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ORIGINAL RESEARCH

Relationship between enteral nutrition and serum levels of inflammatory factors and cardiac function in elderly patients with heart failure

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Objective: To investigate enteral nutrition's effect on serum inflammatory factors and the cardiac function of malnourished elderly patients with heart failure.

Patients and methods: A total of 105 elderly patients with heart failure were randomly divided into 3 groups: Treatment Group A, Treatment Group B, and the Control Group (Group C), each group having 35 patients and being administered conventional heart failure treatment. Group A was treated with 500 mL·d^{-1} of enteral nutrition for 1 month. Group B was given the same dose of enteral nutrition for 3 months. The Control Group was given free diet. Nutritional risk screening 2002 was used to assess the nutritional status before and after the treatment for each group. New York Heart Association status was recorded as were left ventricular ejection fraction, plasma B-type natriuretic peptide, inteleukin-6, C-reactive protein, and tumor necrosis factor-α.

Results: After the treatment, the body mass index, skinfold thickness of upper arm triceps, muscle circumference of the upper arm, upper arm muscle circumference, total protein, albumin, hemoglobin, and left ventricular ejection fraction in the treatment groups all increased, with relatively obvious relief of symptoms of heart failure. The levels of B-type natriuretic peptide, interleukin-6, tumor necrosis factor-α, and C-reactive protein all rose to different extents ($P<0.05$) and Treatment Group B showed more obvious improvement ($P<0.01$). Differences shown by the Control Group in each nutrition indicator, serum levels of inflammatory factors, and cardiac function had no statistical significance ($P>0.05$).

Conclusion: The use of enteral nutrition in conventional treatment of elderly patients with heart failure could improve not only patients' nutritional status and cardiac function, but also their immune function, thus reducing the levels of inflammatory factors. The longer the treatment period is, the more obvious the improvement in patients' cardiac function and inflammatory factors will be observed.

Keywords: enteral nutrition, heart failure, elderly, inflammatory factors, cardiac function

Introduction

Heart failure is a common and complex clinical syndrome that results from functional or structural heart disorder, leading to impaired ventricular filling or ejection of blood to the systemic circulation that is supposed to meet the body's needs. Heart failure can be caused by diseases of the endocardium, myocardium, pericardium, heart valves, and vessels or by metabolic disorders. Most patients with heart failure have symptoms related to impaired left ventricular myocardial function. Patients usually present with dyspnea, fatigue limiting exercise tolerance, and fluid retention characterized by pulmonary and peripheral edema. Heart failure can be caused by several disorders,

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including diseases affecting the pericardium, myocardium, endocardium, cardiac valves, vasculature, or metabolism.[1–3]

The use of diuretics, β-blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, angiotensin receptor neprilysin inhibitor, hydralazine plus nitrate, digoxin, and aldosterone antagonists can relieve symptoms.[4–8] Prolongation of patient survival has been documented after the use of β-blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor neprilysin inhibitor, hydralazine plus nitrate, and aldosterone antagonists. More limited evidence of survival benefit is available for diuretic therapy. The angiotensin-converting enzyme inhibitors or angiotensin receptor blockers were replaced by angiotensin receptor neprilysin inhibitor in the treatment of chronic symptomatic patients with chronic heart failure New York Heart Association (NYHA) class II–III heart failure and adequate blood pressure who could tolerate an optimal dose of these medications. Angiotensin receptor neprilysin inhibitor should not be given within 36 hours after angiotensin-converting enzyme inhibitors dose.

A failing heart is similar to an engine running out of energy. Regulating cardiac energy metabolism is expected to become a new method for the treatment of heart failure. Currently in China, there is limited report on the utilization of energy metabolism to treat heart failure. Below, is the authors' report on the use of enteral nutrition in the conventional treatment of elderly patients with heart failure during the period between January 2014 and July 2015.

Patients and methods

Clinical information

Nutritional risk screening (NRS) 2002[19] scale was used to evaluate the nutritional status of elderly patients with heart failure in our hospital. The selection criterion was that the subjects must be hospitalized heart failure patients aged 65 or above at our hospital. The exclusion criterion included the following: patients that refused to accept nutritional status assessment; patients who were leaving the hospital within 24 hours; patients who would undergo emergency surgery within 24 hours; patients who had infectious diseases or congenital heart disease; and patients who had used enteral nutrition for a long period before they came to our hospital.

