Effectiveness of dentifrices with new formulations for the treatment of dentin hypersensitivity - A meta-analysis

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Abstract: Purpose: This meta-analysis was conducted to evaluate if strontium-acetate- and arginine-containing dentifrices can significantly reduce dentin hypersensitivity (DH). **Methods:** A systematic literature search was performed. The investigation period was from 2006 to 2015 with the search term "dentin hypersensitivity". Nine original articles were relevant. A network meta-analysis of combined z scores was performed. Pooled results from random effects models with their 95% confidence intervals are reported. **Results:** The results from the random effects network meta-analysis show a significant improvement for the agents strontium acetate, arginine, and arginine with whitener, at all times for all stimuli, in comparison with the placebo. Strontium chloride is equivalent to the placebo. None of the dentifrices had a negative effect on DH. This meta-analysis showed that strontium-acetate- and arginine-containing dentifrices can significantly reduce DH. Calcium sodium silicate and potassium nitrate formulas show a tendency for pain relief. Because of the limited power of the available studies, a randomized study with several agents is recommended. (*Am J Dent* 2017;30:221-226).

Clinical significance: The aim of the treatment of dentin hypersensitivity (DH) is pain relief. Dentifrices with formulations of strontium acetate, of arginine or of arginine with whitener seem to have a good impact in the therapy of DH and can be recommended for daily use.

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Introduction

Dentin hypersensitivity is described as a short sharp pain attributable to an external stimulus, which can be thermal, evaporative, tactile, chemical or osmotic and cannot be ascribed to any other form of dental defect, disease or pathology.[1] This occurs on root surfaces or coronal dentin exposed by attrition, abrasion or erosion of the overlying enamel. Periodontal disease, orthodontic treatment or mechanical trauma can result in the removal of the overlying soft tissue from the root surface. The resulting pain is explained by the so-called hydrodynamic theory:[2] pain sensations, which exhibit great inter-individual variability, result from a fluid shift in the dentin tubules and the consequent stimulation of free nerve endings inside the pulp-dentin complex. Dentin hypersensitivity is a widespread problem. Prevalence estimates range as high as 74%.[3] Most studies, however, report estimates between 10-30%.[4] During the last few years, numerous treatments to minimize hypersensitivity reactions have been proposed, differing greatly in invasiveness and cost. They range from the use of toothpastes and mouthwashes, gels and topically applied coatings, adhesive bondings and composite coverage up to endodontic treatment or surgical recession coverage.[5] Some treatments can be applied by the patient, whereas others must be performed by a dental practitioner. Several review articles [6,7] have previously been published, providing information about the effectiveness of the particular treatment methods.

In recent years, however, a clear trend for the development of new formulations of toothpastes for dentin hypersensitivity has become apparent. Toothpastes are the most widespread tool used for the treatment of sensitive teeth.[8] In particular, arginine and calcium sodium phosphosilicates are considered promising approaches. This systematic review provides an overview concerning the effectiveness of newly developed formulations for dentifrices, including the formulations containing arginine or calcium sodium phosphosilicate that have recently been introduced on the market.[9]

Arginine is an amino acid found in toothpastes in combination with bicarbonate and calcium carbonate. These formulations contain 8% arginine and calcium carbonate and 1,450 ppm fluoride as sodium monofluorophosphate. Exposed dentin tubules have been shown to be blocked and sealed by these agents.[10] A clinical study indicated their effectiveness in the treatment of dentin hypersensitivity and in vitro studies have demonstrated their ability to seal dentin tubules.[11]

Calcium sodium phosphosilicate is a bioactive glass that was originally developed for bone regeneration and is characterized by high biocompatibility.[12] This material reacts with liquids and is able to deposit hydoxycarbonate-apatite. It is chemically similar to the apatites contained in enamel and dentin.[13] Added to a dentifrice, apatite is deposited onto the dentin surface and provides mechanical closure of the dentin tubules.[14] The aim of this systematic review and network meta-analysis has been to investigate the potential benefits of arginine and calcium sodium phosphosilicate in comparison with previously available formulations.

