REVIEW ARTICLE

Enamel lesions: Meta-analysis on effect of prophylactic/therapeutic agents in erosive tissue loss

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Abstract This study aims to perform a meta-analysis on the effect of prophylactic/therapeutic agents in enamel tissue loss due to erosion. A paper search was done on Medline, PubMed, Embase, and Cochrane Library, and 732 papers were identified. The inclusion criteria were very restrictive in order to be able to compare different protocols and methodologies used on those studies. Sixteen papers were eligible, grouped according to the measurement method of enamel tissue loss, and a meta-analysis was done for each type of fluoride- and casein-based agent applied. Standardized mean differences were pooled across studies. There was a significant difference between all the treatment groups and their respective control groups. The highest standardized mean difference on enamel tissue loss (mean; 95% confidence interval) was obtained by stannous fluoride (4.789 μm; 1.968–7.610; $P < 0.001$), followed by amine fluoride (2.485 μm; 0.746–4.225; $P < 0.010$), and titanium tetrafluoride (1.787 μm; 1.106–2.469; $P < 0.001$); the lowest difference was obtained by casein phosphopeptide–amorphous calcium phosphate (0.869 μm; 0.007–1.731; $P < 0.050$) and sodium fluoride (0.820 μm; 0.417–1.223; $P < 0.001$). Stannous fluoride as a fluoride-based prophylactic/therapeutic agent allowed the lowest enamel tissue loss in erosive conditions. Standardization among future study protocols will allow better comparison regarding the prophylactic/therapeutic agent with the best clinical efficacy.
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Introduction

Dental erosion is the physical result of a pathologic, chronic, localized, painless loss of dental hard tissues chemically etched away from the tooth surface by acid and/or chelating agents without bacterial involvement. The initial etching results in a mineral partial superficial dissolution—early-stage surface softening,[1] which can reach a few micrometers into enamel or dentine. If the erosive challenge is more prolonged, the outermost layer of the softened surface will eventually be completely dissolved, resulting in permanent loss of tooth structures.[2,3]

Effective measures to control and prevent the erosive wear lesions should include management of dietary and behavioral habits[4] and also daily intervention with effective prophylactic and/or therapeutic agents.[5,6] In principle, there are two possibilities to prevent or control dental erosion: either the active agents are added to an erosive solution in order to decrease its erosive potential; or the active agents are applied directly on the enamel tooth surface to create a protective layer inhibiting enamel demineralization. After an erosive attack, part of the enamel hard tissue surface is lost and cannot be recovered, but there is a partially demineralized softened enamel surface that can be rehardened in the presence of certain substances.[7] The repair process includes the re-precipitation of ions, into the partly demineralized surface enamel, allowing the modification of the tooth surface so that the erosive demineralization is reduced, even under persisting acid challenges (therapeutical agent's effect). The several compounds tested in *in vitro* and *in situ* trials usually have both effects, leading to surface deposits and structural enamel modifications in order to enhance acid resistance. There are different prophylactic/therapeutic agents, several concentrations and ways of delivering, experimentally tested in, *in vitro*, *in situ*, and *in vivo* trials.

The aim of this paper is to perform a meta-analysis on output data of published studies regarding the effects of several prophylactic/therapeutic agents on enamel loss due to tissue demineralization, under erosive conditions.

Materials and methods

Search strategy

The guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement—Transparent Reporting of Systematic Reviews and Meta-Analyses[8] were followed whenever possible. The search was conducted in the Medline, PubMed, Embase, and Cochrane Library for published papers in order to collect and interpret the available evidence on the protective effect of prophylactic/therapeutic agents on enamel tissues due to erosion. Although randomized clinical trials provide the highest level of evidence, this study design is not feasible for measuring enamel tissue loss due to erosive demineralization. Therefore only laboratory *in vitro* and *in situ* studies were included in this review, despite some concerns about the validity of the multiple treatments meta-analysis methods.

There are several agents available to prevent/enhance acid resistance of enamel structure. The most frequently tested agents were fluoride-based agents, namely sodium fluoride (NaF), amine fluoride (AmF), stannous fluoride (SnF_2), titanium tetrafluoride (TiF_4), and casein-derived protein products, delivered as solutions, gels or varnishes.

Full search strategy for literature evidence in databases was performed with the following keywords: #1 ("Dental enamel" [MeSH]) AND ("Tooth Erosion" [MeSH]) OR ("Tooth demineralization" [MeSH]); #2 ("Fluorides" [MeSH]); #3 ("Caseins" [MeSH]); #4 (#1 AND #2); #5 (#1 AND #3); #6 (#4 OR #5). Filters: from 1980 to 01/03/2014, English.

Study selection

The articles identified in all databases were screened for duplicates that were automatically excluded. Two readers independently selected references according to the title and the abstract of each publication. After title/abstracts were screened, the remaining articles were ordered in full text. Figure 1 presents the details of the identification, screening and the article selection process.

Inclusion criteria

In vitro and *in situ* studies on dental erosion, which gather the following conditions. (1) The tested agent must be a single agent, enamel only substrate, an erosive protocol only, human or bovine enamel. (2) The study must provide: sample size, control group without any agent application being only submitted to the erosive protocol, erosion measurement data obtained by the microhardness and profilometry methods, and quantitative results of enamel tissue loss (mean ± standard deviation), and be English published papers (full texts only).