If the total score in NRS 2002 scale was higher than 3, it was considered that a malnutrition and nutritional energy metabolism program needed to be carried out. Patients with a score of less than 3 underwent nutritional risk screening again at a certain time. Follow-up examination was performed until patients left the hospital. Patients' outcome index was recorded with 105 participants, aged 65–82 with an average of 71, included in the malnutrition study. Among them, 63 were male and 42 female, all having met the diagnostic criteria of heart failure and been graded according to the NYHA. Twenty-eight participants were graded as level II, 42 level III, and 35 level IV. Based on the time that participants were hospitalized and their nutritional assessment scores, they were divided into Treatment Group A, Treatment Group B, and the Control Group, each having 35 participants. In terms of the gender, age, disease type, heart function parameter, and nutritional status, the 3 groups did not demonstrate statistically significant difference ($P>0.05$) and were thus comparable (Table 1).

Method treatment

Patients in the 3 groups were all treated with conventional therapies for heart failure, including oxygen absorption, pipe expansion, diuretic, heart strengthening, etc. On such a basis, Group A and B were nasal fed with 500 mL·d^{-1} of enteral nutrition emulsion (product name: RuiDai; Fresenius Kabi Deutschland GmbH, Bad Homburg, Germany; Approval Number: J20090099; specification: 500 mL/bottle) on liquid diet for 1 and 3 months, respectively. In the Control Group, patients were given free diet with the amount of saline controlled.

Index observation

Body mass index, triceps skin fold thickness (TSF), upper arm muscle circumference (AMC), serum total protein, albumin, and hemoglobin's change in index were recorded before the treatment as well as at 1 month and 3 months after the treatment. NYHA of patients in each group was measured before and after treatment. Left ventricular ejection

Table 1 Clinical information of three groups

Clinical information	Group A	Group B	Group C
Sex (M/F)	22/13	21/14	20/15
Age (y)	69.8±4.6	72.4±6.5	71.6±3.9
BMI (kg/m^2)	23.6±1.5	21.8±2.1	22.6±1.1
Grading according to NYHA (I/II/III)	10/15/12	9/13/11	9/14/12
LVEDV (mm)	135.6±15.4	142.8±12.4	141.5±11.9
LVESV (mm)	89.6±12.4	92.4±15.3	95.1±9.6
LVEF (%)	33.8±5.1	34.6±4.4	35.3±3.8
FS (%)	22.5±3.8	23.4±4.1	21.7±2.9
CO (L/min)	4.32±1.35	4.22±1.42	4.46±1.29

Notes: Number of patients in each group =35. Group A: treated with 500 mL·d^{-1} of enteral nutrition for 1 month; Group B: 500 mL·d^{-1} of enteral nutrition for 3 months; Group C: given free diet (control group).

Abbreviations: BMI, body mass index; NYHA, New York Heart Association; LVEDV, left ventricular end diastolic volume; LVESV, left ventricular end-systolic volume; LVEF, Left Ventricular Ejection Fraction; FS, fractional shortening; CO, cardiac output.

fraction, B-type natriuretic peptide (BNP), interleukin-6 (IL-6), C-reactive protein (CRP), and tumor necrosis factor-α (TNF-α) were examined by color B-mode ultrasound.

Ethical considerations

Ethical approval was obtained from the Clinical Research Ethics Committee of The First Affiliated Hospital of Soochow University. Permission to conduct the study in the selected center was also obtained. The subjects participated voluntarily in the study, and were informed of its purposes. A written informed consent was obtained from every eligible subject.

Statistical method

SPSS 22.0 software (IBM Corp., Armonk, NY, USA) was used for statistical analysis. The data were examined by χ^2 and the measurement data were represented by mean ± standard deviation. Student's *t*-test was used for intragroup comparison of indicators before and after treatment. χ^2 test was used for inter-group comparison. $P<0.05$ was considered statistically significant difference.

Result

Comparison of index observation

Table 2 shows the changes in indicators including the body weight, TSF, AMC, total protein, albumin, and hemoglobin among the 3 groups.

