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Role of IL6 and Its Receptors (gp80, gp130) In TEGDMA and HEMA Cytotoxicity

TEGDMA and HEMA do not regulate Inflammation

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Abstract: *The diffusion of residual monomers through the dentin, influence the viability of odontoblasts and the physiological activity of dental pulp. IL-6 is a cytokine that provokes a broad range of cellular and physiological responses, cellular events, including activation of intracellular signaling that controls the cellular and physiological responses, such as the immune response, inflammation, hematopoiesis and oncogenesis, by regulating cell growth, gene activation, proliferation, survival and differentiation. Currently it is not completely understood whether dental resin monomers regulate IL6 gene transcription; therefore, our aim was to evaluate the activation or inhibition of IL6, gp80 and gp130 caused by TEGDMA and HEMA in primary human pulp cells.*

Keyword: *IL6, Inflammation, Cytotoxicity, Receptors, Resins.*

1. INTRODUCTION

The diffusion of residual monomers through the dentin, influence the viability of odontoblasts and the physiological activity of dental pulp [1, 2]. The molecular mechanisms that are behind the genotoxic and cytotoxic effects due to dental resin monomers is not clear at all. In particular TEGDMA (triethylene glycol dimethacrylate) and HEMA (2-hydroxyethyl methacrylate) are deeply investigated because present in the most adhesives and dental composites [1-3]. TEGDMA and HEMA may easily spread into the cytosol and induce cytotoxicity, genetic and oxidative damage in different cell phenotypes [1-3]. Moreover, the monomers are able to control the phenomena of dentinogenesis mainly by means the inhibition of the pulp stem cells (DP-MSCs) differentiation [4]. It has been demonstrated the link between the monomers and the activation of genetic networks, crucial in controlling the cell cycle in carcinogenesis, in the regulation of epithelial-mesenchymal transition process during tooth development and the regulation of inflammatory markers as Interleukin-6 (IL-6) [4, 5].

IL-6 is a cytokine that provokes a broad range of cellular and physiological responses, cellular events, including activation of intracellular signaling that controls the cellular and physiological responses, such as the immune response, inflammation, hematopoiesis and oncogenesis, by regulating cell growth, gene activation, proliferation, survival and differentiation [6, 7]. IL-6 binds to specific receptors present on the cell membrane surface. These receptors include the chain gp80 (or IL-6R) and the two gp130 chains. The high binding affinity between IL-6 and the two membrane-bound receptors (namely, IL-6R and gp130), causes the transduction of the signal with the activation of the intracellular pathways [8, 9]. Membrane-bound IL-6R and gp130 produce, by shedding (loss of both transmembrane and intracytoplasmatic domains), two soluble receptors termed *sIL-6R* and *sgp130*, respectively. [10] sIL-6R is an agonistic circulating receptor of IL-6; this implies that sIL-6 may bind IL-6 and this binary complex (IL-6/sIL-6R) may activate target cells, even those that do not express gp80 on their surface. [10]

Currently it is not completely understood whether dental resin monomers regulate IL6 gene transcription; therefore, our aim was to evaluate the activation or inhibition of IL6, gp80 and gp130 caused by TEGDMA and HEMA in primary human pulp cells.

2. METHODS

We used the pulp of the eighth extracts from different patients to isolate the human pulp fibroblasts (HPCs). HPCs were stimulated with the monomers at different concentrations (TEGDMA 0,1 and 0,5; HEMA 1 and 2mM) after incubation for 24h we evaluated cell viability by MTT. Moreover, we arranged the quantitative analysis (QRT-PCR) of IL6 gene expression by using Taq-Man technology with specific primers and probe (QRT-PCR Step One Applied Biosystem). Statistical analisys of the data was performed using ANOVA ($p<0.05$).

3. RESULTS AND CONCLUSION

HPCs treated with TEGDMA and HEMA for 24h showed significant toxic effect at 0.5mM TEGDMA and 2 mM HEMA (Fig. 1 and 2).

QRT-PCR assay results showed the effect of resins on the mRNA fold increase for IL6, gp80 and gp130 (Fig. 3). In HPCs stimulated with all monomers concentrations tested, there were no differences compared with untreated control (Fig. 3, 4, 5).

IL 6 is an inflammatory cytokine involved in several disorders of the oral cavity; a polymorphism of this cytokine is associated with chronic periodontitis [10].

Recently it has been demonstrated that HEMA was able to control the regulation of the IL-6 gene expression, in dental pulp stem cells (DP-MSCs) [11]. Here, our preliminary data showed that HEMA and TEGDMA did not lead up-regulation of IL-6 in HPCs. Moreover, the behaviour of the gp80 and gp130 genes confirms that the monomers did not trigger an inflammatory process in the dental pulp.

