A Systematic Review of the Effectiveness of Anticalculus Dentifrices

Gopalakrishnan S. Netuveli[a]/Aubrey Sheiham[a]

Purpose: To assess the evidence on the effectiveness of commercially available anticalculus dentifrices.

Materials and Methods: Systematic search for published and unpublished epidemiological data in 7 electronic databases, 5 journals, and the bibliographies of retrieved papers and by making contact with subject experts in this field. Thirty-two reports were identified containing comparisons of one or more active agents with a placebo dentifrice and calculus measured using the Volpe-Manhold Index (VMI).

Results: Random effect model for 3-month studies showed an effect size of –0.6 for all comparisons. The effect sizes varied from –0.3 for dentifrices with zinc chloride 0.5% to –1.1 for pyrophosphate 1.3% and copolymer 1.5% dentifrices. Meta-analysis of all the studies with 6-month follow-up gave an effect size of –1.1 (–1.5 to –0.8) and for 12-month follow-up the effect size was –13.6 (–21.4 to –5.8).

Conclusions: Anticalculus dentifrices containing pyrophosphates, zinc compounds and/or co-polymers were effective in significantly reducing calculus scores (VMI).

Key words: calculus, anti-calculus, dentifrices, pyrophosphate, zinc citrate, co-polymer, toothpaste, systematic review

Oral Health Prev Dent 2004; 2: 49–58. Submitted for publication: 19.05.03; accepted for publication: 18.11.03.

Dental calculus is ubiquitous in humans (Kornman and Löe, 1993). According to the data in the majority of the studies reported in the WHO Global Dental Health Data Bank, over 90% of adults had calculus requiring dental hygiene instruction and professional calculus removal (Miyazaki et al, 1991a,b; Pilot et al, 1992). The cost of professional calculus removal would be beyond the national resources for oral health of most low-income countries (Manji and Sheiham, 1986).

In the early 1960s, when dentifrices containing agents supposed to reduce supra-gingival calculus were reviewed, they were hailed as agents with great public health significance to meet the unmet periodontal needs of an expanding, ageing population (Weinstein and Mandel,1964). Although a wide spectrum of agents, ranging from industrial solvents to enzymes have been tried, the most successful strategy in controlling calculus has been preventing plaque mineralization and most popular anticalculus systems have been those based on zinc or pyrophosphates (Mandel, 1995). The market shares of these dentifrices are increasing (Market Intelligence, 1998).

Since the review by Weinstein and Mandel (1964), many narrative reviews of anticalculus dentifrices have appeared (Stookey et al, 1989; Volpe et al, 1992; Adams, 1995; Sanz, 1996; White, 1997; Davies et al, 1997; Fairbrother and Heasman, 2000). However, a systematic study of their effectiveness is yet to be undertaken. The aim of the present study was to conduct a systematic review to assess the effectiveness of commercially available anticalculus dentifrices.

[a] *Department of Epidemiology and Public Health, University College London Medical School, London, UK.*

Reprint requests: *Professor Aubrey Sheiham, Department of Epidemiology and Public Health, University College London Medical School, 1-19 Torrington Place, London WC1E 6BT, UK. Tel: +44 20 7679 1700. Fax: +44 20 7813 0280. E-mail: a.sheiham@ucl.ac.uk*

METHODS

The search period of interest was from 1966 to June 2002. We searched the following electronic databases for published reports: MEDLINE, EMBASE, CINAHL, PSYCHInfo, PREMEDLINE and HEALTHSTAR. A broad search strategy was deliberately employed in order to maximize the sensitivity of the searches. Using Medical Subject Headings (MeSH) and text words we searched for the following terms: 'anti?calculus' OR 'tartar control' OR 'tooth?paste' OR 'dentifrice' OR 'dental-calculus-prevention- and-control' OR 'pyrophosphates' OR 'zinc citrate'. Standard filters for identifying randomized controlled trials were applied to this search (Dickersin et al, 1994). The review articles and cross references in the trial reports were used to identify more studies. An on-line database of the United States Patent and Trademark Office (http://patents.uspto.gov last accessed July 2003) was searched for further unpublished studies. An advanced search of the Collaboration's trial register CENTRAL was also undertaken. The Journal of Periodontology, Journal of Clinical Periodontology, Clinical Preventive Dentistry, American Journal of Dentistry and Journal of Clinical Dentistry were identified as those most likely to have reports of anticalculus dentifrice trials and were hand searched. Bibliographies of all retrieved papers were scrutinized and authors of relevant papers were contacted in order to identify additional studies.

Study Selection and Appraisal

Both authors reviewed titles and abstracts to identify all potentially eligible RCTs and full text versions of these articles were obtained. Inclusion of studies was decided jointly by the authors, who included those parallel, randomized controlled trials of minimum 3-months duration that tested agents present in commercial dentifrices currently available in the market (pyrophosphates, zinc salts, PVM/MA copolymer and citroxan) with a placebo dentifrice. Our primary outcome measure was Volpe-Manhold index of dental calculus (Volpe et al, 1965). We excluded studies without a placebo control, using different outcome measures with insufficient number of participants, duration and information necessary for meta-analysis.

Quality assessment in this study was done by checking whether the study had acceptable standards in design, analysis, conduct (ethical considerations) and reporting. Acceptable standards included factors such as: specification of minimum significant difference from placebo group, sample size determination, unit of randomization, method of allocation generation, allocation concealment, masking of patient, similarity between placebo and test dentifrices, masking of examiner, treatment of attrition and dropouts, statistical methods, ethical considerations including informed consent and a statement of conflict of interests. Acceptable standards in reporting were judged by whether the report included statements regarding the features described above and whether the report revealed evidence about those statements. A source for this list was the CONSORT descriptor criteria (Moher et al, 2001). Both authors jointly decided the quality of the study. When clarifications regarding their study was required, we contacted the first authors of the papers.

