

Clinical trials with nanoparticle composite in posterior teeth: a systematic literature review

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Abstract

Aim: The aim of this article is to evaluate clinical trials with nanoparticle composite in posterior teeth through a systematic review of the literature. **Methods:** This analysis includes controlled clinical trials with nanoparticle composites, with at least 6 months of evaluation, published in the English language between 1997 and 2009. In vitro and retrospective studies and studies on anterior teeth were excluded. Articles were retrieved from the following full-text electronic journal databases: MEDLINE, LILACS and The Cochrane Library. **Results:** The largest number of articles was found in the MEDLINE database, but only 4 of them met the inclusion and exclusion criteria. No articles were found in the LILACS database; only two articles were selected from The Cochrane Library databases and they coincided with those already included in MEDLINE. **Conclusions:** The nanoparticle composites give a satisfactory performance for use in posterior teeth for at least 2 years of functional activity, but their performance was not superior to that of the other composites. Long-term studies must be conducted to evaluate the performance after 2 years of functional activity. New controlled and randomized clinical trials are necessary.

Keywords: controlled clinical trials, composite resins

Introduction

Restorative composites have undergone continuous improvement in dental practice for over 40 years, since Bowen¹ incorporated inorganic particles into a resinous matrix. Composites comprise a blend of hard, inorganic particles bound together by a soft, resin matrix, and generally encompass three main components: (1) the resin matrix comprising: (i) a monomer system, (ii) an initiator system for free radical polymerization, and (iii) stabilizers to maximize the storage stability of the uncured composite resin and the chemical stability of the cured composite resin; (2) the inorganic filler consisting of particulates such as glass, quartz, and/or fused silica; and (3) the coupling agent, usually an organo-silane, that chemically bonds the reinforcing filler to the resin matrix².

The first formulations contained large load particles of up to 150 μm (macrofilled composites), and had several unsatisfactory physical and mechanical properties³. Investigations conducted in the 1970s and early 1980s concluded that the properties of macrofilled composites, particularly wear, color stability and marginal leakage, were clinically unacceptable for posterior teeth. Research indicated that the inorganic content, geometry and load particle dimensions greatly influenced the final properties of the material⁴⁻⁵.

During the last few decades, new composite formulations have appeared and the mean size of the particles has been drastically reduced. Sub-micrometric particles have been used to

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improve the physical and mechanical properties, namely reduction of the linear thermal expansion coefficient, greater dimensional stability and greater resistance to abrasion and wear^{3,6-7}.

Microfilled composites with a mean filler particle size of 0.04 μm maintain the gloss produced after polishing. Unfortunately, because of their low tensile strength and fracture toughness, microfilled composites are contraindicated for class IV and stress-bearing restorations⁸⁻⁹.

Hybrid composites are materials that contain a blend of pre-polymerized and inorganic fillers. Microhybrid composite has been successful to replace missing tooth structure even though hybrids are less polishable than microfilled composite; they have excellent mechanical properties¹⁰⁻¹¹. According to Peutzfeldt², and Walker and Burgess¹⁰, most improvements in the properties of composites are due to the changes in the inorganic particles.

These aspects have encouraged the use of various nanometric particles in resin-based materials. Nanotechnology, also known as molecular nanotechnology or molecular engineering, is the production of functional materials and structures in the range of 0.1 to 100 nm (the nanoscale) by various physical or chemical methods¹². The use of nanoparticles is useful for many applications including industry, transport, packaging, high-performance coatings, electronics, biomedical, where nanoparticles improve the mechanical properties of materials. In dentistry, posterior class I or II restorations require composites with high mechanical properties; anterior restorations need composites with superior esthetics. The composite resin that meets all the requirements of both posterior and anterior restorations has not yet emerged¹³.

Therefore, nanotechnology is of great interest in composite resin research¹³. The nanocomposite contains a unique combination of two types of nanofillers (5–75 nm) and nanoclusters. Nanoparticles are discrete nonagglomerated and nonaggregated particles of 20–75 nm in size. Nanocluster fillers are loosely bound agglomerates of nano-sized particles. The agglomerates act as a single unit enabling high filler loading and high strength. Due to the reduced dimension of the particles and the wide size distribution, an increased filler load can be achieved with the consequence of reducing polymerization shrinkage and increasing the mechanical properties, such as tensile strength and compressive strength to fracture. These seem to be equivalent or even sometimes higher than those of hybrid composites and significantly higher than microfilled composites. As a consequence, manufacturers now recommend the use of nanocomposites for both anterior and posterior restorations^{11,13-15}.