Materials and Methods

Chosen studies - Studies that were considered eligible had to be randomized or non-randomized controlled clinical trials (RCT or CCT), published between 2006 and 2015 in English language journals, comparing new formulation toothpastes for the treatment of dentin hypersensitivity with established toothpastes or placebo preparations as controls in a parallel group design. At least 30 subjects of any age and gender had to be included per treatment group and followed-up for a mini-

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mum period of 6 weeks. Participating subjects should not have suffered from any form of dental pathology other than dentin hypersensitivity. Eligible treatments were arginine plus calcium carbonite (ACC) or calcium sodium phosphosilicate (CSS) in comparison to potassium nitrate (KNO_3), strontium acetate [$(CH_3COO)_2Sr_2$], strontium chloride ($SrCl_2$), tin fluoride (SnFl) or a placebo (using the same formulation of the dentifrice minus the active ingredient). Pain-inducing stimuli could be thermal, evaporative or tactile. Pain outcomes had to be measured either on a visual analogue scale (VAS) or by dolorimetry.

To identify the relevant publications, we searched PubMed, Embase, the Cochrane Register of Controlled Trials, the National Research Register and the Cochrane Oral Health Group's Trials Register by using the search term "dentin hypersensitivity". The search for "dentin hypersensitivity" resulted in 3,109 hits (Fig. 1).

Two independent reviewers screened the hits according to the criteria indicated above. After screening, 13 original works remained. Since only nine of these 13 articles dealt with ACC and/or CSS, the remaining four were excluded.

The same two independent reviewers extracted information regarding treatments and outcome measurements. The extracted data were recorded in an Excel worksheet.

Statistical methods - We classified study results into short-, mid- and long-term outcomes (ascertained at t = 2 weeks, 5 ± 1 weeks and 10 ± 2 weeks, respectively).

Because of the wide range of pain stimuli (tactile, thermal, evaporative) and measurement methods (VAS, dolorimetry), we transformed all outcome measurements to z scores based on the arithmetic mean and standard deviation of the respective baseline measurements. Thus, all clinical measurements were expressed as differences from the baseline averages by using the baseline standard deviation as the measurement unit. Negative z scores represent better clinical outcomes.

If the original papers were unclear about the variability of results during the follow-up examinations, we imputed a standard deviation of 1 for the z scores.

In a second step, we created a combined outcome measure by averaging the z scores for the outcomes reported in the respective studies. The standard error for this combined outcome measure was calculated from the standard errors of the original z scores by using the delta method.

The network meta-analysis of the combined z scores was performed by using the R package netmeta version 0.8-0 (Gerta Rücker, Guido Schwarzer, Ulrike Krahn, and Jochen König, 2015. netmeta: Network Meta-Analysis Using Frequentist Methods. R package version 0.8-0. http://CRAN.R-project.org/package=netmeta). Network graphs were used to illustrate the evidence base available for the respective time points. In this method, an edge linking two treatments stands for at least one study comparing these two therapies directly. The width of the edges is proportional to the inverse of the standard errors of the respective effect estimates. Thus, wider edges indicate more reliable estimates. Any heterogeneity/inconsistency of the results was assessed by means of the I-squared statistic and the respective P value of the Q test for heterogeneity. Using forest plots, pooled results from random effects models with their 95% confidence intervals were reported.

Results

Table 1 summarizes the main characteristics and raw results of the included studies. The studies selected were conducted in Canada, China, Italy, USA and the United Kingdom. The number of patients ranged from 66[15] to 121.[16] The studies were conducted in universities, in military facilities and in private practices. All studies were funded by pharmaceutical companies.

Table 2 shows the z scores calculated from the raw data. Table 3 gives the combined z scores averaged over the measurements in response to the various stimuli under investigation.

Figure 2 shows the network graphs for the evidence base at times t= 2 weeks, 4 to 6 weeks and 8 to 12 weeks. The I-squared values at these time points were 82.9% (Q= 23.44, df= 4, P= 0.0001), 93.2% (Q= 58.93, df= 4, P< 0.0001) and 97.8% (Q= 91.63, df= 2, P< 0.0001), suggesting considerable heterogeneity within the network.

