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Relationship and Interaction between Anaerobic Sports Branches and Serum Nesfatin-1

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Abstract

Objective: Nesfatin-1, an important molecule for energy balance, is a toughness molecule in the hypothalamus comprising 82 amino acids and having a molecular weight of 9.7 kDa. We investigated whether the level of Nesfatin-1 in athletes before and after anaerobic exercise is affected by engaging in competitive and challenging sports, such as athletics, boxing, and taekwondo.
Material and Methods: Blood samples from a group of athletes who engaged in the aforementioned sports were collected in biochemical tubes. Nesfatin-1 concentrations were determined using a commercially available ELISA kit and the competitive inhibition enzyme immunoassay technique. The Wilcoxon-signed rank, Kruskal–Wallis, and Mann–Whitney U tests were performed. Significance levels were set at 0.01 and 0.05.
Results: Nesfatine-1 level is found to be significantly different before and after the anaerobic competition exercise in athletics, boxing and taekwondo sportsmen that maintain their active sport experience except sedentary group belongs to anaerobic exercise ($p_{athletic}$s= 0.00, p<0.05; p_{boxing}= 0.00, p<0.05; $p_{taekwondo}$=0.00, p<0.05). While this significant difference were seen between the all groups and sedentary group, significant changes were also seen before and after the competition exercise in all group's Nesfatin-1 levels.
Conclusion: The increase in Nesfatin-1 levels may depend on the level of hunger emerging at and immediately after exercising or a neuromuscular stimulus reflex that restores energy balance after excessive energy production that occurs during exercise.
Keywords: Nesfatin-1, anaerobic exercise, energy systems, taekwondo, boxing, athletics

Introduction

Although the twenty-first century is an era in which information and technology facilitates improvements in individuals' lives on both social and conventional scales, it has also resulted in the prevalence of conditions, such as obesity, stress, and cardiovascular diseases. These conditions can be caused by inactivity and monotony, i.e., physical and psychological states that emerged after the replacement of human labor with mechanization during industrialization. Some people now shun activity in outdoor environments in favor of remaining at their desks or on their sofas; such inactivity is greatly influenced by modern and convenient means of communication.

To mitigate physical inactivity that threatens community health and can result in cardiovascular disease; obesity; diabetes; tension; high cholesterol levels; and derivative psychological states, such as boredom and stress, health scientists recommend planned, programmed, and periodic exercise. Through exercise, it is now possible to prevent and cure many chronic physical and psychological diseases. Exercise, which can be defined as regular physical movement, can also result in the production and destruction of the molecules that function as the building blocks of the human organism (1). Exercise regulates the secretion of biomolecules, such as ghrelin, leptin, obestatin, and visfatin, that function in energy metabolism and in many body systems (2-6).

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Furthermore, data on nesfatin demonstrate that intense exercise has a short-term effect on appetite suppression (2,7). Energy is required to perform work. In humans, the ability to do work depends on the conversion of potential energy into mechanical energy through chemical reactions (8). Differences between physical, psychological, and metabolic parameters have been studied through clinical research conducted on athletes engaged in various sports. Adenosine triphosphate (ATP) is formed in both the aerobic and anaerobic metabolic systems. Energy requirements for short-term maximal exercises are mostly obtained through the anaerobic glycolysis and phosphagen systems (9).

Athletics that is expressed as work, games, and competitions comprising running, walking, throwing and jumping, requires physical power, endurance, agility, and speed. The sport of boxing is characterized by short-term dynamic phases that involve almost all muscle groups, and it requires maximal and sub-maximal power intensity that causes body movements to accelerate or slow down (10). Taekwondo is a full contact, tense, and violent martial art that requires heavy physicality and intense training programs (11). When examining exercise and its effects on the body, it is beneficial to make use of qualified aerobic and anaerobic athletes. Along with exercise, several branches of sport are connected to emotional conditions experienced by humans, including aerobic and anaerobic endurance, stress, struggles, and competition. Therefore, in our study, we considered all possibilities by selecting athletes with different stress, endurance, struggle, and competition levels, particularly those athletes who make use of the anaerobic metabolism energy system.

