UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL

FACULDADE DE ODONTOLOGIA

GABRIELA SANTOS DO AMARAL

EVIDÊNCIAS CIENTÍFICAS DO EFEITO ANTI-CÁRIE DE SISTEMAS ADESIVOS E MATERIAIS RESTAURADORES CONTENDO ANTIMICROBIANOS: REVISÃO DA LITERATURA

Porto Alegre

2014

GABRIELA SANTOS DO AMARAL

EVIDÊNCIAS CIENTÍFICAS DO EFEITO ANTI-CÁRIE DE SISTEMAS ADESIVOS E MATERIAIS RESTAURADORES CONTENDO ANTIMICROBIANOS – REVISÃO DA LITERATURA

Trabalho de Conclusão de Curso apresentado ao Curso de Graduação em Odontologia da Faculdade de Odontologia da Universidade Federal do Rio Grande do Sul, como requisito parcial para obtenção do título de Cirurgião-Dentista.

Orientador: Prof. Dr. Rodrigo Alex Arthur

Porto Alegre

2014

CIP - Catalogação na Publicação

Santos do Amaral, Gabriela
Evidências científicas do efeito anti-cárie de sistemas adesivos e materiais restauradores contendo antimicrobianos: revisão da literatura / Gabriela Santos do Amaral. -- 2014.
41 f.

Orientador: Rodrigo Alex Arthur.

Trabalho de conclusão de curso (Graduação) -- Universidade Federal do Rio Grande do Sul, Faculdade de Odontologia, Curso de Odontologia, Porto Alegre, BR-RS, 2014.

1. odontologia. 2. Antimicrobianos. 3. Materiais dentários. 4. Cárie dentária. I. Alex Arthur, Rodrigo, orient. II. Título.

Elaborada pelo Sistema de Geração Automática de Ficha Catalográfica da UFRGS com os dados fornecidos pelo(a) autor(a).

Aos meus pais que sempre motivaram e financiaram meus estudos.

Ao meu orientador que se esmerou na sua missão.

AGRADECIMENTOS

Aos diretamente envolvidos neste trabalho:

Ao meu orientador Professor Rodrigo Arthur que foi meu mestre e guru, fez de mim uma aluna melhor e mais motivada, uma pessoa mais paciente e ainda mais determinada. Vi nele o que é ser um mestre, pela humildade na qual divide o seu conhecimento comigo e disponibilidade incondicional. Obrigada por depositar em mim a confiança concedendo a bolsa de iniciação científica e a oportunidade de realizar contigo esse TCC. Realmente não tenho palavras pra descrever minha gratidão.

À Professora Clarissa Parolo, pela bolsa de monitoria, oportunidade pela qual ingressei no LABIM e que me propiciou a experiência de vivenciar a clínica odontológica por outro ângulo. Aos profissionais do LABIM, pela harmonia da convivência e trabalho em equipe. À Prof. Thaís Negrini e aos alunos da graduação Juliane Krämer e Lucas Pigozzi que cederam e dedicaram seu tempo para me ajudar nas tarefas desse TCC.

À bibliotecária Ida Rossi, pelo trabalho realizado com atenção minuciosa e carinho, no envio de dezenas de artigos científicos.

Aos indiretamente envolvidos:

Aos meus pais pelo apoio pré-vestibular e acadêmico, e por sempre motivarem meus estudos desde a infância. A presença deles até aqui tornou menos árdua essa jornada.

Aos amigos Gabriela Ritt e Willian Girotto que desde o pré-vestibular, e principalmente durante o TCC, vêm me dando apoio emocional e atenção quando precisava ser escutada.

Aos professores do Yázigi Petrópolis, em especial, à Professora Paula Ganzer. Foi graças a dedicação de vocês, há 5 anos, que hoje pude realizar esse trabalho com autonomia.

RESUMO

AMARAL, Gabriela S. do. **Evidências científicas do efeito anti-cárie de sistemas adesivos e materiais restauradores contendo antimicrobianos:** revisão de literatura. 2014. 41 f. Trabalho de Conclusão de Curso (Graduação em Odontologia) – Faculdade de Odontologia, Universidade Federal do Rio Grande do Sul, Porto Alegre, 2014.

A cárie dentária é um processo de doença complexo que, se não tratada adequadamente, pode avançar para a cavitação e uma intervenção restauradora pode ser necessária. Uma das principais causas para a substituição de restaurações é a ocorrência de cárie ao redor dessas restaurações em pacientes cuja atividade de cárie não for adequadamente controlada. Antimicrobianos tem sido incorporados aos materiais restauradores ou adesivos dentinários com a promessa de reduzir a incidência de cárie ao redor de restaurações. Estudos *in vitro* mostraram que a incorporação de compostos antimicrobianos em materiais restauradores dentários é capaz de afetar negativamente a viabilidade das bactérias cariogênicas. No entanto, a relevância clínica desta abordagem na prevenção da cárie dentária ainda é desconhecida. O objetivo desta revisão da literatura foi fornecer uma discussão atualizada sobre o efeito anticárie de antimicrobianos incorporados a materiais restauradores odontológicos ou sistemas adesivos odontológicos com foco sobre as metodologias utilizadas para avaliar o efeito antimicrobiano e sobre a relevância clínica dos resultados publicados. Além disso, buscou-se investigar se a incorporação de compostos antimicrobianos em materiais restauradores odontológicos evita cárie ao redor de restaurações. Através do MEDLINE, via Pubmed, foram procurados artigos publicados de 1980 a 23 de dezembro, 2013 e 1085 artigos foram encontrados. Após a avaliação de inclusão / exclusão, 145 artigos completos foram lidos e incluídos na revisão, que foi composta por 127 in vitro, in situ 1 e 5 em estudos in vivo e 12 revisões de literatura. Conclui-se a partir dos dados desta revisão de literatura que os métodos utilizados para avaliar os efeitos antimicrobianos de materiais restauradores experimentais são simplistas e não representam o dinamismo das condições encontradas na cavidade oral. Portanto, os dados fornecidos por esses estudos devem ser avaliados com cuidado. Além disso, nenhuma contribuição ou evidência foi encontrada, até o momento, sobre o papel dos antimicrobianos incorporados em materiais restauradores na prevenção / controle da cárie dentária e na prevenção da cárie ao redor de restaurações.

Palavras-chave: Odontologia. Antimicrobianos. Materiais dentários. Cárie dentária.

ABSTRACT

AMARAL, Gabriela S. do. **Scientific evidences of the anti-caries effect of antimicrobial-incorporated dental restorative materials/ dentinal adhesives:** a review of the literature. 2014. 41 f. Final Paper. (Graduation in Dentistry) – Faculdade de Odontologia, Universidade Federal do Rio Grande do Sul, Porto Alegre, 2014.

Dental caries is a complex disease process that if not treated properly may advance to frank cavitation and a restorative intervention may be necessary. One of the main causes for restorations replacement is the occurrence of caries around restoration in patients whose carious activity is not adequately controlled. Antimicrobials have been incorporated into restorative materials or dental adhesives with the promise of reducing the incidence of caries around restorations. *In vitro* studies have shown that the incorporation of antimicrobial compounds into dental restorative materials is able to negatively affect the viability of cariogenic bacteria. However, the clinical relevance of this approach in the prevention of dental caries is still unknown. The aim of this review of literature was to provide an updated discussion about anti-caries effect of antimicrobial-incorporated dental restorative materials or dental adhesive systems focusing on the methodologies used to evaluate the antimicrobial effect and on the clinical relevance of the published results. Additionally, we sought to investigate whether the incorporation of antimicrobial compounds to dental restorative materials prevents caries around restorations. MEDLINE, via Pubmed, was searched for papers published from 1980 to December 23, 2013 and 1,085 articles were retrieved. After inclusion/exclusion assessment, 145 full text articles were read and included in the review which was comprised of 127 *in vitro*, 1 *in situ* and 5 *in vivo* studies and 12 reviews of literature. We conclude from the data of this review of literature that the methods used to evaluate the antimicrobial effects of experimental restorative materials are simplistic and do not represent the dynamism of conditions found on oral cavity. Therefore, the data provided by those studies should be evaluated with care. Additionally, no contribution or evidence has been found, so far, regarding the role of antimicrobial incorporated into restorative materials on prevention/control of dental caries and on prevention of caries around restorations.

Keywords: Dentistry. Antimicrobials. Dental Materials. Dental caries.

SUMÁRIO

1 INTRODUÇÃO

A cárie dentária é um processo de doença complexo que tem sido estudado por décadas. Sua etiologia é multifatorial levando à desmineralização dos tecidos dentais em resposta aos ácidos produzidos por bactérias do biofilme dental que degradam carboidratos fermentáveis provenientes da dieta (SELWITZ; ISMAIL; PITTS, 2007). Quando esse processo de desmineralização não é controlado, a área de perda de mineral pode progredir e lesões inicialmente subsuperficiais podem resultar na formação de cavidades na superfície dos dentes (FERREIRA-ZANDONÁ, 2012).

Nesse contexto, o tratamento e prevenção da cárie dentária se dá, principalmente, pelo controle de dieta, reduzindo frequência de ingestão de carboidratos fermentáveis (KIDD, 2011), pela orientação e motivação do paciente para um correto controle mecânico de biofilme dental, que é considerado como fator necessário para desenvolvimento da cárie dentária, e orientação para uso racional do flúor permitindo que baixas concentrações estejam presentes na cavidade bucal de forma constante para interferir nos eventos de des/ e de remineralização (FEATHERSTONE, 2008).

O uso do flúor tem sido considerado como um dos principais fatores responsáveis pelo declínio na prevalência de cárie dentária (MARINHO, 2009) principalmente no que se refere ao uso de dentifrícios fluoretados (ZERO, 2006). Quando flúor está presente no meio bucal, em baixas concentrações e de forma constante, toda vez que houver redução no pH em resposta à fermentação dos carboidratos da dieta pelas bactérias do biofilme, e o pH chegar até 4,5 (esmalte) ou 5,5 (dentina), o mineral do tipo hidroxiapatita que compõe o tecido dental é dissolvido porém, há precipitação na superfície dental de um mineral com maior conteúdo de flúor, denominado de fluorhidroxiapatita. Dessa forma, o flúor atua reduzindo a perda líquida de mineral do dente na medida em que permite a redeposição de parte dos minerais perdidos durante as quedas de pH (TEN CATE et al., 2003; CURY; TENUTA, 2008).

