Original Article High-calorie, whole protein/peptide nutritional formulations for children with cerebral palsy: a retrospective clinical study

Xia Cai, Yingying Qin, Chaoyun Liu, Ling Xie, Juelong Zhu

Child Rehabilitation Department, Yulin First People's Hospital, Yulin 537000, Guangxi, China

Received December 27, 2023; Accepted April 28, 2024; Epub July 15, 2024; Published July 30, 2024

Abstract: Background: Children with cerebral palsy often experience inadequate nutritional intake due to factors like anorexia, intellectual impairments, underdeveloped motor skills of the oral sensory system, and eating and swallowing disorders. These challenges not only hinder their rehabilitation but also impose various degrees of burden on society and their families. Addressing malnutrition in children with cerebral palsy has become a pressing international clinical issue. This study assessed the nutritional status of children with cerebral palsy and examined the impact of a high-calorie enteral nutrition formula as a nutritional intervention. Methods: This retrospective study involved 132 malnourished children with cerebral palsy undergoing rehabilitation at the First People's Hospital of Yulin City from July 2020 to July 2023. Sixty-six children received conventional nutritional interventions after their parents were educated and trained in dietary practices and feeding techniques, forming the general group. The other sixty-six children were given a high-calorie intact protein or short peptide enteral nutrition formula milk powder (Nuiren JUNIOR or Peptamen Junior), and were referred to as the nutrient group. Data on anthropometric measurements, blood indicators, gross motor function, and adverse events were collected at baseline, three months, and six months. Results: After 6 months of intervention, both groups showed improvements in height, weight, weight-forheight Z-score, weight-for-age Z-score and gross motor function. There were statistical differences in height change, body mass index-for-age Z-score, and gross motor function between the two groups (P<0.05). The efficiency of nutritional intervention was significantly higher in the nutrient group than in the general group (P<0.05). In addition, total albumin, albumin, prealbumin, and 25-hydroxyvitamin D levels were higher in the nutrient group than in the general group (P<0.05). An incidence of side effects was observed in 15.15% of the children in the general group and 9.09% in the nutrient group, without significant difference (χ^2 =1.138, P=0.286). Conclusion: High-calorie whole protein or peptide nutritional formulas can significantly improve malnutrition and enhance gross motor function development in children with cerebral palsy and has a low incidence of adverse events. These interventions hold promise for broader clinical application.

Keywords: Cerebral palsy, enteral nutrition intervention, whole protein, peptide, nutritional milk formula

Introduction

Cerebral palsy is a leading cause of physical disability in children [1]. National and international studies indicate that over 50% of children with cerebral palsy are malnourished. For instance, data from the Bangladesh Cerebral Palsy Registry revealed that 70% of children with cerebral palsy were underweight and/or stunted [2]. Similarly, high malnutrition rates have been reported in Indonesia and Uganda [3, 4]. Malnutrition in children with cerebral palsy can impair neurological development,

reduce immunity, weaken respiratory muscles, restrict skeletal growth, and even increase mortality risk [5, 6]. Addressing how to effectively provide nutritional interventions to improve their nutritional status and enhance functional rehabilitation remains a crucial area of clinical research.

In recent years, high-calorie formulas, designed as specialized medical products, have been increasingly utilized in nutritional treatment plans for children due to their high protein content and caloric density, combined with relative safety. These formulas deliver more protein and energy per unit of intake [7]. Previous studies have shown that high-calorie formulas can improve weight gain and enhance gross motor function in children with cerebral palsy [8]. However, these studies often did not include data on body composition and biochemical indicators. Furthermore, reports on nutritional interventions for children with cerebral palsy are scarce and lack detailed information on intervention methods, timing, efficacy assessments, and tolerability.

Therefore, this study evaluated the effectiveness of a high-calorie enteral nutrition formula as a nutritional intervention for children with cerebral palsy. We aim to provide a theoretical basis for nutritional support to address malnutrition in children with cerebral palsy.

Materials and methods

Research subjects

This retrospective study selected malnourished children with cerebral palsy who underwent rehabilitation treatment at the First People's Hospital of Yulin City from July 2020 to July 2023. Inclusion criteria: (1) Children who met the diagnostic criteria for cerebral palsy [9]; (2) Children between 1 and 10 years old; (3) Children with malnutrition according to the American Society for Parenteral and Enteral Nutrition (ASPEN) [10] and the WHO Criteria for Child Growth and Development [11]; (4) Children whose guardians provided informed consent. Exclusion criteria: (1) Those who recently received relevant nutritional interventions; (2) Those with acute or chronic hepatitis, congenital heart disease, genetic metabolic diseases, or other diseases affecting growth and development; (3) Those with severe gastrointestinal diseases or history of milk protein allergy; (4) Those with long-term parenteral nutrition.

