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The effect of parenteral nutrition products on infection parameters in patients receiving long-term mechanical ventilation support

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ABSTRACT

Aim: Malnutrition can increase the frequency of infections by reducing the immune system response. Parenteral nutrition (PN) is considered an important treatment for patients who cannot receive adequate oral or enteral nutrition. The contents of nutritional products may be different. In this study, we aimed to investigate the effects of soy-based and olive oil-based parenteral nutrition products on infection parameters.

Material and Method: A total of 82 patients were included in the study, 50 of which were soy (Group 2) and 32 were olive-based (Group 1) parenteral nutrition. Patient files and laboratory results were reviewed. Age, gender, 1st, 7th, 14th and 21st days in intensive care, leukocyte and platelet counts, Neutrophil lymphocyte ratio (NLR), C-Reactive Protein (CRP) values, Acute Physiology and Chronic Health Evaluation (Apache II) score and first blood culture results after hospitalization were recorded.

Results: The 7th and 21st day CRP values in Group 1 were statistically significantly lower than the 7th and 21st days CRP values in Group 2. In Group 1, growth in blood culture was statistically significantly lower and in Group 2 there was a statistically significant early growth.

Conclusion: As a result, it was found that olive oil-based lipid-containing nutritional solutions were more advantageous in terms of infection on intensıve care than soy-based nutrition products. It was concluded that patients who received postoperative mechanical ventilator support fed with olive oil-based parenteral nutrition products had less infectious growth.

Keywords: Inflammation, immunity, intensive care unit, parenteral nutrition, parenteral nutrition solutions

INTRODUCTION

Nutritional support is one of the most important routine treatments in intensive care units (ICU). Malnutrition can increase the frequency of infections by decreasing the immune system response. Consequently, it may cause increased mortality, longer hospital stay and higher costs (1,2). Parenteral nutrition (PN) is considered an important treatment for patients who can't receive adequate oral or enteral nutrition (3).

In cases where the gastrointestinal tract is functional, it is recommended that patients be fed enterally as soon as possible (4). Parenteral nutrition is recommended for patients who cannot be given enteral nutrition within 24 hours after hospitalization in the ICU (5). Parenteral nutrition should include a balance between glucose, amino acids and lipids and vitamins, minerals and trace elements for the individual nutritional needs of patients. There are many types of parenteral nutrition products such as soy-based and olive oil-based. Although soy-based products are used extensively, olive oil-based products have also been used in recent years.

Adequate nutrition must be provided in the ICU to support immune functions. Nutrition with products containing arginine, nucleotides, ω-3 polyunsaturated fatty acids (PUFA), glutamine, and products that have been shown to increase the cellular immune response to infection in-vivo and in-vitro have been defined as immunonutrition (6). In the studies conducted, it was observed that acute phase reactants such as serum C-Reactive Protein (CRP) were at lower levels in immunonutrition groups. Nutritional products in the market can contain different amounts of amino acids, lipids, vitamins, minerals and trace elements.The amount of oleic acid 24 65 and the oleic acid-linoleic acid ratio was higher in the olive oil-based nutrition product we used in our study. In comparison, the amount of linoleic

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acid in the soy-based nutrition product was higher. We aimed to investigate the effects of soy-based and olive oil-based parenteral nutrition products used in ICU on infection parameters.

MATERIAL AND METHOD

Pursuant to obtaining ethical clearance from the institutional review board (IRB) on December 14th, 2020 (Protocol Number: KAEK-143-09), a retrospective analysis was conducted on the medical records of 868 patients who were admitted to the ICU for various pathologies during the time frame of September 2019 through September 2020. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

As the inclusion criteria;

- were admitted to the ICU with mechanical ventilator support or who received support for the mechanical ventilator on the first day of admission to the intensive care unit
- needed mechanical ventilator support for 21 days
- only parenteral nutrition in the first 24 hours 21 days of only parenteral nutrition
- being a patient of postoperative surgery due to ileus or intestinal ischemia
- nutritional administration with central venous catheter were accepted. Use of only central venous catheter as parenteral feeding route

