CLINICAL SCIENCE OF NUTRITION

Original Article

Clin Sci Nutr 2019; 1(3): 134-40 • DOI: 10.5152/ClinSciNutr.2019.949

Effects of intradialytic parenteral nutrition on antioxidant capacity in hemodialysis patients aged over 60 years

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Cite this article as: Olcay Eminsoy İ, Eminsoy G. Effects of intradialytic parenteral nutrition on antioxidant capacity in hemodialysis patients aged over 60 years. Clin Sci Nutr 2019; 1(3): 134-40.

ABSTRACT

Objective: The aim of the present study was to investigate whether intradialytic parenteral nutrition can affect the antioxidant capacity of hemodialysis patients aged over 60 years.

Methods: The study comprised 20 participants from the Baskent University Umitkoy Dialysis Center; 10 who had intradialytic parenteral nutrition [IDPN, study group (SG)] that included 500 cc of amino acid solution and 500 cc of dextrose were compared with the group that did not have IDPN for 1 month. The randomly selected group had IDPN. Serum albumin, prealbumin, cholesterol, blood urea nitrogen (BUN), creatinine, potassium, and phosphorus; weight; body mass index (BMI); hand muscle strength (HMS); and middle upper arm circumference (MUAC) were measured and compared at baseline and at the end of the study between two groups. After 4 weeks of treatment, thiobarbituric acid reactive substances (TBARS), glutathione peroxidase (GSH-Px), total antioxidant capacity (TAC), and tumor necrosis factor-alpha (TNF-α) values of two groups were compared.

Results: There was no statistically significant difference between the baseline and outcome values of both groups in weight, BMI, HMS, MUAC, BUN, creatinine, potassium, albumin, and cholesterol values during the 1 month period. The SG had 19.97±7.18 kcal/kg/day energy and 0.77±0.21 g/kg/day protein intake. The control group (CG) had 18.66±3.22 kcal/kg/day energy and 0.64±0.11 g/kg/day protein intake. TBARS were 1.84±0.10 μM in the SG and 1.95±0.11 μM in the CG (p=0.031). The mean of TAC was 334.34±23.20 mmol/L in the SG and 290.23±17.72 mmol/L in the CG (p=0.002). The mean of GSH-Px was 305.63±35.31 U/L in the SG and 244.80±17.66 U/L in the CG (p=0.001). The mean of TNF-α was 171.24±25.37 pg/mL in the SG and 193.85±11.82 in the CG (p=0.017).

Conclusion: Results suggest that energy and protein intake were very low in both groups. TBARS and TNF-α were lower in the SG than in the CG. TAC and GSH-Px were higher in the SG than in the CG. IDPN can be used both to increase the protein and energy intake and antioxidant capacity for patients aged over 60 years.

Keywords: Antioxidant capacity, elderly, intradialytic parenteral nutrition, malnutrition

Introduction

Protein energy wasting (PEW), inflammation, impaired immune responsiveness, and oxidative stress (OS) are the strongest risk factors for mortality in chronic dialysis patients. 27.3% of hemodialysis patients (HDPs) have moderate to severe malnutrition (1, 2). Hemodialysis (HD) removes approximately 10–12 g of amino acids and 200–480 kcal of energy in each session. Energy and protein consumption of HDP may be lower than recommended (3). Protein and energy malnutrition is very common in HDP and end-stage renal disease (ESRD) that affects 50% of the patients (4). Inadequate nutrient intake is associated with age, dialysis age, acute or chronic comorbidities, fluid overload, anemia, and poor appetite (5). Intradialytic parenteral nutrition (IDPN) is a mixture of lipid, amino acid, and glucose solution (4). IDPN improves body weight and serum albumin level in malnourished HDP (6). Prealbumin and Subjective Global Assessment (SGA) are important markers for malnutrition. It is suggested that IDPN has to begin in a condition not worse than SGA-B to improve the survival and nutrition status of HDPs (7).