Statistical Methods

For each study the effect size was calculated according to the method of Cohen (1988). Meta-analyses of effect sizes were undertaken using random effects models based on DerSimonian and Laird (1986). The statistical package used for meta-analysis was STATA. Heterogeneity of the studies was measured as the weighted sum of the square of the deviation of study means from the pooled mean (called Q), which has a Chi-squared distribution with degree of freedom equal to one less than number of studies. Both graphical (Light and Pillemer, 1984) and statistical methods (Begg and Mazumdar, 1994; Egger et al, 1997) were used to test for publication bias.

RESULTS

Search Results

The searches yielded 2,807 hits containing terms related to anticalculus toothpastes, which was reduced to 86 when filters for randomized controlled trials were applied. After scrutinizing titles and abstracts, 46 were chosen for full paper retrieval. Of these 31 were finally included in the study.

Table 1 Details of included studies

ID	Author	Year	Duration (months)	Country	Agents	Number of participants*
1	Schiff	1987a	3	USA	Pyrophosphates 3.3%, Pyrophosphates 1.3% & copolymer 1.5%	40, 39, 39
2	Rosling and Lindhe	1987	6	Sweden	Pyrophosphates 3.3%, Pyrophosphates 1.3% & copolymer 1.5%	49, 48, 48
3	Rustogi et al	1991	12	Thailand	Pyrophosphates 1.3% & copolymer 1.5%	62, 62
4	Triratana et al	1991	12	Thailand	Pyrophosphates 3.3% & copolymer 1.0%	54, 54
5	Triratana, Rustogi and Volpe	1991	12	Thailand	Pyrophosphates 1.3% & copolymer 1.5%	58, 58
6	Lobene	1987a	3	USA	Pyrophosphates 1.3% & copolymer 1.5%, Zinc citrate 0.5%	70, 70, 70
7	Petrone et al	1991	3	USA	Pyrophosphates 5.0%, Pyrophosphates 1.3% & copolymer 1.5%	39, 39, 39
8	Lobene	1986	3	USA	Pyrophosphates 3.3%	60, 60
9	Lobene	1987b	3	USA	Pyrophosphates 3.3%	54, 53
10	Fairbrother et al	1997	4	UK	Pyrophosphates 5.0%, Zinc citrate 0.5%,	138, 135, 135
11	Lobene	1989	3	USA	Pyrophosphates 3.3%	56, 57
12	Segretto et al	1998	6	USA	Pyrophosphates 3.3%	129, 131
13	Sowinski et al	1998	3	USA	Zinc citrate 2.0%	38, 37
14	Kohut, Rubin and Baron	1989	3	USA	Pyrophosphates 1.3%	75, 75
15	Stephan et al	1990	6	UK	Zinc citrate 0.5%	50, 42
16	Svatun, Saxton, and Rolla	1990	6	Norway	Zinc citrate 0.5%	38, 40
17	Lobene et al	1987	6	USA	Zinc chloride	30, 27
18	Segretto et al	1991	3	USA	Zinc citrate 0.5%	486, 478
19	Svatun et al	1993	7	Norway	Pyrophosphates 5.0%, Zinc citrate 0.75%, Copolymer 2.0%	46, 48, 48
20	Lobene et al	1991	6	USA	Copolymer 2.0%	42, 37
21	Schiff	1987b	6	USA	Pyrophosphates 3.3%	60, 62
22	Kazmierczak et al	1990	6	USA	Pyrophosphates 3.3%, Zinc citrate 2.0%	63, 61, 61
23	Cohen et al	1994	3	USA	Pyrophosphates 1.3% & copolymer 1.5%	51, 64
24	White et al	1996	6	USA	Pyrophosphates 5.0%	112, 112
25	Singh et al	1990	3	USA	Pyrophosphates 1.3%	49, 47
26	Schiff et al	1990	6	USA	Pyrophosphates 1.3%	37, 38
27	Chikte, Rudolph, and Reinach	1992	3	South Africa	Pyrophosphates 3.3%	45,43
28	Katalin et al	1995	3	Hungary	Zinc citrate 0.75%, Copolymer 2.0%	37, 36
29	Baraya and Soto	1988	6	Colombia	Pyrophosphates 1.3%	30, 30
30	Hagiwara et al	1989	3	Japan	Pyrophosphates 5.0%, Polyphosphates	41, 45
31	Triratana et al	1991	3	Thailand	Pyrophosphates 1.3% & copolymer 1.5%, Zinc citrate 0.5%	50, 50

* Numbers for the placebo group and the agent groups respectively

Study Characteristics

The included studies spanned more than a decade from 1986 to 1998 and except for 3 studies (one each in Spanish, Hungarian and Japanese), all were in English language publications (Table 1). More than half of the studies were done in the USA and, among the remaining studies, 4 were done in Thailand, 5 in Europe, 1 in Japan and another in Colombia. All selected studies had more than 3-months follow-up and about half of them had multiple examinations, usually at 3 and 6 months.