The central results from the random effects meta-analysis are summarized as forest plots in Fig. 3. The effect estimates depicted in the plot are mean differences between the combined z scores for the respective treatment versus the placebo. Negative numbers indicate better clinical outcomes. At all three time points, three treatments appeared superior to the placebo: $(CH_3COO)_2Sr$ 8% and ACC 8% with or without whitener. Mean differences for $(CH_3COO)_2Sr$ were –2.96 (95% CI: –4.68 to –1.23), –4.38 (95% CI: –6.98 to –1.78) and –6.38 (95% CI: –10.84 to –1.93). The corresponding values for ACC 8% without whitener were –2.44 (95% CI: –3.56 to –1.32), –3.27 (95% CI: –4.91 to –1.63) and –4.18 (95% CI: –7.11 to –1.26). Results for ACC 8% with whitener were similar: –2.80 (95% CI: –4.16 to –1.45), –3.92 (95% CI: –5.89 to –1.95) and –4.72 (95% CI: –8.00 to –1.44). No evidence supported any of the other active treatments.

Discussion

Dentin hypersensitivity is defined as a short pain which occurs in teeth with exposed dentin and which is caused by mechanical, tactile, thermal, evaporative, osmotic or chemical stimuli. The concerned teeth have no other defect or pathology. The prevalence is described in the literature with a wide range of 42-74%.[17-20]

The increase is caused, on the one hand, by the higher life expectancy linked with the desire to retain one's own teeth and, on the other hand, by eating habits with erosive and abrasive foods.[21] Dentin hypersensitivity represents, for many patients, a certain impaired quality of life.[22]

The pathological mechanism can be explained by the hydrodynamic theory. Fluid inside the dentin tubules is set into motion at the exposed dentin by the above stimuli. The resulting excitation of nerve endings and the forwarding of this excitation to the central nervous system causes pain. This is still the most recognized theory of the phenomenon of dentin hypersensitivity.[23]

However, a prerequisite is always exposed dentin. The causes of the exposure are multifactorial. Both mechanical effects by improper brushing and especially by erosive substances are critically discussed.[8,22,24] Moreover, scaling and root planing in the treatment of periodontitis can be blamed for the emergence of dentin hypersensitivity.[25]

Table 1. Raw results from the clinical trials included in the network meta-analysis. Results are reported as means and standard deviations (SD) for the different outcome variables at various follow-up times after different stimuli (TC = tactile, TH = thermal, EV). "NA" indicates that the standard deviation was not available from the publication.

