

## RESEARCH ARTICLE

### Dynamics of the content of free amino acids in blood of patients during the long-term use of orthopedic dental metal prostheses

Andrey Yu Nikonov<sup>1</sup>, Olga V Zaytseva<sup>2</sup>, Maksym O Serhienko<sup>1</sup>, Natalia V Krychka<sup>1</sup>, Natalya N Breslavets<sup>1</sup>

<sup>1</sup>Department of Orthopedic Dentistry, Kharkiv National Medical University, Kharkiv, Ukraine, <sup>2</sup>Department of Medical and Biological Physics and Medical Informatics, Kharkiv National Medical University, Kharkiv, Ukraine

Correspondence to: Andrey Nikonov, E-mail: andrew-nikonov65@mail.ru

Received: August 03, 2017; Accepted: October 18, 2017

#### ABSTRACT

**Background:** The effect of materials for dental prostheses on the patient's body remains one of the most relevant issues in orthopedic dentistry. The dentist, more often the orthopedist, has to deal with diseases arising from the toxic effects of chemical mixtures of structural metals on the tissues of the oral cavity and the body as a whole. **Aims and Objectives:** The research purpose is to carry out the dynamics of the content of free amino acids (FAA) in the blood of patients during the long-term use of orthopedic dental metal prostheses. **Materials and Methods:** This paper studies the dynamics of the content of FAA in blood plasma of patients organized into three groups before and after 0.5–1–2 years of the prosthodontic treatment of defected teeth (dentitions) with cast-crowns on the basis of stainless steel alloys and nitride-titanium (NT) coating (Group 1), nickel-chromium alloy (NCA, Group 2), and cobalt-chromium alloy blended with ceramics (CCA, Group 3). **Results:** The study has established a significant increase in FAA levels in blood plasma of Group 1-3 patients during the long-term use of dental orthopedic prostheses, suggesting the disordered processes of protein synthesis and decomposition, the predominance of catabolic over anabolic processes as well as the early manifestations of destructive processes occurring in various organs and tissues. **Conclusion:** Based on the results of studying the effect of metal dental prostheses (stainless steel + NT, NCA, CCA + ceramics) on the FAA pool in patients' blood plasma, a number of preferences are as follows: Stainless steel alloy + NT is more aggressive than NCA; NCA is more aggressive than CCA + ceramic mass. The data obtained in this paper are promising in terms of forecasting various pathologies in the body during prosthodontic treatment with new dental materials.

**KEY WORDS:** Free Amino Acids; Blood Plasma; Orthopedic Dental Metal Prostheses


#### INTRODUCTION

The effect of materials for dental prostheses on the patient's body remains one of the most relevant issues in orthopedic dentistry. The dentist, more often the orthopedist, has to deal with diseases

arising from the toxic effects of chemical mixtures of structural metals on the tissues of the oral cavity and the body as a whole.<sup>[1-5]</sup>

With the intensive use of dental orthopedic prostheses made of various metals in the process of restoration of defected teeth and dentitions, the question inevitably arises as to how the human body can counteract these metallopathic loads, what the capabilities of the body are and how the undesirable effects of structural alloys can be taken into account in preventive and treatment medicines.<sup>[6-8]</sup>

Literature data<sup>[9,10]</sup> and conclusions drawn from the authors' previous studies<sup>[11,12]</sup> indicate the likelihood of developing

Access this article online	
Website: <a href="http://www.njppp.com">www.njppp.com</a>	Quick Response code 
DOI: 10.5455/njppp.2018.8.0829918102017	

National Journal of Physiology, Pharmacy and Pharmacology Online 2018. © 2018 Andrey Nikonov, et al. This is an Open Access article distributed under the terms of the Creative Commons Attribution 4.0 International License (<http://creativecommons.org/licenses/by/4.0/>), allowing third parties to copy and redistribute the material in any medium or format and to remix, transform, and build upon the material for any purpose, even commercially, provided the original work is properly cited and states its license.

common complications in patients using prostheses made of metal alloys including diseases of the digestive tract, liver, and disorders of the nervous system. Thus, it is possible to assume the presence of significant metabolic shifts in the body under the influence of the studied factors.

Amino acids are essential in metabolic transformations and play a key role in the processes of intermediary metabolism. The development of pathological changes and destructive phenomena in many cases is characterized by an amino acid imbalance in the body. The level of free amino acids (FAA) of human blood plasma is known as a diagnostic parameter used in the diagnosis of such diseases as peptic ulcer, severe sepsis and septic shock, pancreatitis, and oncological diseases.<sup>[13-17]</sup>

In this connection, it seems relevant and important to analyze the dynamics of the FAA content of patients' blood plasma during the use of dental metal prostheses.

