	0.220	1.486	0.476
CREA (μmol/L)	155.17 ± 45.77	458.70 ± 51.24	168.40 ± 54.12	183.37 ± 93.75	190.10 ± 108.49	197.60 ± 114.99	2.008	0.157	24.530	< 0.001	0.645	0.724
Urea (mmol/L)	8.84 ± 3.67	8.60 ± 3.33	9.02 ± 3.43	9.69 ± 4.71	9.89 ± 4.63	10.07 ± 4.65	1.103	0.294	2.690	0.261	0.761	0.683
UA (μmol/L)	355.67 ± 82.03	357.53 ± 79.91	382.63 ± 82.45	334.27 ± 63.15	328.27 ± 70.49	362.50 ± 73.47	2.737	0.098	9.005	0.011	0.173	0.917
eGFR (mL/min·1.73 m²)	42.99 ± 13.97	42.38 ± 14.58	39.52 ± 14.21	38.46 ± 15.27	38.44 ± 16.17	36.95 ± 15.75	0.962	0.327	24.407	< 0.001	3.164	0.206
Na (mmol/L)	140.36 ± 1.86	140.39 ± 2.29	140.69 ± 2.08	140.78 ± 1.84	141.19 ± 1.70	140.96 ± 2.05	1.328	0.249	1.386	0.500	1.627	0.443
K (mmol/L)	4.45 ± 0.39	4.50 ± 0.33	4.57 ± 0.45	4.47 ± 0.45	4.60 ± 0.52	4.47 ± 0.43	0.001	0.977	2.938	0.230	3.108	0.211
Ca (mmol/L)	2.36 ± 0.09	2.37 ± 0.10	2.39 ± 0.12	2.34 ± 0.08	2.36 ± 0.08	2.38 ± 0.11	0.129	0.719	9.438	0.009	0.240	0.887
P (mmol/L)	1.11 ± 0.19	1.20 ± 0.29	1.23 ± 0.28	1.12 ± 0.19	1.17 ± 0.21	1.17 ± 0.22	0.278	0.598	13.866	0.001	2.643	0.267

Table 5. Anthropometric results of patients in both groups (mean ± SD)

Indicator	Experimental group			Control group			Wald χ^2 (between groups)	*P* (between groups)	Wald χ^2 (time)	*P* (time)	Wald χ^2 (interaction)	*P* (interaction)
	0 d	45 d	90 d	0 d	45 d	90 d						
Weight (kg)	60.03 ± 13.95	59.65 ± 14.19	59.62 ± 13.93	56.52 ± 10.09	56.71 ± 10.05	56.49 ± 10.16	1.065	0.302	1.253	0.534	4.665	0.097
BMI (kg/m²)	22.40 ± 3.61	22.26 ± 3.62	22.24 ± 3.53	21.21 ± 2.43	21.30 ± 2.32	21.21 ± 2.30	1.926	0.165	1.141	0.565	4.347	0.114
TSF (mm)	11.44 ± 3.24	11.33 ± 3.06	11.42 ± 3.06	10.01 ± 3.45	10.21 ± 3.79	10.11 ± 3.33	2.365	0.124	0.299	0.861	2.194	0.334
AC (cm)	28.62 ± 3.19	28.45 ± 3.13	28.43 ± 3.06	27.63 ± 2.54	27.63 ± 2.42	27.56 ± 2.39	1.585	0.208	2.454	0.293	2.003	0.367
AMC (cm)	25.02 ± 2.69	24.89 ± 2.74	24.84 ± 2.68	24.48 ± 2.51	24.42 ± 2.42	24.39 ± 2.38	0.565	0.452	3.893	0.143	0.388	0.824
Grip strength (kg)	32.94 ± 12.42	33.42 ± 12.13	33.99 ± 12.19	31.90 ± 9.95	31.84 ± 9.64	32.36 ± 10.09	0.260	0.610	2.461	0.292	0.523	0.770

Table 6. Energy, protein, and sodium intake of patients in both groups (mean ± SD)

Indicator	Experimental group			Control group			Wald χ^2 (between groups)	*P* (between groups)	Wald χ^2 (time)	*P* (time)	Wald χ^2 (interaction)	*P* (interaction)
	0 d	45 d	90 d	0 d	45 d	90 d						
Energy intake (kcal)	1,467.23 ± 354.41	1,582.65 ± 243.23	1,532.71 ± 254.54	1,556.83 ± 356.35	1,579.70 ± 366.44	1,548.85 ± 315.46	0.253	0.615	5.064	0.080	1.380	0.501
DEI [kcal/(kg·d)]	25.58 ± 6.10	27.51 ± 3.41	26.64 ± 3.64	27.40 ± 6.35	27.61 ± 5.38	27.15 ± 5.20	0.577	0.447	4.530	0.104	1.647	0.439
ER (%)	0.81 ± 0.21	0.86 ± 0.12	0.83 ± 0.10	0.89 ± 0.24	0.89 ± 0.18	0.87 ± 0.17	1.792	0.181	3.985	0.136	1.769	0.413
Protein intake (g)	48.46 ± 16.94	40.40 ± 9.67	40.20 ± 11.02	47.12 ± 11.50	42.47 ± 10.58	41.64 ± 8.73	0.090	0.764	17.680	< 0.001	0.983	0.612
DPI [kcal/(kg·d)]	0.85 ± 0.30	0.71 ± 0.16	0.69 ± 0.15	0.83 ± 0.23	0.74 ± 0.16	0.73 ± 0.14	0.184	0.668	19.057	< 0.001	0.731	0.694
PR (%)	1.37 ± 0.46	1.14 ± 0.26	1.13 ± 0.22	1.27 ± 0.40	1.13 ± 0.29	1.10 ± 0.24	0.550	0.458	18.978	< 0.001	0.775	0.679
Protein-energy ratio (%)	0.13 ± 0.03	0.10 ± 0.02	0.10 ± 0.02	0.12 ± 0.03	0.11 ± 0.03	0.11 ± 0.03	0.052	0.820	43.121	< 0.001	5.909	0.052
Sodium intake (g)	7.90 ± 2.30	7.30 ± 1.39	6.93 ± 1.34	7.80 ± 1.86	7.40 ± 1.67	6.82 ± 1.00	0.011	0.916	21.427	< 0.001	0.908	0.635

