

BIOCOMPATIBILITY OF DENTAL RESTORATIVE MATERIALS

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ABSTRACT: Biocompatibility is the ability of a material to elicit a biological response, when applied to the body, without causing a chronic inflammatory reaction, foreign body reaction or toxicity, is related to the interaction of the cell or any biomaterial. A few materials are completely inert from the physiological point of view since, most of the components with a variety of potential toxicity. In addition, chemical reactions during cure of the material may also produce undesirable effects. In order to increase knowledge about the characteristics and properties of materials and their interaction with the biological environment, this study aimed, through literature review, guide and inform didactically professionals and academics on the importance of biocompatibility of restorative materials more direct use in dental practice: amalgam, composite resins and glass ionomer cements.

Keywords: biocompatibility, toxicity, biological environment, amalgam, resins.

1. INTRODUCTION

Biocompatibility is defined as the ability of a material to function in a specific application in the presence of an appropriate host response (Williams 1987). There are several biological responses that can occur when a material is placed in contact with living tissue, this response may be inflammatory in nature, allergic, toxic and mutagenic, and this classification is based on pathological and histological analyzes.(McParland and Warnakulasuriya, 2012) The toxicity is dose related material which can cause cell death or tissue. The use of a non biocompatible material of the dental element can cause an increase in the inflammatory response, leading to cell death and tissue necrosis.(Craig, 2019)Autian (1970) was the first to propose a concept consisting of three levels. They are:

- Nonspecific toxicity (cell cultures or small laboratory animals);
- Specific toxicity (usage tests, e.g. in subhuman primates);
- Clinical testing in humans.

According to Autian (1970) the term 'non specific' refers to test systems which do not reflect the application of a material in a clinical situation whilst the term 'specific' applies to the use

of biological models simulating the actual clinical use of the material.(Stein *et al.*, 2005) The following sequence was adopted by the ISO (1984) in Technical Report 7405:

- Initial tests (cytotoxicity, mutagenicity);
- Secondary tests (sensitization, implantation tests, mucosal irritation);
- Usage tests. In both concepts, newly developed materials should be subjected to the three steps in the given sequence from the simple to the complicated test method, from in vitro to animal tests and from preclinical to clinical testing on humans.

The interaction that occurs at the interface material is dynamic and depends on a number of factors such as: the place to be implanted biomaterial, material properties and biological response of the host.(Suzuki *et al.*, 1995) No material in dentistry is completely safe, so the decision about the use of these materials must be balanced in the potential risks and benefits determined by the professional, overlapping the benefits against the possible risks. A material considered to be biologically compatible should not:(Stanislawskiet *al.*, 1999) Damage to the pulp and soft tissues, contain toxic substances that cause problems systemic in nature, have agents that induce allergic responses and submit carcinogenic potential. Significant advances in the use of biomaterials in dentistry, in order to repair bone tissue and teeth lost by some kind of disease or accident, has enabled professionals using innovative therapeutic rehabilitation, re-establishing the physical, psychological and social patients.(Beer *et al.*, 1990) Although a wide range of dental restorative biomaterial on the market, very few materials meet all the necessary requirements for the use of a biomaterial, being the most relevant biocompatibility.(Watahaet *al.*, 1999)

Silver Amalgam

The amalgam is a widely used restorative material for metallic restorations in posterior teeth. Its composition consists of alloy powder and liquid mercury containing silver, tin, copper, zinc among other elements. (Lakshmiet *al.*, 2017)Its major disadvantages are, not present favorable aesthetic properties, adhesiveness has no tooth structure and has mercury in their composition.(Benton *et al.*, 1993) The biocompatibility of amalgam has been a point of controversy for many years, being related to mercury toxicity and the debate over whether mercury from amalgam has toxic effects.(Wylie *et al.*, 2007) Mercury occurs in three forms: as metal (Hg⁰) as inorganic ions (Hg²⁺) or as one of many organic forms of mercury methyl or ethyl. Metallic mercury gains access to the body via the skin or as vapor through the lungs, and inhalation of mercury vapor primary port of entry into the body and then reaches the bloodstream via alveoli, where it is distributed in the body, especially into tissues adipose and nervous.(Schmalz and Garhammer, 2002) Studies have shown that the vapor release amalgams sufficient to cause absorption 1-3 µg of mercury per day, depending upon the amount of alloy present. Mercury is also ingested during the wear of amalgam restorations, about 45 µg per day can reach the gut in the form of amalgam particulate or be dissolved and released as Hg²⁺ ions.