As exclusion criteria;

- having a history of immunosuppression
- being diagnosed with malignancy
- staying in ICU for less than 21 days or weaning from mechanical ventilation before 21 days
- peripheral vascular access was used as a parenteral nutrition route.
- having any growth in cultures taken on the day of admission
- patients using steroids
- patients whose culture results indicate contamination or colonization

Patients with a history of immunosuppression, a history of cancer, patients who were treated for less than 21 days in the ICU, patients with peripheral vascular access to the feeding tract, patients with growth in cultures taken on the day of hospitalization or in cultures other than blood cultures taken later were excluded from the study. Central catheters were not routinely replaced, only reproductive ones. The patients' energy needs were calculated by applying the Harris Benedict formula, Eighty-two (82) patients were enrolled in the study. Patients fed with olive oil-based emulsions used at different times according to their presence in the hospital pharmacy were named Group 1 (n: 32) and the patients fed with soybean oil-based emulsions were divided into two groups, named Group 2 (n: 50). A retrospective chart review was conducted to analyze the medical records of patients admitted to the intensive care unit (ICU). Demographic data, including age and gender, as well as laboratory results including leukocyte and platelet count, Neutrophil lymphocyte ratio (NLR), C-reactive protein (CRP) values, Acute Physiology and Chronic Health Evaluation (APACHE) II score and first blood culture results obtained at the 1st, 7th, 14th and 21st days of ICU admission were recorded.

Calculation of Energy Need

The energy need was calculated with the Harris Benedict formula[(for women; 655.1 + (9.56 x weight kg) + (1.85 x height cm) – (4.68 x age) kcal/day for men; 66.5 + (13.75 x weight kg) + (5.03 x height cm) – (6.75 x age)] kcal/day.

Parenteral Nutrition Ingredients

Soy-based and olive oil-based parenteral nutrition ingredients used with central catheter are shown in **Table 1**.

Table 1. Composition of lipid emulsions used in the study.

	Soyabean oil-based Emulsion	Olive oil-based emulsion
Composition (g/100 ml):		
Soyabean oil	20	0.8
Olive oil	-	3.2
Glycerol	2.20	2.25
Egg phospholipids	1.2	1.2
Sodium oleate	-	0.03
Fatty acid content (%)		
Palmitic acid	11	12
Stearic acid	4	3
Oleic acid 24 65	24	65
Linoleic acid	53	17
a-Linolenic acid	8	3
Oleic:linoleic ratio	0.4	3.8

Statistical Analysis

We based our sample size calculation on data from a study comparing the effects of olive oil-based and soybean oil-based emulsions on infection rate and leukocyte count in critically ill patients receiving parenteral nutrition (7). In the same study, soy-based 16 and olive oil-based 23 patients were compared and no significant difference was found in terms of CRP and Leukocyte values. When α risk was accepted as 0.05 and Power (1-B err probe) as 0.95, 22 participants receiving soy-based nutrition and 32 participants receiving olive oil-based nutrition were statistically required. G * Power 3.1.9.4 program was used for these calculations (8).

Statistical analyzes were performed using the SPSS 26.0 software program (SPSS Inc., Chicago, IL, USA).

After Kolmogorov - Simirnov test was applied to all data, one-way analysis of variance test was used for normally distributed data in intergroup evaluation, and Mann Whitney U test was used for data with skewed distribution. One-way analysis of variance test of repeated measures was used for normally distributed data and Wilcoxon signed rank test was used for data showing skewed distribution. Binary logistic regression analysis was performed to understand whether soy-based and olive-oil-based nutrition has an effect on growth in blood culture. Chi-square test was used for the comparison of nominal values between groups. $p<0.05$ was considered significant.

RESULTS

The majority of the patients included in the study were patients in whom enteral nutrition was not possible due to surgical reasons. Parenteral nutrition was initiated in the first 24 hours of hospitalization in the intensive care unit. No statistically significant difference was observed between the two groups in terms of demographic data. 25 of the Group 1 patients were male and the mean age was 76.56 ± 10.31 years. 36 of the group 2 patients were male and the mean age was 72.92 ± 16.72 (**Table 2**).

