DEVELOPING AN INDIVIDUALIZED TREATMENT PLAN FOR DENTAL PATIENTS WITH ACCOMPANYING SENSITIZATION TO BACTERIA, FOOD, POLLEN, AND MORE.

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ABSTRACT:

Contemporary dental medicine offers a wide range of materials and techniques for the rehabilitation of the dentomaxillofacial system, which in recent years has led to a dramatic increase in allergic reactions in sensitized patients after dental treatment.

Once in the oral cavity, saliva and gastrointestinal tract, dental medication or dental material release products that, under certain conditions, can cause direct cell damage or induce an immunological/allergic reaction. The local and systemic reactivity in each individual is different and this explains why biocompatible materials that persist in the oral cavity elicit an immune/allergic response in some patients while none is evident in others.

Dental medications, and especially materials that permanently remain in the oral cavity (composites, plastics, metal alloys, etc.), cause hypersensitivity reactions mainly of type IV (slow) and less often of type I (fast).

It is very important to develop an individualized treatment plan for dental patients with accompanying sensitization to bacteria, food, pollen, and more.

There is no doubt that the implementation of a holistic approach in the treatment of sensitised patients is a prerequisite for a much more successful treatment performed by the dentist. This imposes work in close collaboration with an interdisciplinary team using the possibilities of the modern achievements of immunology and allergology.

Patients' history data and the results from skin allergy tests are the basis of application of individualized treatment approach and personalized immunotherapy for each separate patient, as well as of treatment result control.

Keyword: allergy, sensitization, individualized treatment plan

INTRODUCTION

Contemporary dental medicine offers a wide range of materials and techniques for the rehabilitation of the dentomaxillofacial system, which in recent years has led to a dramatic increase in allergic reactions in sensitized patients after dental treatment. The treatment of these patients in daily clinical practice is associated with a number of medical and social problems. The biocompatibility of dental materials is individual for each patient. Biocompatible materials and medicines should not cause toxic reactions, immunologically induced rejection, nor contain components that generate an allergic immune response in sensitized patients once in the oral cavity, saliva and gastrointestinal tract, dental medication or dental material release products that, under certain conditions, can cause direct cell damage or induce an immunological/allergic reaction. [1] The local and systemic reactivity in each individual is different and this explains why biocompatible materials that persist in the oral cavity elicit an immune/allergic response in some patients while none is evident in others. The primary clinical manifestations in sensitized patients range from local manifestations (burning sensation, xerostomia, change in taste, lichenoid changes), to systemic hives and edema, and very rarely to life-threatening allergic reactions. Dental medications, and especially materials that permanently remain in the oral cavity (composites, plastics, metal alloys, etc.), cause hypersensitivity reactions mainly of type IV (slow) and less often of type I (fast). Dental material induced adverse reactions are a serious challenge for the dental specialist, since assessing their biocompatibility is a complex, long-term process involving an individual approach for each patient.

When hypersensitivity to a material found in the mouth is proven, together with subjective complaints and an objective finding, the patient should be offered alternative treatment, given that removal of the proven allergen and immunomodulation of the body to enhance antibody production are the priority tasks. It is a challenge

for us to study modern dental biomaterials (plastics, metal alloys, composites, adhesives and cements) that contain a number of individual and group allergens that permanently sensitize patients and affect both the general and the local reactivity of the body, which are recorded through specific clinical and paraclinical studies. The chronic exposure of these sensitizing agents to the oral cavity often evolves into sensitization of the whole organism, the clinical manifestation of which is greatly aggravated over time.

MATERIALS AND METHODS:

Material - total number of patients – 110.

Clinical studies General medical, oral and allergy oriented medical history taken with an individual card. Diagnostic imaging: orthopantomographs and radiographs.

Complex oral and allergic diagnostics, including an in-depth examination of the oral cavity to register the condition of the mucous membrane (oral lesions evident), the dentition (dental status and materials found in the mouth), gingiva and periodontium (CPITN index).

Tests to determine the general and local reactivity of the organism

Tests to determine the local reactivity in the dentomaxillofacial

Measuring of corrosion potentials

Allergy tests.

