International Journal of Psychosocial Rehabilitation, Vol. 24, Issue 04, 2020
ISSN: 1475-7192

IMPROVING THE METHODOLOGY FOR DETERMINING BIOCOMPATIBILITY OF METAL ALLOYS FOR THE PREVENTION OF INTOLERANCE AND GALVANOSIS IN PEOPLE LIVING IN ENVIRONMENTALLY UNFAVORABLE CONDITIONS IN UZBEKISTAN

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Abstract---*The article is devoted tothe improvementof methods for determining the biocompatibility of metal alloys obtained fromvarious dental blanks using the portable expert diagnostic system "Lira-100"; and prevention of the phenomenon of galvanic pathology in the oral cavity, as well as the study of compensatory-adaptive changes in the oral cavity. For this purpose, 103 patients (53 women and 50 men from 39 to 63 years old) wearing metal prostheses of various designs were examined. Among them, there were 59 patients with metal prostheses cast from granules and 44 patients with metal prostheses made from rods, who were previously diagnosed with oral galvanosis and who lived in unfavorable environmental zones.*

Keywords---*biocompatibility of metals, intolerance, biochemical composition of saliva, harmful factors, galvanosis, CoCr alloys.*

I. INTRODUCTION

During orthopedic dental examination ofpatients with metal dentures the number of symptoms are detected: the phenomenon of intolerance of structural materials, galvanosis, toxic stomatitis and contact allergic reactions of a delayed type in the form of inflammation in the areas where the metal parts of the prostheses are adjacent to the mucous membrane of the oral cavity[1]. At the same time, patients complain of a metallic taste, burning and tingling of the tongue, distortion of taste sensitivity, feeling of various aftertastes. Sore throat, xerostomia or, conversely, profuse salivation is noted. A number of patients may noticea soreness on their teeth, redness and swelling of the soft tissues of the face (eyelids, nose, lips, cheeks). Often there are headaches, dizziness, weakness, fatigue, nausea, vomiting, digestive disorders, sleep disorders, heart pain[2], [3], [4].

At the present time, the processes of free radical oxidation occurring in oral cavity associated with the formation of free radicals and reactive oxygen species, attracted the attention of dentists. Under certain conditions, this processesare

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DOI: 10.37200/IJPR/V24I4/PR201316
Received: 22 Sep 2019 | Revised: 13Oct 2019 | Accepted: 15 Jan 2020

protective and compensatory in nature, but in concentrations exceeding physiological, these compounds can lead to the cell structures damage of oral cavity organs, triggering the development of the pathological process[5]. Among antioxidants, reduced glutathione plays an important role: being a hydrophilic compound, it protects the cytoplasm from the damaging effects of free radicals. Also antioxidant protection enzymes provide a powerful and effective metabolism of not only reactive oxygen species, but also active oxidized compounds[6].

As far as we know today, despite the development of new technologies, the number of people with intolerance to certain metals or alloys, such as nickel-chromium alloys, especially stainless steel (the corrosion products of which enter the oral cavity, accumulate in saliva, biological fluids and body tissues) continues to increase[4], [6], [7].

Objective

The objective of this study is to determine the biocompatibility of metal alloys obtained from optimal technological dental blanks: cast bar blanks Ø12mm or granules Ø2-6mmof cobalt-chromium-based (CoCr) alloys, using a portable expert diagnostic system "Lira-100". This system allows to improve the method of determining and preventing the phenomenon of oral cavity galvanosis, as well as to study compensatory and adaptive changes in oral cavity.

II. MATERIALS AND METHODS

Upon receipt of traditional dental blanks for casting cobalt-chromium-based (CoCr) alloys in the form of rods, the main technological stages were melting, sandblasting, tumbling and cutting rods into measured parts[8]. In this case, there was a mechanical effect on structural alloys. To obtain the granules, a vacuum system *Indutherm* (Germany) for smelting granules was used; in addition to melting, only a tumbling of granules was performed in this technological process. To study the structure of cast dental blanks, metallographic studies were performed: macro and microscopic methods of analysis in accordance with accepted standards. The composition of the studied alloys was determined by the method of X-ray microanalysis. The studies were carried out at *Ural's Innovative Technologies (UIT)*.

