Journal of Pathology Research
ISSN: 0976-8068 & E-ISSN: 0976-8076, Volume 2, Issue 1, 2013, pp.-030-032.
Available online at http://www.bioinfopublication.org/jouarchive.php?opt=&jouid=BPJ0000276

CYTOTOXICITY OF RESIN MODIFIED GLASS IONOMER LUTING AGENTS- AN OVERVIEW

HEGDE M.N.* AND SHABIN S.

Dept. of Conservative Dentistry and Endodontics, A.B. Shetty Memorial Institute of Dental Sciences, Nitte University, Mangalore-575 018, Karnataka, India.
*Corresponding Author: Email- drhegdedentist@gmail.com

Received: November 14, 2013; Accepted: December 18, 2013

Abstract- Resin Modified glass ionomer luting agents has attained attention in the past few years due to their increased physical and mechanical properties when compared to conventional glassionomer luting agents. In the recent years, cytotoxic evaluation of this particular luting agents have gained increased popularity due to their composition. A few literatures confirmed the cytotoxicity of resin based glass ionomer luting agents by stating that these luting agents contained monomers such as HEMA, Bis- GMA, etc. This article aims to distill an overview of cytotoxicity of resin based glass ionomer luting agents and the factors which leads to it.

Keywords- Resin modified glass ionomer luting agent, HEMA, Monomers, cytotoxicity

Introduction

The traditional 'glass ionomer luting agent' has been applied to that group of materials that undergoes setting reaction through an acid - base reaction between an ion leachable glass and aqueous polyacid which are characterized by properties such as fluoride release, modulus of elasticity similar to dentin, Coefficient of thermal expansion, bonding to tooth and biocompatibility [1-6]. Despite these advantages, conventional glass ionomer cement possess limitations such as high susceptibility for dehydration, and poor physical properties such as slow setting rate and high solubility [7,8]. Further developments in the field of glass ionomer cement had occurred and a resin modified glassionomer cement has been introduced. The term 'resin modified glass ionomer luting agents' denotes that the basic formulations of glass ionomers are maintained, but modified by the presence of resin [1]. Resin based luting agents have gained increasing attention in the past few years [9]. In 'resin modified glass ionomer cement', hydrophilic monomers and photoinitiaters were added to the conventional glass ionomer cement to improve the physical and mechanical properties of cement [10]. These resin based luting agents are formulated as chemical - cured, light - cured, dual - cured and tri- cured [7]. However, several *in vitro* studies showed that resin modified glass ionomer cement posses more cytotoxicity than the conventional glass-ionomer cement. Therefore, the aim of this review is to distill an overview in the field of cytotoxicity of resin modified glass- ionomer cement.

Composition of Resin Modified Glass Ionomer luting Agent

Resin modified glass ionomer luting cements are basically consists of 80% glassionomer cement and 20% resin. The percentage of the composition can vary with respect to differences in brand [11]. Resin modified glassionomer cements are said to be hybrid material as the cement lies between conventional glassionomer cement and composite resin [12]. [Table-1] shows some of the resin modified glassionomer cement with its composition.

In Resin modified glassionomer cement, polymerisation of methacrylate units in cement can start either light activation or chemical activation. In dual cure resin modified glass ionomer cement, HEMA's polymerisation starts with light activation and it slowly progress to acid- base reaction. In tri cure materials, there is a chemical indicator for HEMA and this HEMA's polymerization starts chemically, followed by a matrix strengthened via progressive acid-base reaction takes place [11]. Studies have been claimed that some of the ingrediants of resin modified glass ionomer cement are cytotoxic.

Table 1- Resin Modified Glass Ionomer Cement and Composition

MATERIAL	COMPOSITION
Rely X luting Cement (3M ESPE, St. Paul, MN, USA)	Powder: Fluoroaluminosilicate, potassium persulfate, ascorbic acid, opacifying agent. Liquid: 30-40% copolymer of acrylic and itaconic acids,25 -35% 2-hydroxy ethyl methacylate, 25-35% water.
Rely X luting Plus Cement	Paste A: Fluoroaluminosilicate glass, Proprietary reducing agent, HEMA, water, opacifying agent. Paste B: Methacrylated carboxylic acid, Bis GMA, HEMA, water, potassium persulfate, zirconia silica filler.
Vitremer (3M ESPE, St. Paul, MN, USA)	Powder: Glass powder, diphenyl- iodonium chloride. Liquid: 10-15% copolymer of acrylic and itaconic acids, 45-55% 2- hydroxyethyl- methacrylate, 35-45% water
Vitrebond (3M ESPE, St.Paul, MN, USA)	Powder: Glass powder(O, SrO, Criolyte, NH4 F,MgO, PsO), 2% diphenyl iodonium chloride. Liquid: 35-45% modified polyacrylic acid, 20-30% 2-hydroxyethyl -methacylate, 30-40% water

Mechanisms of Cytotoxicity

It has been reported in several literatures that Resin modified glass ionomer Cement possess cytotoxicity. This is usually because of HEMA present in the Cement and unbound free monomers released by resin during and after polymerisation. Rather than this, some additional mechanisms also proposed for mechanism of cytotoxicity of resin Cement.

