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Clinical-diagnostic Significance of Recognition of Specific Antibodies in Patients with Allergies to Metal Alloys Used in Prosthetic Dentistry

Ekaterina Stanislavovna Mikhailova^{1*}, Vladimir Valerevich Kostyunichev¹, Lyudmila Alexandrovna Ermolaeva¹, Natalia Alexandrovna Socolovich¹, Natalia Alexandrovna Ogrina¹, Natalia Aleksandrovna Sheveleva¹, Sergey Nikolaevich Zhovtyy¹, Aleksandr Anatolievich Polens²

¹Saint Petersburg State University, St. Petersburg, Russia, 199034, Universitetskaya emb. 7-9 ²St. Petersburg GBUZ «Dental Polyclinic №16», St. Petersburg, Russia, 190005, 4th Krasnoarmeyskaya St., 19

*Correspondence should be addressed to Ekaterina Stanislavovna Mikhailova, Saint Petersburg State University, St. Petersburg, Russia, 199034, Universitetskaya emb. 7-9; Tel: +79219406088; Fax: +78123889222; Email: russia@prescopus.com.

ABSTRACT

A comprehensive survey of 226 patients with an allergy to metal alloys applied in the clinic prosthodontics. In this study, the total Immunoglobulin E (IgE), specific IgE- and Immunoglobulin G (IgG) -antibodies to metal ions in serum and in mixed saliva were measured. In the mixed saliva no significant increasing in IgE-antibodies to metal ions has been revealed, IgG- antibodies to gold, cobalt, chromium, nickel, copper, palladium and platinum ions in low titers were defined in elderly patients. To predict the development of allergic reactions in patients with metal alloys prosthetic constructions, specific serum IgG- antibodies to metal ions that characterize the frequency of contact with the allergen were measured. The content of specific IgE-antibodies to metal ions in serum measured to recognize a primary response to allergens (no history of contact with the metal alloys used in prosthetic dentistry). The investigation of specific IgE- and IgG-antibodies to metal ions in serum has shown the largest number of positive tests to copper (11.3%), gold (10.8%), cobalt (9.9%) and nickel ions (9.3%). The verification of clinical and diagnostic significance of revealing specific antibodies to metal ions in patients with allergies to metal alloys used in prosthetic dentistry, showed that the use of these methods is an auxiliary diagnostic tool and it can only be interpreted in conjunction with the results of clinical examination of the patients.

Key words: Allergic reaction, Dental metallic alloys, Hypersensitivity, Specific IgE-antibodies, Specific IgG-antibodies. Copyright © 2017 Ekaterina Stanislavovna Mikhailova et al. This is an open access paper distributed under the Creative Commons Attribution License. *Journal of Biology and Today's World* is published by *Lexis Publisher*; Journal p-ISSN 2476-5376; Journal e-ISSN 2322-3308.

1. INTRODUCTION

The special literature sources testify that allergy to dental materials as a multifactorial process, depends on the state and interactions of the immune, nervous, endocrine and other systems of the body (1-5). It should be noted that one of the factors contributing to the development of allergies to dental materials can be a decrease in the body's defense ability as a result of agerelated features at the background of common diseases. However, literature sources indicate the great importance state of general and local immune reactivity in the pathogenesis of allergy to dental materials (6-9). In addition to the general immune system in the human body, there are subsystems of immune and biological protection of tissues and organs such as intraepithelial subsystem of nerve, skin and mucosal tissue. The part of intraepithelial subsystem is the oral mucous membrane that consists of cellular elements, humoral factors. This elements are able to response completely autonomously (recognize, process, eliminate by means of specific and nonspecific mechanisms) to a variety of antigens and other factors. At the same time a specific immune response and inflammation develop for protection of organ involved against aggression of immune and non-immune cells (10, 11). The oral mucous membrane is a functional element of the immune system, and one of the most reactive areas of the body, so that it can be involved in the pathological process caused by allergic reactions of local and systemic nature (12, 13). During prosthetic works the mechanical, chemical and toxic, electroplating, microbial factors affect