Quality of Studies

There was only one study which reported sample size calculations and generation of schedule for allocating subjects and treatments (Fairbrother et al, 1997). Allocation concealment was adequately described in 4 studies (Fairbrother et al, 1997; Lobene, 1986; Lobene, 1989; Lobene et al, 1991), not mentioned in 3 (Rosling and Lindhe, 1987; Rustogi, Volpe and Petrone, 1988; Triratana et al, 1991) and indicated in others. Blinding of outcome was adequately described in 4 studies (Fairbrother et al, 1997; Lobene, 1986; Lobene, 1989; Lobene et al, 1991), not mentioned in 2 (Rosling and Lindhe, 1987; Schiff, 1987b) and indicated in others. Only 8 studies adequately described the masking of personnel and subjects (Fairbrother et al, 1997; Lobene, 1986; Lobene, 1989; Lobene et al, 1991; Rosling and Lindhe, 1987; Rustogi, Volpe and Petrone, 1988; Triratana et al, 1991; Triratana, Rustogi and Volpe, 1991), although other studies indicated that such masking was done.

We received a poor response to our queries from the authors that we contacted. Two authors responded, but could not elaborate further on what had already been published.

Heterogeneity

Statistically significant heterogeneity was present (3 months: Q = 215.6, df = 42, P = 0.000; 6 months: Q = 24967.1, df = 19, p = 0.000). In 3-month comparisons, heterogeneity became insignificant when stratified by active agents (Pyrophosphates 5.0%, Pyrophosphates 3.3% + Copolymer 1.0%, Zinc citrate 0.5%, Zinc citrate 2.0%).

Trials of 3-months Duration

There were 43 comparisons between a test dentifrice and placebo in trials of 3-months duration in 27 trial reports. Of these, 17 comparisons were for pyrophosphate dentifrices with concentrations of soluble pyrophosphates of 1.3% (4 studies), 3.3% (8 studies), and 5% (5 studies), and 10 comparisons involved combinations of pyrophosphates and copolymer with different concentrations, 5 studies with 1.3% pyrophosphate and 1.5% copolymer and 5 studies with 3.3% pyrophosphate and 1.0% copolymer. Ten studies involved zinc citrate in different concentrations of 0.5% (6 studies), 0.75% (2 studies), and 2.0% (2 studies). Copolymer (2%) alone was the active agent in 4 reports. One report each was available for polyphosphates and zinc chloride dentifrices.

For all studies the random effects model showed the effect size (d) to be 0.6. When groups were analyzed separately, the effect sizes for 8 groups were statistically significant. They were pyrophosphates 3.3%: –0.4 (95%CI –0.6 to –0.2); pyrophosphates 5.0%: –0.5 (95%CI –0.7 to –0.2); pyrophosphates 1.3% with copolymer 1.5%: –1.1 (95%CI –1.7 to –0.6); pyrophosphates 3.3% with copolymer 1.0%: –0.8 (95%CI –1.1 to –0.6); zinc citrate 0.5%: 0.3 (95%CI –0.5 to –0.1); zinc citrate 2.0%: –0.4 (95%CI –0.7 to –0.1); copolymer 2.0%: –0.8 (95%CI –1.5 to –0.2); and zinc chloride: –0.9 (95%CI –1.4 to –0.3) (Table 2).

Trials of 6-months Duration

There were 20 comparisons between a test dentifrice and placebo in trials of 6-months duration in 14 trial reports. Of these 9 comparisons were for pyrophosphate dentifrices, 5 were for zinc citrate formulations and 2 for copolymer dentifrices. Seventeen comparisons in 11 reports were follow-ups of 3-month trials.

Meta-analysis of all the studies with 6-month follow-up gave an effect size of –1.1 (95%CI –1.5 to –0.8) (Table 3). The numbers of studies in different subgroups were low and some groups had only one study each. All groups had statistically significant effect sizes.

Trials of 12-months Duration

There were only 3 studies included of 12-months duration (Rustogi et al, 1991; Triratana, Rustogi and Volpe, 1991; and Triratana et al, 1991). Two of them were with pyrophosphates 1.3% (effect size –16.2, 95%CI –37.7 to 5.3) and the third was with pyrophosphates 3.3% (effect size –11.7, 95%CI –13.8 to –9.7).

Testing for Publication Bias

Publication bias was tested in the series of studies of 3-month duration. The funnel plot of the inverse

Table 2 Meta-analysis of clinical trials of anticalculus dentifrices of 3-month duration

Agents	Number	Mean effect size (SD units)	95% Confidence limits	
			Lower	Upper
All*	43	– 0.6	– 0.7	– 0.4
Pyrophosphates 1.3%	4	– 0.3	– 0.6	0.1
Pyrophosphates 3.3%	8	– 0.4	– 0.6	– 0.2
Pyrophosphates 5.0%	5	– 0.5	– 0.7	– 0.2
Pyrophosphates 1.3% + Copolymer 1.5%	5	– 1.1	– 1.7	– 0.6
Pyrophosphates 3.3% + Copolymer 1.0%	5	– 0.8	– 1.1	– 0.6
Zinc citrate 0.5%	6	– 0.3	– 0.5	– 0.1
Zinc citrate 0.75%	2	– 0.9	– 2.8	0.9
Zinc citrate 2.0%	2	– 0.4	– 0.7	– 0.1
Copolymer 2.0%	4	– 0.8	– 1.5	– 0.2
Polyphosphates	1	– 0.3	– 0.7	0.2
Zinc chloride	1	– 0.9	– 1.4	– 0.3

* Represent 43 comparisons in 27 reports

Table 3 Meta-analysis of clinical trials of anticalculus dentifrices of 6-month duration