Exclusion criteria

All *in vivo* studies, *in vitro*, and *in situ* studies on erosion, which gather one of the following conditions: the tested
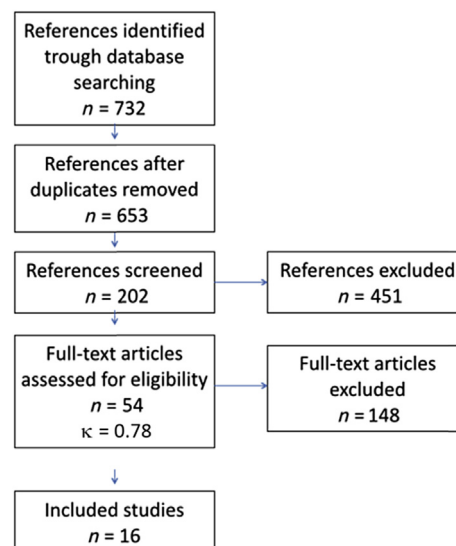

Figure 1   Summary of article selection process.

Table 1 Sample characteristics—size, mean and standard deviation of tissue loss (μm) in control and agent groups, and observed variations, of the selected profilometry studies.

Reference	N	Control group		Tested agent			Variations
		n	Mean ± SD (D n	Type of agent	n	Mean ± SD (D n	
Schlueter et al 2009[10]	144	18	36.1 ± 4.6	TiF$_4$ (6 × 2 min) A	18	2.1 ± 1.9	Difference in agent's
	144	18	19.8 ± 4.2	TiF$_4$ (2 × 2 min) B	18	13.8 ± 3.4	time of application with 2 controls
Magalhães et al 2008[11]	20	10	1.17 ± 0.48	TiF$_4$	10	2.4 ± 0.6	
Yu et al 2010[12]	220	10	2.96 ± 0.55	TiF$_4$ pH 1.2 A	10	1.28 ± 0.36	Different agent pH
				TiF$_4$ pH 4 B	10	2.34 ± 0.38	
				SnF$_2$ pH 1.2 G	10	0.84 ± 0.54	
				SnF$_2$ pH 4 H	10	0.96 ± 0.34	
				NaF pH 1.2 E	10	2.35 ± 0.35	
				NaF pH 4 F	10	2.01 ± 0.34	
				AmF pH 1.2 D	10	0.17 ± 0.32	
				AmF pH 4 C	10	0.16 ± 0.30	
Magalhães & Buzalaf 2007[13]	60	15	3.43 ± 1.13	TiF$_4$ varnish at 2nd day A	15	3.81 ± 0.43	Different time points
				NaF varnish at 2nd day C	15	3.16 ± 0.32	with 2 controls
	60	15	7.31 ± 0.53	TiF$_4$ varnish at 4th day B	15	7.69 ± 0.76	
				NaF varnish at 4th day D	15	7.56 ± 0.90	
Magalhães et al 2008[14]	72	12	2.06 ± 1.49	TiF$_4$ varnish A	12	0.65 ± 0.75	Different agent
				NaF varnish B	12	1.47 ± 1.07	consistencies
				TiF$_4$ solution C	12	2.05 ± 1.49	
Hove et al 2006[15]	24	6	2.0 ± 0.2	TiF$_4$ solution at 2 min etch A	6	0.0 ± 0.1	Different time points
				SnF solution at 2 min etch G	6	0.4 ± 0.2	with 3 controls
				NaF solution at 2 min etch D	6	1.5 ± 0.2	
	24	6	4.4 ± 0.3	TiF$_4$ solution at 4 min etch B	6	0.1 ± 0.1	
				SnF$_2$ solution at 4 min etch H	6	1.5 ± 0.5	
				NaF solution at 4 min etch E	6	3.4 ± 0.3	
	24	6	7 ± 0.3	TiF$_4$ solution at 6 min etch C	6	0.8 ± 0.8	
				SnF$_2$ solution at 6 min etch I	6	3.5 ± 0.7	
				NaF solution at 6 min etch F	6	5.3 ± 0.4	
Hove et al 2007[16]	60	12	2.2 ± 0.6	TiF$_4$ solution at 2 min etch A	12	0 ± 0.4	
				SnF$_2$ solution at 2 min etch I	12	1.2 ± 0.9	
				NaF solution at 2 min etch E	12	2.1 ± 0.7	Different time points
	60	12	5.2 ± 1.0	TiF$_4$ solution at 4 min etch B	12	1.3 ± 1.2	with 4 controls
				SnF$_2$ solution at 4 min etch J	12	4.0 ± 1.7	
				NaF solution at 4 min etch F	12	4.7 ± 1.3	
	60	12	8.1 ± 1.3	TiF$_4$ solution at 6 min etch C	12	4.7 ± 1.7	
				SnF$_2$ solution at 6 min etch K	12	6.6 ± 2.5	
				NaF solution at 6 min etch G	12	7.6 ± 1.7	
	60	12	11.0 ± 1.5	TiF$_4$ solution at 8 min etch D	12	8.4 ± 2.1	
				SnF$_2$ solution at 8 min etch L	12	9.5 ± 3.2	
				NaF solution at 8 min etch H	12	10.6 ± 1.9	
Hove et al 2008[17]	56	14	18.1 ± 9.2	TiF$_4$ solution A	14	0.5 ± 0.9	
				SnF$_2$ solution C	14	1.7 ± 4.0	Type of agent
				NaF solution B	14	21 ± 8.3	
Hove et al 2011[18]	40	8	2.38 ± 0.66	TiF$_4$ pH 1.2 0.5M at 2 min etch A	8	0.45 ± 0.45	Different time-points
				TiF$_4$ pH 1.2 0.05M at 2 min etch B	8	2.07 ± 1.21	with pH 1,2 and different
	40	8	4.68 ± 1.10	TiF$_4$ pH 1.2 0.5M at 4 min etch C	8	2.46 ± 2.35	agent concentrations
				TiF$_4$ pH 1.2 0.05M at 4 min etch D	8	5.05 ± 2.76	
	40	8	7.03 ± 1.49	TiF$_4$ pH 1.2 0.5M at 6 min etch E	8	5.08 ± 3.93	
				TiF$_4$ pH 1.2 0.05M at 6 min etch F	8	10.21 ± 1.82	
	40	8	2.38 ± 0.66	TiF$_4$ pH 2.1 0.5M at 2 min etch G	8	2.08 ± 1.00	Different time-points
				TiF$_4$ pH 2.1 0.05M at 2 min etch H	8	0.72 ± 0.76	with pH 2,1 and different
	40	8	4.68 ± 1.10	TiF$_4$ pH 2.1 0.5M at 4 min etch I	8	4.51 ± 1.71	agent concentrations
				TiF$_4$ pH 2.1 0.05M at 4 min etch J	8	4.05 ± 0.97	
	40	8	7.03 ± 1.49	TiF$_4$ pH 2.1 0.5M at 6 min etch K	8	6.67 ± 1.96	