The purpose of this study is to compare the long-term results of using non-removable dental prostheses made on the basis of various metal alloys in terms of the dynamics of levels of the amino acid content of blood plasma and discuss the prospects for the use of this approach in diagnostic practice.

## MATERIALS AND METHODS

Patients who applied for prosthodontic treatment at the Department of Orthopedic Dentistry of Kharkiv National Medical University (Ukraine) and agreed to participate in the study were organized into three groups:

Group 1 ( $n = 20$ ) - patients who were supposed to have prostheses made of corrosion-resistant steel with a protective nitride-titanium (NT) coating;

Group 2 ( $n = 20$ ) - patients with prostheses based on nickel-chromium alloy (NCA) "Viron 88;"

Group 3 ( $n = 20$ ) - patients with prostheses based on cobalt-chromium alloy (CCA) "Vitalium," blended with ceramic mass "Synspar."

Altogether 60 patients (27 men and 33 women) aged 27-45, who considered themselves somatically healthy, were under supervision. The choice of materials for prosthodontic treatment was due to both medical assessment and patients' financial capabilities.

The object of the study was blood plasma of patients of the same age and gender before and after 1 year of prosthodontic treatment.

The amino acid analysis was performed on an automatic amino acid analyzer AAA T-339 (Czech Republic).<sup>[18]</sup> Patients' blood was taken from the ulnar vein on an empty stomach.

After the separation of the erythrocyte mass,<sup>[18,19]</sup> the plasma was deproteinized by the addition of sulfosalicylic acid in a ratio of 10:1, followed by centrifugation at 2000 rpm for 20 min. The resulting supernatant was ready to be applied to the sampler of an automatic amino acid analyzer.

The statistical processing of the results was carried out by means of the software package Statistica 6.0.<sup>[20]</sup>

## RESULTS

Tables 1-3 summarize data on the FAA content in patients' blood plasma before prosthodontic treatment and 0.5–1–2 years after the use of metal dental prostheses.

Analyzing the results obtained, one can assume that before prosthodontic treatment the total amino acid pool of patient's blood plasma was within the physiological corridor ( $3.220 \pm 0.003$ ). The main amino acids of plasma were glutamine (16.3%), alanine (12.02%), lysine (8.07%), valine (8.04%), and glycine (8.03%).

## DISCUSSION

During the time interval from the moment of prosthodontic treatment to 2 years of the use of corresponding prostheses, in all three groups of patients, there were certain upward shifts in the FAA total concentration as well as the intra-group redistribution of their levels. In this regard, after 1 year, the total -content of all studied amino acids in Group 1 was increased by 6.47 times (by 547%); in Group 2 - by 3.67 times (by 267%); and in Group 3 - by 1.72 times (by 72%). In Group 1, the main amino acids of plasma were serine (18.47%, 30.1 times increase in concentration), alanine (12.48%, 6.72 times increase in concentration), glycine (11.13%, 8.98 times increase in concentration), proline (9.14%, 17.48 times increase in concentration), and lysine (7.95%, 6.37 times increase in concentration).

After 2 years, the FAA pool of blood plasma remained significantly increased in patients with prostheses made of stainless steel (by 5.69 times, or 470%) and NCA (by 3.33 times, or 233%). When using prostheses made of CCA, the fluctuation toward the growth of the FAA content is noticeably less (by 1.45 times, or 45%).

In higher animals and humans, the concentration of amino acids has a tissue and organ specificity, while the blood provides the supply of organs with amino acids and transports them.

Zhukov *et al.*<sup>[21]</sup> observed in their studies that there is a significant increase in the FAA content of blood plasma of experimental animals under the influence of detergents. This is explained by the fact that the intensification of catabolic

