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CLINICAL STUDY

The effectiveness of oral essential aminoacids and aminoacids containing dialysate in peritoneal dialysis

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Abstract

Background/Aim: Oral essential amino acids (AAs) containing supplements (EAS) and AA containing dialysate (ACD) are frequently used in peritoneal dialysis (PD) patients with malnutrition. The present study was conducted to investigate two strategies and compare their effects on the malnutrition status of PD patients. *Materials and Methods*: A total of 31 EAS, 14 ACD patients were enrolled in this study. Serum albumin levels were lower than 3.5 g/dL in all subjects. EAS group patients took five pills containing AAs three times a day with meals. In the other, 2.000 cc of 1.1% ACD was given to patients daily during the study. Demographic and laboratory parameters were analyzed and compared at baseline and 6th month. *Results*: Significant increases in BMI, albumin, and protein in both groups. Mean albumin levels increased significantly by 0.54 g/dL in ACD group ($p < 0.005$) and 0.49 g/dL in EAS group ($p < 0.001$) following 6 months. Mean albumin and delta albumin levels did not differ between two groups. *Conclusion*: These strategies may play an important role in increasing albumin levels and improving the nutritional status of PD patients.

Keywords

Albumin, amino acid, dialysate, malnutrition, peritoneal dialysis

History

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Introduction

Protein-energy malnutrition (PEM) frequently occurs in patients on peritoneal dialysis (PD) and has emerged as an important risk factor in the incidence of morbidity and mortality during therapy.[1,2] PEM has been found among half of patients undergoing PD. Many factors are involved in the development of PEM, such as uremic toxins, inflammation, and loss of serum proteins and amino acids (AAs) from the peritoneal membrane.[3–5] Serum albumin has been used as an acceptable indicator for nutritional status, and a decrease of serum albumin levels is an independent risk factor for morbidity and mortality in end-stage renal disease.[6–9] Inadequate intake of protein and calories also affects nutritional status, and intake of energy and protein for many dialysis patients is lower than the recommended requirements.[9–11] One of the acceptable approaches to improve PEM in patients on maintenance PD is the addition of a dietary nutrient such as AAs containing dialysate (ACD) or oral essential AAs containing supplements (EAS) as part of the therapy.[11–17] Many previous studies have investigated the effects of either ACD or oral EAS for treatment of malnutrition in PD patients.[7,8,12–16] However, to our knowledge, there is no data which compares the effectiveness of these two strategies in patients undergoing PD. In this study, we strove to compare the effects of ACD and oral EAS in PD patients.

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Materials and methods

This retrospective study investigated the effects of AAs containing dialysate and essential AA supplements on patient nutritional profiles for a 6-month period. Oral or intraperitoneal essential AA supplementation was added to treatment of all malnourished patients, whose serum albumin levels were lower than 3.5 g/dL after all interventions in support of positive nitrogen balance. All subjects were 18 years or older, and longer than 3 months under PD. Forty-five PD patients enrolled in the study. Of those, 31 patients were in the EAS group, and 14 were in the ACD group.

Each patient in the EAS group took five pills containing AAs (isolocine, leucine, phenylalanine, valine, methionine, L-lysine, L-thyreonine, L-tryptophan, L-histidine, L-tyrosine) three times a day with meals during a 6-month period. In the ACD group, 2.000 cc of 1.1% AAs containing dialysate was given once a day during the study. Patients with peritonitis,

malignancies, amyloidosis, enteropathy and active-chronic inflammatory disorders and patients who were non-compliant with therapy were excluded. Additionally, patients under oral EAS plus ACD therapy were excluded from the study. Demographic and clinical properties of the patients were noted from the files. Serum albumin, protein, cholesterol, triglyceride, hemoglobin, ESR and hsCRP levels were recorded from the database. The serum albumin level was measured by bromcresol green assay. Demographic and laboratory parameters were analyzed at the baseline and 6 months after commencement of the therapies.

Results are presented as a mean (±standard deviation). All analyses were performed using SPSS 15.0 (SPSS, Chicago, IL). For paired samples at the baseline and at the end of the 6th-month period, the Wilcoxon linear mixed model was used. For analysis of parametric variables, the Student's *t*-test was used, and for non-parametric variables and for comparing the differences (delta values) the Mann–Whitney *U* test was used. Pearson and Spearman correlation tests were performed to assess the correlations between parameters.

Results

At the baseline, there were no significant differences between the EAS and ACD groups regarding gender, age, body mass index (BMI), dialysis duration and diabetes mellitus rates (Table 1). Hemoglobin levels, lipid parameters, serum albumin and protein levels, ESR and C-reactive protein (CRP) levels were not statistically different between the two groups before the therapies (Table 1).

