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Nutritional Status of Hemodialysis Patients with End Stage Renal Disease and Selection and Application of Oral Nutritional Support

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YC collected the samples. YH analyzed the data. YC and YH conducted the experiments and analyzed the results. Both authors discussed the results and wrote the manuscript.

Key words
End stage renal disease, Hemodialysis, Influence status, Diet survey, Nutritional support agent

ABSTRACT

The objective of this study was to analyze the nutritional status of hemodialysis patients with end stage renal disease, and to select oral nutritional support agents with high tolerance. In this experiment, 94 hemodialysis patients with end stage renal disease who were treated in our hospital from August 2020 to July 2022 were selected as research objects. The nutritional status of the patients was evaluated by counting their 24-hour dietary status and using MQSGA (Modified Quantitative Subjective Nutrition Assessment) scale, and was analyzed in combination with the determination of biochemical indicators and body weight. The factors influencing hemodialysis malnutrition of end stage renal disease by single factor linear regression included age, dialysis time, Hb, TG, hs-CRP, BMI, Alb, BUN and Kt/v ratio. The multiple stepwise regression analysis showed that the independent risk factors of malnutrition included age>65 years old, HS-CRP>5 mg/ml and Kt/v<1.2. It was concluded that the incidence of malnutrition in hemodialysis patients with end stage renal disease is relatively high, which is closely related to the age, inflammatory state and dialysis adequacy of the patients. According to nutritional risk characteristics of hemodialysis patients with end stage renal disease, Yixusu (whole nutrient) + whey protein powder can be selected to ensure the demand and consumption of protein during dialysis, improve the immune defense ability of patients and avoid a series of complications caused by malnutrition.

INTRDUCTION

Now that in the new century we are witnessing huge advances in medical science, the pattern of diseases and health care has fundamentally changed and is on the path of increasing life expectancy and improving the quality of life, especially in chronic patients (Shi, 2021). End stage renal disease (ESRD) is also a progressive and irreversible chronic disease in which the activity of the kidneys is disturbed, so that the body is no longer able to establish metabolic actions and maintain the balance of fluids and electrolytes, and following this condition, it has a harmful effect on All body systems (Rodger, 2012).

ESRD is a clinical stage in which the renal function of secondary or primary nephropathy progresses to irreversible loss. The primary clinical treatment is maintenance hemodialysis (MHD) replacement therapy (Wang *et al*., 2012). According to the statistics of Chinese Medical Association, about 89% of ESRD patients receive hemodialysis to prolong their survival time. It can significantly improve their living quality and mortality (Gong and Xu, 2018). With the prolongation of maintenance hemodialysis time, the metabolism, protein and fat consumption ability of the body can be enhanced, and it is also extremely easy to cause malnutrition. According to foreign literature and reports, about 18-75% of maintenance hemodialysis patients with end stage renal disease are malnourished, while related literature in China reports that about 28.9% of these malnourished patients exist. During this period, the infection, low immunity and micro-inflammation caused by malnutrition become the through train between patients and death (Zhu *et al*., 2020). Therefore, this survey evaluated and analyzed the nutritional status of ESRD patients during MHD treatment, and put forward a new, targeted and standardized oral nutritional agent for clinical research practice to provide nutritional support for ESRD patients and avoid adverse clinical outcomes.

MATERIALS AND METHODS

In this study, 94 hemodialysis patients with end stage

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renal disease who were treated in our hospital from August 2020 to July 2022 were selected as research objects, including 52 males and 42 females. They were aged from 35 to 83 years, with an average age of 67.39±7.38 years. Their dialysis time ranged from 7 months to 10 years, with an average of 21.75±7.92 months. The duration of disease was 1-5 years 3.21±2.16 years, and the BMI was 18-27kg/m² 24.58±3.16 kg/m². There were 28 cases of chronic glomerulonephritis, 21 cases of hypertensive glomerulosclerosis, 20 cases of diabetic nephropathy, 11 cases of chronic interstitial nephritis, 10 cases of polycystic renal disease and 4 others. Inclusion criteria: meeting the diagnostic criteria of end stage renal disease in Clinical Diagnosis and Treatment Guide-Nephrology Sub-volume; age ≥ 20 years; continuous hemodialysis for ≥ 3 months; urine volume < 400ml/d, serum protein ≥ 35g/L, glomerular filtration rate < 15ml/min; since the first follow-up dialysis day, the follow-up within the expected time or the death within the expected follow-up time can be completed; maintaining conscious and actively cooperating with the survey. Exclusion criteria: patients with severe cardiovascular and cerebrovascular diseases and malignant tumors; patients with infection, active hepatitis and renal transplantation; previous trauma and surgical history; blood transfusion history and bleeding in recent 6 months; those who quit or transferred to other departments for treatment. By biochemical indicators, anthropological measurement and improved subjective nutrition evaluation scale, 62 of the respondents were malnourished and named as malnourished group, while the remaining 32 were non-malnourished.