(continued on next page)

Table 1 (*continued*)

Reference	N	Control group		Tested agent			Variations
		n	Mean ± SD (D n	Type of agent	n	Mean ± SD (D n	
				TiF_4 pH 2.1 0.05M at 6 min etch L	8	6.68 ± 0.93	
Wiegand et al 2009[19]	130	10	2.3 ± .0.8	SnF_2 0.5% acidic pH H	10	0.6 ± 1.1	Different agents
				SnF_2 1% acidic pH I	10	0.6 ± 0.8	concentrations with
				NaF 0.5% acidic pH D	10	1.2 ± 1.1	acidic pH
				NaF 1% acidic pH E	10	2.3 ± 0.8	
				AmF 0.5% acidic pH C	10	1.1 ± 1.0	
				AmF 1% acidic pH	10	0.9 ± 0.4	
	130	10	2.3 ± .0.8	NaF 0.5% neutral pH F	10	1.4 ± 1.0	Different agents
				NaF 1% neutral pH G	10	2.0 ± 1.3	concentrations with
				AmF 0.5% neutral pH A	10	1.4 ± .1.4	neutral pH
				AmF 1% neutral pH B	10	1.7 ± .0.8	
Schlueter et al 2009[20]	180	20	33.6 ± 15.4	NaF solution	20	24.2 ± 9.2	
White et al 2011[21]	64	8	25.8 ± 4.74	Casein+F NaF solution	8	12.2 ± 1.16	Type of agent
				Casein B	8	20.3 ± 3.14	
				NaF solution A	8	21.6 ± 2.81	
Rees et al 2007[22]	30	10	5.02 ± 1.16	CPP-ACP	10	3.28 ± 1.22	
Poggio et al 2009[23]	30	10	0.5 ± 15	CPP-ACP	10	0.20 ± 0.09	
Vieira et al 2005[24]	42	6	9.77 ± 0.49	TiF_4 1%	6	8.29 ± 0.39	Different agent
				TiF_4 4%	6	8.27 ± 0.55	concentrations
				AmF 1% A	6	8.69 ± 0.66	
Levy et al 2012[25]	120	10	2.68 ± 0.53	TiF_4 varnish A	10	0.53 ± 0.20	Different agent
				NaF varnish C	10	0.94 ± 0.18	consistencies
				TiF_4 solution B	10	3.55 ± 0.59	
				NaF solution D	10	2.84 ± 0.09	

AmF = amine fluoride; CPP-ACP = casein phosphopeptide—amorphous calcium phosphate.

agent is an association of several compounds, dentin substrate, an erosive-abrasion protocol, erosion measurement data obtained by other methods such as: atomic absorption spectroscopy, colorimetric analysis, longitudinal microradiography, or others than these, and studies with incomplete sample or methods information.

In order to minimize the risk of bias, some authors were contacted to clarify issues in their studies, to avoid uncertainty during the data extraction phase of the review.

Disagreements were solved by discussion and consensus. If necessary, the exclusion criteria were adjusted and the abstracts already screened were resubjected to the selection process. Agreement between readers was determined using κ statistics. In the absence of consensus, a third reader was called upon to analyze it. After the publication screening, based on the title and abstracts, full-text copies of the selected articles were assessed for eligibility. A total of 16 studies met the inclusion criteria and were selected for the meta-analysis study.

Synthesis of data

The included studies were grouped according to the method of analysis of enamel tissue loss. Microhardness is considered the method of election for measuring enamel softening (early stages of erosion) and profilometry is the direct method used to measure enamel loss by erosive wear (advanced stages of erosion).[9]

The calculation of the enamel tissue loss was made using the same method for all the studies selected. Treatment and control group tissue hardness mean value differences from pre- to postoperative status were obtained directly, or calculated based on the time-specific mean values obtained from studies results.

Enamel surface microhardness change (SMHC) percentage measurement was calculated as follows:

$$\%SMHC = (SMH_f - SMH_b)/SMH_b \times 100 \qquad (1)$$

where SMH_f is surface microhardness after erosive demineralization and agent application and SMH_b is surface microhardness before erosive demineralization (baseline).

In the studies that used profilometry tests, the enamel tissue loss was measured in μm (micrometers) and calculated as the difference between the reference area and the exposed area to erosive attack and agent application, both in the control and treatment groups.

Statistical analysis

All calculations and graphs were performed using the software R version 3.0.1 (Free Software Foundation, Inc., Boston, USA), with the Metafor package. The statistical heterogeneity among studies was assessed using the inconsistency index, I^2 measure.