Nesfatin-1 has recently received substantial attention as a molecule associated with sports, exercise, and metabolism. An important molecule for energy balance, Nesfatin-1 is a fullness molecule found in the hypothalamus that was first defined by Oh-I et al. (12) in 2006. It comprises 82 amino acids and has a molecular weight of 9.7 kDa. Nesfatin is expressed in many peripheral tissues, such as fat tissue in the gastrointestinal system, and in the brain, which covers the hypothalamic para-ventricular nucleus, supra-optic nucleus, arcuate nucleus, and the lateral hypothalamic area/region. It has a significant effect on metabolic regulation and eating behavior (3,12-18).

After conducting research on energy balance, which is vital for living organisms, Blundell et al. (19) asserted that energy balance signals were more effective with respect to appetite than hunger. The recently discovered Nesfatin-1 hormone is closely associated with energy metabolism, and because it is related to the appetite signal in the neurons of the hypothalamus, it is likely to be the connection point that has been lost or not yet illuminated in terms of energy balance (20). Nesfatin-1 has attracted much attention within the last two years because of its repetitive/reproducible food intake-reducing effect, which is associated with the intake of other hypothalamic peptides and regulates nutritional behaviors. Increasing evidence also promotes the effects that result in several stress-activated endbrain and hindbrain NUCB2/Nesfatin-1 circuits (8,16,17).

In studies on nesfatin and exercise, it has been reported that heavy, continuous physical exercise compresses/reinforces orexigenic (AgRP, NPY, and ghrelin) and anorexigenic peptide/protein (obestatin, leptin, POMS, CART, and visfatin) secretion and concentration in central and peripheral tissues (3-6). Likewise, data related to nesfatin reveals that intense exercise has a short-term effect on appetite suppression (7). In continual attempts to understand new information and specifications, it is unlikely that nesfatin will be disassociated with exercise and sports. Therefore, we studied how training in athletics, boxing, and taekwondo (sports in which stress, struggle, and energy requirements/consumption are similar within the framework of the discipline of competition) influences pre- and post-competition nesfatin values, and we assessed the effects and levels of Nesfatin-1 in the bodies of athletes before and after exercise.

Material and Methods

This research was approved by the Atatürk University Faculty of Medicine Ethical Committee of Clinical Researches (dated 23/01/2014 and assigned number 8). The study was designed to include four groups, each comprising 20 subjects (Table 1): Group 1, voluntary sedentary; Group 2, athletics branch athletes who exercise for 4 hours with daily double training periods, 6 days a week; Group 3, boxing sports branch; and Group 4, taekwondo sports branch. The average ages (in years) of the volunteer members for each group were as follows: athletics: 19.87±1.60; boxing: 20.15±1.52; taekwondo: 20.60±1.65 (athletes with national and international competition experience); and sedentary: 20.40±1.85 (Table 2). Blood samples were drawn from all 80 participants before and after training, and then pre- and post-training serum Nesfatin-1 levels were compared.

The training plans employed in the study were as follows: athletics group, 15-min warm-up exercises and 800 m competition; boxing group, 15-min warm up exercises and 3 × 3 (9)-min round competition; taekwondo group, 15-min warm up exercises and 2 × 3 (6)-min round competition that were organized within the framework of the official rules.

Biochemical Analysis

Blood Sampling

Blood samples were drawn from the participants into biochemical tubes and immediately transported to the biochemistry laboratory. To obtain sera, the samples were centrifuged at 4.000 rpm for 10 min at 5°C. Sera were then stored at –80°C until the biochemical measurements for Nesfatin-1 were performed.

Biochemical Investigations

Nesfatin-1 concentration was determined using a commercially available ELISA kit (USCN Life Science Inc. Export Processing Zone, Economic & Technological Development Zone, Wuhan 430056, P.R. China; catalog number: E90242Hu ELISA kit). The minimum detectable dose of human nesfatin-1 is typically <235.5 pg/mL. Intra-assay precision is CV <10% and inter-assay precision is CV <12%. The sensitivity of this assay or the lower limit of detection was defined as the lowest protein concentration that could be differentiated from zero. It was determined by subtracting two standard deviations from the mean optical

Table 1. Athlete groups and their average ages

Groups	n	Age average (years)
Sedentary	20	20.40±1.85
Athletics	20	19.87±1.60
Boxing	20	20.15±1.52
Taekwondo	20	20.60±1.65
Total	80	20.25±1.66

Table 2. Blood Nesfatin-1 levels obtained from the sports groups before and after participating in sports