A total of 132 malnourished children with cerebral palsy were selected. These children were divided into two groups based on the intervention received: the general group (n=66), receiving a standard diet, and the nutrient group (n=66), receiving a high-calorie enteral nutrition formula milk powder (either intact protein or short peptide type). Data collection occurred at baseline, after 3 months, and after 6 months of intervention. Measurements included anthropometric data, blood indicators, gross motor function, and recording of adverse events. The study protocol was approved by the Medical Ethics Committee of Yulin First People's Hospital (No. YLSY-IRB-CR-2020 078).

Data collection

We collected comprehensive baseline data for each child, including gender, age, type of cerebral palsy, birth history (such as prematurity and birth weight), and current classifications under the Gross Motor Function Classification System (GMFCS) and the Eating and Drinking Ability Classification System (EDACS). Additionally, nutritional risk was assessed for each child through screening. Medical and dietary histories were also compiled to provide insights into each child's dietary patterns and feeding status.

Assessment of nutritional status

Physical measurements: Designated personnel accurately measured the height and weight of the children. Prior to each session, all instruments were calibrated and zeroed. Each measurement was taken twice to ensure accuracy, and the final recorded result is the average of these two measurements.

Nutrition classification: Malnutrition in children was categorized based on WHO child growth and development criteria [11] and ASPEN guidelines [10]. The categories are defined as follows: weight-for-height Z-score (WHZ) or body mass index-for-age Z-score (BAZ) <-1 indicates mild malnutrition, <-2 indicates moderate malnutrition, and <-3 indicates severe malnutrition. Similarly, weight-for-age Z-score (WAZ) or height-for-age Z-score (HAZ) <-2 signifies moderate malnutrition, and <-3 denotes severe malnutrition. See **Table 1**.

Blood indicators: Blood samples (2 mL) were collected into a biochemical tube in the early morning following the child's admission to the hospital, after a period of fasting. The blood samples were analyzed for levels of total albumin, prealbumin, albumin, transferrin, and 25-hydroxyvitamin D by the Laboratory Department.

Motor function evaluation: Motor function and rehabilitation effects in children with dystro-

Z-score	WAZ	HAZ	WHZ	BAZ		
<-1	_	_	Mild malnutrition	Mild malnutrition		
<-2	Moderate malnutrition	Moderate malnutrition	Moderate malnutrition	Moderate malnutrition		
<-3	Severe malnutrition	Severe malnutrition	Severe malnutrition	Severe malnutrition		
Note: WAZ: weight-for-age Z-score; HAZ: height-for-age Z-score; WHZ: weight-for-height Z-score; BAZ: body mass index-for-age						
Z-score.						

Table 1. Classification of malnutrition

Table 2. Calculation formula of Schofield basal metabolic rate

Age (year)	Воу	Girl
<3	0.167 * weight (kg) + 15.174 * height (cm) - 617.6	16.252 * weight (kg) + 10.232 * height (cm) - 413.5
3-10	19.59 * weight (kg) + 1.303 * height (cm) + 414.9	16.969 * weight (kg) + 1.618 * height (cm) + 371.2

phic cerebral palsy were evaluated using the Gross Motor Function Measure (GMFM) [12] and Gross Motor Function Classification System (GMFCS) [13]. The GMFM consists of 88 items, scored out of 100, divided into 5 domains: Area A: lying and turning (17 items, total 51 points); Area B: sitting (20 items, total 60 points); Area C: crawling and kneeling (14 items, total 42 points); Area D: standing (13 items, total 39 points); Area E: walking, running, and jumping (24 items, total 72 points). The GMFCS classifies children into 5 age groups (0-2 years, 2-4 years, 4-6 years, 6-12 years, and 12-18 years), and within each age group, children are divided into 5 levels (I to V) according to their motor function from highest to lowest capability.

Nutrition intervention methods

Estimating energy needs: At baseline, the daily energy needs for children in both study groups were calculated using indirect calorimetry. The formula for estimating target energy intake (kcal/day) is as follows: basal metabolic rate (BMR) * muscle tone * activity level + growth. Specific multipliers included: muscle tone: 0.9 (decreased), 1.0 (normal), 1.1 (increased); activity level: 1.1 (bedridden), 1.2 (wheelchairdependent or crawling), 1.3 (normal walking); growth: 5 kcal/g/day for target weight gain (normal and catch-up growth). The BMR was calculated using the Schofield formula, adjusted by sex and age, as outlined in Table 2. The nutritional goal was a weight gain of approximately 7 g/day, equivalent to an energy target of 35 kcal/day.

Nutrition intervention: Children in general group received a regular daily diet. Parents were pro-

vided with dietary education and training on feeding techniques by study staff.

Children in the nutrient group received a highcalorie protein or peptide enteral nutrition formula in addition to their regular diet. Children with normal gastrointestinal function were given high-calorie protein formulas, while those with gastrointestinal disorders received highcalorie peptide formulas. Formulas were prepared in warm water to an energy density of 1 kcal/ml. Children in GMFCS levels I-III received one-third, and those in levels IV-V received half of their target energy supplement. Children aged 1-2 years consumed the formula 2-3 times daily, while those aged 3-10 years 1-2 times daily.

