A randomised controlled trial to investigate the efficacy of an oxalate strip for the management of dentine hypersensitivity pain

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ABSTRACT

Objectives: To compare a 3.14% potassium oxalate strip and 8% arginine calcium carbonate toothpaste for the reduction of dentine hypersensitivity after 2 and 4 weeks.
Methods: This was an examiner-blind, parallel study in 80 healthy adults with dentine hypersensitivity (Schiff score > 2) in > 1 tooth. After acclimatisation, participants were randomised to the oxalate desensitising strip with fluoride toothpaste or the arginine desensitising toothpaste control which also contained fluoride. Products were applied under supervision of study staff after measuring baseline sensitivity, thereafter the strip or control toothpaste (fingertip application) was applied after 1 and 2 weeks, and teeth brushed twice-daily with the fluoride (test group) or the fluoridated arginine control toothpaste. Sensitivity was assessed following airblast (Schiff and VAS) and tactile stimuli (Yeaple probe) at baseline, 2 and 4 weeks.
Results: Both groups showed significant reductions from baseline in VAS, Schiff and Yeaple sensitivity scores after 2 and 4 weeks (p < 0.0005). The oxalate group had significantly lower Schiff and higher Yeaple probe scores compared to control after both time points (p < 0.0002 and p < 0.05), but while scores favoured the oxalate group, there were no significant differences in VAS.
Conclusions: This study demonstrated application of a 3.14% potassium oxalate strip combined with tooth-brushing with paste was more effective in pain management of dentine hypersensitivity than brushing with arginine toothpaste.
Clinical Significance: Treatment of sensitive teeth with the oxalate strip reduced dentine hypersensitivity after 2 and 4 weeks to a significantly greater degree than a positive control sensitivity toothpaste demonstrating that oxalate strips are an effective targeted treatment for dentine hypersensitivity sufferers.

1. Introduction

Dentine hypersensitivity (DH) is a prevalent condition, studies over the past 10 years reporting figures of 25.5%, 32%, 33% and 12.3% in China, India, Brazil and the US, respectively [1–4]. In Europe the condition is particularly prevalent in young adults, 42% of 18–35 year olds having been shown to suffer from DH [5]. In cohorts of periodontal patients even higher prevalence figures of 73–98% [6] and 68% [7] have been reported. DH most commonly triggered by cold stimuli [8,9], can also be triggered by heat, chemical, tactile and osmotic stimuli which give rise to a short sharp pain characteristic of DH [10]. The pain of DH has been shown to negatively affect quality of life [11], and in a survey of dental practitioners 72% reported that for 10% of their

patients DH was a severe problem [12]. It has been shown that DH can impact on everyday activities such as eating, drinking and tooth-brushing [13] and in a study of DH sufferers receiving periodontal supportive treatment, the pain from DH affected 35% of patients with regards to tooth cleaning ability [14] suggesting that DH can have a more general negative impact on oral health.

For DH to occur, dentine must be exposed and the dentine tubules patent to the pulp [15]. Dentine is frequently exposed by gingival recession which has been shown to be the most common predisposing factor for DH [2,3]. Alternatively, dentine can be exposed by tooth-wear, most commonly erosive toothwear [15]. Non-carious cervical lesions which arise as a result of the combined effect of multiple types of toothwear have been positively associated with DH, with lesion

depth correlating with high levels of DH [16]. Exposed dentine tubules are often covered by a smear layer, protecting against DH [17]. However, the smear layer can readily be removed by dietary acids or surfactants [18], and it has been shown that the more recently an individual has consumed dietary acid, the more likely they are to have DH [19]. In the young, both toothwear and the consumption of dietary acids are increasing [20]. Furthermore, the prevalence of gingival recession has been shown to be high in UK 18–35 year olds [21], therefore DH prevalence, already considerable, is also likely to increase, emphasising the need for new treatments for the condition.