a prosthetic bed tissue and organism as a whole by the development of the subjective and/or objective signs of inflammation (14-17). The response intensity increases in the cooperation of several factors and depends on the immunological status of the organism. For the diagnosis of an allergic response to metal alloys used in dentistry, screening tests are used: patch test method fiberglass evaluation of histamine liberation from blood basophils, evaluation of availability of specific IgE- and IgG-antibodies in the serum of certain haptens by enzyme-linked immunosorbent assay (ELISA), etc. (1, 6). The aim of this research is to verify the clinical and diagnostic

value of specific antibodies to the metal ions definition in patients with allergy to metal alloys used in prosthetic dentistry.

2. MATERIALS AND METHODS

A comprehensive survey of 226 patients aged from 20 years to 80 years with an allergy to metal alloys applied in prosthetic dentistry, has been performed: 44 men (19.5%) and 182 women (80.5%). The distribution of patients by age and gender is shown in Figure 1.

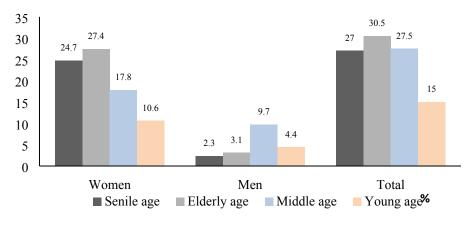
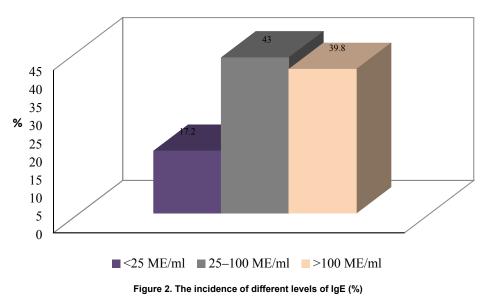


Figure 1. The distribution of patients by age and gender

We used methods, including clinical examination of patients with the assessment of dental and physical status. All the patients underwent patch tests with metal alloys. IgE levels in the blood serum were recognized using commercial ELISA kits MAbs (monoclonal antibodies) produced by "Polignost". Levels of specific IgE- and IgG-antibodies to metals (gold, cobalt, chromium, nickel, copper, palladium, platinum) in mixed saliva and blood serum were recognized by solid phase ELISA using commercial test kits «Doctor Fooke» (Germany). Statistical analysis of the data on a personal computer was performed using STATISTICA for Windows software system (version 10.0).

3. RESULTS AND DISCUSSION

It is known that the development of allergic inflammation may take place due to the intensified synthesis of IgE in the tissues and the availability of specific IgE-antibodies to allergens (3). Therefore, in our research, in patients with allergies to metal alloys, we defined total IgE, specific IgEand IgG-antibodies to metal ions in serum and in mixed saliva. In 39.8% of the examined cases featuring allergic responses to metal alloys the total IgE level in serum tended to increase that could depend on the change of this class of antibody synthesis regulatory mechanisms (Figure 2). No significant differences of this parameter in the examined persons in the age aspect can be traced.



The results of the research reflecting the content IgE- and IgG-antibodies to metal ions in the blood serum of patients are presented in Figure 3. From the 3164 samples tested, positive results were obtained in 206 cases, representing

6.5%. The greatest number of positive tests was revealed in the research of blood serum for the availability of specific IgE- and IgG-antibodies to copper ions (11.3%), and the smallest number of positive tests - to platinum ions (0.4%).

