RESEARCH ARTICLE / ARAŞTIRMA MAKALESİ
DOI: 10.26650/IUITFD.1365883
İst Tıp Fak Derg 2024 / J Ist Faculty Med 2024

THE RELATION OF SERUM NESFATIN-1 LEVELS WITH DISEASE SEVERITY AND COMPLICATIONS IN PATIENTS WITH LIVER CIRRHOSIS*

KARACİĞER SİROZLU HASTALARDA SERUM NESFATİN-1 DÜZEYLERİNİN HASTALIK ŞİDDETİ VE KOMPLİKASYONLARI İLE İLİŞKİSİ

Özlem KANDEMİR ALİBAKAN[1], Hasan ERUZUN[2], İlkim Deniz TOPRAK[3], Uğur YILMAZ[1], Mehmet Alptekin ACAR[1], İpek BİLGE ASLAN[1], Merve POLAT ONMAZ[1], Yasemin GÖKDEN[4], Yücel ARMAN[1], Tufan TÜKEK[5]

[1]University of Health Sciences Turkey, Prof. Dr. Cemil Taşçıoğlu City Hospital, Department of Internal Medicine, İstanbul, Türkiye
[2]Ondokuz Mayıs University, Faculty of Medicine, Department of Gastroenterology, Samsun, Türkiye
[3]University of Health Sciences Turkey, Gaziosmanpaşa Training and Research Hospital, İstanbul, Türkiye
[4]University of Health Sciences Turkey, Prof. Dr. Cemil Taşçıoğlu City Hospital, Department of Gastroenterology, İstanbul, Türkiye
[5]İstanbul University, İstanbul Faculty of Medicine, Department of Internal Medicine, İstanbul, Türkiye

ORCID IDs of the authors: Ö.K.A. 0000-0002-5452-6273; H.E. 0000-0003-0355-1820; İ.D.T. 0000-0002-9320-1252; U.Y. 0000-0001-9398-5774; M.A.A. 0000-0003-0784-8410; İ.B.A. 0000-0001-5253-4336; M.P.O. 0000-0003-0361-3681; Y.G. 0000-0001-6767-3072; Y.A. 0000-0002-9584-6644; T.T. 0000-0002-4237-1163

Cite this article as: Kandemir Alibakan Ö, Eruzun H, Toprak İD, Yılmaz U, Acar MA, Bilge Aslan İ, et al. The relation of serum nesfatin-1 levels with disease severity and complications in patients with liver cirrhosis. J Ist Faculty Med 2024;87(3):209-214. doi: 10.26650/IUITFD.1365883

ABSTRACT

Objective: Nesfatin-1 is an anorectic polypeptide that plays important roles in regulating appetite and energy intake. Cachexia and malnutrition are common in individuals with cirrhosis. We examined the relationship between serum nesfatin-1 levels and stage of cirrhosis, with the hypothesis that an increase in nesfatin-1 levels in patients with cirrhosis may be related to this catabolic process.

Material and Method: The study includes 51 patients with cirrhosis and 30 healthy volunteers. Nesfatin-1 levels in serum samples were compared using the enzyme-linked immunosorbent assay (ELISA). We calculated the Child-Pugh stages and Model for End-Stage Liver Disease (MELD) scores of patients with cirrhosis and examined their relationship with nesfatin-1. We've also investigated the relationship between cirrhosis complications and nesfatin-1.

Results: We found nesfatin-1 levels to be significantly higher in the cirrhosis patient group compared to the control group (p=0.001). The patient group was divided into those with compensated and those with decompensated liver cirrhosis

ÖZET

Amaç: Nesfatin-1, iştahın ve enerji alımının düzenlenmesinde önemli rolleri olan anorektik bir polipeptittir. Kaşeksi ve malnutrisyon sirozlu bireylerde yaygındır. Nesfatin-1 düzeylerinin sirozlu hastalardaki artışının sirozdaki katabolik süreçle alakalı olabileceği hipoteziyle nesfatin-1 serum düzeyleri ve siroz aşamaları ilişkisini inceledik.

