



An over View on Cytotoxicity of Glass Ionomer Cements

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Abstract

Since their introduction in the market, some 30 years ago, the biocompatibility aspects of glass-ionomer cements (GICs) have been intensively studied for the past 30 years, since their introduction in the market. In general, cytotoxicity of fully set conventional preparations in previous studies was shown to be minimal. However if GIC was placed in direct contact with the pulp tissue, abscess formation was observed. A resin-modified preparation proved to be cytotoxic under these conditions. This product was also observed to be mutagenic. The biological effects of glass ionomer cements as used in clinical dentistry are described in this article. For any restorative material to be used in clinical dentistry, they should be biocompatible and non-toxic to the tissues it comes in contact. Generally, conventional GICs are suggested to have minimal toxicity, whereas, resin-modified GICs are shown to exert cytotoxicity and genotoxicity.

Key words: biocompatibility, cytotoxicity, glass ionomer cement

Introduction

No dental material meets all requirements to be considered as an ideal restorative material should meet all the requirements, and should be biocompatible and non-toxic to the tissues. Biomaterials 1993;14: 906–16]. Most of these materials have to contact or interact with body tissue and fluids, so material's selection must take into consideration not only mechanical and physical properties but also biological compatibility. The need for evaluating the cytotoxicity and biocompatibility of specific material is as important as the assessment of its physiological or mechanical properties [Six N, Lasfargues JJ, Goldberg M. In vivo study of the pulp reaction to Fuji IX, a glassionomer cement. J Dent 2000;28: 413–22]. Since glass ionomer cements were first introduced in the early70s by WILSON & KENT (1972), major changes have occurred in their chemical composition. Conventional glass-ionomer cements were characterized by an acid-base reaction between polycarboxylic acids and alumina silicate glass particles that formed a set matrix. They presented favourable characteristics such as their ability to chemically adhere to dental tissues and to release fluoride ions. As reported by MOUNT (1995) the leaching of fluoride ions from conventional glass-ionomer cements provided them with excellent anti-cariogenic properties. However, their clinical indications were limited because they exhibited poor mechanical and aesthetic qualities (UM & OILO 1992).

Later, light-curing glass-ionomer cements incorporating BISGMA and TEGDMA dental resins have been developed. With this new formulation, both the conventional acid-base reaction and the photo-polymerization of the resins produced a mixed network of glass ionomer and resin matrix. Despite improved mechanical properties and reduced sensitivity to moisture, light curing glass-ionomer cements remained mostly used as liners or bases under composite resin restorations (UM & OILO 1992). As a restorative material, the major weakness of light curing glass-ionomer cements was a lack of translucency and post-operative sensitivities were frequently observed after placement [STANLEY HR(1992) Local and systemic response to dental composites and glass ionomers. Advances in Dental Research 6 55-64] .

Biocompatibility

Biocompatibility of dental materials is the ability of the material to produce an appropriate biological response in a given application in the body [K.J Anusavice, Phillips science of dental materials, eleventh edition, Elsevier, St.Louis, Missouri;2003,171]. For any dental restorative material this is now considered as a fundamental

requirement. The most common biological reactions to materials include toxic, inflammatory, allergic and mutagenic reactions. Of these toxicity is the earliest response and for almost all materials the first screening test is the toxicity test. In patients body materials release substances which can cause overt toxicity.

Local and Systemic Effects of Materials

Local and systemic effects are primarily caused by substances that are released from the material and the biological response to those substances [K.J Anusavice, Phillips science of dental materials, eleventh edition, Elsevier, St.Louis, Missouri; 2003, 177]. The distribution of released substances determines the nature severity and location of these effects. For dental materials the local effects are seen in the pulp of the tooth, in the periodontium at the root apex or in oral tissues such as the buccal mucosa or tongue. Systemic effects from dental materials gain access to the body through ingestion and absorption in the gut, inhaled vapour, release at the tooth apex or absorption through the oral mucosa. The biological response to the systemic effects depends on the site of exposure, the excretion rate of the substance and the concentration and duration of the exposure.[K.J Anusavice, Phillips science of dental materials, eleventh edition, Elsevier, St.Louis, Missouri; 2003, 177].