The response of the patient's oral cavity tissues to the sample material was evaluated using the "Lira-100bt" expert diagnostic complex developed and manufactured in Russia, which meets the requirements of government standards GOST 19687-89, GOST R 50444-92 and technical specifications TU 9442-001-41971715-2007. A total of 103 patients (53 women and 50 men from 39 to 63 years old) wearing metal prostheses of various designs were examined; among them - 59 patients wearing metal prostheses cast from granules and 44 wearing metal prostheses made from a rod who were previously diagnosed with oral cavitygalvanosis. The study was carried out by comparing the values of the coefficient of functional asymmetry of the initial measurement and the coefficient of functional asymmetry obtained when measuring with the test sample. The coefficients were calculated using the software of the expertdiagnostic complex "Lira-100". The "Lira-100" expert diagnostic complex is based on the analysis of changes in the bioelectrical reactivity parameters of living organ tissues — an electromagnetic response signal, which determines the presence of pathological processes in the studied tissues with high accuracy. Bioelectrical reactivity values are closely related to real microcirculation and the intensity of metabolic processes.

In order to study the content of reduced glutathione and the activity of glutathione-dependent enzymes of oral liquid at various degrees of secondary adentia in patients, we identified the following groups: in case of dental restoration with whole-cast bridges (group IV),we used clinical group I (absence of 1-3 teeth) as comparison group.For groups V (bugel prosthesis) and VI (laminar prosthesis) we used clinical group II (absence of 4-10 teeth) and III (complete adentia) as comparison groups, respectively.

DOI: 10.37200/IJPR/V24I4/PR201316
Received: 22 Sep 2019 | Revised: 13Oct 2019 | Accepted: 15 Jan 2020

The study effect of saliva pH on dentures in patients, “pH-410” pH meter-millivolt meter was used during the initial examination, on the day the dentures were fixed and after 6 months. The electrochemical potentials of metallic inclusions in the oral cavity were measured using the “Multifunctional Ionomer EV-74” device.

Observing the patients, a clinical evaluation of the manufactured prostheses was performed according to the modified basic criteria [6], [9], [1]. The surfaces of prosthetic crowns, fasings, solders, plastic and ceramic veneers, and the prosthetic field were examined. The condition of dentures in the examined patients was evaluated on the manufacture day of new dentures and after 6 months.

To assess the secretory immunity, the oral fluid was taken, which consisted of mixed saliva. In oral fluid, the concentration of lactoferrin (LF) and secretory immunoglobulin A (IG A) was determined by the solid-phase heterogeneous enzyme-linked immunosorbent assay using the “Vector-Best” test system.

In order to assess the nonspecific resistance of oral mucosa, the adsorption reaction of microorganisms by buccal epithelial cells was used.

Statistical processing of the results was carried out based on the principles of variation statistics according to Student's t-test using the statistical software *Statistica 8.0*. To analyze the correlation between the characteristics, Spearman correlation analysis was used. The differences were considered statistically significant at $p < 0.05$.

III. RESULTS AND DISCUSSION

The amount of usable metal in traditional technology is 45-50%, with metal losses up to 18-20%. Granulation technology allows to obtain up to 80-90% of usable metal, with 1.5% losses. The study of dental technician-caster work showed that using the granular form of blanks allows quickly and evenly warm up metal, because the weight of the granules Ø 2.0-6.0 mm is 0.1-0.6 g, while the weight of the bar blanks Ø12 mm is 12.0-15.0 g. The melting time of 50 grams of bar blanks is an average of 190±2 seconds, and it drops down to 100±2 sec when using this new form of blanks.

Comparative analysis of the structure and composition of metal alloys after casting, carried out by metallographic and chemical spectral methods showed that the average distance between the axes of dendrites in samples of CoCr alloys obtained from rods reaches 24 microns, while the average distance between the axes of dendrites in alloy samples cast from granules is only 13 microns. Segregation in the first group is higher ($\Delta Mo=6.5\pm5.2\%$; $\Delta Cr=28.0\pm3.1\%$) than in the second ($\Delta Mo=6.5\pm1.5\%$; $\Delta Cr=28.0\pm0.9\%$). The number of non-metallic inclusions in products made of rods is also more: it reaches 11 per unit area against 5 per unit area in dentures cast from granules. Another important indicator - the melting loss- for the alloy in bars reaches 0.24%, while in samples obtained from granules it is only 0.16%.

The most suitable for patients was the CoCr alloy, produced in the form of granules, in which the coefficient of functional asymmetry is close to the control line. The subsequent prosthetics with the use of CoCr alloy in granules, showed the absence of complaints in all the studied patients[10], [11].