Hemodialysis patients have increased OS because of an increased pro-oxidative activity and a decreased antioxidant system. Glutathione peroxidase (GSH-Px) is one of the enzymes that protect membrane lipids and cellular

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Submitted: 23.08.2019 **Accepted:** 13.12.2019

and extracellular components from oxidative damage (8). During lipid peroxidation, thiobarbituric acid reactive substances (TBARS) are produced (9). HDPs have significantly higher level of TBARS than peritoneal dialysis patients (10). Total antioxidant capacity (TAC) is decreased when OS occurs (11). HDPs have increased OS that they have greater risk for cardiovascular disease. Antioxidative treatment can be beneficial for reducing OS (12). Tumor necrosis factor-alpha (TNF-α) is a pro-inflammatory cytokine that increases during damages in HDPs (13).

There are many factors that affect muscle loss, but the most important ones are inadequate protein intake and inactivity for elderly individuals. Consuming the proper amounts of dietary protein can slow down sarcopenia in aging. A daily protein intake of 1.3–1.4 g/kg/day can be safe and useful for healthy older adults (14). Serigne et al. (15) found that elderly HDPs have an energy intake of 20–25 kcal/kg/day and a protein intake of 0.84–0.95 g/kg/day. Protein and energy malnutrition ranges from 50% to 60% in dialysis patients (16). According to the results of the European study in chronic kidney disease stage 4 patients (EQUAL study), PEW was higher among women, increasing with age (17). Hand muscle strength (HMS) is an important parameter that can show sarcopenia, malnutrition, and/or frailty. The method is inexpensive, rapid, and simple for elderly individuals, but it is less common in HDPs (18).

Intradialytic parenteral nutrition can be a useful tool for elderly HDPs' malnutrition. OS is an important factor for all chronic patients, and HD can increase the OS for all patients. We attempt to understand the effects of IDPN for both antioxidant capacity and malnutrition in elderly HDPs in which the number of these patient groups increases each day.

Methods

This was a randomized, clinical, two-group comparison trial of nutritional counseling plus IDPN versus nutritional counseling alone in HDPs aged over 60 years. The study protocol was approved by the ethics committee of Baskent University (no. KA09/201, 08.05.2009). The study included approximately 20 HDPs who were aged over 60 years, with a dialysis age over at least 6 months, with three times a week HD session for 4 h, not using any medication that affects protein metabolism, and with no diabetes mellitus and cancer. A total of 20 patients were randomly selected, with 10 who could tolerate IDPN as the study group (SG) and the other 10 as the control group (CG).

All patients received nutritional counseling and followed their diet programs that were prepared for each patient, containing 35 kcal/kg/day energy and 1.2 g/kg/day protein. The dry weight of all patients was used for calculations. Daily food consumption of all patients was collected twice a week in which 1 day was a dialysis day for both groups at 0, 1, 2, 3, and 4 weeks of the study. Food consumption of all patients was calculated by the BEBIS program after one portion of the food was determined.

The SG included five female and five male patients who were given 500 cc of amino acid solution and 10% dextrose for 1 month in every dialysis session. The CG comprised two female and eight male participants who did not use any additives. Serum albumin, prealbumin, cholesterol, creatinine, potassium, and phosphorus; weight; body mass index (BMI); HMS; and upper middle arm circumference were measured at baseline and at the end of the study. After 4 weeks of treatment, TBARS, GSH-Px, TAC, and TNF-α values were measured for two groups. Normal laboratory values were based on the BU laboratory normal values.

Statistical analysis

Anthropometric measurements, biochemical results, and food consumption were analyzed by Statistical Package for the Social Sciences 17 (SPSS Inc., Chicago, IL, USA). The significance of the intra-group variability of HD energy, protein, carbohydrate, fat, and other nutrients was tested using the Freidman test. HDPs' energy, protein, and other nutrients were tested by using the independent samples t-test. The inter-group Mann–Whitney U test and the in-group Wilcoxon test were used to test the significance of the energy, protein, and other nutrients received by the HDPs.

Results

The average ages of the SG were 69.40±5.49 years in women and 69.80±5.49 years in men. The average ages of the CG were 67.50±10.60 years in women and 70.00±5.70 years in men.

The results of anthropometric measurements are shown in Table 1. There were no any differences between the initial and week 4 measurements of weight, BMI, HMS, and MUAC. BMI was 23.99±2.38 kg/cm^2 in the CG and 23.41±3.34 kg/cm^2 in the SG (p=0.986).