Dessa forma, o foco do tratamento da doença cárie deve incidir sobre a sua causa e não sobre a sua consequência (cavidade de cárie). Por isso, o ato de restaurar um elemento dentário não deve ser considerado um tratamento em si, mas sim a resolução de uma sequela dessa doença. Sendo assim, cavidades de cárie

nas superfícies dentais que impossibilitem uma adequada limpeza e remoção de biofilme, que fragilizem o remanescente dentário, que comprometam a função mastigatória e que apresentem comprometimento estético podem ser restauradas.

Quando uma lesão cariosa surge em um tecido previamente hígido, ela é classificada como *cárie primária*. Porém, quando ocorre lesão cariosa adjacente à margem de restaurações, estas são chamadas, segundo MJOR, 2005, de *cárie recorrente* ou *cárie secundária*. Vale ressaltar que esses termos estão em desuso, uma vez que apresentam ocorrências de uma mesma doença. A denominação usada atualmente classifica como “cárie adjacentes às restaurações” as lesões de cárie que se desenvolvem nas proximidades de uma restauração ou na interface do dente hígido com o material restaurador (MJOR, 2005) apenas como uma forma de diferenciá-las das lesões de cárie que não se desenvolvem associadas ou nas proximidades das restaurações. É sabido que a microinfiltração bacteriana ao redor da interface dente/restauração de resina composta cria um nicho para colonização bacteriana que pode levar ao desenvolvimento de lesão de cárie ao redor dessas restaurações (KHALICHI et al., 2009). Além disso, essa microinfiltração pode contribuir para a sensibilidade pós-operatória e, se intervenção adequada não for realizada, o processo carioso pode progredir causando dor e comprometimento pulpar (KHALICHI et al., 2009).

Segundo Silva e Maltz (2004), a ocorrência de cárie ao redor das restaurações é considerada como uma das principais causas de substituição de restaurações. Em virtude disso, tem sido discutido que materiais restauradores contendo antimicrobianos em suas formulações possam ser usados para controlar esse processo (HAMOUDA et al., 2012).

Inúmeros estudos *in vitro* têm demonstrando que a incorporação de antimicrobianos aos materiais restauradores é capaz de inibir o crescimento de *Streptococcus* ssp e de *Lactobacillus* ssp (GARCÍA-CONTRETAS et al., 2011; CHEN; SHEN; SUH, 2012; IMAZATO, 2003; MELO et al., 2013. Porém, não existe evidência científica da relevância clínica dessa abordagem no tratamento e prevenção de cárie dentária.

Dessa forma, o objetivo desse trabalho foi fornecer uma discussão atualizada sobre efeito anti-cárie de antimicrobianos incorporados em materiais restauradores e sistemas adesivos levando-se em conta as metodologias utilizadas para avaliação

desses materiais bem como a relevância clínica dos resultados publicados. Adicionalmente, esta revisão objetivou investigar se a incorporação de antimicrobianos aos materiais restauradores previne a ocorrência de cárie ao redor das restaurações.

ARTIGO CIENTÍFICO

SCIENTIFIC EVIDENCES OF THE ANTI-CARIES EFFECT OF ANTIMICROBIAL-INCORPORATED DENTAL RESTORATIVE MATERIALS/ DENTINAL ADHESIVES: A REVIEW OF THE LITERATURE

ABSTRACT

Dental caries is a complex disease process that if not treated properly may advance to frank cavitation and a restorative intervention may be necessary. One of the main causes for restorations replacement is the occurrence of caries around restoration in patients whose carious activity is not adequately controlled. Antimicrobials have been incorporated into restorative materials or dental adhesives with the promise of reducing the incidence of caries around restorations. *In vitro* studies have shown that the incorporation of antimicrobial compounds into dental restorative materials is able to negatively affect the viability of cariogenic bacteria. However, the clinical relevance of this approach in the prevention of dental caries is still unknown. The aim of this review of literature was to provide an updated discussion about anti-caries effect of antimicrobial-incorporated dental restorative materials or dental adhesive systems focusing on the methodologies used to evaluate the antimicrobial effect and on the clinical relevance of the published results. Additionally, we sought to investigate whether the incorporation of antimicrobial compounds to dental restorative materials prevents caries around restorations. MEDLINE, via Pubmed, was searched for papers published from 1980 to December 23, 2013 and 1,085 articles were retrieved. After inclusion/exclusion assessment, 145 full text articles were read and included in the review which was comprised of 127 *in vitro*, 1 *in situ* and 5 *in vivo* studies and 12 reviews of literature. We conclude from the data of this review of literature that the methods used to evaluate the antimicrobial effects of experimental restorative materials are simplistic and do not represent the dynamism of conditions found on oral cavity. Therefore, the data provided by those studies should be evaluated with care. Additionally, no contribution or evidence has been found, so far, regarding the role of antimicrobial incorporated into restorative materials on prevention/control of dental caries and on prevention of caries around restorations.

INTRODUCTION

Dental caries is a complex disease process that has been studied for decades. Briefly, dental caries is a multifactorial disease characterized by demineralization of dental tissues in response to acids produced due to the degradation of fermentable dietary carbohydrates by dental biofilm bacteria. This leads to a pH decrease on tooth surface resulting in loss of dental mineral structure (FEATHERSTONE, 2008). In this context, mutans streptococci, mainly *Streptococcus mutans*, and *Lactobacillus casei* have been considered as the main bacteria responsible for the metabolic-induced dental tissue loss, because they are able to survive under acidic-pH environment and to produce acids from rapidly fermentable carbohydrates (TAKAHASHI; NYVAD, 2008). This process, known as "Ecological Plaque Hypothesis" (MARSH, 1994), takes into account the role of diet on microbial shifts of dental biofilm and the impact of this microbial changes on tooth surfaces integrity. Recently, an extension of the above mentioned Hypothesis has been postulated by Takahashi and Nyvad (2008). These authors consider that the frequent episodes of acidification of dental biofilm lead to a transition of microbial composition of dental biofilm from a dynamic stage, where there is a predominance of non-mutans streptococci and *Actinomyces* on biofilms, to an acidogenic stage characterized by the predominance of non-mutans streptococci able to withstand low pH environments. For instance, this latter stage might be converted into an aciduric one, due to the perpetration of low-pH environment, where mutans streptococci and other acid-tolerant bacteria prevail. These shifts alter the phenotypic/genotypic traits of dental biofilm microbiota resulting in an imbalance on mineral equilibrium between tooth and surrounding aqueous phase leading to a net mineral loss.

Once the mineral loss progresses as a response to the altered microbiota composition and to a sucrose-rich diet, a cavitation may be clinically seen on tooth surface. This cavitation may need to be sealed with dental restorative materials in order to restore chewing function and in order to decrease biofilm accumulation on that particularly site. In this context, it has been suggested that the main cause for restoration flaw and need for replacement is the occurrence of caries around restorations (SILVA; MALTZ, 2004), which is caused by the penetration of bacteria into tooth/restoration interface leading to demineralization of the surrounding tooth walls. Therefore, in an effort to increase the longevity of restorations, the incorporation

of antimicrobial substances into dental restorative materials has been encouraged (HAMOUDA et al., 2012) with the aim to reduce biofilm formation on the surface of these restorative materials. Long-term restorations are clinically attractive since they may reduce the costs of restoration replacement and the discommodity for the patient due to several re-interventions (WENG et al., 2012).

Among the antimicrobials incorporated into dental restorative material, monomer 12-methacryloyloxydo-decylpyridinium bromide (MDPB), chlorhexidine digluconate (CHX) and Silver Nanoparticle (NAg) are the most frequently used (CHEN et al., 2012). MDPB is a cationic agent and exhibits biocidal activity by reacting with negatively charged bacterial surfaces (IMAZATO et al., 1994) irreversibly damaging the cytoplasmic membrane of the bacteria (KWON et al., 2010; LI et al., 2009). CHX acts on bacterial cell wall provoking leakage of intracellular constituents, which lead to cell death (MCDONELL; RUSSELL, 1999). Additionally, it has been reported that silver ions of silver nanoparticles (Nag) inactivate important bacterial enzymes and affect the replication mechanism of the microbial DNA leading to a reduction on bacterial viability (MORONES et al., 2005). It has also been shown that silver attaches to the outer membrane and affects permeability as well as induces structural changes in the cell ultimately leading to cell death (FAN et al., 2011). Several articles have shown that the incorporation of these above mentioned antimicrobials to dental adhesives and restorative materials is able to inhibit *Streptococcus* ssp and *Lactobacillus* ssp growth under laboratorial conditions (GARCÍA-CONTRETAS et al., 2011; IMAZATO et al., 1994; FOLEY; BLACKWELL, 2003).

Besides these before mentioned antimicrobial substances, other antimicrobial compounds such as quaternary ammonium dimethacrylate (QADM), chitosan, triclosan, furanone and poly quaternary ammonium salt (PQAS) have also been also incorporated into dental restorative materials (IMAZATO, 1995b; WENG et al., 2012; IMAZATO, 2003). Overall, these compounds act on microbial cell surfaces provoking leakage of intracellular content (REGOS; HITZ, 1974; KIM et al., 2013; JEON et al., 2014).

Under laboratorial conditions, it has been shown that the incorporation of antimicrobial compounds into dental restorative materials is able to negatively affect the viability of cariogenic bacteria (CARVALHO et al., 2012; SEVINÇ; HANLEY, 2010;

CHENG et al., 2012d; ELSAKA, 2012; FAN et al., 2011; HE et al., 2012). However, the clinical relevance of this approach in the prevention of dental caries is still unknown (PEREIRA-CENCI et al., 2013). Therefore, the aim of this review of literature is to provide an updated discussion about anti-caries effect of antimicrobial-incorporated dental restorative materials or dental adhesive systems focusing on the methodologies used to evaluate the antimicrobial effect and on the clinical relevance of the published results. Additionally, we sought to investigate whether the incorporation of antimicrobial compounds to dental restorative materials prevents caries around restorations.