To identify galvanic phenomena causing galvanosis in oral cavity we used a special D2 sensor of the "Lira-100" device with metal tip. As a result of calculations, it was revealed that V1> V2 was less than 30% in all examined patients, whose dentures were made of CoCr alloy in granules, which indicates the permissible values of electrical potentials. No data suggesting the presence of galvanosis in oral cavity was found.

Pathological changes in oral cavity against the background of constant interaction with harmful physical and chemical products of metallurgical production, primarily associated with functional and organic disorders in the salivary glands, which is confirmed by our data. Complaints of frequent thirst were made by patients in the Main Group (MG): wearing

DOI: 10.37200/IJPR/V24I4/PR201316
Received: 22 Sep 2019 | Revised: 13Oct 2019 | Accepted: 15 Jan 2020

prostheses made from a rod - 19.23%; and wearing prostheses made from granules - 5.88%;patients in the Control Group (CG) did not have such complaints. Dry mouth occurred in 34.62% of patients in Main Group, and in 11.76% of patients from Control Group. The nature of changes in the indicators of secretory immunity of oral liquid depended on the type of material of the manufactured prosthesis. A decrease in the level of lactoferrin by 23.2% ($p \leq 0.05$) and of secretory IG A by 26.3% ($p > 0.05$) were observed compared with the Control Group (Table 1).

Table 1. Indicators of lactoferrin, secretory IG A, adsorption of microorganisms

Patient group	Lactoferrin ng/m	Secretory IGA mg/ml	Adsorption of microorganis average cytochemical coeffici (ACC)
Control Group	6005,6± 328,0	165,0±12,4	2,0±0,3
Main Group	3915±231,3	137±16,9	1,6±0,4

Analysis of the examined patients indicates that the average value of the PMA index in the Main Group was 47.4±1.36%, which corresponds to moderate severity, and in the Control Group 14.9±1.62%. We did not reveal significant differences in the degree of inflammation of the gingival membrane in individuals with dentures made from granules or rods. But in patients from the Main Group there were various pathologies of oral mucosa such as: benign tumors - 8.2%; leukoplakia - 4.3%; cheilitis - 5.9%; tongue and cheek swelling - 44.9%; tongue plaque - 68.2%; fissured tongue - 12.7%; tongue burning - 9.4%; dry mouth -46.4%; bitter taste in oral cavity - 23.2%; inflammatory diseases of periodontal tissues - 60.5%.These symptoms were rather less common in the Control Group: 1.7%; 0%; 3.3%; 23.7%; 31.7%; 2.4%; 0%; 17.8 %, 5.4%; 59.7%, respectively.

Based on the obtained values of electrochemical potentials, we made a galvanogram and calculated EMF. The results of the study of EMF in patients of different groups are presented in Table 2.

Table 2. Potential difference indices in patients of different groups

Surveyed groups	Types of dentures	Indicators of the electrochem potentials difference
Control group	Porcelain fused metal	40±10
n = 44; male = 16	Metal acrylic dentures	50±10
female = 28	All-metal dentures	30±10
Main group:	Porcelain fused metal	30±10
n = 59; male = 22	Metal acrylic dentures	40±10
female = 37	All-metal dentures	40±10

Note: Significance of differences P <0.05

The study of oral fluid pH showed, that despite a slight shift in pH to the acidic side - patients with all-metal prostheses made of rod and patients with prostheses made of granules had comparable results: 7.0 ± 0.2 and 5.8 ± 0.4, respectively ($p < 0.05$). The pH of saliva had a significant shift to the acidic side in patients with dentures made of CoCr alloys from rods[12].In our opinion this was due not only to the presence of dentures in oral cavity made of CoCr alloys,

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but also to the effects of microbiological, immunological and biochemical factors that contribute to the progression of inflammatory diseases in oral cavity[13].

One of the non-specific and informative indicators of the local immune reactivity of the oral mucous membrane, is the rate of adsorption of microorganisms to epithelial cells. It can be judged by the average cytochemical coefficient (ACC), which did not differ significantly between the groups. However, in a detailed analysis of the distribution of cells of different categories, it was found that the number of cells adsorbed more than 50 microbial bodies (p=0.04) was reduced by one and a half times when using traditional-type blanks in the form of rods. This indicates a partial inhibition of the immunoreactivity mechanisms of the oral mucous membrane in the presence of metal dentures cast from blanks in the form of rods, whose indicators of dendritic structure dispersion and liquation heterogeneity (ΔMo±5,2%; ΔCr±3,1%) are worst and a large number of non-metallic inclusions are present[14]. Corrosion products (iron, copper, manganese, chromium, etc.) enter the oral cavity and accumulate in saliva, biological fluids and body tissues[15].