Gereç ve Yöntem: Çalışmamıza 51 sirozlu hasta ve 30 sağlıklı gönüllü alındı. Serum örneklerinden nesfatin-1 düzeyleri ELISA kullanılarak karşılaştırıldı. Sirozlu hastaların Child-Pugh evreleri ve multifaktöriyel son dönem karaciğer hastalığı modeli (MELD) skorları hesaplanarak nesfatin-1 ile ilişkileri incelendi. Ek olarak siroz komplikasyonları ile nesfatin-1 arasındaki ilişki araştırıldı.

Bulgular: Nesfatin-1 düzeyleri sirozlu hasta grubunda kontrol grubuna göre anlamlı olarak yüksek bulundu (p=0,001). Hasta grubu kompanse ve dekompanse olarak ayrılıp, kontrol grubu ile karşılaştırıldı. Kompanse siroz grubunda nesfatin-1 düzeyleri anlamlı olarak yüksek bulundu (p=0,01). Sirozlu hastalar Child-Pugh

* This study was presented as a poster at the European Association for the Study of the Liver (EASL) Congress in Vienna in June 2023.

Corresponding author/İletişim kurulacak yazar: Hasan ERUZUN – hasaneruzun@gmail.com

Submitted/Başvuru: 26.09.2023 • **Revision Requested/Revizyon Talebi:** 10.10.2023 •
Last Revision Received/Son Revizyon: 03.04.2024 • **Accepted/Kabul:** 28.04.2024 • **Published Online/Online Yayın:** 08.07.2024

and compared with the control group. Nesfatin-1 levels were found to be significantly higher in the compensated liver cirrhosis group (p=0.01). When classifying the patients with cirrhosis based on their Child-Pugh stages and MELD scores, no significant relationship was detected between these groups and their nesfatin-1 levels.

Conclusion: Nesfatin-1 may have antioxidant, anti-inflammatory, and anti-apoptotic effects in maintaining the state of patients with compensated liver cirrhosis. Low levels of nesfatin-1 in decompensated liver cirrhosis may result from defense mechanisms and inadequate production.

Keywords: Nesfatin-1, liver, cirrhosis, decompensation, anti-inflammatory, antioxidant

evrelerine ve MELD skorlarına göre sınıflandırıldığında bu gruplar ile nesfatin-1 düzeyleri arasında anlamlı bir ilişki saptanmadı.

Sonuç: Sirozlu hastalarda kompanze halin sürdürülmesinde nesfatin-1'in antioksidan, antiinflamatuar ve antiapoptotik etkileri olabilir. Dekompanse sirozda nesfatin-1 düzeylerinin düşük olması savunma mekanizması ve yetersiz üretimden kaynaklanabilir.

Anahtar Kelimeler: Nesfatin-1, karaciğer, siroz, dekompansasyon, antienflamatuvar, antioksidan

INTRODUCTION

Cirrhosis develops as a result of hepatocellular damage leading to extensive fibrosis and nodular regeneration in the liver. Advanced cirrhosis usually involves anorexia. Taste and smell disorders in patients increase anorexia. Weight loss, cachexia, sarcopenia, and chronic disease are common. Body mass index (BMI) has been previously shown to be insufficient at revealing malnutrition, especially in patients with overt ascites (1, 2).

Nesfatin-1 is a polypeptide that has important roles in the regulation of food intake, energy homeostasis, and water intake. Nesfatin-1 is the amino-terminal portion of nucleobindin-2 (NUCB2) detected in the hypothalamic nuclei and has proven to be effective in appetite control in rats. Intracerebroventricular (ICV) injection of nesfatin-1 dose-dependently reduced food intake in rats with leptin receptor mutation (3). Nesfatin-1 has been shown to be expressed in many peripheral tissues other than the central nervous system (4, 5). Recent studies have highlighted the anti-inflammatory, antioxidant, and anti-apoptotic effects of nesfatin-1 (6).

We aim to determine the level of nesfatin-1 in the cirrhosis and control groups in order to investigate its relationship with the severity and complications of cirrhosis and also to determine whether nesfatin-1 has a role in decompensated liver cirrhosis by considering how the anorectic nesfatin-1 peptide might be responsible for the frequently encountered cachexia and malnutrition in patients with cirrhosis.