MATERIALS AND METHODS

MEDLINE, via Pubmed, was searched for papers published from 1980 to December 23, 2013. The search strategy used was (((dental material) AND antimicrobial) OR antibacterial) AND restorative. Titles and abstracts of all identified studies based on the above search strategy were read. Whenever there was not enough information available, the full-text article was read. Only articles written in English, reporting antimicrobial effect of antimicrobial-incorporated- dental restorative material or dentinal adhesives against cariogenic bacteria or reporting an anti-caries effect were included in the review and fully read. It was excluded from the review articles reporting antimicrobial effect of fluoride, antimicrobial effect of dental materials other than restorative/dentinal adhesives, reports of mechanical properties of the studied materials, remineralization effects due to fluoride incorporation into the tested materials and difficulty to access the full-text. References of eligible articles and narrative reviews were hand-searched to detect other potential studies of interest. Duplicated studies were excluded. Data about type of study (*in vitro*, *in situ* or *in vivo*), dental material/dentinal adhesives used, antimicrobial tested, microorganisms against antimicrobials were tested, methodology used to evaluate the antimicrobial effect and the antimicrobial effect (positive or negative) were extracted from the selected articles. Number of volunteers, collection of clinical samples, presence of an adequate control group and anti-caries effect were also collected from *in situ* and *in vivo* studies.

RESULTS

The search retrieved 1,085 articles. 145 full text articles were read and included in the review. Figure 1 shows a flow diagram of the articles that were identified, screened, excluded and included in the review. Out of the included articles, 127 were *in vitro*, 1 *in situ* and 5 *in vivo* studies and 12 reviews of literature.

Within all the selected studies, composite resin was the dental restorative material most tested (n=36 studies), followed by Glass Ionomer Cement (GIC; n=25), dentinal adhesives (n=23) and dentinal primers (n=19). The most incorporated antimicrobials were MDPB, CHX and NAg, comprising for 45,2% of the selected studies, followed by silver ions, QADM, triclosan, Cetrimide, PEI (Polyethyleneimine nanoparticles) and NACP (nanoparticles of amorphous calcium phosphate) (26,9%) (Figure 2). Another 18 antimicrobial were also incorporated into restorative materials and they comprised 27,9% of the selected studies (Figure 3). The results of Figures 2 and Figure 3 were taken from the appendage.

Within the *in vitro* studies, regarding the methodology used to evaluate the antimicrobial effects of the materials, inhibition of bacterial growth by direct contact with the tested material surface and inhibition of bacterial growth in broth were used by all of them. The time elapsed for the evaluation of the antimicrobial effect varied from 2 hours to 90 days, but the vast majority of studies evaluated bacterial viability only after 24 hours. Positive results in the inhibition of bacterial growth were seen in more than 70% of the studies for any of the tested antimicrobials, either for composite resins, GIC, dentinal adhesives or dentinal primers.

A positive result in decreasing bacterial viability due to the use of experimental antimicrobial-incorporated dental restorative materials/ dentinal adhesives was found in all of the selected *in situ* and *in vivo* studies. In only one of them the antimicrobial effect was evaluated after a long-time exposure to intraoral environment (up to 6 months), while all the other articles reported antimicrobial effects in a period shorter than a week (Table 1).

None of the selected articles (*in vitro*, *in situ, in vivo*) evaluated the anti-caries effect or the ability of the incorporated-antimicrobial restorative materials/dentinal adhesives on the prevention of caries around restoration.

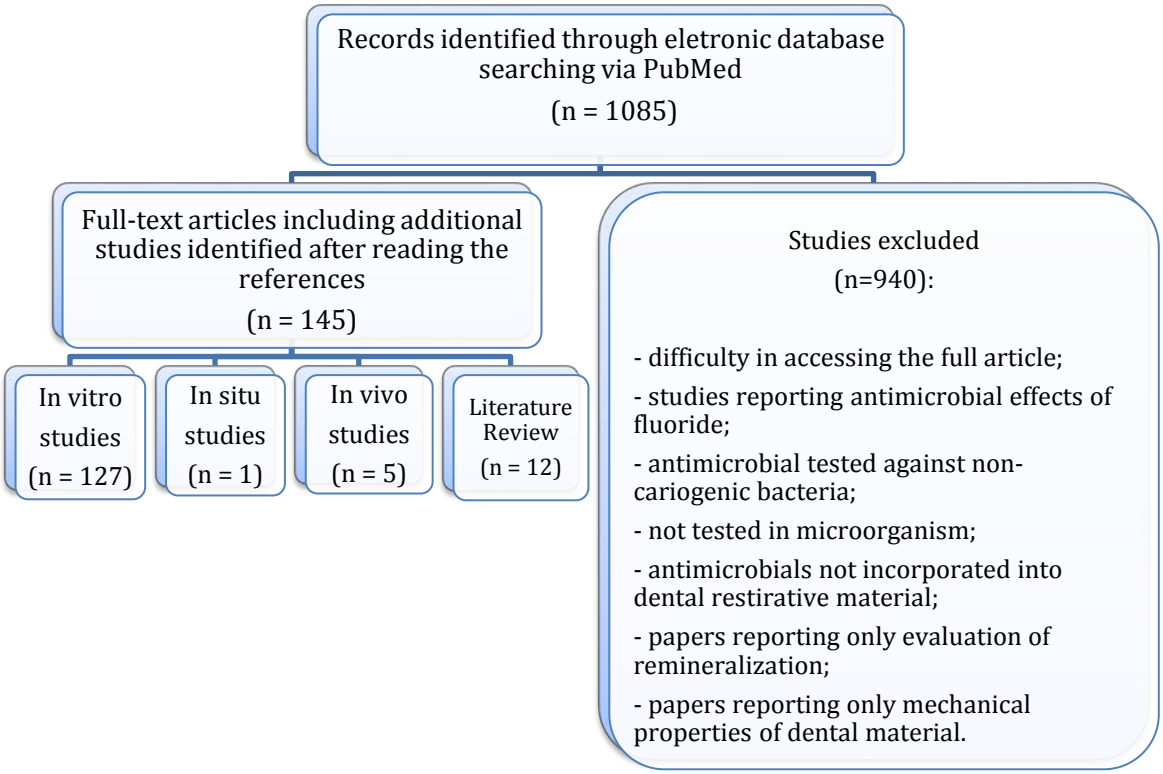

Figure 1. Flow diagram showing included and excluded studies retrieved from the electronic search.

Figure 2 – Descriptive analysis of the most incorporated antimicrobials into restorative materials / Adhesive systems.

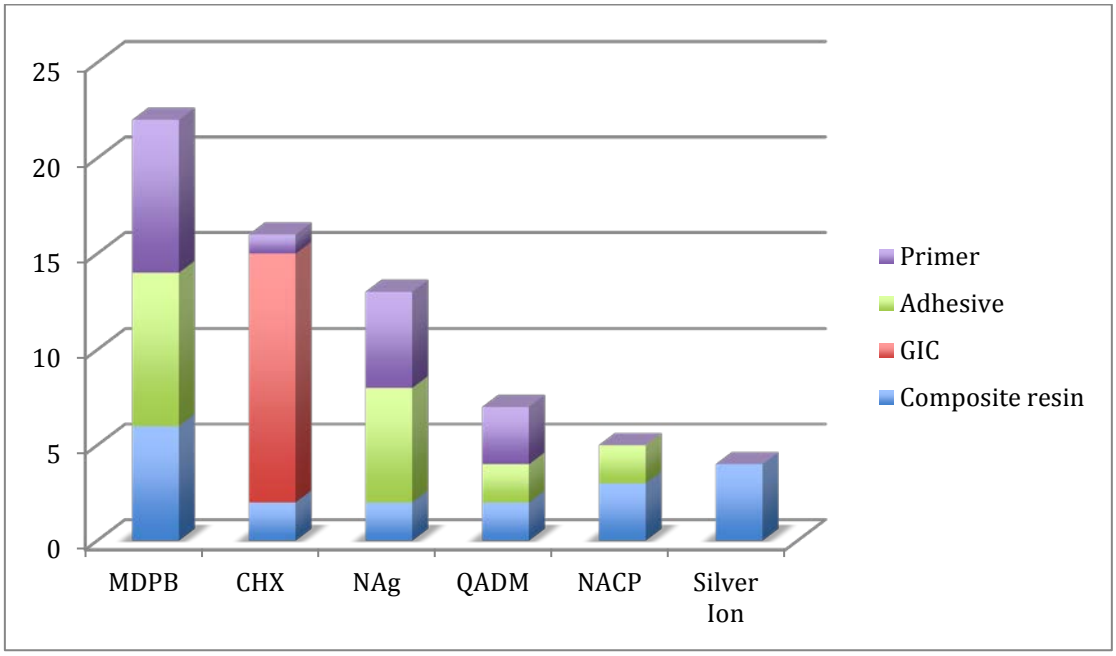

Figure 3 - Descriptive analysis of the less incorporated antimicrobials into restorative materials / Adhesive systems.