			Average ± Standard deviation	p value
Nesfatin-1	Athletics	Before	1175.26±509.28	0.000*
		After	2601.06±599.63	
	Boxing	Before	924.26±449.07	0.000*
		After	1988.69±545.56	
	Taekwondo	Before	1177.89±248.89	0.000*
		After	3923.90±1362.09	

Results were expressed as average ± standard deviation
*Statistical significance, p<0.005

Table 3. Descriptive statistics for each treatment group

Group		n	Minimum	Maximum	Median
Sedentary	Measurement	20	920.44	1866.17	1213.74
Athletics	Before	20	616.69	1816.67	1038.36
	After		1297.36	3232.87	2849.46
Boxing	Before	20	565.71	1547.47	637.23
	After		1027.62	2556.69	1848.42
Taekwondo	Before	20	675.23	1507.74	1134.91
	After		2141.45	5606.21	3754.9

density value of twenty zero standard replicates and then calculating the corresponding concentration.

The competitive inhibition enzyme immunoassay technique was employed in the biochemical investigations. A monoclonal antibody specific to human Nesfatin-1 was pre-coated onto a microplate. A competitive inhibition reaction was launched between biotin-labeled human Nesfatin-1 and unlabeled human Nesfatin-1 (standards or samples) with the pre-coated antibody specific for human Nesfatin-1. After incubation, the unbound conjugate was washed off. Subsequently, avidin conjugated to horseradish peroxidase (HRP) was added to each microplate well and incubated. The amount of bound HRP conjugate was reverse proportional to the concentration of Nesfatin-1 in the sample. After addition of the substrate solution, the intensity of the color developed was reverse proportional to the concentration of Nesfatin-1 in the sample.

Statistical Analysis

In this study, the minimum and maximum values of the nesfatin values in the blood samples taken from the athletes in the treatment and control groups were obtained, and the average and standard deviation for groups were calculated. Analyses were made to determine whether the normality hypothesis of the data was met. In the two measurements that would compare the sample averages, since the test conditions could not be provided due to abnormalities in the distribution of the inter-measurement differences, the existence of a difference between the measurements was tested using the Wilcoxon-signed rank test, which is a non-parametric comparison test that can be used as an alternative to the Student's t-test for associated samples. The Kruskal–Wallis test was also performed to compare the averages of the measurements of the four groups, and the Mann–Whitney U test was performed to determine any significant inter-group differences. Following the Mann–Whitney U test, the Bonferroni correction was made and the alpha level, which was normally 0.05, was divided by the number of tests performed (0.05/6). Therefore, a new critical alpha value was calculated to be 0.0083, and statistical significance was determined on the basis of this value.

Table 4. Comparison of the measurements on the basis of exercise before and after Nesfatin-1 values by Wilcoxon-signed rank test

	After Measurement-Before Measurement	n	Rank average	Rank total	z	p
Sedentary	Negative ranks	-	-	-	.000	1.000
	Positive ranks	-	-	-		
	No difference	20				
Athletics	Negative ranks	1	1.00	1.00	-3.893	.00
	Positive ranks	19	11.00	209.00		
	No difference	-				
Boxing	Negative ranks	-	.00	0.00	-3.932	.00
	Positive ranks	20	10.50	210.00		
	No difference	-				
Taekwondo	Negative ranks	-	.00	.00	-3.927	.00
	Positive ranks	20	10.50	210.00		
	No difference	-				

Table 5. Comparison of the measurements on the basis of exercise before and after Nesfatin-1 values by Kruskal–Wallis test

Groups (before)	n	Rank average	Median	Sd	X^2	p	Significant difference
1. Sedentary	20	48.45	1213.74	3	8.566	0.036	Unavailable
2. Athletics	20	44.15	1038.37				
3. Boxing	20	28.1	637.23				
4. Taekwondo	20	41.3	1134.91				
Groups (after)	**n**	**Rank average**	**Median**	**Sd**	**X^2**	**p**	**Significant difference**
1. Sedentary	20	13.75	1213.74	3	53.563	0.00	Available 1<2, 1<3, 1<4, 2>3, 2<4, 3<4,
2. Athletics	20	51.7	2849.46				
3. Boxing	20	32.75	1848.42				
4. Taekwondo	20	63.8	3754.9				