MATERIALS and METHODS

Study group

Our study involves a patient group consisting of 51 patients with cirrhosis and 30 healthy volunteers who were admitted to the internal medicine clinic in our hospital. We determined sample size according to a power analysis based on previous articles about nesfatin-1. Volunteers over 18 years old who'd been diagnosed with cirrhosis of the liver and followed up in our clinic and who'd been supported by clinical, laboratory, and radiologic data were included in the study as the patient group. Volunteers over 18 years old without liver cirrhosis were included in the study as the control group. Persons under 18 years of age, who did not give consent, who were pregnant, who have a BMI > 35 kg/m^2, who'd been diagnosed with schizophrenia and anorexia nervosa, or who are patients with a malignancy were excluded from the study.

We noted the age, sex, height, and weight of the participants after obtaining informed consent from all volunteers, then questioned them about comorbidities and drug use before measuring basic biochemical parameters, international normalized ratio (INR), C-reactive protein (CRP), and glycated hemoglobin (HbA1c) levels. We then asked about any complications of cirrhosis and the etiology of cirrhosis. The only complications of cirrhosis in the patient group were hepatic encephalopathy, ascites, and variceal bleeding. The Model for End-Stage Liver Disease (MELD) scores and Child-Pugh stages were also calculated. The primary endpoint of the study is to determine and compare the levels of nesfatin-1 in the patient and control groups. The secondary endpoint of our study is to determine the relationship between cirrhosis complications and nesfatin-1 levels. Our study was approved by Türkiye's University of Health Sciences Prof. Dr. Cemil Taşçıoğlu City Hospital Ethics Committee (Date: 05.03.2019, No: 1143).

Measuring nesfatin-1

A blood sample was taken from the participants in one biochemistry tube and centrifuged. The supernatant portion was stored at -80°C. All stored blood samples were thawed only once on the day of analysis. Nesfatin-1 levels were measured using a human nesfatin-1 enzyme-linked immunosorbent assay (ELISA) kit (Cloud-Clone Corp. ELIZA Kit for Nesfatin 1 [NES1] CEA242Hu 96 Tests), with nesfatin-1 levels able to be detected between 617.3-50,000 pg/mL.

Data analysis

The descriptive statistics use mean, standard deviation, median, and 25%-75% values for the numerical variables, with numbers and percentages being used for the cat-

egorical variables. The independent samples t-test was used to analyze the differences between the two groups of variables through parametric distribution, while the Mann-Whitney U test was used to analyze differences between the two groups of variables with non-parametric distribution and the Kruskal-Wallis test to analyze the differences between more than two groups of variables with non-parametric distribution. Pearson's chi-square test was used for intergroup comparisons of the categorical variables. When a significant difference was detected in the comparisons between more than two groups, a post-hoc analysis was performed to understand from which group the difference had originated. Correlation analysis was performed using Spearman's non-parametric correlation test, with the confidence interval set at 95% and the significance level being accepted as $p < 0.05$.

RESULTS

The patient group includes a total of 51 patients (21 females, 30 males), while the control group includes a total of 30 participants (17 females, 13 males). The groups are similar in terms of age (p=0.201) and sex (p=0.177, Table 1).

When examining the etiology of cirrhosis, liver cirrhosis was seen to be due to cryptogenic liver disease in 15 (29.4%) patients, alcoholic liver disease in 12 (23.5%), nonalcoholic steatohepatitis (NASH) in nine (17.6%), cardiac causes in five (9.8%), hepatitis B virus (HBV) infection in four (7.8%), hepatitis C virus (HCV) infection in three (5.9%), and other causes in three (6%) patients. Nesfatin-1 levels were found to be significantly higher in the NASH group (p=0.003). BMI was higher in the NASH group, but not at a statistically significant level.

The levels of nesfatin-1 were compared between the cirrhosis and control groups and found to be statistically significantly higher in the cirrhosis group (p=0.001, Table 1).

A significant difference was found among the control group, the compensated liver cirrhosis group, and the decompensated liver cirrhosis group in terms of nesfatin-1 levels (p=0.001). Post-hoc analysis was performed to examine from where the difference had originated. Accordingly, the levels of nesfatin-1 in the compensated group were found to be significantly higher than in the control group (p=0.010, Table 2).