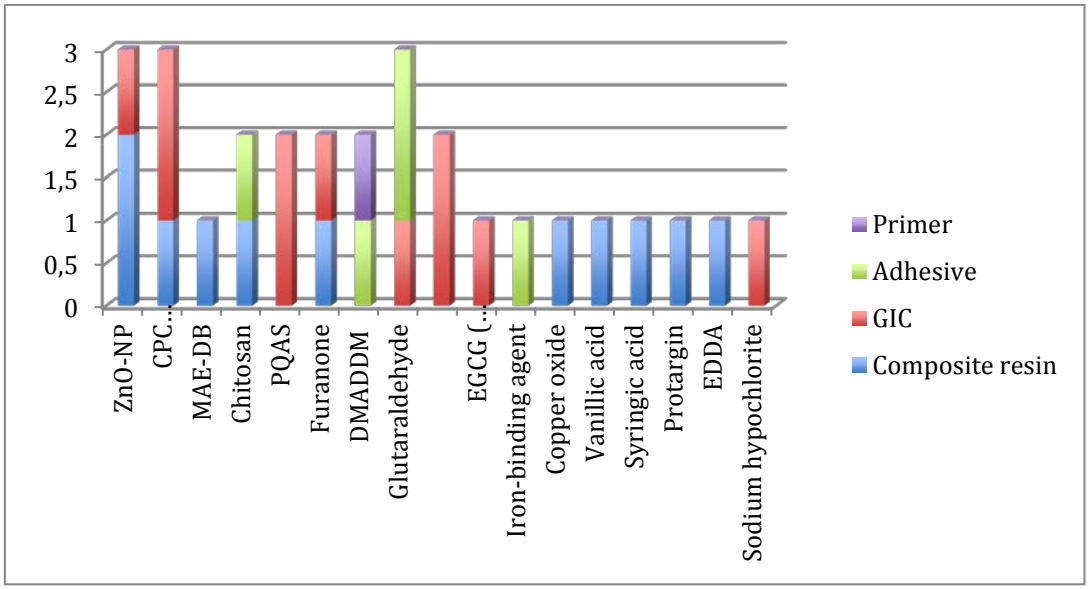

Table 1 - Descriptive analysis of the short-term clinical studies included in the review of the literature:

Authors	Year	Study	Patients	Clinical sample	Antimicrobial	Material	Control	Microorganisms	Anti-caries effect	Methods	Time	Results
Rupf et al.	2012	*In situ*	6	No	Octenidine dihydrochloride 3% and 6%	Composite resin	Composite resin without antimicrobial	Multispecies biofilm formed *in situ*	Not tested	SEM/ FM	3 and 7 days	Antimicrobial +
Rolland et al.	2011	*In vivo*	36	Root caries	MDPB (Concentration not informed)	Clearfill SE Bond Clearfill Protect Bond	Root caries sampling before primer application	*Streptococci Lactobacilli Yeasts Anarobes*	Not-tested	Viable cells counts	20 seconds	Antimicrobial +
Du et al.	2012	*In vivo*	8	No	CHX 2%	Experimental GIC Experimental GICRM	GIC w.o CHX GICRM w.o CHX	Multispecies biofilm formed *in vivo*	Not-tested	CLSM SEM	4h, 24h	Antimicrobial +
Foley; Blackwell	2003	*In vivo*	45	Dentinal caries	Copper phosphate (Concentration not informed)	Experimental Liner	No liner application	Mutans streptococci Lactobacilli Anaerobes	Not-tested	Viable cells counts	1 month, 6 months	Antimicrobial +
Frencken et al.	2007	*In vivo*	50	Dentinal caries	CHX (Concentration not informed)	GIC	GIC w.o CHX	Mutans streptococci Lactobacilli Total Aerobes Total Anaerobes	Not-tested	Viable cells counts	7 days	Antimicrobial +
Imazato et al.	2004	*In vivo*	5 beagle dogs	Dentin	MDPB (Concentration not informed)	Primer	not clear	*Streptococcus mutans*	Not-tested	Viable cells counts	30 minutes	Antimicrobial +

,MDPB: 12-methacryloyloxydo-decylpyridinium bromide; CHX: Chlorhexidine digluconate; GIC: glass ionomer cement; GICRM: glass ionomer cement resin modified; SEM: scanning electronic microscopy; FM: fluorescence microscopy; CLSM: Confocal scanning laser microscopy.

Discussion

Irrespective to the antimicrobial incorporated into restorative material/dentinal adhesives, a reduction in bacterial viability has been found (ESTEVES et al., 2010; GUPTA et al., 2011; RATHKE et al., 2010). The effects of MDPB and CHX have been extensively tested by *in vitro* and short-term clinical studies (IMAZATO et al*.,* 2002; TURKUN et al., 2008; CHENG et al., 2013; RUPT et al., 2012; ROLLAND et al., 2011; DU et al., 2012; FOLEY; BLACKWELL, 2003; FRENCKEN et al*.,* 2007; IMAZATO et al., 2004) (Figure 2). The antimicrobial effects of silver nanopaticules have been tested only under *in vitro* conditions. It has been discussed though that in a nanoparticulate form, silver ions are released more effectively from the materials and therefore they have better bactericidal activity than higher size silver particles due to its high surface area-to-volume ratio (KUMAR, 2008) and that could also be a promising approach to be used as an antimicrobial therapy in fields other than dentistry (FAN et al., 2011). There is no report so far regarding it antimicrobial effect under clinical conditions.

However, it is important to discuss that, although the methods used to assess the antimicrobial effects of experimental restorative materials present a first screening and the first evidence about the a potential effect, they are simplistic, limited and only provide a short-time effect on bacterial cell viability. Most of the selected articles evaluated whether the incorporation of an antimicrobial into a restorative material is able to reduce bacterial growth on its surface by a direct contact inhibition or by preventing biofilm formation. Keeping in mind that the most frequent cause of restorations replacement is due to caries around restoration (MJOR, 2005), it is reasonable to think that the prevention of biofilm formation, mainly on tooth/restoration interface, could contribute to the prevention of caries around restorations. However, the tested conditions and the available data do not allow any conclusions to be drawn in this respect.

Additionally, it has been shown that the tested materials are able to release the antimicrobial to the surrounding aqueous environment and inhibits the growth of the bacteria. In fact, the release of the antimicrobial to the oral

cavity might be a desirable behavior of a restoration since it could inhibits, at a distance, the growth of cariogenic microorganisms on oral cavity leading to a more favorable and health-related microflora (MARSH, 1994). However, although we have learnt from those studies that the incorporation of antimicrobials into restorative materials effectively reduces the bacteria viability, in most of them the antimicrobial effect of an experimental restorative material was evaluated in a short period of time (up to 24 hours) (BOTELHO, 2005; LI et al., 2013; FRENCKEN et al., 2007; HERRERA et al., 2001; HU et al., 2013; KIM; SHIN, 2013; HOMORI et al., 1999; SAKU et al., 2010). In only 3 *in vitro* studies the antimicrobial effect was studied over a period of time of 6 months (ZHANG et al., 2013b), but it seems that the antimicrobial effect is reduced over the time. Considering that a restoration has a high longevity in oral cavity, it is questionable whether a short-time bacterial inhibition has any clinical relevance.

It has been argued that the incorporation of antimicrobials into dentinal adhesives aims to impair biofilm colonization on tooth/restoration interface as a consequence of composite resin contraction and degradation of adhesive interface (KHALICHI et al., 2009). However, we consider that once a restoration is placed under the standard and well-controlled clinical steps, the chance of failure is low and, therefore, there is no need for adding antimicrobials to dentinal adhesives. Additionally, clinical studies have suggested that once a carious cavity is restored and it is well sealed, mainly in respect to the surrounding dentine walls, any microorganism left on the remaining dentine is inhibited and no progression of carious lesion is observed (BJORNDAL et al., 1997; ORHAN et al., 2010; LULA et al., 2011; MALTZ et al. 2002; 2007; 2012). Therefore, it may be clinically irrelevant the incorporation of antimicrobial into dentinal adhesives aiming its anti-caries effect. Additionally, it has been proposed that dentinal primers with antimicrobial effect could be used as a minimally invasive treatment for root caries (ROLLAND et al., 2011). However, that assumption was done based on microbiological counts of carious dentine samples obtained before and after only one short-time primer application. There was not any kind of follow-up for lesion activity assessment. Therefore, no conclusion can be drawn

based on those data.

We could also observe the lack of clinical studies evaluating the role of antimicrobials incorporated into restorative materials and its potential anti-caries effect. Only 6 studies evaluated the effect of experimental restorative materials under *in situ* or *in vivo* conditions (Table 1), but they focused only on the antimicrobial effect *per se*. No investigation was carried out in an attempt to verify whether the presence of the antimicrobial indirectly affects carious lesions development or not.

Ideally, in a first attempt to explore the antimicrobial effect of restorative materials, clinical conditions must be simulated under *in vitro* conditions but in a more realistic way. That means further studies need to be better design and their experimental designs should consider tooth/restoration as substrates for biofilm formation under a dynamic and constant flow of saliva in order to mimic the release of these antimicrobials as it would happen in oral cavity. Once *in vitro* results are promising, well-controlled short-term clinical studies should be designed and the extent of demineralization around restorations needs to be better explored in response to the experimental restorative materials. Standardized gaps could be generated *ex-vivo* on tooth/restoration interfaces, simulating a clinical condition appealing for bacterial colonization, and the tested tooth samples should be fixed on intra-oral appliances in order to allow biofilm accumulation on its surface. Additionally to these factors, biofilm could be grown under a high cariogenic challenge simulating the use of antimicrobial-incorporated restorations by caries active patients. It is demanded, afterwards, well designed, long-term and controlled clinical studies. Whether the incorporation of antimicrobial to the restorative material truly inhibits biofilm formation, it may be expected a low demineralization which could be monitored by means of mineral-content sensitive methods such cross-sectional hardness (FAN et al., 2011), transversal microradiography (ELSAKA; HAMOUDA; SWAIN, 2011). Clinical studies evaluating the topical effect of antimicrobial incorporated dentinal adhesives for controlling or preventing dentine root caries need to be conducted for longer periods of time in order to provide better evidences regarding its antimicrobial and/or cariostatic effects.

Considering the multiplicity of factors involved in carious process and the limitations of the data provided by this narrative review of the literature, we restate that the best evidence for dental caries control and treatment is based on diet advise (reduction of frequency of exposure to rapidly fermentable carbohydrates), individual motivation for a frequent and adequate mechanical biofilm removal from tooth surfaces and constant exposure to low-fluoride concentration provided by daily use of fluoridated toothpastes (KIDD, 2011).

Therefore, we conclude from the data of this review of literature that the methods used to evaluate the antimicrobial effects of experimental restorative materials are simplistic since they do not represent the dynamism of conditions found on oral cavity. Therefore, the data provided by those studies should be evaluated with care. Additionally, no contribution or evidence has been found, so far, regarding the role of antimicrobial incorporated into restorative materials on prevention/control of dental caries and on prevention of caries around restorations or whether this is a rational approach to prevent dental caries.

REFERENCES

ANTONUCCI, J. M. et al. Synthesis and characterization of dimethacrylates containing quaternary ammonium functionalities for dental applications. **Dent Mater,** Copenhagen, v. 28, no. 2, p. 219-228, Fev. 2012.