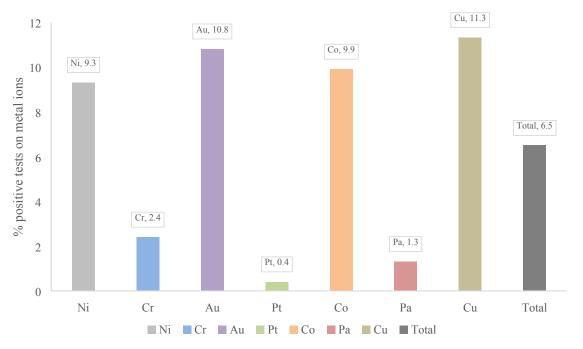
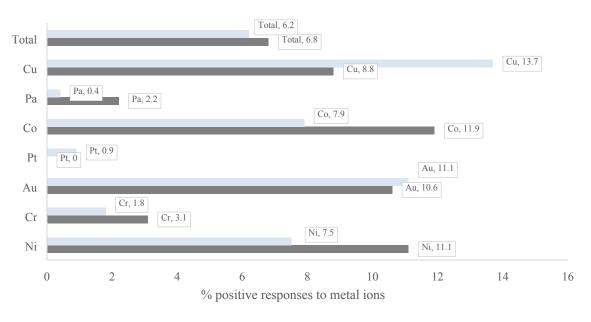


Figure 3. The number of positive tests on metal ions (%)

According to the obtained data specific IgE-antibodies to the metal ions were revealed in 6.8% cases, IgG-specific antibodies to metal ions - in 6.2% of cases. No significant differences between the number of positive tests with revealed specific IgE-antibodies to the gold ions and the number of positive tests of IgG-antibodies to this metal have been revealed (Figure 4). The number of positive tests with the acute phase response (IgE-antibodies) to palladium ions (2.2%), cobalt (11.9%), chromium (3.1%) and nickel (11.1%) exceeds the cytotoxicity indications (IgG -antibodies) to these metals. Positive tests with identified specific IgG-antibodies to copper ions (13.7%) exceeds the indications in the acute phase response (IgEantibodies) on the ions of the metal (8.8%). Acute-phase response (IgE-antibodies) is more expressed to cobalt ions (11.9%) and nickel (11.1%) and the cytotoxic response (IgG-antibodies) - to copper ions (13.7%). IgG-antibodies to metal ions in the serum of patients are diagnosed with higher frequency in patients already having prosthetic constructions in the oral cavity made of metal alloys. The detection frequency of IgG-antibodies to metal ions increases with the growing terms of wearing prosthetic constructions made of metal alloys (r = 0,612, p <0.05). IgE-antibodies to metal ions were recognized more frequently in patients not previously exposed to the metal alloys used in clinic prosthetic dentistry, but in those patients with allergic history (r = 0,522, p <0.05).



IgG IgE

Figure 4. Contents of specific IgE- and IgG-antibodies to metal ions in the blood serum of patients with allergy to metal alloys (%)

In women, the serum content of specific IgE-antibodies to the metal ions amounts to 7.3% of all samples studied. Consequently, with each of the fourteenth women surveyed specific IgE- antibodies to metal ions were revealed in serum. In the serum samples of women specific IgE-antibodies to cobalt ions were identified in 13.7% of cases, to gold ions in 12.6% of cases, to nickel ions - in 12.1% of cases, to copper ions - in 6.6 % of cases, to chrome ions - in 3.3% of cases, to palladium ions - in 2.7% of cases. IgE-specific antibodies to platinum ions were not revealed in the samples (Figure 5). IgE-specific antibodies to ions of metals in male serum reflecting an acute phase responses of the immune system, were revealed in 4.9% of cases (every twenty male patients surveyed). In the samples of men specific IgE-antibodies to copper ions (18.2%) were revealed most often. Specific IgE-antibodies to nickel ions were revealed in 6.8% cases, to cobalt ions – in 4.6% cases, to gold and chrome ions in 2.3% of cases. IgE-specific antibodies to platinum and palladium ions were not revealed in the samples.