The results of the analysis (Table 2) indicate that in Group A and B, after adjuvant therapy with enteral nutrition, patients had obvious increase (all $P<0.05$ or $P<0.01$) in body mass, TSF, AMC, total protein, albumin, and hemoglobin. In the Control Group, compared with the pretreatment level, the above indicators all increased, but without statistical significance ($P>0.05$). This indicates that free diet alone did not significantly improve malnourished elderly patients' nutritional status. In Group B, the levels of all the above indicators increased substantially after treatment (all $P<0.01$). Compared with Group A, Group B exhibited an increase in all indicators, showing that the longer the treatment period was, the more obvious the effect would be.

Changes in cardiac function and serum inflammatory factors

As can be seen in Table 3, in Treatment Groups A and B, the average concentration of BNP, IL-6, TNF-α, and CRP in patients' serum all increased to levels higher than normal. Patients' cardiac function was improved compared with that before treatment. Inflammatory cytokine levels decreased compared with the normal value, and Group B demonstrated the most obvious decrease. With heart function improved, serum concentrations of inflammatory factors BNP, IL-6, TNF-α, and CRP considerably decreased ($P<0.05$). Group B had more significant improvement in cardiac function and the most obvious decrease in serum inflammatory factors ($P<0.01$). In the Control Group, patients did not have obvious improvement in cardiac function and the decrease in serum inflammatory factors was not statistically significant ($P>0.05$).

Safety evaluation

Major adverse cardiovascular events include the following three: cardiovascular death, myocardial infarction, and stroke. In this study, no adverse events were found in the two enteral nutrition-supported groups. On the contrary, in the Control Group, one patient died of myocardial infarction. But the correlation between the major adverse cardiovascular events and enteral nutrition needs further data validation.

Table 2 Comparison of nutrition indicators among the 3 groups of patients before and after the treatment

Group	BMI [kg·(m²)⁻¹]	TSF (mm)	AMC	Total protein (g·L⁻¹)	Albumin	Hemoglobin
Group A						
Before	23.6±1.5	6.6±1.2	16.4±2.2	54.6±6.3	31.5±4.3	114.2±9.2
After	25.4±2.1*	7.4±1.1*	17.5±2.3*	68.3±6.1*	36.7±5.6*	119.8±10.2*
Group B						
Before	21.8±2.1	6.8±1.1	15.9±3.1	52.7±5.8	32.4±6.1	111.7±8.1
After	23.9±2.2*	8.6±0.9**	18.4±2.5**	72.6±8.5**	37.9±4.8**	125.3±7.6**
Group C						
Before	22.6±1.1	6.5±1.8	17.4±1.6	55.5±5.2	32.6±5.8	113.3±8.5
After	23.1±2.2	6.8±2.1	18.3±2.5	56.3±6.1	33.2±5.6	115.6±9.2

Notes: Compared to this group before treatment, *$P<0.05$, **$P<0.01$. Group A: treated with 500 mL·d⁻¹ of enteral nutrition for 1 month; Group B: 500 mL·d⁻¹ of enteral nutrition for 3 months; Group C: given free diet (control group).

Abbreviations: BMI, body mass index; TSF, triceps skin fold thickness; AMC, upper arm muscle circumference.

Table 3 Comparison of serum inflammatory factors and LVEF among 3 groups before and after the treatment

Group	LVEF (%)	BNP (pg/mL)	IL-6 (pg/mL)	TNF-α (nmol/L)	CRP (mg/L)
Group A					
Before	33.8±5.1	425.6±41.5	223.5±19.4	28.6±2.9	13.3±2.2
After	35.5±6.2*	331.2±36.6*	214.2±18.5*	25.1±3.2*	10.2±1.8*
Group B					
Before	34.6±4.4	429.7±39.7	226.7±21.2	27.7±3.1	14.5±2.3
After	37.8±6.7**	313.9±37.5**	209.6±17.8**	24.1±3.4**	9.2±2.3**
Group C					
Before	35.3±3.8	421.4±45.7	231.4±20.2	28.2±4.4	13.8±2.7
After	35.4±4.2	418.6±39.8	225.9±25.8	28.4±5.1	14.1±3.1

Notes: Compared to this group before treatment, *$P<0.05$, **$P<0.01$. Group A: treated with 500 mL·d^{-1} of enteral nutrition for 1 month; Group B: 500 mL·d^{-1} of enteral nutrition for 3 months; Group C: given free diet (control group).

Abbreviations: LVEF, left ventricular ejection fraction; BNP, B-type natriuretic peptide; IL-6, interleukin-6; TNF-α, tumor necrosis factor-α; CRP, C-reactive protein.

