ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

REVIEW ARTICLE

Toxicology and Biocompatibility of Dental Materials: A Review

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ABSTRACT

During the past few years, the biocompatibility of dentalmaterials has evolved into a comprehensive, complex, and independent discipline of dental materials science. As dentists we must know about which materials are biocompatible and which are not, as then only we can provide proper care and service to our patients. At the same time knowing about their biocompatibility and toxicology we can ensure that both the dentists and the dental technicians are safe from the side effects of dental materials. In this article we will discuss about the various dental materials used in day to day dentistry and about their biocompatibility and toxicology.

Keywords: Biocompatibility, toxicology, dental materials, mercury, nickel, polymethyl methacrylate

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ISSN: 0975-8585

INTRODUCTION

For more than 2000 years, attempts have been done to improve life quality of dental patients with the use of various new materials and devices. Evidence of use of materials such as extracted animal & human teeth to fabricate bridges dates back to 400 B.C. Hippocrates in the same era of 460-370 B.C., had put forward & emphasized on the concept of ethical treatment of patients. A biomaterial can be defined as any substance, otherthan a drug, that can be used for any period as part of a system that treats,augments or replaces any tissue, organ or Function of the body.So the first requirement for material is its biocompatibility. Therefore one should differentiate between biocompatibility and toxicology.

Definition

1. Biocompatibility is formally defined "as the ability of a material toelicit an appropriate biological response in a given application in the body".
2. Toxicology is the study of the adverse effects of chemical, physical or biological agents on living organisms and the ecosystem, including the prevention of such adverse effect (2012 Society of Toxicology)
3. Toxicity of a material describes the ability to damage abiological system by chemical meansOR It is a dose related potential of a material to cause cell or tissue death [1].

Therefore it is essential to know the biocompatibility of a material otherwise it can lead to adverse reactions. The science of dental biomaterials must be based on a broad information base of certain biologic considerations that are associated with the use of materials designed for the oral cavity.

Based on these criteria, the requirements for dental material biocompatibility include the following:

- It should not be harmful to the pulp and soft tissues.
- It should not contain toxic diffusible substances that can be released and absorbed into the circulatory system to cause a systemic toxic response.
- It should be free of potentially sensitizing agents that are likely to cause an allergic response.
- It should have no carcinogenic potential.

Relevance to Dentists

Dentist's potential concerns about biocompatibility can be organized in to 4 areas:

1) Safety of the patient.

One of the primary concerns of any dental practitioner is to avoid harming the patient. Evidence has shown that, although adverse reactions to dental materials are not common, they can occur for many types of materials, including alloys, resins and cements.

2) Safety of Dental staff

ISSN: 0975-8585

In many situations, the risk of adverse effects of biomaterials is much higher for dental staff than for the patient. The staff may be chronically exposed to materials when they are being manipulated or setting.

E.g:- Amalgam – Mercury vapour.

Chronic exposure to latex and resin based materials.

3) Regulatory compliance issues.

Biocompatibility issues are closely linked to regulations that affect dental practice.

Ex: Dental amalgam.

Because of the biologic concerns about mercury, regulators have considered monitoring and restricting amount of mercury in waste water for dental practice.

4) Legal Liability.

Biocompatibility issues also influence liability issues that affect dental practitioners. Because dental materials can affect the well-being of patients and dental auxiliaries, practitioners assume a legal risk when using these materials.

Allergic responses to Dental materials:

Allergic Contact Dermatitis:

It is most common occupational disease. The incubation period is 2 days to several years. Dermatitis occurs where the body surface makes direct contact with the allergen.

An allergic contact dermatitis associated with the monomers of bonding agents frequently involves the distal parts of fingers and the palmar aspects of the finger tips.

Allergy to Latex Products:

Hypersensitivity to latex containing products may represent a true latex allergy or a reaction to accelerators and antioxidants used in latex processing [2]. Thiuram a chemical used in fabrication of latex articles and polyether component of latex rubber gloves worn by dentists were the causes of allergic reactions.

