

## **Intraoral Contact Hypersensitivity to Dental Methacrylates A Review of Clinical And Research Literary Sources**

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**Abstract:** *Methacrylate-based materials are used daily in dental practice. Specialized publications report these materials as allergens with a high sensitizing potential. The present review of literature discusses the incidence, clinical manifestations, immunological mechanisms and methods of proving sensitization to dental acrylic compounds.*

**Keywords:** *allergy, contact hypersensitivity, dental methacrylates, intraoral manifestation sensitizing potential,*

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### **I. Introduction**

Modern dental medicine uses all possible applications of methacrylates for the purposes of achieving high aesthetic and functional results. An abundance of di- and polyfunctional compounds curing after application of chemical or light stimuli are used in conservative dental treatment as sealants, adhesives, cements, composite filling materials. Most of the trade products available are a mixture of high and low viscosity dimethacrylates, the combination of which results in resins possessing the necessary rheological properties (11, 15). Treatment involving removable complete and partial dentures, temporary crowns and bridges, as well as fabrication of orthodontic appliances also uses restorations made of methyl methacrylate (MMA) liquid monomer and pre-cured MMA polymer as powder. The polymerization process achieves conversion of the free monomer radicals into polymer molecules with three-dimensional spatial structure. The formation of high quality polymers is of particular importance to dental practice. The small percentage of unbound radicals characterizes the final product as possessing better physical, mechanical and biological properties (16, 20, 21). When curing is performed intraorally, or in cases when the technological process has not been properly adhered to, the free radicals are greater in amount. The release of such molecules increases the risk of developing toxic or allergic reactions. Signs of non-specific inflammation are observed intraorally. If skin sensitization has been proved by performing allergy tests, these symptoms can be explained with immunological mechanisms of delayed hypersensitivity.

### **II. Amount Of Residual Monomer**

The degree of polymerization of dental acrylics is in the range of 46% - 80%, which practically means that from 20% to 50% of the monomer molecules remain unbound (16, 21, 32). Ten per cent of them freely diffuse and come into contact with the oral mucosa and the pulp tissue. The components that have not reacted, as well as the products of degradation, have been defined as substances with a sensitizing, cytotoxic, genotoxic and endocrine effect (16, 20, 28, 39). The smaller the molecules, the more severe the adverse biological effects they exert. This is due to their lipophilicity and ability to react chemically with the lipid molecules of cell membranes. The comparison of heat-curing, light-curing and self-curing materials allows us to classify them on the basis of their increasing antigenic and toxic potential. Light-curing materials possess the lowest sensitizing potential, followed by the heat-curing ones, whereas the self-curing materials have the highest allergizing potential. (1, 2, 4, 6, 18, 20, 29).

### **III. Incidence Of Allergic Reactions To Dental Acrylic Resins**

Allergic reactions to dental materials have been frequently discussed in literature. There is a multitude of examples of contact reactions occurring in medical and auxiliary staff. Cases of patients with intraoral complaints following treatment involving methacrylate-based materials have been reported rather scarcely.

The results of investigations conducted on a greater scale showed that the incidence of intraorally manifested allergic reactions differed in the different populations. Khamaysi et al. (37) investigated 134 patients with pathologic changes in the orofacial area and found sensitization to methacrylates in 5.8% of them. The study of Kanerva et al. (35) involved 4000 subjects and proved sensitization in 2.8% of them. Goon et al. (31) reported an incidence of 2.3% among 1322 patients. Bauer (19) analysed the results from dermatological departments that had tested in the course of a year 291 people with problems following prosthetic procedures,

proving sensitization in 5.5% of them. Long-term observations in the course of 10 years showed an incidence of reactions to MA in the range of 2% (19, 31, 35, 37). The results reported by the respective authors referred to investigations of dental patients only.

Bulgarian authors have rarely discussed the immune toxicity of plastic materials and results of such studies can be cited mostly from dissertations. Popova has reported 9-10%, Stoeva 6.2% sensitization incidence (4, 6). The patients referred for proving a diagnosis of allergy had complaints following dental treatment. Interpreting the data in this light and comparing them to the great number of patients wearing prostheses suggests a comparatively low likelihood of developing a reaction to the monomers contained in the prosthetic materials. This fact can be explained by the resistance of oral mucosa to irritants and sensitizing factors. Saliva with its neutralizing and washing-off effect, as well as the good vascularization of mucosa, do not allow a continuous contact. The small amount of Langerhans cells and T-lymphocytes, as compared to the one in other body surfaces, also contributes to the greater resistance (25). Publications dealing with intraoral manifestations of allergy to methacrylates have described mainly single clinical cases, and these types of reactions are considered a pathology of minor consequence to health in the greater number of these articles.

#### **IV. Pathophysiological mechanisms**

The symptoms and pathologic alterations in the oral mucosa are a diagnostic problem engaging specialists in different medical areas, and the patients frequently cannot obtain a final solution to their problem, in spite of all possible efforts made. Besides carrying out general medical investigations, it is advisable to interpret the clinical situation as manifestation of hypersensitivity (14). Dental materials are predominantly considered to be contact allergens inducing reactions of a delayed type. They are haptens by nature which initially have to bind to a protein from the mucosa, after which they obtain the qualities of sensitizing factors. Antigen-presenting cells (Langerhans cells) process the allergen and attach it to the surface by means of the molecules of the main histocompatibility complex. Then the allergen is presented to the T-lymphocytes in the local lymph nodes. The next step is the release of lymphokines 1 and 2 and cytokines; these mediators bring about a clonal expansion of T-lymphocytes and their migration to the mucosal area contacting the allergen. Histologically and clinically these reactions have the signs of a non-specific inflammation. The epithelial layer and the submucosal connective tissue show intracellular edema and cell vesiculation. The area contacting the allergen may be infiltrated by lymphocytes, basophils, neutrophils and eosinophils (18, 25, 28).

