J Clin Periodontol 2006; 33: 1–13 doi: 10.1111/j.1600-051X.2005.00860.x

Journal of Clinical Periodontology

A review of the effects of stannous fluoride on gingivitis

S. Paraskevas and G. A. van der Weijden

Department of Periodontology, Academic Center for Dentistry Amsterdam (ACTA), Amsterdam, The Netherlands

Paraskevas S, van der Weijden GA. A review of the effects of stannous fluoride on gingivitis. J Clin Periodontol 2006; 33: 1–13. doi: 10.1111/j.1600-051X.2005.00860.x.

Abstract

Aim: To review the literature on the effects of stannous fluoride on gingivitis.

Material and Methods: The Medline and cochrane central register of controlled trials were searched up to August 2005 to identify appropriate studies. The primary outcome measure was gingivitis.

Results: Independent screening of titles and abstracts of 542 papers resulted in 36 publications (inter-reviewer ê score of 0.76), out of which 15 papers finally fulfilled the criteria of eligibility. For SnF_2 *dentifrices,* a statistically significant reduction in gingivitis was noted in comparison with control (weighted mean difference (WMD) of 0.15 (gingival index) and 0.21 (gingivitis severity index) (test for heterogeneity $p < 0.00001$, $I^2 = 91.1\%$ and $p = 0.03$, $I^2 = 80.1\%$, respectively)). With regard to plaque reduction inconsistent results existed. On using the plaque index no differences were found, whereas meta-analysis of the Turesky index provided a WMD of 0.31 ($p = 0.01$, test for heterogeneity $p < 0.0001$, $I^2 = 91.7\%$). Because of insufficient data, a meta-analysis for SnF_2 *mouth rinse* and *dentifrice/mouthrinse* formulations was not performed.

Conclusions: The use of SnF_2 dentifrices results in gingivitis and plaque reduction when compared with a conventional dentifrice. The precise magnitude of this effect was difficult to assess because of a high level of heterogeneity in study outcomes.

Key words: gingivitis; plaque; review; stain; stannous fluoride; tin fluoride

Accepted for publication 28 September 2005

During the last few decades, a decline in the prevalence of dental caries has been noticed, possibly as a result of the use of fluoridated products (National Institute of Dental Research 1987, Ainamo & Osterberg 1992). However, the universal prevalence of gingivitis suggests that individuals are not capable of reaching adequate oral hygiene levels (Brown et al. 1996, Hugoson et al. 1998, Morris et al. 2001). Both primary prevention of gingivitis and primary and secondary prevention of periodontitis are based on the achievement of sufficient plaque control. In fact, in patients exercising meticulous oral hygiene, it has been shown that periodontal disease progression could be arrested (Axelsson et al. 1991).

The concept of the primary prevention of gingivitis derived from the assumption that gingivitis is the precursor of periodontitis, and that maintenance of healthy gingiva will prevent periodontitis and tooth loss (Addy & Adriaens 1998, Garmyn et al. 1998). Consequently, prevention of gingivitis could have a major impact on the costs of periodontal care (Baehni & Takeuchi 2003).

The use of chemical agents with anti-plaque or anti-gingivitis action as adjuncts to self-performed oral hygiene is based on the shortcomings of the latter. The challenge with the chemical plaque control is to develop an active anti-plaque agent that does not disturb the natural flora of the oral cavity. For instance, a powerful product would be an antibiotic rinse, but this would increase the risks of bacterial resistance, hypersensitivity reactions, or super-infections (Seymour & Heasman 1992). Both industry and science have been searching for products whose side effects are balanced against the benefits. Several agents have been tested through the years and studies have provided information on their efficiency in controlling or inhibiting plaque growth (for a review see Mandel 1988). The most effective agent known to date is chlorhexidine (CHX). However, side effects such as an unpleasant taste, alterations in taste sensation, non-aesthetic discoloration of the teeth and, in some cases, desquamative oral lesions may prohibit the prolonged use of CHX. In the search for agents that exert anti-plaque and/or anti-gingivitis efficacy without the sides effects known for CHX, research has turned its interest toward several agents such as triclosan, sanguinarine, quartenary ammonium chloride compounds and metal salts. From the latter, tin combined with fluoride (SnF_2) is a well-known agent that has been used in dentifrice formulations as early as the beginning of the 1940s (van Loveren

1990, 2001, Miller et al. 1994). Several formulations including dentifrices, gels and mouth rinses and regimes have been tested throughout the years. Although most of the studies agree upon the fact that the SnF_2 products have a plaque-reducing effect, there is inconclusive evidence with regard to the effects of varying SnF_2 formulations on the parameters of gingivitis.

The present systematic review was undertaken in an attempt to address this question.

Material and Methods

The focused question for this search was as follows.

In patients with gingivitis what is the effect of use of SnF_2 on the parameters of gingival inflammation?

Literature Search.

Two sources of evidence were selected in the search for appropriate papers for this study purpose: The national Library of Medicine, Washington DC (MEDLINE-PubMed) (1965 up to and including August 2005) and the cochrane central register of controlled trials (1965 up to and including August 2005).

The eligibility criteria were as follows:

(a) randomized controlled trials (RCTs) and controlled clinical trials (CCTs) (gingivitis in the SnF_2 group against its own baseline status);
(b) studies of at least 6-month duration;
(c) no periodontitis;
(d) subjects with no systemic disorders; and
(e) no recent history of systemic medications including antibiotics and non-steroidal anti-inflammatory drugs (within the last 6 months).

Only papers written in English language were accepted. Case reports, letters, and historical reviews were not included in the search. Papers without abstracts whose title suggested that they were related to the objectives of this review were also selected so that the full text could be screened.

Factors that were recorded to be able to investigate the heterogeneity of the primary outcome across studies were as follows:

(a) evaluation period;
(b) number of subjects;
(c) the mean age and range of subjects;
(d) oral hygiene (baseline values of plaque index (PI), gingivitis and stain);
(e) oral hygiene instruction/reinforcement during the study examinations;
(f) smoking status;
(g) industry funding; and
(h) methodological study quality assessment.

Search strategy

MEDLINE search

- (Intervention) fluorides/all subheadings OR tin fluorides/all subheadings, ''fluorid*'' OR ''tin fluorides'' OR ''tin fluoride'' OR ''tin-fluoride'' OR ''stannous fluoride''.

AND

- (Outcome) GINGIVITIS/all subheadings OR GINGIVAL HEMORRHAGE/all subheadings OR PERIODONTAL INDEX/all subheadings, ''gingivitis'' OR ''gingivit*'' OR ''gingival bleeding'' OR ''bleeding on probing'' OR ''bleeding on marginal probing''.

Cochrane library search

The search strategy applied for the Cochrane search was as follows.

- (Intervention) FLUORIDES OR TIN FLUORIDES, ''fluoride'' OR ''fluorid*'' OR ''tin fluoride'' OR ''stannous fluoride'' OR ''stannous-fluoride''

AND

- (Outcome) GINGIVITIS OR PERIODONTAL INDEX OR GINGIVAL HEMORRHAGE, ''gingivit*'' OR ''gingivitis'' OR ''gingival bleeding'' OR ''bleeding-on-probing'' OR ''bleeding on probing''

Screening and selection of papers

The papers were screened independently by two reviewers (S. P and G. A. W). At first, they were screened by title and abstract. As a second step, full text papers were obtained when they fulfilled the criteria of the study aim. ê scores evaluated the inter-examiner agreement. Any disagreement between the two reviewers was resolved after additional discussion.

For full-text screening, the following criteria were taken into consideration:

- studies of $\geqslant$6-month duration;
- RCTs or CCTs; and
- parameters mentioned (gingivitis, plaque, stain).

Additionally, information concerning the methodological study quality assessment was extracted based upon the following aspects.