Hemodialysis

All ESRD patients were treated with hemodialysis at the frequency of 500ml/min dialysate flow, 200-260ml blood flow, 2-3 times a week and 4 hours each time during MHD.

Mass measurement method

BMI (kg/m2) = body weight (kg)/ height (m)2 (El-Gamasy *et al*., 2018).

Evaluation of nutritional status

The nutritional status was evaluated by MQSGA (Modified Quantitative Subjective Evaluation Form). The survey contents of the scale included 7 items such as the changes of diet, exercise ability, body weight, gastrointestinal symptoms, subcutaneous fat reduction, complications and muscle consumption of patients in the past 6 months. Each item was scored on the basis of 5 scales of Likert 1-5, with the total score ranging from 7 to 35 points. The scores ≤10 points indicate normal nutrition. The scores between 11 and 20 points indicate moderate malnutrition. The scores between 21 and 35 points indicate severe malnutrition. The total scores < 10 points were classified into malnutrition group.

Nutrition intake

One-to-one inquiry was adopted, and the size and variety of food for each meal of patients for three consecutive days were counted. The intake of energy and protein in patients' diet was calculated by medical recipe calculator, and the daily standard weight protein intake (DPI) and energy intake (DEI) were calculated. The actual daily intake of nutrients was calculated according to the dietary review.

Biochemical indicators detection

5ml of peripheral venous blood was drawn before dialysis and 3ml of that was drawn after dialysis with an empty stomachin the morning. It is mainly used to detect the biochemical indicators including plasma albumin (Alb), hemoglobin (Hb), total cholesterol (TG), high-sensitivity C-reactive protein (hs-CRP) and serum urea nitrogen (BUN) (González-Ortiz *et al*., 2019).

Indicators of dialysis adequacy

The formula kt/v =-in (R-0.008XT) + (4-3.5×R) × UF/W was adopted for calculation. The ratio before and after dialysis was BUN, namely the R in the formula. The single dialysis time was t in the formula. The ultrafiltration volume was the UF in the formula, and the body weight after dialysis was the W in the formula. Kt/V< 1.2 indicated inadequate dialysis (Yang *et al*., 2021).

Data collection

Data collectors were nurses who did not participate in the survey to avoid data collection nurses and nurses who participated in the survey being in the same group, which would affect the authenticity of the results. 2 nurses who did not participate in this survey were selected for data collection of the tested patients. Original data shall be retained and shall not be smeared or modified. In this study, 61 samples were collected from the non-malnutrition group, and one patient voluntarily withdrew from the survey; 32 cases in the malnutrition group were recovered, all of which met the exclusion criteria. The total effective recovery result rate was 98.94%.

Statistical analysis

The collected data are processed by SPSS23.0 statistical software, and the measurement data are tested by t value and expressed by x±s; the independent samples of the comparison of differences between groups are subject

to x^2 test. The factors that may affect the malnutrition of ERSD patients during MHD treatment are independent variables and subject to single factor linear regression analysis. After that, significant factors are selected for multiple stepwise regression analysis. The test standard is α=0.05.

Table I. Single-factor linear regression analysis of influencing the nutritional status of patients.

Indicator	Assignment	Non-malnutrition group (n=61)	Malnutrition group (n=32)	X^2/t	P value
Gender					
Male	0	41	23	0.213	0.645
Female	1	20	9		
Age (years)					
≤65	0	39	10	8.995	0.003
> 65	1	22	22		
Dialysis time (months)					
≤25	0	41	11	9.182	0.002
> 25	1	20	21		
Hb (g/L)					
≥110	0	41	13	6.094	0.014
< 110	1	20	19		
TG (mmol/L)					
<1.70	0	27	11	0.849	0.357
≥1.70	1	34	21		
hs-CRP (mg/ml)					
≤5	0	51	17	9.922	0.002
>5	1	10	15		
BUN (mmol/L)					
2.9~7.5	0	39	27	4.256	0.039
>7.5	1	22	5		
BMI (kg/m2)					
18.5-24.9	0	51	20	5.178	0.023
≥25	1	10	12		
Alb (mg/L)					
35~55	0	33	10	4.408	0.036
< 35	1	28	22		
Kt/v [n (%)]					
≥1.2	0	46	16	6.098	0.014
< 1.2	1	15	16		

RESULTS

Table I shows the single-factor linear regression analysis of nutritional status of patients. There was no significant difference in gender and TG under different nutritional status (P > 0.05). However, there were statistically significant differences in age, dialysis time, Hb, hs-CRP, BUN, BMI, Alb and Kt/v (P<0.05).