Each agent [TiF_4, AmF, NaF, SnF_2, and casein phosphopeptide—amorphous calcium phosphate (CPP-ACP)] was compared to the control group, where an erosive protocol was done with no agent applied. The analysis was done using the standardized mean difference with 95% confidence intervals (95%CI).

The bias analysis was done with the Begg and the Egger tests, and an analysis of the results sensitivity was also performed. For this, the results were excluded one at a time to test their consistency.

Results

Profilometry studies results

A high heterogeneity ($I^2 > 50\%$) was found in all groups, which led us to use the random effects model. Table 1

presents all the mean and standard deviation of enamel tissue loss (μm) in the control and agent groups, from all the studies selected.

The outcomes from each treatment analysis are presented on the forest-plots (Figs. 2—6).

Table 2 presents the overall obtained standardized mean difference between tissue loss of each control group and the treatment group (μm), defined according to the agent applied. There is a significant difference between all the treatment groups and their respective control groups. The highest standardized mean difference was obtained with the SnF_2, followed by the AmF and TiF_4 and the
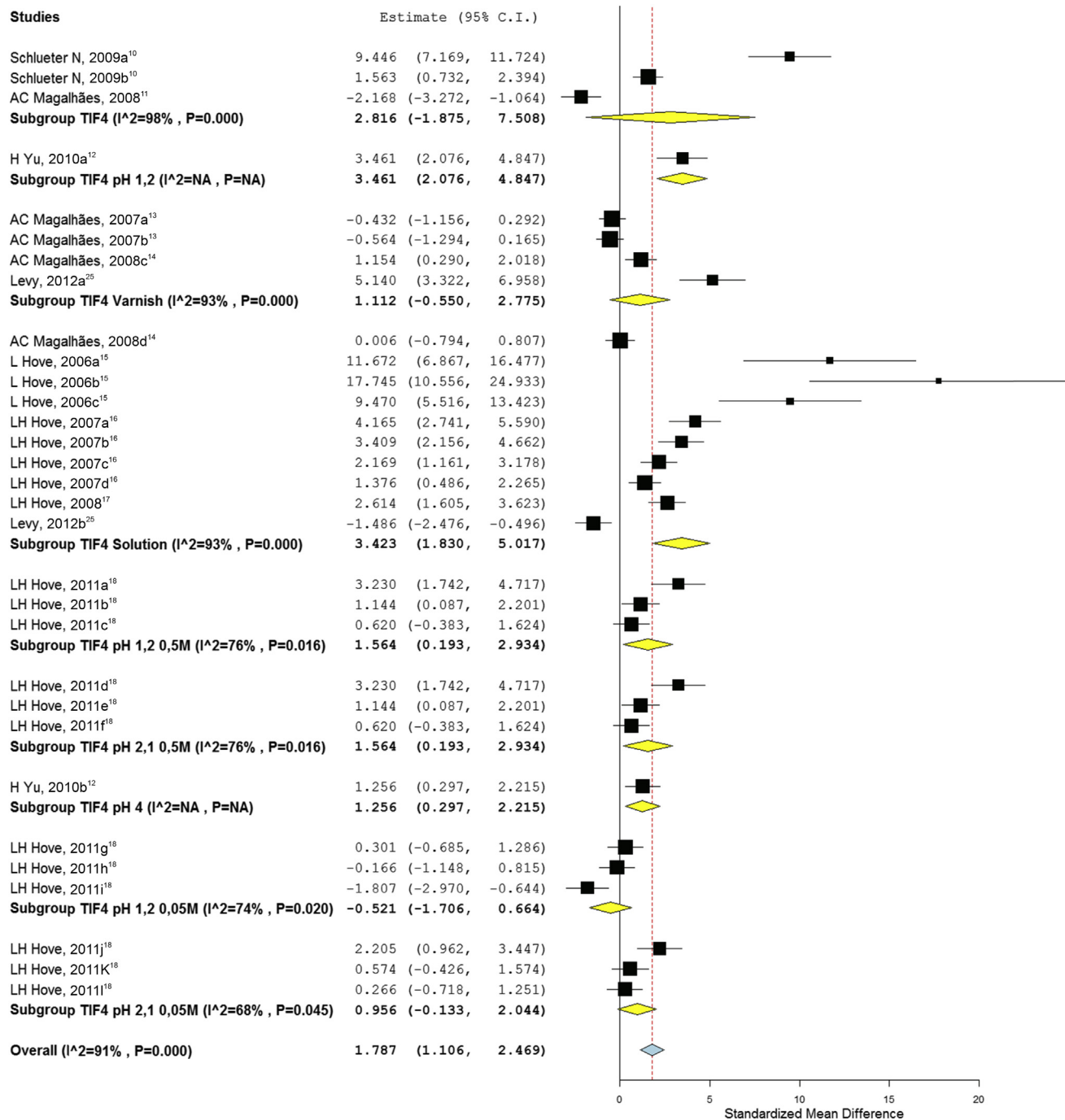