There are also composites on the market which are not exclusively nanoparticles, but contain nanometric and micrometric particles, and this has led to better performance. These materials are considered the precursors of nanoparticle composites and some refer to them as nanohybrids¹³.

Within the context of nanotechnology, the aim of this study was to analyze, by means of a systemic review of the literature, studies that conducted clinical trials with nanoparticle composite in posterior teeth in order to verify the performance of these composites in real conditions.

Material and methods

The systematic review of the literature was conducted using the

following full-text electronic journal databases: MEDLINE (International Literature in Health Sciences), LILACS (Latin American and Caribbean Literature in Health Sciences) and The Cochrane Library.

For inclusion in this review, an article had to meet the following specifications: it should be a controlled clinical trial investigating nanoparticle composite in posterior teeth, with at least 6 months of evaluation, published in the English language between 1997 and 2009. Articles with the following characteristics were excluded: *in vitro* studies, retrospective studies and studies on anterior teeth.

The search strategy for the MEDLINE and LILACS databases was: nanofiller or (nanocomposite) or (nanofill) or (nanofilled) [Words] and "CLINICAL TRIAL" or "CONTROLLED CLINICAL TRIAL" or "CLINICAL TRIAL PHASE I" or "CLINICAL TRIAL PHASE II" or "CLINICAL TRIAL PHASE III" or "CLINICAL TRIAL PHASE IV" or "RANDOMIZED CONTROLLED TRIAL" or "MULTICENTER STUDY" or "EVALUATION STUDIES" [Publication type] and "ENGLISH" [language].

In The Cochrane Library, the search was conducted as follows: nanofiller or (nanocomposite) or (nanofill) or (nanofilled).

After application of the search strategy, two examiners reviewed the titles and abstracts of the articles and performed the selection by consensus. With the objective of complementing the database searches, non-automated manual searches were also conducted on the References within the selected articles.

Results and Discussion

Nanoparticle composites were developed with the aim of combining high mechanical properties and maximum polishing. Laboratory tests provide useful information on material performance and its manipulation characteristics, but they cannot provide answers about its clinical longevity. Only controlled and randomized clinical trials can provide conclusions on the use of composites¹⁶.

After application of the search strategy, 79 articles were found in the MEDLINE database, but only four of them met the pre-established criteria; no studies were found in LILACS. Thirteen articles were found in The Cochrane Library, but only two met the inclusion criteria, and these coincided with those selected from MEDLINE database. The searches conducted from within the references of the selected articles yielded no additional articles fulfilling the inclusion requirements. Table 1 explains the objectives, methodology, results and conclusions of the selected articles.

Although controlled and randomized clinical trials have a reference pattern, only controlled clinical trials were included in this review, except for Dresch et al.¹⁷ who indicated that randomization was used and explained how it was accomplished.

With regard to the sample size, all articles included at least 30 restorations *per* group, which is considered as a satisfactory number. In the study by Ernst et al.¹⁸, a split mouth design was used and 56 restorations were performed in each group, but the total number of subjects was 50 because some individuals received more than one restoration *per* group. This contradicts the recommendations of Hickel et al.¹⁹ who affirmed that each research subject must have, at most, one sample unit *per* group. In the research by Efes et al.¹⁶ each patient received only one restoration, but the ideal condition of all the groups in the same mouth was not followed. Dresch et al.¹⁷ designed 4 groups in the same patient, giving a total of 148 restorations and 37 *per*

Table 1 – Title, author, year, aims, methodology, results and conclusion of articles