- Methods of randomization (i.e. method used to generate the randomization sequence) were considered as adequate when random number table or tossed coin or shuffled cards were used; inadequate when other methods of randomization were used (such as alternate assignment, hospital number, odd/even birth date); and unclear when the method of randomization was not reported or explained.
- Allocation concealment (i.e. how the randomization sequence was hidden from the examiners?) was considered as adequate when examiners were kept unaware of the randomization sequence (for example, by means of central randomization, pharmacy sequentially numbered/coded containers, sequentially numbered, opaque envelopes); inadequate when other methods of allocation concealment were used (such as alternate assignment, hospital number, odd/even birth date); and unclear when the method of allocation concealment was not reported or explained.
- Blinding of examiners with regard to treatment alternatives used in the trial was determined. In the present assessment, ''single'' blinding was considered to be the proper approach because it was unreasonable to assume that a patient could be blinded to the treatment.
- Completeness of follow-up by answering the following questions. (a) Was the number of patients at baseline and at completion of the follow-up interval reported for both groups? (b) Were all the patients who entered the trial prop-

Table 1. Overview of the studies (in alphabetic order) that were excluded after full-paper reading, and reasons for exclusion

Author(s) (year)	Reason for rejection
Binney et al. (1996)	Not relevant to SnF_2
Birkeland et al. (1973)	Not relevant to SnF_2
Boyd et al. (1988)	Baseline and end size per group not known, presentation of data in the form of graphs (no numerical data)
Brayer et al. (1979)	Not relevant to SnF_2
Hoffmann et al. (2001)	Presentation of data in the form of box plots (no numerical data)
Klock et al. (1985)	Presentation of data (only bleeding sites) in the form of graphs (no numerical data)
Laine et al. (1993)	Non-healthy (lymphoma) patients
Larson et al. (1985)	Short-term (2 months) study
Lindhe et al. (1971)	Animal study
Mankodi et al. (2002)	NaF in combination with other agents
Perdok et al.(1988)	Short-term (7 days) study
Spindel et al. (1986)	Not relevant to SnF_2
Tinanoff et al. (1989)	Patients having overdentures, end-sample values per group not known
Wenderoth et al. (1999)	Not relevant to SnF_2
Winer et al. (1986)	Not relevant to SnF_2
Yankell et al. (1982)	Short-term (5 days) study
Yates et al. (2003)	Short-term (42 days) study
Yoon & Berry (1979)	Short-term (3 weeks) study

erly accounted for at completion? (c) Does the analysis take into account the drop-outs/losses to follow-up or the excluded patients?

Statistical analysis

Both for the title/abstracts screening and for the screening of the full papers, ê coefficients were calculated to evaluate the agreement between the reviewers.

The mean values and standard deviations were collected by data extraction. In some studies where standard errors of the mean were reported, standard deviations were calculated by the authors based on the sample size.

Only one paper provided data of increments during the experimental period. All other papers supplied data for baseline and end-trial assessments. Consequently, it was not possible to perform a meta-analysis of the difference because the standard deviation of the difference could not possibly be calculated. Therefore, the data for baseline and end were presented separately. An analysis for both time points was performed. Weighted means of baseline and end were calculated by means of the Review Manager 4.2 software of the Cochrane Collaboration using a random effect model.

Results

The MEDLINE-PubMed search resulted in 519 papers. The Cochrane search resulted in 227 papers. After extracting those papers that were present in both searches, 542 titles/abstracts remained to be screened.

The screening of the titles/abstracts initially resulted in 36 full articles. The inter-examiner ê was 0.76, indicating good agreement between the reviewers. Some of the papers required additional screening of the full text because the information given in the abstract was not adequate to be able to judge their suitability. In total, 18 papers had to be excluded. The reasons leading to their exclusion are explained in Table 1. There were also two papers (Leverett et al. 1986, Boyd 1994) reporting results on the same study population presented in other articles (Leverett et al. 1986 and Boyd & Chun 1994, respectively). Therefore, the data from these studies were used only once. The remaining full papers ($n = 15$) were read by the reviewers and were processed for data extraction. An overview of the papers and the study characteristics is presented in Table 2a. As SnF_2 may be present in different formulations and different concentrations, it was decided to categorize the suitable studies according to the formulation used during the screening and data extraction. Thus, the data analysis included three regimens conforming to the use of SnF_2 in *dentifrice/gel*, *mouth rinse* or combined as *dentifrice/mouth rinse*. Comparisons were made against NaF (or Sodium Monofluorophosphate (MFP))-containing dentifrices or placebo products when appropriate.

Assessment of heterogeneity

(a) Evaluation period.

With the exception of five studies (Leverett et al. 1984, Wolff et al. 1989, Zimmerman et al. 1993, Boyd & Chun 1994, Mengel et al. 1996), the selected studies were of 6-month durations. The studies by Zimmerman et al. (1993) and Mengel et al. (1996) lasted for 7 and 9 months, respectively; whereas the studies by Wolff et al. (1989) and Boyd & Chun (1994) had a duration of 18 months. The longest study was conducted by Leverett et al. (1984) and lasted for 2 years.

(b) Number, mean age, and range of subjects.

The number of participants varied per group and study. Information on the study characteristics is displayed in Table 2a. The studies by Boyd & Chun (1994) and Sgan-Cohen et al. (1996) were carried out in healthy adolescents, whereas the study by Leverett et al. (1984) involved schoolchildren. The remaining studies included adult individuals.

(c) Oral hygiene (baseline values of PI, gingivitis and stain).

As expected, varying levels of plaque and gingivitis have been described in the various studies (Table 2a).

(d) Prophylaxis, oral hygiene instruction/reinforcement during the study examinations.

The majority of the studies reported dealt with a parallel design where the test/control products were used by the participants at home without supervision. In only one study (Leverett et al. 1984) the was rinsing supervised. Also, eight studies used professional prophylaxis after the assignment of the products (Table 2a). The Boyd & Chun study used oral hygiene instruction and

Table 2a. Overview of the studies processed for full-paper reading and data extraction

Author(s) (year)	Study design	Evaluation period (months)	# subjects base–end	Subjects/age
Dentifrice/gel				
Wolff et al. (1989)	Parallel	18	546–281 SnF_2: ?–89 NaF: ?–87 Placebo: ?–105	Healthy adults Mean age: 27.6
Boyd & Chun (1994), Boyd (1994)	Parallel with prophylaxis at start	18	65–55 NaF: 35–32 SnF_2: 30–23	Healthy adolescents Mean age: 13.4
Perlich et al. (1995)	Parallel with prophylaxis at start	6	383–328 NaF: 191–174 SnF_2: 192–154	Healthy (gingivitis only ?) adults NaF mean age: 36.5 SnF_2mean age: 37.2
Beiswanger et al. (1995)	Parallel with prophylaxis at start	6	620–549 NaF: 153–136 $SnF_{2\ high}$: 153–140 $SnF_{2\ low}$: 157–140	Healthy (mild-to-moderate gingivitis) adults NaF mean age: 32.6 SnF_2mean age: 33.7–34.5 (both groups)
Beiswanger et al. (1997)	Parallel with prophylaxis at start	6	918–635 NaF: 143–140 SnF_2: 278–267	Healthy adults NaF mean age: 36.1 SnF_2mean age: 36.3
Williams et al. (1997)	Parallel with prophylaxis at start	6	124–112 NaF: ?–58 SnF_2: ?–54	Healthy adults (baseline Q–H score >1.5 and GI score >1) NaF mean age: 34.8 SnF_2mean age: 29.5
Mankodi et al. (1997)	Parallel with prophylaxis at start	6	119–104 NaF: ?–54 SnF_2: ?–50	Healthy adults (baseline Q–H score >1.5 and GI score >1) NaF mean age: 38.5 SnF_2 mean age: 41.4
McClanahan et al. (1997)	Parallel with prophylaxis at start	6	570–483 NaF: 191–174 SnF_2 : 192–154	Healthy adults NaF mean age: 36.5 SnF_2mean age: 37.3
Mankodi et al. (2005)	Parallel	6	143–130 Control: ?–66 SnF_2: ?–64	Healthy adults Mean age: control: 38.5 SnF_2: 37.1
Sgan-Cohen et al. (1996)	Parallel, Normal unsupervised OH	6	300–246 NaF: ?–121 AmF/SnF_2:. ?–125	Healthy adolescents Mean age: 15–16
Shapira et al. (1999)	Parallel	6	119–103 NaF: 60–52 AmF/SnF_2: 59–51	Healthy adults Mean age: ? Range: 25–65
Mouth rinse				
Leverett et al. (1984), Leverett et al. (1986)	Parallel	28	511–268 NaF: 255–127 SnF_2: 256–141	Healthy schoolchildren Mean age: ? Range: 12–15
Zimmerman et al. (1993)	Parallel	7	120–102 Placebo: 60–50 AmF/SnF_2: 60–52	Healthy adults with gingivitis Mean age: 26.2
AmF/SnF_2 dentifrice/mouth rinse				
Mengel et al. (1996)	Parallel	9	150–130 NaF mouth rinse/dentifrice ?–? AmF/SnF_2 mouth rinse/dentifrice: ?–? AmF/SnF_2 dentifrice/NaF mouth rinse ?–?	Healthy Adolescents and adults (gingivitis or early signs of periodontitis) Mean age: 28
Paraskevas et al. (2005)	Parallel	6	301–281 NaF dentifrice 154–147 AmF/SnF_2 mouth rinse/dentifrice 147–134	Healthy adults (>50% gingival bleeding) NaF mean age: 35.7 SnF_2mean age: 34.6

GI, gingival index; Q–H; Quigley & Hein index.

Table 2b. Overview of the clinical parameters of the studies processed for full-paper reading and data extraction.