Author, year	Treatment (no. of subjects) A	B	C	Stimulus	Outcome measurement	Time (weeks)	Mean A	SD A	Mean B	SD B	Mean C	SD C
Litkowski 2010	CSS 2.5% (22)	CSS 7.5% (22)	Placebo (22)	TC	VAS (0-100 mm)	0	48.40	10.32	49.20	10.32	47.50	10.79
						2	34.80	NA	28.10	NA	42.40	NA
						4	29.80	NA	21.70	NA	33.80	NA
						8	30.80	NA	13.20	NA	31.00	NA
				TH	VAS) 0-100 mm	0	50.00	7.97	49.40	8.44	48.70	8.91
						2	44.90	NA	45.50	NA	46.10	NA
						4	35.50	NA	45.00	NA	41.90	NA
						8	34.50	NA	44.70	NA	34.20	NA
Que 2010	ACC 8.0% with whitener (40)	ACC 8.0% (40)	Placebo (41)	TC	Dolorimetry (10-50 grams)	0	16.38	7.51	15.00	6.89	16.59	7.54
						2	36.50	12.26	35.75	11.91	22.20	10.37
						4	45.50	6.58	44.62	7.79	26.59	11.64
						8	48.50	4.11	48.00	4.91	30.12	12.57
				EV	Scale (0-3)	0	2.13	0.29	2.13	0.32	2.13	0.34
						2	1.18	0.56	1.16	0.68	1.99	0.45
						4	0.75	0.55	0.76	0.64	1.82	0.38
						8	0.44	0.56	0.38	0.52	1.72	0.46
Sharma 2010	KNO_3 5.0% (40)	SnFl 0.4% (40)	CSS 7.5% (40)	TH	VAS (0-10 cm)	0	5.78	1.12	5.68	1.05	5.60	0.98
						2	3.83	1.57	4.18	1.38	2.88	0.91
						4	2.93	1.10	2.95	0.99	1.68	0.66
						12	1.20	0.97	0.85	0.86	0.53	0.68
				EV	VAS (0-10 cm	0	5.85	1.03	5.83	1.01	5.73	0.99
						2	3.80	1.32	4.10	1.13	3.15	0.92
						4	2.98	0.80	3.18	1.01	1.80	0.91
						12	0.95	0.88	0.75	0.93	0.73	0.78
Hughes 2010	$(CH_3COO)_2Sr_2$ 8.0% (39)	ACC 8.0% (39)		TC	Dolorimetry (10-50 grams)	0	10.60	2.05	10.80	2.93		
						2	16.80	NA	15.50	NA		
						4	24.50	NA	21.20	NA		
						8	33.80	NA	26.90	NA		
				EV	Scale (0-3)	0	2.40	0.42	2.40	0.45		
						2	2.00	NA	2.00	NA		
						4	0.80	NA	0.70	NA		
						8	0.10	NA	0.20	NA		
				EV	VAS (0-100 mm)	0	43.10	23.13	43.40	23.12		
						2	33.90	NA	35.80	NA		
						4	25.80	NA	27.70	NA		
						8	17.70	NA	22.40	NA		
Pradeep 2010	CSS 5% (36)	KNO_3 5% (37)	Placebo (37)	TH	VAS (0-10 cm)	0	8.43	1.26	7.66	1.52	6.91	1.28
						2	6.37	1.02	6.51	1.52	6.00	1.09
						6	2.57	0.84	3.94	1.28	4.31	1.09
				EV	VAS (0-10 cm)	0	7.17	1.5	6.57	1.52	6.40	1.09
						2	4.71	1.38	5.66	1.34	5.20	1.09
						6	1.97	0.84	3.66	1.09	3.83	0.73
Docimo 2009a	ACC 8.0% (40)	KNO_3 5% (40)		TC	Dolorimetry (10-50 grams)	0	11.75	3.11	11.50	3.24		
						1	17.25	8.08	13.38	4.44		
						2	25.87	8.16	18.63	4.67		
						4	40.75	7.30	31.62	8.04		
						8	45.63	3.95	40.88	5.18		
				EV	Scale (0-3)	0	2.49	0.42	2.39	0.33		
						1	1.98	0.63	2.05	0.39		
						2	1.59	0.59	1.91	0.36		
						4	0.89	0.82	1.21	0.37		
						8	0.45	0.34	0.68	0.31		
Docimo 2009b	ACC 8.0% (40)	KNO_3 2% (40)		TC	Dolorimetry (10-50 grams)	0	12.13	3.74	13.63	4.38		
						2	26.45	6.99	19.30	6.99		
						4	40.98	7.87	31.52	7.87		
						8	45.40	5.30	40.47	5.30		
				EV	Scale (0-3)	0	2.49	0.37	2.51	0.40		
						2	1.65	0.51	2.17	0.51		
						4	0.92	0.56	1.35	0.56		
						8	0.49	0.39	0.69	0.39		
Ayad 2009	ACC 8.0% (38)	KNO_3 2% (39)		TC	Dolorimetry (10-50 grams)	0	14.08	6.24	13.46	5.52		
						2	23.12	6.87	19.90	6.87		
						4	36.21	6.75	29.59	6.75		
						8	47.34	3.35	39.00	3.35		
				EV	Scale (0-3	0	2.67	0.35	2.64	0.30		
						2	1.86	0.41	2.22	0.41		
						4	1.09	0.35	1.54	0.35		
						8	0.34	0.39	0.93	0.39		
Du Min 2008	CSS 5% (25)	Placebo (25)	$SrCl_2$ (25)	TH	VAS (0-10 cm)	0	4.08	1.49	4.68	1.49	3.72	1.49
						2	3.96	NA	4.80	NA	3.60	NA
						6	2.40	NA	3.96	NA	2.88	NA
				EV	VAS (0-10 cm)	0	5.94	1.20	6.22	1.20	5.73	1.20
						2	4.70	NA	5.40	NA	4.90	NA
						6	3.87	NA	4.90	NA	5.21	NA