Processing of latex:

Natural rubber products

↓

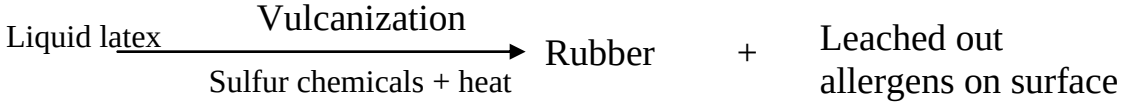
White milky sap from tropical trees.

↓

Ammonia is added to pressure.

↓

Hydrolyzes and degrades the sap proteins to produce allergens.



Reactions vary from simple types such as localized rashes and swelling to more serious types such as wheezing and anaphylaxis.Rankin et al, 1993 stated that Dermatitis of hands is the most common adverse reaction [2]. In 1984, Blinkhorn and Leggate described generalized angioneurotic edema, chest pains and a rash on the neck and chest of a 15 years old boy as a reaction to a dental rubber dam [3].

To avoid these allergic reactions non latex gloves were introduced their composition is elastyrene (block copolymer), neolon, tactylon, Qualitoch (corn starch).

Allergy to denture base material:

Basker et al 1976, demonstrated that free residual methyl methacrylate monomer in autopolymerized acrylic dentures or appliances can cause allergic reactions. To avoid this, authors recommended that autopolymerized appliances and denture should be immersed in water for 24 hours before being worn[4].Laeijendecker and Van Josst 1994, presented cases of females wearing complete denture suffering from oral lichen planus and "burning mouth syndrome". When patch testing was done they developed papular reactions. Clinical improvement occurred when gold in dentures was replaced [5].

Pulpal Responses to specific Agents and Techniques:

1. Mercury

In 1968 SOREMARK and associates showed that radioactive mercury reached pulp in humans after 6 days if no cavity liner was used. They also stated that "rate of diffusion into enamel and dentin was inversely related to the degree of mineralization" [6]. Kurosaki and Fusayama (1975) showed that mercury from amalgam restorations in humans and dogs did not reach pulp. In fact, it did not penetrate dentin that was demineralized intentionally [7]. Van Der Linden and VanAken 1973, studying on human teeth found no mercury in more radiopaque dentin beneath amalgam restorations. Previously, it had been thought that this layer was prominent because of mercury diffusion [8].Mortazavi Vet al2000 stated that greatest amount of mercury was released during dry polishing of an amalgam restoration [44 micro grams].Total amount of mercury generated during placement [6-8micro grams], wetpolishing [2-4 micrograms] and trituration [1-2 micrograms] was also measured [9].

2. Composites

The addition of mineral fillers to the direct filling chemically cured resin composites in 1960's and 1970's did not reduce their potential for creating severe pulp responses. If not lined properly, they cause chronic pulpitis that persists for an indefinite time.Level of pulp response to resin composite restorations is especially intensified in deep cavities when an incomplete curing of resin permits a higher concentration of residual unpolymerized monomer to reach the pulp.

Hallstrom reported the case of a 6-year-old girl who suffered anaphylactic shock after application of a pit and fissure sealant. Intraorally, blister like lesions of the gingiva next to the treated teeth were visible [10].

Precautions while using them include, firstly, Use twice the recommended time exposure and secondly cure in increments.

3. Zinc phosphate cement

When used as a base, it is not a highly toxic substance. However, if a thin mix of Zinc phosphate cement is used to cement a crown or inlay, a strikingly different response occurs. When patient bites down on a tongue blade to seat restoration, the phosphoric acid within the mix of zinc phosphate cement is forced into the dentinal tubules in such a quantity that it creates, after 3 or 4 days a widespread three – dimensional lesion involving all the coronal pulp tissue.Schmalz etal documented that the toxicity of zinc phosphate cements in mouse fibroblast cultures and PDL cell cultures was dependent on the setting time [11].

4. Glass ionomer cement:

When first introduced, pulp responses were classified as bland, moderate and less irritating than other cements. The blandness of GIC was attributed to absence of strong acids and toxic monomers. Polyacrylic acid and related poly acid is much weaker than phosphoric acid, as polymers, they possess higher molecular weights that may limit their diffusion through the dentinal tubules to the pulp.Pamerjir and Stanley 1984, permitted an anhydrous GIC to set under continuous pressure (Simulating Crown cementation), pulp abscesses and intense (severe) hemorrhage occurred when the reparative dentin thickness was 0.5 mm or less. Therefore, it is recommended to use a small dab of calciumhydroxide in areas of extensive crown preparation; when it is within 1 mm of pulp before the cementation procedure [12].