Serum protein and albumin levels, lipid parameters, ESR, CRP and BMI were compared at the beginning of the therapy and after 6 months of therapy (Table 2). There were significant increases in BMI, serum albumin levels and serum protein levels in both groups, but triglyceride levels had increased significantly only in the ACD group (Table 2). The ESR was significantly reduced in both groups after 6 months, but during the same time period, hsCRP levels did not change significantly (Table 2). Mean albumin levels increased to 0.54 g/dL (22%) in the ACD group and 0.49 g/dL (19%) in the EAS group after 6 months of therapy. Mean albumin and delta albumin levels did not differ between the two groups (Table 3). There was a significantly positive correlation between serum protein and blood hemoglobin levels ($p < 0.005$, $r = 0.72$) in the ACD group. However, there was neither a significant correlation between serum albumin, protein, hsCRP and ESR levels, nor was there a significant change in these levels after therapy. Serum bicarbonate levels between the two groups were similar at the beginning of the study. In contrast, at the 6-month mark, serum bicarbonate levels were higher in the oral EAS group than the ACD group. Despite this variance, the reduced amount of serum bicarbonate levels was not statistically significant ($p > 0.05$) in the ACD group (Table 2). Four patients in the oral EAS supplement group and five in the ACD group were given oral bicarbonate supplements ($p > 0.05$). Serum calcium decreased slightly in both groups, although the decline was not considered statistically significant. Serum phosphate levels decreased slightly in the ACD group and increased slightly in the oral EAS group, without statistically significance (Table 2).

Table 1. Demographic and laboratory characteristics of both groups.

	EAS group ($n = 31$)	ACD group ($n = 14$)	p Value
Age	48.7 ± 16.4	47.4 ± 13.5	NS
Gender (F/M)	14/17	7/7	NS
Dialysis duration (m)	24.1 ± 20.5	32.9 ± 22.6	NS
Diabetes mellitus	12	5	NS
BMI (kg/m^2)	25.1 ± 5.1	25.8 ± 5.5	NS
Hemoglobin (g/dL)	11 ± 1.2	11.1 ± 1.6	NS
Serum albumin (g/dL)	2.69 ± 0.39	2.85 ± 0.46	NS
Serum protein (g/dL)	6.03 ± 0.81	6 ± 0.62	NS
Cholesterol (mg/dL)	209.5 ± 68.2	190.4 ± 30.7	NS
Triglyceride (mg/dL)	165.9 ± 87	152.4 ± 51.3	NS
ESR (mm/h)	51.5 ± 20.2	54.8 ± 34.7	NS
hsCRP (mg/dL)	1.98 ± 1.80	1.11 ± 1.16	NS

Note: EAS, essential amino acid supplements; ACD, amino acid containing dialysate; m, month; BMI, body mass index; ESR, erythrocyte sedimentation rate; hsCRP, high-sensitive C-reactive protein.

Discussion

In this study, we observed that ACD and EAS increased BMI, serum albumin and protein levels in PD patients with malnutrition. Additionally, the ESR decreased during the follow-up period, but no change in serum hsCRP levels was observed in either group. There was no difference in the rate of change of serum albumin, protein levels and BMI when comparing both groups at the end of the follow-up period.

During PD, loss of AAs of approximately 2–4 g/d and protein loss of 5–15 g/d from dialysate were reported.[8,18] Additionally, inadequate intake of protein and calories leads to malnutrition in many patients.[9–11] It has been reported that a decrease in albumin levels is closely related to morbidity and mortality in patients undergoing PD treatment.[19] Therefore, adequate protein and calorie supplementation is essential for improvement of malnutrition and leads to decreases in morbidity and mortality in these patients.

In a study conducted by Poole et al., oral protein supplements were added to the meal of a total of 33 PD patients.[12] The mean albumin levels were 3.23 g/dL at the baseline, and these increased slightly to 3.26 g/dL at the end of 3 months in 33 patients. Poole et al. argued that oral protein supplements are not efficient in PD patients.[12] In another study, daily protein supplements were added to the meal of incident-PD patients, who were then followed-up for 12 months.[20] The mean albumin level of 90 patients was 3.75 g/dL, and no significant increase was observed in these studies following their completion.[12] However, patients with peritonitis were not excluded from these studies. During their follow-up periods,[12,20] Eustace et al. revealed that oral essential AAs are more effective in patients with very low serum albumin levels than in patients who have subnormal albumin levels.[21]

In our study, the albumin levels were around 2.8 g/dL, which is lower than albumin levels in patients who were enrolled in the other studies referenced herein, and data from patients with peritonitis were excluded. These results reflect the fact that the nutritional status of patients in our study was

Table 2. Clinical and laboratory results of both groups at baseline and after 6 months.