Triggers of DH elicit pain by causing movement of the fluid within dentine tubules and activating sensory neurones in the pulp [22], thus strategies to treat DH either aim to block the pulpal nerve response or occlude dentine tubules to prevent fluid movement [23]. While there is some evidence to support the efficacy of nerve depolarising oral healthcare products for the reduction of DH pain, data suggests that these formulations need to be used for several weeks before a true benefit is felt by the DH sufferer [24,25]. Products that aim to occlude dentine tubules can act much more quickly providing the benefit of immediate relief from DH pain [26,27]. Recent systematic reviews support the efficacy of arginine, stannous fluoride and calcium sodium phosphosilicate-containing occluding formulations for the reduction of DH pain, although more high quality studies are recommended to confirm findings [28,29].

Oxalate products work by tubule occlusion, calcium ions in oral fluids interacting with oxalate salts to precipitate both on the dentine surface and within the tubule depth [25,30]. Recent in vitro studies have shown oxalate crystals within dentine tubules at depths of 5–25 μm [31]. However, a 2011 systematic review failed to find evidence to support oxalate product use for the treatment of DH [32]. More recently a novel oxalate formulation has been incorporated into dental strips which can be applied to the specific areas where there are sensitive teeth, allowing a steady release of oxalate solution [33]. In a feasibility study it was shown that oxalate strips were well tolerated by patients [34] and in 2 randomised controlled trials, strips containing 1.5% oxalate (3.14% potassium oxalate) have been shown to provide a larger reduction in DH pain than a potassium nitrate toothpaste [35], and a similar reduction in pain to a professionally applied 3% oxalic-acid paint-on solution [36]. However, further randomised controlled trials to confirm the efficacy of oxalate strips for the treatment of DH are needed.

The present study was designed to determine the efficacy of the 1.5% oxalate strip as compared to a positive control arginine containing toothpaste for the reduction of DH pain. An arginine toothpaste was chosen as the comparator product for this study as there is sufficient evidence of efficacy for the treatment of DH [23,28,29] and it has been shown to be effective when applied using fingertip application directly onto exposed sensitive dentine [37].

2. Materials and methods

2.1. Study design

This was a single site, parallel, two treatment clinical study blind with respect to the pain assessor, completed at a UK dental school between June and September 2016. Ethical approval was gained from the UK National Research Ethics Service (NHS REC Ref 16/SW/0050) and the study was carried out in accordance with good clinical practice guidelines. This study was undertaken with the understanding and written consent of each subject and conducted in accordance with the Declaration of Helsinki (2009). The study reported here is the first part of a 2-part study registered on the ISRCTN clinical trials register (ISRCTN10406748). The second (follow on) part of the study conducted using an in situ model to assess tubule occlusion after 2 weeks following test or control product application, will be reported in a second publication.

2.2. Participant recruitment, randomisation and treatment

Individuals aged 18 or over with a self-reported history of DH were invited to take part in the study. Participants who gave informed consent were assessed for eligibility. Eligible participants were those in good general health with at least one tooth with a Schiff sensitivity score of > 2 in response to an air blast [38]. Individuals with periodontal disease, long term use (> 7 days) of analgesics or other medications such as anti-histamines that could interfere with pain perception, or who had used desensitising toothpastes within the 3 months preceding the screening visit were excluded from the study. All teeth were assessed for sensitivity and up to four sensitive teeth were identified and selected to ensure that a tooth with persistent sensitivity could be chosen at baseline.

Eligible participants were given a manual toothbrush (Oral-B Indicator®) and sodium fluoride toothpaste (Crest Decay Prevention®, 1450 ppm F), both Procter & Gamble Company, OH, USA, to use twice daily for 7–14 days before the baseline study visit. Participants were asked not to change their normal flossing habits. Prior to the baseline appointment participants were asked to refrain from taking any analgesics in the eight hours before the appointment, brushing their teeth within four hours of the appointment and eating and drinking within an hour of the appointment.

At the baseline visit the sensitive teeth identified at screening were re-assessed for DH following an evaporative air challenge by examiner Schiff and patient reported VAS scores (scale: 0 = no tooth pain to 100 = worse tooth pain ever experienced), and tactile stimulus delivered by Yeaple probe. One or two of these teeth that demonstrated persistent sensitivity (Schiff score > 2; Yeaple score of < 20 g) were chosen for treatment. Participants without persistent sensitivity were withdrawn from the study. Eligible participants were stratified based on age, gender, and baseline Schiff and VAS scores, and randomly assigned using a sponsor supplied computer generated program to either test (Crest® Sensi-Stop Strips and Crest® Decay Protection Toothpaste, 1450 ppm F; Procter & Gamble Company, OH, USA) or positive control (Colgate ProRelief® Toothpaste, 1450 ppm F (Pro-Argin); Colgate-Palmolive Company, NY, USA). Randomisation was undertaken by study staff according to their study numbers which were allocated in the order participants were enrolled. Randomisation and product dispensing were conducted in an area distinct from that of clinical examinations, and the strips and dentifrice tubes were overwrapped and packaged in identically appearing test kit boxes.

