Antibacterial agents in composite restorations for the prevention of dental caries (Review)

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This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2009, Issue 3

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[Intervention Review]

Antibacterial agents in composite restorations for the prevention of dental caries

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Editorial group: Cochrane Oral Health Group.
Publication status and date: New, published in Issue 3, 2009.
Review content assessed as up-to-date: 9 March 2009.

Citation: Pereira-Cenci T, Cenci MS, Fedorowicz Z, Marchesan MA. Antibacterial agents in composite restorations for the prevention of dental caries. *Cochrane Database of Systematic Reviews* 2009, Issue 3. Art. No.: CD007819. DOI: 10.1002/14651858.CD007819.pub2.

ABSTRACT

Background

Dental caries is a multifactorial disease in which the fermentation of food sugars by bacteria from the biofilm (dental plaque) leads to localised demineralisation of tooth surfaces, which may ultimately result in cavity formation. Resin composites are widely used in dentistry to restore teeth. These restorations can fail for a number of reasons, such as secondary caries, excessive wear, marginal degradation, tooth sensitivity, pulpal death, and restorative material fracture. Caries adjacent to restorations is one of the main causes for restoration replacement. The presence of antibacterials in both the filling material and the bonding systems would theoretically be able to affect the initiation and progression of caries adjacent to restorations.

Objectives

To assess the effects of antibacterial agents incorporated into composite restorations for the prevention of dental caries.

Search methods

We searched the following databases in February 2009: the Cochrane Oral Health Group's Trials Register; the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2009, Issue 1); MEDLINE via OVID (1950 to February 2009) without filter; and EMBASE via OVID (1980 to February 2009) without filter.

Selection criteria

Randomised controlled clinical trials (RCTs) comparing resin composite restorations containing antibacterial agents with non-antibacterial containing composite restorations.

Data collection and analysis

Two review authors conducted screening of studies in duplicate and independently, and although no eligible trials were identified, the two authors had planned to extract data independently and assess trial quality using standard Cochrane Collaboration methodologies.

Main results

We retrieved 128 references to studies, none of which matched the inclusion criteria for this review and all of which were excluded.

Authors' conclusions

We were unable to identify any randomised controlled trials on the effects of antibacterial agents incorporated into composite restorations for the prevention of dental caries. The absence of high level evidence for the effectiveness of this intervention emphasises the need for well designed, adequately powered, randomised controlled clinical trials.

PLAIN LANGUAGE SUMMARY

Antibacterial agents in composite restorations for the prevention of dental caries

When tooth decay (caries) has caused a cavity in a tooth a range of materials can be used as fillings. These include resin composite, glass ionomer cement, amalgam and compomers. Secondary caries (tooth decay that may appear near or underneath a filling at a later stage) is a common concern in dental practice and may reduce the life span of these fillings. Antibacterial agents may be incorporated in some dental fillings i.e. resin composites to help prevent the development of secondary caries. This review failed to find any trials supporting or refuting the effectiveness of antibacterial agents incorporated into composite restorations to prevent dental caries. The authors concluded that future research should aim to provide evidence for clinicians to make informed decisions about whether antibacterial agents are effective in improving clinical outcomes in composite restorations and that further randomised controlled trials should be well designed and reported according to the Consolidated Standards of Reporting Trials (CONSORT) Statement.

BACKGROUND

Dental caries is a multifactorial disease in which the fermentation of food sugars by bacteria from the biofilm (dental plaque) leads to localised demineralisation of tooth surfaces, which may ultimately result in cavity formation. This process is triggered by ecological pressure (such as alteration in salivary flow or increase in sugars consumption) which results in microbiological shifts and other changes within this biofilm (Marsh 2006; Selwitz 2007).

