Research Article / Özgün Araştırma

DOI: 10.4274/cayd.galenos.2022.07830
J Pediatr Emerg Intensive Care Med 2023;10:39-43

Investigation of the Role of Nesfatin-1 Levels in the Evaluation of Nutrition Monitoring in the PICU

Nesfatin-1 Düzeylerinin ÇYBÜ'de Beslenme Monitorizasyonu Değerlendirilmesindeki Rolünün Araştırılması

Yasemin Çoban[1], Alper Köker[2], Sultan Aydın[3], Yılmaz Akbaş[4], Ahmet Ufuk Kömüroğlu[5]

[1]Hatay State Hospital, Clinic of Pediatric Intensive Care, Hatay, Turkey
[2]Antalya University Faculty of Medicine, Department of Pediatrics, Division of Pediatric Intensive Care, Antalya, Turkey
[3]Hatay State Hospital, Clinic of Pediatric Neurology, Hatay, Turkey
[4]Hatay State Hospital, Clinic of Pediatric Haematology, Hatay, Turkey
[5]University of Health Sciences Turkey, Van Training and Research Hospital, Clinic of Biochemistry, Van, Turkey

Abstract

Introduction: Although nutrition is very effective on mortality in critically ill children, patients cannot be fed adequately. There is no suitable biomarker for enteral nutrition monitoring and management. The aim of this study; To investigate the usability of nefsatin-1 for nutritional monitoring and management in critically ill children.

Methods: In the January-September 2019 period, 35 critically ill children who were hospitalized in the tertiary pediatric intensive care unit without any signs of inflammation were included in the study. Nesfatin-1, vitamin D level, prealbumin, albumin was evaluated for the study.

Results: Thirty-five patients who were admitted to the pediatric intensive care unit and whose hospitalization reasons had regressed were evaluated. The mean nesfatin-1 values of the patients were measured as 9.95±0.78 ng/mL (4.25-18.93 ng/mL). There was a negative and low (r=-0.214) relationship between target calorie intake and nesfatin-1, a positive and low (r=0.172) relationship with prealbumin, and a positive and high relationship with vitamin D (r=0.529). Similar relationships were determined between the weight change ratio and nesfatin-1 (r=-0.266), prealbumin (r=0.154) and vitamin D (r=0.337).

Conclusion: Based on the study findings, it was concluded that serum nefsatin-1, albumin and prealbumin are not appropriate indicators for nutritional monitoring and management in critically ill children.

Keywords: Nesfatin-1, child critical ilness, nutrition

Öz

Giriş: Kritik hasta çocuklarda beslenme mortalite üzerinde oldukça etkili olmasına rağmen, hastalar yeterince beslenememektedir. Enteral beslenme monitorizasyonu ve yönetimi için uygun bir biyobelirteç mevcut değildir. Bu çalışmanın amacı; nefsatin-1'in kritik hasta çocuklarda nütrisyonel monitorizasyon ve yönetimi için kullanılabilirliğini araştırmaktır.

Yöntemler: Ocak-Eylül 2019 periyodunda 3. basamak çocuk yoğun bakım ünitesinde yatan, enflamasyon bulgusu olmayan 35 kritik hasta çocuk çalışmaya alınmıştır. Nesfatin-1, vitamin D düzeyi, prealbümin, albümin, çalışma için değerlendirilmiştir.

Bulgular: Çocuk yoğun bakım ünitesine yatan, enfeksiyon belirteçlerinin gerilediği 35 hasta değerlendirilmiştir. Hastaların ortalama nesfatin-1 değerleri 9,95±0,78 ng/mL (4,25-18,93 ng/mL) olarak ölçülmüştür. Hedef kalori alım oranı ile nesfatin-1 arasında negatif ve düşük (r=-0,214), prealbümin ile pozitif ve düşük (r=0,172), vitamin D ile ise pozitif ve yüksek (r=0,529) ilişki bulunmuştur. Benzer ilişkiler ağırlık değişim oranı ile nesfatin-1 (r=-0,266), prealbümin (r=0,154) ve vitamin D (r=0,337) arasında belirlenmiştir.