The results of laboratory findings are shown in Table 2. Increases in prealbumin levels were statistically significant in the CG at baseline and the end of the study. Prealbumin levels were 23.94±10.95 mg/dL at baseline and 29.79±8.17 at the end of the study in the CG (p=0.037). Potassium levels were 5.42±0.58 mmol/dL at baseline

Table 1. Anthropometric measurement of the control group and study group

	Control group		Study group		
Measurements	$\bar{\chi}$	**SD**	$\bar{\chi}$	**SD**	**p**
Initial weight (kg)	67.16	11.95	59.77	12.36	0.288
Weight week 4 (kg)	67.13	12.23	60.91	12.64	0.540
BMI initial (kg/cm^2)	24.00	2.25	23.34	3.23	1.000
BMI week 4 (kg/cm^2)	23.99	2.38	23.41	3.34	0.986
HMS initial	16.00	10.02	11.99	7.41	0.342
HMS week 4	16.84	10.65	12.21	6.70	0.210
MUAC initial (cm)	16.00	10.02	23.70	6.16	0.209
MUAC week 4 (cm)	16.84	10.65	24.70	4.87	0.379
Height (cm)	166.50	10.53	160.60	10.03	0.036

p: Mann–Whitney U test, $p<0.05$. BMI: body mass index; HMS: hand muscle strenght; MUAC: middle upper arm circumference; SD: standard deviation

and 5.28±0.88 mmol/dL at the end of the study in the CG (p=0.838), which was slightly lower, but was not statistically significant. There were no changes in blood cholesterol level of the patients.

Table 3 shows the average nutrient intake level of both the control and study groups. The average energy intake of both groups was very low. Energy intake was 18.66±3.22 kcal/kg/day in the CG and 19.97±7.18 kcal/kg/day in the SG (p=0.597). Protein intake was 0.64±0.11 g/kg/day in the CG and 0.77±0.21 g/kg/day in the SG (p=0.131). The average potasium consumption was 1094.06±230.14 mg in the CG and 889.63±339.39 in the SG (p=0.174). The average phosphorus consumption was 639.63±99.25 mg in the CG and 533.94±164.04 in the SG (p=0.151). The average zinc intake was 5.90±0.72 mg/day in the CG and 4.74±1.23 in the SG (p=0.028), and it is statistically important.

TBARS (μM), TAC (mmol/L), GSH-Px (U/L), and TNF-α (pg/mL) evaluation in the CG and SG are shown in Table 4. The blood levels of TBARS, TAC, GSH-Px, and TNF-α were evaluated for both the CG and SG. TBARS levels were 1.95±0.11 μM in the CG and 1.84±0.10 μM in the SG (p=0.031). TAC levels were 290.23±17.72 in the CG and 334.34±23.20 in the SG (p=0.002). GSH-Px levels were 244.80±17.66 U/L in the CG and 305.6±35.31 U/L in the SG (p=0.001). TNF-α levels were 193.85±11.82 pg/mL in the CG and 171.24±25.37 in the SG (p=0.017).

The rate of elderly individuals keeps growing. The elderly population rate was 7.7% in 2013, and it was 8.5% in 2017. According to the Turkey Institution of Statistics projections, it will be 16.3% in 2040 and 25.6% in 2080 in elderly individuals aged over 65 years (19). The percentage of HDPs aged 65 years and older followed up for >90 days in 2016 was 47.7% of all dialysis patients (20). By the time the elderly population rate increases, the HDP number will also increase in Turkey. The rate of elderly individuals in the general population keeps growing, and the dialysis population is increasing in Europe. Protein–energy malnutrition is common in HDPs (18, 21, 22). Malnutrition rates were 5%–10% for patients who were living at home, 30%–60% for patients who were living in some facilities, and 35%–60% for patients who were in the hospital (23).

OS in an important risk factor for cardiovascular disease in HDPs. Glutathione plays a key role for cellular resistance against oxidative damage. Studies about TAC in HDPs show controversial results. The use of multivitamin preparation, including vitamin E, can affect the level of TAC capacity (24, 25). In our study, the level of TAC was higher in the SG, and the amino acid solution can affect the level of TAC. Healthy dietary interventions, including low carbohydrates and Mediterranean diets, may have some beneficial effects on blood pressure, quality of life, and lipid profile, but the effects on OS is uncertain (26, 27). HD causes significant depletion of antioxidants. Vitamin C deficiency was associated with an increased level of several antioxidants and a decreased level of antioxidant GSH-Px (28). In our study, GSH-Px levels were higher in the SG than in the CG. On the other hand, vitamin C, fiber, and vitamin E were similar for the CG and SG. In one randomized, controlled study, the effects of the supplementation of soy or whey protein or placebo during dialysis treatment on the biomarker of inflammation (C-reactive pro-