Author(s) (year)	Product(s)	Plaque index (SD)			Gingivitis index(SD)		
		baseline	end	Δ plaque[†]	baseline	end	Δ gingivitis[†]
Dentifrice/gel							
Wolff et al. (1989)		PI			Bleeding index		
	a. 0.75% sodium monofluorophosphate (NaMFP) Dentifrice+0.4% SnF_2 gel	?	?	?	a. 0.97 (0.50)	a. 0.90 (0.55)	0.07
	b. 0.75% (NaMFP) Dentifrice+0.22% NaF gel				b. 0. 92 (0.45)	b. 0.85 (0.45)	0.07
	c. 0.75% (NaMFP) Dentifrice+placebo (fluoride-free) gel				c. 0.91 (0.52)	c. 0.89 (0.54)	0.02
Boyd & Chun (1994), Boyd (1994)		PI			GI		
	a. NaF Dentifrice	a. 0.74 (0.69)	a. 1.06 (0.73)[‡]	− 0.32	a. 0.76 (0.05)	a. 1.35 (0.60)[‡]	− 0.59
	b. NaF Dentifrice+high availability Sn^{++} (HASn) gel	b. 0.66 (0.58)	b. 0.68 (0.49)	− 0.02	b. 0.64 (0.55)	b. 0.81 (0.52)	− 0.17
Perlich et al. (1995)		Turesky mod Q–H			GI		
	a. 0.243% NaF dentifrice	a. 1.90 (0.48)	a. 2.23 (?)	–0.33	a. 0.71 (0.25)	a. 0.51 (?)[‡]	0.20
	b. 0.454% stabilized SnF_2 dentifrice	b. 1.93 (0.50)	b. 2.16 (?)	–0.25	b. 0.68 (0.24)	b. 0.41 (?)	0.27
Beiswanger et al. (1995)		PI			GI		
	a. 0.243% NaF dentifrice	a. 0.95 (0.38)	a. 0.73 (?)	0.22	a. 0.71 (0.22)	a. 0.45 (?)[‡]	0.26
	b. 0.454% SnF_2 stabilized with 4.16% sodium gluconate dentifrice	b. 1.03 (0.46)	b. 0.71 (?)	0.32	b. 0.67 (0.24)	b. 0.36 (?)	0.31
	c. 0.454% SnF_2 stabilized with 2.08% sodium gluconate dentifrice	c. 0.96 (0.40)	c. 0.72 (?)	0.24	c. 0.69 (0.22)	c. 0.37 (?)	0.32
Beiswanger et al. (1997)		Pl			GI		
	a. 0.243% NaF dentifrice	a. 0.67 (0.35)	a. 0.54 (0.23)	0.13	a. 0.84 (0.23)	a. 0.78 (0.23)[‡]	0.06
	b. 0.454% stabilized SnF_2 dentifrice	b. 0.73 (0.49)	b. 0.55 (0.33)	0.21	b. 0.86 (0.33)	b. 0.64 (0.16)	0.22
Williams et al. (1997)		Turesky mod Q–H			GI*		
	a. 0.243% NaF dentifrice in silica base	a. 2.49 (0.45)	a. 2.2 (0.46)[§]	0.29	a. 1.28 (0.19)	a. 1.30 (0.15)[‡]	− 0.02
	b. 0.454% stabilized SnF_2dentifrice	b. 2.48 (0.49)	b. 1.7 (0.40)	0.78	b. 1.27 (0.18)	b. 1.01 (0.13)	0.26
Mankodi et al. (1997)		Turesky mod Q–H			GI*		
	a. 0.243% NaF dentifrice in silica base	a. 2.60 (0.48)	a. 2.61 (0.53)[‡]	− 0.01	a. 1.18 (0.12)	a. 1.19 (0.16)[‡]	− 0.01
	b. 0.454% stabilized SnF_2 dentifrice	b. 2.68 (0.43)	b. 2.08 (0.41)	0.60	b. 1.17 (0.14)	b. 0.94 (0.14)	0.23
McClanahan et al. (1997)		Turesky mod Q–H			GI		
	a. 0.243% NaF dentifrice containing	a. 1.90 (0.52)	a. 2.23 (0.40)	− 0.33	a. 0.71 (0.26)	a. 0.52 (0.13)[‡]	0.19
	b. 0.454% stabilized SnF_2 dentifrice	b. 1.94 (0.50)	b. 2.16 (0.37)	− 0.22	b. 0.68 (0.25)	b. 0.41 (0.12)	0.27
Sgan-Cohen et al. (1996)		PHP index			GI		
	a. AmF/SnF_2 dentifrice	a. 0.57 (0.14)	a. 0.55 (0.14)	0.02	a. 0.95 (0.24)	a. 0.72 (0.24)	0.23
	b. 0.31% NaF dentifrice	b. 0.57 (0.15)	b. 0.57 (0.14)	–	b. 1.01 (0.37)	b. 0.78 (0.28)	0.23
Mankodi et al. (2005)		Turesky mod Q–H			Mod GI		
	a. 0.454% SnF_2+sodium hexametaphosphate dentifrice	a. 2.73 (0.41)	a. 2.14 (0.40)	0.59	a. 2.03 (0.10)	a. 1.57 (0.24)	0.46
	b. 0.76% sodium monofluorophosphate	b. 2.91 (0.35)	b. 2.30 (0.41)[‡]	0.61	b. 2.04 (0.10)	b. 2.01 (0.24)[‡]	0.03
Shapira et al. (1999)		Pl			GI		
	a. AmF/SnF_2 dentifrice	a. 1.19 (0.29)	a. 0.76 (0.21)	0.43	a. 1.43 (0.21)	a. 1.33 (0.21)	0.04
	b. NaF dentifrice	b. 1.28 (0.22)	b. 0.83 (0.14)	0.45	b. 1.43 (0.22)	b. 1.39 (0.14)	0.1
Leverett et al. (1984), Leverett et al. (1986)		PI (Ramfjord teeth)	Whole population		GI (Ramfjord teeth)	Whole population	
	a. 0.1% SnF_2 mouth rinse	a. 1.05 (0.34)	a. 0.94 (0.38)	0.11	a. 1.00 (0.35)	a. 0.90 (0.38)	0.10
	b. 0.05% NaF mouth rinse	b. 1.05 (0.34)	b. 1.03 (0.39)	0.02	b. 0.98 (0.34)	b. 0.95 (0.40)	0.03

Table 2b. (Contd.)

Author(s) (year)	Product(s)	Plaque index (SD)			Gingivitis index(SD)		
		baseline	end	Δ plaque†	baseline	end	Δ gingivitis†
Dentifrice/gel							
			Compliant population			Compliant population	
			a. 0.99 (0.38)	0.06		a. 0.91 (0.37)	0.09
			b. 1.10 (0.37)‡	–0.05		b. 0.95 (0.40)	0.03
Zimmerman et al. (1993)		API			Mod SBI		
	a. AmF/SnF_2 mouth rinse	a. 61.3%	a. 50.6%	10.7%	a. 52%	a. 29.3%	22.7%
	b. Placebo mouth rinse	b. 55.1%	b. 53.4%	1.7%‡	b. 43.7%	b. 41.8%	1.9%‡
		PlI (teeth 14/34)			GI (teeth 14/34)		
		a. 1.17 (0.57)	a. 0.68 (0.57)	0.49	a. 1.36 (0.48)	a. 0.95 (0.36)	0.41
		b. 0.96 (0.52)	b. 0.86 (0.51)	0.1‡	b. 1.25 (0.45)	b. 1.19 (0.41)	0.06‡
AmF/SnF_2 dentifrice/mouth rinse							
Mengel et al. (1996)		API			Mod SBI		
	a. Combination NaF mouth rinse and dentifrice	a. 55.1 (SD)%	a. 56.15%		a. 24.64 (SD)%	a. 17.24%	8.5%
	b. Combination of AmF/SnF_2 mouth rinse and dentifrice	b. 69.98%	b. 49.54%		b. 21.59%	b. 13.10%	7.4%
	c. Combination of AmF/SnF_2 dentifrice and NaF mouth rinse	c. 68.92%	c. 53.93%		c. 19.86%	c. 14.86%	5.0%
		PlI (teeth 14/34)			GI (teeth 14/34)		
		a. 1.09 (0.47)	a. 0.56 (0.40)	0.53	a. 0.82 (0.28)	a. 0.68 (0.28)	0.14
		b. 1.12 (0.48)	b. 0.52 (0.33)	0.60	b. 0.82 (0.20)	b. 0.67 (0.32)	0.15
		c. 1.03 (0.33)	c. 0.51 (0.30)	0.52	c. 0.80 (0.19)	c. 0.64 (0.27)	0.16
Paraskevas et al. (2005)		PlI			BOMP		
	a. Combination of AmF/SnF_2 mouth rinse and dentifrice	a. 1.16 (0.4)	a. 0.95 (0.4)	0.21 (0.3)	a. 0.77 (0.16)	a. 0.71 (0.16)	0.06 (0.13)
	B. NaF dentifrice (control)	b. 1.13 (0.4)	b. 0.99 (0.4)	0.14 (0.3)‡	b. 0.78 (0.17)	b. 0.73 (0.17)	0.05 (0.12)

*Mandel–Chilton modif of Silness–Löe.