Sonuç: Çalışma bulgularına göre, kritik hasta çocuklarda, nutrisyon monitorizasyonu ve yönetimi için serum nefsatin-1, albümin ve prealbüminin uygun göstergeler olmadığı sonucuna varılmıştır.

Anahtar Kelimeler: Nesfatin-1, kritik hasta çocuk, beslenme

Address for Correspondence/Yazışma Adresi: Yasemin Çoban, Hatay State Hospital, Clinic of Pediatric Intensive Care, Hatay, Turkey
E-mail: yasemincoban83@gmail.com **ORCID ID:** orcid.org/0000-0002-5283-239X
Received/Geliş Tarihi: 17.06.2022 **Accepted/Kabul Tarihi:** 23.12.2022

©Copyright 2023 by Society of Pediatric Emergency and Intensive Care Medicine
Journal of Pediatric Emergency and Pediatric Intensive Care published by Galenos Yayınevi.

Introduction

Despite recent technological developments, malnutrition is commonly seen in pediatric intensive care units. Acute or chronic malnutrition is observed at a rate of 24-55% with deterioration of nutritional status during hospital stay.[1]

Malnutrition observed at the time of hospitalization, increased basal metabolic rate during critical illness, severe protein catabolization, and limited energy stores of the pediatric patient increase the severity of malnutrition and thus the mortality and morbidity of the patient.[2]

Monitoring is recommended in order to start feeding in the early period and to achieve ideal nutritional goals in critical pediatric patient follow-up. However, no method has been identified as the ideal method.[3] The condition of the critically ill child is even more complex, and fluid leaks into the third space make accurate anthropometric evaluation difficult.[4]

Some peptides and neurotransmitters play a role in both appetite regulation and stress response, and nesfatin is one of these peptides. Nesfatin-1, which was first described by Oh et al.[5] in 2006, is a satiety molecule found in the hypothalamus, with a molecular weight of 9.7 kDa, consisting of 82 amino acids. Nesfatin-1 is found not only in brain tissues, but also in peripheral tissues such as adipose tissue, stomach, pancreatic islets, liver and testis.

Nesfatin-1, originating from NEFA/nucleobindin2, is a recently discovered hormone that suppresses food intake via melanocortin in the hypothalamus.[5]

The relationship of the nesfatin-1 molecule with thermogenesis, especially in ischemic brain injuries, neuroprotective, reproductive physiology, cardiovascular functions, blood glucose balance, gastrointestinal functions, energy metabolism, and even anxiety and depression has been investigated.[6,7] Nesfatin-1, which was considered an anorexigenic hormone when it was first discovered, has been shown to have an effect on many systems in later studies. Especially in animal studies, it was observed that food intake decreased when serum and tissue nesfatin levels increased.[8,9]

Low levels of albumin in serum are known as an indicator of malnutrition. In emergency and critical situations, albumin level decreases by 30% in a very short time. Prealbumin level (normal range: 16-35 mg/dL) is not considered as a marker for malnutrition since it is also affected by inflammation; however, it has been stated that it can be useful to determine the nutritional level by measuring it with C-reactive protein (CRP) at certain periods even in cases where inflammation persists.[10]

Nutrition is an important part of treatment in the critically ill patients. During the enteral nutrition period, the difference between the planned/calculated nutrient formulation to be given to the patient and the amount that the patient can take in practice is quite high. In addition, the effect of nutrition on the patient emerges in the future. Therefore, monitoring and standardization are very important in intensive care nutrition management from the first day of the hospitalization of critically ill patient.[10]

The aim of this study is to investigate the usability of nesfatin-1 in nutritional monitoring and management by examining the relationship between serum nesfatin-1 levels and anthropometric measurements and some blood parameters in patients hospitalized in the pediatric intensive care unit. Studies on nesfatin-1, which is reported to be closely related to nutrition and affect almost all systems in the literature, almost completely examine the issue of obesity in adults and children. According to the published literature, this study was carried out on pediatric intensive care patients for the first time.