Agents	Number	Mean effect size (SD units)	95% Confidence limits	
			Lower	Upper
All*	20	– 0.6	– 1.1	– 1.5
Pyrophosphates 1.3%	2	– 0.3	– 3.6	– 10.8
Pyrophosphates 3.3%	4	– 0.4	– 0.6	– 1.0
Pyrophosphates 5.0%	3	– 0.5	– 0.4	– 0.6
Pyrophosphates 1.3% + Copolymer 1.5%	3	– 1.1	– 3.1	– 5.6
Pyrophosphates 3.3% + Copolymer 1.0%	1	– 0.8	– 0.7	– 1.1
Zinc citrate 0.5%	3	– 0.3	– 0.7	– 1.0
Zinc citrate 0.75%	1	– 0.9	– 0.8	– 1.2
Zinc citrate 2.0%	2	– 0.4	– 0.6	– 1.6
Copolymer 2.0%	1	– 0.8	– 2.9	– 3.8

* Represent 20 comparisons in 14 reports

of standard error of effect size against effect size was asymmetrical suggesting publication bias (Figure 1). Statistical tests (Begg and Majumdar, 1994; Egger et al, 1997) used to estimate the bias also showed statistically significant results when all 43 trials were considered together.

Adverse Effects

Of the 32 reports included in the systematic review, 20 reports reported on the absence of adverse effects. The other 11 reports did not mention whether adverse effects were present or not.

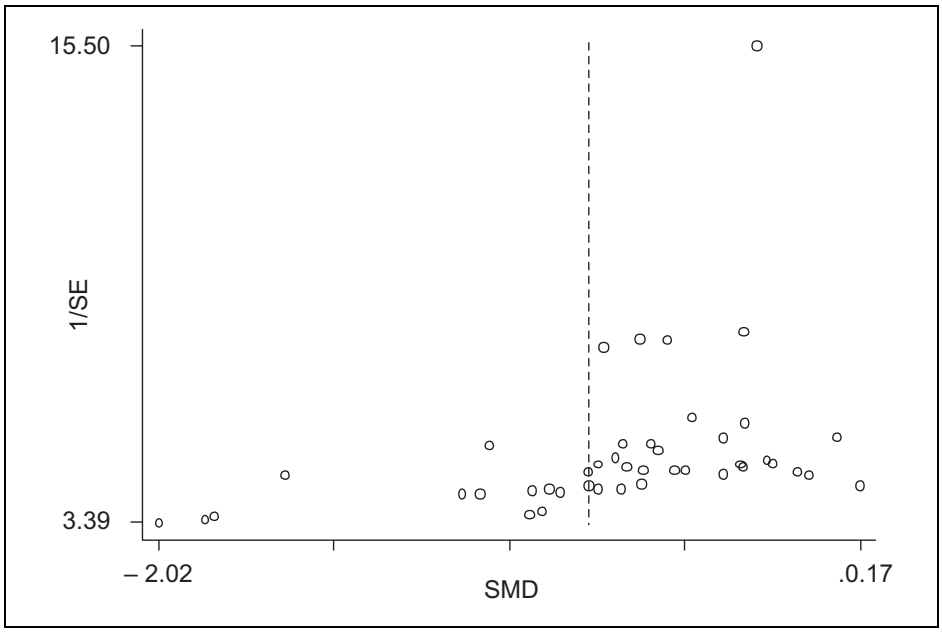

Fig 1 Funnel plot to detect publication bias in the 3-month studies selected for the systematic review of anticalculus dentifrices. SMD: Standardized Mean Difference of effect size. SE: Standard error of effect size.

Excluded Studies

15 studies that tested dentifrices containing the agents included in the review (pyrophosphates, zinc compounds, copolymer, and citroxan) but excluded for other reasons are described in Table 4.

DISCUSSION

This systematic review of anticalculus dentifrices indicated that they are effective in inhibiting calculus formation. However, anticalculus dentifrices can vary in their effectiveness depending on their active agents and their concentrations. The most effective anticalculus dentifrices were those containing pyrophosphates and PVM/MA copolymer with the best performance from the dentifrice with 1.3% pyrophosphates and 1.5% copolymer. The anticalculus dentifrices reduce calculus by 0.8 to 1.1 standard deviation units. Individually, pyrophosphates and copolymer did not do as well as zinc citrate. Again, the best combination had a lower concentration of pyrophosphates (1.3%) and higher concentration of the copolymer (1.5%). Copolymer by itself was better than pyrophosphates. Only 0.75% zinc citrate showed better anticalculus effect than copolymer. The results also showed that the effect fell off after a certain concentration of the agent, and, therefore, higher calculus reduction was not found at the highest concentration of the agent. The benefit of anticalculus dentifrices increased with duration of use.

Scope of the Review

The review was limited in scope to agents available in commercial dentifrices. The earliest attempts in calculus prevention were by trying to dissolve calculus, and were doomed to fail due to collateral damage to the dental tissues (Weinberg and Mandel 1964; Stookey et al, 1989; Mandel 1995). The advent of crystal growth inhibitors like pyrophosphates, zinc salts and polyvinyl ester and maleic acid could be considered to mark the real beginning of the anticalculus dentifrice age, which began about four decades ago. Therefore in specifying the research question, as postulated here, no loss has occurred in the general scope of the subject of anticalculus dentifrices. Recent narrative reviews also support this assertion.

Another limitation of the review is the limited number of long-term studies included. Volpe et al (1965) had shown that 3 months were sufficient for anticalculus clinical trials and described a study design for clinical trials of anticalculus dentifrices (Volpe et al, 1992), which has been followed by most investigators in this area.