When the CRP, Leukocyte, Platelet and Neutrophil Lymphocyte Ratio (NLR) values were compared between and within the groups, no statistically significant change was observed between the four measurement values in terms of leukocyte, platelet and neutrophil lymphocyte ratio (NLR) values among the groups. Leukocyte values on the 7th and 21st days in Group 1 and on the 7th and 14th days in Group 2 were found to be statistically significantly lower than the leukocyte values on the 1st day. The 7th day platelet value in Group 1 and Group 2 was found to be statistically significantly lower than the 1st day platelet value. While the NLR value on the 21st day in Group 1 was found to be statistically significantly lower than the NLR value on the 1st day, there was no statistically significant difference between the four measurement values in Group 2. 14th and 21st days in Group 1, 7th, 14th in Group 2. and 21st day CRP values were found to be statistically significantly higher than the 1st day. The 7th and 21st day CRP values in Group 1 were found to be statistically significantly lower than the 7th and 21st day CRP values in Group 2 (**Table 3**, **Figure 1**).

Table 2. Demographic data of the cases. (Values are expressed as mean ± SD)

	Group 1		Group 2		P
	Mean	SD	Mean	SD	
Age (Year)	76.56	10.31	72.92	16.72	0.27
Gender(M/F)	25/7		36/14		0.53

SD: Standart deviation, F: Female, M; Male

Table 3. Comparison of CRP, Leukocyte, Platelet and values of the groups

		1st Day			7th Day			14th Day			21th Day	
		Mean	SD	P 1-7th Day	Mean	SD	P 1-14th Day	Mean	SD	P 1-21th Day	Mean	SD
Crp (mg/l)												
	Group 1	93.36	89.91	0.48	92.38	54.35	0.03*	127.49*	71.50	0.004€	131.54£	58.84
	Group 2	98.95	89.10	0.004†	139.76†	84.42	0.008ß	150.18ß	92.76	0.001^	190.88^	102.20
	P	0.75			0.009			0.25			0.010	
Leukocyte 10^3/µl												
	Group 1	13.78	5.45	0.002**	10.24**	4.26	0.09	11.73	11.39	0.001≠	10.42≠	5.00
	Group 2	13.74	7.62	0.03††	11.32††	4.27	0.02η	11.39η	6.57	0.43	12.43	6.79
	P	0.64			0.17			0.86			0.19	
Platelet 10^3/µl												
	Group 1	267.53	122.93	0.010^^	217.22^^	108.78	0.13	230.22	130.30	0.06	215.28	150.55
	Group 2	258.26	108.01	0.001ǂ	206.84ǂ	123.22	0.65	285.58	291.85	0.08	233.42	197.52
	P	0.87			0.38			0.52			0.93	
NLR												
	Group 1	24.08	49.30	0.13	11.48	8.88	0.56	15.95	19.99	0.007µ	11.08µ	19.66
	Group 2	18.98	18.84	0.14	11.78	7.97	0.12	12.45	9.90	0.25	13.83	13.88
	P	0.85			0.54			0.96			0.76	

*: p 0.03=When day 1 and day 14 are compared, day 14 was found to be significantly higher.
£: p 0.01=When the 1st day and the 21st day are compared, the 21st day was found to be significantly higher.
+: P 0.04=When the 1st day and the 7th day were compared, the 7th day was found to be significantly higher.
B: p 0.01=When day 1 is compared with day 14, day 14 was found to be significantly higher.
^: p 0.01=When day 1 and day 21 are compared, day 21 was found to be significantly higher.
**: p 0.01=When the 1st day and the 7th day are compared, the 7th day was found to be significantly lower.
≠: p 0.01=When day 1 and day 21 are compared, day 21 was found to be significantly lower.
††: p 0.03=When the 1st day and the 7th day were compared, the 7th day was found to be significantly lower.
η: p 0.02=When day 1 and day 14 are compared, day 14 was found to be significantly lower.
^^: p 0.01=When the 1st day and the 7th day are compared, the 7th day was found to be significantly lower.
ǂ: p 0.01=When the 1st day and the 7th day were compared, the 7th day was found to be significantly lower.
µ: p 0.01=When day 1 and day 21 are compared, day 21 was found to be significantly lower.

