REVIEW ARTICLE

Biohazards associated with materials used in prosthodontics

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Abstract

Dental materials for permanent restorations are manufactured with the intent to be stable and insoluble, but they do not fully achieve this goal. The amount of dissolved components is small and their detection sometimes requires sophisticated analytical equipment. The minute amounts of components that leach out of permanent dental restorative materials are most unlikely to cause toxic reactions, locally or systemically. Reliable research information using robust methodology is thus needed to clarify the various safety issues and frequency of adverse reactions in general dentistry, including prosthodontic treatment.

Key words: Adverse effects, biocompatibility, formaldehyde, nanoparticles, polymeric restorative materials

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Introduction

The development in prosthodontics is characterized by an increasing number of new prosthetic materials. There are, however, a large number of properties of the prosthetic materials, which must be as close to ideal as increasing demands of the patients, biologic, physical, chemical, and aesthetic compatibility that have to be taken into consideration. Prosthodontics practice requires contact with restorative and auxillary dental materials of widely different composition such as metals, resin-based synthetic polymers, cements, impression materials, and restorative materials like dental amalgam, composites, and dental ceramics. How safe are these materials? Leakage and transfer of potentially allergic components from such materials carry the risk of hypersensitive reactions among patients, dental personnel, and laboratory technicians. Biocompatibility of dental amalgam has indeed been debated for long with results of diversified opinions and how safe are the materials used in place of amalgam? Short-term and long-term reaction whether severe or mild should be documented widely so that due precautions can be practiced. Occupational exposures have been reported to arise from work in several industries and from work in dental clinics with poor mercury handling practices.[1]

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Biological side effects to materials used in dentistry are rare. An overall estimate indicates the frequency of such adverse effects to occur in the 1:1000 to 1:10,000 of all dental treatments,[2] but it is dependent on the type of practice and the materials used.[3] All artificial materials release substances into the oral environment and imply some risk of side effects and adverse reactions.[4,5] Amalgam has been associated with general health concerns,[6] while local oral effects from different restorative materials are reported.[7] The biocompatibility of dental restorative materials is being evaluated in different test settings.[8] Red blood cells (RBCs) and associated materials have been elucidated with respect to effect on cellular and sub-cellular levels related to resin constituents[9-11] and also filler particles[12] [Figure 1].

Adverse reactions may occur in different ways [Figure 2].

Frequent dermatological reactions include transient redness, irritation or decreased tactile sensitivity to seriously incapacitating blisters, desquamation, soreness, bleeding fissures, and pain. Frequent causes include acrylic resins,

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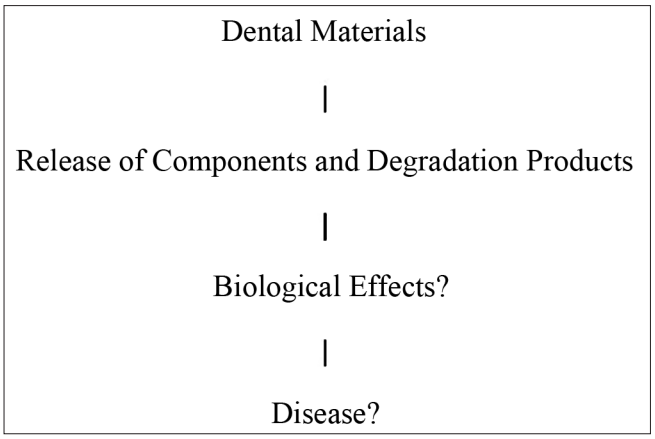

Figure 1: Sequence of events that may lead to biological side effects to dental materials

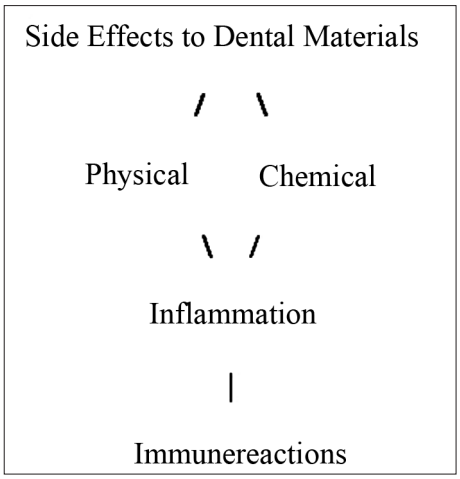

Figure 2: Possible routes that may lead to biological side effects to dental materials

latex gloves, impression materials, eugenol containing temporary cements. Nondermatological reactions include damage to eyes due to UV light and visible light used in everyday practice. Respiratory reactions are attributed to vapors from acrylic resin monomers and cyanoacrylates. Materials left in the inaccessible areas like subgingival regions where elastomeric impression materials are not removed, cell viability is affected. Hence due care should be taken before disposing the patients from our clinics. Functional and aesthetic improvement of stomatognathic system with added psychological advantages should be assessed in light of their contribution to the dental, oral, and general health and well being of the patient. Due precautions should be practiced in handling the materials and equipments to avoid occupational hazards on one hand and due care taken to avoid any insult to oral tissues and general health of patients on the other.