Patients in the study group were tested by allergy skin prick with a standard panel of inhalant and food allergens (Bul Bio NCIPD, Bulgaria). The test panel includes the following allergens:

A1 House dust 1000 BU; A13 Dermatophagoides pteronyssinus 1000 BU; B1 Mixed grass pollen 1000 PNU; D1 Streptococcus a-haemolyticus 1000 BU; D2 Streptococcus b- haemolyticus 1000 BU; D3 Staphylococcus epidermidis 1000 BU; D4 Staphylococcus aureus 1000 BU/ml; E7 Candida albicans 1000 BU; EI Mixed fungal allergen 1000 BU; C4 Cow milk; C7 Egg white; C68 Soy bean.

The allergens; histamine hydrochloride standard 1 mg/ml and the negative control (50 % glycerinated Coca solution) were applied simultaneously on the forearm of the patients. The size of the wheal and flare reaction was measured 15-20 minutes after pricking. The tests were considered positive if the wheal diameter was 3 mm or greater with a flare of at least 5 mm.

Statistical methods:

- Descriptive statistics.
- Spearman non-parametric correlation test – Spearman R, r was used to estimate correlation dependencies. A significant correlation is considered to be a value of the coefficient $R > 0.3$ with a degree of statistical significance $p < 0.05$.

- Frequency analysis.

- Linear regression analysis.

Data is processed using Statistica ver. 13.3 (28. 10. 2017), GraphPad Prism ver. 8.1 (2018), SPSS ver. 23 (16. 06. 2018) and Microsoft Excel 2016.

RESULTS:

Following establishing sensitivity to dental materials present in the mouth and those used in future dental treatment, patients are referred for determination of sensitisation to a standard series of allergens (bacterial, food, pollen, domestic etc. allergens) by intradermal and percutaneous skin allergy test. The test is performed in the allergy surgery in the allergy laboratory of the NCCPD (National Centre of Contagious and Parasite Diseases). The establishment of concomitant sensitisation to bacterial, fungal, food, domestic, industrial, professional etc. allergens is of particular importance for the individual treatment plan of dental patients. The removal of the established allergens from the group of dental materials is the first and main stage of specific therapy for patients with evidence of allergy.

We present data from analysis of 110 patients with evidence of allergy to dental materials at a mean age of $49,9 \pm 14,3$ - 29 (26,4%) men and 81 (73,6%) women examined by a standard series of allergens (bacterial, food, pollen, domestic etc.) through a prick and intradermal test (table 1 and fig. 1).

Table 1. Sensitised patients according to gender and age.

	Min	Max	Mean $\pm$ SD	p-value
Men (n=29)	17	75	$45,2 \pm 16,6$	0,04
Women (n=81)	27	79	$51,6 \pm 13,1$	
Total (n=110)	17	79	$49,9 \pm 14,3$	

Fig. 1. Sensitised patients according to gender and age

The results are presented on the basis of: there is/ isn't sensitisation to the tested allergen, i.e. diameter ≥ 3 mm or ≥ 7 mm, respectively, are perceived as positive.

In 107 (97, 3%) patients sensitisation to one or more of the examined allergens was established (table 2 and fig. 2).

Table 2. Sensitised patients according to the number of positive tests

Number of positive tests per a patient	Number of patients (%)
1 sensitisation	17 (15,9)
2 sensitisations	28 (26,2)
3 sensitisations	30 (28,0)
4 sensitisations	17 (15,9)
5 sensitisations	12 (11,02)
6 sensitisations	2 (1,9)
8 sensitisations	1 (0,9)

The highest percentage of sensitisations are recorded to G3staphepiderm (90.2%), followed by G1Strhaem (87, 0%) and G2strhaem (86, 2%). There is no positive result for cow's milk in the examined group. In

Fig. 2. Sensitised patients according to the number of positive tests

the distribution according to gender, there is a significantly higher share of men with sensitisation to household dust and DI fungi in comparison to women (table 3 and fig. 3 and 4).

Table 3. Sensitised patients according to the number of positive tests?

	Total Num. (%)	Men Num. (%)	Women Num. (%)	p-value
Household dust (n=100)	33 (33,7)	14 (51,9)	19 (26,0)	0,018
G1Strhaem (n=23)	20 (87,0)	8 (88,9)	12 (85,7)	1
G2strhaem (n=29)	25 (86,2)	9 (90,0)	16 (84,2)	1
G3Staphepiderm (n=61)	55 (90,2)	15 (93,8)	40 (88,9)	1
G4Staphaureus (n=104)	43 (41,3)	14 (50,0)	29 (38,2)	0,37
D7Candidaalb (n=106)	70 (66,0)	19 (70,4)	51 (64,6)	0,644
DIFungal (n=106)	16 (15,1)	8 (27,6)	8 (10,4)	0,036
A1 Grass (n=23)	7 (30,4)	2 (25,0)	5 (33,3)	1
A1Dpteron (n=107)	28 (26,2)	11 (37,9)	17 (21,8)	0,136
B7Egg protein (n=90)	5 (5,6)	2 (8,3)	3 (4,5)	0,606
B4 Cow's milk (n=17)	0 (0,0)	0 (0,0)	0 (0,0)	-
Soy (n=93)	9 (9,7)	3 (12,0)	6 (8,8)	0,698