Finally, we should mention the bias that could be introduced by not screening the study independently.

Table 4 Details of excluded studies

Study	Active Agents	Duration	Results, summary and reason for exclusion
Kranz et al (1991)	Citroxan	3 months	34% reduction against positive control, 51% against placebo. A double-blind parallel trial involving 128 subjects, half mouth scaling. Only point estimates reported. Excluded due to study design, lack of information.
van der Burgt and Klassen (1988)	Pyrophosphate	8 weeks	Pyrophosphate – 53% reduction in VMI (Phase 1) (significant). The study design was a cross over study involving 36 subjects divided equally between AB and BA groups. It was excluded because the results were presented without any information on treatment-period interaction and duration of study was only 8 weeks.
Kurbad et al (1991)	Pyrophosphate	12 weeks	Pyrophosphate – 25.5% reduction in VMI (significant). The study design was a crossover study involving 60 subjects divided equally between AB and BA groups. It was excluded because the results were presented jointly for both periods with out any information on treatment-period interaction.
Lu KH et al (1988)	Pyrophosphate (2 dentifrices, 3.3% vs. 5%)	4 months	5% paste – 14.5% reduction compared to 3.3% paste. A double-blind parallel trial involving 206 subjects, limited to a head to head comparison of two active agents. Comparison of effect on different levels of calculus formation at baseline given.
Sowinski J et al (1999)	Pyrophosphate (2 dentifrices, one of them contains copolymer)	12 weeks	Copolymer paste – 34.6% reduction compared to other (significant). A double-blind parallel trial involving 48 subjects, limited to a head to head comparison of two active agents.
Sowinski J et al (1998)	Pyrophosphate (2 dentifrices, one of them improved version of other)	12 weeks	Improved version – 44.1% reduction compared to other (significant). A double-blind parallel trial involving 73 subjects, limited to a head to head comparison of two active agents. Information supplied is insufficient to describe the improvement made and attribute it properly to the results.
Bollmer BW et al (1995)	Pyrophosphate 3.3%	6 months	Pyrophosphate – 21.8% (3 months, nonsignificant) 21.7% (6 months, significant) reduction in whole mouth VMI. A double-blind parallel trial involving 163 subjects. The subjects used chlorhexidine, known to promote calculus formation. Reported results were for adjusted mean whole mouth VMI with out mentioning SD or SE. Excluded because of presence of a calculus promoting agent, a condition different from other studies. Only study giving change in the number of teeth with calculus – 26% after 3 months and 20% after 6 months.
Taller SH (1990)	Pyrophosphate 3.3% (2 dentifrices)	4 months	Non-significant differences. The study had in sufficient number of subjects in each group (9 to 10), the VMI index score was nonstandard (included facial surfaces also).
Rustogi KN et al (1988)	Pyrophosphate, Zinc chloride	3 months	Pyrophosphate – 27.3% reduction in VMI (compared to zinc chloride, significant). 107 subjects participated in a two phase study. In the first phase they used a placebo dentifrice for 3 months and then was divided into two groups. In the second phase the subjects used the test dentifrices. Authors use the results of the first phase to compare test dentifrices to placebo. The results of second phase is limited to a head to head comparison of two active agents. Excluded due to study design.
Santos et al (1999)	Pyrophosphates (3.3% & 5%), Casein phosphopep tide	2 weeks	3.3% paste – 13%, 5% paste – 16%, CPP – 8% reductions. 3 double-blind randomized controlled trials using a toothshield to protect lower anterior teeth from brushing and delivering the dentifrice. Excluded due to the use of the experimental model. VMI presented for labial side also and showed greater reduction.
Sanz et al 1994	Zinc lactate	6 months	No difference from control group. A double-blind, stratified parallel study involving 208 people. The test dentifrice contained chlorhexidine. Calculus data presented graphically only. Excluded for the presence of calculus promoting agent, insufficient information.
Disney et al 1989	Zinc citrate 0.5%, 1%, 2% & 4%	1 week accumulation	No difference from control group for 0.5% group, modest differences in 1% & 2% group and large difference in 4% group (equivalent to positive control (pyrophosphate toothpaste). A double-blind clinical trial involving 12 to 16 subjects in 6 groups. Calculus assessment using mylar strips ligated to lingual of two lower central incisors. Excluded due to the study design and calculus outcome measure.
Taner et al 1990	Pyrophosphate	3 months	No significant differences. A study involving 35 subjects. Calculus outcome was Marginal line calculus Index. Excluded due to calculus outcome measure used and small number of subjects in each group.
Gaengler et al 1993	Pyrophosphate	3 months	25.5% reduction. A double-blind crossover study involving 60 subjects comparing a SEM method with VMI and MLCI. No data on VMI presented. Excluded due to study design, lack of information
Triratana et al 1989	Pyrophosphate 3.3% & copolymer 1%	6 months	37.07% reduction. A double-blind crossover trial involving 50 subjects. Not enough information to calculate effect size. Excluded due to study design, lack of information.

External Validity of Studies

A possible criticism of the study design might be that participants are selectively chosen for high calculus formation and might enjoy exaggerated benefits (Hagiwara et al, 1989). Therefore, in a population where calculus levels were low, the anticalculus dentifrices might have lesser impact than expected. However, studies done in populations known to produce large amounts of calculus, for example, a Thai population (Triratana et al, 1991) did not show any large effect. Bollmer et al (1995) showed that in the presence of a calculus promoting agent, chlorhexidine, and the anticalculus effect might become significant only after longer use. Sanz et al, (1994) did not find any significant calculus reduction for zinc lactate in their study where subjects used chlorhexidine. Some authors had tried to overcome the effect of baseline risk by adjusting for baseline VMI scores while reporting their results. Where both adjusted and unadjusted results were available, there was not much difference in the effect sizes between the two results (Fairbrother et al, 1997; Segretto et al, 1998; Kohut et al, 1997).