Table 2. Z scores derived from the raw data, based on the mean and standard deviation of the baseline measurement. Negative values indicate better clinical outcomes. Imputed standard deviations are marked with an asterisk.

	Treatment (no. of subjects)						Z scores (mean ± SD)		
Author, year	A	B	C	Stimulus	Outcome measurement	Time (weeks)	A	B	C
Litkowski 2010	CSS 2.5% (22)	CSS 7.5% (22)	Placebo (22)	TC	VAS (0-100 mm)	0	0.00 ± 1.00	0.00 ± 1.00	0.00 ± 1.00
						2	-1.32 ± 1.00*	-2.04 ± 1.00*	-0.47 ± 1.00*
						4	-1.80 ± 1.00*	-2.67 ± 1.00*	-1.27 ± 1.00*
						8	-1.71 ± 1.00*	-3.49 ± 1.00*	-1.53 ± 1.00*
				TH	VAS (0-100 mm)	0	0.00 ± 1.00	0.00 ± 1.00	0.00 ± 1.00
						2	-0.64 ± 1.00*	-0.46 ± 1.00*	-0.29 ± 1.00*
						4	-1.82 ± 1.00*	-0.52 ± 1.00*	-0.76 ± 1.00*
						8	-1.94 ± 1.00*	-0.56 ± 1.00*	-1.63 ± 1.00*
Que 2010	ACC 8.0% with whitener (40)	ACC 8.0% (40)	Placebo (41)	TC	Dolorimetry (10-50 grams)	0	0.00 ± 1.00	0.00 ± 1.00	0.00 ± 1.00
						2	-2.68 ± 1.63	-3.01 ± 1.73	-1.73 ± 0.74
						4	-3.88 ± 0.88	-4.30 ± 1.13	-1.33 ± 1.54
						8	-4.28 ± 0.55	-4.79 ± 0.71	-1.79 ± 1.67
				EV	Scale (0-3)	0	0.00 ± 1.00	0.00 ± 1.00	0.00 ± 1.00
						2	-3.28 ± 1.93	-3.03 ± 2.13	-0.41 ± 1.32
						4	-4.76 ± 1.90	-4.28 ± 2.00	-0.91 ± 1.12
						8	-5.83 ± 1.93	-5.47 ± 1.63	-1.21 ± 1.35
Sharma 2010	KNO_3 5.0% (40)	SnFl 0.4% (40)	CSS 7.5% (40)	TH	VAS (0-10 cm)	0	0.00 ± 1.00	0.00 ± 1.00	0.00 ± 1.00
						2	-1.74 ± 1.40	-1.43 ± 1.31	-2.78 ± 0.93
						4	-2.54 ± 0.98	-2.60 ± 0.94	-4.00 ± 0.67
						12	-4.09 ± 0.87	-4.60 ± 0.82	-5.17 ± 0.69
				EV	VAS (0-10 cm)	0	0.00 ± 1.00	0.00 ± 1.00	0.00 ± 1.00
						2	-1.99 ± 1.28	-1.71 ± 1.12	-2.61 ± 0.93
						4	-2.79 ± 0.78	-2.62 ± 1.00	-3.97 ± 0.92
						12	-4.76 ± 0.85	-5.03 ± 0.92	-5.05 ± 0.79
Hughes 2010	$(CH_3COO)_2Sr_2$ 8.0%	ACC 8.0%		TC	Dolorimetry (10-50 grams)	0	0.00 ± 1.00	0.00 ± 1.00	
						2	-3.02 ± 1.00*	-1.60 ± 1.00*	
						4	-6.78 ± 1.00*	-3.55 ± 1.00*	
						8	-11.32 ± 1.00*	-5.49 ± 1.00*	
				EV	Scale (0-3)	0	0.00 ± 1.00	0.00 ± 1.00	
						2	-0.95 ± 1.00*	-0.89 ± 1.00*	
						4	-3.81 ± 1.00*	-3.78 ± 1.00*	