Historically, various materials have been used to make impressions for removable and fixed prosthodontics. Early materials included rigid and semi-rigid compositions such as plaster, zinc-oxide eugenol, impression compound, and waxes; these materials still have limited uses in dentistry. Prosthodontic restorations and appliances consist of many designs including conventional and implant-supported crowns, fixed prostheses (dental bridges), and removable prostheses or dentures. Some are fixed using precision attachment and screws or cemented to teeth or implants with minimal contacts with gingival or other oral soft tissues. Others are either fully supported by the oral mucosa or removable and are resting on both hard tissues of teeth or their analogues (implants) and soft tissues. Different materials, including metals, polymeric materials, ceramics, and several types of cements are used when fabricating and fitting Prosthodontic appliances for patients. In fact more than 75% of all the existing dental materials are directly or indirectly used or involved when fabricating and providing prosthodontics restorations to be placed in the oro-facial complex of patients. For the purpose of this review, prosthodontic materials are defined as those used in the making of indirect restorations. These restorations are constructed in the dental laboratory on casts obtained from impressions and other chair-side recordings. Some of these materials including gypsum, casting waxes, and investment are required only in the fabrication of prostheses in the laboratory. These usually do not come in direct contact with the patient tissues. Thus, any adverse effects, if any, are largely limited to dental personnel handling them. The consequent adversities that arise during laboratory procedures may be due to their contact with skin, exposure to dust from mixing, grinding and polishing, and inhalation of fumes and vapors. Of particular concern are all those who are frequently exposed to particles or dust in the dental laboratory and dental clinical area including staff and patients during the chair-side adjustment and finishing of prostheses. Most of these potential problems can be handled by using the recommended safety or protective devices to improve the working environment, for example, use of face masks, gloves, local, and central dust and fumes extraction systems. When evaluating adverse reactions to materials used in prosthodontic appliances, a variety of situations must therefore be taken into consideration. This is because some materials come only in brief contact with the patients such as when making an impression or registering a bite of the patient. In contrast, dental prostheses are intended to remain *in situ* for decades. A number of factors need to be taken into account when estimating adverse biological reactions to prosthodontic materials. Among these include: the type, form, contour, extent of the prosthesis, any medication used by the patient, salivary flow rate, xerostomia, oral hygiene, quality of fit, and function of the prosthesis. All these conditions may affect local reactions in addition to those caused by the materials *per se*. Biological films, 'pellicles', of salivary origin will also accumulate on the materials. They differ in composition depending on the material and

on the properties of the patients' saliva. The irrigating effect of saliva is also difficult to assess. However, a distinct difference exists between material reactions intra-orally and extra-orally, with those on skin being more frequent and more severe.[13] Skin patch testing is therefore of limited value, even if specifically designed series of tests for dental materials are employed.[14]

Biocompatibility tests

Many preclinical biocompatibility tests are available to minimize the risk of adverse reactions to dental materials.[15] These tests are categorized on the basis of their applicability levels. Initial tests include cell culture tests, hemolytic tests, systemic toxicity tests, and tests estimating teratogenic and carcinogenic effects and potential. Secondary tests cover implantation tests, skin and mucous membrane irritation tests, and sensitization tests. Usage tests take into account the manner in which the materials are intended to be used in clinical practice. Oral mucosa tests based on reactions to materials in contact with the hamster-cheek pouch is considered to be a short-term usage test for prosthodontic materials and relatively less invasive and traumatic especially to suturing the skin to secure the material in contact with the mucosa. If a holding device is used, uncertainty exists regarding the position and pressure exerted by the test specimen. Plaque accumulation around the test specimen will also affect the reactions. Specially designed appliances for testing prosthodontic materials have not received widespread use, probably because of the inherent problems with the test or the cost involved.[16] Development of usage tests for prosthodontic materials should therefore receive greater attention and should become a research priority.