Short Term Release of Free Monomers During the Monomer-polymer Conversion

Due to the defective photopolymerisation, thermal, mechanical or chemical factors, unbound monomers will release within the first few hours after initial polymerisation and these free monomers, can

exhibit cytotoxic effects. It was expected that at the end of polymerisation, most of the monomers will react to polymer network and the quantity of residual monomers left have been evaluated as no more than 1.5-5% [12]. However, studies shows that these unbound monomers is enough to contribute cytotoxic effects [13].

Residual dentin thickness and dentin permeability also plays a role in the cytotoxicity. Residual dentin layer absorbs unbound monomers and contribute to decrease in the cytotoxicity level [12].

Release of Ions

RM- GIC release ions such as fluoride, aluminium and strontium and some of these are present in tooth paste especially fluoride. Fluoride content of tooth paste and the other ions reload the material and the RM- GIC wont become porous. Other ions will implicate the color of restorative material and these metal ions such as Cu^{2+}, Al^{3+}, and Fe^{2+} produce reactive Oxygen species (ROS) that are cytotoxic [12]. Studies shows that cytotoxicity will be enhanced by metals such as aluminium and iron that are present in RM -GIC [13,14].

Role of Bacteria at the Interface Between luting Agent and Dental Tissues

The presence of bacteria at the interface of luting agent and dental tissues plays a role in cytotoxicity. Ingredient present in resin modified luting agent such as TEGDMA promotes proliferation of cariogenic microrganisms such as lactobacillus acidophilus and streptococcus Sobrinus, etc. These bacteria produces exotoxins which has a noxious effects on pulp cells and thus leads to cytotoxicity [12].

Cytotoxicity Tests

Cell cultures derived from animals and humans have been used for the last 40 years for the evaluation of the cytotoxic effects caused by resin based luting agents. Permanent cell lines and primary cells which are derived from oral tissues have been used [15,16].

One must know to select the type of cell for determining the cytotoxic effect on resin based dental luting agents. It has been shown that permanent cells which have been cultured for years shows a homogenous morphology and physiology whereas primary cell cultures which are deriving from target tissues shows a limited life span and are heterogenous. Thus an *in vitro* test is better simulated by primary cultures [15].

Cytotoxicity tests commonly performed to evaluate the cell cultures of enzyme activities, membrane integrity, cell growth inhibition determination, alteration of cell morphology, and determination of effective dose that cause 50% reduction of cell proliferation. The most commonly used and recognised indicators for cytotoxicity are counting survival cells, determination of enzyme activities, measurement of proliferation rates, and synthesis of cellular macromolecules [15]. MTT test is the most widely used method for cytotoxic evaluation, however succinic dehydrogenase (SDI) and alkaline phosphatase responses have also been used [17].

***In vitro* and *In vivo* Studies**

A few studies that have been conducted in the field of cytotoxicity of resin modified glassionomer cement shows that the material is cytotoxic [18-22].

In vitro cytotoxicity of contemporary resin modified glass ionomer cements on subcutaneous tissue of rats (MDPC-23 cells) have been shown the material to be cytotoxic. Authors reported that HEMA present in RM-GIC is responsible for the cytotoxicity and the mechanism of action of uncured leached monomers on the cell membrane may be responsible for the cytotoxic effect. Authors also concluded that decomposition products of the initiator diphenyliodoniumchloride releasing from the RMGIC may also cause cytotoxic effects to the culture of cells [18].

Cytotoxicity of four categories of dental cements on L-929 fibroblast cell culture test have been shown the material to be cytotoxic in different rank orders. Authors noted that fresh specimens of tested cements showed significant cytotoxicity which diminished after 7 days and dual cured specimens showed lower toxicity than chemical cured [19]. This result concurs with the result of Aranha et al who pointed that light activation will reduce the cytotoxicity of resin modified glass ionomer lining cements [20].