Another consideration is that a placebo effect might be present. Two studies where 'no treatment' groups were present suggested the possibility of a placebo effect (Triratana et al, 1991; Rustogi et al, 1991).

Heterogeneity among Studies

The heterogeneity among studies can be another limiting factor. Although only 3 active agents were involved, the review revealed that the studies could be divided into 9 strata depending on active agents, singly and in combination, and their concentrations. In addition, comparisons could be classified in terms of duration of studies into three, as those with 3-month, 6-month and 12-month duration. Heterogeneity was controlled to a great extent when studies were sub-grouped on the basis of agents and concentration.

Outcome Measure

The VMI is the standard measurement used in screening commercial dentifrices and therefore, we limited ourselves to this single outcome. But only three studies were excluded on this criterion. Two of them used Marginal Line Calculus Index (Gaengler et al, 1993; Taner et al, 1990), and a third used an experimental design with mylar strips (Disney et al, 1989). Although the limiting to the VMI is a potential source of bias, it should be noted that available evidence is also limited to studies with VMI often done with industry support on limited number of products.

Cohen's d was chosen as effect size because it was easy to calculate and interpret.

The decision to perform meta- analysis on the standardized mean difference rather than weighted mean difference was based on the facts that: 1) there were differences in the way VMI was reported in different studies; 2) VMI is a partial scoring technique and therefore the absolute values have limited utility; and 3) standardized mean difference has a simple population level interpretation. The standardized mean difference can be interpreted as the standard deviation units by which the location of a distribution is shifted due to the intervention.

Publication Bias

The significance of publication bias, in recent years, was highlighted by the controversy over environmental exposure to tobacco smoke and cancer (Misakian and Bero, 1998). The traditional approach to the examination of publication bias is the funnel plot. The funnel plot of the 43 comparisons for 3-month studies showed considerable asymmetry suggestive of existence of publication bias.

Quality of Studies

This systematic review did reveal that the quality of reporting clinical trials in dentistry should be improved. Despite the fact that these clinical trials had a design specified for them (Volpe et al, 1992), there are obvious lacunae. Two significant lapses are: 1) not specifying whether a sample size has been determined for the trial and assumptions used to determine that sample size; and 2) not reporting whether consent was obtained from the subjects. In addition, most reports limited themselves to indicating allocation concealment and blinding.

Clinical, Research and Policy Implications

Dentistry had already witnessed the impact of fluoride toothpastes on dental caries prevalence. The

current review was prompted by the question whether such an impact is possible with anticalculus dentifrices. The results of this review, albeit modest, suggest that these dentifrices could exert some influence on dental treatment needs. The long-term use of anticalculus dentifrices could reduce the amount of calculus accumulation and thereby influence the requirement of routine scaling, in terms of time and interval between scalings. Such beneficial effects may be manifested only at population levels. When we tested these assumptions in suitable models, we found them to be tenable (Netuveli, 2002). Thus, future clinical trials should be directed towards testing the health service benefits of dentifrices containing anticalculus agents.

Another implication is in the labelling of toothpastes as anticalculus dentifrices. The results of this suggest that anticalculus dentifrices can vary in their effectiveness depending on their active agents and their concentrations. This is obscured when dentifrices are marketed under the rubric 'tartar-control'. This brand related effectiveness would not be found for anti-caries or gum protection dentifrices, since all brands would use the same active agent. In the case of toothpastes it might be essential to be explicit when declaring the active agent.

ACKNOWLEDGEMENT

This paper has benefited from the comments from an anonymous reviewer.
Competing interests: None.