†the differences were calculated by the reviewers.

‡statistically significant in comparison with the test group (SnF_2).

In the original papers, in place of standard deviations SEMs, when were presented, they have been converted into SDs by the authors based on the sample size when reported.

API, approximal plaque index; BOMP, bleeding on marginal probing; GI, gingival index; Mod GI, modified gingival index, Mod SBI, modified sulcus bleeding index; PI, plaque index; PHP, patient hygiene performance, SD, standard deviations.

reinforcements during the periodic orthodontic appointments.

(e) Smoking status.

There were no studies reported on smoking habits of the participants. Therefore, this factor could not be investigated.

(f) Industry funding.

In a few studies information was found with respect to industry involvement in the financial support of the studies (Zimmerman et al. 1993, Mengel et al. 1996, Sgan-Cohen et al. 1996, Shapira et al. 1999, and Paraskevas et al. 2005). In other studies, no information was given although the authors or co-authors were actively involved in industrial research departments (Beiswanger et al. 1995, 1997, Mankodi et al. 1997, Perlich et al. 1995, McClanahan et al. 1997, Williams et al. 1997).

(g) Study quality

- *Method of Randomization*

With the exception of the study by Boyd & Chun (1994) all other studies were randomized. There were however some studies where the method of randomization was unclear (Leverett et al. 1984, Boyd & Chun 1994, Mengel et al. 1996, Mankodi et al. 1997, Williams et al. 1997, Shapira et al. 1999).

- *Allocation concealment*

Four papers (Zimmerman et al. 1993, Mengel et al. 1996, Sgan-Cohen et al. 1996, Shapira et al. 1999) gave information and addressed the issue of allocation concealment. For the remaining papers this issue was judged as unclear.

- *Blindness*

Two studies were conducted as single (operator) blinded experiments (Boyd & Chun 1994, Paraskevas et al. 2005), whereas the remaining were double blind.

- *Completeness in follow-up*

In the majority of the studies, there were drop-outs i.e. data are reported based on decreasing number of subjects. Three studies gave additional information about the reasons for the drop-outs (Zimmerman et al. 1993, Mengel et al. 1996, Paraskevas et al. 2005), whereas for the remaining papers the reasons were not explained. Three studies reported $>10\%$ subject losses (Wolff et al. 1989, Beiswanger et al. 1995, Perlich et al. 1995).

Information on examiner-related factors such as calibration of the examiners, intra/inter-examiner variability etc. was not available for the selected studies.

Clinical parameters

- *Gingivitis*

Analysis of the selected studies showed that gingivitis was investigated by means of several indices. All but six studies used either the gingival index (GI) (Löe & Silness 1963) for gingivitis assessment or the Mandel–Chilton modification of the GI (Table 2b). One study used the modified gingival index (Lobene et al. 1986). Two papers used the modification of the sulcus bleeding index (Lange 1981) for the evaluation of the gingival inflammation, whereas one paper provided results on bleeding index (Table 2b). One study reported data on gingivitis based on the bleeding on marginal probing (van der Weijden et al. 1994b). Finally, some studies (Beiswanger et al. 1995, 1997, Perlich et al. 1995, Mankodi et al. 1997, Williams et al. 1997) provided additional information on the gingival condition of the participants as the mean number (gingivitis severity index (GSI)) (Palomo et al. 1989) or percentage of bleeding sites.

With regard to its anti-gingivitis effect, SnF_2 produced a variation of results: in dentifrice/gel formulations all but one study described a statistically significant change in gingivitis in favour of the SnF_2 compared with NaF, whereas two studies reporting on AmF/SnF_2 dentifrice showed no significant differences in gingivitis in comparison with NaF. In mouth-rinse formulations, two studies reported significant effects in favour of the SnF_2 in comparison with placebo or NaF (Table 2b). Finally, when a combined regimen was used, two studies were identified which found no statistically significant differences between AmF/SnF_2 and the NaF alone or combined regimens with respect to the parameters of gingival inflammation (Table 2b).

- *Plaque*

Several plaque indices were used in order to evaluate the presence of plaque: seven studies used the PI, five studies used the Turesky (1970) modification of the Quigley & Hein Index (1962), and five studies gave additional details on the plaque severity index (Palomo et al. 1989, Beiswanger et al. 1995, 1997, Perlich et al. 1995, Mankodi et al. 1997, Williams et al. 1997), whereas the approximal plaque index (Lange et al. 1977) was used in two papers. Additionally, one paper used the patient hygiene performance index (Podshadley & Haley 1968) (Table 2b).

For all the three different regimens, a variation in results existed between the studies. When SnF_2 was used in a dentifrice/gel formulation 4 studies reported statistically significant plaque reduction compared with NaF and six others reported no difference, whereas none of the selected papers reported an effect in favour of NaF (Table 2b). When SnF_2 (alone or in combination with AmF) was used as a mouth rinse, two studies reported a statistically significant decrease in plaque compared with placebo or NaF (Table 2b). With regard to the combined regimen one study showed no significant differences between treatment groups whereas another demonstrated a significant drop in plaque in comparison to control (Table 2b).

- *Stain*

In total, eight studies provided information on dental staining. Several indices were used in these studies in order to assess the presence of staining: the Meckel stain index (Lang et al. 1982, Perlich et al. 1995, McClanahan et al. 1997), the stain intensity score or area (Beiswanger et al. 1995, 1997), the modified stain index (Podshadley & Haley 1968, Wolff et al. 1989), the stain index (Lobene 1968, Sgan-Cohen et al. 1996) or the modified stain index by Gründemann et al. (2000) and Paraskevas et al. (2005). One study (Boyd & Chun 1994) made the distinction between light, moderate, or heavy staining. Regardless of the index used, a statistically significant increase of the prevalence of staining in comparison with NaF (Beiswanger et al. 1995, 1997, Perlich et al. 1995, McClanahan et al. 1997, Paraskevas et al. 2005) or placebo (Wolff et al. 1989) seemed to be

a common finding after the use of different SnF_2 formulations.

Weighted means

A number of papers provided inappropriate or inadequate data presentation and were therefore unsuitable for weighted mean calculation. The remaining studies provided data on the baseline and end values, giving no information on the size and the standard deviation of the difference for the weighted mean calculation. Therefore, the reviewers used the baseline and end-point data and calculated the weighted mean for these points in order to combine the data of the various studies.

- *Dentifrice regimes*

Six papers presented sufficient mean data and standard deviation in order to be included in the weighted mean calculation. For the GI, on study basis, baseline values between the test and the control groups were of the same magnitude (Table 2b), indicating that the test and control groups were comparable. The pooled estimate from all studies included demonstrated very little heterogeneity between studies (Fig. 1. Weighted mean difference (WMD) -0.01, *Test for heterogeneity* $p = 0.52$, $I^2 = 0\%$)). At the end of the experimental period the weighted mean GI favoured the SnF_2 group (WMD -0.15, $p < 0.00001$, Test for heterogeneity $p < 0.00001$, $I^2 = 91.1\%$).

As the GSI represents the number of sites with a score two or three of the GI (i.e. sites with bleeding), a separate analysis was performed for the studies reporting on this index (Fig. 2). Again, baseline scores were compared for the use of dentifrice containing SnF_2 and favoured a significant ($p < 0.00001$) drop of 0.21 in the GSI (Test for heterogeneity $p = 0.03$, $I^2 = 80.1\%$) as opposed to the use of NaF-containing dentifrice at the end of the studies.

The two papers referring to the PI (Silness & Löe 1964) found no differences in baseline and end values (Beiswanger et al. 1997, Shapira et al. 1999). However, the rest of the articles using the Turesky modification found that at the conclusion of the studies, the use of a dentifrice containing 0.452% SnF_2 resulted in a significant decrease in plaque (calculated weighted mean 0.31, $p = 0.01$, test for heterogeneity $p < 0.0001$, $I^2 = 91.7\%$, Fig. 3).

- *Mouth rinse*.

For mouth-rinse formulations, two articles Leverett et al. (1984) and Zimmerman et al. (1993) presented data that were impossible to combine.

- *Dentifrice/mouth-rinse combination*

There was only one article available (Mengel et al. 1996).

In some of the analyses performed, there was an obvious heterogeneity in the clinical outcome of the selected studies. In case the testing for heterogeneity was significant the reader should take caution in using the WMD as the exact measure of the effect.

Discussion

This review was undertaken in order to reveal the effect of SnF_2 on parameters of gingival inflammation. As SnF_2 can be used in different formulations, the results of the present review were categorized according to the use of this agent in a dentifrice/gel, a mouth rinse or a combination of dentifrice and mouth rinse.

Evidence-based dentistry relates the evidence and professional expertise to the patient's preferences and values. In search of this evidence, the authors identified papers providing information that was relevant to the focused question.