Tests for Biocompatibility

For measuring the biocompatibility of dental materials three basic types of tests are available the in vitro test, the animal test and the usage test which are performed either in animals or in humans.[K.J Anusavice, Phillips science of dental materials, eleventh edition, Elsevier, St.Louis, Missouri; 2003, 189]. The first screening test to evaluate a new material are the in vitro tests and are performed outside of an organism. They are performed separately from an intact organism and may be conducted in a test tube, cell-culture dish, flask or other container. The material or an extract of a material should communicate with some biological system which may consist of mammalian cells, cellular organelles, tissues, bacteria or some sort of enzyme. The contact between the material and the biological system may be direct or indirect which involves exposure of a material directly with the biological system if it's a direct contact. In indirect contact there is some sort of a barrier such as agar, membrane filter or dentin.[K.J Anusavice, Phillips science of dental materials, eleventh edition, Elsevier, St.Louis, Missouri; 2003, 189]. In animal tests the material is placed in to an intact organism of some type. Common animals used for this type of test are mice, rats, hamsters, ferrets or guinea pigs. In animal tests an intact animal is used rather than cells or tissues from an animal and the advantage of an animal test is its ability to allow an intact biological system to respond to a material for usage test the material should be placed in an environment clinically relevant to the use of the material and are performed in humans or animals.

Cytotoxicity

Cytotoxicity is a substance's quality of being poisonous to cells. Chemicals like acids or immune cells are among cytotoxic substances. Cytotoxicity is the quality of being toxic to cells. Cells exposed to a cytotoxic compound can respond in a number of ways. The cells may undergo necrosis, in which they lose membrane integrity and die rapidly as a result of cell lysis; they can stop growing and dividing; or they can activate a genetic program of controlled cell death, termed apoptosis. Cells undergoing necrosis typically exhibit rapid swelling, lose membrane integrity, shut down metabolism, and release their contents into the environment upon lysis. Apoptosis is characterized by well-defined cytological and molecular events, including a change in the refractive index of the cell, cytoplasmic shrinkage, nuclear condensation, and cleavage of DNA.

Cytotoxicity of Glass Ionomer Cements

Generally, the biocompatibility of conventional GICs is considered to be good, with minimal release of organic components[Kuhn A T, Lesan WA& Painter H A, 1983; Release of organic species from glass ionomer cements Journal Material Science 224]. Mjor, Nordahl and Tronstad(1991) filled Class V cavities of dog teeth with GIC and found that only slight pulpal reactions occurred [Mjor IA, Nordahl I & Tronstad L (1991) Glass ionomer cements and dental pulp Endodontics& Dental Traumatology 7(2) 59-64]. Nevertheless, if GIC was placed in direct contact with the pulp tissue, abscess formation was observed [Peterson RC&Watts A,(1987); Toxicity to the pulp of a glass ionomer cement British Dental Journal 162(3)110-112]. This reaction may result from the release of toxic ingredients from GIC, because GIC (Ketac-Fil, ESPE) eluents may inhibit the proliferation of gingival fibroblasts and rat osteosarcoma cells[Peltola M, Salo T & Oikarinen K ,(1992) Toxic effects of various retrograde root-filling materials on gingival fibroblasts and rat sarcoma cells Endodontics& Dental Traumatology 8(3) 120-124]. In another study samples of glass-ionomer cement were prepared in sterile tissue culture medium either by direct contact between the fluid and standard cement samples or through a layer of human dentin, and then tested for toxicity to cultured mouse fibroblasts (L929). The directly-prepared eluates of the cements were highly cytotoxic, but those prepared through dentin were of either limited or no cytotoxicity. The degree of toxicity of some directly-prepared eluates was reduced by adjustment of the pH to neutrality. It was apparent that dentin reduced the potential for cytotoxicity of glass-ionomer cements to a large degree. Proposed mechanisms for the reduction were limited availability of water at the dentin-cement interface and thus limited dissolution of components, buffering of acid components of the cements by dentin, or other chemical interactions with dentin[Hume WR& Mount GJ,(1988) In vitro studies on the potential for pulpal cytotoxicity of glass ionomer cements Journal of Dental Research 67(6) 915-918]. In addition, few studies have investigated the pulpal effects of resin-modified GICs. Felton and others(1991)