Table I also shows multiple stepwise regression analysis of factors influencing nutritional risk status. Table II shows the multiple stepwise regression analysis of factors influencing nutritional risk status. The independent risk factors influencing nutritional risk status by multiple stepwise regression analysis include age > 65 years old, HS-CRP>5mg/ml and KT/V<1.2. Malnutrition was taken as the dependent variable. Multiple step wise regression analysis was carried out by taking gender (assignment: male =0, female =1), age (assignment: ≤ 65 years old =0, > 65 years old =1), dialysis time (assignment: ≤25 months =0, > 25 months =1), Hb (assignment: ≥110g/L=0, < 110g/L=1), TG (assignment: <1.70mmol/L=0, ≥1.70mmol/L=1), hs-CRP (assignment: ≤5mg/ml=0, > 5mg/ml=1), BUN (assignment: 2.9-7.5mmol/L=0, > 7.5mmol/L=1), BMI (assignment: 18.5-24.9kg/m2=0, ≥25kg/m2=1), Alb (assignment: 35-55g/L=0, < 35mg/L=1), Kt/v (assignment: ≥1.2%=0, < 1.2%=1) as independent variables. The results showed that age > 65 years old, hs-CRP > 5mg/ml, Kt/v < 1.2% were the influencing factors of malnutrition in hemodialysis patients with end-stage renal disease (P<0.05).

Table II. Multiple stepwise regression analysis of factors influencing nutritional risk status.

Factor	β	SE	Wald value	P value	OR value	95% CI
Age > 65 years	0.693	0.218	14.582	0.000	2.000	1.304-3.066
hs-CRP >5mg/ml	0.743	0.319	7.301	0.007	2.102	1.125-3.928
Kt/v>1.2[n(%)]	0.873	0.281	11.056	0.001	2.394	1.380-4.153

DISCUSSION

ESRD is the manifestation of the end stage development of chronic renal disease, which is second only to cardiovascular diseases and malignant tumors. Patients may suffer from damage to immune organs and cytokines and other damages. Renal transplantation is the most effective treatment, but most patients can't accept it because of various factors such as organ source and high cost. With the continuous development of dialysis

technology, peritoneal dialysis and hemodialysis have become the best treatment options, which can effectively prolong the life cycle. According to incomplete statistics, the number of ESRD patients in China is as high as 120 million. The MHD population progresses to ESRD at a rate of 2%. Among them, about 15%-75% are malnourished, and about 6%-8% are severely malnourished (Tsuchida *et al*., 2016). Looking back on 2008, the International Society of Renal Nutrition and Metabolism discussed that the state of decreasing energy and protein reserves during the progress of chronic renal disease, namely, low serum albumin, low body mass indicator, insufficient intake of calories and dietary nutrients, progressive skeletal muscle consumption and micro-inflammation, was named protein-energy consumption syndrome (Günalay *et al*., 2018). Therefore, the accurate nutritional evaluation of ESRD patients can provide a favorable basis for clinical diagnosis and treatment, and it is vitally important to ensure the living quality of patients.

Maintenance hemodialysis is the main alternative therapy for patients with end-stage chronic kidney disease. It can purify the blood by removing the excess residue in the blood of patients through the principle of semi-permeable membrane. On the one hand, this treatment can delay the damage of stasis to the kidney and accelerate the rate of kidney failure; on the other hand, it can improve the quality of life of patients after the replacement kidney has completed the filtration of stasis. But prolonged treatment with maintenance blood techniques can cause inflammation in the body, which can lead to a lack of L-carnitine, resulting in adverse effects such as anemia and malnutrition. In this survey, the patients were divided into non-malnutrition and malnutrition groups according to the score of MASGA scale. Through the analysis of related factors and multiple factors, the final statistics showed that the independent risk factors of malnutrition in patients with ESRD during MHD included patient age, HS-CRP > 5 mg/ml and KT/V < 1.2, which suggested that the above biochemical indicators were closely related to ESRD with malnutrition. Alb is clinically recognized as the response indicator of protein storage capacity in the body, and hypoproteinemia is the most effective biochemical indicator to judge whether there is malnutrition. This statement is also confirmed in the results of this survey. It is analyzed that the reasons are mainly due to the decrease of gastric acid secretion, digestive enzymes and digestive juices in elderly patients over 65 years old, the imbalance of body synthesis and metabolism, the decrease of normal cell function, the change of organ physiological function, and then the impact on the absorption and digestion of food nutrients (Zolnoori *et al*., 2012); in addition, the metabolic rate of elderly patients is reduced, and the period of being sensitive to accumulated toxins in the body is delayed. There is no obvious difference between the appetite of patients after hemodialysis and that before dialysis. Moreover, patients with ESRD are prone to endocrine dysfunction during long-term glucocorticoid treatment, such as hyperinsulinemia, insulin resistance, hyperthyroidism, insensitivity to growth hormone and insulin-like growth factor, etc., which can inhibit protein synthesis and promote protein decomposition (Zhou *et al*., 2013).