BAPNA, M. S.; MUKHERJEE, S.; MURPHY, R. The antimicrobial effect of an iron-binding agent on *Streptococcus mutans.* **J. Oral Rehabil.**, Oxford, v. 19, no. 2, p. 111-113, Mar. 1992.

BAPNA, M. S.; MURPHY, R.; MUKHERJEE, S. Inhibition of bacterial colonization by antimicrobial agents incorporated into dental resins. **J. Oral Rehabil.**, Oxford, v. 15, no. 5, p. 405-411, Sept. 1988.

BARBACHAN E SILVA, B.; MALTZ, M. Secondary caries: a review of the literature. **R. Fac. Odonto**., Porto Alegre, v. 45, no.1, p. 29-33, jul. 2004.

BARKHORDAR, R. A. et al. Technical note: Antimicrobial action of glass-ionomer lining cement on S. sanguis and S. mutans. **Dent. Mater.**, Copenhagen, v. 5, no 4, p. 281-282, July 1989.

BEYTH, N. *et al*. Long-term antibacterial surface properties of composite resin incorporating polyethyleneimine nanoparticles. **Quintessence Int.**, Berlin, v. 41, no. 10, p. 827-835, Nov/Dec. 2010.

BEYTH, N., et al. Antibacterial activity of dental composites containing quaternary ammonium polyethylenimine nanoparticles against Streptococcus mutans. **Biomaterials,** Guilford, v. 27, no. 21, p. 3995–4002, July. 2006.

BJORNDAL, L.; LARSEN, T.; THYLSTRUP, A. A clinical and microbiological study of deep carious lesions during stepwise excavation using long treatment intervals. **Caries Res.**, Basel, New York, v. 31, no. 6, p. 411-417, 1997.

BOECKH, C. et al. Antibacterial activity of restorative dental biomaterials in vitro. **Caries Res.**, Basel, New York, v. 36, no. 2, p. 101-107, Mar/Apr. 2002.

BOTELHO, M. G. Inhibitory effects on selected oral bacteria of antibacterial agents incorporated in a glass ionomer cement. **Caries Res.**, Basel, New York, v. 37, no. 2, p. 108-114, Mar/Apr. 2003.

BOTELHO, M. G. The antimicrobial activity of a dentin conditioner combined

with antibacterial agents. **Oper Dent.**, Seattle, v. 30, no. 1, p. 75-82, Jan/Feb. 2005.

BRAMBILLA *et al*. Influence of different adhesive restorative materials on mutans streptococci colonization. **Am. J. Dent**., San Antonio, v. 18, no. 3, p. 173-176, Jun. 2005.

BURGUERS, R. et al. The anti-adherence activity and bactericidal effect of microparticulate silver additives in composite resin materials. **Arch. Oral Biol.**, New York, v. 54, no. 6, p. 595–601, Jun. 2009.

CARVALHO et al. Analysis by confocal laser scanning microscopy of the MDPB bactericidal effect on *S. mutans* biofilm CLSM analysis of MDPB bactericidal effect on biofilm. **J. Appl. Oral Sci.,** Bauru, v. 20, no.5, p. 568-575, Sept. 2012.

CEHRELI, Z. C.; STEPHAN, A.; SENER, B. Antimicrobial properties of self-etching primer-bonding systems. **Oper. Dent.**, Seattle, v. 28, no. 2, p. 143-148, Mar/Apr. 2003.

CHEN, L.; SHEN, H.; SUH, B. I. Antibacterial dental restorative materials: A state-of-the-art review. **Am. J. Dent.**, San Antonio, v. 25, no. 6, p. 337-346, Dec. 2012.

CHENG, L. et al. Anti-biofilm dentin primer with quaternary ammonium and silver nanoparticles. **J. Dent. Res.**, Chicago**,** v. 91, no. 6, p. 598-604, Jun. 2012.

CHENG, L. et al. Antibacterial amorphous calcium phosphate nanocomposites with a quaternary ammonium dimethacrylate and silver nanoparticles. **Dent. Mater.,** Copenhagen, v. 28, no. 5, p. 561–572, May. 2012b.

CHENG, L. et al. Antibacterial and physical properties of calcium–phosphate and calcium–fluoride nanocomposites with chlorhexidine. **Dent. Mater.**, Copenhagen, v. 28, no 5, p. 573–583, May. 2012c.

CHENG, L. et al. Dental primer and adhesive containing a new antibacterial quaternary ammonium monomer dimethylaminododecyl methacrylate. **J. Dent.,** Bristol, v. 41, no. 4, p. 345–355, Apr. 2013b.

CHENG, L. et al. Effect of amorphous calcium phosphate and silver nanocomposites on dental plaque microcosm biofilms. **J. Biomed. Mater. Res. B Appl. Biomater**., Hoboken, v. 100, no. 5, p. 1378–1386, July. 2012d.

CHENG, L. et al. Effects of antibacterial primers with quaternary ammonium and nano-silver on Streptococcus mutans impregnated in human dentin blocks. **Dent. Mater.,** Copenhagen, v. 29, no. 4, p. 462–472, Apr. 2013.

da SILVA, R. C. et al. Antibacterial activity of four glass ionomer cements used in atraumatic restorative treatment. **J. Mater. Sci. Mater. Med.**, London, v. 18, no. 9, p. 1859-1862, Sept. 2007.

DAVIDOVICH, E. et al. Surface antibacterial properties of glass ionomer cements used in atraumatic restorative treatment. **J. Am. Dent Assoc.**, Chicago, v. 138, no. 10, p. 1347-1352, Oct. 2007

DEEPALAKSHMI, M. *et al*. Evaluation of the antibacterial and physical properties of glass ionomer cements containing chlorhexidine and cetrimide: an in-vitro study. **Indian J. Dent. Res**., Ahmedabad, v. 21, no. 4, p. 552-556, Oct/Dec. 2010.

DU, X. et al. Inhibition of early biofilm formation by glass-ionomer incorporated with chlorhexidine in vivo: a pilot study. **Aust. Dent. J.**, Sydney, v. 57, no. 1, p. 58–64, Mar. 2012.

DUQUE, C. et al. Inhibitory activity of glass-ionomer cements on cariogenic bacteria. **Oper. Dent**., Seattle, v. 30, no. 5, p. 636-640, Sept/Oct. 2005.

EBI, N. et al. Inhibitory effects of resin composite containing bactericide-immobilized filler on plaque accumulation. **Dent. Mater.**, Copenhagen, v. 17, no. 6, p. 485-491, Nov. 2001.

EI-TATARI, A. et al. Influence of salvadora persica (miswak) extract on physical and antimicrobial properties of glass ionomer cement. **Eur. Arch. Pediatr. Dent.,** Leeds, v. 12, no. 1, p. 22-25, Feb. 2011.

ELSAKA, S. E. Antibacterial activity and adhesive properties of a chitosan-containing dental adhesive. **Quintessence Int.,** Berlin, v. 43, no. 7, p. 603-613, Jul/Aug. 2012.

ELSAKA, S. E.; HAMOUDA, I. M.; SWAIN, M. V. Titanium dioxide

nanoparticles addition to a conventional glass-ionomer restorative: influence on physical and antibacterial properties. **J. Dent.**, Bristol, v. 39, no. 9, p. 589-598, Sept. 2011.

EMILSON, C. G.; BERGENHOLTZ, G. Antibacterial activity od dentinal bonding agents. **Quintessence Int.,** Berlin, v. 24, no. 7, p. 511-515, July. 1993.

ESTEVES, C. M. *et al*. Antibacterial activity of various self-etching adhesive systems against oral streptococci. **Oper. Dent.**, Seattle, v. 35, no. 4, p. 448-453, July/Aug. 2010.

FAN, C. et al. Development of an antimicrobial resin—A pilot study. **Dent. Mater.**, Copenhagen, v. 27, no. 4, p. 322-328, Apr. 2011.

FEATHERSTONE, J. D. Dental caries: a dynamic disease process. **Aust. Dent. J.**, Sydney, v. 53, no. 3, p. 286-291, Sept. 2008.

FEUERSTEIN, O. et al. Antibacterial properties of self-etching dental adhesive systems. **J. Am. Dent. Assoc.**, Chicago, v. 138, no. 3, p. 349-354, Mar. 2007.

FOLEY, J.; BLACKWELL, A. In vivo cariostatic effect of black copper cement on carious dentine. **Caries Res.**, Basel, v. 37, no. 4, p. 254-260, July/Aug. 2003.

FRAGA, R. C.; SIQUEIRA Jr., J. F.; UZEDA, M. In vitro evaluation of antibacterial effects of photo-cured glass ionomer liners and dentin bonding agents during setting. **J. Prosthet. Dent.**, St. Louis, v. 76, no. 5, p. 483-486, Nov. 1996.

FRENCKEN, J. E. *et al*. Antibacterial Effect of Chlorhexidine- Containing Glass Ionomer Cement in vivo: A Pilot Study. **Caries Res,** Basel, v. 41, p. 102–107, 2007.

GARCÍA-CONTRETAS, R. et al. Perspectives for the use of silver nanoparticles in dental practice. **Int. Dent. J.**, London, v. 61, no. 6, p. 297-301, Dec. 2011.

GIAMMANCO, G. M. et al. In vitro evaluation of the antibacterial activity of cured dentin/enamel adhesive incorporating the antimicrobial agent MDPB. **New Microbiol.**, Pavia, v. 32, no. 4, p. 385-390, Oct. 2009.

GOHO, C.; AARON, G. R. Enhancement of antimicrobial properties of cavity varnish: a preliminary report. **J. Prosthet. Dent.**, St. Louis, v. 68, no. 4, p. 623-625, Oct. 1992.

GROBLER, S. R.; BASSON, N. J.; ROSSOUW, R. J. Shear bond strength, microleakage and antimicrobial properties of AElitebond. **Am. J. Dent.**, San Antonio, v. 9, no. 3, p. 120-124, Jun. 1996.

GUPTA, A. et al. An *ex vivo* study to evaluate the remineralizing and antimicrobial efficacy of silver diamine fluoride and glass ionomer cement type VII for their proposed use as indirect pulp capping materials – Part I. **J. Conserv. Dent.**, [Amritsar], v. 14, no. 2, p. 113-116, Apr/Jun. 2011.