Studies have shown that the content of glutathione (GSH)in oral cavity of patients with partial adentiawith the absence of 1-3 teeth before prosthetics, decreased by 21% (p<0.02) compared to healthy people. In patients with the absence of 4-10 teeth level of GSH in oral liquid decreased by 37,0% (p<0,001), and in patients with complete adentia– by 54,0% (p<0,001) compared with the control group.

The activity of glutathione-dependent enzymes in oral liquid of patients with adentia before prosthetics also decreased (Table 3). Thus, the activity of glutathione peroxidase (GP) decreased by 22,7% (p<0.001), and glutathione reductase (GR)– by 30,2% (p<0.001) in patients with the absence of 1-3 teeth; by 48,3% (p<0.001) and 32.7% (p<0.001) in patients with the absence of 4-10 teeth compared with the activity of enzymes in the group of people with intact dentition. The most pronounced decrease in the activity of oxidase and reductase enzymes involved in glutathione metabolism was observed in the group of patients suffering from complete adentia. Glutathione peroxidase activity in the III clinical group decreased by 58.3% (p<0.001), and glutathione reductase - by 38.8% (p<0.001) compared with the control group.

Table 3. The content of reduced glutathione and the activity of glutathione-dependent oral fluid enzymes at various degrees of secondary adentia in patients not subjected to dental prosthetics (M±m)

Examined Groups	**n**	**GSH, µmol/l**	**GP, µmol/ (min • g protein)**	**GR, µmol/ (min • g protein)**
I (patients with 1-3 teeth missing)	21	48,13±3,22 p_{1-7}<0,02	38,69±2,39 p_{1-7}<0,001	21,45±1,60 p_{1-7}<0,001
II (patients with partial adentia, with 4-10 teeth missing)	10	38,36±2,04 p_{2-7}<0,001 p_{1-2}<0,02	25,86±1,51 p_{2-7}<0,001 p_{1-2}<0,001	20,68±1,24 p2-7<0,001 p_{1-2}>0,5
III (patients with complete adentia in the upper and lower jaws)	10	28,05±1,10 p_{3-7}<0,001 p_{1-3}<0,001 p_{2-3}<0,001	20,88±1,65 p_{3-7}<0,001 p_{1-3}<0,001 p_{2-3}<0,05	18,81±1,17 p_{3-7}<0,001 p_{1-3}<0,5 p_{2-3}<0,5

DOI: 10.37200/IJPR/V24I4/PR201316
Received: 22 Sep 2019 | Revised: 13Oct 2019 | Accepted: 15 Jan 2020

IV (patients with solid cast fixed bridges prostheses made of CoCr alloys)	21	31,21±1,98 p_{4-7}<0,001 p_{4-1}<0,001	13,16±3,00 p_{4-7}<0,001 p_{4-1}<0,001	16,77±1,11 p_{4-7}<0,001 p_{4-1}<0,02
V (patients with bugel dentures)	10	13,3±0,79 p_{5-7}<0,001 p_{5-2}<0,001 p_{5-4}<0,001	6,99±1,93 p_{5-7}<0,001 p5-2<0,001 p5-4<0,5	11,72±0,75 p_{5-7}<0,001 p5-2<0,001 p5-4<0,5
VI (patients with removable laminar dentures made of methyl methacrylate)	10	12,35±2,42 p_{6-7}<0,001 p_{6-3}<0,001 p_{6-4}<0,001 p_{6-5}>0,5	5,08±0,59 p6-7<0,001 p6-3<0,001 p6-4<0,02 p6-5<0,5	6,75±0,81 p6-7<0,001 p6-3<0,001 p6-4<0,001 p6-5<0,001
VII (healthy, with intact dental arch)	21	60,92±4,44	50,02±2,02	30,74±1,43

According to the obtained data, in the oral fluid of patients of the IV clinical group, the level of GSH was 35.2% ($p<0.001$) lower compared to the group I. The content of reduced glutathione in the group V was lower by 65.3% ($p<0.001$) compared to the group II. The maximum decrease in the concentration of GSH was found in the group with removable laminar prostheses. The content of reduced glutathione in the clinical group VI was 12.35±2.42 μmol/g, which was lower by 56.0% ($p<0.001$) compared to the group III.