Cytotoxic effects of hard setting cements applied on the odontoblast cell line MDPC-23 have been shown significant cytotoxicity. Authors noted that uncured leached monomers on the cell membrane played a very important role in the cytotoxicity. Authors concluded that cytotoxic effects can also be caused by release of chlorine benzene, iodine benzene, and bromide benzene, which are the decomposition products of the initiator diphenyliodoniumchloride. Authors also showed the significant relation of the cytotoxic effects of some resin monomers, such as BIS-GMA, UDMA and TEGDMA [22]. Literatures shows that these resin monomers can be able to deplete intracellular glutathione as well as interfere with the expression of some proteins such as osteonectin, dentin sialoprotein, and collagen which plays an important role in the pulp repair [23].

Assessing the cytotoxicity on the effect of reduced curing time in five resin luting cements polymerized by high power LED curing light on the viability of a cell of L-929 fibroblast cell showed that cell survival rate results for 40 s exposure time were significantly higher than 20 s cell survival rate. Authors concluded that period of photoactivation of luting agent is related to the cytotoxic effects on luting agents [24].

Conclusion

A lot of factors such as HEMA, BIS GMA, TEG DMA, unbound free monomers released by resin during and after polymerisation, and reactive oxygen species released by ions can contribute to the cytotoxicity of resin modified glass ionomer luting agent. A care must be taken to provide technology towards different techniques to decrease the unbound free monomers after polymerisation of resin modified glass ionomer luting agent which are need to be studied.

Conflicts of Interest: None declared.

References

[1] McCabe J.F. (1998) *Biomaterials,* 19, 521-527.

[2] Gao W. and Smales R.J. (2001) *Journal of Dent.,* 29, 301-306.

[3] Bullard R.H., Leinfelder K.F. and Russel CM. (1998) *J. Am. Dent. Assoc*.,116, 871-874.

[4] Erickson R.L. and Glass Poole E.A. (1994) *J. Esthet. Dent*., 6, 227-244.

[5] Costa C.A.S., Giro E.M., Nascimento A.B.L., Teixeira H.M. and Hebling J. (2003) *Dental Materials*, 19, 739-746.

[6] Leyhausen G., Abtahi M., Karbakhsch M., Sapotnick A. and Geurtsen W. (1998) *Biomaterials*, 19, 559-564.

[7] Cho E., Kopel H. and White S.N. (1995) *Quint Int.,* 26, 351-358.

[8] Mount G.J. (1994) *Oper. Dent*., 19, 82-90.

[9] El-Badrawy W.A. and El-Mowafy O.M. (1995) *The Journal of Prosthetic Dentistry*, 73(6), 515-524.

[10] Cattani-Lorente M.A., Godin C. and Meyer J.M. (1994) *Dental Materials*, 10(1), 37-44.

[11] Sümer E. and Deger Y. (2011) *Int. Dent. Res*., 1, 26-31.

[12] Goldberg M. (2008) *Clin. Oral Invest*., 12, 1-8.

[13] Stanislawski L., Daniau X., Lauti A. and Goldberg M. (1999) *J. Biomed. Mater. Res*., 48, 227-288.

[14] Stanislawski L., Lefeuvre M., Bourd K., Soheili-Majd E., Goldberg M. and Perianin A.J. (2003) *Biomed. Mater. Res*., 66, 476-482.

[15] Geurtsen W. (2000) *Crit. Rev. Oral. Biol. Med*., 11(3), 333-335.

[16] Ratanasathein S., Wataha J.C., Hanks C.T., Dennison J.B. (1995) *J. Dent. Res*., 74, 1602-1606.

[17] Chen C.C., Chen R.C. and Huang S.T. (2002) *J. Biomed. Mater Res*., 60, 452-457.

[18] Souza P.P., Aranha A.M., Hebling J., Giro E. and Costa C.A. (2006) *Dental Materials*, 22(9), 838-844.

[19] Schmid-Schwap M., Franz A., König F., Bristela M., Lucas T., Piehslinger E. and Schedle A. (2009) *Dental Materials*, 25(3), 360-368.

[20] Aranha A.M., Giro E.M., Souza P.P., Hebling J., de Souza Costa CA. (2006) *Dental Materials*, 22, 864-869.

[21] Melo de Mendonça A.A., Chaves Souza P.P., Hebling J. and de Souza Costa C.A. (2007) *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology and Endodontology*, 104(4), e102-e108.

[22] Engelmann J., Janke V., Volk J., Leyhausen G., Von Neuhoff N., Schlegelberger B. and Geurtsen W. (2004) *Biomaterials*, 25 (19), 4573-4580.

[23] Camps J., Mitsiadis T.A., Bottero M.J., Butler W. and Franquin J.C. (2002) *Journal of Biomedical Materials Research*, 63(4), 418-423.

[24] Ergun G., Egilmez F. and Yilmaz S. (2011) *J. Appl. Oral Sci*., 19 (3), 286-292.