Symptoms of the toxicity of mercury are related to the form of the mercury being the lowest level to any known toxic effect is 3 µg / kg. Acute symptoms are neurological or renal going paresthesiaie, at levels ≥ 500 µg / kg to ataxia at the level of ≥ 1000 µg / kg, joint pain at the level of ≥ 2,000 µg / kg and death at the level of ≥ 4000 µg / kg. Symptoms of chronic exposure include weakness, fatigue, anorexia, weight loss, insomnia, irritability,dizziness and tremors in the extremities or eyelids . However, studies conducted in populations exposed to mercury professionally, no evidence that dental amalgam mercury released is harmful.(Geurtsen, 2002)

Glass Ionomer Cement

The conventional glass ionomer cements (GICs) are presented commercially in the form of powder and liquid. The powder is composed of silica (SiO₂), alumina (Al₂O₃), calcium fluoride (CaF₂), aluminum fluoride (AlF₃), aluminum phosphate (Al PO₄) and sodium aluminum fluoride (Na₃AlF₆) the liquid comprises by an alkenoic acid, and polyacrylic acid as used (30%), itaconic acid (15%), tartaric acid (10%) and water (45%). These materials exhibit unique properties that include: ability to ion exchange with the tooth surface, release fluoride for a lifetime membership to the restoration and maintenance of tooth structure with marginal sealing for long periods.(Dahl, 1978) Limitations in clinical use are related to their mechanical properties, i.e. mechanical strength of this material is inferior when compared with amalgam and composite resin, also presenting a negative characteristic as a slow polymerization reaction.(Batchelor and Todd, 2010)To improve the physical and mechanical properties, these materials have undergone some changes in its composition. One was the inclusion of hydrophilic monomers such as 2-hydroxyethyl-methacrylate (HEMA) and polymerization initiators, thus resulting in the glass ionomer cements, resin-modified (RMGICs)

The biocompatibility of ionomer cements is attributed to some reasons such as the ability to adhere to tooth structure, high molecular weight polyacrylic acid present in the composition, minimally exothermic curing reaction and rapid pH neutralization. The cytotoxicity of these materials is a property that is a point of discussion in the literature because there is no unanimity of opinion.(Mittermüller *et al.*, 2012)

The canals or dentinal tubules are responsible for the diffusion of fluids through the dentin and are directly related to this protective function. These tubules are shown grouped and cross the dentin throughout its thickness, containing the cytoplasmic cell - the odontoblasts present in dental pulp.(Mobeeriek and Eshiekh, 1998) Residues of methacrylate monomers can be incorporated into the lipid bilayer of the cell membrane leads to solubilization of odontoblasts this structure and consequent irreversible cell damage. Thus, the RMGICs should not be placed in direct contact with the pulp tissue, however, studies show the compatibility of these biological cements when used in contact with gums and oral mucosa.(Gangemiet *et al.*, 2009)

Composite Resin

Dental composites are complex mixed materials which generally consist of an organic polymerizable matrix, reinforcing fillers, which are mainly inorganic and a silane-coupling agent.[2] The polymerizable matrix contains one or more monomers: e.g., Bis GMA and/or UDMA, comonomers (EGDMA,DEGDMA,TEG-DMA) and various additives, like an initiator (camphorquinone), co initiator (e.g., dimethyl-aminobenzoic acid ester), an inhibitor of polymerization (e.g., BHT), and a photostabilizer (e.g., benzophenone), various inorganic materials are used as fillers: quartz, borosilicate, lithium aluminum silicate glasses, and amorphous silica. In order to achieve radiopacity, oxide glasses with barium, strontium, zinc or other metals are added to fillers of modern resin composites.(Silvestre *et al.*, 2005)

Absorption of organic substances from unpolymerized material and also unbound resin components may leach into saliva during the initial phase after polymerization said to predispose both patients and dental personnel to allergic reactions.(Kaufman and Keila, 1989) Systemic reactions are expressed generally as allergic skin reactions. Some brands of dental restorative materials possess the ability to release histamine from human blood basophils in sensitive patients.(Deshpande, Verma and Macwan, 2014)

Restorative resins are said to be cytotoxic before polymerization and immediately after placement. When glass-ionomer cements (GICs) were first introduced, with just one acid (polyacrylic), pulpal responses were classified as bland. With the addition of many more acids to enhance certain characteristics and reduce the setting time, GICs have become more irritating. A co-polymerized new resin composite, in which the filler particle is trimethylolpropane-trimethacrylate is chemically bonded to the resin matrix, demonstrated no pulpal irritation or inflammation when was placed on vital dentin of teeth with complete enamel removal.(Calişkan, Türkün and Alper, 1994)