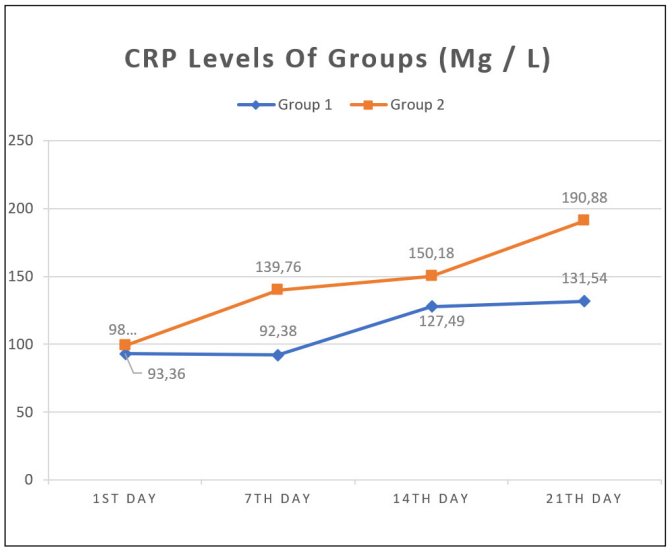

Figure 1. CRP Levels Of Groups

When the blood culture reproduction of the groups were compared, the growth in blood culture was found to be statistically significantly lower in Group 1 (p =0.03). Reproduction was detected in 6 of 32 patients in Group 1, while growth was detected in 20 of 50 patients in Group 2. The most reproductive microorganism in Group 1 was Enterococcus Faecium, in Group 2 Acinetobacter Baumannii and Klebsiella Pneumoniae were the most reproducing microorganisms. When the first blood culture reproduction days of the groups were compared, it was found that there was statistically significantly earlier growth in Group 2 (p =0.03, **Figure 2**).

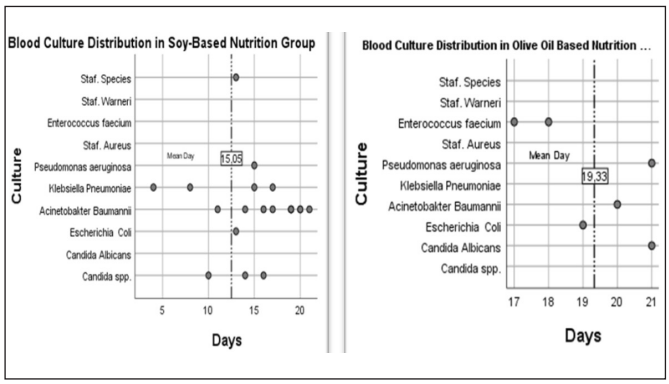

Figure 2. First Blood Culture Breeding Days of Groups

When the APACHE II scores calculated within and between the groups on the 1st, 7th, 14th and 21st days were compared, no statistically significant difference was found between the groups.

In the logistic regression analysis, it was found that age and gender had no effect on blood culture growth and that there was 3 times more growth in blood culture in patients who received soy-based nutrition compared to patients who received olive oil-based nutrition (**Table 4**).

Table 4. Coefficient Estimates of the Logistic Regression Model

Variables	β	S.E.	Wald	df	Sig.	Exp(B)	95% C.I. for EXP(B)	
							Lower	Upper
Gender	0.497	0.607	0.670	1	0.413	1.643	0.500	5.394
Age	0.022	0.019	1.413	1	0.235	1.022	0.986	1.060
Group (1)	1.192	0.555	4.618	1	0.032	3.293	1.111	9.762
Constant	-2.735	1.499	3.328	1	0.068	0.065		
Cox & Snell R2 =.071, Nagelkerke R2=.100, -2 Log Likelihood = 96.394								

DISCUSSION

As a result of this study, it is seen that olive oil-based emulsions are more advantageous in terms of CRP, growth in blood culture and breeding day in mean blood culture among the patient groups who received parenteral nutrition products containing two different lipids. There was no significant difference between the groups in terms of leukocyte, platelet, NLR and APACHE II Scores.