Study characteristics – study quality assessment

The studies presented in this review are all prospective clinical trials using a parallel design. With the exception of one study, the studies were considered as randomized. The data extraction and analysis performed by the reviewers showed, however, that in the majority of the studies several issues were not always adequately addressed. Quality assessment of individual studies that are summarized in systematic reviews is necessary to limit bias in conducting the systematic review, gain insights into potential comparisons and guide the interpretation of the findings. With regard to the study quality, many of the studies did not provide additional information on the randomization method, and allocation concealment was not addressed with the exception of three studies. In some papers the presentation of the results was given by means of graphs or plots, making the interpretation of the results rather difficult, if not impossible. Data approximation based on graphic representations was not attempted. Furthermore, some studies did not report valuable information (such as sample size, standard deviations or standard errors of the mean) and therefore had to be excluded from further analysis. Subject drop-out was another issue to be evaluated. In most studies, data assessment was based on a decreasing number of individuals. Information on the reasons for drop-outs was not always provided. In some papers, drop-outs reached a level of $>10\%$ of the original baseline size (Wolff et al 1989, Beiswanger et al. 1995, Perlich et al. 1995, McClanahan et al. 1997). It is not known what the impact of these drop-outs on the study results could be, because no study reported separate analyses for the subjects dropping out until the time of exit. Additionally, there was considerable variation observed with regard to the sample size or the duration of the studies. For example, the studies by Boyd & Chun (1994) and Wolff et al. (1989) lasted 18 months and could be considered as the longest investigations reporting on dentifrice/gel formulations identified by this review. However, the study by Boyd & Chun (1994) was conducted on orthodontic patients – a fact that may limit the value of their results because it is well known that orthodontic appliances could hinder the plaque control performed by the individuals and promote the development of gingivitis. This study should therefore be regarded separately and therefore, was not included in the pooled GI estimate. The study by Wolff et al. (1989) initially recruited high numbers of patients ($N = 546$) but suffered from the relatively high numbers of drop-outs that occurred during the study (only 281 subjects completed the study). Also this study could not be included in the meta-analysis because of the presentation of data for GI and Plaque in the form of graphs.

Evidence

The majority of the studies lasted 6 months, which is considered the minimum requirement when the anti-gingivitis or anti-plaque efficacy of a given product is assessed (Council on Dental Therapeutics 1986). The reviewers identified one study (Zimmerman et al. 1993) that satisfied all the criteria of

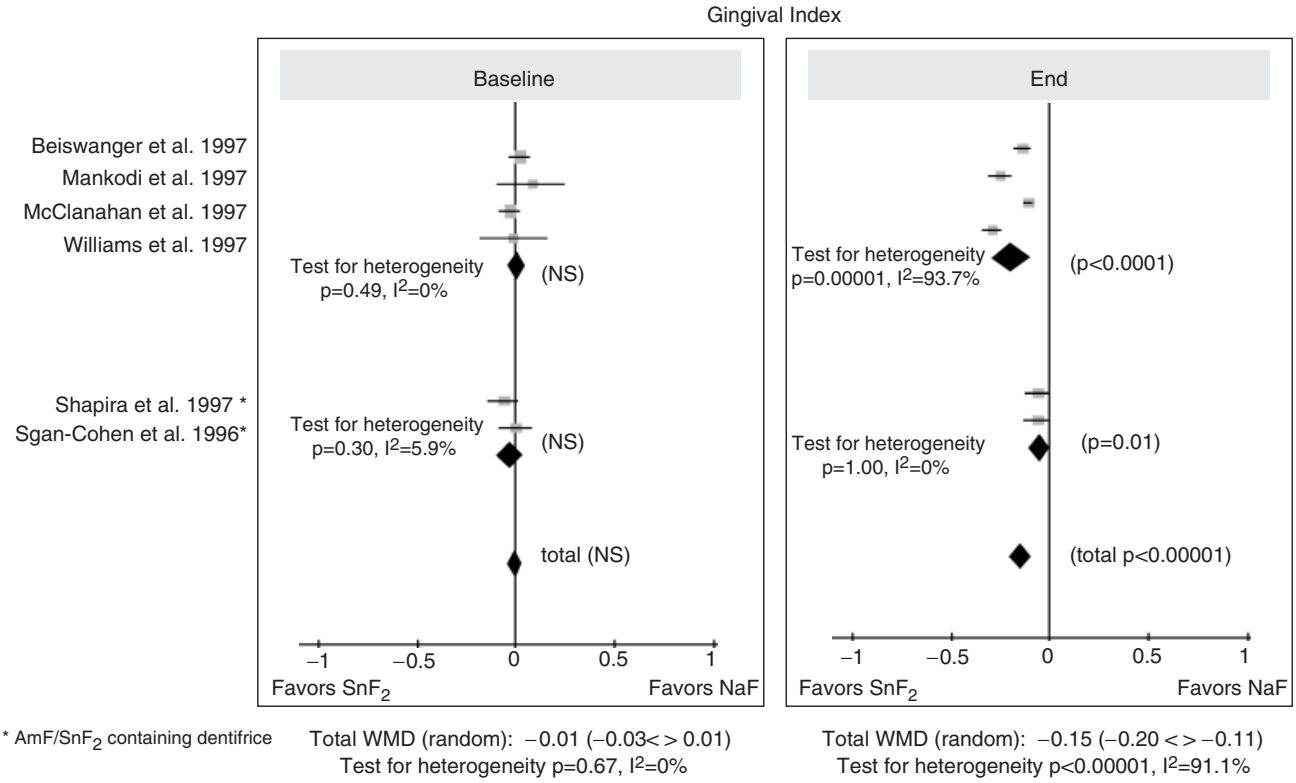

Fig 1. Forrest plot demonstrating baseline and end values for the gingival index for the studies using the *dentifrice* formulations. The size of the box signifies the ''weight'' or importance of the study. Weighted mean differences (WMD) are provided including the 95% confidence interval (CI).

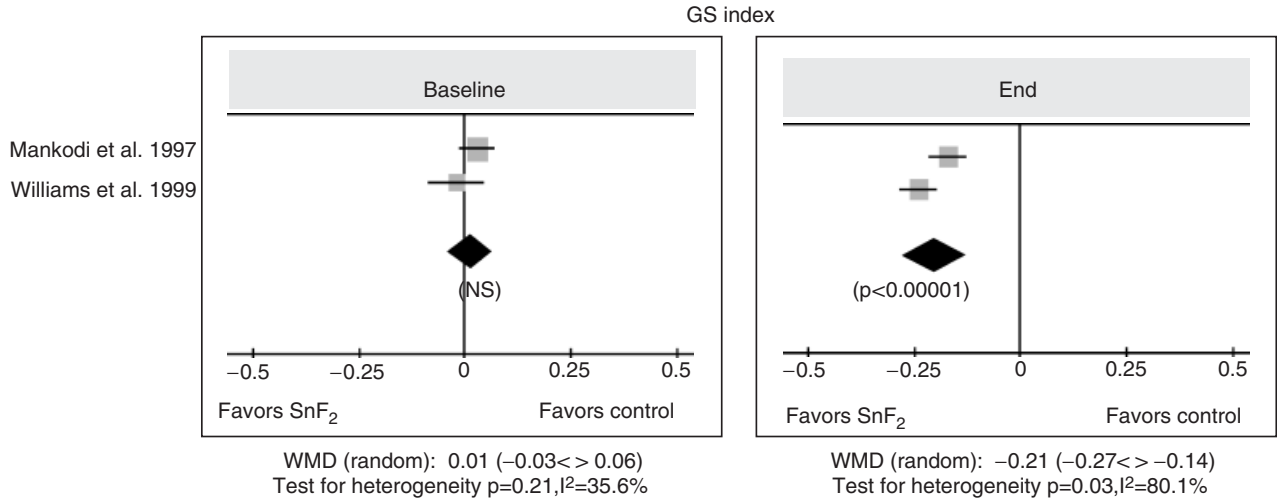

Fig 2. Forrest plots for baseline and end values for the gingivitis severity index for the studies using the *dentifrice* formulations. The size of the box signifies the ''weight'' or importance of the study. Weighted mean differences (WMD) are provided including the 95% confidence interval (CI).

study quality assessment. This could be considered as the highest level of evidence. In this particular study the effect of a mouth rinse containing AmF/SnF_2 on plaque and gingivitis was compared with the use of a placebo mouth rinse during a 7-month period. At the end of the experiment, significant differences between the two groups were observed in terms of plaque and gingivitis in favour of the AmF/SnF_2 group (Table 2b). These results are in line with the results as observed in the present review as shown in the weighted mean calculation that comprise the results of various studies (Figs 1–3).