Participants randomised to the test product were provided with gel test strips in over-labelled foil pouches plus their over-labelled toothpaste and a manual toothbrush. Participants were instructed to remove a strip from the pouch and apply it directly onto their identified sensitive study teeth with the gel directed onto tooth surfaces sufficient to cover the exposed facial dentine and surrounding region for a period of 10 min. The first application was supervised by study personnel at the baseline visit. Participants in this group re-applied strips to their identified study teeth after one week at home and after 2 weeks under supervision in the clinic according to the manufacturer's instructions. In addition, this group was instructed to brush twice daily using the toothbrush and toothpaste provided.

Participants randomised to the positive control product received this over-labelled toothpaste together with a manual toothbrush. These participants were instructed to apply with their finger, a pea-sized amount of the control paste onto the facial surface of their identified sensitive study teeth for one minute per each tooth as directed by the manufacturer. This application of toothpaste was supervised by study personnel at the baseline visit. Participants in this group re-applied the control toothpaste by fingertip application, as described in the manufacturer's instructions, to their identified study teeth after one week at home and after 2 weeks under supervision in the clinic at the same timepoints as the test group applied the strip. In addition, this group was instructed to brush twice daily using the positive control toothpaste

and toothbrush provided. Throughout the study, the study dentist was in an area separate from randomisation, product distribution, oral hygiene instruction and supervised use of treatment phase products.

Study participants returned to the study site 2 and 4 weeks after the baseline visit for assessment of their DH by Schiff, VAS and Yeaple probe score. Sensitivity assessments were undertaken prior to supervised product application at the 2 week visit, no product was applied at visit 4.

2.3. Clinical assessments

All clinical assessments were carried out by the study dentist who at each visit carried out an oral soft and hard tissue exam to monitor tolerability.

The evaporative air stimulus was a one second perpendicular application of cold air from a standard dental unit syringe delivered to the labial surface of each tooth at approximately a 1 cm distance. Each test tooth was isolated mesially and distally from adjacent teeth. Schiff scores (0 = participant does not respond to stimulus, 1 = participant responds to stimulus but does not request discontinuation of stimulus, 2 = participant responds to stimulus and requests discontinuation or moves from stimulus, 3 = participant responds to stimulus, considers stimulus to be painful and requests discontinuation of the stimulus) were discretely recorded by the examiner.

DH in response to a tactile stimulus was measured by Yeaple calibrated each morning [39]. The study dentist made two horizontal sweeps across the exposed cervical dentine beginning at 10 g and increasing pressure in 10 g increments to a maximum of 20 g (baseline visit) or 50 g (subsequent visits) until the participant expressed discomfort. After a 'yes' response tactile pressure was repeated at this force after a 5 min interval. If a second 'yes' was not obtained, the force was increased by 10 g and the tactile assessment repeated until a pressure which elicited two consecutive 'yes' responses was identified. If no sensitivity was found up to 50 g, then 50 g was recorded as the threshold.

2.4. Statistical analysis

The planned sample size of 80 participants in total was based on a previous study of the same size and parallel design in which significant differences were observed between the positive control toothpaste used in this study and a test toothpaste containing Stannous Fluoride after 3 days and 2 weeks treatment [40]. Sensitivity scores for the up to two enrolled teeth were averaged for each subject and separately for each visit and measure. Baseline and demographic data were summarized by treatment group to assess baseline comparability. For each post-baseline visit, the mean change from baseline in the cold air sensitivity Schiff score, the cold air VAS and Yeaple score were compared to zero for each treatment group using a paired t-test. Analysis of covariance models using baseline as the covariate were used to compare treatment groups. All statistical comparisons were two-sided with a level of significance of α = 0.05.