HAMOUDA, I. M. Current perspectives of nanoparticles in medical and dental biomaterials. **J. Biomed. Res.**, Nanjing, v. 26, no. 3, p. 143-151, May. 2012.

HE, J. et al. Incorporation of an antibacterial and radiopaque monomer in to dental resin system. **Dent. Mater.,** Copenhagen, v. 28, no. 8, p. 110-117, Aug. 2012.

HE, J. et al. Preparation and Evaluation of Dental Resin with Antibacterial and Radio-Opaque Functions. **Int. J. Mol. Sci.**, Basel, v. 14, no. 3, p. 5445-5460, Mar. 2013.

HERNÁNDEZ, M.; COBB, D. SWIFT, E. J. Jr. Current strategies in dentin remineralization. **J. Esthet. Restor. Dent.**, Hamilton, v. 26, no. 2, p. 139-145, Mar/Apr. 2010.

HERRERA, M. et al. Antibacterial activity of glass-ionomer restorative cements exposed to cavity- producing microorganisms. **Oper. Dent**., Seattle, v. 24, no. 5, p. 286-291, Sept/Oct. 1999.

HERRERA, M. et al. Antibacterial activity of resin adhesives, glass ionomer and resin-modified glass ionomer cements and a compomer in contact with dentin caries samples. **Oper. Dent.**, Seattle, v. 25, no. 4, p. 265-269, July/Aug. 2000.

HERRERA, M. et al. In vitro antibacterial activity of glass-ionomer cements. **Microbios.**, Cambridge, v. 104, n.409, p. 141-148, 2001.

HIRAISHI, N. et al. Effect of chlorhexidine incorporation into a self-etching

primer on dentine bond strength of a luting cement. **J. Dent.,** Bristol, v. 38, no. 6, p. 496-502, Jun. 2010.

HOJATI, S. T. et al. Antibacterial, physical and mechanical properties of flowable resin composites containing zinc oxide nanoparticles. **Dent. Mater.,** Copenhagen, v. 29, no. 5, p. 495-505, May. 2013.

HOTWANI, K. *et al*. Antibacterial effects of hybrid tooth colored restorative materials against Streptococcus mutans: An in vitro analysis. **J. Conserv. Dent.**, [Amritsar], v.16, no. 4, p. 319-322, July. 2013.

HU, J. et al. Antibacterial and physical properties of EGCG-containing glass ionomer cements. **J. Dent.**, Bristol, v. 41, no. 10, p. 927-934. Oct. 2013

HUANG, L. et al. Antibacterial effect of a resin incorporating a novel polymerizable quaternary ammonium salt MAE-DB against *Streptococcus mutans*. **J. Biomed. Mater. Res. B Appl. Biomater.**, Hoboken, v. 100, no. 5, p. 1353- 1358, July. 2012.

IMAZATO et al**.** Antibacterial resin monomers based on quaternary ammonium and their benefits in restorative dentistry. **Japanese Dental Science Review,** v. 48, no. 2, p. 115-125, Aug. 2012.

IMAZATO et al. Antibacterial activity and bonding characteristics of an adhesive resin containing antibacterial monomer MDPB. **Dent. Mater.,** Copenhagen, v. 19, no. 4, p. 313-319, Jun. 2003.

IMAZATO et al. Comparison of antibacterial activity of simplified adhesive systems. **Am. J. Dent.**, San Antonio, v. 15, no. 6, p. 356-360, Dec. 2002.

IMAZATO et al. Incorporation of bacterial inhibitor into resin composite. **J. Dent. Res.,** Chicago, v. 73, no. 8, p. 1437-1443, Aug. 1994.

IMAZATO, S; IMAI, T.; EBISU, S. Antibacterial activity of proprietary self-etching primers. **Am. J. Dent.**, San Antonio, v. 11, no. 3, p. 106-108, Jun. 1998c.

IMAZATO, S. et al. Antibacterial activity of bactericide-immobilized filler for resin-based restoratives. **Biomaterials**, [Guilford, England], v. 24, no. 20, p. 3605–3609, Sept. 2003.

IMAZATO, S. et al. Antibacterial activity of cured dental resin incorporating the antibacterial monomer MDPB and an adhesion-promoting monomer. **J. Biomed. Mater. Res**., Hoboken, v. 39, no. 4, p. 511–515, 1998b.

IMAZATO, S. et al. Antibacterial activity of dentine primer containing MDPB after curing. **J. Dent.,** Bristol, v. 26, no. 3, p. 267-271, Mar. 1998.

IMAZATO, S. et al. In vivo antibacterial effects of dentin primer incorporating MDPB. **Oper. Dent**., Seattle, v. 29, no. 4, p. 369-375, July/Aug. 2004.

IMAZATO, S. et al. Antibacterial activity of MDPB polymer incorporated in dental resin. **J. Dent.**, Bristol, v. 23, no. 3, p. 177-181, 1995.

IMAZATO, S. et al. Antibacterial properties of resin composites and dentin bonding systems. **Dent. Mater.**, Copenhagen, v. 19, no. 6, p. 449-457, Sept. 2003b.

IMAZATO, S. et al**.** Bactericidal effect of dentin primer containing antibacterial monomer methacryloyloxydodecylpyridinium bromide (MDPB) against bacteria in human carious dentin. **J. Oral. Rehabil**., Oxford, v. 28, no. 4, p. 314-319, Apr. 2001.

IMAZATO, S. et al. Comparison of antibacterial activity of simplified adhesive systems. **Am. J. Dent.**, San Antonio, v. 15, no. 6, p. 356-360, Dec. 2002.

IMAZATO, S. et al. In vitro antibacterial effects of the dentin primer of Clearfil Protect Bond. **Dent. Mater.**, Copenhagen, v. 22, no. 6, p. 527-532, Jun. 2006.

IMAZATO, S. et al. Incorporation of antibacterial monomer MDPB into dentin primer. **J. Dent. Res.**, Chicago, v. 76, no. 3, p. 768-772, Mar. 1997.

IMAZATO, S. et al. Incorporation of bacterial inhibitor into resin composite. **J. Dent. Res.,** Chicago, v. 73, no. 8, p. 1437-1443, Aug. 1994.

IMAZATO, S. et al**.** Penetration of an antibacterial dentine-bonding system into demineralized human root dentine in vitro. **Eur. J. Oral Sci.**, Copenhagen, v. 110, no. 2, p. 168-174, Apr. 2002.

IMAZATO, S.; TORRI, M.; TSUCHITANI, Y. Antibacterial effect of composite incorporating Triclosan against *Streptococcus mutans*. **J. Osaka Univ. Dent. Sch.**, Osaka, v. 35, p. 5-11, Dec. 1995.

JEDRYCHOWSKI, J. R.; CAPUTO, A. A.; KERPER, S. Antibacterial and mechanical properties of restorative materials combined with chlorhexidines. **J. Oral Rehabil.,** Oxford, v. 10, no. 5, p. 373-381, Sept. 1983.

JEON, S. J. et al. Underlying mechanism of antimicrobial activity of chitosan microparticles and implications for the treatment of infectious diseases. **PLoS One.,** San Francisco, v. 9, no. 3, Mar. 2014.

KARANIKA-KOUMA, A. et al. Antibacterial properties of dentin bonding systems, polyacid-modified composite resins and composite resins. **J. Oral Rehabil.,** Oxford, v. 28, no. 2, p. 157–160, Feb. 2001.

KHALICHI, P. et al. The influence of triethylene glycol derived from dental composite resins on the regulation of Streptococcus mutans gene expression. **Biomaterials,** [Guilford, England], v. 30, no. 4, p. 452–459, Feb. 2009.

KIDD, E. The implications of the new paradigm of dental caries. **J.Dent.**, Bristol, v. 39s2 s3–s8, Sept. 2011.

KIM, J. S.; SHIN, D. H. Inhibitory effect on *Streptococcus mutans* and mechanical properties of the chitosan containing composite resin. **Restor. Dent. Endod.**, Seoul, v. 38, no. 1, p. 36-42, Feb. 2013.

KITASAKO, Y. et al. Growth-inhibitory effect of antibacterial self-etching primer on mutans streptococci obtained from arrested carious lesions. **J. Esthet. Restor. Dent.**, Hamilton, v. 16, no. 3, p. 176-182, 2004.

KUDOU, Y. et al. Addition of Antibacterial Agents to MMA-TBB Dentin Bonding Systems – Influence on Tensile Bond Strenght and Antibacterial Effect. **Dent. Mater. J.**, Tokyo, v. 19, no. 1, p. 65-74, Mar. 2000.

KUMAR, C. S. S. R. Nanomaterials: toxicity, health and environmental issues. **Wiley-VCH**, v. 96, p. 306–308, 2006.

KURAMOTO, A. et al. Inhibition of root caries progression by an antibacterial adhesive. **J. Dent. Res.**, Chicago, v. 84, no. 1, p. 89-93, Jan. 2005.

KWON, T. Y. et al. Antibacterial effects of 4-META/ MMA-TBB resin containing chlorhexidine. **J. Biomed. Mater. Res. B Appl. Biomater.**, Hoboken, v. 92, no. 2, p. 561-567, Feb. 2010.

LEUNG, D. et al. Chlorhexidine-releasing methacrylate dental composite materials. **Biomaterials**, [Guilford, England], v. 26, no. 34, p. 7145–7153, Dec. 2005.

LEWINSTEIN, I. et al. Antibacterial properties of aged dental cements evaluated by direct-contact and agar diffusion tests. **J. Prosthet. Dent.,** St. Louis, v. 93, no. 4, p. 364-371, Apr. 2005.

LI, F. et al. Anti-biofilm effect of dental adhesive with cationic monomer. **J. Dent. Res.**, Chicago, v. 88, no. 4, p. 372-376, Apr. 2009b.

LI, F. et al. Comparison of quaternary ammonium-containing with nano-silver-containing adhesive in antibacterial properties and cytotoxicity. **Dent. Mater.**, Copenhagen, v. 29, no. 4, p. 450–461, Apr. 2013.