Table 1: A comparison of some parameters between the cirrhosis and control groups

	Cirrhosis group (min-max) (n=51)	Control group (min-max) (n=30)	p value
Age (year)	65.8±12.5	61.9±13.9	0.201
Female, n (%) Male, n (%)	21 (42) 30 (58)	17 (56) 13 (44)	0.177
DM (+), n (%) DM (-), n (%)	24 27	17 13	0.404
HT (+), n (%) HT (-), n (%)	23 28	15 15	0.669
IHD (+), n (%) IHD (-), n (%)	11 40	4 26	0.357
BMI (kg/m^2)	27.4±4.2	26.6±3.6	0.439
Nesfatin-1 (ng/mL)	11.3 (8.4-13.1)	7.2 (6-10.1)	**0.001**
Fasting blood glucose (mg/dL)	110 (96-149)	97 (88-174)	0.152
Creatinine (mg/dL)	0.94 (0.6-1.4)	0.73 (0.5-1.2)	0.286
Sodium (mmol/L)	138 (133-140)	139 (137-143)	0.089
ALT (U/L)	20 (14-30)	15 (11.7-19)	**0.007**
AST (U/L)	29 (22-40)	18 (14.7-23.2)	**< 0.001**
Platelet (10^3/uL)	98 (68-125)	211.5 (175.5-271)	**< 0.001**
Total Bilirubin (mg/dL)	1.5 (0.9-2.2)	0.4 (0.3-0.5)	**< 0.001**
INR	1.2 (1.1-1.3)	1.0 (0.9-1.1)	**< 0.001**
Albumin (g/dL)	3.0 (2.4-4.1)	3.7 (3.1-4.1)	**0.004**
HbA1c (%)	6.2 (5.4-7.8)	7 (5.7-8.6)	0.079
CRP (mg/L)	14 (5-63.5)	15.6 (5.2-35.6)	0.835

ALT: Alanine transaminase, AST: Aspartate transaminase, CRP: C reactive protein, DM: Diabetes mellitus, HbA1c: Hemoglobin A1C, HT: Hypertension, INR: International correction ratio, IHD: Ischemic heart disease, BMI: Body mass index

Patients with cirrhosis were grouped as Child A, Child B, Child C (for the Child-Pugh stage) and as having MELD scores equal to or greater than 15 or less than 15. No significant difference was found between the groups in terms of nesfatin-1 levels (Table 3).

Table 2: Nesfatin-1 level comparisons among the control, compensated, and decompensated cirrhosis groups

Nesfatin-1 (ng/mL)	Control A (n=30)	Compensated cirrhosis B (n=20)	Decompensated cirrhosis C (n=31)	A-B-C p value	A-B p value	A-C p value	B-C p value
Median	7.2 (6-10.1)	11.9 (10.2-14.8)	10.4 (6.6-12.6)	**0.001**	**0.010**	0.077	0.218
BMI		(28.01±4.09)	(26.9±4.27)				0.38

BMI: Body mass index

Table 3: Nesfatin-1 level comparison according to the Child A, B, and C as well as MELD <15 and MELD ≥15 groups

Nesfatin-1 (ng/mL)	CHILD A (n=14)	CHILD B (n=28)	CHILD C (n=9)	p value
Mean	11	12.4	11.9	0.667
Median	11.3 (10.1-13.1)	11 (8.1-14.6)	10.4 (6.4-12.6)	
	Cirrhotic patients with MELD ≥15 (n=17)		**Cirrhotic patients with MELD score <15 (n=34)**	
Mean	11.6		12.1	0.589
Median	12.4 (8-14.8)		10.9 (8.3-13.1)	

CHILD: Child-Pugh Score, MELD: Model for End-Stage Liver Disease score

We examined the relationship between nesfatin-1 levels and the amount of ascites (absent, minimal, overt; p=0.727), the presence of encephalopathy (absent, present; p=0.499), and variceal bleeding (absent, present; p=0.902) and found no significant difference.

We then examined the relationship between complications and nesfatin-1 levels and again found no significant correlation (ascites: r=-0.096, p=0.504; encephalopathy: r=-0.096, p=0.505; variceal bleeding: r=0.017, p=0.903).

DISCUSSION

Our study has found serum nesfatin-1 levels to be significantly higher in the cirrhosis of the liver patient group than in the control group. Increased nesfatin-1 levels may be one of the mechanisms of malnutrition and cachexia in patients with cirrhosis. When making a triple comparison among the compensated liver cirrhosis, decompensated liver cirrhosis, and control groups, a significant difference was found in terms of nesfatin-1 levels. When comparing the groups with one another in pairs, a significant difference was found only between the compensated liver cirrhosis group and the control group.