3. Results

The study was conducted between July and September 2016. Ninety-two participants were screened, 80 individuals were randomised and completed the study (Fig. 1). There were no adverse events recorded. The demographics of the participant population are shown in Table 1. There were no significant differences between the groups with respect to age, gender or ethnicity (p > 0.09).

3.1. Clinical Efficacy of the oxalate strip

Sensitivity scores are shown in Table 2 for all measures (Schiff, VAS and Yeaple probe) at all time points (baseline, 2 and 4 weeks). There

were no significant differences between the groups at baseline with respect to any of the measures used (p > 0.2). At both Week 2 and Week 4 post-treatment visits, both groups exhibited significantly improved mean pain scores relative to baseline for all measures (p ≤ 0.0005). The change from baseline is shown in Table 3 and Fig. 2.

When comparing treatments, at Week 2 and Week 4 post treatment visits, the test group had significantly lower mean Schiff and higher mean Yeaple scores than the control group (Table 4; p < 0.0001 and p < 0.05, respectively). However, there were no statistically significant differences in the patient reported VAS at Week 2 [treat diff (SE) 4.551 (3.368), p = 0.18] or Week 4 [treat diff (SE) 4.385 (4.081), p = 0.29], although scores favoured the Sensi-Stop strip.

4. Discussion

Home use products containing arginine, stannous fluoride, calcium sodium phosphosilicate and potassium for the treatment of DH have been shown to have efficacy, systematic reviews recognizing there is sufficient evidence [28,29], although Hu *et al,* [29] still suggest more high quality randomized controlled trials are needed to confirm their findings. Of the home use products available, systematic reviews of arginine containing products have consistently demonstrated their efficacy for the treatment of DH pain [23,41]. Evidence from individual studies supporting the use of professionally applied oxalate formulations for the treatment of DH pain exist [42,43], but a systematic review in 2011 found that while data indicates that 3% monohydrogen-monopotassium may be able to reduce DH pain, there was insufficient evidence to confirm that oxalate treatments are of benefit to DH sufferers [32]. Subsequent to this review, a dental strip delivery system for formulations of oxalates was developed and the present study compared the ability of a strip containing 3.14% potassium oxalate to alleviate DH with that of an arginine calcium carbonate positive control toothpaste, both products being used in accordance with manufacturer's instructions.

It was demonstrated that DH scores for both treatment groups fell progressively from baseline to 4 weeks as determined by all three measures, Schiff, Yeaple and VAS score, scores suggesting that both treatments achieved a clinically relevant reduction in DH. Similarly, a reduction in DH after 2 and 4 weeks has been demonstrated with a self-administered 1.4% oxalate mouthrinse used in combination with a standard fluoride toothpaste twice daily [44] and reductions of DH after 4 and 8 weeks were observed in 3 studies of mouthrinses containing 1.5–2.0% oxalate [45], although only one of these studies demonstrated better efficacy than a placebo control.

By contrast, in the present study it was demonstrated that the strip provided significantly greater DH relief than the positive control toothpaste after both 2 and 4 weeks as measured by Schiff and Yeaple scores. Occlusion by oxalates has been shown to be better than that achieved by arginine formulations in two previous in vitro studies, with a 1.4% potassium oxalate containing mouthrinse and a 1.5% oxalate strip reducing dentine permeability significantly more than an arginine containing mouthrinse and/or toothpaste [46,47]. Interestingly in the latter study it was also demonstrated that the oxalate strip performed better than an oxalate mouthrinse, suggesting that the strip method of applying oxalate is particularly effective. In the present study the demonstration of a residual desensitising effect 2 weeks after the last application of the strip also suggests that oxalates have a longer term efficacy for the treatment of DH pain. Strips as a mode of treatment delivery enable the localisation of the formulation to the target area at a therapeutic concentration, minimising wastage of product and preventing unnecessary or over treatment. Similar to another recent study [35] participants in the present study did not complain of any difficulties with the oxalate strip.