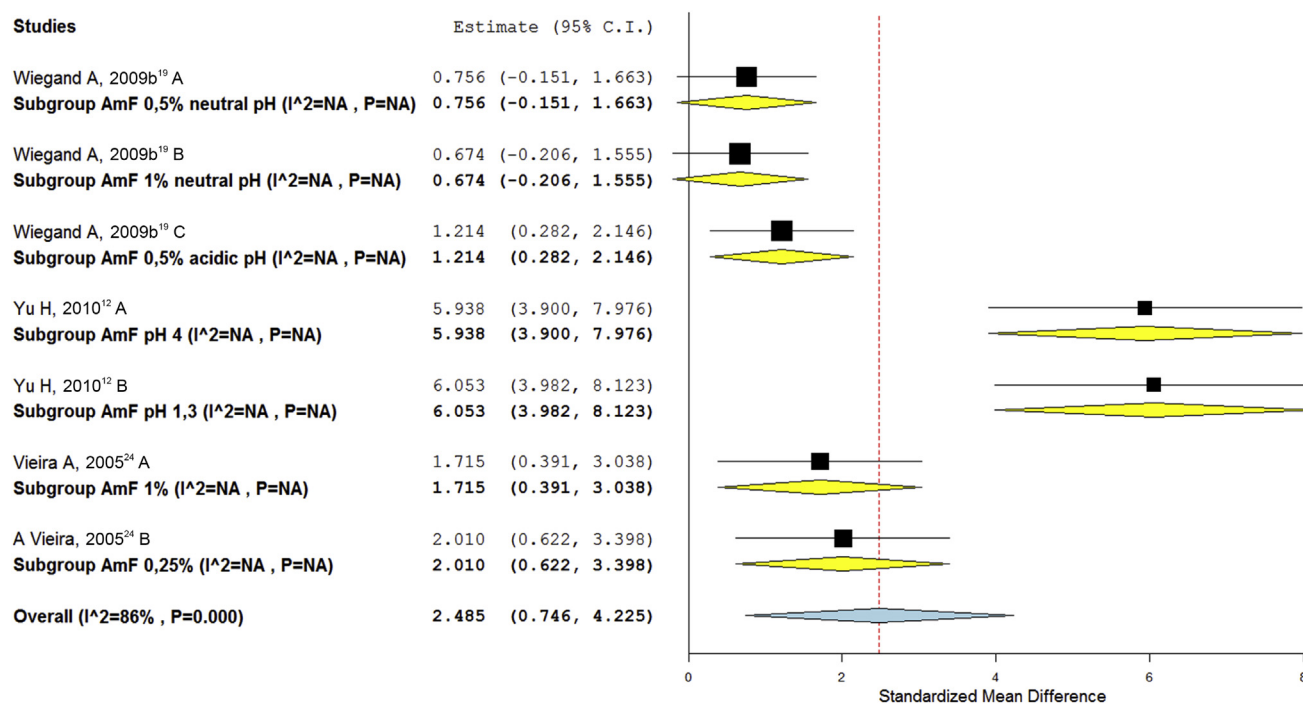**Figure 2** Forest plot: control group versus TiF_4 group.

Figure 3   Forest plot: Control group versus amine fluoride group.

lowest difference was obtained with the NaF and CPP-ACP agents.

Microhardness studies results

In studies where microhardness testing was used as the method for enamel tissue loss measurement, the only agents compared were the TiF$_4$ and NaF. Table 3[11,13,21,26] presents the mean and standard deviation of SMHC% in the control and agent groups from the selected studies. In the comparison between the control group and the TiF$_4$ group, the heterogeneity was high ($I^2 > 50\%$) so the random effects model was used. In the case of the control group compared with the NaF group the heterogeneity found was low ($I^2 < 50\%$), and the methodology used was based on the fixed effects model.

The main outcomes are presented for both comparisons (control vs. TiF$_4$; Figure 7, and control vs. NaF; Figure 8) individually and with combined results. Figure 7 shows the overall results (random effects); it appears that the control group has significantly higher surface microhardness change means than the TiF$_4$ group. The application of the Begg test (Z = 1.019, P = 0.308) and Egger test [t(2) = 2.059, P = 0.176] showed no bias (P ≥ 0.05) between studies.

When sensitivity was evaluated, the overall result found was 0.873 (95%CI, 0.054—1.691). Omitting the Magalhães AC[11] or Magalhães AC[14] studies, the standardized mean of the control group remains significantly higher than the TiF$_4$ group. If the Magalhães AC[26] or Magalhães AC[13] studies are excluded, the statistically significant differences between the control group and the group TiF$_4$ disappear.

Figure 8 shows the overall results (fixed effects) of the standardized mean difference between the control group and NaF group. The enamel tissue loss means from the control groups are significantly higher than in the NaF groups. According to the results of Begg test (Z = 1.045; P = 0.296) and Egger test [t(1) = 12.050, P = 0.053], there was no bias (P ≥ 0.05) between studies.

When analyzed, the sensitivity, and if omitting any of the three studies,[13C,13D,21] the same result remains: the standardized mean difference from the control groups was significantly higher than the NaF groups, with an overall result from the sensitivity tests of 2.051 (95%CI, 1.285—2.817).

Discussion

Studies to test possible methods and agents to prevent enamel erosion should ideally be conducted *in vivo*, using intraoral measurement of tooth tissue loss.[27] Unfortunately, the available methods have a low accuracy.[28] There is also uncertainty about the pattern of erosion progression, which implies a need for long-term monitoring studies; it is also difficult to control the enamel tissue loss that results from erosion alone or from attrition/abrasion processes. There are only two *in vivo* trials that had, as purpose, to evaluate the effect of therapeutic agents against enamel erosion.[29,30]