When the combined (dentifrice/mouth rinse) regimen was taken into account, only one study was found that provided evidence of this regimen (Mengel et al. 1996). This study found

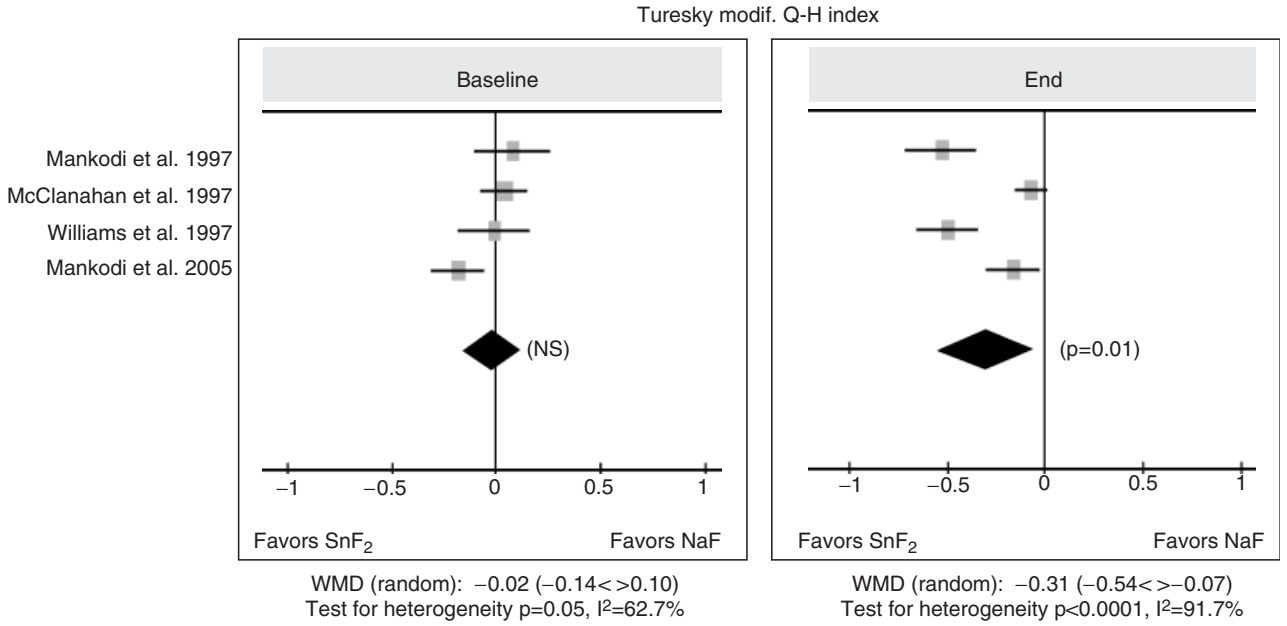

Fig 3. Forrest plot for the baseline and end values for the Turesky modification of the Quigley & Hein index for the studies using the *dentifrice* formulations. The size of the box signifies the ''weight'' or importance of the study. Weighted mean differences (WMD) are provided including the 95% confidence interval (CI).

no differences between treatment groups in terms of gingivitis and plaque. For both the mouth rinse and the dentifrice/mouth-rinse formulations, more research is necessary in order to gain further insight in the effects of SnF_2 (alone or in combination with AmF) on plaque and gingivitis.

Compliance

Compliance of the individuals with the given instructions should also be considered as an important factor that could affect the results of a given study. Two studies reported details on the compliance of individuals (Leverett et al. 1984, Wolff et al. 1989). In the Leverett et al. study, patients showing $>75\%$ compliance appeared to have greater reduction in gingivitis and plaque, whereas the Wolff et al. (1989) study stated that compliance is an important issue as it is impossible to determine the relative efficacy of the products not used. Klock et al. (1985) mentioned that their study population was ''unreliable'', thus providing scope for cautious interpretation of their results. Obviously, compliance should also be addressed in future studies on the use of oral hygiene products as this factor may affect study outcomes.

The fact that in some dentifrice studies a decrease of gingivitis was not always accompanied by a decrease in the amount of plaque can be explained by the fact that SnF_2 promotes qualitative changes of plaque towards a less pathogenic one (Perdok et al. 1989, Zimmerman et al. 1993, Mengel et al. 1996). Another explanation could be that this agent promotes the deposition of a pellicle protein layer as a result of topical application of this agent (Tinanoff & Weeks 1979, Rykke et al. 1991). It is speculated that the ''thickened'' pellicle layer may interfere with the measurements of plaque and may give an obscure interpretation of the actual plaque present (Skjorland et al. 1978, Leverett et al. 1984, Hasreiter 1989). Another factor to be taken into account when interpreting the results of various studies is the diversity in the study characteristics: variation in study populations (schoolchildren *versus* young *versus* older individuals) and baseline characteristics (plaque, gingivitis scores), oral hygiene reinforcement and compliance of individuals (supervision *versus* no supervision), possible unknown effects of smoking and socio-economic status of the individuals may help explain the observed differences.

Depending on the formulation and index used, a variation of results was observed when plaque was analysed. When the Turesky modification of the Quigley & Hein index was used (this index measures plaque area rather than thickness), a mean weighted difference of -0.31 was found between groups. Out of the five studies reporting on this index, there were three studies that found significant reductions in favour of the SnF_2 groups (Mankodi et al. 1997, 2005, Williams et al. 1997) and one study reported an increase in plaque levels after six months (McClanahan et al. 1997) for both the test and control group. However, the increase was less for the SnF_2 group. There was insufficient information available to perform a meta-analysis with respect to the use of the PI (Silness & Löe 1964). The two papers identified by this review (Beiswanger et al. 1997, Shapira et al. 1999) failed to report a significant effect on plaque between groups.

The presence of staining was assessed in a few studies. Despite variation in the methodology used for stain assessment, majority of them reported a statistically significant increase in staining after the use of SnF_2 when compared with NaF or placebo. Tooth stain may have social implications for the patient, may impair patient compliance, and may increase the time spent for polishing the dentition. It is recommended that patients and clinicians be aware of this adverse effect when evaluating the cost–benefit ratio of this oral hygiene agent (Guarnelli et al. 2004).

Important considerations

The GI uses a scale from 0 to 3 in order to express visual changes in the gingival tissues. One could say that such a reduction (-0.15) observed in relation to the control group is small when one considers the scale of the above-mentioned index. However, the magnitude of this reduction is better understood when one considers the individually reported percentage differences between test and control groups of the studies selected for the WMD calculation. The ADA and the Council on Dental Therapeutics state in their acceptance programme guidelines for chemotherapeutic products for the control of gingivitis that in terms of efficacy the test product should demonstrate a $>15\%$ reduction in gingivitis in comparison with placebo or, where applicable, with an active control product. In the present review, out of the seven studies included in the WMD calculation five of them complied with the $>15\%$ threshold of this guideline. In fact, 4 of them demonstrated $>20\%$ reduction in comparison with control.

The results of the present review should be viewed in the light of search limitations. It was restricted to two databases in order to identify studies conforming to the selection criteria. Although these databases are quite extensive, they may have missed papers reported in other bibliographic sources that report on subjects using the products in question. It was also restricted to papers written in English language. The possibility exists that there are papers written in other languages. Furthermore, no effort was made to retrieve information from industry on unpublished data.

At baseline no heterogeneity was observed meaning that at the start of the studies the test and control groups included were comparable. Therefore, the heterogeneity observed in the meta-analysis of the data at the end of the study reflected different behaviours of the study populations to the study product, differences in study designs and all other factors that may influence the outcomes. Heterogeneity is not a poor attribute in a meta-analysis, but it shows that the results of the different studies are inconclusive. A meta-analysis helps to detect whether the outcomes are in favour of the study product. However, in case the testing for heterogeneity was significant the reader should take caution in using the WMD as the exact measure of the effect.

Conclusions

The present literature search found insufficient information with regard to the effect of SnF_2 mouthrinses as well as the combined (dentifrice/mouthrinse) regimen on gingivitis and plaque in order to make any conclusion.

Regarding dentifrices, the reviewed literature showed that the use of SnF_2 dentifrice results in a reduction in gingivitis and plaque compared with control (NaF) dentifrices. The magnitude of this effect was relatively small and because the test for heterogeneity was significant, the reader should take caution in using the WMD as the exact measure of the effect.

References

Addy, M. & Adriaens, P. (1998) Consensureport of Group A. Epidemiology and etiology of periodontal diseases and the role of plaque control in dental caries. In: Lang, N., Attström, R. & Löe, H. (eds). *Proceedings of the European Workshop on Mechanical Plaque Control*, pp. 98–101. Berlin: Quintessence Publishing Co. Verlag.

Ainamo, A. & Osterberg, T. (1992) Changing demographic and oral disease patterns and treatment needs in the Scandinavian populations of old people. **42**, 311–322.

Axelsson, P., Lindhe, J. & Nystrom, B. (1991) On the prevention of caries and periodontal disease. Results of a 15-year longitudinal study in adults. *Journal of Clinical Periodontology* **18**, 182–189.

Baehni, P. C. & Takeuchi, Y. (2003) Anti-plaque agents in the prevention of biofilm-associated oral diseases. *Oral Diseases* **9** (Suppl. 1), 23–29.