Nesfatin-1 has been shown to be an anorectic polypeptide and to be expressed in peripheral tissues such as the liver and the hypothalamus (4, 7). In the decompensated period, hepatic expression of nesfatin-1 may decrease with the deterioration of liver functions. Again, in patients with encephalopathy, central expression of nesfatin-1 may decrease due to possible central nervous system involvement. These mechanisms may explain the relatively lower release of nesfatin-1 in decompensated liver cirrhosis than in compensated liver cirrhosis. On the other hand, when comparing the control group and the decompensated cirrhosis group, p was found to be 0.070, which is not significant; however, we might have reached a significant difference if we'd had more patients. Clearly, more studies with larger patient groups are needed on this subject.

The Child-Pugh classification and MELD are prognostic scoring systems created using biochemical parameters and the complications of cirrhosis. With its antioxidant and anti-inflammatory properties, nesfatin-1 can be thought to be more prominent in cirrhosis. Although not statistically significant, the relative elevation of nesfatin-1 in the Child B group supports our view that this may be due to antioxidant and anti-inflammatory activities of nesfatin 1 in compensated liver cirrhosis.

Ogiso et al. found serum nesfatin-1 levels to be lower in patients with anorexia nervosa restricting type when compared to controls (8). When considering this information alongside our results, we can say that the possible defense mechanisms and insufficient production in decompensated liver cirrhosis suppress nesfatin-1 values. Aydın et al. studied 97 patients with cirrhosis in their study on prolidase, urotensin-2, and nesfatin-1 levels. Their study found the serum nesfatin-1 levels to be significantly higher in the

cirrhosis group and the decompensated cirrhosis group when comparing these to the control group (9). The difference between our results and those of Aydın et al. may be due to the patients having comorbid chronic diseases and the differences in the etiologic causes of cirrhosis. Due to the insufficient number of patients, we were unable to make a separate etiologic evaluation. Our study also examined the relationship between complications of cirrhosis and nesfatin-1 and found no significant difference.

The production of free oxygen radicals such as nitric oxide (NO), which plays an active role in the hemodynamic changes developing in liver failure and the regulation of hepatocyte function (10), can be stimulated by endotoxins formed in liver failure, by a portosystemic shunt, by decreased reticuloendothelial cell function, and by bacterial products of gastrointestinal origin being cleared less (11). Úbeda et al. study on rats found increased concentrations of activated helper T cells, monocytes, and proinflammatory cytokines in the peripheral blood of rats with cirrhosis that had not yet developed ascites. They concluded the activation of the immune system to have occurred before the development of ascites in experimental cirrhosis, as well as bacterial DNA fragments to have reached the mesentery lymph nodes and caused local inflammation in compensated cirrhosis (12). Recent studies support nesfatin-1 as having anti-inflammatory, antioxidant, and anti-apoptotic effects (13-16). Another study has also shown nesfatin-1 levels to decrease in sepsis (17). Nesfatin-1 may balance the negative effects of inflammatory cytokines, NO, and free oxygen radicals through its antioxidant and anti-inflammatory mechanisms in those with compensated liver cirrhosis. A decrease in nesfatin-1 levels may accelerate the decompensation process by the decrease in anti-inflammatory, antioxidant, and anti-apoptotic activities.

Mean arterial blood pressure increase induced by nesfatin-1 had been shown to be abolished through the melanocortin-3/4 receptor antagonist or phentolamine (18). Another study showed the blood pressure raising effect of nesfatin-1 to be blocked by the oxytocin receptor antagonist ornithine vasotocin (19). Another study examining the relationship among nesfatin-1, blood pressure, and sympathetic activity showed ICV nesfatin-1 injections to increase the sympathetic activity of the melanocortin system in kidneys and to cause an increase in blood pressure (20). Hyperdynamic circulation occurs in cirrhosis. In hepatorenal syndrome (HRS) and ascites in particular, sympathetic nervous system activation is known to occur due to effective arterial volume reduction. Increased nesfatin-1 levels may play a role in the pathogenesis of cirrhosis and its complications, and the maintenance of compensation through the activation of the sympathetic nervous system.