#### **V. Clinical Manifestation**

Intraoral contact hypersensitivity is clinically manifested mostly by findings on examination. When taking the history, the symptoms as reported by the patients are likely to be subjective complaints. The latter most frequently include burning sensation, pain, dryness, change in taste, sensing the tissues as edematous, although such a condition of the tissues may not actually be found on examination. The pathologic changes in tissues are extra- and intraoral. Intraoral findings include erythema, ulceration and erosions, and very rarely edema. In a great number of the cases the lichenoid alterations are a manifestation of contact hypersensitivity to methacrylates. Such lesions are a sign of prolonged contact with dental materials and they frequently develop in direct spatial interrelation. The extraoral findings include labial edema, erythema, fissure formation and angular cheilitis. Interesting are some cases describing symptoms occurring in remote organs and tissues and even anaphylactic reactions, the mechanism of which is not sufficiently clarified (10, 11, 17, 19, 22, 23, 24, 34, 36, 38, 40).

#### **Onset Of Reaction**

Observation of patients with proved sensitization to dental resins does not aid in determining the exact period of time after which clinical symptoms will develop. It should be noted that the application of bonds, photo composite materials and adhesives more frequently causes reactions initiated hours following or almost immediately following a visit to the dental office. In larger restorations, such as complete dentures and orthodontic appliances, 2, 3, 7 and up to 30 days are likely to pass after their placement before development of symptoms. There are examples of much shorter periods following contact with dental plastic materials when symptoms resembling an immediate reaction can be observed, e.g. difficulty breathing, edema of the tongue, lips and eyelids (10, 13, 17, 19, 23, 24, 30, 36, 38).

#### **VI. Risk Factors For Occurrence Of Sensitization**

Professional contact with methacrylates is the sensitizing factor most frequently found in specialized publications. Medical care providers, cosmeticians working with glues and adhesives are the most frequent dental patients exhibiting intraoral symptoms when methacrylates are used. Dental treatment alone has been commented as the only cause of sensitization in a very small number of cases, so its likelihood is negligible (13, 24, 36).

### **Monomers With Highest Sensitizing Potential**

The main allergens to which sensitization has occurred in patients with removable plastic restorations are MMA (methyl methacrylate), 2-HEMA (2-hydroxyethyl methacrylate), TEGDMA (triethyleneglycol dimethacrylate), EGDMA (ethyleneglycol dimethacrylate). Reaction to composite materials has been observed most frequently in epoxy acrylates, such as Bis-GMA (2,2-bis[4-(2-hydroxy-3-methacryloxypropoxy)phenyl]propane), Bis-EMA (2,2-bis(4-(2-Methacryloxyethoxy)phenyl)propane) (5, 6, 7, 10, 13, 23, 40).

### **Methods Of Testing Allergy To Dental Plastic Materials**

Since their introduction in 1930, methacrylates have been widely used in dental practice. In the 1950s the first systematized observations were published focusing on the likelihood of sensitization to monomer methacrylate constituents in patients with dentures. Attempts at performing dermatological tests have been made with the aim of proving sensitization. The first methodologies involved direct placement of the complete dentures on the skin of the forearm for a period of 48 hours (26, 27). Testing patients without complaints in the same way showed that skin changes were in fact non-specific and caused by the pressure of the denture. Later attempts to improve the diagnostic process involved fabrication of discs the size of a coin and made of heat-curing or self-curing plastic, which were also placed on the skin. Other methods involved fabrication of allergens *ex tempore* – a certain amount of the monomer and polymer were mixed with olive oil or petroleum jelly, placed on a cotton gauze and attached to the skin surface of the back with a plaster tape (40). The analysis of the results showed that either active sensitization to the constituents tested or chemical burning of the skin was likely to occur. Mixing up with different types of inert carriers led to an excessive dilution of the components of lower percentage in the composition, thus false negative results were likely. Testing the fabricated dental materials could not demonstrate to which specific constituent sensitization had occurred (33).

Modern protocols for proving sensitization to dental plastic materials include application of allergenic preparations where the individual monomer molecules are precisely dosed. The carrier in which the methacrylate molecules are dispersed is petroleum jelly. The percent content of the tested substance is the result of a multitude of clinical and laboratory experiments aiming at obtaining optimum doses that do not induce reactions in healthy patients but provoke an immune response in sensitized patients. The entire diagnostic process follows a protocol with requirements and criteria, providing reliability of the results obtained and their interpretation in every individual clinical case (7, 8, 12).

## **VII. Conclusion**

Sensitization to dental plastic materials occurs rarely in dental patients. The intraoral clinical manifestation of hypersensitivity involves non-specific mucosal alterations at the site of direct contact with the material. Sensitization to methacrylates occurs more frequently in professional environment; the likelihood of its occurrence following dental treatment is minimal. It is advisable to confirm the sensitization using allergens fabricated in laboratory conditions (not trade products found on the market) by directly applying them to the skin.

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