Unpolymerized resin monomers in RMGIC and Cu^{2+} and Ag^+ in metal-reinforced glass ionomer are responsible for cytotoxicity of the materials.(Subbarao, Neelakantan and Subbarao, 2012) The biocompatibility of a fast-setting glass-ionomer cement assessed based on a comparative biological study, which concluded that Ketac-bond is an acceptable restorative material.(Sainulabdeen *et al.*, 2010)Fluoride-releasing resin biocompatibility is comparable to that of nonfluoride dental resin. Therefore it can be considered as a biologically safe material as an adhesive or a dental restorative resin.(Tamilselvam, Divyanand and Neelakantan, 2013)

Zinc Phosphate

Zinc phosphate dental cement is one of the oldest and widely used cements, and is commonly used for luting permanent metal and zirconium dioxide restorations and as a base for dental restorations. Zinc phosphate cement is used for cementation of inlays, crowns, bridges, and orthodontic appliances and occasionally as a temporary restoration. It is prepared by mixing zinc oxide and magnesium oxide powders with a liquid consisting principally of phosphoric acid, water, and buffers. It is the standard cement to measure against. It has the longest track record of use in dentistry. It is still commonly used; however, resin-modified glass ionomer cements are more convenient and stronger when used in a dental setting.(Hurrell-Gillingham *et al.*, 2003)

Chlorhexidine

Chlorhexidine is a cationic bisbiguanide with optimal antimicrobial action. It is active against a wide range of microorganisms present in the oral cavity, such as Gram-positive and Gram-negative bacteria, bacterial spores, lipophilic virus, yeast and dermatophytes. It seems to act by adsorbing onto the cell wall of the microorganism and causing leakage of intracellular components (Leonardo *et al.* 1999). It is bacteriostatic in nature, at low concentrations and bactericidal in nature, at high concentrations and adsorbs to dental tissue and mucous membrane resulting in its prolonged gradual release at therapeutic levels (Jeansonne & White 1994, White *et al.* 1997). Chlorhexidine was found to be an effective antimicrobial agent when used as an endodontic irrigation solution and when used as an intracanal antimicrobial dressing further reduction of remaining bacteria within the root-canal system were seen.

The toxicity of chlorhexidine to gingival cells is due to the toxic potency of chlorhexidine is dependent on the length of exposure and the composition of the exposure medium . These findings suggest that similar reactions within a root canal may reduce the potential of a cytotoxic reaction in the periapical tissues. Boyce *et al.* (1995) found 0.05% chlorhexidine is uniformly toxic to both cultured human cells and microorganisms. Agarwal *et al.* In 1997 found that the chlorhexidine rapidly disrupts the cell membrane of both crevicular and peripheral blood neutrophils at concentrations above 0.005% in 5 min, indicating that its

inhibitory effect on neutrophil function is mostly due to its lytic properties. Yesilsoy et al. (1995) assessed the short-term toxic effects of chlorhexidine in the subcutaneous tissue of guinea pigs and found a moderate inflammation present after 2 days, followed by a foreign-body granuloma formation at 2 weeks. (Yli-Urpo, Närhi and Söderling, 2003)

Sodium Hypochlorite

The antimicrobial efficacy of the solution is due to its ability to hydrolyse and oxidise the cell proteins and, to some extent, it osmotically draws fluids out of cells due to its hypertonicity (Pashley et al. 1985). Sodium hypochlorite has a pH of approximately 11-12 and when hypochlorite contacts tissue proteins, nitrogen, formaldehyde and acetaldehyde are formed within a short time and peptide links are broken resulting in dissolution of the proteins. (Engfelt 1922).

Complications of the use of sodium hypochlorite is due to accidental injection beyond the apex which can cause violent tissue reactions characterized by pain, swelling, haemorrhage, and in some cases the development of secondary infection and paraesthesia (Reeh& Messer 1989, Becking 1991, Ehrich et al.1993). Hypersensitivity reactions to sodium hypochlorite have also been reported. A great deal of care should be taken when using sodium hypochlorite during endodontic irrigation. Ehrich et al. (1993) suggested that a clinician should check, both clinically and radiographically, for immature apices, root resorption, apical perforations or any other conditions that may result in larger than normal volumes of irrigant to be extruded from the root-canal system into the surrounding tissue. (Ribeiro, Marques and Salvadori, 2006)

ETDA

The disodium salt of ethylene diaminetetraacetic acid (EDTA) is generally accepted as the most effective chelating agent and lubricant in current endodontic practice. It is used in endodontic therapy to enhance the chemomechanical enlargement of canals (Walton & Torabinejad 1996), to remove smear layer (Meryonet al.1987) and to clean and aid in disinfecting the dentinal walls (Yoshida et al. 1995). A great deal of care should therefore be exercised when using sodium hypochlorite during endodontic irrigation. Ehrich et al. (1993) suggested that a clinician should check, both clinically and radiographically. Irrigation should be performed slowly with gentle movement of the needle to ensure that it is not binding in the canal. That leakage of EDTA to periapical tissues during root-canal preparation may inhibit macrophage function, and thus alter the inflammatory response in periapical lesions. EDTA has been shown to have weak antibacterial and antifungal properties.