Resin composite is a material widely used in dentistry to restore teeth. These restorations can fail for a number of reasons, such as secondary caries, excessive wear, marginal degradation, tooth sensitivity, pulpal death, and restorative material fracture (Hickel 2007). Caries adjacent to restorations, also described as secondary or recurrent caries, is one of the main causes for restoration replacement (Brunthaler 2003; Mjör 2005; Opdam 2007), representing up to 55% of the causes of failure reported by dentists (Mjör 2005). These carious lesions are mediated by biofilm accumulation at the tooth/restoration interface (Kidd 2004; Thomas 2007). To prevent a recurrence of caries and improve their longevity, attempts have been made to add antibacterials into composite restorative materials (Imazato 2003).

Composite restorations consist of two major components: a resin composite for filling and the bonding systems to be applied to the cavity before the placement of filling materials. The incorporation of antibacterial substances in these two components would have different roles relating to the prevention of the harmful effects caused by bacteria within the biofilm covering the tooth/restoration interface. The antibacterial effects of composites for filling would be mainly relevant to inhibition of plaque accumulation on the surface of the materials and tooth around the restoration. In contrast, for bonding systems, their antibacterial effects are discussed in terms of disinfection of the cavity as well as inactivation of bacteria which could invade the adhesive interface due to microleakage (Imazato 2003). The presence of antibacterials in both the filling material and the bonding systems would theoretically be able to affect the initiation and progression of caries adjacent to restorations.

Since the incorporation of antimicrobials in restorative materials and bonding systems could represent additional cost to the consumers or affect the mechanical properties of composites, it would be important to review the benefits and cost-effectiveness of such products in dentistry. Additionally, consumers would benefit when other possible adverse effects of these products are studied.

OBJECTIVES

To assess the effects of antibacterial agents incorporated into composite restorations for the prevention of dental caries.

METHODS

Criteria for considering studies for this review

Types of studies

Only randomised controlled clinical trials (RCTs) were considered in this review.

Types of participants

Adults and adolescents in any age group with restorations in the permanent dentition and children with restorations in the primary dentition.

Types of interventions

Resin composite restorations containing antibacterial agents compared to non-antibacterial containing composite restorations, considering similar materials in composition.

Types of outcome measures

Primary outcome

(1) Secondary caries.

Secondary outcomes

(1) Longevity of restorations, recorded by the time to failure in months. Failures included replacement of the restoration, tooth extraction, pulpotomy, or natural exfoliation adjusted extraction, these last two if primary dentition is being considered, or any inability or inadequacy to perform as expected.
(2) Postoperative sensitivity, marginal adaptation, anatomic form and other clinical outcomes (tooth vitality and pulpitis) proposed to assess restoration's quality based on the US Public Health Service (USPHS) criteria and its evolution (Hickel 2007).
(3) Patient's view and satisfaction with the treatment, according to the evaluation proposed by Hickel 2007.

Costs

Direct costs of interventions including financial losses to patients, evaluated by direct and indirect cost regarding materials and time to revisit the dental office.

Adverse effects

Any specific adverse effects related to any clinically diagnosed reactions to any of the active interventions will be noted.

Search methods for identification of studies

Electronic searches

For the identification of studies included or considered for this review, detailed search strategies were developed for each database to be searched. These were based on the search strategy developed for MEDLINE but revised appropriately for each database.
We searched the following databases on 25th February 2009:

- Cochrane Oral Health Group's Trials Register;
- Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2009, Issue 1);
- MEDLINE (1950 to February 2009) without filter;
- EMBASE (1980 to February 2009) without filter.

For the detailed search strategies applied to each of the databases *see* Appendix 1; Appendix 2; Appendix 3; Appendix 4.
There were no language restrictions on included studies.

Searching other resources

We did not conduct handsearching of any journals but searched the reference lists of relevant articles and the review authors' personal database of trial reports.