Materials and Methods

The study was planned as a controlled prospective clinical trial. In the January-September 2019 period, 35 critically ill children, who were hospitalized in the tertiary pediatric intensive care unit and had no signs of inflammation, were included in the study. Informed consent was obtained from their families.

Body weights, height measurements, demographic data, complications, daily calorie intake, and reasons for admission to the intensive care unit of the patients included in the study were recorded. After the patient's inflammation markers (CRP, procalcitonin) regressed, routine biochemistry and hematological examinations were performed. Vitamin D level, prealbumin, and albumin were evaluated for the study. During these tests, serum was separated for serum nesfatin-1 level. The serums were stored at -40 °C. After the study was completed, serum nesfatin-1 levels were measured with Bio-Tek ELX-800 brand ELISA method in Van Yüzüncü Yıl University Health Services Vocational School, Research and Application Laboratory.

The study was approved by the Hatay Mustafa Kemal University, Tayfur Ata Sökmen Faculty of Medicine Clinical Research Ethics Committee (approval number: 03, date: 20.02.2020).

Statistical Analysis

The daily calorie intake and the required calorie intake were determined according to the Schofield method (target calorie) and recorded. In order to prevent differences between patients, the caloric intake-target calorie/target calorie*100 was formulated. Entry and exit weights of the patients were formulated with exit weight-entry weight/entry weight*100. Patients were considered to have lost weight if they had a weight loss of more than 10%.

The normality test of nesfatin-1 values was performed with the Shapiro-Wilk and it was determined that it did not show normal distribution. The correlation between demographic and blood parameters and nesfatin-1 was calculated using the Spearman's rho. The differences in nesfatin-1 between those who maintained their weight and those who lost their weight were analyzed by using the Mann-Whitney U test, one of the non-parametric tests, and the difference between the percentage of reaching the target calorie (95% and above, 94-75% and below 75%) and nesfatin-1 by using the Kruskal-Wallis test. Normally distributed albumin, prealbumin and vitamin D levels were compared with t-test for pairwise comparison, with One-Way ANOVA for triple comparison, and with Duncan test for multiple comparison test. Values below p<0.05 were considered significant in the multiple comparison test. The analysis of the obtained data was made with the SPSS 22.0 statistical program.

Results

In 35 patients included in the study, the number of boys/girls was 19/16 and their mean age was calculated as 40.6±7.1 months (12 months-144 months). Eighteen of the patients were hospitalized in the intensive care unit for central nervous system diseases, 10 for respiratory failure, 4 for cardiogenic reasons, and 3 for renal reasons. 88.5% (n=31) of the patients were fed enterally. Two patients were fed only parenterally, and 2 patients were fed enterally + parenterally. The mean nesfatin value of the patients included in the study was measured as 9.958±0.78 ng/mL (4.25-18.93 ng/mL).

The correlation coefficient values calculated between measured levels of nesfatin-1, albumin, prealbumin and vitamin D and some nutritional parameters are presented in Table 1.

Targeted calorie intake had a negative and low correlation with nesfatin-1 (r=-0.214; p>0.05), a positive and low correlation with prealbumin (r=0.172; p>0.05), and a positive and high correlation with vitamin D (r=0.529; p<0.01). Similar relationships were determined between weight change ratio and nesfatin-1 (r=-0.266; p>0.05), prealbumin (r=0.154; p>0.05) and vitamin D (r=0.337; p>0.05). Correlation coefficient was calculated as r=-0.337 between serum nesfatin-1 level and vitamin D (p<0.05). A positive and moderate correlation (r=0.329) was found between hospitalization time and prealbumin level (p<0.05).

Nesfatin-1, albumin, prealbumin and vitamin D levels of those who maintained their weight and lost weight during the intensive care period are presented in Table 2.

It was observed that weight change during hospitalization did not affect serum nesfatin-1, albumin, prealbumin and vitamin D levels (p<0.05).