The improved efficacy of the oxalate strip over the arginine toothpaste in DH pain reduction in the present study may be due to the deposition of calcium oxalate crystals deep within the dentine tubules,
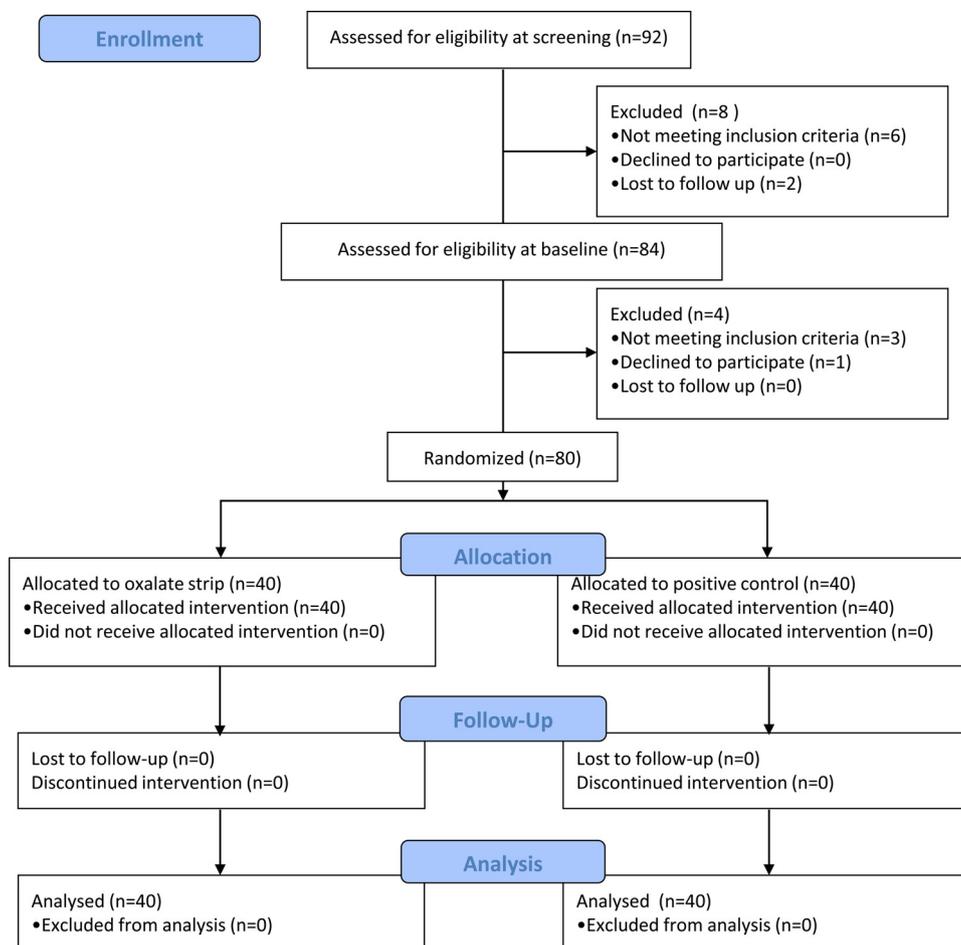
Fig. 1. CONSORT Flow diagram showing participant flow through the study.

Table 1
Demographics of study participants.

Characteristic	Positive control toothpaste (n = 40)	Strip (n = 40)	Total (n = 80)
Age (Years)			
Mean	37.2	33	35.1
SD	11.65	10.27	11.11
Min – Max	21 – 67	19 - 61	19 – 67
Ethnicity (%)			
Asian Oriental	1 (3%)	1 (3%)	2 (3%)
Black	1 (3%)	0 (0%)	1 (1%)
Caucasian	38 (95%)	37 (93%)	75 (94%)
Other	0 (0%)	2 (5%)	2 (3%)
Sex			
Female	29 (73%)	38 (70%)	57 (71%)
Male	11 (28%)	12 (30%)	23 (29%)

in vitro studies having shown that these form at depths of 15–25 μm [31,48], protecting them from being dislodged mechanically. Furthermore, data suggests that they are resistant to dissolution by acids [49]. By contrast, in the same study, microgranules initially deposited in dentine tubules by an arginine toothpaste were removed following acid challenge. Oxalate precipitates have also been shown to be acid resistant when delivered as a 3% gel in vitro [30]. While some resistance to acid challenge has been demonstrated for arginine formulations in another in vitro study [50] the greater depth of penetration of oxalates may provide better protection from acid dissolution. The ability of precipitates that occlude dentine tubules to resist dietary acid challenges is important for persistence of the occlusion and a sustained

relief in sensitivity.