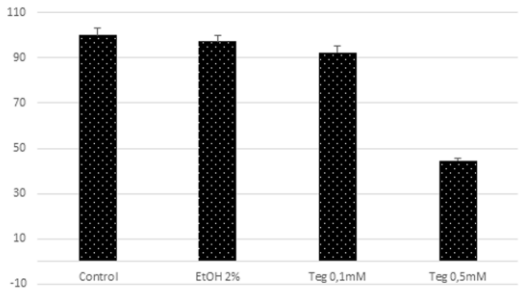

Fig. 1 HPCs treated with TGDMA 0,1 and 0,5 mM

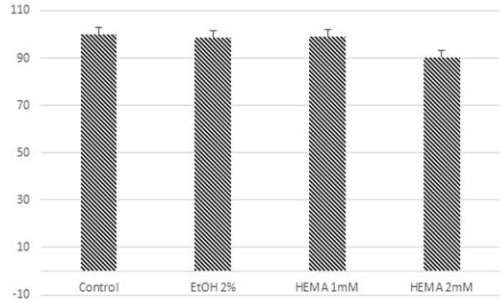

Fig. 2 HPCs treated with TGDMA 0,1 and 0,5 mM

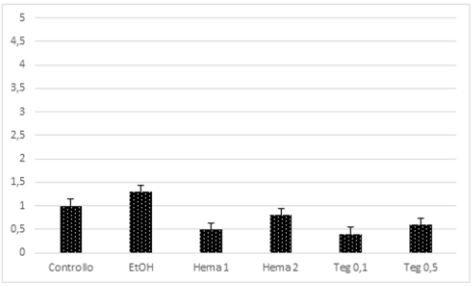

Fig. 3 mRNA fold increase of IL6. The data were the results of five experiments with $p < 0,01$

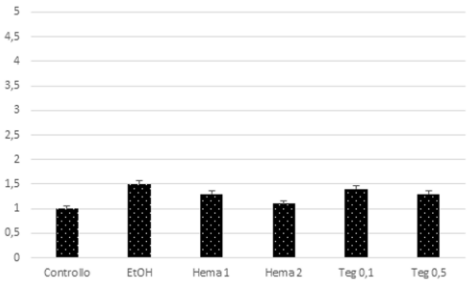

Fig. 4 mRNA fold increase of gp130. The data were the results of five experiments with $p < 0,01$

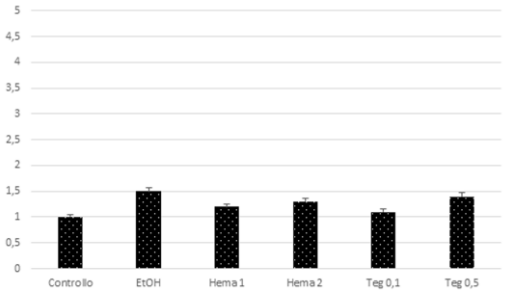

Fig. 5 mRNA fold increase of gp80. The data were the results of five experiments with $p < 0,01$

REFERENCES

[1] Schweikl H.Schweikl H, Spagnuolo G, Schmalz G.Genetic and cellular toxicology of dental resin monomers. J Dental Res. 2006 Oct; 85(10):870-7.

[2] Krifka S, Spagnuolo G, Schmalz G,A review of adaptive mechanisms in cell responses towards oxidative stress caused by dental resin monomers. Biomaterials. 2013 Jun; 34(19):4555-63.

[3] Schweikl H, Hiller KA, Eckhardt A, Bolay C, Spagnuolo G, Stempfl T, Schmalz G. Differential gene expression involved in oxidative stress response caused by triethylene glycol dimethacrylate. Biomaterials 29(2008)1377-1387.

[4] Bakopoulou A, Leyhausen G, Volk J, Tsiftsoglou A, Garefis P, Koidis P, Geurtsen W. Effects of HEMA abd TEGDMA on the vitro odontogenic differentiation potential of human pulp stem/progenitor cells derived from deciduos teeth. Dental Materials 27 (2011) 608-617.

[5] Heinrich, P. C., Behrmann, I., Muller-Newen, G., Schaper, F. and Graeve, L. (1998) Interleukin-6-type cytokine signalling through the gp130/Jak/STAT pathway. Biochem. J. 334, 297–314

[6] Heinrich, P. C., Graeve, L., Rose-John, S., Schneider-Mergener, J., Dittrich, E., Erren, A., Gerhartz, C., Hemmann, U., Lutticken, C., Wegenka, U. et al. (1995) Membrane-bound and soluble interleukin 6 receptor: studies on structure, regulation of expression and signal transduction. Ann. N.Y. Acad. Sci. **762**, 222–236

[7] Murakami M, Hibi M, Nakagawa N, et al: IL-6-induced homodimerization of gp130 and associated activation of a tyrosine kinase. Science 260:1808-1810, 1993

[8] Rose-John S, Ehlers M, Grotzinger J, et al: The soluble interleukin 6 receptor. Ann N Y Acad Sci 762:207-220, 1995

[9] Gaillard JP, Pugniere M, Tresca JP, et al: Interleukin 6 receptor signaling. II. Bio-availability of interleukin 6 in serum. Eur Cytokine Netw 10:337-344, 1999.

[10] Relationship between inteleukin-6 gene-572C/G polymorphism and chronic periodontitis. Guan ZM, Liu JJ, Ma X, Wu DH, Yu J, Huang GQ.Zhonghua Kou Qiang YiXue Za Zhi. 2008 Jul; 43(7):410-3. Chinese.PMID:19031817.

[11] Trubiani O, Cataldi A, De Angelis S, D'Arcangelo C, Caputi S. Overexpression of interleukin-6 and -8, cell growth inhibition and morphological changes in 2-hydroxyethyl methacrylate-treated human dental pulp mesenchymal stem cells. Int Endod J 2012 jan; 45(1):19-25.