the administration frequency, likely due to individual intolerance to high-nutrition foods.

4.2. Effects of the new low-protein enteral nutrition formula and full-nutritional FSMP

Chronic renal failure can lead to the accumulation of metabolic substances such as urea and creatinine, electrolyte disturbances, acid-base imbalances, and hormonal dysregulation, resulting in conditions such as anorexia and mild inflammation. These changes enhance catabolism and lead to insufficient protein and energy intake, causing malnutrition [1,27]. In this study, there were no statistically significant differences in the nutritional adequacy or clinical effectiveness indicators between the two groups at any time point, suggesting that both formulas were equally effective in improving the nutritional status and maintaining kidney function in CKD stages 3–4 patients. Anthropometric indicators also showed no significant differences between groups or over time, possibly due to the short follow-up duration and the relatively good baseline nutritional status of the outpatient participants. Furthermore, individualized dietary guidance and frequent follow-ups by dietitians ensured high adherence and accuracy in implementing dietary plans, ultimately maintaining good nutritional status [28,29].

As the intervention progressed, some indicators showed significant changes over time. For nutritional indicators, PAB, which reflects short-term nutritional status, demonstrated an upward trend in both groups despite no statistical significance, indicating that both formulas could potentially improve patients' nutritional status. Regarding clinical progression, while TP, Ca, and P levels fluctuated over time, they remained within normal reference ranges. CREA levels increased over time, and UA showed fluctuations within normal ranges, while eGFR decreased over time. However, there were no significant differences between groups, and no interaction effects between time and intervention were observed, suggesting that both enteral nutrition formulas were similarly effective in maintaining kidney function. FSMPs and enteral nutrition formulas, as food products rather than medicines, aim to enhance nutrient intake, improve nutritional status, and reduce malnutrition, thereby aiding in delaying disease progression and reducing adverse clinical outcomes caused by malnutrition [17].

4.3. The importance of nutritional management in chronic kidney disease management

Previous studies have confirmed that individualized dietary guidance effectively helps CKD patients correct poor dietary habits and reduce the risk of malnutrition [28-31]. In this study, although there were no differences in dietary intake between the experimental and control groups, protein and sodium intake significantly decreased as the intervention progressed. During the intervention, DPI and the proportion of protein-derived energy decreased, with DPI dropping from above the guideline recommendations to within the recommended range. Although sodium intake remained higher than recommended, it was significantly reduced compared to pre-intervention levels. These dietary changes contributed to reducing the renal burden and slowing disease progression while maintaining patients' nutritional status [31,32].

However, significant challenges remain in implementing individualized nutritional management. First, clinicians often overlook or undervalue nutritional management during diagnosis and treatment, initiating dietary interventions only when patients are hospitalized or already at high risk of malnutrition. Second, there is a shortage of nutrition professionals, with clinical dietitians comprising a small proportion of healthcare teams. Third, patients often lack awareness of the importance of nutritional management and hold misconceptions about CKD-related diets. Lastly, dietary habits in China, which primarily include rice- and wheat-based foods, may lead to resistance to prolonged consumption of starch-based foods like lotus root powder or vermicelli. Additionally, low-protein rice, with its relatively coarse texture compared to regular rice, is less palatable, resulting in poor long-term adherence to low-protein diets [33-35]. In contrast, enteral nutrition formulas offer advantages such as a variety of flavors, convenience, comprehensive nutrition, and individualized options. These features make them valuable as meal replacements in the individualized nutritional management of CKD patients, particularly for those with insufficient oral intake, high risk of malnutrition, or existing malnutrition.

This study has several limitations. First, as a pre-market exploratory study, the sample size was small, and the long-term effects of the nutritional formulas on patients could not be observed. Second, the COVID-19 pandemic led to a higher dropout rate during the third follow-up, introducing potential bias. Lastly, recruitment challenges due to the pandemic and other practical constraints resulted in the absence of a blank control group, preventing a comprehensive analysis of the independent effects of enteral nutrition formulas and dietary guidance on patients. Future research should focus on hospitalized or malnutrition-risk CKD patients in large-scale, multicenter prospective follow-up studies to further explore the role of low-protein enteral nutrition formulas in improving nutritional status and filling the gap in FSMP applications for kidney disease.

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Disclosure statement

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