Title (author, year)	Aims	Methodology	Results and conclusions
Clinical evaluation of a nanofilled composite in posterior teeth: 12-month results (Dresch et al., 2006) ¹⁷	To compare the clinical performance of a nanoparticle composite with two microhybrid composite and one compactable composite in posterior restorations after 12 months	Thirty-seven patients with at least four class I or II cavities and with normal occlusion were selected. A total of 148 restorations were performed, 25% of each material (Filtek Supreme/3M ESPE, St Paul, MN, USA; Pyramid/Bisco, Schaumburg, IL, USA; Esthet-X/Dentsply, Konstanz, Germany or Tetric Ceram/Ivoclar-Vivadent, Bredenerstrasse Liechtenstein, Germany). Two calibrated operators performed the treatment, in accordance with the manufacturer's instructions. The adhesive systems used were from the same manufacturers as the resin, and in the case of deep cavities, calcium hydroxide cement and/or glass ionomer cement was applied. Finishing and polishing were done 1 week later. Two independent examiners assessed the restorations at baseline and 12 months later according to the United States Public Health Service (USPHS) modified criteria	All the patients were assessed 12 months later. At baseline, post-operative sensitivity was observed in seven restorations, which disappeared at the 12-month evaluation. No secondary caries, marginal discoloration or lack of retention was observed after 1 year. Color match and marginal adaptation were the items that received the highest number of Bravo scores (11 and 12, respectively). Only four restorations were classified as Bravo in the anatomic form item. Six restorations showed poor surface texture after 12 months. No statistically significant difference was observed between materials, and their performance at baseline and after 1 year was statistically similar. The authors concluded that the Filtek Supreme, Pyramid, Esthet-X and Tetric Ceram composites exhibited excellent clinical performance after 1 year
Clinical evaluation of an ormocer, a nanofill composite and a hybrid composite at 2 years (Efes et al., 2006)	During a period of 2 years evaluate the clinical performance of an ormocer, a nanoparticle composite, and as control, a hybrid composite, in small class I cavities in permanent molars	Ninety class I cavities were prepared in 90 patients, who had primary caries. The teeth were restored incrementally, in oblique layers with ormocer (Admira/VOCO, Cuxhaven, Germany), nanoparticle (Filtek Supreme/3M ESPE) or hybrid (Renew/Bisco) composite by a single operator. The restorations were examined using the Ryge criteria (USPHS modified) at baseline, after 6 months, 1 year and 2 years	At the follow-up examinations, 100%, 100%, and 97% of 90 restorations were evaluated at 6 months, 1 year and 2 years, respectively. The scores for all the performance criteria were either Alpha or Bravo. None of the restorative materials presented secondary caries or postoperative sensitivity at 6 months, 1 year or 2 years. After 2 years, there were no clinically unacceptable criteria, except in one Admira restoration (ormocer) which failed. According to the cavosurface marginal discoloration and the surface texture criteria, there were no significant differences between the restorative materials. The marginal adaptation rate was 100% for the nanofill composite and hybrid composite and 97% for the ormocer at both 1 and 2 years. There were no significant differences between the restorative materials. The composites studied resulted in high clinical performance after 2 years
Two-year clinical evaluation of ormocer, nanohybrid and nanofill composite restorative systems in posterior teeth (Mahmoud et al., 2008) ²⁰	To evaluate and compare the 2-year clinical performance of an ormocer, a nanohybrid, and a nanofill resin composite with that of a conventional microhybrid composite in restorations of small occlusal cavities made in posterior teeth	Forty dental students from the Faculty of Dentistry at Mansoura University were enrolled in this study. The criteria for their inclusion were the presence of primary caries or replacement of existing amalgam for esthetic reasons. Each patient received at least 4 occlusal restorations. A total of 140 restorations was carried out, 25% for each material: ormocer-based, Admira (Voco); a nanohybrid resin composite, Tetric EvoCeram (Ivoclar-Vivadent); a nanofill resin composite, Filtek Supreme (3M ESPE); and a microhybrid resin composite, Tetric Ceram (Ivoclar-Vivadent). Two operators carried out all restorations according to the manufacturers' instructions. Two independent examiners made all evaluations according to the USPHS-modified Ryge criteria immediately after placement of restorations and after 6 months, 1 year and 2 years	All patients attended the 2-year recall visit. The scores for all the performance criteria were either Alpha or Bravo. Only one ormocer and one microhybrid composite restoration had failed after 2 years. The color match of 13 microhybrid composite restorations was scored as Bravo at the baseline examination. This criterion did not change during the 2-year period. Regarding clinical performance, there were no statistically significant differences among the materials used. After 2 years, the ormocer, nanohybrid, and nanofill composites showed acceptable clinical performance similar to that of the microhybrid resin composite

group. Mahmoud et al.²⁰ placed 140 restorations, 35 for each restorative composite, with each patient receiving at least 4 occlusal restorations.