The composition of high-calorie whole protein or peptide enteral nutrition formulas is shown in **Table 3**.

Rehabilitation training: Individualized rehabilitation programs were tailored to each child's motor function level, including training for abnormal posture correction, muscle strength, endurance, joint mobility, motor function, swallowing function, guided education, physical therapy, and other treatments. Rehabilitation training was conducted at the hospital on weekdays, and functional rehabilitation training was continued at home on other days.

Adverse events

Parents monitored children for adverse events related to feeding intolerance, such as diarrhea, bloating, vomiting, and constipation. Any incidents were reported to the researchers and recorded for analysis.

0	<u> </u>	
Composition and composition	Nuiren Junior	Peptamen Junior
Type of protein	50% whey protein + 50% casein	100% hydrolyzed whey protein (100% peptide)
Protein content (g/100 ml)	3.1	3.0
Fat content	18% MCT, vegetable oil	58% MCT, soybean oil, sunflower oil
Carbohydrates	Maltodextrin, white sugar	Starch, maltodextrin, sucrose
Calories (kcal/100 ml)	100	100
Calcium (mg/100 ml)	68	90
Vitamin D (ug/100 ml)	1.1	1.4

Table 3. High-calorie whole protein or peptide enteral nutrition formulas

Note: MCT: medium chain triglycerides.

Statistical analysis

Data analysis was conducted using SPSS software, version 23.0, with a significance level set at α =0.05. For categorical variables, such as gender and cerebral palsy type, were described using case counts and percentages, and analyzed with the Chi-square test. Continuous variables following a normal distribution, such as birth weight and height, were represented by means and standard deviations ($\overline{x} \pm sd$), and analyzed using the t-test. For non-normal distributed continuous variables, like nutritional parameter changes (comparing 3-month and baseline values, as well as 6-month and baseline differences), median (M) with 25th (P_{25}) and 75th (P₇₅) percentiles were used for representation, and the Mann-Whitney U test was employed. Ordinal data, such as nutritional status classifications before and after intervention, were analyzed using the rank sum test. For comparisons within groups at different time points, for instance, changes in GMFM before and after intervention, one-way repeated measures ANOVA was applied. A *p*-value less than 0.05 was considered statistically significant.

Results

Baseline data

Of the 132 children, boys were the majority (61.36%), and spastic cerebral palsy was the most common type of cerebral palsy (41.67%). The most common GMFCS level was III (30.30%), and the most common EDACS classification was IV (35.61%). See **Table 4**.

Nutritional status change

Repeated measures ANOVA test showed that height, weight, WHZ, and WAZ of children

increased in both groups after baseline (P<0.05). The non-parametric test results showed that the increases in height in the nutrient group after 3 and 6 months of intervention were greater than those in the general group (P<0.05). Also, the children in the nutrient group exhibited higher BAZ values than the general group after 3 months (P<0.05). See **Tables 5** and **6**.

Nutritional grading

After 6 months of intervention, the effective rate of nutritional intervention in the nutrient group was significantly higher than that in the general group, and the difference was statistically significant (P<0.05). See **Table 7**.

Gross motor function changes

The GMFM scores of children in both groups were significantly higher at 3 and 6 months after intervention than at the baseline (P<0.05). The increase in the GMFM score in the nutrient group was greater than that of the general group at 3 and 6 months after the intervention (P<0.05). See **Tables 8** and **9**.

Comparison of blood indexes

After 6 months of intervention, the levels of total albumin, albumin, prealbumin, and 25-hydroxyvitamin D in the nutrient group were significantly higher than those in the general group (P<0.05). See **Table 10**.

Comparison of adverse events

The incidence of side effects was 15.15% in the general group and 9.09% in the nutrient group, showing no significant difference (χ^2 =1.138, *P*=0.286). See **Table 11**.

Baseline data	General group (n=66)	Nutrient group (n=66)	t/χ² value	P value
Gender			0.289	0.592
Воу	39 (59.09)	42 (63.64)		
Girl	27 (40.91)	24 (36.36)		
Age (Month)	22.35±7.09	23.16±7.14	0.654	0.514
Cerebral palsy type			0.790	0.852
Dyskinetic	19 (28.79)	23 (34.85)		
Spasm type	28 (42.42)	27 (40.91)		
Mixed	13 (19.70)	10 (15.15)		
Ataxia	6 (9.09)	6 (9.09)		
Premature	20 (30.30)	22 (33.33)	0.140	0.709
Birth weight (kg)	2.78±0.55	2.70±0.63	0.777	0.438
GMFCS level			-0.027	0.978
I	11 (16.67)	10 (15.15)		
II	8 (12.12)	13 (19.70)		
III	24 (36.36)	16 (24.24)		
IV	14 (21.21)	15 (22.73)		
V	9 (13.64)	12 (18.18)		
EDACS level			-0.322	0.747
I	8 (12.12)	10 (15.15)		
II	15 (22.73)	13 (19.70)		
III	21 (31.82)	18 (27.27)		
IV	22 (33.33)	25 (37.88)		
GMFM	34.10±19.44	32.02±15.97	0.672	0.503
Height (cm)	82.64±7.23	81.64±8.56	0.725	0.470
Body weight (kg)	8.87±1.54	8.83±1.57	0.148	0.883