REFERENCES

1. Adams D. Calculus inhibition agents: A review of recent clinical trials. Adv Dent Res 1995;9:410-418.
2. Baraya A, Soto J. Effect of a dentifrice containing soluble pyrophosphates and sodium fluoride on dental calculus deposits. Rev Fed Odontol Colomb 1988;38:41-55.
3. Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. Biometrics 1994;50: 1088-1101.
4. Bollmer BW, Sturzenberger OP, Vick V, Grossman E. Reduction of calculus and Peridex stain with Tartar-Control Crest. J Clin Dent 1995;6:185-187.
5. Chikte UM, Rudolph MJ, Reinach SG. Anticalculus effects of dentifrice containing pyrophosphate compared with control. Clin Prev Dent 1992;14:29-33.
6. Cohen S, Schiff T, McCool J, Volpe A, Petrone ME. Anticalculus efficacy of a dentifrice containing potassium nitrate, soluble pyrophosphate, PVM/MA copolymer, and sodium fluoride in a silica base: a twelve-week clinical study. J Clin Dent 1994;5:93-96.
7. Davies RM, Ellwood RP, Volpe AR, Petrone ME. Supragingival calculus and periodontal disease. Periodontology 2000 1997;15:74-83.
8. DerSimonian R, Laird N. Meta-analysis in clinical trials. Controlled Clinical Trials 1986;7:177-188.
9. Dickersin K, Scherer R, Lefebvre C. Systematic Reviews: Identifying relevant studies for systematic reviews. BMJ 1994;309:1286-1291.
10. Disney JA, Graves RC, Cancro L, Payonk G, Stewart P. An evaluation of 6 dentifrice formulations for supragingival anticalculus and anti plaque activity. J Clin Periodontol 1989;16: 525-528.
11. Fairbrother KJ, Heasman PJ. Anticalculus agents. J Clin Periodontol 2000;27:285-301.
12. Fairbrother KJ, Kowolik MJ, Curzon ME, Muller I, McKeown S, Hill CM, Hannigan C, Bartizek RD, White DJ. The comparative clinical efficacy of pyrophosphate/triclosan, copolymer/triclosan and zinc citrate/triclosan dentifrices for the reduction of supragingival calculus formation. J Clin Dent 1997;8:62-66.
13. Gaengler P, Kurbad A, Weinert W. Evaluation of anticalculus efficacy. An SEM method of evaluating the effectiveness of pyrophosphate dentifrice on calculus formation. J Clin Periodontol 1993;20:144-146.
14. Hagiwara M, Osada T, Miyake M, Yogo M, Suganuma N, Takahashi A. Clinical study of the anticalculus effect of a dentifrice containing sodium polyphosphate. Nippon Shishubyo Gakkai Kaishi 1989;31:948-959.
15. Katalin S, Schiff TG, Katalin G, Ildiko T, Jolan B. Clinical comparison of the calculus inhibiting effect of three commercially available toothpastes. Fogorv Sz 1995;88:393-398.
16. Kazmierczak M, Mather M, Ciancio S, Fischman S, Cancro L. Clinical evaluation of anticalculus dentifrices. Clin Prev Dent. 1990;12:13-17.
17. Kohut BE, Rubin H, Baron HJ. Relative clinical effectiveness of three anticalculus dentifrices. Clin Prev Dent 1989;11:13-16.
18. Kornman KS, Loe H. The role of local factors in the etiology of periodontal diseases. Periodontology 2000;1993;2:83-97.
19. Kranz S, Boffa J, Frankl SN, Glaser C. A comparative clinical study of two anticalculus dentifrices for efficacy in the inhibition and removal of surface stain and calculus. Pract Periodontics Aesthet Dent 1991;3:28-31.
20. Kurbad A, Gangler P, Hoffmann T, Kirchner T, Weinert W. Inhibiting effect of a pyrophosphate-dentifrice on calculus formation. Dtsch Zahnarztl Z 1991;46:277-280.
21. Light RJ, Pillemer DB. Summing Up: The Science of Reviewing Research. Cambridge, MA: Harvard University Press 1984.
22. Lobene RR. A clinical study of the anticalculus effect of a dentifrice containing soluble pyrophosphate and sodium fluoride. Clin Prev Dent 1986;8:5-7.
23. Lobene RR. Anticalculus effect of a dentifrice containing pyrophosphate salts and sodium fluoride. Compend Contin Educ Dent 1987a;8:175-178.
24. Lobene RR. A clinical comparison of the anticalculus effect of two commercially-available dentifrices. Clin Prev Dent 1987b;9:3-8.
25. Lobene RR. A study to compare the effects of two dentifrices on adult dental calculus formation. J Clin Dent 1989;1:67-69.
26. Lobene RR, Battista GW, Petrone DM, Volpe AR, Petrone ME. Clinical efficacy of an anticalculus fluoride dentifrice containing triclosan and a copolymer: A 6-month study. Am J Dent 1991;4:83-85.