Data collection and analysis

Selection of studies

Two review authors (Tatiana Pereira-Cenci (TPC) and Maximiliano Sergio Cenci (MSC)) independently assessed the abstracts of studies resulting from the searches. Full copies of all relevant and potentially relevant studies, those appearing to meet the inclusion criteria, or for which there were insufficient data in the title and abstract to make a clear decision, were obtained. The full text papers were assessed independently and in duplicate by two review authors and any disagreement on the eligibility of included studies was resolved through discussion and consensus or through a third party (Zbys Fedorowicz (ZF)). All irrelevant records were excluded and details of the studies and the reasons for their exclusion were noted in the Characteristics of excluded studies table in Review Manager (RevMan) 5 (RevMan 2008).

Data extraction and management

Although no studies were identified for inclusion in this review the following methods of data extraction, assessment of risk of bias and data management will apply for subsequent updates, and when future studies are identified.
Study details will be entered into the 'Characteristics of included studies' table in RevMan 5. The review authors (TPC and MSC)

will collect independently and in duplicate outcomes data using a pre-determined form designed for this purpose. The review authors will only include data if there is an independently reached consensus, any disagreements will be resolved by consulting with a third review author (ZF).
The following details will be extracted.
(1) Trial methods:
(a) method of allocation
(b) masking of participants, trialists and outcomes
(c) exclusion of participants after randomisation and proportion of losses at follow up.
(2) Participants:
(a) country of origin
(b) sample size
(c) age
(d) sex
(e) inclusion and exclusion criteria.
(3) Intervention:
(a) type
(b) duration and length of time in follow up.
(4) Control:
(a) type
(b) duration and length of time in follow up.
(5) Outcomes:
(a) primary and secondary outcomes mentioned in the outcome measures section of this review.
If stated, the sources of funding of any of the included studies will be recorded.
The review authors will use this information to help them assess heterogeneity and the external validity of the trials.

Assessment of risk of bias in included studies

An assessment of the risk of bias in included studies will be undertaken following the recommendations as described in Chapter 8 of the *Cochrane Handbook for Systematic Reviews of Interventions* 5.0.1 (Higgins 2008).
A specific tool for assessing risk of bias in each included study will be adopted. This comprises a description and a judgement for each entry in a risk of bias table, where each entry addresses a specific feature of the study:

- Adequate sequence generation
- Allocation concealment
- Blinding
- Incomplete outcome data addressed
- Free of selective reporting
- Free of other bias.

The judgement for each entry involves answering a questions, with answers 'Yes' indicating low risk of bias, 'No' indicating high risk of bias, and 'Unclear' indicating either lack of information or uncertainty over the potential for bias. An assessment of the overall risk of bias will be summarized involving the consideration of the relative importance of different domains.
Two review authors will independently and in duplicate assess the risk of bias of all included studies. Any disagreement will be discussed and where necessary a third review author will be consulted to achieve consensus. Where uncertainty cannot be resolved, effort will be made to contact authors directly for clarification.

Assessment of heterogeneity

We plan to assess clinical heterogeneity by examining the characteristics of the studies, the similarity between the types of participants, the interventions and the outcomes as specified in the criteria for included studies. Statistical heterogeneity will be assessed using a Chi^2 test and the I^2 statistic where I^2 values over 50% indicate moderate to high heterogeneity (Higgins 2003).

Assessment of reporting biases

If sufficient randomised controlled trials are identified, an attempt will be made to assess publication bias using a funnel plot (Egger 1997).

Data synthesis

The Cochrane Collaboration's statistical guidelines will be followed for data synthesis. The data will be analysed by TPC using RevMan 5 and reported according to Cochrane Collaboration criteria.
For continuous data the mean difference and 95% confidence intervals will be calculated. Risk ratios and their 95% confidence intervals will be calculated for all dichotomous data.
Results of clinically and statistically homogeneous trials will be pooled to provide estimates of the efficacy of the interventions only if the included studies have similar interventions received by similar participants.
For the synthesis and meta-analysis of any quantitative data we will use the fixed-effect and random-effects models as appropriate. If it is established that there is significant statistical heterogeneity between the studies we will use the random-effects model with studies grouped by action.
In the event that there are insufficient clinically homogeneous trials for any specific intervention or insufficient study data that can be pooled, a narrative synthesis will be presented.

