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Carboxylesterase expression in human dental pulp cells: Role in regulation of BisGMA-induced prostanoid production and cytotoxicity

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ABSTRACT

Biocompatibility of dentin bonding agents (DBA) and composite resin may affect the treatment outcome (e.g., healthy pulp, pulpal inflammation, pulp necrosis) after operative restoration. Bisphenol-glycidyl methacrylate (BisGMA) is one of the major monomers present in DBA and resin. Prior studies focused on salivary esterase for metabolism and degradation of resin monomers clinically. This study found that human dental pulp cells expressed mainly carboxylesterase-2 (CES2) and smaller amounts of CES1A1 and CES3 isoforms. Exposure to BisGMA stimulated CES isoforms expression of pulp cells, and this event was inhibited by catalase. Exogenous addition of porcine esterase prevented BisGMA- and DBA-induced cytotoxicity. Interestingly, inhibition of CES by bis(*p*-nitrophenyl) phosphate (BNPP) and CES2 by loperamide enhanced the cytotoxicity of BisGMA and DBA. Addition of porcine esterase or *N*-acetyl-L-cysteine prevented BisGMA-induced prostaglandin E_2 (PGE_2) and $PGF_{2\alpha}$ production. In contrast, addition of BNPP and loperamide, but not mevastatin, enhanced BisGMA-induced PGE_2 and $PGF_{2\alpha}$ production in dental pulp cells. These results suggest that BisGMA may induce the cytotoxicity and prostanoid production of pulp cells, leading to pulpal inflammation or necrosis via reactive oxygen species production. Expression of CES, especially CES2, in dental pulp cells can be an adaptive response to protect dental pulp against BisGMA-induced cytotoxicity and prostanoid release. Resin monomers are the main toxic components in DBA, and the ester group is crucial for monomer toxicity.

1. Introduction

Various tooth-colored restorative materials such as dentin bonding agents (DBA), composite resin and resin-modified glass ionomer cements have been widely used, with differing success, to restore dental caries. However, indirect pulp capping by resin composites is shown to induce reactive odontoblasts and pulpal inflammation in some treated teeth [1]. Direct capping of the exposed human dental pulp with DBA followed by composite resin filling is also found to induce moderate to severe pulp inflammation with abscess formation [2]. After polymerization, some of the unpolymerized monomers such as triethyleneglycol di-methacrylate (TEGDMA), 2-hydroxy-ethyl-methacrylate (HEMA) and bisphenol-glycidyl methacrylate (BisGMA) may be released from DBA or dental composites [3]. The released monomers may directly contact the surrounding pulp tissue or diffuse through dentinal tubules to affect the biological activities of dental pulp. The extent of pulpal effects from resin monomers depends on the solubility of monomers, remaining dentin thickness, the diffusion capacity of monomers and the content/proportion of various monomers [4]. Application of DBA to restore deep caries cavities in human teeth may cause obvious cytotoxicity and pulpal inflammatory responses which delay the pulpal healing with failure of dentin bridge formation [5,6]. Prostaglandin E_2 (PGE_2) and $PGF_{2\alpha}$ are two major inflammatory mediators elevated during pulpal inflammation [7,8]. The released monomers may possibly lead to cytotoxicity and induce tissue inflammatory response of dental pulp. It is also important to delineate why some dental pulp maintains vitality, whereas some dental pulp becomes inflamed or even necrotic after operative restoration.

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