The studies addressed here were not unanimous with regard to the type of adhesive system used. The manufacturers of the composites recommend the use of an adhesive system from the same manufacturer. This rule was followed by Efes et al.¹⁶, Dresch et al.¹⁷ and Mahmoud et al.²⁰. However, Ernst et al.¹⁸ decided to vary only the composite and used the same adhesive for both groups. They reported that the influence of the adhesive on the result of the clinical studies can first be seen in marginal discoloration or in the presence of open margins. These aspects were not verified in this study, which corroborates the clinical evidence that composite performance might not be compromised when used with an adhesive other than the one recommended.

All restorations were assessed blindly, since the examiners did not know the restorative material. Agreement among the examiners was high in all the articles (≥ 0.87).

The experimental designs of the three studies had some differences, shown in Table 2, but these particularities did not result in distinct outcomes among the articles.

The restorations of the articles selected were evaluated by the Modified USPHS (United States Public Health Service) criteria, which is a long-established method used in clinical trials. The criteria

evaluated in common in the 4 articles were color match, retention, marginal adaptation, anatomic form, surface roughness, marginal staining, sensibility and secondary caries. The restorations were classified in Alpha, Bravo, Charlie and Delta. Alpha and Bravo scores mean excellent and clinically acceptable results, while Charlie and Delta scores mean clinically not acceptable, an indication to replace the restoration to prevent future damage or to repair present damage¹⁸.

In the research by Dresch et al.¹⁷, no differences were found between the nanoparticle composite, Filtek Supreme, the compactable Pyramid and two microhybrids (Esthet-X and Tetric Ceram) for the study periods. The majority of the scores were Alpha and Bravo, that is, all the materials exhibited excellent clinical performance after 1 year. No restorations failed. Efes et al.¹⁶ ratified these results as they reported that the scores for color match, marginal discoloration, anatomical form, marginal adaptation and surface texture for all the restorative materials, changed from Alpha to Bravo at most. For the retention criteria, except for one Admira (ormocer) restoration considered clinically unacceptable (score Delta, restoration was partially or totally missing); all the others were Alpha. There was no secondary caries, or postoperative sensitivity in the patients assessed. Consequently, Admira Filtek Supreme (nanoparticle) and Renew (hybrid) resulted in high clinical performance after 2 years.

Table 2 – Particular characteristics of the selected articles.

Study	Number of professionals who performed the restorations	Sample per group	Total number of restorations	Reason for performing the restoration	Patient age	Isolation	Type of cavity	Adhesive system	Pulp capping	Follow-up period	Final return rate (%)	Number of failures with nanofill composite
Dresch et al., 2006 ¹⁷	2	37	148	The majority was replacement of existing amalgam for esthetic reasons	Not given	Rubber dam	Classes I and II	One per group, from the same composite manufacturer	Adhesive system (AS). In deep cavities: calcium hydroxide and/or glass ionomer cement before the adhesive system	1 year	100	0
Efes et al., 2006 ¹⁶	1	30	90	Primary caries	18–48 years	Cotton rolls and suction	Class I minimally invasive	One per group, from the same composite manufacturer	Adhesive system	2 years	97	0
Ernst et al., 2006 ¹⁸	6	56	112	Primary caries or deficient restoration	Mean 35.7 years (SD 11.3)	Rubber dam	Class II	One for all the groups	Adhesive system	2 years	100	1
Mahmoud et al., 2008 ²⁰	2	35		Primary caries or replacement of existing amalgam for esthetic reasons	Not given	Cotton rolls and suction	Class I	One per group, from the same composite manufacturer	Adhesive system. In cavities extending for more than 2mm into the dentin, a glass-ionomer cement before AS	2 years	100	0

In the study of Ernst et al.¹⁸, the two composites used (Tetric Ceram-hybrid (fine particles) and Filtek Supreme (nanoparticles) gave acceptable clinical performance at the end of 2 years. According to the USPHS criteria, global clinical success (Alpha and Bravo scores) was 98%. With regard to color match, good performance was 95% for the nanoparticle composite and 98% for the hybrid. Two fractures of restorations were observed within the observation period of 2 years: one chipping fracture (cohesive-type fracture) of a distal marginal ridge in a Filtek Supreme restoration placed in a mandibular molar and one bulk fracture in the mesial part of a Tetric Ceram restoration placed in a mandibular premolar.

The study by Mahmoud et al.²⁰ also corroborates the findings of the articles mentioned above. The scores for all the performance criteria were either Alpha or Bravo. Only one ormocer and one microhybrid composite restoration had failed after 2 years, showing secondary caries.