Results

Table 2 shows the effects of athletics, boxing, and taekwondo on Nesfatin-1 levels. The t-test for the associated samples determined a significant difference between the averages of the nesfatin levels that were measured before exercise ($\bar{X}_{Athletics\text{-}Before}$=1175.26, $\bar{X}_{Boxing\text{-}before}$=924.26, and $\bar{X}_{Taekwondo\text{-}before}$=1177.89,) and the averages of the nesfatin values that were measured after exercise ($\bar{X}_{Athletics\text{-}after}$=2601,06, $\bar{X}_{Boxing\text{-}After}$=1988.69, and $\bar{X}_{Taekwondo\text{-}after}$=3923,90): ($t_{athletics\ (19)}$ =-9.21, p<0.05; $t_{boxing(19)}$ =-7.97, p<0.05; and $t_{taekwondo\ (19)}$ =-9.76, p<0.05).

The descriptive statistical values for Nesfatin-1 levels measured before and after sedentary, athletics, boxing, and taekwondo sports are provided in Table 3. Considering the arithmetic averages of the Nesfatin-1 levels in athletes from the treatment groups before and after athletics, boxing, and taekwondo (Table 3), all post-application values were higher than the pre-application values and the averages of the individuals in the sedentary group. To determine whether these differences were statistically significant and compare the parametric tests, it was necessary to confirm whether the hypotheses of the related test were met.

On the basis of the results of the data normality test, the data were not normally distributed (Shapiro–Wilk test, p<0.05). In the two measurements comparing the sample averages, since the test conditions could not be provided due to abnormalities in the distribution of the inter-measurement differences, the difference between the measurements was tested by the Wilcoxon Signed Rank test. The results of the Wilcoxon-signed rank test, which was chosen because of the lack of normality, are provided in Table 4. On the basis of the Wilcoxon-signed rank test, a statistically significant difference was observed between the before and after exercise Nesfatin-1 levels of participating athletes ($Z_{athletics}$=-3.893, p<0.05; Z_{boxing}=-3.932, p<0.05; $Z_{taekwondo}$=-3.927, p<0.05). These results demonstrate that the various sports applications had significant effects on Nesfatin-1 levels (Figure 1).

Table 5 shows the results of Kruskal–Wallis tests for inter-group differences in Nesfatin measurements taken before and after exercise in the sedentary, athletics, boxing, and taekwondo groups. The data for the Kruskal- Wallis test are provided in Table 5.

When we examine Table 5, based on the Kruskal-Wallis test performed to determine whether there was a difference between the Nesfatin-1 values of the four groups before and after the application of exercise, significant differences in average Nesfatin-1 levels were observed both before and after exercise among the groups ($X^2_{before(3)}$=8.566, p<0.05; $X^2_{after(3)}$=53.563, p<0.05). In multiple comparisons using the Mann–Whitney U test, although there were no significant differences among the groups before the application of exercise, the post-application nesfatin levels significantly differed between groups as follows: the sedentary group differed from the athletics group in favor of the athletics group; the sedentary group differed from the boxing group in favor of the boxing group; the sedentary group differed from the taekwondo group in favor of the taekwondo group; the athletics group differed from the boxing group in favor of the athletics group; the athletics group differed from the taekwondo group in favor of the taekwondo group; and the boxing group differed from the taekwondo group in favor of the taekwondo group. When the Bonferroni correction was applied and the alpha level, which is typically 0.05, was divided into the number of tests performed (.05/6), a new critical alpha value was determined to be 0.0083, and the significance was determined on the basis of this value.

Discussion

In this study, significant differences were found between the pre- and post-competition nesfatin values of athletes participating in athletics, boxing, and taekwondo. These groups contained participants who maintained active sports lives at the national and international competition level within the scope of anaerobic metabolism, and they were in contrast to participants in the healthy sedentary group. Nesfatin-1 was found in

