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Research Paper

The effect of restorative materials on cytokines in gingival crevicular fluid☆

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ABSTRACT

Objective: Composition of the restorative materials may cause inflammatory responses by monocyte activation and changes in the levels of cytokine released from different cells. Interleukin-6 (IL-6), interleukin-8 (IL-8) and Tumor necrosis factor alpha (TNF-α) are important cytokine for evaluating of the inflammatory process. The aim of this study was to evaluate the different restorative materials used in class V cavities effect on gingival crevicular fluid inflammatory cytokine levels.

Design: 60 individuals having Class V carious cavities participated in the study. Cavities were restored with FiltekZ250, DyractXP, Fuji IX, Cavex avalloy restorative materials. Changes in clinical and biochemical parameters were evaluated before restorations, seven and 21 days after restorations. Contralateral tooth intact enamel surface was determined as control side. Periotron8000 device was used for detection of GCF volume. Cytokine level of GCF was evaluated by Human ELISA kits. Data were analyzed using Mann-Whitney *U* test and Wilcoxon signed ranks test. The correlations between clinical parameters and biochemical parameters were examined by Spearman's rank correlation analysis.

Results: After restorative treatments PI and GI scores were decreased compared with baseline evaluations. There was a significant difference in GCF levels between experimental and control sites in all groups. GCF IL-6 levels in all groups except Filtek Z250, GCF IL-8 levels in all groups except Fuji IX, GCF TNF-α level in only Fuji IX showed significant differences between experimental and control sites.

Conclusions: The obtained data supported that all of the tested materials caused changes in GCF cytokine levels.

1. Introduction

The main purpose of restorative dentistry is to restore and maintain tooth health by an adequate restorative treatment. Although developing technology in the field of dentistry, there is a continuing need for biomaterials with high biocompatibility, mechanical competence and antimicrobial effects (Costa, Giro, do Nascimento, Teixeira, & Hebling, 2003; Eskandarizadeh et al., 2015; Grieve, Alani, & Saunders, 1991; Modena et al., 2009; Six, Lasfargues, & Goldberg, 2000). Dental restorative materials are in direct or indirect contact with various tissues, such as enamel, dentin, pulp and gingiva. Therefore, dental materials should be risk-free for all oral tissues and should not cause toxic, mutagenic or cancerogenic effects (Costa et al., 2003).

Dental restorative materials rarely cause local or systemic side effects, such as toxic, irritative or allergic reactions. Local effects are inflammatory changes or hypersensitivity reactions against the material. Various studies have demonstrated that organic compound and the degradation products of various metals, including mercury, silver, copper, tin, nickel, chrome and cobalt and composite resins may cause allergic reactions (Bergman, 1990; Syed, Chopra, & Sachdev, 2015).

Researches has indicated that the compounds released from restorative materials can increase the growth of bacteria and the consumption of glutathione, which is important in pulpal and gingival cell apoptosis and the production of reactive oxygen products (Goldberg, 2008; Gul, Akgul, Alp, & Kiziltunc, 2014). Composition of the materials may cause inflammatory responses by monocyte activation and changes in the levels of cytokine released from monocytes. This condition causes variations in the levels of some cytokines, such as interleukin-1β (IL-1β), interleukin- 6 (IL-6) and tumor necrosis factor alpha (TNF-α) in the gingival crevicular fluid (GCF) of the infected region (Nelson, Wataha, Cibirka, & Lockwood, 2001).

Cytokines are glycoproteins with a low molecular weight, which play a role in important biological events, such as cellular growth, inflammation, immunity, tissue repair and hematopoiesis (Gornowicz et al., 2012). They also play an important role in the inflammatory response related to gingivitis, tissue destruction in periodontal diseases

☆ In the study changes of clinical and biological parameters level were determined after restorative treatment.

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Table 1
The distribution of teeth according to the location.

Groups	Sex	Dental Arch	Tooth Distrubition			n
			Anterior	Premolar	Molar	
1	Female	Lower	2	4	0	6
		Upper	2	2	0	4
	Male	Lower	1	0	1	2
		Upper	0	2	1	3
2	Female	Lower	1	2	0	3
		Upper	3	2	0	5
	Male	Lower	1	2	1	4
		Upper	1	2	0	3
3	Female	Lower	0	7	2	9
		Upper	0	1	0	1
	Male	Lower	0	2	2	4
		Upper	0	1	0	1
4	Female	Lower	0	0	8	8
		Upper	0	0	3	3
	Male	Lower	0	0	3	3
		Upper	0	0	1	1

and the regulation of the adaptive immune response. Together with other elements of the cytokine network, IL-6 and IL-8 regulate the periodontal cellular inflammatory response. Tissue reaction, as a response to bacterial infection, occurs as a result of proinflammatory cytokines, while anti-inflammatory cytokines try to control this process (Giannopoulou, Kamma, & Mombelli, 2003; Seymour & Gemmell, 2001). Proinflammatory cytokines play a role in vascular dilation, increased permeability and inflammatory response. Since periodontal diseases have an inflammatory character, proinflammatory cytokines have been held responsible for the local tissue destruction in these diseases, and it has been reported that the level of these cytokines are increased both in saliva and GCF (Garlet, 2010).