						8	-5.48 ± 1.00*	-4.89 ± 1.00*	
				EV	VAS (0-100 mm)	0	0.00 ± 1.00	0.00 ± 1.00	
						2	-0.40 ± 1.00*	-0.33 ± 1.00*	
						4	-0.75 ± 1.00*	-0.68 ± 1.00*	
						8	-1.10 ± 1.00*	-0.91 ± 1.00*	
Pradeep 2010	CSS 5% (36)	KNO_3 5% (37)	Placebo (37)	TH	VAS (0-10 cm)	0	0.00 ± 1.00	0.00 ± 1.00	0.00 ± 1.00
						2	-1.63 ± 0.81	-0.76 ± 1.00	-0.71 ± 0.86
						6	-4.65 ± 0.67	-2.45 ± 0.84	-2.04 ± 0.86
				EV	VAS (0-10 cm)	0	0.00 ± 1.00	0.00 ± 1.00	0.00 ± 1.00
						2	-1.64 ± 0.92	-0.60± 0.88	-1.10 ± 1.00
						6	-3.47 ± 0.56	-1.91 ± 0.72	-2.35 ± 0.67
Docimo 2009a	ACC 8.0% (40)	KNO_3 5% (40)		TC	Dolorimetry (10-50 grams)	0	0.00 ± 1.00	0.00 ± 1.00	
						1	-1.77 ± 2.60	-0.58 ± 1.37	
						2	-4.54 ± 2.62	-2.20 ± 1.44	
						4	-9.32 ± 2.35	-6.21 ± 2.48	
						8	-10.89 ± 1.27	-9.07 ± 1.27	
				EV	Scale (0-3)	0	0.00 ± 1.00	0.00 ± 1.00	
						1	-1.21 ± 1.50	-1.03 ± 1.18	
						2	-2.14 ± 1.40	-1.45 ± 1.09	
						4	-3.81 ± 1.95	-3.58 ± 1.12	
						8	-4.86 ± 0.81	-5.18 ± 0.94	
Docimo 2009b	ACC 8.0% (40)	KNO_3 2% (40)		TC	Dolorimetry (10-50 grams)	0	0.00 ± 1.00	0.00 ± 1.00	
						2	-3.83 ± 1.87	-1.29 ± 1.60	
						4	-7.71 ± 2.10	-4.08 ± 1.80	
						8	-8.90 ± 1.42	-6.13 ± 1.21	
				EV	Scale (0-3)	0	0.00 ± 1.00	0.00 ± 1.00	
						2	-2.27 ± 1.38	-0.85 ± 1.28	
						4	-4.24 ± 1.51	-2.90 ± 1.40	
						8	-5.41 ± 1.05	-4.55 ± 0.98	
Ayad 2009	ACC 8.0% (38)	KNO_3 2% (39)		TC	Dolorimetry (10-50 grams)	0	0.00 ± 1.00	0.00 ± 1.00	
						2	-1.45 ± 1.10	-1.17 ± 1.24	
						4	-3.55 ± 1.08	-2.92 ± 1.22	
						8	-5.33 ± 1.05	-4.63 ± 0.61	
				EV	Scale (0-3	0	0.00 ± 1.00	0.00 ± 1.00	
						2	-2.31 ± 1.17	-1.40 ± 1.37	
						4	-4.51 ± 1.00	-3.67 ± 1.00	
						8	-6.66 ± 1.11	-6.66 ± 1.17	
Du Min 2008	CSS 5% (25)	Placebo (25)	$SrCl_2$ (25)	TH	VAS (0-10 cm)	0	0.00 ± 1.00	0.00 ± 1.00	0.00 ± 1.00
						2	-0.08 ± 1.00*	+0.08 ± 1.00*	-0.08 ± 1.00*
						6	-1.13 ± 1.00*	-0.48 ± 1.00*	-0.56 ± 1.00*
				EV	VAS (0-10 cm)	0	0.00 ± 1.00	0.00 ± 1.00	0.00 ± 1.00
						2	-1.03 ± 1.00*	-0.68 ± 1.00*	-0.69 ± 1.00*
						6	-1.72 ± 1.00*	-1.10 ± 1.00*	-0.43 ± 1.00*