In contrast to clinician scored data, in the present study there were no differences between treatments for participant reported VAS at 2 or 4 weeks although scores slightly favoured the oxalate test group. These results may be due to difficulties inherent in the use of VAS. Participants vary in their tolerance and perception of DH pain [51], thus participants with the same pain experience can record markedly different VAS scores. However, it is important to gain an idea of how the participant perceives their pain and VAS is a well-established method of measuring patient reported pain [52] that is commonly used in DH studies [53]. Interestingly in the present study if analysis was restricted to only those with greater than median sensitivity at baseline (VAS 63 mm or more), by week 4 there was a significant difference observed between the 2 groups in favour of the oxalate strip [treat diff (SE) 13.287 (5.808), p = 0.03].

It is possible that improvements in pain scores in the present study were influenced by study participation (Hawthorne effect) [54] in the present study, participants were advised to use their study products in line with their normal oral hygiene regimen, and they participated in the study for over 4 weeks.

5. Conclusions

The results of the present study demonstrate the efficacy of a strip containing 3.14% potassium oxalate gel in reducing the pain of DH. Clinician scores suggest the efficacy is greater than that of an arginine calcium carbonate positive control toothpaste for which efficacy is supported by numerous systematic reviews [23,28,41] and that efficacy persisted up to 2 weeks after treatment. Study participants reported no

Table 2
Baseline, week 2 and week 4 scores for Schiff, VAS and Yeaple scores.

Treatment	n	Schiff (score)		VAS (mm)		Yeaple (g)	
		Mean (SD)	Median	Mean (SD)	Median	Mean (SD)	Median
Baseline							
Positive control toothpaste	40	2.23 (0.44)	2.00	60.16 (18.86)	64.75	12.75 (3.75)	10.00
Strip	40	2.26 (0.34)	2.00	55.38 (18.45)	58.75	12.75 (3.91)	10.00
Week 2							
Positive control toothpaste	40	1.69 (0.54)	1.50	49.95 (20.55)	53.00	18.50 (10.01)	15.00
Strip	40	1.18 (0.51)	1.00	42.43 (17.07)	42.75	24.50 (14.71)	20.00
Week 4							
Positive control toothpaste	40	1.49 (0.66)	1.50	41.59 (22.73)	43.25	25.38 (13.75)	25.00
Strip	40	0.88 (0.50)	1.00	34.83 (18.68)	35.00	31.50 (13.83)	30.00

Table 3
Change from baseline in Schiff, VAS and Yeaple score.

Treatment	n	Schiff (score)		VAS (mm)		Yeaple (g)	
		Mean (SD)	p-value[*]	Mean (SD)	p-value[*]	Mean (SD)	p-value[*]
Week 2							
Positive control toothpaste	40	−0.54 (0.46)	< 0.0001	−10.21 (16.11)	0.0003	5.75 (9.51)	0.0005
Strip	40	−1.09 (0.53)	< 0.0001	−12.95 (16.79)	< 0.0001	11.75 (14.03)	< 0.0001
Week 4							
Positive control toothpaste	40	−0.74 (0.61)	< 0.0001	−18.58 (18.05)	< 0.0001	12.63 (13.01)	< 0.0001
Strip	40	−1.39 (0.52)	< 0.0001	−20.55 (23.15)	< 0.0001	18.75 (13.43)	< 0.0001