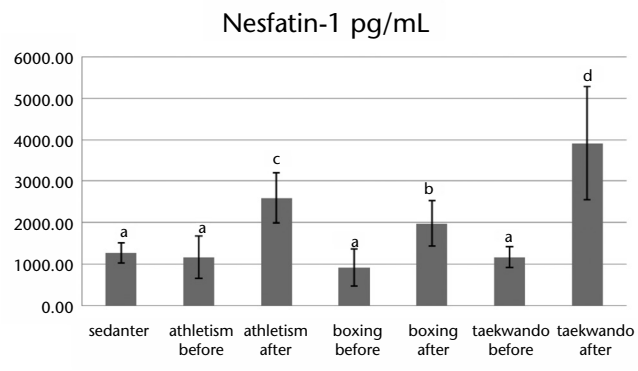

Figure 1. Serum Nesfatin-1 levels of all groups

all groups before and after competition. After exercise within the framework of competition discipline, a significant difference was determined between the sedentary group and the athletics group in favor of the athletics group; between the sedentary group and the boxing group in favor of the boxing group; and between the sedentary group and the taekwondo group in favor of the taekwondo group. Furthermore, on the basis of the comparisons between the sports branches, significant differences in Nesfatin-1 levels were determined between the athletics group and the boxing group in favor of the athletics group; between the athletics group and the taekwondo group in favor of the taekwondo group; and between the boxing group and the taekwondo group in favor of the taekwondo group.

It has been reported that heavy, continuous physical exercise compresses/reinforces orexigenic (AgRP, NPY, and ghrelin) and anorexigenic peptide/protein (obestatin, leptin, POMS, CART, and visfatin) secretion and its concentration in central and peripheral tissues (3-6). Furthermore, some data reveals that intense exercise has a short-term effect on suppressing appetite (7). In the literature, Oh-I et al. (12) demonstrated that Nesfatin-1 is an amino terminal fragment derived from NEFA/nucleobinding2 (NUKB2). Rat cerebrospinal fluid contains Nesfatin-1 that is an amino terminal fragment derivative of NUKB2, and its concentration decreases in the hypothalamic nucleus during conditions of hunger. NUKB2's conversion into Nesfatin-1 is required for the suppression of food intake (12), and studies have demonstrated that although the continuous infusion of Nesfatin-1 into cerebral ventricles via an osmotic pump leads to a substantial reduction in food intake, body weight, and mesenteric, subcutaneous, and epididymal fat mass, it does not lead to changes in skeletal muscle (12,21,22). Algül and Özçelik (22) stated that the hypothalamus controls the weight–energy balance of the body; the lateral hypothalamus controls nutrition, whereas the ventral-medial hypothalamus controls the feeling of satiety. These parts of the hypothalamus act in conjunction with stimulant and suppressive signals.

The Nesfatin-1 hormone, secreted from the neurons in the hypothalamus, is believed to be key to the balance of energy related to appetite (22). Additionally, Nesfatin-1 and body mass index (BMI) are negatively correlated in non-obese people, and the concentration of Nesfatin-1 is substantially lower in groups with higher BMIs (22). Plasma Nesfatin-1 levels have been demonstrated to be lower in patients with anorexia neurosis, a condition characterized by chronic food intake restriction (23,24).

In the present research, we found that anaerobic exercise substantially increased Nesfatin-1 levels in athletes engaging in athletics, boxing, and taekwondo. All branch athletes who have participated in our competition protocol in official competition rules and periods, and all athletes' being weight athletes and their obligation to keep their body weights at an optimum level by training. Therefore, their preparation for the competitions usually requires losing excessive weight can express that nesfatin's increase as a fullness molecule at the time of struggle occurs within the framework of physiological and psychological conditions.

Another study by Ghanbari-Niaki et al. (2), which was similar to our study, assessed the effects of anaerobic exercise on nesfatin that were influenced by metabolic stress and other hormones. Their study demonstrated that exercise protocols lead to metabolic stress despite substantial changes in glucose-regulating hormone circulation, plasma glucose, and lactate but that there was no substantial change in plasma Nesfatin-1. In contrast to exercise protocols, the deficiency of Nesfatin-1 can be partially because of regimen, diet, state, or the condition of hunger.

When we consider all previous studies and this study, we can conclude that along with releasing high levels of energy, anaerobic exercise increases nesfatin levels in athletes because of the disintegration of ATP (which is required for short-term muscular contractions) into creatinine and phosphate ions. ATP revelation to be used by muscles and suppressing energy requirement are dependent on the feeling of hunger, which occurs because of the discharge of energy stores, and the secretion of nesfatin. Thus, a reflex of neuromuscular stimulants can provide the feeling of fullness and energy balance. The increase in nesfatin secretion does not have any adverse effects on nerve–muscle coordination, which is a determinant of an athlete's performance during competition.