Table 2. Laboratory findings according to groups and gender					
Laboratory	**Groups**	**Gender**	**Baseline X±SD**	**End X±SD**	**p**
BUN (mg/dL)	Control	Male	74.75±31.88	78.50±17.60	0.499
		Female	70.50±36.06	62.50±0.70	0.655
		Total	73.90±30.63	75.30±16.93	0.813
	Study	Male	69.60±14.89	78.20±15.58	0.345
		Female	55.80±18.74	76.00±14.83	0.138
		Total	62.70±17.53	77.10±15.38	0.059
Creatinine (mg/dL)	Control	Male	9.79±3.29	9.87±2.21	0.779
		Female	5.54±1.06	9.25±3.43	0.180
		Total	8.94±3.43	9.75±2.27	0.285
	Study	Male	9.25±1.76	10.09±1.74	0.345
		Female	7.01±1.67	7.90±1.66	0.138
		Total	8.13±2.00	9.00±1.97	0.139
Potassium (mmol/dL)	Control	Male	5.50±0.55	5.4±0.69	0.833
		Female	5.10±0.84	4.65±1.62	0.655
		Total	5.42±0.58	5.28±0.88	0.838
	Study	Male	5.44±0.52	5.66±0.99	0.345
		Female	5.20±1.39	5.36±1.01	0.684
		Total	5.32±1.00	5.51±0.92	0.306
Phosphorus (mg/dL)	Control	Male	4.55±1.50	5.46±1.60	0.161
		Female	3.88±0.21	7.04±0.92	0.180
		Total	4.42±1.35	5.77±1.59	0.047*
	Study	Male	4.62±1.02	5.88±0.87	0.080
		Female	4.33±1.49	5.05±2.05	0.225
		Total	4.47±1.21	5.46±1.55	0.028*
Albumin (mg/dL)	Control	Male	4.05±0.38	3.97±0.41	0.726
		Female	3.78±0.21	3.90±0.00	0.180
		Total	3.99±0.36	3.96±0.36	0.443
	Study	Male	4.04±0.49	3.95±0.24	0.686
		Female	3.77±0.52	3.94±0.39	0.225
		Total	3.90±0.50	3.95±0.30	0.575
Prealbumin (mg/dL)	Control	Male	26.20±9.51	30.65±7.35	0.123
		Female	14.90±15.55	26.35±13.93	0.180
		Total	23.94±10.95	29.79±8.17	0.037*
	Study	Male	25.92±7.86	25.30±8.46	0.588
		Female	27.16±6.48	33.98±5.69	0.080
		Total	26.54±6.87	29.64±8.19	0.153

Table 2. Laboratory findings according to groups and gender (continued)					
Laboratory	**Groups**	**Gender**	**Baseline X±SD**	**End X±SD**	**p**
Total cholesterol	Control	Male	162.87±34.44	178.75±45.57	0.141
		Female	183.50±6.36	199.50±62.93	0.655
		Total	167.00±31.64	182.90±46.17	0.153
	Study	Male	147.20±20.49	147.20±31.71	0.893
		Female	190.60±50.03	204.40±57.65	0.500
		Total	168.90±42.67	175.80±53.22	0.575
SD: standard deviation; BUN: blood urea nitrogen					