Adverse/Side effects of prosthodontic materials

Unexpected biological side effects to prosthodontic materials may occur as a result of their direct contact with soft or mineralized tissues, or by exposure to leachable components resulting from corrosion and degradation products.[16] Concurrent and combined presence of dental prosthetic restorations made in more than one alloys with differing compositions will tend to enhance the corrosion caused by galvanic action. Since these components may be indigested, both local and systemic reactions may occur. Prosthodontic materials and their corrosion/degradation products comprise components that are known to be allergic, toxic, and carcinogenic in specific situations. Local mechanical irritation due to an overhanging margin of a restoration or an overextended denture must also be considered as adverse effects. Thus, a number of potential problems exist. However, few side effects of prosthodontic materials have been reported in the literature. Similarly, no detailed investigations have been carried out to assess the incidence of adverse effects. An assessment of biological side effects to prosthodontic materials is therefore challenging and it is important to differentiate between potential and documented side effects. It should be kept in mind that prosthodontic materials are manufactured with the aim of being inert and insoluble. Thus, the amounts of leachable components are small, which make toxic reactions unlikely to occur. However, the initiation of an allergic reaction in a sensitized individual requires minimal amounts of the allergen to be present. Contact allergic reactions (type IV reactions) are the most common side effects to prosthodontic materials.

Incidence of adverse/side effects

An overall incidence of side effects to dental materials of 1 per 500 patients, or of one patient per approximately 3.5 years of practice was reported in one study.[17] Over 13,000 patients were examined for acute and long-standing adverse effects during a 2 week period. Prosthodontics and orthodontic treatments were somewhat over-represented compared with dental treatments of general nature with involvement of many dental materials. The incidence for individual materials or group of materials was too low to establish an incidence rate. Lichenoid reactions in the oral mucosa related directly to a restorative material were the most commonly reported side effects. Many of the signs of the noted reactions were symptom-less in patients and even remaining un-noticed to them. A questionnaire survey among prosthodontists indicated adverse patient reactions in 1 out of 300 patients or one patient in approximately 2 years per prosthodontist.

Adverse reactions to prosthodontic materials

In May 2008, a Scientific Committee of the European Commission addressed the use of dental amalgam and the available alternative restorative materials.[18,19] The committee concluded that dental amalgams are effective and noted that none of the dental materials—amalgam and alternatives—was without clinical limitations and toxicological hazards. Because dental amalgam is neither tooth-colored nor adhesive to remaining tooth tissues, its use has been decreasing in recent years and the alternative tooth-colored filling materials have become increasingly more popular.

Due to the low incidence of side effects to prosthodontic material, it will be pertinent to limit this discussion to groups of materials rather than specific types of materials including polymeric materials, alloys, implant materials, and cements. Ceramic materials are generally regarded as inert, but dust particles of these materials arising during handling, manipulating, adjusting, and finishing the fabrication represent a potential problem, both for the laboratory and clinical personnel as well as patient.[20]

Polymeric restorative materials

Polymerization of resin-based materials may be initiated by heat, light, or by chemical activators at room or mouth

temperature. Apart from containing accelerators (amines), they contain co-polymers, such as butyl-methacrylate (BMA), plasticizing agents such as dibutyl-phthalate, and inhibitor such as hydroquinone. In addition, cadmium salts-based coloring agents are also added, these ingredients as well as the added cadmium salts are not considered to represent any problems for patients but they may pose potential hazard to technicians routinely grinding and finishing prosthesis made in resin-based materials. Methyl methacrylate (MMA) monomer may result in toxic reactions and allergic responses in previously sensitized individuals, especially in under cured appliances. It is often difficult to differentiate between these two fundamentally different types of reactions because the clinical manifestations are similar, that is, redness and swelling of the affected mucosa. Physical trauma caused by overextended or poorly fitting dentures may also present as local reactions. These are difficult to differentiate from other types of local lesions. It is important to keep in mind that FORMALDEHYDE is a degradation product of several monomers used in dentistry, including denture-base polymers and restorative resin-based composites. Heat cured acrylics are well tolerated by the gingival tissues. In comparison, cold-curing acrylic resins may result in gingival reactions, due to presence of higher concentration of the residual monomer in cold-cured resins as compared with heat-cured acrylics. The consequent diffused or localized burning sensation in the mouth because of direct mucosal irritation may be erroneously taken for the entity of "Burning Mouth Syndrome (BMS)". In fact the burning sensation may result from the intra-oral manipulation of resin or because of the presence of residual monomer. Allergic reactions to an ethylene amine activator used in several polymeric materials, including impression materials and temporary crown materials are one of two most commonly reported adverse effects to prosthodontic materials.[21] Recurrent facial dermatitis was observed with dental work because of epoxy acrylate bisphenol-A glycidildimethacrylate (BIS-GMA).[22]