In situ and *in vitro* models have been developed as attempts to overcome these problems. Here, standardized controls can be implemented, allowing for the examination of one variable at a time, the introduction of new variables stepwise, and accurate measurement technologies over defined time periods, and can be used to determine dental tissue loss.[27] These two types of studies are the most used in evaluating agents' action on dental erosion. This study aims to synthesize large amounts of information of *in situ* and *in vitro* trials, providing estimated effect sizes that
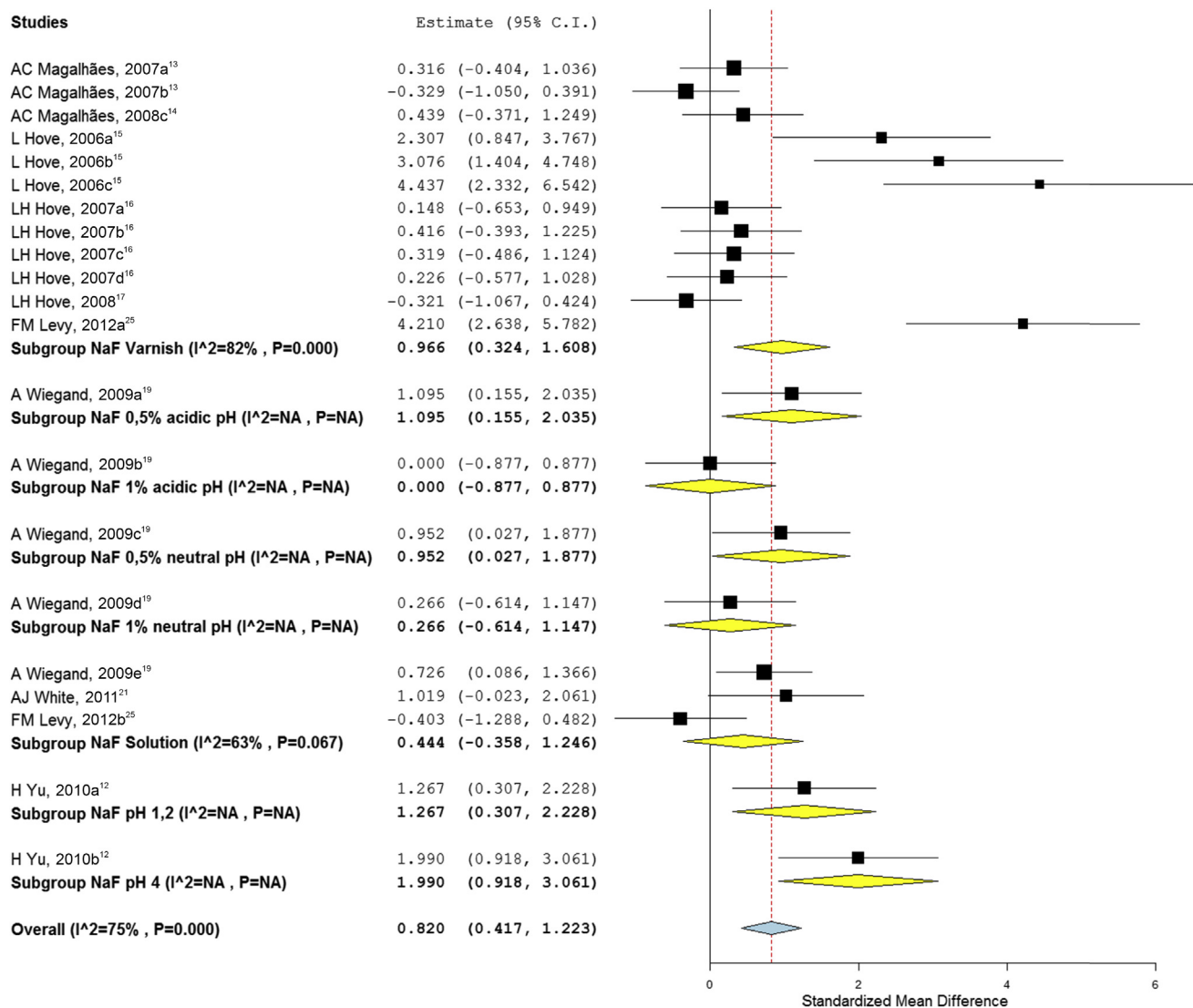
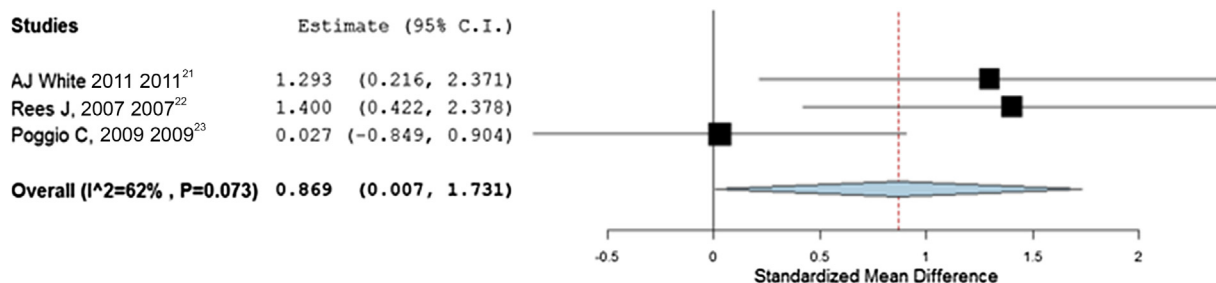**Figure 4**   Forest plot: Control group versus NaF.