Various therapeutic approaches have been established for the treatment of dentin hypersensitivity. The aim is to seal the exposed dentin tubules and to prevent the transmission of stimuli.[26] For this purpose, a variety of coatings, solutions and gels containing various fluoride compounds and preparations of their combinations are available.[27,28] The use of mouthwashes

Table 3. Combined z scores, averaged over the outcome variables at three follow-up time points. Negative values indicate better clinical outcomes.

Author, year	Treatment (no. of subjects) A	B	C	Time (weeks)	Combined Z scores (mean ± SD) A	B	C
Litkowski 2010	CSS 2.5% (22)	CSS 7.5% (22)	Placebo (22)	2	-0.98 ± 1.00	-1.25 ± 1.00	-0.38 ± 1.00
				4 – 6	-1.81 ± 1.00	-1.59 ± 1.00	-1.02 ± 1.00
				8 – 12	-1.83 ± 1.00	-2.02 ± 1.00	-1.58 ± 1.00
Que 2010	ACC 8.0% with whitener (40)	ACC 8.0% (40)	Placebo (41)	2	-2.98 ± 1.79	-3.02 ± 1.94	0.17 ± 1.35
				4 – 6	-4.32 ± 1.48	-4.29 ± 1.63	-0.21 ± 1.35
				8 – 12	-5.05 ± 1.42	-5.13 ± 1.26	-0.29 ± 1.52
Sharma 2010	KNO_3 5.0% (40)	SnFl 0.4% (40)	CSS 7.5% (40)	2	-1.87 ± 1.34	-1.57 ± 1.22	-2.69 ± 0.92
				4 – 6	-2.67 ± 0.89	-2.61 ± 0.97	-3.99 ± 0.81
				8 – 12	-4.42 ± 0.86	-4.82 ± 0.87	-5.11 ± 0.74
Hughes 2010	$(CH_3COO)_2Sr_2$ 8.0% (39)	ACC 8.0% (39)		2	-1.46 ± 1.00	-0.94 ± 1.00	
				4 – 6	-3.78 ± 1.00	-2.67 ± 1.00	
				8 – 12	-5.96 ± 1.00	-3.76 ± 1.00	
Pradeep 2010	CSS 5% (36)	KNO_3 5% (37)	Placebo (37)	2	-1.64 ± 0.87	-0.68 ± 0.94	-0.90 ± 0.93
				4 – 6	-4.06 ± 1.63	-2.18 ± 0.78	-2.19 ± 0.77
Docimo 2009a	ACC 8.0% (40)	KNO_3 5% (40)		2	-3.34 ± 2.10	-1.83 ± 1.28	
				4 – 6	-6.57 ± 2.16	-4.89 ± 1.93	
				8 – 12	-7.88 ± 1.07	-7.13 ± 1.31	
Docimo 2009b	ACC 8.0% (40)	KNO_3 2% (40)		2	-3.05 ± 1.64	-1.07 ± 1.44	
				4 – 6	-5.98 ± 1.83	-0.79 ± 1.00	
				8 – 12	-7.15 ± 1.25	-5.34 ± 1.10	
Ayad 2009	ACC 8.0% (38)	KNO_3 2% (39)		2	-1.88 ± 1.14	-1.28 ± 1.31	
				4 – 6	-4.03 ± 1.04	-3.29 ± 1.20	
				8 – 12	-5.99 ± 0.88	-5.16 ± 1.01	
Du Min 2008	CSS 5% (25)	Placebo) (25)	$SrCl_2$ (25)	2	-0.56 ± 1.00	-0.30 ± 1.00	-0.39 ± 1.00
				4 – 6	-1.43 ± 1.00	0.79 ± 1.00	-0.50 ± 1.00

containing potassium nitrate or sodium fluoride seem to have a positive effect.[26]