Prosthodontic alloys

Some of the metals used in dental alloys are known to be biologically active or potentially hazardous, such as nickel, chromium, cobalt, cadmium and beryllium. About one in four reactions to materials used in prosthodontic treatments are related to metals, especially chromium, cobalt nickel and gold alloys used for metal ceramic restorations.Literature indicates that allergic reactions to gold-based restorations were more common than to nickel-containing alloys.[23] Hildebrand *et al.* reviewed 139 published cases of allergy to base-metal alloys in removable partial dentures.[24] Gingivitis and stomatitis were the most common clinical symptoms, but remote reactions occurred in almost 25% patients. However, mucosal reactions to metal-based partial dentures are rare. The most frequently observed gingival signs and symptoms could be considered as effects of direct pressure contact and the consequent trauma ensuing from the same rather than the side effects of alloys or materials used in the Removable Partial Denture RPD fabrication. Biological reactions to casting alloys are dependent on the release of components from the alloys, which would seem to indicate that they should be dependent on the degree of corrosion. However, no correlation seems to exist between mucosal reactions to fixed prosthesis and corrosion and tarnish. This lack of correlation may indicate that the biological reactions observed are caused by factors other than the material *per se*. Palladium alloys are generally better tolerated than base-metal alloys or gold alloys for metal–ceramic restorations, although they tend to tarnish more than other casting alloys. However, technicians who frequently braze alloys above their melting point are at risk because in the process of soldering and welding, cadmium will evaporate. This represents a problem with the need for availability of an adequate fume extraction system. In response to this hazard, the use of solders containing cadmium has also been largely discontinued. Alloys are among the materials used for the making of conventional cast posts and cores. A variety of metal combinations are in common use, sometimes with stainless steel pins. Of particular concern is to exercise care not to combine the simultaneous use of two different alloys for the post and cast core/crown when preparing post retained crowns because the galvanic corrosion may cause root fractures.

Implant materials

A wide variety of materials have been used in dental implants, including polymeric materials, alloys, ceramic, and synthetic hydroxyl-apatite. The most frequently used materials have been cobalt–chromium alloys, vitreous carbon, titanium, and aluminium oxide. Numerous investigations have been performed to assess the biological properties of dental implants. Much attention has focused on the bone tissue/implant interface and on the ingrowth of bone into the porous implant fixture. The concept of "osseointegration" associated with the titanium implants, as demonstrated by Branemark, has proved much of the biological basis for modern implantology. The failure commonly results because of improper surgical procedures, problem with the loading of the implant, and infection. So far our understanding is clear regarding the inert nature of pure titanium implants.

Much attention has been paid to the nanoparticles (NPs) that are produced for applications in various areas, Understanding the NP–cell interaction is critical for the safe development of nanomaterials, and the biological evaluation of NPs have been prone to be a necessity or a pioneering step in interdisciplinary nanotechnological fields. Biological response in joint tissues irritated by particulate debris that consist of metals, polyethylene (PE), and ceramics as the primary cause of periprosthetic osteolysis and the subsequent implant loosening in total joint replacements. Then we should also survey the osteo-effects of nanosized wear

particles and discuss the NPs' biohazards when they are exposed within the privileged sites in the human body. With an increasing application of nanotechnology in life sciences and medicine, further studies are required on biosafety evaluations of NPs with attention to nanotoxicology not only from the angle of environmental science but also based on the aspect of biomedical applications.[25]

Cements

Zinc phosphate cement has been, and still is, the most frequently used luting agent for crown and bridges. Eugenol is a known cytotoxic and allergic substance. Clinical reports have indicated a high frequency of postluting sensitivity with Glass Ionomer cements. Pulp studies generally indicate slight reactions, but somewhat more to the luting type than to the restorative type of glass ionomer materials. A recent clinical study of pulp sensitivity following cementation with zinc phosphate and glass ionomer cements showed less sensitivity to zinc phosphate than to glass ionomer during the first 2 weeks, but after 3 months, there were no differences. Espelid *et al*.[26] compared the clinical behavior of silver reinforced glass ionomers and resin modified glass ionomers, and found that after 24 months, the resin modified glass ionomers have the best overall performance with respect to retention, marginal integrity, and secondary caries. The pressure on the dentine exerted during cementation was thought to play a possible role on the observation. Modern resin-based luting cements are also well tolerated to pulp.[6]

Research agenda related to dental restorations

The participants of the World Health Organization (WHO) consultation in 1997 devoted considerable time to a discussion of a research agenda related to dental restorations[27]. The Consultation unanimously agreed to establish the following research topics: *Oral Health Program*

1) Global registry of biological and adverse health effects for monitoring of dental material-related symptoms/diseases in various populations.
2) Studies to identify special risk groups and individuals highly sensitive to various restorative materials.
3) Development of criteria regarding the replacement of failed restorations.

Conclusion

Many potential problems exist, but few documented adverse reactions have been published. Much attention has been focused on the presence of nickel, based on the fact that, nickel is a potent allergen, a carcinogen and can be distributed to various organs in experimental studies in animals. It is expected that one requirement will be for clinicians and manufacturers to report biological side effects associated with use of the materials to certifying bodies or health authorities. With the low incidence of adverse effects of the materials in present use, this will satisfy the needs of the patients and those handling the materials. Reliable research information using robust methodology is thus needed to clarify the various safety issues and frequency of adverse reactions in general dentistry, including prosthodontic treatment.

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