Table 1. Relationships between some parameters of patients and nesfatin-1, prealbumin, albumin, and vitamin D levels

	Age (month)	PELOD2	PIM3	Weight-1 (kg)	Weight-2 (kg)	AF (%)	HKF (%)	Length of hospitalization (day)	Nesfatin-1 (ng/mL)	Prealbumin (mg/dL)	Albumin (mg/dL)	Vitamin D (ng/mL)
PELOD2	-0.18											
PIM3	-0.17	0.81**										
Weight-1 (kg)	0.37*	0.17	0.15									
Weight-2 (kg)	0.42*	0.18	0.19	0.99**								
AF (%)	0.18	0.13	0.29	-0.07	0.09							
HKF (%)	0.13	-0.14	-0.11	-0.18	-0.10	0.44**						
Length of hospitalizaiton (day)	-0.02	0.15	0.08	0.00	0.03	0.16	0.43*					
Nesfatin-1 (ng/mL)	-0.11	0.18	0.15	0.01	-0.04	-0.32	-0.21	-0.12				
Prealbumin (mg/dL)	0.29	-0.17	-0.11	0.07	0.10	0.13	0.17	0.33	0.01			
Albumin (mg/dL)	0.11	-0.21	-0.22	0.17	0.15	-0.08	0.09	0.23	-0.08	0.60**		
Vitamin D (ng/mL)	0.03	-0.09	-0.08	-0.24	-0.21	0.17	0.52**	0.52**	-0.34	0.42*	0.40*	
CRP	0.21	0.17	0.21	0.15	0.15	0.01	-0.16	-0.02	0.20	0.19	-0.15	0.06

PELOD2: Pediatric logistic organ dysfunction 2, PIM3: Pediatric index of mortality 3, Weight-1: Weight on the first day of hospitalization in the intensive care unit, Weight-2: Weight on the day when blood sample was collected for nesfatin-1, AF: (Weight2 - Weight1)/Weight1*100, HKF: (Calorie intake- target calorie)/target calorie, CRP: C-reactive protein, *: p<0.05, **: p<0.01

Table 2. Serum nesfatin-1, prealbumin, albumin and vitamin D levels of patients who could maintain their weight (normal) and lost weight during hospitalization

	n	Nesfatin-1 (ng/mL)	Prealbumin (mg/dL)	Albumin (mg/dL)	Vitamin D (ng/mL)
Normal	28	9.54±4.41	17.93±7.85	3.34±0.61	28.14±13.30
Weight loss	7	11.61±5.63	17.43±5.62	3.40±0.39	31.43±6.80
p		0.219	0.299	0.176	0.056

Table 3. Nesfatin-1, albumin, prealbumin and vitamin D levels with the rate of reaching the target calorie

Rate of reaching the target calorie	n	Nesfatin (ng/mL)	Prealbumin (mg/dL)	Albumin (mg/dL)	Vitamin D (ng/mL)
>95%	10	8.169±1.160	19.5±2.271	3.42±0.44	37.00±2.923[a]
94-75%	13	12.691±1.541	15.60±2.609	3.18±0.21	25.90±3.089[b]
<75%	12	9.506±1.219	18.00±1.747	3.35±0.57	23.46±3.459[b]
p		0.177	0.478	0.533	0.011

[a,b]Mean values followed by different letters within a column are significantly different (p<0.05)

In Table 3, the rates of reaching the targeted calories and nesfatin-1, albumin, prealbumin and vitamin D levels of patients who could take the targeted daily calorie amount are presented. It was determined that target calorie intake rates did not change nesfatin-1, albumin and prealbumin levels. It was calculated that the vitamin D level of patients who reached at least 95% of their target calorie intake (37.00±2.923 ng/mL) was higher than those with lower calorie intake (25.90±3.089 and 23.46±3.459 ng/mL) (p<0.05).