**Table 1:** The FAA content in blood plasma of patients using prostheses made of stainless steel with NT coating

Amino acids	Amino acid content, mM/ml (% of the amount)			
	Before prosthodontic treatment	After 6 months	After 1 year	After 2 years
Cysteic acid	0.186±0.001 (5.77)	0.986±0.002* (4.71)	0.934±0.004* (4.48)	0.875±0.003* (4.77)
Aspartic acid	0.212±0.001 (6.58)	0.731±0.004* (3.49)	0.666±0.003* (3.19)	0.534±0.002* (2.91)
Threonine	0.162±0.005 (5.03)	0.789±0.003* (3.77)	0.701±0.005* (3.36)	0.684±0.002* (3.73)
Serine	0.128±0.006 (3.97)	3.971±0.005* (18.96)	3.850±0.009* (18.47)	3.756±0.006* (20.47)
Glutamine	0.525±0.001 (16.3)	1.723±0.003* (8.23)	1.608±0.008* (7.41)	1.412±0.004* (7.70)
Proline	0.109±0.006 (3.38)	2.012±0.007* (9.61)	1.906±0.008* (9.14)	1.531±0.004* (8.34)
Glycine	0.258±0.003 (8.01)	2.505±0.005* (11.96)	2.319±0.006* (11.33)	2.113±0.007* (11.52)
Alanine	0.387±0.004 (12.02)	2.783±0.006* (13.29)	2.602±0.003* (12.48)	2.562±0.008* (13.96)
Valine	0.259±0.003 (8.04)	1.168±0.002* (5.58)	1.172±0.008* (5.62)	0.931±0.005* (5.07)
Isoleucine	0.123±0.001 (3.82)	0.203±0.002* (0.97)	0.330±0.006* (1.58)	0.165±0.004* (0.90)
Tyrosine	0.080±0.001 (2.48)	0.471±0.005* (2.25)	0.586±0.009* (2.81)	0.632±0.007* (3.44)
Lysine	0.260±0.003 (8.07)	1.854±0.005* (8.85)	1.656±0.003* (7.95)	1.174±0.006* (6.40)
Histidine	0.125±0.001 (3.88)	0.481±0.002* (2.30)	0.683±0.004* (3.28)	0.373±0.005* (2.03)
Arginine	0.144±0.002 (4.47)	0.417±0.003* (1.99)	0.358±0.008* (1.72)	0.294±0.007* (1.60)
Leucine	0.135±0.004 (4.19)	0.324±0.006* (1.55)	0.538±0.007* (1.72)	0.406±0.005* (2.21)
Cystine	0.127±0.001 (3.94)	0.522±0.002* (2.49)	0.934±0.004* (4.48)	0.906±0.004* (4.94)
Total	3.220±0.003 (100)	20.940±0.004*	20.843±0.006*	18.348±0.004*

\* - differences with data "before prosthodontic treatment" are reliable,  $P < 0.05$ . NT: Nitride-titanium, FAA: Free amino acids

processes in tissues under various kinds of intoxications is a manifestation of an adaptive reaction aimed at maintaining homeostasis. The increase in the FAA pool as a result of the enhanced protein breakdown contributes to the directed synthesis of a number of cellular structures and other body needs. At the same time, a high content of amino acids in the blood can indicate the predominance of catabolic over anabolic processes in the body.

In the clinical examination of organs and tissues of the oral cavity in Group 1 patients 0.5–1–2 years after the use of metal dental prostheses, the first degree of metallotoxicosis was established. It is characterized by the absence of the objective signs of mucosal lesions, but by periodic pains in the tongue, gums, dry mouth, a sense of viscosity on the lips, a taste of metal, a change in taste.<sup>[12]</sup>

The increase in the total FAA pool of blood plasma in this group of patients, due to the influence of prosthetic material (stainless steel + NT), may indicate not only the disordered processes of protein synthesis and decomposition but also the early manifestations of destructive processes occurring in various organs and tissues.

Patients with non-removable metal prostheses based on NCA (Group 2) after 0.5–1–2 years had no complaints about prostheses or discomfort in the oral cavity. Visible changes from the mucosa, supporting teeth, antagonist teeth, and gum retraction were not detected. This indicates the effectiveness and quality of prosthodontic treatment performed. Although everything seems quite in order, the dynamics of the amino acid content of patients' blood plasma in this group makes it possible to assess their well-being as unstable. The reason