Nesfatin-1 is a pleiotropic molecule with different effects in many tissues. Many unknown factors could change the results of the study. In addition, the etiology of cirrhosis may also affect nesfatin-1 levels. Therefore, studies with larger numbers of patients are needed to demonstrate the effects of the nesfatin-1 molecule. Our study found no significant difference between BMIs in the control and cirrhosis groups, whereas the nesfatin-1 levels of NASH patients were found to be significantly higher than in the control group. Controversial results about this subject are found in the literature (21, 22). One study showed nesfatin-1 levels to be low in patients with NASH, while another showed them to be high, albeit not a statistically significant level. While our study did find nesfatin-1 levels to be significantly higher in patients with NASH, we refrain from making a definitive interpretation due to their cirrhotic stage and the low number of patients. In patients who develop decompensated ascites, relative weight gain secondary to ascites may be misleading because it may hide malnutrition and sarcopenia when evaluated using BMI alone. The limitations of our study are the lack of additional evaluations for malnutrition and the small sample size.

CONCLUSION

Our study has found nesfatin-1 levels to be significantly higher in the cirrhosis group and compensated liver cirrhosis group compared to in the control group. Nesfatin-1 may be involved in the maintenance of compensation with its antioxidant, anti-inflammatory, and anti-apoptotic effects. Based on the control group, the decrease in serum nesfatin-1 levels in decompensated liver cirrhosis compared to compensated liver cirrhosis may be due to its defense mechanisms and insufficient production. Nesfatin-1 has blood pressure increasing effects on the central and sympathetic nervous system, which may contribute to the maintenance of homeostasis in patients with cirrhosis involving hyperdynamic circulation.

Ethics Committee Approval: The study has ethical approval from the Türkiye's University of Health Sciences Prof. Dr. Cemil Taşçıoğlu City Hospital Ethics Committee (Date: 05.03.2019, No: 1143).

Informed Consent: All participants gave informed consent and volunteered to be interviewed.

Peer Review: Externally peer-reviewed.

Author Contributions: Conception/Design of Study- Ö.K.A., H.E., İ.D.T., Y.A., U.Y., İ.B.A., M.P.O., M.A.A.; Data Acquisition- Ö.K.A., U.Y., H.E., Y.G.; Data Analysis/Interpretation- Ö.K.A., U.Y., H.E., İ.D.T., Y.A., T.T., Y.G.; Drafting Manuscript- Ö.K.A., M.P.O., İ.B.A., M.A.A., H.E.; Critical Revision of Manuscript- Ö.K.A., Y.G., İ.B.A., M.P.O., M.A.A., H.E., Y.A.; Final Approval and Accountability- Ö.K.A., H.E., Y.A., T.T., Y.G.; Material and Technical Support – U.Y., M.A.A., M.P.O., İ.B.A.; Supervision- T.T., Y.G., Y.A., H.E.