found that light-cured GICs induce few toxic effects on the pulp, whereas, various GIC preparations have recently been reported to exhibit differential toxic effects on tissues. Sasanaluckit and others(1993) tested nine different GICs (including resin-modified GIC) and found that Vitrebond(3M, St Paul, MN, USA, a resin-modified GIC) is an extremely toxic GIC, whereas ChemFil, KetacFil and Ketac Silver exhibited few toxic effects on cultured cells [Sasanaluckit P, Albustany KR, Doherty PJ, Williams DF. Biocompatibility of glass ionomer cements. *Biomaterials* 1993;14: 906–16]. These differential toxic effects may be due to disparities in the compositions of GICs, such as poly-acrylic acid, itaconic acid, tartaric acid, resin monomers and more(Stanley, 1992). In several studies it has been shown that toxicity of GIC are related to changes in pH [Hume WR & Mount GJ, (1988) In vitro studies on the potential for pulpal cytotoxicity of glass ionomer cements *Journal of Dental Research* 67(6) 915-918, Consiglio R, Rengo S, Liguoro D, Riccitiello F, Formisano S, Palumbo G & Di Jeso B (1998) Inhibition by glass-ionomer cements of protein synthesis by human gingival fibroblasts in continuous culture *Archives of Oral Biology* 43(1) 65-71] and the possible release of fluoride [Consiglio R, Rengo S, Liguoro D, Riccitiello F, Formisano S, Palumbo G & Di Jeso B (1998) Inhibition by glass-ionomer cements of protein synthesis by human gingival fibroblasts in continuous culture *Archives of Oral Biology* 43(1) 65-71] HEMA and aluminium ion. In addition to the contents of common ingredients of conventional GICs such as aluminium silicate glass, calcium, fluoride and polyacrylic acid liquid, HEMA which is released in resin modified glass ionomers may be the major contributing factor to pulp toxicity [Palmer G, Anstice HM, Pearson GJ. The effects of curing regime on the release of hydroxyethyl methacrylate (HEMA) from resin modified glass ionomer cements. *J Dent* 1999;27:303–11.]. In other studies it has been shown that both conventional and resin modified GICs may suppress the protein synthetic activity of gingival fibroblasts and inhibit the proliferation of gingival fibroblasts. Generally, conventional GICs are suggested to have minimal toxicity, whereas, resin-modified GICs are shown to exert cytotoxicity and genotoxicity [Sidhu SK & Schmalz G (2001) The biocompatibility of glass ionomer cement materials. A status report for the American journal of dentistry. *American journal of dentistry* 14(6) 387-396]. Differential cytotoxicities of GICs and resin-modified GICs may be due to disparities in the composition of powder and liquid and possibly particle size and setting properties.

Conclusion

To conclude the clinical relevance of the observed toxicity of GICs on pulp cells is not fully clear. Thus more in vivo studies are needed to confirm the toxicity of GICs to pulp tissues when used as restorative materials and their clinical relevance.

References

1. Sasanaluckit P, Albustany KR, Doherty PJ, Williams DF. Biocompatibility of glass ionomer cements. *Biomaterials* 1993;14: 906–16.
2. Six N, Lasfargues JJ, Goldberg M. In vivo study of the pulp reaction to Fuji IX, a glass ionomer cement. *J Dent* 2000; 28: 413–22.
3. Wilson AD, Kent BE. The glass-ionomer cement: a new translucent dental filling material. *J Appl Chem Biotechnol* 1971; 21:313–8.
4. Palmer G, Anstice HM, Pearson GJ. The effects of curing regime on the release of hydroxyethyl methacrylate (HEMA) from resin modified glass ionomer cements. *J Dent* 1999;27:303–11.
5. Stanislawski L, Daniau X, Lauti A, Goldberg M. Factors responsible for pulp cell cytotoxicity induced by resin-modified glass ionomer cements. *J Biomed Mater Res* 1999;48:277–88.
6. Wataha JC, Hanks CT, Craig RG. In vitro synergistic, antagonistic, and duration of exposure effects of metal cations on eukaryotic cells. *J Biomed Mater Res* 1992; 26:1297–309.
7. Lewis J, Nix L, Schuster G, Lefebvre C, Knoernschild K, Caughman G. Response of oral mucosal cells to glass ionomer cements. *Biomaterials* 1996; 17:1115–20.
8. Oliva A, Ragione D, Salerno A, Riccio V, Tartaro G, Gozzolino A. Biocompatibility studies on glass ionomer cements by primary cultures of human osteoblasts. *Biomaterials* 1996;17:1351–6.
9. Kuhn A T, Lesan WA & Painter H A, 1983; Release of organic species from glass ionomer cements *Journal Material Science* 224
10. Mjor IA, Nordahl I & Tronstad L (1991) Glass ionomer cements and dental pulp *Endodontics & Dental Traumatology* 7(2) 59-64
11. K.J Anusavice, Phillips science of dental materials, eleventh edition, Elsevier, St. Louis, Missouri; 2003.
12. Sidhu SK & Schmalz G (2001) The biocompatibility of glass ionomer cement materials. A status report for the American journal of dentistry. *American journal of dentistry* 14 (6) 387-396.
13. Peltola M, Salo T & Oikarinen K, (1992) Toxic effects of various retrograde root-filling materials on gingival fibroblasts and rat sarcoma cells *Endodontics & Dental Traumatology* 8(3) 120-124

14. Hume WR& Mount GJ,(1988) In vitro studies on the potential for pulpal cytotoxicity of glass ionomer cements Journal of Dental Research 67(6) 915-918
15. Peterson RC&Watts A,(1987); Toxicity to the pulp of a glass ionomer cement British Dental Journal 162(3)110-112
16. Stanleyhr (1992) Local and systemic responseto dental composites and glass ionomers. Advances in Dental Research 6 55-64