Figure 5   Forest plot: Control group versus casein phosphopeptide—amorphous calcium phosphate group.

have greater precision and generalizability than individual studies.[31]

The inclusion criteria were very restrictive, in order to turn the studies comparable. Even so, there was a wide range of protocols on the enamel demineralization time/method, on the agent's composition/method of delivery, and also on methods of measuring enamel tissue loss. This posed a serious restriction on this attempt to review the literature in a quantitative, systematic manner. Including studies that compare control groups with single agents applied, excluding the association of several compounds, may be a limitation of this meta-analysis. However, this was necessary in order to allow some standardization among experiments and a better comparison regarding their
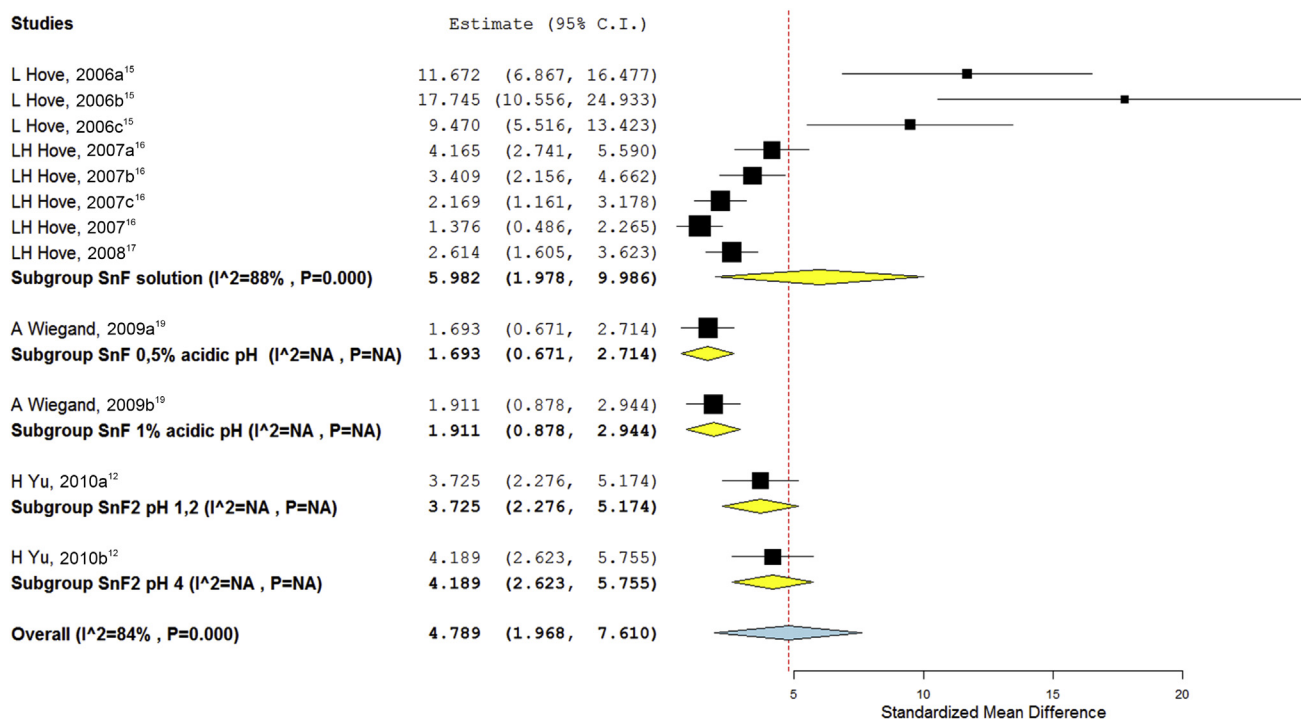
Figure 6 Forest plot: control group versus SnF$_2$ group.

effect. Several fluoride- and casein-based agents are available to prevent/enhance acid resistance of enamel structure, but, for this review, the most frequently used (NaF, AmF, SnF$_2$, TiF$_4$, CPP-ACP) were selected. Methods for measuring enamel tissue loss are also very different, and in some studies are not the most adequate. The choice of the method for evaluating erosion depends primarily on the stage of the lesion, the expected changes in the structure of the erosive lesion during the study and on the tissue of interest.[32] Microhardness is considered the method of choice for measuring enamel softening (early stages of erosion)[9] and profilometry is the direct method used to measure tissues loss by erosive wear (advanced stages of erosion).[32] Study protocols analyzed are very different, which makes it difficult to compare them and to establish which one is the most adequate agent to prevent/control

enamel tissue loss. Standardization of protocols is needed to ensure a valuable and scientific comparison between agent efficacies.

The lowest erosive tissue loss values were obtained by SnF$_2$, considering enamel tissue loss mean difference values between the control and the SnF$_2$ treatment groups, followed by the AmF and TiF$_4$ groups. The lowest difference was obtained with the NaF and the CPP-ACP, in both methods of enamel tissue loss measurement. SnF$_2$ was the agent that allowed the best enamel demineralization-protection in erosive conditions. The studies included in this review were performed under laboratory conditions, which limits the extrapolation of the actual usefulness of these agents application to the clinical situation. Despite this, the results might guide the researcher on evidence-based *in vitro* and *in situ* erosive enamel tissue loss data and suggest best practice given current knowledge. The erosion protection mechanism by tin effect is due to the reaction products which emerge from the interaction between hydroxyapatite and the tin fluoride preparation.[20] Lower pH-value solutions, are more protective against erosive enamel wear, partially due to the increased formation of CaF$_2$-like deposit and better incorporation of metal ions (Sn) into enamel.[12,20] Several studies tested the SnF$_2$ prophylactic/therapeutic effect against enamel erosion[12,15–17,19,33–36] or tin-and fluoride-containing solutions.[37] Considering the literature review, under mild-erosive conditions, tin and titanium seemed to be the ions that combined with fluoride obtained higher levels of consensuses by the authors.[10,33,35,38–41] In severe-erosive conditions the Sn-fluoride compounds showed better results on preventing enamel erosive tissue loss.[10] The problem with titanium fluoride agents, is that the titanium ion is

Table 2 Overall obtained standardized mean difference between the control and treatment group tissue loss (μm), defined according to the agent applied, on selected profilometry studies.