Indeed, the amount of GCF is very small in the healthy sulcus and when the gingiva is healthy, this fluid is similar to transudate in the sulcus or serum exudate (Lamster, Hartley, & Vogel, 1985; Pollanen, Salonen, & Uitto, 2003). Transudate increase with inflammation of the gingiva and transform into an inflammatory exudate including high amounts of molecules derived from gingival tissues, vascular cellular components of inflammation and serum originating molecules (Ebersole, 2003).

An increased volume of GCF is positively associated with the degree of gingival inflammation (Emingil, Cinarcik, Baylas, Coker, & Huseyinov, 2001). In the detection of inflammatory activity, investigating the levels of the inflammatory mediators in the biological fluids is a diagnostic marker. Therefore, biochemical and immunological factors in GCF are frequently evaluated in the search for the pathogenesis of gingival and periodontal infections. Previous studies have demonstrated that restorative treatments also affect GCF volume (van Dijken & Sjostrom, 1998).

Clinical studies are the ultimate test to evaluate the clinical effectiveness and durability of restorative materials. The objective of this study was to evaluate the biological effects of restorative materials, which were used in restorative treatment of class V carious lesion. This study tested the null hypothesis that different classes of restorative materials: composite, compomer, glass ionomer, and amalgam effect IL-6, IL-8 and TNF- α level in GCF.

2. Materials and methods

2.1. Patients and study design

60 voluntary patients (21 male and 39 female) in good oral and general health, having class V carious lesion associated with gingiva participated in this study. The study was granted ethical approval (2012.5.1) by the Institute of Health Sciences at Ataturk University and conducted in accordance with the Declaration of Helsinki.

The sample size was calculated using G*power analysis with α error at 5%, β error at 20% and large effect size 0.50, thus maintaining the power of the study at 80%. The estimated sample size was 48 (n = 12) which was rounded off to 60 samples.

Inclusion criteria: Class V carious cavity with sub-gingival margins without invasion of biological width, good general health, no use of anti-inflammatory and no antibiotic therapy within the previous six months, good periodontal health, with generalized probing depths ≤3mm and no radiographic evidence of periodontal bone loss. Exclusion criteria were cigarette smoking, diabetes, immunocompromise, pregnancy and breast-feeding in women, use of orthodontic devices. All patients were motivated to good oral hygiene during the study.

2.2. Cavity preparation and restoration

Participants between 25 and 40 years of age were assigned to four groups (n = 15). The teeth were randomly prepared with restorative materials but amalgam was preferred primarily in molar teeth due to aesthetic reasons. The distribution of teeth according to the location were given in Table 1.

Group 1 was restored with composite resin (Filtek TM Z250, 3M-ESPE, St. Paul MN, USA), group 2 was restored with compomer resin (Dyract XP, Dentsply DETREY GmbH, Konstanz, Germany), group 3 was restored with glass ionomer cement (Fuji IX GP capsule, GC Corporation, Tokyo, Japan) and group 4 was restored with amalgam (Cavex Avalloy, Cavex Holland BV Haarlem, Holland). Material details are listed in Table 2.

The cavities prepared by a diamond bur in a conventional high-

Table 2
Restorative materials used in this study. Information about the materials was obtained from the "Instructions for use" and MSDS forms on the manufacturers.

Materials	Content	Product code	Manufacturer
Filtek Z250	TEGDMA, Bis-GMA, UDMA, Bis-EMA, Zirkonia/Silica (%60)	N110464	3 M ESPE, St.Paul, MN, USA
Cavex Avalloy	% 45 Ag, %30,5 Sn, %24 Cu, % 0,5 Zn	13072	CAVEX HOLLAND BV, Haarlem, HOLLAND
Dyract XP	UDMA, TCB resin, TEGDMA, trimethacrylate ve dimethacrylate resin, BHT, Strontium-alumino-sodium-fluoro-phosphor-silicate glass, Strontium fluoride	1208000178	DENTSPLY, DETREY Gmbh, Konstanz, GERMANY
Fuji IX GP	Powder: fluoroalumino-silicate glass, polyacrylic acid powder, iron oxide, titanium diokside; Liquide: the aqueous solution of polyacrylic acid, distilled water, tartaric acid	1012243	3 M ESPE, St. Paul, MN, USA
Clearfil SE Primer[a]	MDP, HEMA, hydrophilic aliphatic dimethacrylate, di- camphorquinone, water	01089A	KURARAY, Sakazu, Kurashiki, Okayama, JAPAN
Clearfil SE Bond[a]	MDP, Bis-GMA, HEMA, hydrophobic aliphatic dimethacrylate, di- camphorquinone, colloidal silica	01630A	KURARAY, Sakazu, Kurashiki, Okayama, JAPAN
Prime & Bond NT[a]	Di ve trimethacrylate resin, functional amorphous silica, PENTA, setilamin hydroflorid, acetone	1202000758	DENTSPLY, DETREY Gmbh, Konstanz, GERMANY

[a] materials were used for composite and compomer resins bonding in clinical usage.