Table 4. Baseline data $[\overline{x} \pm s, n (\%)]$

Note: Percentage is calculated by rounding method. GMFCS: Gross Motor Function Classification System; EDACS: Eating and Drinking Ability Classification System; GMFM: Gross Motor Function Measure.

Discussion

Malnutrition is a condition resulting from inadequate intake of energy and/or protein, failing to meet an individual's physiological demands [14]. In children with cerebral palsy, the factors contributing to malnutrition are multifaceted, with a significant one being central nervous system pathologies. These pathologies can lead to orofacial sensorimotor disorders, impaired coordination between swallowing and respiration, and esophageal motility disorders. Consequently, these children often struggle with mouth movements and swallowing, leading to feeding difficulties and insufficient nutritional intake [3]. As a result, the incidence of malnutrition is notably higher in children with cerebral palsy than in normal children [15]. Malnourished children with cerebral palsy generally exhibit a lower quality of life compared to well-nourished children. Their health and living conditions are considerably poorer, and malnutrition can severely impact the development of skeletal, neurological, and respiratory systems [5, 6, 16]. Additionally, children with cerebral palsy face extensive and challenging rehabilitation tasks. The presence of malnutrition complicates the conduct and diminishes the effectiveness of rehabilitation training [17]. Therefore, nutritional guidance and interventions cannot be neglected for such children. Our findings showed that nutritional interventions with high-calorie whole protein or peptide formulas could significantly improve malnutrition and promote the development of gross motor function in children with cerebral palsy, offering more benefits than general daily dietary interventions alone.

The measurement of energy intake is a key component of nutritional interventions. Children with cerebral palsy have different nutri-

	-				
Group	Baseline	3 months	6 months	<i>F</i> value	P value
Height (cm)					
General group (n=66)	82.64±7.23	85.81±8.02	88.50±8.39*	5.024	0.007
Nutrient group (n=66)	81.64±8.56	87.38±9.71*	93.45±10.87*	14.201	< 0.001
Body weight (kg)					
General group (n=66)	8.87±1.54	10.35±1.77*	11.89±1.90*	22.178	< 0.001
Nutrient group (n=66)	8.83±1.57	10.81±2.08*	13.02±2.41*	43.194	< 0.001
WHZ					
General group (n=66)	-1.48±1.04	-1.21±0.79	-0.98±0.78*	3.295	0.039
Nutrient group (n=66)	-1.49±0.72	-1.16±0.74	-0.76±0.74*	12.795	< 0.001
WAZ					
General group (n=66)	-1.90±0.82	-1.41±0.86*	-0.84±0.90*	15.147	< 0.001
Nutrient group (n=66)	-1.90±0.74	-1.31±0.78*	-0.73±0.85*	26.427	< 0.001
HAZ					
General group (n=66)	-1.84±0.80	-1.72±0.63	-1.76±0.66	0.291	0.748
Nutrient group (n=66)	-1.84±0.78	-1.74±0.81*	-1.70±0.68*	0.883	0.415
BAZ					
General group (n=66)	-1.31±0.77	-1.15±0.76	-1.00±0.77*	2.015	0.136
Nutrient group (n=66)	-1.29±0.64	-0.88±0.62*	-0.74±0.76*	8.980	<0.001

Table 5. Nutritional status changes in the two group $(\overline{x} \pm s)$

Note: Compared with baseline, *P<0.05. WAZ: weight-for-age Z-score; HAZ: height-for-age Z-score; WHZ: weight-for-height Z-score; BAZ: body mass index-for-age Z-score.