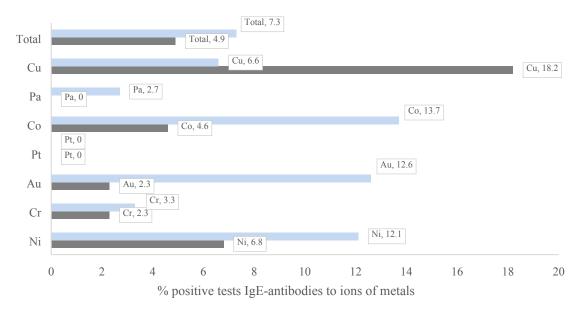




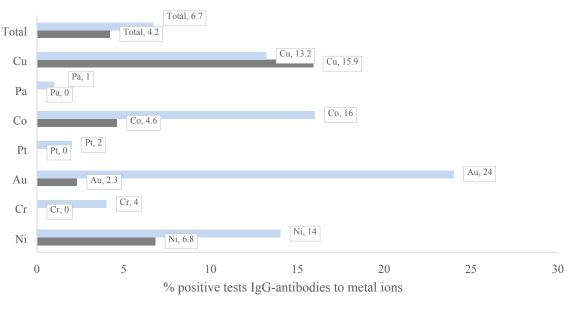
Figure 5. The content of the specific IgE-antibody to the metal ions in the serum of patients with allergy to metal alloys (%)

Thus, the largest number of positive tests illustrating an acute phase of immune system response to metal alloys, were obtained from men to copper and nickel ions, to cobalt, from women to nickel and gold ions. In women, the content of specific IgG-antibodies to metal ions the blood

serum amounted to 6.7% of all the samples (Figure 6). Thus, the specific IgG-antibodies to metal ions were revealed in each fifteenth woman of the surveyed and in each twenty-fourth of the surveyed men. In the blood serum of women IgG-antibodies to the gold ions (24%)

and cobalt ions (16%), men IgG-antibodies to copper ions (15.9%) were most frequently revealed. The availability of specific IgG- antibodies to chrome, palladium and

platinum ions, was observed only in the blood serum of women.



Women Men

Figure 6. The content of IgG-antibodies specific to metal ions in the blood serum of patients with allergy to metal alloys (%)

The frequency analysis of the recognition for specific IgEand IgG-antibodies to metal ions in the blood serum of different age groups of patients with allergy to metal alloys is shown in Figure 7. With young patients the metal alloys used for prosthetic works often cause severe allergic response mediated by the increased levels of specific IgEantibodies in blood serum. If young women have allergic response realized only through an acute phase response, the young men in 8.4% of cases have an acute phase response (recognized by specific IgE-antibodies to metal ions) and in 2% cases - cytotoxic response (recognized by the specific IgG-antibodies to metal ions). With middleaged patients with allergic response to metal alloys the detection rate of IgE- antibodies to metal ions is reduced compared to the indicators found with younger persons (by 2.7 times with women and 4.4 times with men), but it does

not exceed the parameters of elderly patients. The detection rate of IgE -antibodies to metal ions (34.7%) in the blood serum of patients of middle age is higher than the detection rate of IgG-antibodies to metal ions (18.6%). The detection rate of specific IgG-antibodies to metal ions in blood serum reaches maximum values with elderly patients (47.9%) and it is 2.3 times higher than the detecting frequency parameters of specific IgE-antibodies to metal ions in this age group. The detection rate of specific IgE-antibodies to metal ions in the blood serum of elderly patients is the lowest value (7.4%) relative to values of this parameter identified in another age groups and lower than frequency indicators of IgG-antibodies to metal ions found with the patients in this age group (15.4%).