5. Resin based composite cements (Dual cure)

These are indicated for all – ceramic crowns, metal ceramic crowns, ceramic veneers, and porcelain inlays.In 1992, Stanley compared pulp responses to dual – cured resin – based cementation agents. They observed that only when dual – cure resin cement received no visible light energy average pulp response levels exceed the accepted level of biocompatibility [13].

6. Conditioning (etching) Agents

Conditioning procedures are used with both resin composite systems and GIC's.Brannstrom 1980 showed that conditioning of dentin and removal of the smear unit allows the ingress of bacteria and outward flow of dentinal fluid and possibly contributes to formation of a biofilm that interferes with adhesion.Conditioning techniques that are associated with weaker acids, shorter periods of application, and elimination of subbing and scrubbing procedures produce a minimal pulp response [14].

7. Bonding Agents

A variety of dentin bonding agents has developed and is applied to cut dentin during restoration of teeth.Many of these reagents are cytotoxic to cells in -vitro if tested alone. However, when placed on dentin and rinsed with tap water between applications of subsequent reagents, cytotoxicity is decreased. Long term in- vitro studies suggest however that sufficient components of many bonding agents permeate up to 0.5 mm of dentin to cause significant suppression of cellular metabolism for up to 4 weeks after their application.Hydroxy ethyl methacrylate (HEMA) is at least 100 times less cytotoxic in tissue culture than Bis – GMA.Douglas et al 1999 stated that major components of DBA like Bis-GMA,UDMA suppress mitochondrial enzymes such as succinic dehydrognase indicating that at sufficient concentrations these components alter macrophage function [15].

Reaction of other Oral soft tissues

1. Restorative materials

Restorative materials may cause reactions in the oral soft tissues such as gingiva.In general, conditions those promote retention of plaque, such as rough surfaces or open margins, increase inflammatory reactions in gingiva around these materials. However, released products of restorative materials also contribute either directly or indirectly to this inflammation, particularly in areas where the washing effects of saliva are less, such as in interproximal areas, in deep gingival pockets or under removable appliances.

Cements exhibit some cytotoxicity in the freshly set state, but this decreases substantially with time. The buffering and protein – binding effects of saliva appear to militate against cytotoxic effects.Composites are initially very cytotoxic in in-vitro tests of direct contact with fibroblasts. The cytotoxicity is most probably primarily from unpolymerized components in the air – inhibited layer that leach out from the materials.Amalgam restorations carried in to gingival crevice may cause inflammation of gingiva because of products of corrosion or bacterial plaque. Gold is a stable and relatively insoluble restorative material.Extremely rare cases (1:1 million) may react to gold restorations.

Reactions include Burning sensations, Lichenoid lesions and General systemic reactions [16].

2. Denture base material:

Denture base materials, especially methacrylates, have been associated with immune hypersensitivity reactions of gingiva and mucosa probably more than any other dental material.The greatest potential for hyper sensitization is for dental and laboratory personnel who are exposed repeatedly to a variety of unreacted components.Hypersensitivity has been documented to the acrylic and diacrylic monomers, certain curing agents, antioxidants, amines and formaldehyde.

3. Soft denture liners

Soft tissue responses to soft denture liners and adhesives are of concern because of intimate contact between these materials and gingiva. Plasticizers,which are incorporated into some materials to make them soft and flexible, are released in vivo and in-vitro.In animal tests, several of these materials have caused significant epithelial changes, presumably from the released plasticizers.

4. Implant materials.

These are four basic materials used in implant fabrication:ceramics, carbon, metals and polymers. Interest in biocompatibility of implant materials has grown as the use of implants in clinical practice has increased dramatically in the past 10 yrs.Most ceramic implant materials have very low toxic effects on tissues, either because they are in an oxidized state or are corrosion resistant. These are toxic and are non-immunogenic and non-carcinogenic. These are brittle and lack impact and shear strength, and therefore have been used as porous or dense coatings on metals or other materials.If root surface porosities are more than 150 mm in diameter, the implants often become firmly bound to bone. If porosities are smaller, the tissue usually forms only fibrous in growth.