Discussion

It is known that nesfatin-1 is effective on appetite tendencies, simple carbohydrate and fat intake behavior that will cause obesity in experimental animals. However, the mechanism of action has not yet been clearly explained. In addition, most studies have aimed to find new therapeutic solutions for obesity.[11,12]

Studies in experimental animals have shown that increased levels of nesfatin-1 suppress appetite and play a role in the regulation of eating behavior and body weight in rats.[5]

Nesfatin-1 level was found to be significantly lower in obese children compared to those with normal body mass index.[12] On the contrary, another study reported a positive and high correlation between the amount of body fat and serum nesfatin-1 concentration.[13]

In the literature, there are many studies on serum nesfatin-1 levels in obese adults. However, the number of studies measuring blood nesfatin-1 levels in obese children and adolescents is extremely limited. First, the relationships between anthropometric and metabolic characteristics and serum nesfatin-1 were investigated in obese children and adolescents in South Korea.[14]

All of these studies aimed to understand the relationship between the mechanism of obesity and nesfatin-1 secretion. In one of the studies conducted on this subject,[14] the mean serum nesfatin-1 level was found to be 1.4 ng/mL (0.1-10.7 ng/mL) in obese children and 2.0 ng/mL (0.1-20.0 ng/mL) in children with a normal body mass index. The difference between the two groups was found to be statistically very significant. According to the findings of the same study, it was stated that the serum nesfatin-1 level tended to decrease as the adolescent period approached.[14] In our study, the mean blood nesfatin-1 level was found to be 9.95±0.78 ng/mL (4.25-18.93 ng/mL), which was higher than in previous studies. This result was attributed to the fact that the patients were prepubertal and they had baseline malnutrition.

There are conflicting reports in the results of studies to determine the relationship between childhood serum nesfatin-1 and anthropometric properties. For example, Anwar et al.[15] reported a positive relationship between serum nesfatin-1 level and body mass index in obese children.

In our study, in critically ill children, no difference was detected in serum nesfatin-1 levels between those with and without weight loss and between those who reached the target calories and those who did not. It was thought that the results of our study could not be compared to those of previous studies since they were performed in healthy and homogeneous (age-physiological period-sex etc.) populations and/or groups of obese children. However, based on the current findings, it has been evaluated that nesfatin-1 cannot be used as a marker for nutritional monitoring and management to monitor the feeding level in the intensive care unit. On the other hand, nesfatin-1 level was found to be significant in terms of measuring it for the first time in critically ill children and it provided a reference value.

In our study, it was observed that weight differences during hospitalization did not change serum albumin and prealbumin levels and were among the reference values in all groups.

However, a positive and moderate correlation was calculated between the length of stay in the intensive care unit and the serum prealbumin level. However, Keller[16] reported that although albumin and prealbumin levels were associated with nutritional levels in non-diseased individuals, these two parameters should be used as an indicator of inflammation rather than nutritional level in acute diseases. In this study, the increased prealbumin with longer hospitalization period and the short half-life of prealbumin (2-3 days) were explained by the effectiveness of enteral nutrition during hospitalization. Researchers reported that there was no difference in blood vitamin D levels in obese and normal children.[14] Currently, vitamin D supplementation is given in enteral formulas used in intensive care nutrition and the current research. However, in the current study, children who lost weight and did not achieve their target caloric intake had significantly lower vitamin D levels than patients who achieved the target caloric intake and did not lose weight.

Study Limitations

The limitations of this study are that the basal nesfatin-1 levels of the patients were not determined and the number of patients was low.

Conclusion

This is the first study to evaluate nesfatin-1 as a nutritional indicator in critically ill children. According to the study findings, serum nesfatin-1, albumin and prealbumin, which are selected as biomarkers for nutritional monitoring and management in critically ill children, are not appropriate indicators; however, it was concluded that the level of vitamin D could indicate the level of reaching the target calorie. Traditionally, calorie and weight monitoring have already been considered a good indicator.

Ethics

Ethics Committee Approval: The study was approved by the Hatay Mustafa Kemal University, Tayfur Ata Sökmen Faculty of Medicine Clinical Research Ethics Committee (approval number: 03, date: 20.02.2020).