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

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

REFERENCES

1. Moctezuma-Velázquez C, García-Juárez I, Soto-Solís R, Hernández-Cortés J, Torre A. Nutritional assessment and treatment of patients with liver cirrhosis. Nutrition 2013;29:1279-85. [CrossRef]
2. Traub J, Reiss L, Aliwa B, Stadlbauer V. Malnutrition in patients with liver cirrhosis. Nutrients 2021;13(2):540. [CrossRef]
3. Oh-I S, Shimizu H, Satoh T, Okada S, Adachi S, Inoue K, et al. Identification of nesfatin-1 as a satiety molecule in the hypothalamus. Nature 2006;443(7112):709-12. [CrossRef]
4. Psilopanagioti A, Nikou S, Papadaki H. Nucleobindin-2/nesfatin-1 in the human hypothalamus is reduced in obese subjects and colocalizes with oxytocin, vasopressin, melanin-concentrating hormone, and cocaine-and amphetamine-regulated transcript. Neuroendocrinol 2019;108(3):190-200. [CrossRef]
5. Prinz P, Stengel A. Nesfatin-1: current status as a peripheral hormone and future prospects. Curr Opin Pharmacol 2016;31:19-24. [CrossRef]
6. Xu Y, Chen F. Antioxidant, anti-inflammatory, and anti-apoptotic activities of nesfatin-1: a review. J Inflamm Res 2020;13:607-17. [CrossRef]
7. Schalla MA, Stengel A. Current understanding of the role of nesfatin-1. J Endocr Soc 2018;2(10):1188-206. [CrossRef]
8. Ogiso K, Asakawa A, Amitani H, Nakahara T, Ushikai M, Haruta I, et al. Plasma nesfatin-1 concentrations in restricting-type anorexia nervosa. Peptides 2011;32(1):150-3. [CrossRef]
9. Aydin F, Cindoglu C, Kirhan I, Uyanikoglu A, Yenice N. Serum prolidase, urotensin-2, and nesfatin levels in patients with compensated or uncompensated cirrhosis. Ann Med Res 2019;26(8):1666-9 [CrossRef]
10. Di Pascoli M, Sacerdoti D, Pontisso P, Angeli P, Bolognesi M. Molecular mechanisms leading to splanchnic vasodilation in liver cirrhosis. J Vasc Res 2017;54(2):92-9. [CrossRef]
11. Frances R, Munoz C, Zapater P, Uceda F, Gascon I, Pascual S, et al. Bacterial DNA activates cell-mediated immune response and nitric oxide overproduction in peritoneal macrophages from patients with cirrhosis and ascites. Gut 2004;53(6):860-4. [CrossRef]
12. Úbeda M, Munoz L, Borrero MJ, Díaz D, Francés R, Monserrat J, et al. Critical role of the liver in the induction of systemic inflammation in rats with preascitic cirrhosis. Hepatology 2010;52(6):2086-95. [CrossRef]
13. Özsavcí D, Erşahin M, Şener A, Özakpinar ÖB, Toklu HZ, Akakín D, et al. The novel function of nesfatin-1 as an anti-inflammatory and antiapoptotic peptide in subarachnoid hemorrhage–induced oxidative brain damage in rats. Neurosurgery 2011;68:1699-708. [CrossRef]
14. Yavuz M, Ozsoy M, Celep B, Gülsari Y, Aslan E, Bozbiyik O, et al. Anti-inflammatory and anti-apoptotic effect of nesfatin-1 on liver ischemia-reperfusion injury. Ann Ital Chir 2020;91:207-14.
15. Thébault E, Purucker M, Whaler KA, Langlais B, Sabaka TJ. The magnetic field of the Earth's lithosphere. Space Sci Rev 2010;155:95-127. [CrossRef]
16. Kolgazi M, Ozdemir-Kumral Z, Cantali-Ozturk C, Demirci E, Yuksel M, Sirvanci S, et al. Anti-inflammatory effects of nesfatin-1 on acetic acid-induced gastric ulcer in rats: involvement of cyclo-oxygenase pathway. J Physiol Pharmacol 2017;68(5):765-77.
17. Toprak İ, Eruzun H, Kutlu Y, Arman Y, Yumuştutan P, Yoldemir Aydın Ş, et al. Diagnostic and prognostic value of Nesfatin-1 in sepsis and septic shock. J Exp Clin Med 2022;39(1):1-6. [CrossRef]
18. Wernecke K, Lamprecht I, Jöhren O, Lehnert H, Schulz C. Nesfatin-1 increases energy expenditure and reduces food intake in rats. Obesity (Silver Spring) 2014;22(7):1662-8. [CrossRef]
19. Yosten GL, Samson WK. The anorexigenic and hypertensive effects of nesfatin-1 are reversed by pretreatment with an oxytocin receptor antagonist. Am Physiol-Regul Integr Comp Physiol 2010;298(6):R1642-47. [CrossRef]
20. Tanida M, Mori M. Nesfatin-1 stimulates renal sympathetic nerve activity in rats. Neuroreport 2011;22(6):309-12. [CrossRef]
21. Başar Ö, Akbal E, Köklü S, Koçak E, Tuna Y, Ekiz F, et al. A novel appetite peptide, nesfatin-1 in patients with non-alcoholic fatty liver disease. Scand J Clin Lab Invest 2012;72(6):479-83. [CrossRef]
22. Ayyildiz T, Dolar E, Barbaros O, Arıkan Ş, Balaban S. Non-alcoholic Fatty Liver Disease and Its Association with Serum Nesfatin-1. Anatol Clin J Med Sci 2022;26(1):45-53. [CrossRef]