BIOCOMPATABILITY OF METALS

Laboratory techniques performed with metals may expose us occasionally or routinely to excessively high concentrations of beryllium and nickel dust and beryllium vapour.

1. Beryllium

Although the beryllium concentration in dental alloys rarely exceeds 2 wt % the amount of beryllium vapor released in to the breathing space during melting of Ni-Cr-Be alloys may be significant over an extended period. The risk of beryllium vapour exposure is greatest for dental technicians during alloy melting especially in the absence of an adequate exhaust and filtration system.High levels of beryllium have been measured during finishing and polishing when a local exhaust system was not used. They were reduced to levels considered safe when exhaust fan was used.Exposure of beryllium may result in acute and chronic forms of beryllium disease – BERYLLIOSIS.Symptoms range from coughing, chest pain and general weakness to pulmonary dysfunction.

2. NICKEL

It is a great concern to dental patients with a known allergy to this element.Dermatitis resulting from contact with nickel solutions was described as early as 1989.Inhalation, ingestion and dermal contact of nickel or nickel containing alloys are common because nickel is found in environmental sources such as air, soil and food as well as in synthetic objects such as coins, kitchen utensils, and jewelry.Nickel allergy was determined by PATCH TEST. Menne T

1987described a standard patch test consisting of 5% Nickel sulfate solution or 5% Nickel sulfate solution on a petrolatum base, in center portion of a square Band-Aid of good quality. This is applied on medial aspect of upper arm, which was cleaned with a alcohol swab. This is left in place for 48hr undisturbed. A Band-Aidwithout any reagent is placed adjacent to the first acts a control. After 48 hours, Band-Aid is removed and area is cleaned. It is read after 20 min [17].

0 →noreaction.
+ →erythema is seen.
++ →erythema, papules are seen.
+++→erythema, papules, vesicles are seen.
++++→edema with vesicles is seen.

Dimethyl glyoxime test

Shore stated that few drops of 1% alcohol solution of dimethyl glyoxime, few drops of ammonium hydroxide added to a metallic object, skin on solution will produce a strawberry red insoluble salt in presence of nickel [18].

Lamster (1987), showed 2 cases demonstratingLoss of alveolar bone about Ni rich nonprecious alloy and porcelain crown within 18 months of placement. Reason for this was thought that the electrolysis of metal leading to corrosion and biocompatibility of Nickel [19].John. C. Wataha 1998 stated that transient exposure of casting alloys to an acidic oral environment is likely to significantly increase elemental release from Ni-based alloys, but not from high noble alloys.He also stated that brushing dental casting alloys may increase their cytotoxicity in vitro, but the increase depends heavily on the alloy type and brushing technique. He observed that with tooth paste Nickel based alloys were significantly more lost, Ni-Cr-Be was the worst, increasing more than 60% toxicity over controls [20]. J. Geis-Gerstorfer1991 stated that from point of corrosion resistance Beryllium free Ni-Cr-Mo alloys should be preferred in clinical use [21].Craig 2002 stated that of pure metals Au, Pd, Ti were least cytotoxic. Followed by Ag, Ni, single phase alloys with moderate copper.Symptoms of sensitivity range from urticaria, pruritis, Xerostomia, eczema or vesicular eruptions.Release of Ni ions from dental alloys is high enough to be clinically significant. If so as a result, of potential alteration in endocrine functions, changes in vital functions such as bloodpressure, pulse, temperature may be expected. Ni containing alloys have been linked to decrease in lymphocytes in human [22].

CONCLUSION

The biocompatibility of a dental material depends on its composition, location and interactions with oral cavity. Diverse biological responses to these materials depend on whether they release their components and whether those components are toxic, immunogenic, or mutagenic at released concentrations.The location of a material in the oral cavity partially determines its biocompatibility.Today, in development of any biomaterial one must consider not only strength, esthetics, or functional aspects of the material, but its biocompatibility as well. Furthermore, demands for appropriate biological responses are

increasing as we ask materials to perform more sophisticated functions in body. Thus considerations of biocompatibility are important to manufactures, practitioners, scientists and patients.

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