**Table 2:** The FAA content in blood plasma of patients using prostheses made of NCA

Amino acids	Amino acid content, mcM/ml (% of the amount)			
	Before prosthodontic treatment	After 6 months	After 1 year	After 2 years
Cysteic acid	0.186±0.001 (5.77)	0.383±0.002* (3.60)	0.683±0.008* (5.78)	0.421±0.007* (3.93)
Aspartic acid	0.212±0.001 (6.58)	0.302±0.001* (2.84)	0.230±0.007* (1.94)	0.228±0.006* (2.13)
Threonine	0.162±0.005 (5.03)	0.304±0.007* (2.86)	0.206±0.008* (1.74)	0.196±0.004* (1.83)
Serine	0.128±0.006 (3.97)	1.736±0.005* (16.31)	1.802±0.008* (15.24)	1.829±0.005* (17.07)
Glutamine	5.25±0.001 (16.3)	0.281±0.005* (2.64)	0.379±0.009* (3.21)	0.487±0.002* (4.55)
Proline	0.109±0.006 (3.38)	1.123±0.007* (10.55)	1.008±0.005* (8.53)	0.971±0.004* (9.06)
Glycine	0.258±0.003 (8.01)	1.452±0.007* (13.64)	1.350±0.008* (11.42)	1.254±0.006* (11.70)
Alanine	0.387±0.004 (12.02)	0.926±0.002* (8.70)	1.719±0.006* (14.54)	1.637±0.005* (15.28)
Valine	0.259±0.003 (8.04)	0.871±0.001* (8.20)	0.921±0.004* (7.79)	0.614±0.007* (5.73)
Isoleucine	0.123±0.001 (3.82)	0.287±0.008* (2.70)	0.345±0.007* (2.92)	0.305±0.006* (2.85)
Tyrosine	0.080±0.001 (2.48)	0.497±0.007* (4.67)	0.500±0.005* (4.23)	0.516±0.003* (4.82)
Lysine	0.260±0.003 (8.07)	0.812±0.004* (7.63)	0.740±0.007* (6.26)	0.639±0.005* (5.96)
Histidine	0.125±0.001 (3.88)	0.393±0.002* (3.69)	0.459±0.003* (3.88)	0.481±0.008* (4.49)
Arginine	0.144±0.002 (4.47)	0.302±0.003* (2.84)	0.286±0.004* (2.42)	0.275±0.005* (2.57)
Leucine	0.135±0.004 (4.19)	0.386±0.003* (3.63)	0.540±0.007* (4.57)	0.497±0.006* (4.64)
Cystine	0.127±0.001 (3.94)	0.591±0.005* (5.55)	0.656±0.003* (5.55)	0.364±0.007* (3.40)
Total	3.220±0.003 (100)	10.646±0.004*	11.824±0.006*	10.714±0.005*

\*differences with data “before prosthodontic treatment” are reliable,  $P < 0.05$ . NCA: Nickel-chromium alloy, FAA: Free amino acids

lies in the biochemical abnormalities in the body, induced by metal structures based on NCA. The tendency to decrease the levels of sulfur-containing amino acids was established in comparison with the period before prosthodontic treatment, and the signs of endotoxemia appeared.

It should be mentioned that patients with prostheses based on NCA, who had, for example, chronic diseases of the gastrointestinal tract, noted that the attacks happened more frequently. This suggests the etiological role of NCA in inducing the pathology of the digestive system. The data obtained coincide with the opinion of the researchers<sup>[6,10,22-25]</sup> on the importance of the presence of chronic inflammatory diseases in the pathogenesis of intolerance to dental structural materials.

Analyzing the FAA content in blood plasma of Group 3 patients (CCA + ceramic coating), one should note that

during the biennium they did not undergo such profound changes in the parameters of homeostasis, as in the case of metal structures made of stainless steel with NT coating or NCA.

The findings obtained are in tune with the data presented by Ivantsov,<sup>[26]</sup> who conducted a comprehensive study in a comparative aspect of the long-term results of the use of non-removable metal-ceramic prostheses made on the basis of titanium and CCA. It is determined that these materials show good results in terms of clinical effectiveness. By objective criteria, it is proved that titanium is the most optimal metal in terms of biocompatibility as against CCA with respect to influencing the parameters of homeostasis of the oral fluid.

Thus, the study of the FAA content of patients' blood plasma before prosthodontic treatment and 0.5–1–2 years