Fig. 3. Sensitised patients according to the number of positive tests (x>40%)

Fig. 4. Sensitised patients according to the number of positive tests ($x > 40\%$)

Results from the conducted test of statistical hypotheses at significance level $p = 0.05$: P-value is high and it may be suggested that the correlation is due to random sampling and is in normal ranges for the studied sensitized patients according to the number of positive tests. When choosing the non-parametric Spearman test, the confidence interval of the correlation coefficient by reasonable approximation was calculated. This approximation shows the use of a small confidence interval (table 2 and 3 and fig. 2–4).

The P-value for non-parametric correlation of Spearman is high and the data suggests that the correlation is real. It will change from negative to a positive correlation. The whole interval consists of values close to 1 which are considered correct, and then we have serious proof that there is a correlation in the conducted tests.

The chief aim of our study, related to the treatment of biocompatible dental materials of sensitized patients, determined the necessity, in parallel with all the specific dental methods used, to take the necessary measures to correct the altered immunological reactivity of these patients. Generally speaking, we can claim that as people with various allergic diseases, they have a suppressed Th1 immunological reactivity and predominance of that of Th2 type which is related to the release of larger amounts of IL-4 and IL-13, which stimulate Ig-antibody synthesis. Therefore, it is important for these patients, as a concomitant therapy, to be treated, if possible, with preparations stimulating Th1 immunological reactivity which is manifested by increased secretion of IL-2 and gamma interferon, which suppress IgE class antibody synthesis. In this regard, one possibility is the use of some polybacterial immunostimulants such as the Bulgarian agent Respivax. It has experimentally and clinically established ability to stimulate the Th1 immunological reactivity with increased synthesis of gamma-interferon, higher IgG-antibody levels, of lung surfactant and potent activation of

phagocytic activity. Its intake by sensitized patients would have a positive effect and would lead to the reduction of their allergic predisposition which would facilitate the work of the dentist. [2, 3, 4]

Apart from the strife to alter the immunological reactivity from Th2 to Th1 type of allergic patients, it is extremely important to influence their specific sensitization to certain allergens. Our effort should focus on three directions: restricting the contact with the respective allergen/s, applying an appropriate symptomatic/pathogenic treatment and the most important of all – conducting allergen-specific immunotherapy/ vaccination which is the only etiopathogenic treatment method for allergic diseases leading to a continuous and lasting clinical response of patients.

For this purpose, apart from the well-taken targeted history and the specialised clinical examination, it is necessary to perform the necessary allergy tests, in vivo/skin-allergy samples and in vivo/serological tests together with clinical allergologists in order to establish the etiological causative agent- allergen responsible for the observed allergic disease. This would allow performing a quality allergen-specific immunotherapy/vaccination.

DISCUSSION:

In the cases of concomitant hypersensitivity to allergens present simultaneously in the internal and external environment of the body, it is obligatory for them to be identified and, if possible, removed or limited in their proximity and duration of impact. In cases of unambiguously established hypersensitivity to the main group of allergens, their elimination begins simultaneously with the dental treatment, the specific desensitisation including not only removal of allergens but also concomitant immunomodulating therapy with the purpose of increasing the level of specific antibodies in saliva and the body as a whole.

CONCLUSIONS:

There is no doubt that the implementation of a holistic approach in the treatment of sensitised patients is a prerequisite for a much more successful treatment performed by the dentist. This imposes work in close collaboration with an interdisciplinary team using the possibilities of the modern achievements of immunology and allergology.

Patients' history data and the results from skin allergy tests are the basis of application of individualized treatment approach and personalized immunotherapy for each separate patient, as well as of treatment result control.

Abbreviations:

IgA – Immunoglobulin A

IgG – Immunoglobulin G

IgM – Immunoglobulin M

IL – Interleukin

Th1 – Th1 immunological reactivity

Th2 – Th2 immunological reactivity

NCCPD – National Centre of Contagious and Parasite Diseases

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