Informed Consent: Informed consent was obtained from their families.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Y.Ç., A.K., Y.A., Concept: Y.Ç., A.K., Y.A., Design: Y.Ç., A.K., Y.A., Data Collection or Processing: Y.Ç., A.K., A.U.K., Analysis or Interpretation: Y.Ç., A.K., A.U.K., Literature Search: Y.Ç., S.A., Writing: Y.Ç.

Conflict of Interest: No conflict of interest was declared by the authors.

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

References

1. Feferbaum R, Delgado AF, Zamberlan P, Leone C. Challenges of nutritional assessment in pediatric ICU. Curr Opin Clin Nutr Metab Care. 2009;12:245-50.
2. De Menezes FS, Leite HP, Nogueira PCK. What are the factors that influence the attainment of satisfactory energy intake in pediatric intensive care unit patients receiving enteral or parenteral nutrition? Nutrition. 2013;29:76-80.
3. Collins S. Community-based therapeutic care: a new paradigm for selective feeding in nutritional crises. Overseas Development Institute (ODI). 2004;48:1-30.
4. Keehn A, O'Brien C, Mazurak V, Brunet Wood K, Joffe A, et al. Epidemiology of interruptions to nutrition support in critically ill children in the pediatric intensive care unit. JPEN J Parenter Enteral Nutr. 2015;39:211-7.
5. Oh IS, Shimizu H, Satoh T, Okada S, Adachi S, et al. Identification of nesfatin-1 as a satiety molecule in the hypothalamus. Nature. 2006;443:709-12.
6. Erfani S, Moghimi A, Aboutaleb N, Khaksari M. Nesfatin-1 improve spatial memory impairment following transient global cerebral ischemia/reperfusion via inhibiting microglial and caspase-3 activation. J Mol Neurosci. 2018;65:377-84.
7. Schalla MA, Stengel A. Current understanding of the role of nesfatin-1. J Endocr Soc. 2018;2:1188-206.
8. Albayrak A, Demiryıldız I, Albayrak Y, Aylu B, Ozogul B, et al. The role of diminishing appetite and serum nesfatin-1 level in patients with burn wound infection. Iran Red Crescent Med J. 2013;15:389-92.
9. Ari M, Ozturk OH, Bez Y, Oktar S, Erduran D. High plasma nesfatin-1 level in patients with major depressive disorder. Prog Neuropsychopharmacol Biol Psychiatry. 2011;35:497-500.
10. Berger MM, Reintam-Blaser A, Calder PC, Casaer M, Hiesmayr MJ, et al. Monitoring nutrition in the ICU. Clin Nutr. 2019;38:584-93.
11. Dore R, Krotenko R, Reising JP, Murru L, Sundaram SM, et al. Nesfatin-1 decreases the motivational and rewarding value of food. Neuropsychopharmacology. 2020;45:1645-55.
12. Abaci A, Catli G, Anik A, Kume T, Bober E. The relation of serum nesfatin-1 level with metabolic and clinical parameters in obese and healthy children. Pediatr Diabetes. 2013;14:189-95.
13. de Dios O, Herrero L, Gavela-Pérez T, Soriano-Guillén L, Garcés C. Sex-specific association of plasma nesfatin-1 concentrations with obesity in children. Pediatr Obes. 2019;14:e12567.
14. Kim SH, Ahn MB, Cho WK, Cho KS, Jung MH, et al. The relation of serum nesfatin-1 level with anthropometric and metabolic parameters in children and adolescents: A prospective observational study. Medicine (Baltimore). 2019;98:e15460.
15. Anwar GM, Yamamah G, Ibrahim A, El-Lebedy D, Farid TM, et al. Nesfatin-1 in childhood and adolescent obesity and its association with food intake, body composition and insulin resistance. Regul Pept. 2014;188:21-4.
16. Keller U. Nutritional Laboratory Markers in Malnutrition. J Clin Med. 2019;8:775.