Table 6.	Comparison	of the changes in	nutritional parameters	between the two g	groups $[M(P_{25}, P_{75})]$
----------	------------	-------------------	------------------------	-------------------	------------------------------

Variable	Changes	General group (n=66)	Nutrient group (n=66)	Zvalue	<i>P</i> value
Height (cm)	Δ (3 months - baseline)	2.80 (1.70, 380)	3.65 (2.28, 5.23)	-2.889	0.004
	Δ (6 months - baseline)	5.40 (3.98, 6.50)	8.35 (5.18, 12.03)	-5.126	<0.001
Body weight (kg)	Δ (3 months - baseline)	1.30 (0.70, 1.93)	1.40 (0.80, 2.53)	-1.283	0.200
	Δ (6 months - baseline)	2.60 (1.60, 3.90)	3.10 (1.90, 5.13)	-1.896	0.058
WHZ	Δ (3 months - baseline)	0.26 (0.13, 0.51)	0.32 (0.08, 0.66)	-0.544	0.586
	Δ (6 months - baseline)	0.47 (0.16, 0.96)	0.55 (0.23, 1.05)	-1.270	0.204
WAZ	Δ (3 months - baseline)	0.38 (0.24, 0.62)	0.40 (0.17, 1.01)	-0.685	0.493
	Δ (6 months - baseline)	1.03 (0.59, 1.27)	0.96 (0.511, 1.75)	-0.651	0.515
HAZ	Δ (3 months - baseline)	-0.04 (-0.23, 0.36)	0.14 (-0.14, 0.31)	-1.206	0.228
	Δ (6 months - baseline)	-0.10 (-0.38, 057)	0.10 (-0.12, 0.48)	-1.750	0.080
BAZ	Δ (3 months - baseline)	0.18 (-0.25, 0.61)	0.29 (0.06, 0.73)	-1.966	0.049
	Δ (6 months - baseline)	0.29 (-0.14, 0.81)	0.48 (-0.05, 1.00)	-1.245	0.213

Note: WAZ: weight-for-age Z-score; HAZ: height-for-age Z-score; WHZ: weight-for-height Z-score; BAZ: body mass index-for-age Z-score.

tional needs. For example, some of them have increased energy consumption due to spasticity and involuntary movements, while severe cases are bedridden or need to use wheelchairs for long periods of time due to severe motor limitations, so their physical activity as well as energy needs are reduced. Walker et al. [18] showed that spasticity accounts for about 10% of the energy consumption in children with cerebral palsy, while those who cannot walk expend 60%-70% of the energy compared to their ambulatory peers of the same age. Therefore, applying standard energy intake recommendations for healthy children of the same age may result in inappropriate energy intake in children with cerebral palsy, either exceeding or being insufficient relative to their actual needs. We estimated nutritional needs for both groups

	Group	Mild malnutrition	Moderate malnutrition	Severe malnutrition	Normal	Z	Ρ
Baseline	General group (n=66)	17 (25.76)	32 (48.48)	17 (25.76)	0 (0)	1.831	0.067
	Nutrient group (n=66)	23 (34.85)	35 (53.03)	8 (12.12)	0 (0)		
3 months	General group (n=66)	24 (36.36)	35 (53.03)	6 (9.09)	1 (1.51)	1.152	0.250
	Nutrient group (n=66)	32 (48.48)	27 (40.91)	4 (6.06)	3 (4.55)		
6 months	General group (n=66)	27 (40.91)	33 (50.00)	5 (7.58)	1 (1.51)	2.169	0.030
	Nutrient group (n=66)	45 (68.18)	10 (15.15)	4 (6.06)	7 (10.61)		

Table 7. Nutritional classification of the two groups before and after intervention [n (%)]

Note: Percentage is calculated by rounding method.

Table 8. GMFM changes before and after intervention in two groups $(\overline{x} \pm s)$

Group	Baseline	3 months	6 months	<i>F</i> value	P value	
General group (n=66)	34.10±19.44	41.86±20.02	51.60±19.04*	8.997	< 0.001	
Nutrient group (n=66)	32.02±15.97	45.10±18.02*	59.28±21.33*	25.139	< 0.001	

Note: Compared with baseline, *P<0.05.

Table 9. Comparison of changes in GMFM between the two groups $[M(P_{25}, P_{75})]$

			e · 25· 75/			
	Changes	General group (n=66)	Nutrient group (n=66)	Zvalue	P value	
GMFM	Δ (3 months - baseline)	6.20 (3.57, 8.53)	9.55 (5.15, 20.58)	-3.241	0.001	
	Δ (6 months - baseline)	14.85 (8.26, 21.98)	25.00 (12.65, 35.93)	-3.555	< 0.001	
Nata: CM						

Note: GMFM: Gross Motor Function Measure.

Group	General group (n=66)	Nutrient group (n=66)	t value	P value
Total albumin (g/L)				
Baseline	56.93±8.80	54.39±10.50	1.506	0.134
6 months	65.77±7.71	71.47±4.97	5.048	< 0.001
Albumin (g/L)				
Baseline	37.10±4.96	36.31±6.45	0.789	0.432
6 months	44.75±6.35	48.69±4.39	4.146	< 0.001
Prealbumin (mg/L)				
Baseline	156.91±21.53	153.89±39.50	0.545	0.587
6 months	193.92±20.84	211.73±31.37	3.842	< 0.001
Transferrin (g/L)				
Baseline	1.94±0.45	1.91±0.45	0.383	0.702
6 months	2.20±0.46	2.33±0.33	1.866	0.064
25-hydroxyvitamin D (ng/mL)				
Baseline	82.31±15.19	84.25±40.00	0.368	0.713
6 months	109.87±16.34	133.74±24.00	6.679	<0.001