Table 3. Nutrient intake of the control group and study group			
Nutrients	**Control group X±SD**	**Study group X±SD**	**p**
Energy (kcal/day)	1239.86±166.12	1158.26±324.36	0.684
Energy (kcal/kg/day)	18.66±3.22	19.97±7.18	0.597
Carbohyrdate (g/day)	144.76±19.95	130.24±47.89	0.326
Fiber (g/day)	10.87±2.25	8.95±3.85	0.247
Protein (g/day)	42.59±8.05	45.63±9.05	0.143
Protein (g/kg/day)	0.64±0.11	0.77±0.21	0.131
Total fat (g/day)	53.60±10.03	43.79±12.24	0.165
Vitamin A (mg/day)	669.80±88.41	590.41±70.26	0.353
Vitamin E (mg/day)	5.65±1.41	5.08±1.95	0.257
Vitamin K (mg/day)	170.16±45.17	136.61±41.99	0.257
Vitamin B_1 (mg/day)	0.41±0.07	0.36±0.14	0.545
Vitamin B_2 (mg/day)	0.79±0.12	0.67±0.21	0.290
Niasin (mg/day)	6.13±2.10	4.87±2.33	0.112
Vitamin B_{12} (mg/day)	2.15±0.39	1.75±0.52	0.070
Vitamin B_6 (mg/day)	0.64±0.13	0.54±0.20	0.151
Vitamin C (mg/day)	47.93±19.97	41.02±25.72	0.406
Potassium (mg/day)	1094.06±230.14	889.62±339.36	0.174
Calcium (mg/gün)	421.66±69.69	346.80±109.76	0.082
Phosphorus (mg/day)	639.63±99.25	533.94±165.04	0.151
Iron (mg/day)	6.07±0.96	5.14±1.79	0.199
Zinc (mg/day)	5.90±0.72	4.74±1.23	0.028*
Sodium (mg/day)	2444.03±370.15	2225.89±772.50	0.326
p: Mann–Whitney U test, p<0.05. SD: standard deviation			

tein (CRP) and interleukin (IL)-6) were investigated. At the end of the study, it was found that intradialytic protein supplementation during a 6-month intervention reduced inflammation and improved the physical function of HDPs (29). The mean of TNF-α, which is one of the biomarkers of inflammation, was lower in the SG than in the CG.

Table 4. TBARS (μM), TAC (mmol/L), GSH-Px (U/L), and TNF-α (pg/mL) evaluation in the control group and study group

	Control group X±SD	Study group X±SD	p
TBARS (μM)	1.95±0.11	1.84±0.10	0.031
TAC (mmol/L)	290.23±17.72	334.34±23.20	0.002
GSH-Px (U/L)	244.80±17.66	305.63±35.31	0.001
TNF-α (pg/mL)	193.85±11.82	171.24±25.37	0.017

p: Mann–Whitney U test, p<0.05. TBARS: thiobarbituric acid reactive substances; TAC: total antioxidant capacity; GSH-Px: glutathione peroxidase; TNF-A: tumor necrosis factor-alpha; CG: control Group; SG: study group SD: standard deviation

Protein energy wasting is common in ESRD, and it is strongly associated with mortality and adverse outcomes. Intradialytic oral nutrition supplement was found to be beneficial. It reduced the mortality rate and improved some incidence of nutritional status for hypoalbuminemic HDPs (30). IDPN is especially effective with such low serum albumin values. While non-nutritional interventions should also be considered that lead to less inflammation or protein loss (31), it is important to help maintain good nutritional status. Inadequate food intake during HD days is a common practice, and in many countries, the meal is served during dialysis session (31).

A total of 20 HDPs with a serum albumin <39 g/L received 100 mL of 10% ω-3 polyunsaturated fatty acid (PUFA) emulsion during 11 consecutive HD sessions. BMI, serum albumin, transferrin, and lipids were measured before and after treatment. Serum IL-6 and high-sensitivity CRP levels were determined before and after the HD session at baseline and after 4 weeks of treatment. Short-term parenteral administration of ω-3 PUFA is safe and well-tolerated by HDPs. The intervention does not significantly influence markers of inflammation or change the nutritional status of chronic HDPs, but it may attenuate the inflammatory response to HD sessions (32). In our study, we only used amino acid and dextrose in the SG, so there was no effect of any lipid solution on the patients' inflammation parameters (1).

Elderly HDPs are increasing each day. Nutrition is one of the most important factors that affect the survival of the patients. IDPN can both affect the nutritional status and antioxidative capacity of the patients in our study. More longitudinal studies are needed to identify the effects of IDPN on antioxidant capacity in HDPs.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Başkent University (03.06.2009/181 KA09/201).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – M.G.E.; Design – İ.O.E.; Supervision – M.G.E., İ.O.E.; Resources – İ.O.E.; Materials – İ.O.E.; Data Collection and/or Processing – İ.O.E.; Analysis and/or Interpretation – İ.O.E.; Literature Search – İ.O.E.; Writing Manuscript – İ.O.E., M.G.E.; Critical Review – M.G.E.

Conflict of Interest: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

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