Subgroup analysis and investigation of heterogeneity

We will consider conducting subgroup analyses for different restorative materials if there are sufficient numbers of included trials.

Sensitivity analysis

If there are sufficient included studies we plan to conduct sensitivity analyses to assess the robustness of our review results by repeating the analysis with the following adjustments: exclusion of studies with unclear or inadequate allocation concealment, unclear or inadequate blinding of outcomes assessment and completeness of follow up.

RESULTS

Description of studies

See: Characteristics of excluded studies.
No studies were included in this review.

Results of the search

De-duplication of the search results produced 128 references to potentially eligible studies (Cochrane Oral Health Group's Trials Register 5, CENTRAL 10, MEDLINE 90, EMBASE 45). After examination of the titles and abstracts of these references, all but two were eliminated and excluded from further review. Full text copies of the remaining studies (Ergucu 2007; Ohta 1984) in addition to two literature reviews (Imazato 2003; Wiegand 2007) were obtained and then subjected to further evaluation which included an examination of their bibliographical references which provided no additional citations to potentially eligible trials. We also identified one study (Ohta 1984) which was in the Japanese language and which we arranged to be translated and evaluated against our inclusion criteria but subsequently excluded it as it was ineligible.
The review authors discussed the eligibility of the potentially eligible studies, resolved any uncertainties by consensus and finally excluded all the studies, *see* Characteristics of excluded studies table.

Included studies

We retrieved a number of studies in our searches of the literature but none were eligible and therefore no trials were included in this review.

Excluded studies

We excluded all records which did not match our inclusion criteria and noted the reasons for exclusion in the Characteristics of excluded studies table.

Risk of bias in included studies

No trials were included.

Effects of interventions

None of the studies retrieved in our searches met our inclusion criteria and therefore no data were available for analysis.

DISCUSSION

Over the past decades, new developments in dental technology, patient demands for tooth-coloured restorations and a need to find alternatives to amalgam were some reasons for the increased use of resin composite materials. An increasing number of composite restorations is placed as a routine in dental practice, and it is the most widely used direct restorative material.

Failure of composite restorations is usually attributed to the development of caries lesions adjacent to these restorations. In order to prevent the development of dental caries adjacent to or underneath these restorations, antibacterial or bactericidal agents have been added to resin composite adhesives as a way to provide an adjunct treatment contributing to suppression of residual infection and increasing the survival of the restored tooth.

However, no randomised controlled trials (RCTs) on resin composite containing antibacterial agents compared to a control group were retrieved by the literature search. Therefore, it is difficult to draw conclusions to support any difference in the inhibition of caries development and progression or clinical performance of antibacterial containing resin composites and other restorations. Given the absence of RCTs comparing antibacterial versus non-antibacterial containing resin composites, we could not conclude anything on significant differences regarding these materials. However, this lack of evidence does not rule out major differences on secondary caries development, longevity or postoperative sensitivity related to antibacterial containing materials.

To allow a controlled comparison of materials, well-designed trials should be planned and conducted. When evaluating antibacterial and non-antibacterial containing resin composites, clinicians and analysts will probably be unable to recognize the materials used from their appearance and are possible to fit into the blinded format. Additionally, independent assessment of restorations is a key factor in quality assessment and data extraction when considering longevity of restorations. Assessment should be performed by independent evaluators to avoid biased assessment of the restorations even after long periods between recalls. Decisions should be taken according to a set of pre-determined criteria. The decision to replace a restoration should be made by an independent evaluator and not the operator or private practitioner whose practice management situation may influence the outcome.

Most analyses planned in the protocol could not be conducted in this review because of the lack of relevant well-designed RCTs. Therefore, we foresee a great need to conduct high quality RCTs to investigate the potential advantages of antibacterial containing composites before recommending the routine use of these materials. Further analyses are expected in future updates of this review, with reports that fulfil the inclusion criteria.