Table 10. Blood indexes of the two groups before and after intervention $(\bar{x} \pm s)$

of children to align their energy intake more closely with their needs. After a 6-month nutritional intervention, children in the nutrient group showed a significant increase in height and weight. The research results of Soylu et al. [19] and Zhao et al. [8] also support the effectiveness of high-calorie whole protein or peptide-based nutritional formulas. The potential mechanisms may include the following. (1) Energy and nutrient supplementation: Highcalorie formulas provide elevated levels of energy and essential micronutrients, which

0	Adverse events				
Group	Diarrhea	Constipation	Vomiting	Rash	n (%)
General group (n=66)	7 (10.61)	1 (1.51)	2 (3.03)	0 (0)	10 (15.15)
Nutrient group (n=66)	2 (3.03)	1 (1.51)	1 (1.51)	2 (3.03)	6 (9.09)
X ²					1.138
Р					0.286

Table 11. Comparison of adverse events in the two groups [n (%)]

Note: Percentage is calculated by rounding method.

may help bridge the energy and nutrient gaps created by increased metabolic demands or insufficient nutrient intake in children with cerebral palsy. (2) Improved nutrient absorption: These formulas are often easier to digest and absorb, especially for children with cerebral palsy who may struggle with swallowing difficulties or have impaired digestive function. (3) Promotion of growth and development: Highcalorie formulas are rich in vital nutrients such as proteins, fats, and vitamins, all crucial for normal growth. Improved nutritional status through these formulas can directly contribute to increases in height and weight.

In recent years, enteral nutrition, including home-based approaches, has gained prominence as a primary method for managing dietary needs in children with cerebral palsy, many of whom suffer from gastrointestinal issues such as dysphagia and gastroesophageal reflux. Therefore, we opted for enteral nutrition due to its suitability for our patient group. Our findings indicate that enteral nutrition significantly outperformed standard nutritional approaches in improving nutritional status. Specifically, the nutrient group saw a greater reduction in moderate and severe malnutrition compared to the general group. This aligns with prior research that has documented similar benefits of enteral feeding in children with cerebral palsy [20-22]. In this study, we employed anthropometric methods to evaluate the nutritional status of children with cerebral palsy, finding this approach to be more accurate, universal, and convenient than other nutritional screening tools. In addition, we monitored blood indicators including total albumin, albumin, prealbumin, and 25-hydroxyvitamin D. After 6 months of nutritional intervention, all blood indicators showed improvement, with the nutrient group displaying higher levels than the general group. The enhanced absorption of high-calorie peptide nutrients, which were pre-

treated to be absorbed directly by the intestinal mucosal epithelium without breakdown, likely contributed to this result [23]. Conversely, whole protein enteral nutrition stimulates the secretion of digestive juices, mimicking normal food digestion and absorption, thereby providing essential nutrients and energy, and improving nutritional status. Despite the overall improvement in nutritional status among the children in our study, approximately 1/3 of the children still had moderate or severe malnutrition after the intervention, indicating that 6 months of nutritional intervention may be far from sufficient, and further expansion of the sample size and longer follow-up observations are needed to assess the long-term effects and safety of enteral nutrition interventions.

In this study, both groups of children with cerebral palsy demonstrated significant improvements in gross motor function. Notably, those in the nutrient group exhibited more substantial enhancements. This outcome may be attributed to the high-protein and high-energy content of the whole protein or peptide nutritional formulas used. These formulas effectively correct nutritional intake and nitrogen balance, promoting muscle growth and increased energy intake. Consequently, the children were better equipped physically to participate in and benefit from rehabilitation training, leading to significant improvements in gross motor function.

The monitoring of adverse events is a critical aspect of nutritional interventions. In this study, the incidence of adverse events was 15.15% in the general group and 9.09% in the nutrient group. Most reported events were mild gastrointestinal symptoms, such as constipation, bloating, and diarrhea. Notably, two children in the nutrient group developed rashes. Investigation revealed that one child had a known allergy, which might have contributed to

the rash, while the other causes could not be ruled out. The other child had experienced transient rashes previously, suggesting other potential causes. These findings indicate that gastrointestinal intolerance was not exacerbated by the high-calorie nutritional formulas. Overall, the children tolerated the high-calorie whole protein or peptide formulas well, aligning with results from previous studies documented in the literature [24, 25].