There was a significant imbalance in the work of glutathione-dependent oral enzymes in patients of clinical groups IV, V and VI at the time of examination.

In the mixed saliva of patients of group IV, the activity of GP and GR decreased by 66.0% ($p<0.001$) and 21.8% ($p<0.02$) respectively, compared with the corresponding indicators before prosthetics. In patients of group V, the activity of GP was lower by 73.0% ($p<0.001$), and GR - by 43.3% ($p<0.001$) compared to these indicators in group II. When using removable laminar prostheses for the treatment of adentia, the general tendency to inhibit the activity of glutathione-dependent enzymes of oral antiradical protection, observed in the IV and V clinical groups, was maintained.

GP activity in group VI was by 75.7% lower ($p<0.001$) compared to the group III. The activity of GR when wearing laminar prostheses was lower by 64.1% ($p<0.001$) compared to the group III.

Thus, in the oral fluid of patients with secondary adentia, both before prosthetics and after the use of fixed and removable orthopedic structures, we found significant violations in the exchange of one of the main cellular antioxidants - reduced glutathione - capable both independently restore reactive oxygen species, and together with GP catalyze the reduction of hydrogen peroxide and organic peroxides[16].

Apparently, the oxidation of functionally important thiol groups of GSH occurs by direct action of oxidizing agents with thiolopriv effect on them. In conditions of adentia without prosthetics, as well as in prosthetics with fixed bridges, the most likely mechanism for decreasing the content of reduced glutathione in patients oral liquid is the fact of accumulation of metal ions with variable valence (for example, iron, cobalt, nickel, chromium ions) found by a number of authors[12]. The decrease in the activity of the GR-enzyme, which regenerates the reduced glutathione, contributed to the decrease in the concentration of GSH in the oral cavity.

DOI: 10.37200/IJPR/V24I4/PR201316
Received: 22 Sep 2019 | Revised: 13Oct 2019 | Accepted: 15 Jan 2020

When using removable laminar dentures for prosthetics, the leading mechanism contributing to the reduction of GSH in the oral fluid of patients, in our opinion, was the presence of a residual monomer in the prosthesis, which did not enter into the polymerization reaction of the methyl methacrylate residue, which by its chemical nature is a free radical[17].

Bugel dentures used in this study were made of methyl methacrylate, imitating the shapes of the crown of missing teeth, and a metal arch connecting them, and therefore both described mechanisms of activation of free radical oxidation of biomolecules took place in patients of the V clinical group.

The decrease in the activity of GP and GR in the oral fluid of patients whose defects in the dentition were replaced by fixed and removable prostheses, was apparently associated with the oxidative modification of the functional groups of enzymes that occurred under the influence of an excess of active oxygen species and free radicals. The conformational rearrangements of the enzyme molecules resulting from this, the dissociation of proteins into subunits, as well as an increase in the rate of their degradation, could be the cause of the phenomenon we observed. The described metabolic disorders, which occurred in the oral cavity of patients with adentia both before and after dental prosthetics, indicated the formation of oxidative stress and required timely correction with antioxidant drugs[18].

IV. CONCLUSION

Studies have shown the obvious advantages of producing cobalt and chromium alloys in the form of granules. According to X-ray microanalysis, the greatest chemical heterogeneity was observed in the blanks in the form of rods, which is confirmed by metallographic studies.

Producing CoCr alloy in the form of granules allows using it in individuals living in adverse environmental conditions. CoCr alloy blanks in the form of granules is one of the structural materials that can be used as a means of preventing complications when using metallic inclusions in people employed in metallurgical production.

A personalized approach to the selection of materials for the manufacture of dentures for patients is required, especially for those engaged in work under adverse physical and chemical conditions.

The clinical use of CoCr alloy, produced in the form of granules, showed its good tolerance by patients. The use of dental alloy blanks in the form of granules is a preventive measure against the development of galvanic processes and corrosion of CoCr.

Dental alloy manufacturers should switch to the production of metal alloy blanks in the form of granules. The use of the “Lira-100” expert diagnostic complex provides high-precision measuring of bioelectrical reactivity parameters of living organ tissues and detects the presence of pathological processes in the oral cavity, which are closely related with real microcirculation and metabolic rate.

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DOI: 10.37200/IJPR/V24I4/PR201316
Received: 22 Sep 2019 | Revised: 13Oct 2019 | Accepted: 15 Jan 2020