Discussion

The study found that the main cause of heart failure was the exhaustion of heart energy. Compared with other organs, heart requires more energy. Myocardial energy metabolism influences not only its systolic function, but also its diastolic function.[9,10] If the body cannot produce enough energy, it causes operating problems in the heart, which lead to heart diseases. Elderly patients with heart failure usually have congested system circulation or pulmonary circulation featured by long course of disease, bad nutritional status, and substantial weight loss, which easily aggravates heart energy metabolism and leads to heart failure.[11] Due to intestinal congestion and seroperitoneum, elderly patients usually have anorexia or eat less. Therefore, they often suffer from malnutrition or even intestinal protein loss. Also due to high metabolism and high consumption, the protein catabolic rate is quite high with abnormal amino acid protein metabolism. This may cause negative nitrogen balance, leading to cachexia. A vicious circle between malnutrition and heart failure is thus formed, resulting in higher incidence of complications and mortality. Thus, for elderly patients with heart failure who have just been admitted to the hospital, besides treatment for heart failure, assessment of malnutrition and nutritional risk should also be performed so as to carry out timely therapy to regulate the patient's nutrition energy metabolism.

The result of this research indicates that the use of enteral nutrition during conventional treatment of elderly patients with heart failure helps to maintain patients' gastrointestinal function, promote protein synthesis, improve patients' nutrition status, adjust inflammatory cytokine levels, and improve cardiac function.[12–14] The longer the treatment period is, the more obvious the improvement in cardiac function and inflammatory cytokine levels will be. Patients on free diet showed no obvious improvement in nutrition indicators after the treatment, the levels of some indicators having even decreased. The cardiac function and inflammatory cytokine levels were improved, but not to a large extent, indicating that elderly patients with heart failure had a negative balance. It is shown that patients had not only digestion and absorption barriers to nutrient substrate, but also inadequate intake of energy and protein.

Researches at AMARE and others also proved that malnutrition had greater influence on elderly patients with heart failure.[15] Applied at early stages, enteral nutrition energy metabolism regulation therapy could considerably improve patients' life quality.[16] Also, the time period of enteral nutrition therapy was closely related to the improvement of patients' nutrition status. Inflammatory cytokines CRP and IL-6 had negative correlation with left ventricular ejection fraction, indicating that inflammatory cytokines could directly damage the heart. Therefore, based on heart failure control, comprehensive treatment could be achieved by strengthening the nutrition energy metabolism regulation therapy and improving patients' physical fitness. Meanwhile, in this study, right ventricular ejection fraction also showed a negative correlation with two inflammatory factors (CRP and IL-6). For patients supported by enteral nutrition, the value of right ventricular ejection fraction could be improved, but there was no significant difference ($P>0.05$, data not shown).

Enteral nutrition is an intestinal immune compound preparation. It is a polymer readily metabolized with reasonable combination and designed in accordance with human metabolic characteristics. Anabolically, it is high in calorie, protein, and fat, yet low in carbohydrate. RruiDai nutrient solution contains immune nutrients ω3 fatty acid, nucleotides, and antioxidant vitamins A, E, and C.[17] ω3 fatty acid has a strong anti-inflammatory effect, which could inhibit the production of immune inhibitor prostaglandin II. Vitamins A, E, and C could improve the body's antioxidant capacity,

remove free radicals, and improve immunity. RruiDai nutrient solution contains a small amount of dietary fiber, which is easy to digest and absorb. It could protect intestinal mucosal barrier and prevent intestinal bacteria shift. It could also protect intestinal tract and the immune function, significantly reducing the incidence of intestinal infection and prevent flora imbalance.[18]

Conclusion

Most elderly patients with heart failure have different levels of malnutrition. It needs to be diagnosed in time and treated with nutrition energy metabolism regulation therapy making use of the enteral nutrition. The treatment of malnutrition should be carried out in parallel with that of heart failure. For one thing, it could improve patients' nutrition status, immunity, and life quality. For another, it could reduce inflammatory cytokine levels, improve patients' cardiac function, and enhance the effect of treatment for heart failure. Therefore, it is more than necessary to properly use nutrition energy metabolism regulation therapy. At the same time, it could prevent the occurrence of respiratory infection, respiratory failure, and other complications, avoiding the development of cachexia and reducing time spent in hospital and mortality.

Disclosure

The authors report no conflicts of interest in this work.

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