Advantages and disadvantages

Our study contributes valuable insights into the efficacy of high-calorie formula nutritional interventions for children with cerebral palsy, an area that has been relatively underexplored. The findings indicate that these interventions hold significant potential for enhancing clinical outcomes in this population. Despite its contributions, this study has several limitations. Firstly, the sample size of this study is small and exclusively comprises children attending our hospital. Secondly, the intervention period was only 6 months, so the long-term nutritional improvement needs to be studied by extending the intervention period. Thirdly, while the control group received dietary education and feeding training, variations in the dietary content and formula milk composition between the groups could influence the results. Lastly, our study may not have adequately accounted for all possible confounding factors that could impact the children's prognosis, such as family economic status, social support, and underlying health conditions.

To build on the findings of this study, we plan to conduct long-term follow-up studies to evaluate the sustained impacts of nutritional interventions on the health, growth, development, and quality of life of children with cerebral palsy. Increasing the sample size through multicenter studies will enhance the generalizability and reliability of the research findings. Additionally, we will explore the combined effects of nutritional interventions with other therapies, such as physical and occupational therapy, to promote comprehensive development in children with cerebral palsy.

Conclusion

Our study demonstrates that nutritional interventions using high-calorie whole protein or peptide formulas can significantly improve malnutrition and enhance gross motor function development in children with cerebral palsy, with a low incidence of adverse events, underscoring their safety and effectiveness. Given these positive outcomes, such nutritional interventions hold great promise for broader clinical application.

Acknowledgements

This work was supported by Yulin City Scientific Research and Technology Development Plan Project (Clinical Study on Nutritional Intervention for Children with Cerebral Palsy in Yulin City) [grant number 20204304].

Written informed consent was given from the guardians of all participants.

Disclosure of conflict of interest

None.

Address correspondence to: Xia Cai, Child Rehabilitation Department, Yulin First People's Hospital, Yulin 537000, Guangxi, China. Tel: +86-1387752-9820; E-mail: cxlwx200801@163.com

References

- [1] Li N, Zhou P, Tang H, He L, Fang X, Zhao J, Wang X, Qi Y, Sun C, Lin Y, Qin F, Yang M, Zhang Z, Liao C, Zheng S, Peng X, Xue T, Zhu Q, Li H, Li Y, Liu L, Huang J, Liu L, Peng C, Kaindl AM, Gecz J, Han D, Liu D, Xu K and Hu H. In-depth analysis reveals complex molecular aetiology in a cohort of idiopathic cerebral palsy. Brain 2022; 145: 119-141.
- [2] Jahan I, Muhit M, Karim T, Smithers-Sheedy H, Novak I, Jones C, Badawi N and Khandaker G. What makes children with cerebral palsy vulnerable to malnutrition? Findings from the Bangladesh cerebral palsy register (BCPR). Disabil Rehabil 2019; 41: 2247-2254.
- [3] Jahan I, Muhit M, Hardianto D, Karim T, Al Imam MH, Das MC, Smithers-Sheedy H, Badawi N and Khandaker G. Nutritional status of children with cerebral palsy in remote Sumba Island of Indonesia: a communitybased key informants study. Disabil Rehabil 2021; 43: 1819-1828.
- [4] Kakooza-Mwesige A, Tumwine JK, Eliasson AC, Namusoke HK and Forssberg H. Malnutrition is common in Ugandan children with cerebral palsy, particularly those over the age of five and those who had neonatal complications. Acta Paediatr 2015; 104: 1259-1268.

- [5] Eveleens RD, Dungen DK, Verbruggen SCAT, Hulst JM and Joosten KFM. Weight improvement with the use of protein and energy enriched nutritional formula in infants with a prolonged PICU stay. J Hum Nutr Diet 2019; 32: 3-10.
- [6] Jahan I, Sultana R, Muhit M, Akbar D, Karim T, Al Imam MH, Das MC, Smithers-Sheedy H, McIntyre S, Badawi N and Khandaker G. Nutrition interventions for children with cerebral palsy in low- and middle-income countries: a scoping review. Nutrients 2022; 14: 1211.
- [7] Bogen DL, Hanusa BH, Baker R, Medoff-Cooper B and Cohlan B. Randomized clinical trial of standard- versus high-calorie formula for methadone-exposed infants: a feasibility study. Hosp Pediatr 2018; 8: 7-14.
- [8] Zhao Y, He L, Peng T, Liu L, Zhou H, Xu Y, Yang X, Huang Y, Chen Z, Xu Y, Li J, Hou X, Tang H and Xu K. Nutritional status and function after high-calorie formula vs. Chinese food intervention in undernourished children with cerebral palsy. Front Nutr 2022; 9: 960763.
- Novak I, Morgan C, Adde L, Blackman J, Boyd [9] RN, Brunstrom-Hernandez J, Cioni G, Damiano D, Darrah J, Eliasson AC, de Vries LS, Einspieler C, Fahey M, Fehlings D, Ferriero DM, Fetters L, Fiori S, Forssberg H, Gordon AM, Greaves S, Guzzetta A, Hadders-Algra M, Harbourne R, Kakooza-Mwesige A, Karlsson P, Krumlinde-Sundholm L, Latal B, Loughran-Fowlds A, Maitre N, McIntyre S, Noritz G, Pennington L, Romeo DM, Shepherd R, Spittle AJ, Thornton M, Valentine J, Walker K, White R and Badawi N. Early, accurate diagnosis and early intervention in cerebral palsy: advances in diagnosis and treatment. JAMA Pediatr 2017; 171: 897-907.
- [10] Becker P, Carney LN, Corkins MR, Monczka J, Smith E, Smith SE, Spear BA and White JV; Academy of Nutrition and Dietetics; American Society for Parenteral and Enteral Nutrition. Consensus statement of the Academy of Nutrition and Dietetics/American Society for Parenteral and Enteral Nutrition: indicators recommended for the identification and documentation of pediatric malnutrition (undernutrition). Nutr Clin Pract 2015; 30: 147-161.
- [11] WHO Multicentre Growth Reference Study Group. WHO child growth standards based on length/height, weight and age. Acta Paediatr Suppl 2006; 450: 76-85.
- [12] Russell DJ, Rosenbaum PL, Cadman DT, Gowland C, Hardy S and Jarvis S. The gross motor function measure: a means to evaluate the effects of physical therapy. Dev Med Child Neurol 1989; 31: 341-352.