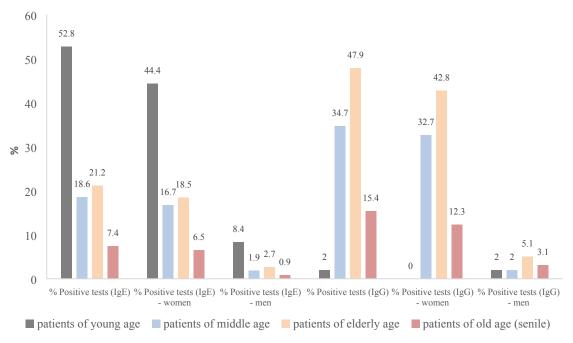


Figure 7. Detection rate of IgE- and IgG-antibodies in blood serum to metal ions of different age groups of patients with allergy to metal alloys (%)

Thus, in younger patients with an allergic response to metal alloys and/or those having allergic history a significant increase in the level of specific IgE-antibodies to metal ions mediating immediate type hypersensitivity was revealed. The number of positive tests that revealed IgE-antibodies to metal ions is reduced (2.8 times) with the middle age patients, significantly increased with elderly patients compared to the data of the middle age group and reaches a minimum value (7.4%) with patients of senile (old) age. The number of positive tests that has revealed IgG-antibodies to metal ions reaches a maximum value

with elderly patients (47.9%) and it has a minimum value with younger patients (2%). No increases in total IgE levels in mixed saliva of patients with an allergy to metal alloys have been revealed. In mixed saliva of patients with allergy to metal alloys specific IgE-antibodies to metal ions (cobalt, chromium, nickel, palladium, platinum) were absent. Only with a few elderly people with positive patch test to metal alloys used in prosthesis, IgE-antibodies to gold and copper ions have been revealed in a very low titers (Figure 8).

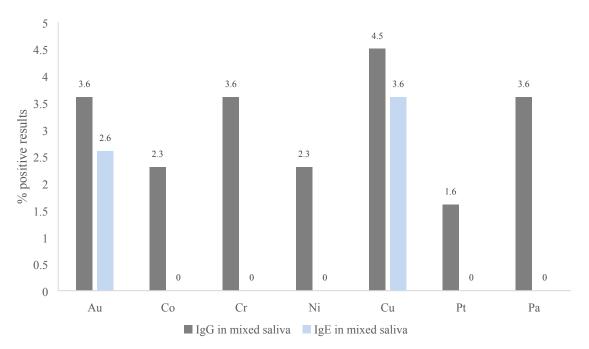


Figure 8. The incidence of IgE- and IgG-antibodies to metal ions in mixed saliva of patients with allergy to metal alloys (%)

In mixed saliva IgG antibodies to ions of metals (gold, cobalt, chromium, nickel, copper, palladium, platinum) were revealed in low titers and in a few cases with elderly

patients.

4. CONCLUSION

The development of intolerance to dental materials has a value of hypersensitivity to metal alloys used in the clinic prosthodontics that is mediated by immediate type allergic response only in 6.5% of cases. The mixed saliva of patients with allergy to metal alloys no significant raise of IgE-antibodies mediating immediate type allergic reaction was revealed. In mixed saliva IgG- antibodies to metals (gold, cobalt, chromium, nickel, copper, palladium, platinum) were revealed in low titers and in a few cases with elderly patients. The research antibody contents with respect to specific IgE- and IgG-antibodies to metal ions in blood serum with patients allergic to metal alloys showed that the highest number of positive tests was found to copper ions (11.3%), gold (10.8%), cobalt (9.9%) and nickel (9.3%). In the blood serum of men specific IgE- and IgG-antibodies to copper ions (18.2% and 15.9% respectively), to nickel (6.8%) and cobalt ions (4.6%) were most often revealed. The samples of blood serum of women specific IgE- and IgG-antibodies to gold ions (12.6% and 24% respectively), to cobalt ions (13.7% and 16% respectively), to nickel ions (12.1 % and 14%, respectively) and copper ions (6.6% and 13.2% respectively) were most frequently revealed. The age differences in the number of positive tests on the content of specific IgE- and IgG-antibodies to metal ions in blood serum have been identified. With younger patients allergic to metal alloys and/or those with an allergic history a hypersensitivity reaction is realized primarily through the acute phase response. With middle age, elderly and senile age patients as compared to the surveyed young age group a high frequency of positive tests recognizing specific IgGantibodies to metal ions has been revealed. Consequently, in order to predict the development of allergic reactions in those patients having prosthetic constructions of metal alloys it is possible to define specific IgG-antibodies to metal ions in blood the serum that characterizes the frequency of contacts with the allergen. To identify the primary reaction to allergens for patients with a history bearing no information on contact with metal alloys used in prosthetic dentistry specific IgE-antibodies to metal ions in blood serum should be identified.