LI, F. et al. Effects of a dental adhesive incorporating antibacterial monomer on the growth, adherence and membrane integrity of *Streptococcus mutans*. **J. Dent.**, Bristol, v. 37, no. 4, p. 289-296, Apr. 2009.

LOBO, M. M. et al. In vitro evaluation of caries inhibition promoted by self-etching adhesive systems containing antibacterial agents. **J. Biomed. Mater. Res. B Appl. Biomater.**, Hoboken, v. 75, no. 1, p. 122-127, Oct. 2005.

LULA, E. C.; ALMEIDA, L. J. Jr.; ALVES, C. M.; MONTEIRO-NETO, V.; RIBEIRO, C. C. Partial caries removal in primary teeth: association of clinical parameters with microbiological status. **Caries Res.**, Basel, v. 45, no. 3, p. 275-280, May. 2011.

MALATON, S. et al. In vitro antibacterial evaluation of flowable restorative materials. **Quintessence Int.**, Berlin, v. 40, no. 4, p. 327-332, Apr. 2009.

MALATON, S. et al. Surface antibacterial properties of compomers. **Eur. Arch. Paediatr. Dent.**, Leeds, v. 7, no. 3, p. 136-141, Sept. 2006.

MALATON, S.; SLUTZKY, H.; WEISS, E. I. Surface antibacterial properties of packable resin composites: Part I. **Quintessence Int.**, Berlin, v. 35, no. 3, p.189-193, Mar. 2004.

MALTZ, M.; DE OLIVEIRA, E. F.; FONTANELLA, V.; BIANCHI, R. A clinical, microbiologic, and radiographic study of deep caries lesions after incomplete caries removal. **Quintessence Int.**, Berlin, v. 33, no. 2, p. 151-159, 2002.

MALTZ, M.; DE OLIVEIRA, E. F.; FONTANELLA, V.; CARMINATTI, G. Deep caries lesions after incomplete dentine caries removal: 40-month follow-up study. **Caries Res.**, Basel, v. 41, no. 6, p. 493-496, Oct. 2007.

MALTZ, M.; HENZ, S. L.; DE OLIVEIRA, E. F.; JARDIM, J. J. Conventional caries removal and sealed caries in permanent teeth: A microbiological evaluation. **J. Dent.**, Bristol, v. 40, no. 9, p. 776-782, Sept. 2012.

MARSH, P. D. Microbial Ecology of dental plaque and its significance in health and disease. **Adv. Dent. Res.**, [Washington, DC], v. 8, no. 2, p. 263-271, July. 1994.

MCDONELL, G.; RUSSELL, A. D. Antiseptics and Disinfectants: Activity, Action, and Resistance**. Clin. Microbiol. Rev.**, [Washington, DC], v. 12, no. 1, p. 147-179, Jan. 1999.

MEIERS, J. C.; MILLER G. A. Antibacterial activity of dentin bonding systems, resin-modified glass ionomers, and polyacid-modified composite resins. **Oper. Dent,** Seattle, v. 21, no. 6, p. 257-264, Nov/Dec. 1996.

MELO, M. A. et al. Novel dental adhesive containing antibacterial agents and calcium phosphate nanoparticles. **J. Biomed. Mater. Res. Part B Appl. Biomater.**, Hoboken, v. 101, no. 4, p. 620-629, May. 2013.

MELO, M. A. et al. Novel dental adhesives containing nanoparticles of silver and amorphous calcium phosphate. **Dent. Mater.**, Copenhagen, v. 29, no. 2, p. 199-210, Feb. 2013b.

MJOR, I. A. Clinical diagnosis of recurrent caries. **J. Am. Dent. Assoc.**, Chicago, v. 136, no. 10, p. 1426-1433, Oct. 2005.

MOREAU, J. L. et al. Mechanical and acid neutralizing properties and bacteria inhibition of amorphous calcium phosphate dental nanocomposite. **J. Biomed. Mater. Res. B Appl. Biomater.**, Hoboken, v. 98, no. 1, p. 80-88, July. 2011.

MORONES, J. R. et al. The bactericidal effect of silver nanoparticles. **Nanotechnology**, Bristol, v. 16, no. 10, p. 2346–2353. Oct. 2005.

NAMBA, N. et al. Antibacterial effect of bactericide immobilized in resin matrix. **Dent. Mater.**, Copenhagen, v. 25, no. 4, p. 424-430, Apr. 2009.

OHMORI, K.; MAEDA, K.; KOHNO, A. Evaluation of antibacterial activity of three dentin primers using an in vitro tooth model. **Oper. Dent.**, Seattle, v. 24, no. 5, p. 279-285, Sept/Oct. 1999.

ORHAN, A. I.; OZ, F. T.; ORHAN, K. Pulp exposure occurrence and outcomes after 1- or 2-visit indirect pulp therapy VS complete caries removal in primary and permanent molars. **Pediatr. Dent.**, Chicago, v. 32, no. 4, p. 347-355, July/Aug. 2010.

ORSTAVIK, D. Antibacterial properties of and element release from some dental amalgams. **Acta Odontol. Scand.**, Stockholm, v. 43, no. 4, p. 231-239, Aug. 1985.

OSINAGA, P. W. et al. Zinc sulfate addition to glass-ionomer-based cements: influence on physical and antibacterial properties, zinc and Fuoride release. **Dent. Mater.,** Copenhagen, v. 19, no. 3, p. 212-217, May. 2003.

OZER, F. et al. Antibacterial activities of MDPB and fluoride in dentin bonding agents. **Eur. J. Prosthodont. Restor. Dent.,** Larkfield, v. 13, no. 3, p.139-142, Sept. 2005.

PALENIK, C. J.; SETCOS, J. C. Antimicrobial abilities of various dentine bonding agents and restorative materials. **J. Dent.**, Bristol, v. 24, no. 4, p. 289-295, July. 1996.

PEREIRA-CENCI, T.; CENCI, M. S.; FEDOROWICZ, Z.; AZEVEDO, M. Antibacterial agents in composite restorations for the prevention of dental caries (Review). **Cochrane Database Syst. Rev.**, Oxford, v. 12, Dec. 2013.

PRATI, C. et al. Antibacterial effectiveness of dentin bonding systems. **Dent. Mater.,** Copenhagen, v. 9, no. 6, p. 338-343, Nov. 1993.

RATHKE, A. et al. Antibacterial activity of a triclosan-containing resin composite matrix against three common oral bacteria. **J. Mater. Sci. Mater. Med.,** London, v. 21, no. 11, p. 2971-2977, Nov. 2010.

REGOS, J; HITZ H, R. Investigations on the mode of action of Triclosan, a broad spectrum antimicrobial agent**. Zentralbl Bakteriol Orig A.**, Stuttgart, v. 226, no. 3, p. 390-401, Mar. 1974.

RIBEIRO, J.; ERICSON, D. In vitro antibacterial effect of chlorhexidine added

to glass-ionomer cements. **Scand. J. Dent. Res.**, Copenhagen, v. 99, no. 6, p. 533-540, Dec. 1991.

ROLLAND S. L. et al. A randomised trial comparing the antibacterial effects of dentine primers against bacteria in natural root caries. **Caries Res.**, Basel, v. 45, no. 6, p. 574-580, Dec. 2011.

RUPF, S. et al. Biofilm inhibition by an experimental dental resin composite containing octenidine dihydrochloride. **Dent. Mater.**, Copenhagen, v. 28, no. 9, p. 974-984, Sept. 2012.

SAINULABDEEN, S. et al. Antibacterial activity of triclosan incorporated glass ionomer cements--an in vitro pilot study. **J. Clin. Pediatr. Dent.**, Birmingham, v. 35, no. 2, p. 157-161. 2010.

SAKU, S. et al. Antibacterial activity of composite resin with glass-ionomer filler particles. **Dent. Mater. J.,** Tokyo, v. 29, no. 2, p. 193-198, Mar. 2010.

SANDERS, B. J. et al. Antibacterial and physical properties of resin modified glass-ionomers combined with chlorhexidine. **J. Oral Rehabil.,** Oxford, v. 29, no. 6, p. 553–558, Jun. 2002.

SCHERER, W.; LIPPMAN, N.; KAIM, J. Antimicrobial properties of glass-ionomer cements and other restorative materials. **Oper. Dent.**, Seattle, v. 14, no. 2, p. 77-81, 1989.

SETTEMBRINI, L. et al. A comparison of antimicrobial activity of etchants used for a total etch technique. **Oper. Dent.**, Seattle, v. 22, no. 2, p. 84-88, Mar/Apr. 1997.

SEVINÇ B. A.; HANLEY, L. Antibacterial Activity of Dental Composites Containing Zinc Oxide Nanoparticles. **J. Biomed. Mater. Res. B Appl. Biomater.**, Hoboken, v. 94, no. 1, p. 22–31, July. 2010.

SHVERO, D. K. et al. Antibacterial effect of polyethyleneimine nanoparticles incorporated in provisional cements against Streptococcus mutans. **J. Biomed. Mater. Res. Part B Appl. Biomater.,** Hoboken, v. 94, no. 2, p. 367–371, Aug. 2010.

SLUTZKY, H. et al. Antibacterial Properties of Temporary Filling Materials. **J. Endod.**, New York, v. 32, no. 3, p. 214-217. Mar. 2006.

SLUTZKY, H. et al. Surface antibacterial properties of resin and resin-modified dental cements. **Quintessence Int.,** Berlin, v. 38, no. 1, p. 55–61, Jan. 2007.

SLUTZKY, H.; MALATON, S.; WEISS, E. I. Antibacterial surface properties of polymerized single-bottle bonding agents: Part II. **Quintessence Int.**, Berlin, v. 35, no. 4, p. 275-279, Apr. 2004.

SVANBERG, M.; MJOR, I. A.; ORSTAVIK, D. Mutans streptococci in plaque from margins of amalgam, composite, and glass-ionomer restorations. **J. Dent. Res.**, Chicago, v. 69, no. 3, p. 861-864, Mar. 1990.

TAKAHASHI, N.; NYVAD, B. Caries Ecology Revisited: Microbial Dynamics and the Caries Process. **Caries Res.,** Basel, v. 42, no. 6, p. 409-418, 2008.