- [13] Palisano R, Rosenbaum P, Walter S, Russell D, Wood E and Galuppi B. Development and reliability of a system to classify gross motor function in children with cerebral palsy. Dev Med Child Neurol 1997; 39: 214-223.
- [14] Scarpato E, Staiano A, Molteni M, Terrone G, Mazzocchi A and Agostoni C. Nutritional assessment and intervention in children with cerebral palsy: a practical approach. Int J Food Sci Nutr 2017; 68: 763-770.
- [15] Jahan I, Muhit M, Hardianto D, Laryea F, Amponsah SK, Chhetri AB, Smithers-Sheedy H, McIntyre S, Badawi N and Khandaker G. Epidemiology of malnutrition among children with cerebral palsy in low- and middle-income countries: findings from the global LMIC CP register. Nutrients 2021; 13: 3676.
- [16] Karim T, Jahan I, Dossetor R, Giang NTH, Van Anh NT, Dung TQ, Chau CM, Van Bang N, Badawi N, Khandaker G and Elliott E. Nutritional status of children with cerebral palsy-findings from prospective hospital-based surveillance in vietnam indicate a need for action. Nutrients 2019; 11: 2132.
- [17] Ruiz Brunner MLM, Cieri ME, Rodriguez Marco MP, Schroeder AS and Cuestas E. Nutritional status of children with cerebral palsy attending rehabilitation centers. Dev Med Child Neurol 2020; 62: 1383-1388.
- [18] Walker JL, Bell KL, Boyd RN and Davies PS. Energy requirements in preschool-age children with cerebral palsy. Am J Clin Nutr 2012; 96: 1309-1315.
- [19] Soylu OB, Unalp A, Uran N, Dizdarer G, Ozgonul FO, Conku A, Ataman H and Ozturk AA. Effect of nutritional support in children with spastic quadriplegia. Pediatr Neurol 2008; 39: 330-334.
- [20] Arrowsmith F, Allen J, Gaskin K, Somerville H, Clarke S and O'Loughlin E. The effect of gastrostomy tube feeding on body protein and bone mineralization in children with quadriplegic cerebral palsy. Dev Med Child Neurol 2010; 52: 1043-1047.
- [21] Dipasquale V, Catena MA, Cardile S and Romano C. Standard polymeric formula tube feeding in neurologically impaired children: a five-year retrospective study. Nutrients 2018; 10: 684.
- [22] van Waardenburg DA, de Betue CT, Goudoever JB, Zimmermann LJ and Joosten KF. Critically ill infants benefit from early administration of protein and energy-enriched formula: a randomized controlled trial. Clin Nutr 2009; 28: 249-255.
- [23] Mohamed Elfadil O, Steien DB, Narasimhan R, Velapati SR, Epp L, Patel I, Patel J, Hurt RT and

Mundi MS. Transition to peptide-based diet improved enteral nutrition tolerance and decreased healthcare utilization in pediatric home enteral nutrition. JPEN J Parenter Enteral Nutr 2022; 46: 626-634.

- [24] Evans S, Twaissi H, Daly A, Davies P and Macdonald A. Should high-energy infant formula be given at full strength from its first day of usage? J Hum Nutr Diet 2006; 19: 191-197; quiz 199-201.
- [25] Devaera Y, Syaharutsa DM, Jatmiko HK and Sjarif DR. Comparing compliance and efficacy of isocaloric oral nutritional supplementation using 1.5 kcal/mL or 1 kcal/mL sip feeds in mildly to moderately malnourished Indonesian children: a randomized controlled trial. Pediatr Gastroenterol Hepatol Nutr 2018; 21: 315-320.