AUTHORS' CONCLUSIONS

Implications for practice

There is no evidence to suggest benefit of using antibacterial containing composites or adhesives to prevent the development of dental caries. However, as no data are available, the question of whether or not these antibacterial agents are beneficial is still critical to suggest implications for practice. Considering that new materials containing antibacterial agents are expected to have additional costs in comparison to the commercially available resin composites, the use of such materials on clinicians' daily practice cannot be justified or recommended until convincing evidence is available.

Implications for research

In light of the disappointing results from the literature search, we strongly recommend that well-designed clinical trials of antibacterial containing resin composite restorations are undertaken and reported. Reports must include high quality descriptions of all aspects of methodology to enable appraisal and interpretation of results. Important factors such as random allocation sequence, blind assessment, reason for sample size and dealing with withdrawals should be carefully considered when planning, conducting and reporting clinical studies. Studies with a long follow-up should be undertaken to confirm the long-term effects of this treatment. Future publications which fulfil the inclusion criteria for this review will be incorporated in subsequent updates of the review.

ACKNOWLEDGEMENTS

We wish to thank Anne Littlewood (Cochrane Oral Health Group) for her assistance with literature searching and the Cochrane Oral Health Group for their help in developing the protocol and conducting this review.

REFERENCES

References to studies excluded from this review

Ergucu 2007 ***{published data only}***
Ergucu Z, Turkun LS. Clinical performance of novel resin composites in posterior teeth:18-month results. *Journal of Adhesive Dentistry* 2007;**9**(2):209–16.

Ohta 1984 ***{published data only}***
Ohta Y. Antibacterial activity of plastic restorative materials. *Shikwa Gakuho* 1984;**84**(1):83–8.

Additional references

Brunthaler 2003
Brunthaler A, König F, Lucas T, Sperr W, Schedle A. Longevity of direct resin composite restorations in posterior teeth. *Clinical Oral Investigations* 2003;**7**(2):63–70.

Egger 1997
Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997;**315**(7109):629–34.

Hickel 2007
Hickel R, Roulet JF, Bayne S, Heintze SD, Mjör IA, Peters M, et al.Recommendations for conducting controlled clinical studies of dental restorative materials. *Clinical Oral Investigations* 2007;**11**(1):5–33.

Higgins 2003
Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003;**327** (7414):557–60.

Higgins 2008
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Imazato 2003
Imazato S. Antibacterial properties of resin composites and dentin bonding systems. *Dental Materials* 2003;**19**(6): 449–57.

Kidd 2004
Kidd EA, Fejerskov O. What constitutes dental caries? Histopathology of carious enamel and dentin related to the action of cariogenic biofilms. *Journal of Dental Research* 2004;**83 Spec No C**:C35–8.

Marsh 2006
Marsh PD. Dental plaque as a biofilm and a microbial community - implications for health and disease. *BMC Oral Health* 2006;**6 Suppl 1**:S14.

Mjör 2005
Mjör IA. Clinical diagnosis of recurrent caries. *Journal of the American Dental Association* 2005;**136**(10):1426–33.

Opdam 2007
Opdam NJ, Bronkhorst EM, Roeters JM, Loomans BA. A retrospective clinical study on longevity of posterior composite and amalgam restorations. *Dental Materials* 2007;**23**(1):2–8.

RevMan 2008
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Selwitz 2007
Selwitz RH, Ismail AI, Pitts NB. Dental caries. *Lancet* 2007;**369**(9555):51–9.

Thomas 2007
Thomas RZ, Ruben JL, ten Bosch JJ, Fidler V, Huysmans MC. Approximal secondary caries lesion progression, a 20-week in situ study. *Caries Research* 2007;**41**(5):399–405.

Wiegand 2007
Wiegand A, Buchalla W, Attin T. Review on fluoride-releasing restorative materials--fluoride release and uptake characteristics, antibacterial activity and influence on caries formation. *Dental Materials* 2007;**23**(3):343–62.

* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Ergucu 2007	Non-RCT and both groups received antibacterial bonding agent
Ohta 1984	Non-RCT in vitro study. In Japanese translated by Ken Yaegaki

RCT = randomised controlled trial.

DATA AND ANALYSES

This review has no analyses.

APPENDICES

Appendix 1. MEDLINE (OVID) search strategy

1. DENTAL RESTORATION, PERMANENT/
2. DENTAL CAVITY PREPARATION/
3. ((dental or tooth or teeth) and (fill$ or restor$ or "cavity preparation$")).mp.
4. or/1-3
5. exp COMPOSITE RESINS/
6. (composite$ or Bisphenol A-Glycidyl Methacrylate or compomer$).mp.
7. or/5-6
8. exp ANTI-BACTERIAL AGENTS/
9. (antibacterial$ or anti-bacterial$ or antimicrob$ or anti-microb$ or "12-methacryloyloxydodecylpyridinium bromide$").mp.
10. or/8-9
11. 4 and 7 and 10

Appendix 2. Cochrane Oral Health Group's Trials Register search strategy

((fill* or restor*) and (composite* or componer*) and (antibacterial* or anti-bacterial* or antimicrob* or anti-microb*))

Appendix 3. CENTRAL search strategy

#1 DENTAL RESTORATION, PERMANENT
#2 DENTAL CAVITY PREPARATION
#3 ((dental* or tooth or teeth) and (fill* or "cavity preparation*"))
#4 (#1 or #2 or #3)
#5 COMPOSITE RESINS explode all trees
#6 (composite* or "Bisphenol A-Glycidyl Methacrylate" or compomer*)
#7 (#5 or #6)
#8 ANTI-BACTERIAL AGENTS explode all trees
#9 (antibacterial* or anti-bacterial* or antimicrob* or anti-microb* or
"12-methacryloyloxydodecylpyridinium bromide*")
#10 (#8 or #9)
#11 (#4 and #7 and #10)

Appendix 4. EMBASE (OVID) search strategy

1. DENTAL RESTORATION, PERMANENT/
2. DENTAL CAVITY PREPARATION/
3. ((dental or tooth or teeth) and (fill$ or restor$ or "cavity preparation$")).mp.
4. or/1-3
5. exp COMPOSITE RESINS/
6. (composite$ or Bisphenol A-Glycidyl Methacrylate or compomer$).mp.
7. or/5-6
8. exp ANTI-BACTERIAL AGENTS/
9. (antibacterial$ or anti-bacterial$ or antimicrob$ or anti-microb$ or "12-methacryloyloxydodecylpyridinium bromide$").mp.
10. or/8-9
11. 4 and 7 and 10

HISTORY

Protocol first published: Issue 2, 2009

Review first published: Issue 3, 2009

CONTRIBUTIONS OF AUTHORS

Tatiana Pereira-Cenci (TPC), Maximiliano Sergio Cenci (MSC), Melissa Marchesan (MM) and Zbys Fedorowicz (ZF) were responsible for: organising the retrieval of papers, writing to authors of papers for additional information, screening search results, screening retrieved papers against inclusion criteria, appraising the quality of papers, data collection for the review, extracting data from papers and obtaining and screening data on unpublished studies.

TPC and MSC were going to enter the data into RevMan.

MSC was responsible for analysis and interpretation of the data.

All review authors contributed to writing the review.

TPC, MSC and ZF were responsible for designing and co-ordinating the review, and data management for the review.

TPC and MSC conceived the idea for the review and are the guarantors for the review.

DECLARATIONS OF INTEREST

There are no financial conflicts of interest and the review authors declare that they do not have any associations with any parties who may have vested interests in the results of this review.

INDEX TERMS

Medical Subject Headings (MeSH)

*Dental Restoration, Permanent; Anti-Bacterial Agents [*therapeutic use]; Composite Resins [*therapeutic use]; Dental Caries [*prevention & control]

MeSH check words

Humans