Casting Alloys

Dental casting alloys play a prominent role in the treatment of dental disease. alloys continue to be used as the principal material for fixed prosthetic restorations and will likely be the principal material for years to come. No other material has the combination of strength, modulus, wear resistance, and biologic compatibility that a material must have to survive long term in the mouth as a fixed prosthesis. (Schiteaet al., 2020) Today's practitioner may select from alloys based on palladium, silver, nickel, cobalt, and titanium, among others. Furthermore, alloys within each of these groups are diverse, and the practitioner faces a bewildering array of choices. Although uses for pure metals such as gold foil and platinum foil exist in dentistry, the main role for metals in dentistry has been in alloys [10]. Alloys are used for fixed prostheses rather than pure metals because pure metals do not have the

appropriate physical properties to function in these types of restorations. Thus, the use of alloys provides physical and biologic properties that are required for successful, long-term fixed prostheses (Greenwood, 2018).

The biocompatibility of cast metallic restorations is primarily determined by the amount and nature of released cations. The biological effects of these metal ions are significantly different. Although contradictory data have been documented, many investigators have reported that Cu, Ni, and Be have pronounced cytotoxic potency. There is also evidence from in vitro investigations that various metallic elements, like Ni, Co, and Cr, can modulate the immune response. Local and systemic allergic reactions to many metals have been observed, with Ni being the most frequent allergenic element. Additionally, various other factors could contribute to biological interactions of metallic restorations, such as physicochemical surface parameters (atomic ratio of noble to non noble metals, etc.), phase formation, wear, and the quality of the manufacturing process itself.

Dental Implants

A dental implant is an artificial tooth root that is placed into your jaw to hold a replacement tooth or bridge. Dental implants may be an option for people who have lost a tooth or teeth due to periodontal disease, an injury, or some other reason. Although titanium is the preferred choice for dental implants as it is an inert material, if used in oral implants, it may encourage toxic or allergic type I or IV reactions. Allergy due to titanium might be accountable for the failure of implants in some cases (known as “cluster patients”). It has been documented that the risk of titanium allergy is more prevalent in patients having sensitivity to other metals. In such types of cases, an allergy assessment is suggested to exclude problems related with titanium implants.

Titanium and zirconium are highly reactive metals, and when exposed to fluid media or air they quickly develop a layer of titanium dioxide (TiO_2) or zirconium dioxide (ZrO_2). This layer of metal dioxide forms a boundary at the interface between the biological medium and the metal structure and prevents further deterioration of materials. It produces passivation of the metal, determining the degree of biocompatibility and the biological response to the implant. Any rupture of the oxide layer may produce corrosion of these metals and affect compatibility. (SoheiliMajd, Goldberg and Stanislawski, 2003)

Impression Materials

Allergic reactions are reported to polyether impression materials which manifest as swelling, itching and redness. It was seen on patch testing that a component of the catalyst paste caused the allergy and on replacement of this component, no allergic reactions were observed. Another retrospective study documented results of multiple allergy tests with polyether impression material and its components (between 2007 and 2009). The results of patch tests showed a positive reaction to mixed polyether impression materials, base paste or to the base component. (SoheiliMajd, Goldberg and Stanislawski, 2003)

There is only a single allergic case reported in which a patient developed hypersensitivity reaction to polysulfide material in the form of redness, itching and oedema following secondary impression for upper and lower complete dentures and on treatment with topical corticosteroids (Betamethasone valerate ointment 0.1%) she recovered. A retrospective case report of fatal anaphylactic shock to alginate impression material has also been documented. (Schmalz and Arenholt-Bindslev, 2009) Because of the isolated allergic cases

reported to alginate and polysulphide materials, there is inconclusive evidence of the incidence of these reactions.

2. CONCLUSION

It is essential to achieve genuine dental products to shield patients from the trivial form of danger. To accomplish this, an amalgamation of multi-spectral tests currently available to us should be used before declaring any material safe. All materials in current use are considered acceptable, in terms of their biocompatibility with local tissues, when properly handled and placed. Adverse systemic reactions are believed to be rare and self-limiting and tend to be of an allergenic nature. Local reactions have been documented in a small percentage of individuals, and systemic toxic reactions have been reported in the scientific literature.

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