TAKAHASHI, Y. et al. Antibacterial effects and physical properties of glass-ionomer cements containing chlorhexidine for the ART approach. **Dent. Mater.,** Copenhagen, v. 22, no. 7, p. 647–652, July. 2006.

TANAGAWA, M. et al. Inhibitory effect of antibacterial resin composite against Streptococcus mutans. **Caries Res.**, Basel, v. 33, no. 5, p. 366-371, Sept/Oct. 1999.

THOMÉ, T. et al. In vitro analysis of inhibitory effects of the antibacterial monomer MDPB-containing restorations on the progression of secondary root caries. **J. Dent.**, Bristol, v. 37, no. 9, p. 705-711, Sept. 2009

TOBIAS, R. S. et al. A further study of the antibacterial properties of dental restorative materials. **Int. Endod. J.**, Oxford, v. 21, no. 6, p. 381-392, Nov. 1988.

TOBIAS, R. S.; BROWNE, R. M.; WILSON, C. A. Antibacterial activity of dental restorative materials. **Int. Endod. J.**, Oxford, v. 18, no. 3, p. 161-171, July. 1985.

TOPCUOGLU, N. et al. *In vitro* antibacterial effects of glass-ionomer cement containing ethanolic extract of propolis on *Streptococcus mutans.* **Eur. J. Dent.**, Ankara, v. 6, no. 4, p. 428-433, Oct. 2012.

TURKUN, L. S. et al. Long-term antibacterial effects and physical properties of a chlorhexidine-containing glass ionomer cement. **J. Esthet. Restor. Dent.**,

Hamilton, v. 20, no. 1, p. 29-44, 2008.

TUZUNER, T. et al. Antibacterial activity and physical properties of conventional glass-ionomer cements containing chlorhexidine diacetate/cetrimide mixtures. **J. Esthet. Restor. Dent.**, Hamilton, v. 23, no. 1, p. 46-55, Feb. 2011.

VAIDYANATHAN, M. et al. Antimicrobial properties of dentine bonding agents determined using in vitro and ex vivo methods. **J. Dent.**, Bristol, v. 37, no. 7, p. 514-521, July. 2009.

WALTER, R. et al. In Vitro Inhibition of Bacterial Growth Using Different Dental Adhesive Systems. **Oper. Dent.**, Seattle, v. 32, no. 4, p. 388-393, Jul/Aug. 2007.

WENG, Y. et al. A novel antibacterial dental glass-ionomer cement. **Eur. J. Oral Sci.**, Copenhagen, v. 118, no. 5, p. 531-534, Oct. 2010.

WENG, Y. et al. A novel antibacterial resin composite for improved dental restoratives. **J. Mater. Sci. Mater. Med.**, London, v. 23, no. 6, p. 1553-1561, Jun. 2012b.

WENG, Y. et al. A novel furanone-modified antibacterial dental glass ionomer cement. **Acta Biomater.**, v. 8, no. 8, p. 3153-3160, Aug. 2012.

WICHT, M. J. et al. A triclosan-containing compomer reduces Lactobacillus spp. predominant in advanced carious lesions. **Dent. Mater.,** Copenhagen, v. 21, no. 9, p. 831–836, Sept. 2005.

XIAO, Y. H. et al. Antibacterial activity and bonding ability of an adhesive incorporating an antibacterial monomer DMAE-CB. **J. Biomed. Mater. Res. B Appl. Biomater.**, Hoboken, v. 90, no. 2, p. 813-817, Aug. 2009.

XIE, D. et al. Preparation and evaluation of a novel glass-ionomer cement with antibacterial functions. **Dent. Mater.**, Copenhagen, p. 27, no. 5, p. 487-496. May. 2011.

YAMAMOTO, K. et al. Antibacterial activity of silver ions implanted in Si0 2 filler on oral streptococci. **Dent. Mater.,** Copenhagen, v. 12, no. 4, p. 227-229, July. 1996.

YESILYURT, C. et al. Antibacterial Activity and Physical Properties of Glass-ionomer Cements Containing Antibiotics. **Oper. Dent.**, Seattle, v. 34, no. 1**,** p. 18-23, Jan/Feb. 2009.

YOSHIDA, K. et al. Antibacterial activity of resin composites with silver-containing materials. **Eur. J. Oral Sci.**, Copenhagen, v. 107, no. 4, p. 290-296, Aug. 1999.

YOSHIDA, K.; TANAGAWA, M.; ATSUTA, M. Characterization and inhibitory effect of antibacterial dental resin composites incorporating silver-supported materials. nc. **J. Biomed. Mater. Res.**, Hoboken, v. 47, no. 4, p. 516–522, Dec. 1999b.

YUDOVIN-FARBER, I. et al. Surface Characterization and Biocompatibility of Restorative Resin Containing Nanoparticles **Biomacromolecules**, Washington, v. 9, no. 11, p. 3044–3050, Nov. 2008.

ZHANG, K. et al. Effects of dual antibacterial agents MDPB and nano-silver in primer on microcosm biofilm, cytotoxicity and dentine bond properties. **J. Dent.,** Bristol, v. 41, no. 5, p. 464-474, May. 2013b.

ZHANG, K. et al. Effect of quaternary ammonium and silver nanoparticle-containing adhesives on dentin bond strength and dental plaque microcosm biofilms. **Dent. Mater.,** Copenhagen, v. 28, no. 8, p. 842-852, Aug. 2012.

ZHANG, K. et al. Effect of water-ageing on dentine bond strength and anti-biofilm activity of bonding agent containing new monomer dimethylaminododecyl methacrylate. **J. Dent.,** Bristol, v. 41, no. 6, p. 504-513, 2013b.

3 CONCLUSÃO

Conclui-se a partir dos dados desta revisão de literatura que os métodos usados para avaliar o efeito antimicrobiano de materiais restauradores são muito simples e não representam o dinamismo de condições encontradas na cavidade bucal. Por isso, os dados fornecidos por esses estudos precisam ser analisados com cuidado. Em adição, nenhuma contribuição ou evidência tem sido encontrada em relação ao efeito da incorporação de antimicrobianos em materiais restauradores na prevenção/controle de cárie dental e na prevenção de cárie ao redor de restaurações.

REFERÊNCIAS

CURY, J. A.; TENUTA, L. M. A. How to maintain a cariostatic fluoride concentration in the oral environment. **Adv. Dent. Res.,** [Washington, DC], v. 20, no. 1, p. 13-16, July 2008.

FEATHERSTONE, J. D. B. Caries prevention and reversal based on the caries balance. **Pediatr. Dent.**, Chicago, v. 28, no. 2, p. 128-132, Mar./Apr. 2006.

FEATHERSTONE, J. D. B. Prevention and reversal of dental caries: role of low level fluoride. **Community Dent. Oral Epidemiol.,** Copenhagen, v. 27, no. 1, p. 31-40, Feb. 1999.

FEJERSKOV, O.; KIDD, E. **Dental Caries**: the disease and its clinical management. 2nd ed. Oxford: Blackwell Munksgaard, 2008. p. 58-60.

FERREIRA-ZANDONÁ. The natural history of dental caries lesions **-** A 4-year observational study. **J. Dent. Res.**, Chicago, v. 91, no. 9, p. 841-846, Sept. 2012.

GARCÍA-CONTRETAS, R. et al. Perspectives for the use of silver nanoparticles in dental practice. **Int. Dent. J.**, London, v. 61, no. 6, p. 297-301, Dec. 2011.

HAMOUDA, I. M. et al. Current perspectives of nanoparticles in medical and dental biomaterials. **J. Biomed. Res.**, Nanjing, China, v. 26, no. 3, p. 143-151, May 2012.

HARA, A. T.; ZERO, D. T. The caries environment: saliva, pellicle, diet, and hard tissue ultrastructure**. Dent. Clin. North Am.**, Philadelphia, v. 54, no. 3, p. 455-467, July 2010.

IMAZATO, S. et al. Incorporation of bacterial inhibitor into resin composite. **J. Dent. Res.,** Chicago, v. 73, no. 8, p. 1437-1443, Aug. 1994.

KHALICHI, P. et al. The influence of triethylene glycol derived from dental composite resins on the regulation of Streptococcus mutans gene expression. **Biomaterials,** [Guilford, England], v. 30, no. 4, p. 452–459, Feb. 2009.

KIDD, E. The implications of the new paradigm of dental caries. **J. Dent.,** England, v. 39, Suppl 2, p. S3-S8, Dec. 2011.

KWON, T. Y. et al. Antibacterial effects of 4-META/ MMA-TBB resin containing chlorhexidine. **J. Biomed. Mater. Res. B Appl. Biomater.**, Hoboken, v. 92, no. 2, p. 561-567, Feb. 2010.

LI, F. et al. Anti-biofilm effect of dental adhesive with cationic monomer. **J. Dent. Res.**, Chicago, v. 88, no. 4, p. 372-376, Apr. 2009.

MARINHO, V. C. Cochrane reviews of randomized trials of fluoride therapies for preventing dental caries. **Eur. Arch. Paediatr. Dent**., Leeds, v. 10, no. 3, p. 183-191, Sept. 2009.

MCDONELL, G.; RUSSELL, A. D. Antiseptics and disinfectants: activity, action, and resistance**. Clin. Microbiol. Rev.**, [Washington, DC], v. 12, no. 1, p. 147-179, Jan. 1999.

MJOR, I. A. Clinical diagnosis of recurrent caries. **J. Am. Dent. Assoc.**, Chicago, v. 136, no. 10, p. 1426-33, Oct. 2005.

MORONES, J. R. et al. The bactericidal effect of silver nanoparticles. **Nanotechnology**, Bristol, v. 16, no. 10, p. 2346–2353, Oct. 2005.

SELWITZ, R. H.; ISMAIL, A.; PITTS, N. B. Dental caries. **Lancet**, London, v. 369, no. 9555, p. 51-59, Jan. 2007.

WENG, Y. et al. A novel furanone-modified antibacterial dental glass ionomer cement. **Acta Biomater.**, Kidlington, v. 8, no. 8, p. 3153-3160, Aug. 2012.

ZERO, D. T. Dentifrices, mouthwashes, and remineralization/caries arrestment strategies. **BMC Oral Health**, London, v. 6, Suppl. 1, p. s9, 2006.