Beiswanger, B. B. Doyle, P. M. Jackson, R. D. Mallatt, M. E. Mau, M. Bollmer, B. W. Crisanti, M. M. Guay, C. B. Lanzalaco, A. C. Lukacovic, M. F. Majetti, S. & McClanahan, S. F. (1995) The clinical effect of dentifrices containing stabilized stannous fluoride on plaque formation and gingivitis – a six-month study with ad libitum brushing. *Journal of Clinical Dentistry* **6** (Spec No.), 46–53.

Beiswanger, B. B. McClanahan, S. F. Bartizek, R. D. Lanzalaco, A. C. Bacca, L. A. & White, D. J. (1997) The comparative efficacy of stabilized stannous fluoride dentifrice, peroxide/baking soda dentifrice and essential oil mouthrinse for the prevention of gingivitis. *Journal of Clinical Dentistry* **8** (Spec No.), 46–53.

Binney, A., Addy, M., Owens, J., Faulkner, J., McKeown, S. & Everatt, L. (1996) A 3-month home use study comparing the oral hygiene and gingival health benefits of triclosan and conventional fluoride toothpastes. *Journal of Clinical Periodontology* **23**, 1020–1024.

Birkeland, J. M., Jorkjend, L. & von der Fehr, FR. (1973) The influence of fluoride mouth rinsing on the incidence of gingivitis in Norwegian children. *Community Dental Oral Epidemiology* **1**, 17–21.

Boyd, R. L. (1994) Long-term evaluation of a SnF_2 gel for control of gingivitis and decalcification in adolescent orthodontic patients. *International Dental Journal* **44** (Suppl. 1), 119–130.

Boyd, R. L. & Chun, Y. S. (1994) Eighteen-month evaluation of the effects of a 0.4% stannous fluoride gel on gingivitis in orthodontic patients. *American Journal of Orthodontics and Dentofacial Orthopedics* **105**, 35–41.

Boyd, R. L., Leggott, P. J. & Robertson, P. B. (1988) Effects on gingivitis of two different 0.4% SnF_2 gels. *Journal of Dental Research* **67**, 503–507.

Brayer, L., Antal, M., Sela, M., Gedalia, I. & Stabholtz, A. (1979) Effect of toothbrushing with a fluoride-free and fluoride-containing dentifrice on oral hygiene and number of leukocytes in the gingival fluid. *Journal of Periodontology* **50**, 604–606.

Brown, L. J., Brunelle, J. A. & Kingman, A. (1996) Periodontal status in the United States, 1998–1991: prevalence, extent, and demographic variation. *Journal of Dental Research* **75** (Spec No.), 672–683.

Council on Dental Therapeutics (1986) Guidelines for acceptance of chemotherapeutic agents for the control of supragingival plaque and gingivitis. *Journal of American Dental Association* **112**, 529–532.

Garmyn, P. D., van Steenberghe, D. & Quirynen, M. (1998) Efficacy of plaque control in the maintenance of gingival health: plaque control on primary and secondary prevention. In: Lang, N., Attström, R. & Löe, H. (Eds.) *Proceedings of the European Workshop on Mechanical Plaque Control*, pp. 107–120. Berlin: Quintessence Bublishing Co. Verlag.

Gründemann, L. J., Timmerman, M. F., IJzerman, Y. & Van der Weijden, G. A. (2000) Stain, plaque and gingivitis reduction by combining chlorhexidine and peroxyborate. *Journal of Clinical Periodontology* **27**, 9–15.

Guarnelli, M. E., Zangari, F., Manfrini, R., Scapoli, C. & Trombelli, L. (2004) Evaluation of additional amine fluoride/stannous fluoride-containing mouthrinse during supportive therapy in patients with generalized aggressive periodontitis. *Journal of Clinical Periodontology* **31**, 742–748.

Hasreiter, R. J. (1989) Is 0.4% stannous fluoride gel an effective agent for the prevention of oral diseases? *Journal of American Dental Association* **118**, 205–208.

Hoffmann, T., Bruhn, G., Richter, S., Netuschil, L. & Brecx, M. (2001) Clinical controlled study on plaque and gingivitis reduction under long-term use of low-dose chlorhexidine solutions in a population exhibiting good oral hygiene. *Clinical Oral Investigations* **5**, 89–95.

Hugoson, A., Norderyd, O., Slotte, C. & Thorstensson, H. (1998) Oral hygiene and gingivitis in a Swedish adult population 1973,

1983 and 1993. *Journal of Clinical Periodontology* **25**, 807–812.

Klock, B., Serling, J., Kinder, S., Manwell, M. A. & Tinanoff, N. (1985) Comparison of effect of SnF_2 and NaF mouthrinses on caries incidence, salivary *S. mutans* and gingivitis in high caries prevalent adults. *Scandinavian Journal Dental Research* **93**, 213–217.

Laine, P., Meurman, J. H., Murtomaa, H., Lindqvist, C., Torkko, H., Pyrhonen, S. & Teerenhovi, L. (1993) One-year trial of the effect of rinsing with an amine fluoride–stannous-fluoride-containing mouthwash on gingival index scores and salivary microbial counts in lymphoma patients receiving cytostatic drugs. *Journal of Clinical Periodontology* **20**, 628–634.

Lange, D. E. (1981) *Parodontogie in der täglichen Praxis*. Berlin: Quintessenz Verlag, pp. 96–98.

Lang, N. P., Hotz, P., Graf, H., Geering, A. H., Saxer, U. P., Sturzenberger, O. P. & Meckel A, H. (1982) Effects of supervised chlorhexidine mouthrinses in children. A longitudinal clinical trial. *Journal of Periodontal Research* **17**, 101–111.

Lange, D. E., Plagmann, H.-Chr., Eenboom, A. & Promesberger, A. (1977) Klinische Bewertungsverfahren zur Objektievierung der Mundhygiene. *Deutsche Zahnärztliche Zeitschrift* **32**, 44–47.

Larson, L. C., Allen, J. M., Hyman, J. J. & Pelleu, G. B. Jr. (1985) Effect of a 0.2% SnF_2 mouthrinse on gingival tissues and associated microflora. *Clinical Preventive Dentistry* **7**, 5–8.

Leverett, D. H. McHugh, W. D. & Jensen, O. E. (1984) Effect of daily rinsing with stannous fluoride on plaque and gingivitis: final report. *Journal of Dental Research* **63**, 1083–1086.

Leverett, D. H., McHugh, W. D. & Jensen, O. E. (1986) Dental caries and staining after twenty-eight months of rinsing with stannous fluoride or sodium fluoride. *Journal of Dental Research* **65**, 424–427.

Lindhe, J., Hansson, B. O. & Branemark, P. I. (1971) The effect of topical application of fluorides on the gingival tissues. *Journal of Periodontal Research* **6**, 211–217.

Lobene, R. R. (1968) effects of dentifrices on tooth stains with controlled brushing. *Journal of American Dental Association* **77**, 849–855.

Lobene, R. R., Weatherford, T., Ross, N. M., Lamm, R. A. & Menaker, L. (1986) A modified gingival index for use in clinical trials. *Clinical Preventive Dentistry* **8**, 3–6.

Löe, H. & Silness, J. (1963) Periodontal disease in pregnancy I. Prevalence and severity. *Acta Odontologica Scandinavica* **21**, 533–551.

Mandel, I. D. (1988) Chemotherapeutic agents for controlling plaque and gingivitis. *Journal of Clinical Periodontology* **15**, 488–498.

Mankodi, S. Bartizek, R. D. Winston, J. L. Biesbrock, A. R. McClanahan, S. F. & He, T. (2005) Anti-gingivitis efficacy of a stabilized 0.454% stannous fluoride/sodium hexametaphosphate dentifrice. *Journal of Clinical Periodontology* **32**, 75–80.

Mankodi, S., Lopez, M., Smith, I., Petrone, D. M., Petrone, M. E., Chaknis, P. & Proskin, H. M. (2002) Comparison of two dentifrices with respect to efficacy for the control of plaque and gingivitis, and with respect to extrinsic tooth staining: a six-month clinical study on adults. *Journal of Clinical Dentistry* **13**, 228–233.

Mankodi, S. Petrone, D. M. Battista, G. Petrone, M. E. Chaknis, P. DeVizio, W. Volpe, A. R. & Proskin, H. M. (1997) Clinical efficacy of an optimized stannous fluoride dentifrice, Part 2: a 6-month plaque/gingivitis clinical study, northeast USA. *Compendium of Continuing Education in Dentistry* **18** (Spec No.), 10–15.

McClanahan, S. F. Beiswanger, B. B. Bartizek, R. D. Lanzalaco, A. C. Bacca, L. & White, D. J. (1997) A comparison of stabilized stannous fluoride dentifrice and triclosan/copolymer dentifrice for efficacy in the reduction of gingivitis and gingival bleeding: six-month clinical results. *Journal of Clinical Dentistry* **8** (Spec No), 39–45.