It was found in this survey that the proportion of patients with hs-CRP > 5mg/ml in non-malnutrition group was significantly lower than that in malnutrition group, suggesting that high hs-CRP level directly affected the nutritional status of the body. hs-CRP was the most sensitive and specific biochemical indicator of chronic inflammatory state. Analysis showed that the accumulation of toxins and chemicals in the body promoted the retention of inflammatory metabolites, leading to inflammatory state (Silva *et al*., 2017). The mechanism of ESRD complicated with malnutrition in inflammatory state is as follows: (1) In inflammatory state, inflammatory factors inhibit mRNA expression in liver through the actions of IL-1, IL-6, TNF-α, etc. Protein synthesis in skeletal muscle decreases, which induces hypoproteinemia and increases albumin decomposition (Shih *et al*., 2015). (2) Inflammatory cells can stimulate the increase of fat leptin in plasma, while leptin receptor can be expressed in hypothalamus, adipocytes, adrenocortical cells, thyroid follicular epithelial cells and other tissues and organs. The most important thing is hypothalamus, which can reduce appetite, reduce energy intake and inhibit fat synthesis, and also increase metabolic rate and energy consumption, eventually leading to malnutrition (Allegra *et al*., 1991).

According to this survey, for patients in non-malnutrition group, the age over 65 years and Kt/v<1.2 are the main risk factor for malnutrition in maintenance hemodialysis patients, which is consistent with the research report of (Hermans *et al*., 2006). The reasons are as follows: (1) Although maintenance hemodialysis is an alternative method for end stage renal disease, it can't completely replace the normal physiological function of kidney. Long-term maintenance hemodialysis can lead to the changes of various organ functions. (2) Inadequate dialysis can reduce gastrointestinal function, cause acidosis and insulin resistance, and accelerate the decomposition and metabolism of protein (Tan *et al*., 2019). (3) During maintenance hemodialysis, patients have poor appetite, protein and insufficient calorie intake. When dialysis fluid volume and ultrafiltration volume increase, dialysis frequency decreases. Besides, the dialysis equipment is reused repeatedly, resulting in insufficient dialysis and a

large number of protein loss (Ruperto *et al*., 2016).

CONCLUSION

Maintenance hemodialysis patients are affected by many physiological and pathological factors, which can easily lead to malnutrition. There are many ways of clinical nutrition agent and nutrition supply, but oral nutrition supplement is considered as a more conventional and effective method, especially the supplementation of protein and energy. In this study, for the elderly, inflammatory patients and patients with incomplete dialysis, they could choose the combination of Yixusu (Hangzhou Newquxing Biotechnology Co., Ltd.) and Whey Protein Powder (Tomson Beijian Co., Ltd.) during dialysis. Yixusu contains 1762KJ of energy, 4.5g of protein, 8.0g of fat and 82.8g of carbohydrate per hundred grams. Whey protein contains 1683KJ of calories, 80.0g of protein, 4.7g of fat, 10.0g of carbohydrates and 175mg of sodium per hundred grams (Wei *et al*., 2020). Chiu E's research found that (Chiu *et al*., 2019), maintenance hemodialysis patients lack about 1046-2092J of energy and 10-20g of protein every day, and the oral nutritional agent composed of this nutritional component agent can meet the consumption requirements. However, consulting the relevant literature, it was found that oral nutritional agents were well tolerated in a short time, and some patients' compliance was reduced due to factors such as bad taste after long-term application. Therefore, in the future research, we should also aim at the large-sample and multi-center-controlled trials in the same period, expand the size of patient samples, analyze the factors affecting the loss and solve thethirsty caused by oral agents.

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IRB approval

This research was carried out with the approval of Research Guidance Workshop Committee (The First Affiliated Hospital of Harbin Medical University).

Ethical approval

The study was carried out in compliance with guidelines issued by ethical review board and institutional biosafety committee of The First Affiliated Hospital of Harbin Medical University. The official letter would be available on fair request to corresponding author.

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