27. Lu KH, Ruhlman CD, Chung K, Adams A. A clinical comparison of anticalculus dentifrices over 4 months of use. J Indiana Dent Assoc 1988;67:17-18.
28. Mandel ID. Calculus update: prevalence, pathogenicity and prevention. J Am Dent Assoc 1995;126:573-580.
29. Manji F, Sheiham A. CPITN findings and the manpower implications of periodontal treatment needs for Kenyan children. Community Dent Health 1986;3:143-151.
30. Market Intelligence. Oral Hygiene. London: Mintel 1998.
31. Misakian AL, Bero LA. Publication Bias and Research on Passive Smoking – Comparison of Published and Unpublished Studies. JAMA 1998;280:250-253.
32. Miyazaki H, Pilot T, Leclercq MH et al. Profiles of periodontal conditions in adolescents measured by CPITN. Int Dent J 1991a;41:67-73.
33. Miyazaki H, Pilot T, Leclercq MH et al. Profiles of periodontal conditions in adolescents measured by CPITN. Int Dent J 1991b;41:74-80.
34. Moher D, Schulz KF, Altman DG. Quality of reports of parallel-group randomized trials The CONSORT statement: Revised recommendations for improving the quality of reports of parallel-group randomized trials. Ann Intern Med 2001;134: 657-662.
35. Netuveli GS. Public health aspects of oral calculus: an analysis of trends and future scenarios. Ph. D. Thesis. University of London 2002.
36. Petrone M, Lobene RR, Harrison LB, Volpe A, Petrone DM. Clinical comparison of the anticalculus efficacy of three commercially available dentifrices. Clin Prev Dent 1991;13:18-21.
37. Pilot T, Miyazaki H, Leclercq MH, Barmes DE. Profiles of periodontal conditions in older age cohorts, measured by CPITN. Int Dent J 1992;42:23-30.
38. Rosling B, Lidhe J. The anticalculus efficacy of two commercially available anticalculus dentifrices. Compend Contin Educ Dent 1987;278-282.
39. Rustogi KN, Volpe AR, Petrone ME. A clinical comparison of two anticalculus dentifrices. Compendium 1988;9:78-79.
40. Santos SL, Putt MS, Feinberg CA, Fernandez PM. Development and validation of a short term clinical model for assessing calculus inhibiting agents. J Clin Periodontol 1999; 26:169-176.
41. Sanz M. Anticalculus efficacy. In: Lang NP, Karring T, Lindhe J (Eds). Proceedings of 2nd European Workshop on Periodontology. Chemicals in Periodontics. Berlin: Quintessence Verlag 1996.
42. Sanz M, Vallcorba N, Fabregues S, Muller I, Herkstroter F. The effect of a dentifrice containing chlorhexidine and zinc on plaque, gingivitis, calculus and tooth staining. J Clin Periodontol 1994;21:431-437.
43. Schiff TG. Comparative clinical study of two anticalculus dentifrices. Compend Contin Educ Dent 1987a;275-277.
44. Schiff TG. The effect of a dentifrice containing soluble pyrophosphate and sodium fluoride on calculus deposits. A 6-month clinical study. Clin Prev Dent 1987b;9:13-16.
45. Segreto VA, Collin EM, D'Agostino R, Cancro LP, Pfeifer HJ, Gilbert RJ. Anticalculus effect of a dentifrice containing 0.5% zinc citrate trihydrate. Community Dent Oral Epidemiol 1991; 19:29-31.
46. Segretto VA, Stevens DP, Schulte MC, Fortna RH, Gerlach RW. Safety and efficacy of novel tartar control dentrifrice containing 3.3% pyrophosphate: a controlled six-month clinical trial. J Clin Dent 1998;9:26-29.
47. Singh SM, Petrone ME, Volpe AR, Rustogi KN, Norfleet J. Comparison of the anticalculus effect of two soluble pyrophosphate dentifrices with and without a copolymer. J Clin Dent 1990;2:53-55.
48. Sowinski J, Petrone DM, Battista G, Petrone ME, Crawford R, Patel S, DeVizio W, Chaknis P, Volpe AR, Proskin HM. The clinical anticalculus efficacy of a tartar control whitening dentifrice for the prevention of supragingival calculus in a three-month study. J Clin Dent 1999;10:107-110.
49. Sowinski J, Petrone DM, Battista G, Petrone ME, DeVizio W, Volpe AR. Clinical comparison of two tartar control dentifrices: a twelve-week study. J Clin Dent 1998;9:101-104.
50. Stephen KW, Saxton CA, Jones CL, Ritchie JA, Morrison T. Control of gingivitis and calculus by a dentifrice containing a zinc salt and triclosan. J Periodontol 1990;61:674-679.
51. Stookey GK, Jackson RD, Beiswanger BB, Stookey KR. Clinical efficacy of chemicals for calculus prevention. In: ten Cate JM (ed). Recent advances in the study of dental calculus. Oxford: IRL Press 1989;235-258.
52. Svatun B, Saxton CA, Rolla G. Six-month study of the effect of a dentifrice containing zinc citrate and triclosan on plaque, gingival health, and calculus. Scand J Dent Res 1990;98:301-304.
53. Svatun B, Saxton CA, Huntington E, Cummins D. The effects of three silica dentifrices containing Triclosan on supragingival plaque and calculus formation and on gingivitis. Int Dent J 1993;43:441-452.
54. Taller SH. Clinical study of the anticalculus effect of two pyrophosphate containing dentifrices and baking soda. JNJ Dent Assoc 1990;61:20-23.
55. Taner IL, Kebudi E, Taplamacioglu B. A clinical study to evaluate the anticalculus effect of a dentifrice on calculus formation 1990;17:45-49.
56. Triratana T, Kerdvongbundit V, Chutapimol N, Thepbanterng S. The effect of a dentifrice containing soluble pyrophosphate and a copolymer on calculus deposit: a six-month clinical study. J Dent Assoc Thai 1989;39:142-147.
57. Triratana T, Kietprajuk C, Banditsing P, Kraiwaphan P. Clinical comparison of anticalculus dentifrices: a three-month study of Thai children and teenagers. J Clin Dent 1991;3:B23-B25.
58. Triratana T, Rustogi KN, Volpe AR. The effect of an anticalculus dentifrice on supragingival calculus formation and gingival recession in Thai adults: a one-year study. J Clin Dent 1991;3:22-26.
59. van der Burgt TP, Klaassen PP. The effect of a dentifrice containing pyrophosphates on calculus accumulation. Ned Tijdschr Tandheelkd 1988;95:108-111.
60. Volpe AR, Manhold JH, Hazen SP. In vivo calculus assessment: Part I. a method and its examiner reproducibility. J Periodontol 1965;36:292-298.
61. Volpe AR, Petrone ME, DeVizio W, Davies RM. A review of plaque, gingivitis, calculus and caries clinical efficacy studies with a dentifrice containing triclosan and PVM/MA copolymer. J Clin Dent 1992;4:31-41.
62. Weinstein E, Mandel ID. The present status of anticalculus agents. J Oral Therapeut Pharmacol 1964;1:327-334.
63. White DJ, McClanahan SF, Lanzalaco AC, Cox ER, Bacca L, Perlich MA, Campbell SL, Schiff T, Stains A. The comparative efficacy of two commercial tartar control dentifrices in preventing calculus development and facilitating easier dental cleanings. J Clin Dent 1996;7:58-64.
64. White DJ. Dental calculus: recent insights into occurrence, formation, prevention, removal and oral health effects of supragingival and subgingival deposits. Eur J Oral Sci 1997;105:508-522.