	EAS group ($n=31$)			ACD group ($n=14$)		
	Baseline	6 months	p Value	Baseline	6 months	p Value
BMI (kg/m^2)	25.1 ± 5.1	25.3 ± 4.8	<0.05	25.8 ± 5.5	26.5 ± 5.1	<0.01
Hemoglobin (g/dL)	11 ± 1.2	11.1 ± 1.7	NS	11.1 ± 1.6	11.3 ± 2.2	NS
Serum Albumin (g/dL)	2.69 ± 0.39	3.18 ± 0.49	<0.001	2.85 ± 0.46	3.4 ± 0.37	<0.005
Serum Protein (g/dL)	6.03 ± 0.81	6.28 ± 0.67	<0.01	6 ± 0.62	6.45 ± 0.77	<0.05
Cholesterol (mg/dL)	209.5 ± 68.2	218.5 ± 55.6	NS	190.4 ± 30.7	226.8 ± 54	NS
Triglyceride (mg/dL)	165.9 ± 87	178.7 ± 96.9	NS	152.4 ± 51.3	263.1 ± 122.2	<0.01
ESR (mm/h)	51.5 ± 20.2	42.4 ± 19.6	<0.01	54.8 ± 34.7	36.8 ± 20.2	<0.005
hsCRP (mg/dL)	1.98 ± 1.80	1.84 ± 2.21	NS	1.11 ± 1.16	1.23 ± 1.15	NS
Serum bicarbonate	19.6 ± 1.95	19.8 ± 1.86	NS	19.1 ± 2.1	18.7 ± 1.5	NS
Serum creatinine (mg/dL)	7.4 ± 3.1	7.8 ± 2.7	NS	6.6 ± 2.1	7.2 ± 2.4	NS
Serum cCa (mg/dL)	9.53 ± 0.73	8.96 ± 1.12	NS	8.99 ± 1.02	8.93 ± 0.63	NS
Serum phosphat (mg/dL)	4.7 ± 1.48	4.93 ± 1.64	NS	4.41 ± 0.81	4.67 ± 0.85	NS
Serum potassium (mg/dL)	4.63 ± 0.84	4.69 ± 095	NS	4.77 ± 0.62	4.61 ± 0.77	NS
İPTH (pg/mL)	343.7 ± 348.6	342.7 ± 232.6	NS	325.7 ± 277.8	357.6 ± 182.9	NS

Note: BMI, body mass index; ESR, erythrocyte sedimentation rate; hsCRP, high-sensitive C reactive protein; cCa, corrected calcium; iPTH, intact parathyroid hormone.

Table 3. The comparison of changed ratio of laboratory parameters.

	EAS group ($n=31$)		ACD group ($n=14$)		p Value
	Δ mean	Δ%	Δ mean	Δ%	NS
BMI (kg/m^2)	0.25	1	0.68	3	NS
Serum albumin (g/dL)	0.49	19	0.54	22	NS
SERUM PROTEIN (G/DL)	0.25	4	0.45	8	NS
ESR (mm/h)	−9	18	−16	29	NS
hsCRP (mg/dL)	−0.14	7	0.12	9	NS

Note: BMI, body mass index; ESR, erythrocyte sedimentation rate; hsCRP, high-sensitive C reactive protein.

poorer at the baseline than the nutritional status of patients taking part in the other studies, and the negative effects of inflammatory situations were eliminated from our collected data. All of these conditions may explain the different results when comparing our study with other relevant research endeavors.

During the exchange period of 2 L of 1.1% AAC dialysate (4–6 h), approximately 80% (∼18 g) of AAs is absorbed from the peritoneal membrane.[7,22] This AAs replacement may contribute AA's recruitment in PD patients who are experiencing malnutrition. Many studies have revealed improvements in nutritional parameters, such as a significant increase in serum protein, albumin levels, nitrogen balance, BMI and recovery of plasma AAs profile after 1.1% AAC dialysate initiation in PD patients.[7,23,24] A review of Reinhart reveals the argument that the ESR reflects chronic inflammatory situations more so than hsCRP, while hSCRP reflects acute inflammatory or infective illness rather than the ESR.[25] Similarly, in our study significant increases in BMI, serum albumin and protein levels were observed in malnourished patients after initiation of AAC dialysate. Additionally, decreases in the ESR absent changes in hsCRP levels at the end of study reflect the fact that malnutrition-related chronic inflammation improved after initiation of AA supplements. These results indicate that AA supplementation by any method may play an important role in the improvement of malnutrition/inflammation syndrome in PD patients.

There were some limitations to our study. Objective nutritional indicators, such as the subjective global assessment index, protein catabolic rate, the protein equivalent of nitrogen appearance, anthropometric measurements, clinical outcomes and cost-effectiveness, were not assessed because of insufficient data and the overall design of the study.

Conclusions

Efficient oral EAS and AAC dialysate were found to have a similar effect on nutritional parameters in malnourished patients who were treated with PD. These results reflect that both oral and intra-peritoneal protein supplements may be employed to improve malnutrition in PD patients. However, these results must be confirmed through prospective, well-designed studies in order to fully reveal the effects of protein supplements with respect to these treatment modalities in PD patients.

Declaration of interest

The authors have no financial relation with companies associated to the findings of this study.

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