**Table 3:** The FAA content in blood plasma of patients using prostheses made of CCA with ceramics

Amino acids	Amino acid content, mcM/ml (% of the amount)			
	Before prosthodontic treatment	After 6 months	After 1 year	After 2 years
Cysteic acid	0.186±0.001 (5.77)	0.201±0.002 (3.98)	0.246±0.003* (4.44)	0.198±0.002 (4.25)
Aspartic acid	0.212±0.001 (6.58)	0.252±0.005* (4.99)	0.248±0.004* (4.48)	0.241±0.003* (5.17)
Threonine	0.162±0.005 (5.03)	0.211±0.006* (4.18)	0.189±0.004 (3.41)	0.191±0.005 (4.10)
Serine	0.128±0.006 (3.97)	0.481±0.007* (9.52)	0.681±0.006* (11.15)	0.384±0.004* (8.24)
Glutamine	0.525±0.001 (16.3)	0.603±0.002* (11.94)	0.634±0.008* (11.44)	0.572±0.005* (12.27)
Proline	0.109±0.006 (3.38)	0.325±0.004* (6.44)	0.418±0.004* (7.54)	0.316±0.004* (6.78)
Glycine	0.258±0.003 (8.01)	0.527±0.002* (10.44)	0.512±0.04* (9.24)	0.404±0.005* (8.67)
Alanine	0.387±0.004 (12.02)	0.511±0.001* (10.12)	0.688±0.008* (12.42)	0.643±0.007* (13.80)
Valine	0.259±0.001 (3.82)	0.276±0.002 (5.47)	0.313±0.003* (5.65)	0.298±0.006* (6.39)
Isoleucine	0.123±0.001 (3.82)	0.156±0.002* (3.09)	0.189±0.003* (3.41)	0.165±0.002* (3.54)
Tyrosine	0.080±0.001 (2.48)	0.092±0.003 (1.82)	0.106±0.002* (1.91)	0.101±0.001* (2.17)
Lysine	0.260±0.003 (8.07)	0.573±0.005* (11.35)	0.528±0.004* (9.53)	0.396±0.006* (8.50)
Histidine	0.125±0.001 (3.88)	0.208±0.004* (4.12)	0.189±0.003* (3.41)	0.167±0.002* (3.58)
Arginine	0.144±0.002 (4.47)	0.165±0.003* (3.27)	0.192±0.002* (3.46)	0.181±0.005* (3.88)
Leucine	0.135±0.004 (4.19)	0.273±0.006* (5.41)	0.286±0.005* (5.16)	0.251±0.003* (5.39)
Cystine	0.127±0.001 (3.94)	0.196±0.002* (3.88)	0.183±0.002* (3.30)	0.153±0.001* (3.28)
Total	3.220±0.003 (100)	5.050±0.0035*	5.602±0.004*	4.661±0.004*

\*differences with data “before prosthodontic treatment” are reliable,  $P < 0.05$ , CCA: Cobalt-chromium alloy, FAA: Free amino acids

after the use of metal dental prostheses revealed an increase in the total pool of amino acids, which may indicate the pronounced destructive processes developing in organs and tissues.

## CONCLUSIONS

The method of ion exchange chromatography was used to study the FAA content in patients' blood plasma before and after 0.5–1–2 years of the prosthodontic treatment of defected teeth and dentitions with cast-crowns on the basis of stainless steel alloys and NT coating, NCA, and CCA blended with ceramic mass.

The analysis of the FAA content in blood plasma of patients using prostheses made of various metal alloys (duration

of use is 0.5–1–2 years) indicates a significant increase in FAA concentrations, suggesting the disordered course of metabolic processes, and highlights the early symptoms of possible deeper pathological processes. When using various orthopedic metal structures, there is a significant difference in the amino acid status of blood.

Based on the results of studying the effect of the given metal alloys on the FAA pool in patients' blood plasma, a number of preferences are as follows: Stainless steel alloy with NT coating is more aggressive than NCA; NCA is more aggressive than CCA blended with ceramic mass.

The data obtained are promising in terms of forecasting possible pathologies in the body during prosthodontic treatment with new dental materials.