Nutritional support is an important part of intensive care treatments. Nutrition has been found to have positive effects on immunological functions, helps wound healing, and reduces mortality and morbidity. As in all patients, the first choice in intensive care patients is oral nutrition, which is a natural diet. Oral nutrition is often not possible in intensive care patients. This has led clinicians to find different ways of nutrition. As a result, enteral and parenteral nutrition types have been developed (9).

Parenteral nutrition is the administration of high concentrations of hypertonic solutions that meet the nutritional needs of patients with a limited absorption capacity of the gastrointestinal system and a problem that prevents nonfunctional or enteral nutrition, via central catheter or peripheral venous route.In our study, all of the patients were patients whose gastrointestinal tract was unsuitable for enteral nutrition due to the operation.

Hyperglycemia, electrolyte inbalance, hypertriglyceridemia, kidney and liver function disorders are frequently encountered metabolic complications of parenteral nutrition (10). These complications that develop in addition to the disease cause an increase in inflammatory response (11).

One of the most important treatments in the ICU is to support immune functions, and adequate nutritional support must be provided for this. Since products containing arginine, nucleotides, ω-3 polyunsaturated fatty acids (PUFA), glutamine have been shown to increase the cellular immune response to infection in-vivo and in-vitro, the term 'immunonutrition' is used for feeding with these products. Studies have shown that acute phase reactants such as serum CRP and fibrinogen have a lower course in patient groups

receiving immunonutrition (6). Arginine, nucleotides and PUFA are found in different proportions in the nutritional products used in our study.

Linoleic acid forms a large part of PUFA in soy-based lipid emulsions (12). Linoleic acid reduces the release of proinflammatory cytokines, impairs reticuloendothelial functions, and inhibits macrophage and lymphocyte functions (7). Cury-Boaventura et al. (13) showed that soy-based lipid emulsion decreased lymphocyte proliferation and even caused death of neutrophils and lymphocytes. In the light of this information, soy-based lipid emulsions negatively affect immune functions (7).

Olive oil-based emulsions contain monounsaturated fatty acids (Monounsaturated fatty acids: MUFA) rich in oleic acid (14). MUFA is thought to be ineffective on immune functions (7,15).In the study of Ockenga et al. (16) on patients with acute pancreatitis, it was reported that parenteral nutrition was associated with CRP, which is an inflammation marker. There are other similar studies in the literature (17,18). Gürsoy et al. (10) reported that soy-based and olive-oil-based nutritional products lower CRP, but there was no statistically significant difference between them. Mateu-de Antonio et al. (7) reported that soy-based lipid-containing emulsion had more suppressive properties on the amount of leukocytes than olive-oil-based lipid-containing emulsions. In our study, the leukocyte, platelet and NLR values between the groups were similar. CRP was found to be close on the 1st and 14th days, and significantly lower in the olive oil-based nutrition group on the 7th and 21st days. When the blood culture results and mean reproduction days of the groups were compared, it was found that the growth was statistically significantly less and later in the olive oil-based nutrition group. No significant difference was observed between the APACHE II scores of the groups.

The limitations of our study can be seen as the different diagnoses of the patients in hospitalization, the absence of additional diseases, the different central catheterization sites, and the limited number of patients.Negative cultures can be false-negative and need to be repeated, which is a limitation of our study.

CONCLUSION

As a result, it was found that olive oil-based lipid-containing nutritional solutions were more advantageous in terms of immune response than soy-based nutrition products. It was concluded that patients who received postoperative mechanical ventilator support fed with olive oil-based parenteral nutrition products had less infectious growth.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Kastamonu University Medical Faculty Clinical Researches Ethics Committee (Date: 14.12.2020, Decision No: KAEK-143-09).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

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

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