Another likely mechanism for the increase in nesfatin levels in exercisers is the effects of Nesfatin-1 on the central nervous system. Nesfatin-1 affects the hypophysis-adrenal axis and the sympathetic nervous system, leading to a wide effect spectrum that promotes organ function and emotions. These central activities, along with the activation of NUCB2/Nesfatin-1 neurons in the brain by various types of stress, are an adaptive reaction stimulated under stressful conditions (13,25-27). The effects of Nesfatin-1 on psychological metabolism have also been examined in several studies and were shown to play a role in adaptation to stress (28).

Bez et al. (29) compared the plasma levels of Nesfatin-1 in patients with panic disorder and those in a healthy control group; they found that there was a positive correlation between plasma Nesfatin-1 levels and panic attack scores in patients with panic disorder. Thus, they stated that there may be an association between anxiety and plasma Nesfatin-1 levels in these patients. Furthermore, it was shown that Nesfatin-1 regulates

cardiac function, reduces blood glucose levels, and induces behaviors such as fear and anxiety. Therefore, Nesfatin-1 is known as a multifunctional peptide with an anorectic effect (29-31).

These findings can be used to explain the Nesfatin-1 levels observed in our study. Specifically, heart rate and blood pressure increased during the exercises that required short-term exertion, fierce competition, and aggressive struggle, and this led to irregularity of cardiac function; anaerobic exercise can lead to high secretion levels of Nesfatin-1, which stimulates metabolism-induced cardiac functional disorders and blood glucose imbalance as a reaction to psychological traumas, such as stress, anxiety, fear, or panic attacks, on the basis of the reduction in blood sugar associated with energy requirements.

Nesfatin-1 is found in brain tissues as well as in peripheral tissues, such as adipose tissue, the stomach, pancreas islets, liver, and testis (17,18). It has been demonstrated to have a nesfatin-like immuno-effect in the first pancreatic β-cells, and studies have been conducted to study and characterize whole-body energy homeostasis, insulin secretion, and the effect of Nesfatin-1 with respect to glycemic history. It has been demonstrated that glucose-reaction Nesfatin-1 regulates insulin secretion, glucose homeostasis, and whole-body energy balance in rats (32). Similarly, a study by Fingar et al. (33) reported that central nesfatin-1 increased continuous, partial insulin sensitivity, and glucose tolerance by activating the insulin signal route.

On the basis of the findings of these studies, during the fast discharge of muscle and liver glucose and glycogen stores during anaerobic exercise, secretion of the energy balance molecule nesfatin may have increased to balance the increasing blood sugar levels (i.e., the glucose level) in the case of the revelation of energy requirements and the high energy levels in the exercisers. In other words, the energy requirement for an organism is supplied primarily through glucose in the blood for short-term and intense exercises and muscle contractions; thus, blood sugar naturally decreases. Glycogen, which is stored in the muscles and liver, is carried by means of glucagon hormones to the blood as glucose. At this phase of transition, the body could have secreted a high amount of Nesfatin-1 as an energy regulator to avoid entering into shock. Alternatively, Nesfatin-1 may have been secreted to provide energy and insulin balance because of the increase in primary ATP production by glucose and glycogen stores in the blood, muscles, and liver for short-term contractions, i.e., the organism perceived the high energy levels as high blood sugar.

Conclusion

In our study, the level of blood nesfatin increased in the participants after sports activity. Levels of Nesfatin-1 may depend on 1) Secretion to suppress the feeling of hunger, which originates because of energy requirements during and immediately after exercise; 2) A reflex of neuromuscular stimulants to provide energy balance in excessive energy production, which emerges during exercise; 3) Secretion to regulate both cardiac functional disorders and any blood glucose imbalance caused by psychological traumas, such as stress, anxiety, fear, or panic attacks, which emerge because of exercise; or 4) Secretion to provide energy and insulin balance because of a perceived excess in ATP production due to exercise, which is detected as high blood sugar. However, further advanced and developed studies should be conducted to examine these claims in detail.

Ethics Committee Approval: Ethics committee approval was received for this study from Atatürk University Faculty of Medicine Clinical Investigations Ethics Committee.

Informed Consent: Information was given to the patients verbally about research and approval of the patients was verbally received.

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