## REFERENCES

1. Volozhin AN, Babakhin AA. Immunomodulating activity of dental materials. *Stomatologiya*. 2006;1:18-20.
2. Volozhin AN, Babakhin AA, Tsurulnikov LP. Biocompatibility of prosthetic materials. *Stomatologiya*. 2004;83(5):57-61.
3. Marko BP, Kozin VN, Yu AD. Complex approach to the problem of individual intolerance of prosthetic devices from various materials. *Stomatologiya*. 2003;3:47-51.
4. Whittingham-Jones PM, Dunstan E, Altaf H, Cannon SR, Revell PA, Briggs TW. Immune responses in patients with metal-on-metal hip articulations: A long-term follow-up. *J Arthroplasty*. 2008;23(8):1212-8.
5. Shang X, Wang L, Kou D, Jia X, Yang X, Zhang M, et al. Metal hypersensitivity in patient with posterior lumbar spine fusion: A case report and its literature review. *BMC Musculoskelet Disord*. 2014;15:314.
6. Lebede KA, Deynikov AI, Robustova TG. Importance of chronic inflammatory diseases in the origin of polyallergone intolerance to prosthetic materials. *Stomatologiya*. 2006;3:19-27.
7. Yu NM, Goman MV, Uryasyeva EV. Intolerance of materials of prosthetic devices. *Med News N Caucasus*. 2014;9(3):286-91.
8. Rozhnova OM, Pavlov VV, Sadovoy MA. Biological compatibility of medical products based on metals, causes of the formation of pathological reactivity (foreign literature review). *Bull Siberian Med*. 2015;14(4):110-8.
9. Tushina TV. Influence of Metal Alloys Used in Orthopedic Dentistry on Oral Tissues in Patients with Essential Hypertension. Moscow: Doctoral Dissertation; 2007. p. 22.
10. Tsimbalistov AV, Mikhaylova ES, Shabashova NV. Immunological aspects of the pathogenesis of intolerance to dental structural materials. *Stomatologiya*. 2006;4:37-40.
11. Yu NA. Disturbance of prooxidant-antioxidant homeostasis upon the administration of nickel and titanium nitride. *Probl Med Nauky Osvity*. 2005;2:49-52.
12. Yu NA. Pathogenetic Mechanisms of the Formation of Metal-Toxicosis Caused by Metal Prosthetic Devices: Symptoms, Diagnosis, Treatment and Prevention. Kyiv: Doctoral Dissertation; 2012. p. 38.
13. Zhabitskaya ED, Shtemenko NI, Puchenko AA, Sorochan OA. Study of the composition of free amino acids of healthy people and people suffering from anemia. *Visnyk Dnipropetrovsk Univ*. 2002;10(2):78-81.
14. Zaporozhchenko BS, Shishlov VI. Change in the levels of free amino acids in plasma of patients with acute pancreatitis and their correction with the help of early parenteral nutrition. *Klin Khir*. 2000;1:13-5.
15. Maslakova ND, Nefedov LN. Amino acid pool in patients with obstructive jaundice before and after operative removal of obstructions to outflow of bile. *Klin Khir*. 1994;5:42-5.
16. Shishlov VN, Zaporozhchenko BS. Effect of amino acids on the functional activity of the pancreas. *Klin Khir*. 2000;9:49-52.
17. Mariani A, Mezzi G, Masci E, Soldarini A, Calori G, Zerbi A, et al. Accuracy of the plasma amino acid-consumption test in detecting pancreatic diseases is due to different methods. *Pancreas*. 1999;18(2):203-11.
18. Microtech. Instruction Manual for the Automatic Analyzer of Amino Acids AAA T-339. Prague: Microtech; 1981.
19. Bazarnova MA, Morozova VT, editors. *Clinical Biochemistry, Part 3*. Kyiv: Vyscha Shkola; 1986. p. 408.
20. Kim JO, Mueller CW, Klekka WR, Aldenderfer MS, Blashfield RK. *Factorial, Discriminant and Cluster Analysis*. Moscow: Finansy and Statistika; 1989.
21. Zhukov VI, Popova LD, Zaytseva OV. *Simple and Macrocyclic Ethers: The Scientific Basis for the Protection of Water Bodies*. Kharkiv: Tornado; 2000. p. 438.
22. Banchenko GV, Borovskiy EV, Rabinovich IM. Mucosal diseases (allergic diseases). In: Borovsky EV, editor. *Therapeutic Dentistry*. Moscow: MID; 2004. p. 666-77.
23. Karpuk NA, Yu KI, Novikov DK, Kurbakov KM. Use of application samples for diagnosing allergies in patients with intolerance to nickel. *Allerg Immunol*. 2012;4:123-30.
24. Minayev SS, Stryuk RN, Yu MA. Allergic reactions to dental prostheses from gold-based alloys as a stimulating factor for autoimmune processes (clinical observation). *Stomatologiya*. 2006;8:18-21.
25. Tsimbalistov AV, Mikhaylova ES. Problems of adaptation in patients with intolerance to dental structural materials and prosthetic devices. *Parodontologiya*. 2006;38(1):48-9.
26. Ivantsov OA. Comparative Analysis of the Use of Non-Removable Metal-Ceramic Prostheses Based on Titanium and Cobalt-Chromium Alloy. Samara: Doctoral Dissertation; 2004. p. 22.

**How to cite this article:** Nikonov AY, Zaytseva OV, Serhienko MO, Krychka NV, Breslavets NN. Dynamics of the content of free amino acids in blood of patients during the long-term use of orthopedic dental metal prostheses. *Natl J Physiol Pharm Pharmacol* 2018;8(1):118-123.

**Source of Support:** Nil, **Conflict of Interest:** None declared.