[*] 2-sided paired *t*-test.
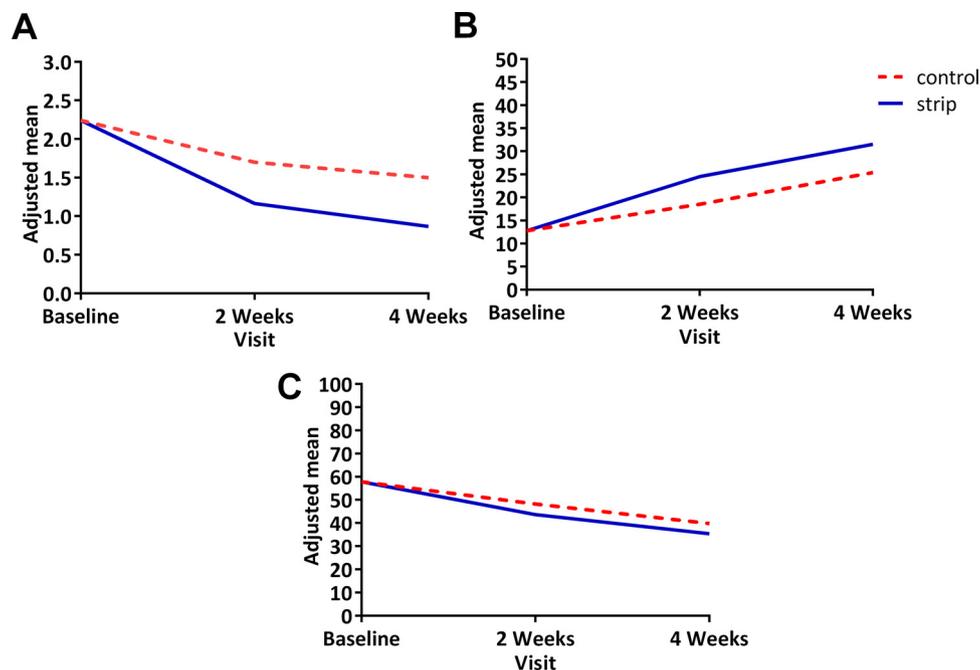
Fig. 2. Mean sensitivity scores from baseline to 4 weeks (a) Schiff Air Index (b) Yeaple Probe (c) VAS.

difficulties with using the strip at home, thus study findings support this method of delivery of oxalate agents which allows for a localised application to DH areas within the mouth.

Table 4
Comparison Schiff and Yeaple Score between treatments at 2 and 4 weeks using Analysis of Covariance Model.

Treatment	n	Schiff					Yeaple				
		Adj Mean (SE)	%* difference	Treat Diff (SE)	95% CI Treat Diff	2-sided p-value	Adj Mean (SE)	% Difference	Treat Diff (SE)	95% CI Treat Diff	2-sided p-value
2 weeks											
Positive control toothpaste	40	1.699 (0.075)	32	0.535 (0.106)	(0.324, 0.746)	<0.0001	18.500 (1.907)	−32	−6.000 (2.697)	(−11.371, −0.629)	0.0291
Strip	40	1.164 (0.075)					24.500 (1.907)				
4 weeks											
Positive control toothpaste	40	1.498 (0.086)	42	0.633 (0.122)	(0.390, 0.876)	<0.0001	25.375 (2.104)	−24	−6.125 (2.976)	(−12.050, −0.200)	0.0429
Strip	40	0.865 (0.086)					31.500 (2.104)				

* Percent Change versus Colgate Pro-Relief® Toothpaste. Treat Diff = treatment difference.

References

[1] X. Liang, Z. Wei, D. Hu, J. Ruan, Prevalence of dentin hypersensitivity among the residents of Xi'an city, China. Acta Odontol. Scand. 75 (2017) 387–393, https://doi.org/10.1080/00016357.2017.1323348.

[2] G.M. Naidu, K.C. Ram, N.R. Sirisha, Y.S. Sree, R.K. Kopuri, N.R. Satti, C. Thatimatla, Prevalence of dentin hypersensitivity and related factors among adult patients visiting a dental school in Andhra Pradesh, Southern India, J. Clin. Diagn. Res. 8 (2014), https://doi.org/10.7860/JCDR/2014/9033.4859 ZC48-51.

[3] R.S. Costa, F.S. Rios, M.S. Moura, J.J. Jardim, M. Maltz, A.N. Hass, Prevalence and risk indicators of dentin hypersensitivity in adult and elderly populations from Porto Alegre, Brazil. J. Periodontol. 85 (2014) 1247–1258, https://doi.org/10.1902/jop.2014.130728.

[4] J. Cunha-Cruz, J.C. Wataha, L.J. Heaton, M. Rothen, M. Sobieraj, J. Scott, J. Berg, Northwest Practice-based Research Collaborative in Evidence-based DENTistry. The prevalence of dentin hypersensitivity in general dental practices in the northwest United States, J. Am. Dent. Assoc. 144 (2013) 288–296.