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AUTHORS CONTRIBUTION

This work was carried out in collaboration among all authors.

CONFLICT OF INTEREST

The authors declared no potential conflicts of interests with respect to the authorship and/or publication of this paper.

REFERENCES

1. Büdinger L, Hertl M. Immunologic mechanisms in hypersensitivity reactions to metal ions: an overview. Allergy. 2000;55(2):108-15.

2. Hornstein O. Inflammatory and systemic reactions of the mouth mucosa. Archives of oto-rhino-laryngology. 1975;213(1):287-331.

3. Holgate ST, Church M, Lichtenstein LM. Allergy: Mosby Elsevier; 2006.

4. Merritt K, Rodrigo JJ. Immune response to synthetic materials: sensitization of patients receiving orthopaedic implants. Clinical orthopaedics and related research. 1996;326:71-9.

5. Sugawara S, Uehara A, Tamai R, Takada H. Innate immune responses in oral mucosa. Journal of endotoxin research. 2002;8(6):465-8.

 Gill M, Ockelford P, Morris A, Bierre T, Kyle C. Diagnostic Handbook. 2000.
Nokiba K. Immunological studies on the peripheral blood mononuclear cells in metal allergy patients. Kokubyo Gakkai zasshi The Journal of the Stomatological Society, Japan. 2005;72(2):159-71.

8. Vreeburg K, De Groot K, Von Blomberg M, Scheper R. Induction of immunological tolerance by oral administration of nickel and chromium. Journal of dental research. 1984;63(2):124-8.

9. Zhang X, Wei LC, Wu B, Yu LY, Wang XP, Liu Y. A comparative analysis of metal allergens associated with dental alloy prostheses and the expression of HI A DR in ginglight tiggue. Maloguilar medicine reports 2016;12(1):01.9

of HLA-DR in gingival tissue. Molecular medicine reports. 2016;13(1):91-8. 10. Axéll T. Hypersensitivity of the oral mucosa: clinics and pathology. Acta odontologica Scandinavica. 2001;59(5):315-9.

11. Fisher AA. Reactions of the mucous membrane to contactants. Clinics in dermatology. 1987;5(2):123-36.

12. Gawkrodger D. Investigation of reactions to dental materials. British journal of dermatology. 2005;153(3):479-85.

13. Yue L, Xiao-ping W, Xia D, Hong-ying S, Ya-tong D, Xin Z. Comparative study of sensitivity of different dental metal materials. Shanghai Journal of Stomatology. 2014;23(2).

14. Siddiqi A, Payne AG, De Silva RK, Duncan WJ. Titanium allergy: could it affect dental implant integration? Clinical oral implants research. 2011;22(7):673-80.

15. MAGNUSSON B, BERGMAN M, Bergman B, SÖREMARK R. Nickel allergy and nickel-containing dental alloys. European Journal of Oral Sciences. 1982;90(2):163-7.

16. Thomas P, Maier S, Summer B. Allergic reactions to metal implants. Materialwissenschaft und Werkstofftechnik. 2004;35(12):997-1000.

17. Thomas P, Weik T, Roider G, Summer B, Thomsen M. Influence of Surface Coating on Metal Ion Release: Evaluation in Patients With Metal Allergy. Orthopedics. 2016;39(3):S24-S30.