Mengel, R. Wissing, E. Schmitz-Habben, A. & Flores-de-Jacoby, L. (1996) Comparative study of plaque and gingivitis prevention by AmF/SnF_2 and NaF. A clinical and microbiological 9-month study. *Journal of Clinical Periodontology* **23**, 372–378.

Miller, S., Truong, T., Heu, R., Stranick, M., Bouchard, D. & Gaffar, A. (1994) Recent advances in stannous fluoride technology: antibacterial efficacy and mechanism of action towards hypersensitivity. *International Dental Journal* **44**, 83–94.

Morris, A. J., Steele, J. & White, D. A. (2001) The oral cleanliness and periodontal health of UK adults in 1998. *British Dental Journal* **191**, 186–192.

National Institute of Dental Research (NIDR) (1987) Oral Health of United States adults. National Findings. US Department of Healthy and Human Services, Washington, DC, N.I.H. Publication No. 87-2868.

Palomo, F., Wantland, L., Sanchez, A., DeVizio, W., Carter, W. & Baines, E. (1989) The effect of dentifrice containing triclosan and a copolymer on plaque formation and gingivitis. A 14-week clinical study. *American Journal of Dentistry* **2**, 231–237.

Paraskevas, S. Versteeg, P. A. Timmerman, M. F. Van der Velden, U. & Van der Weijden, G. A. (2005) The effect of a dentifrice and mouthrinse combination containing amine fluoride/stannous fluoride on plaque and gingivitis. A six-month field study. *Journal of Clinical Periodontology* **32**, 757–764.

Perdok, J. F., Busscher, H. J., Weerkamp, A. H. & Arends, J. (1988) The effect of an amine-fluoride-stannous fluoride-containing mouthrinse on enamel surface free energy and the development of plaque and gingivitis. *Clinical Preventive Dentistry* **10**, 3–9.

Perlich, M. A. Bacca, L. A. Bollmer, B. W. Lanzalaco, A. C. McClanahan, S. F. Sewak, L. K. Beiswanger, B. B. Eichold, W. A. Hull, J. R. Jackson, R. D. & Mau, M. S. (1995) The clinical effect of a stabilized stannous fluoride dentifrice on plaque formation, gingivitis and gingival bleeding: a six-month study. *Journal of Clinical Dentistry* **6** (Spec No.), 54–58.

Podshadley, A. G. & Haley, J. V. (1968) A method for evaluating oral hygiene performance. *Public Health Reports* **83**, 259–264.

Quigley, G. & Hein, J. (1962) Comparative cleansing efficacy of manual and power brushing. *Journal of American Dental Association* **65**, 26–29.

Rykke, M., Ellingsen, J. E. & Sonju, T. (1991) Chemical analysis and scanning electron microscopy of acquired pellicle formed *in vivo* on stannous fluoride treated enamel. *Scandinavian Journal of Dental Research* **99**, 205–211.

Seymour, A. & Heasman, A. (1992) Anti-plaque and anti-calculus agents. In: Seymour, A. & Heasman, A. (eds) *Drugs, Diseases, and the Periodontium*, p. 156. New York: Oxford University Press.

Sgan-Cohen, H. D. Gat, E. & Schwart, Z. (1996) The effectiveness of an amine fluoride/stannous fluoride dentifrice on the gingival health of teenagers: results after six months. *International Dental Journal* **45**, 340–345.

Shapira, L. Shapira, M. Tandlich, M. & Gedalia, I. (1999) Effect of amine fluoride-containing toothpast (Meridol) on plaque and gingivitis in adults: a six-month clinical study. *Journal of the International Academy of Periodontology* **4**, 117–120.

Silness, J. & Löe, H. (1964) Periodontal disease in pregnancy II. Correlation between oral hygiene and periodontal condition. *Acta Odontologica Scandinavia* **22**, 121–135.

Skjorland, K., Gjermo, P. & Rolla, G. (1978) Effect of some polyvalent cations on plaque formation *in vivo*. *Scandinavian Journal of Dental Research* **86**, 103–107.

Spindel, L. M., Chauncey, H. H. & Person, P. (1986) Plaque reduction unaccompanied by gingivitis reduction. *Journal of Periodontology* **57**, 551–554.

Tinanoff, N., Manwell, M. A., Zameck, R. L. & Grasso, J. E. (1989) Clinical and microbiological effects of daily brushing with either NaF or SnF_2 gels in subjects with fixed or removable dental prostheses. *Journal of Clinical Periodontology* **16**, 284–290.

Tinanoff, N. & Weeks, D. B. (1979) Current status of SnF_2 as an antiplaque agent. *Pediatric Dentistry* **1**, 199–204.

Turesky, S., Gilmore, N. D. & Glickman, I. (1970) Reduced plaque formation by the chloromethyl analogue of vitamin C. *Journal of Periodontology* **41**, 41–43.

Wenderoth, C. J., Weinstein, M. & Borislow, A. J. (1999) Effectiveness of a fluoride-releasing sealant in reducing decalcification during orthodontic treatment. *American Journal of Orthodontics and Dentofacial Orthopedics* **116**, 629–634.

Winer, R. A., Epstein, S. & Chauncey, H. H. (1986) Effect of an experimental dentifrice on plaque accumulation and gingival inflammation. *Special Care Dentistry* **6**, 228–230.

Williams, C. McBride, S. Bolden, T. E. Mostler, K. Petrone, D. M. Petrone, M. E. Chaknis, P. DeVizio, W. Volpe, A. R. & Proskin, H. M.

(1997) Clinical efficacy of an optimized stannous fluoride dentifrice, Part 3: a 6-month plaque/gingivitis clinical study, southeast USA. *Compendium of Continuing Education in Dentistry* **18** (Spec No.), 16–20.

Wolff, L. F. Pihlstrom, B. L. Bakdash, M. B. Aeppli, D. M. & Bandt, C. L. (1989) Effect of toothbrushing with 0.4% stannous fluoride and 0.22% sodium fluoride gel on gingivitis for 18 months. *Journal of American Dental Association* **119**, 283–289.

Van Loveren, C. (1990) The antimicrobial action of fluoride and its role in caries inhibition. *Journal of Dental Research* **69** (Spec No.), 676–683.

Van Loveren, C. (2001) Antimicrobial activity of fluoride and its *in vivo* importance: identification of research questions. *Caries Research* **35** (Suppl. 1), 65–70.

Van der Weijden, G. A., Timmerman, M. F., Saxton, C. A., Russell, J. I., Huntington, E. & Van der Velden, U. (1994b) Intra-/inter-examiner reproducibility study of gingival bleeding. *Journal of Periodontal Research* **29**, 236–241.

Yankell, S. L., Shern, R. J., Stoller, N. H. & Green, P. A. (1982) Effects of topically applied stannous fluoride and acidulated phosphate fluoride alone and in combination on dental plaque. *Journal of Periodontal Research* **17**, 380–383.

Yates, R. J., Shearer, B. H., Morgan, R. & Addy, M. (2003) A modification to the experimental gingivitis protocol to compare the antiplaque properties of two toothpastes. *Journal of Clinical Periodontology* **30**, 119–124.

Yoon, N. A. & Berry, C. W. (1979) An *in vivo* study of the effects of fluoride (SnF2 0.4%, APF 1.23%, and neutral NaF 0.05%) on levels of organisms resembling Actinomyces, gingival inflammation and plaque accumulation. *Journal of Dental Research* **58**, 535–536.

Zimmerman, A. Flores-de-Jacoby, L. & Pan, P. (1993) Gingivitis, plaque accumulation and plaque composition under long-term use of Meridol®. *Journal of Clinical Periodontology* **20**, 346–351.

Address:
S. Paraskevas
Department. of Periodontology
Academic Center for Dentistry Amsterdam (ACTA)
Louwesweg 1
1066 EA Amsterdam
The Netherlands
E-mail: s.paraskevas@acta.nl

Clinical Relevance

Scientific rationale: Tin combined with fluoride (SnF_2) is a well-known agent that has been used for many decades in the formulations of dentifrices. Although most of the studies agree upon the fact that the SnF_2 products have a plaque-reducing effect, there is inconclusive evidence with regard to the effects of several SnF_2 formulations on gingivitis.

Principal findings: There is little and conflicting information with respect to the effect of SnF_2 mouthrinses and the combined (dentifrice/mouthrinse) regimen on gingivitis and plaque. However, there is substantial information on dentifrice formulations. Meta-analysis demonstrated a significant reduction in gingivitis and plaque in favour of the SnF_2-containing dentifrices when compared with a conventional dentifrice. The precise magnitude of the effect was difficult to assess because of a high level of heterogeneity in the study outcomes.

Implications for practice: SnF_2 dentifrice/gel formulations result in a reduction of plaque and gingivitis. However, whether this reduction will lead to long-term clinical benefits for the patients remains to be determined.