The precipitation of calcium fluoride crystals leads both to the dentin tubules being closed and to the promotion of a certain amount of remineralization. Sealants are applied in the dental practice and must be repeated several times. The indirect sealing of the tubules is only temporary. If sodium fluoride is repeatedly applied within 1 year, pain relief can be achieved in 41% of the patients.[29] In other studies,[28] the necessity for multiple applications and the unstable results are described as disadvantages of this therapy.

Furthermore, the use of lasers in the treatment of dentin hypersensitivity is described in the literature, but only poor results have been achieved.[30]

Another approach in the relief of dentin hypersensitivity is the use of special dentifrices. An advantage is that it can be carried out by the patient at home. Dentifrices containing e.g. strontium or potassium nitrate for daily home use were reported to achieve good results.[28,31] Freda et al[32] described in their meta-analysis a benefit of CSS either in toothpastes of prophylaxis pastes whereas the effect with the toothpaste is superior to the one with the prophylaxis paste. Some of the evaluated studies were industry-sponsored.

The available data and the study designs with respect to the impact and effectiveness of the various agents in the dentifrice leading to a reduction of dentin hypersensitivity, however, are extremely heterogeneous.

For this meta-analysis, only nine studies according to the chosen inclusion criteria could be taken into account. Because of this, we had to summarize the results of the various stimuli for the same time points. In the present study, we found that a significant relief of dentin hypersensitivity occurred over the whole period for the two active components strontium and arginine compared with the placebo.

Dentifrices containing strontium acetate cause a strong adsorption of the strontium in calcium-containing dentin. This leads to a stable occlusion of the dentin tubules.[33,34] Surprisingly, the present study shows a positive effect produced by the dentifrice containing strontium acetate compared with strontium chloride. This can be explained by the better occlusion of the dentin tubule by strontium acetate than by strontium chloride.[34] The result could also be influenced by the small power of the available studies. A comparative study of strontium-acetate- and strontium-chloride-containing dentifrices is thus desirable.

A new therapeutic approach in the year 2002 was the use of preparations based on amino acids, whereby, dentin hypersensitivity is treated with arginine and calcium carbonate, which interlock into the exposed dentin tubules by a mechanical layer.[10]

Based upon this finding, ProArgin Technology was launched as a new product (Colgate Sensitive ProRelief) on the market in 2009. The arginine containing dentifrices mechanically close dentin tubules and lead to a pain relief.[35] This can be confirmed by the results of this meta-analysis. These results are similar to those following the use of strontium-acetate-containing dentifrices. An admixture of whitener seems to have no negative impact.

Dentifrices containing calcium sodium silicate and potassium nitrate showed no significant improvement compared with the placebo in the meta-analysis. The small study number might also be responsible for this result. Only a tendency to reduce the dentin hypersensitivity at all times can be seen. None of the dentifrices included in this meta-analysis had a negative effect on dentin hypersensitivity. Similar results were found by Levenson.[20]

Recently a systematic review[23] compared the effectiveness between strontium acetate and arginine-based dentifrices to relieve dentin hypersensitivity. Magno et al[19] reported, similar to our study, a good effect for both agents, but only in one study a superior pain relief of strontium acetate. The present findings can be paired with the results of Yan et al[36] who reported the positive effect of arginine-containing toothpastes for dentin hypersensitivity in this meta-analysis. A direct compari-

son in a controlled randomized study, with various agents that have played a role in this meta-analysis e.g. ACC vs CSS would be desirable in the future.

In conclusion, this meta-analysis has shown that strontium-acetate- and arginine-containing dentifrices can significantly reduce dentin hypersensitivity. Interestingly, the strontium chloride formula had no effect, which may have been caused by the limited power of the study. Calcium sodium silicate and potassium nitrate formulas only show a tendency for pain relief but without significance. A randomized study with direct comparison of the various pain relief agents is recommended.

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