Although all the articles included in this review obtained good results, the authors¹⁶⁻¹⁸ warned about the need for longitudinal follow-up studies in order to obtain long-term answers about this new type of composite because the trials described were of short duration. Notwithstanding the fact that all the articles included in this review were, in general, well designed, there is the need for additional controlled and randomized clinical trials that could shed light on some of the questions still not completely resolved.

The following conclusions may be drawn: The performance of nanoparticle composites is satisfactory for use in posterior teeth for at least 2 years of functional activity; Nanoparticle composites can be used in posterior teeth, although their performance was not superior to that of the other composites studied; Longer-term studies must be conducted to evaluate performances after 2 years of functional activity; New controlled and randomized clinical trials are necessary to further evaluate some of the issues and questions that have not been fully addressed by current studies.

References

- Bowen RL. Properties of a silica-reinforced polymer for dental restorations. *J Am Dent Assoc.* 1963; 66: 57-64.
- Peutzfeldt A. Resin composites in dentistry: the monomer systems. *Eur J Oral Sci.* 1997; 105: 97-116.
- Leinfelder KF. Posterior composite resin: the materials and their clinical performance. *J Am Dent Assoc.* 1995; 126: 663-76.
- Adabo GL, Cruz CAS, Fonseca RG, Vaz LG. The volumetric fraction of inorganic particles and the flexural strength of composites for posterior teeth. *J Dent.* 2003; 31: 353-9.
- Willems G, Lambrechts P, Braem M, Celis JP, Vanherle G. A classification of dental composites according to their morphological and mechanical characteristics. *Dent Mater.* 1992; 8: 310-9.
- Bryant RW. Direct posterior composite resin restorations: a review 1—factors influencing case selection. *Aust Dent J.* 1992; 37: 81-7.
- Lu H, Lee YK, Oguri M, Powers JM. Properties of a dental resin composite with a spherical inorganic filler. *Oper Dent.* 2006; 31: 734-40.
- Lambrechts P, Ameye C, Vanherle G. Conventional and microfilled composite resins. Part II. Chip fractures. *J Prosthet Dent.* 1982; 48: 527-38.
- Fortin D, Vargas MA. The spectrum of composites: new techniques and materials. *J Am Dent Assoc.* 2000; 131: 265-305.
- Walker R, Burgess JO. Comparing resin-based composites. *Compend Contin Educ Dent.* 2004; 25: 424-35.
- Mitra SB, Wu D, Holmes BN. An application of nanotechnology in advanced dental materials. *J Am Dent Assoc.* 2003; 134: 1382-90.
- Kirk RE, Othmer DF, Kroschwitz J, Howe-Grant M. *Encyclopedia of chemical technology.* 4th ed. New York: Wiley; 1991. p.397.
- Beun S, Glorieux T, Devaux J, Vreven J, Leloup G. Characterization of nanofilled compared to universal and microfilled composites. *Dent Mater.* 2007; 23: 51-9.
- Condon JR, Ferracane JL. Reduced polymerization stress through non-bonded nanofiller particles. *Biomaterials.* 2002; 23: 3807-15.
- Yap AUJ, Yap SH, Teo CK, Ng JJ. Comparison of surface finish of new aesthetic restorative materials. *Oper Dent.* 2004; 29: 100-4.
- Efes BG, Dörter C, Gömeç Y. Clinical evaluation of an ormocer, a nanofill composite and a hybrid composite at 2 years. *Am J Dent.* 2006; 19: 236-40.
- Dresch W, Volpato S, Gomes JC, Ribeiro NR, Reis A, Loguercio AD. Clinical evaluation of a nanofilled composite in posterior teeth: 12-month results. *Oper Dent.* 2006; 31: 409-17.
- Ernst CP, Brandenbusch M, Meyer G, Canbek K, Gottschalk F, Willershausen B. Two-year clinical performance of a nanofiller vs a fine-particle hybrid resin composite. *Clin Oral Investig.* 2006; 10: 119-25.
- Hickel R, Roulet JF, Bayne S, Heintze SD, Mjör IA, Peters M et al. Recommendations for conducting controlled clinical studies of dental restorative materials. *Clin Oral Investig.* 2007; 11: 5-33.
- Mahmoud SH, El-Embaby AE, AbdAllah AM, Hamama HH. Two-year clinical evaluation of ormocer, nanohybrid and nanofill composite restorative systems in posterior teeth. *J Adhes Dent.* 2008; 10: 315-22.