Group analysis	Standardized mean difference (μm) of tissue loss (95% CI)
TiF$_4$ vs. Control	1.787 (1.106−2.469) P < 0.001
AmF vs. Control	2.485 (0.746−4.225) P < 0.010
NaF vs. Control	0.820 (0.417−1.223) P < 0.001
SnF$_2$ vs. Control	4.789 (1.968−7.610) P < 0.001
CPP-ACP vs. Control	0.869 (0.007−1.731) P = 0.073

AmF = amine fluoride; CPP-ACP = casein phosphopeptide −amorphous calcium phosphate.

Table 3 Sample characteristics: size, mean and standard deviation of surface microhardness change percentage (SMHC%) in control and agent groups, and observed variations, of the selected microhardness studies.

| Reference	N	Control group		Tested agent			Variations
		n	Mean ± SD (%)	Type of agent	n	Mean ± SD (%)	
Magalhães et al 2009[26]	20	10	84.42 ± 14.05	TiF$_4$ solution	10	73.32 ± 11.65	
Magalhães et al 2008[11]	20	10	83.4 ± 4.64	TiF$_4$ solution	10	73.40 ± 5.12	
Magalhães & Buzalaf 2007[13]	60	15	87.96 ± 2.23	TiF$_4$ varnish at 2nd day A	15	88.28 ± 3.2	Different time points
				NaF varnish at 2nd day C	15	77.26 ± 5.05	with 2 controls
	60	15	94.15 ± 1.14	TiF$_4$ varnish at 4th day B	15	92.04 ± 2.55	
				NaF varnish at 4th day D	15	88.59 ± 5.11	
White et al 2011[21]	64	8	58.2 ± 810.5	NaF solution A	8	13.3 ± 25.3	Type of agent
				Casein solution	8	21.8 ± 20.3	
				Casein+ NaF	8	19.1 ± 32.5	
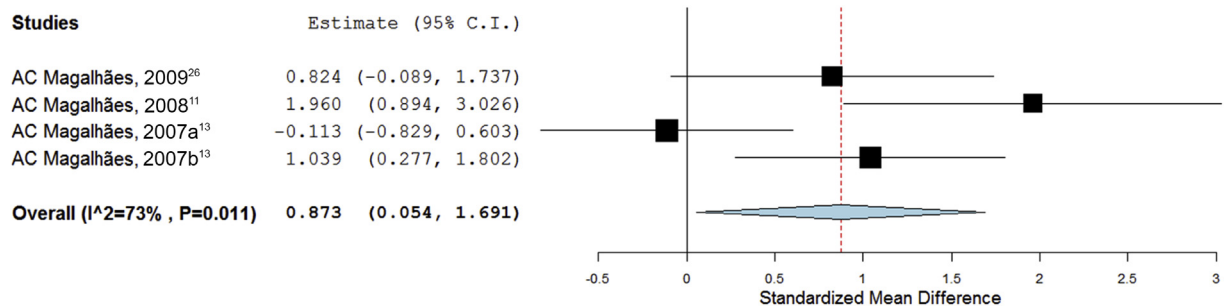
Figure 7 Forest plot: individual and pooled results of control group versus TiF$_4$.
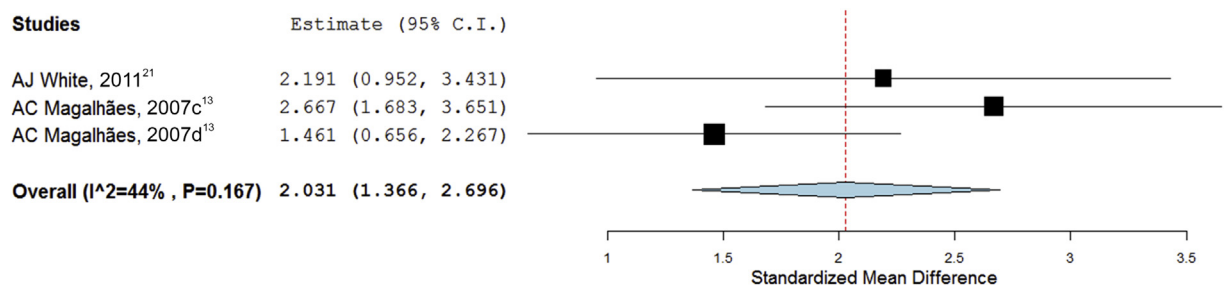

Figure 8 Forest plot: individual and pooled results of control group versus NaF group.

highly dependent on pH medium, meaning that the solutions must be very acidic to obtain the maximum effect regarding enamel demineralization prevention.[42,43] The need for high concentration and low pH limits its use as a mouth rinse.[10] Outputs from some studies showed a 50–90% enamel tissue loss reduction.[17,20,44] According to Schlueter et al,[45] high concentrations of Sn and fluoride are very effective in reducing erosive tissue loss, and their efficacy increases with increasing ratios of Sn to fluoride concentrations.

Dealing with heterogeneity among study treatment effects, or the situation in which differences in study outcomes are not readily accounted for by sampling variation, is one of the most important challenges a meta-analysis has to face.[46] The next step includes the examination of moderator variables impact on this study effect sizes by using regression-based techniques, in order to reinforce stannous fluoride's importance on enamel erosion.

Conflict of interests

The authors received no financial support and declare no potential conflicts of interest with respect to the authorship and/or publication of this article.

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