[5] N.X. West, M. Sanz, A. Lussi, D. Bartlett, P. Bouchard, D. Bourgeois, Prevalence of dentine hypersensitivity and study of associated factors: a European population-based cross-sectional study, J. Dent. 41 (2013) 841–851, https://doi.org/10.1016/j.jdent.2013.07.017.

[6] M.B. Chabanski, D.G. Gillam, J.S. Bulman, H.N. Newman, Clinical evaluation of cervical dentine sensitivity in a population of patients referred to a specialist periodontology department: a pilot study, J. Oral Rehabil. 24 (1997) 666–672, https://doi.org/10.1111/j.1365-2842.1997.tb01079.x.

[7] J.S. Rees, L.J. Jin, S. Lam, I. Kudanowska, R. Vowles, The prevalence of dentine hypersensitivity in a hospital clinic population in Hong Kong, J. Dent. 31 (2003) 453–461.

[8] H.J. Shiau, Dentin hypersensitivity, J. Evid, Based Dent. Pract. 12 (2012) 220–228, https://doi.org/10.1016/S1532-3382(12)70043-X.

[9] D.G. Gillam, A new perspective on dentine hypersensitivity - guidelines for general dental practice, Dent. Update 44 (33-36) (2017) 39–42, https://doi.org/10.12968/denu.2017.44.1.33.

[10] Canadian Advisory Board on Dentin Hypersensitivity, Consensus-based recommendations for the diagnosis and management of dentin hypersensitivity, J. Can. Dent. Assoc. 69 (2003) 221–226.

[11] K. Bekes, C. Hirsch, What is known about the influence of dentine hypersensitivity on oral health-related quality of life? Clin. Oral Investig. 17 (Suppl 1) (2013) S45–S51, https://doi.org/10.1007/s00784-012-0888-9.

[12] D.G. Gillam, J.S. Bulman, M.A. Eijkman, H.N. Newman, Dentists' perceptions of dentine hypersensitivity and knowledge of its treatment, J. Oral Rehabil. 29 (2002) 219–225, https://doi.org/10.1046/j.1365-2842.2002.00812.x.

[13] O.V. Boiko, S.R. Baker, B.J. Gibson, D. Locker, F. Sufi, A.P. Barlow, P.G. Robinson, Construction and validation of the quality of life measure for dentine hypersensitivity (DHEQ, J. Clin. Periodontol. 37 (2010) 973–980, https://doi.org/10.1111/j.1600-051X.2010.01618.x.

[14] V. Goh, E.F. Corbet, W.K. Leung, Impact of dentine hypersensitivity on oral health-related quality of life in individuals receiving supportive periodontal care, J. Clin. Periodontol. 43 (2016) 595–602, https://doi.org/10.1111/jcpe.12552.

[15] N. West, J. Seong, M. Davies, Dentine hypersensitivity, Monogr. Oral Sci. 25 (2014) 108–122, https://doi.org/10.1159/000360749.

[16] D.N.R. Teixeira, L.F. Zeola, A.C. Machado, R.R. Gomes, P.G. Souza, D.C. Mendes, P.V. Soares, Relationship between noncarious cervical lesions, cervical dentin hypersensitivity, gingival recession, and associated risk factors: A cross-sectional study, J. Dent. 76 (2018) 93–97, https://doi.org/10.1016/j.jdent.2018.06.017.

[17] D.H. Pashley, How can sensitive dentine become hypersensitive and can it be reversed? J. Dent. 41 (Suppl 4) (2013) S49–55, https://doi.org/10.1016/S0300-5712(13)70006-X.

[18] E.G. Absi, M. Addy, D. Adams, Dentine hypersensitivity-the effect of toothbrushing and dietary compounds on dentine in vitro: an SEM study, J. Oral Rehabil. 19 (1992) 101–110.

[19] R.C. Olley, R. Moazzez, D. Bartlett, The relationship between incisal/occlusal wear, dentine hypersensitivity and time after the last acid exposure in vivo, J. Dent. 43 (2015) 248–252, https://doi.org/10.1016/j.jdent.2014.11.002.

[20] R.C. Olley, H. Sehmi, The rise of dentine hypersensitivity and tooth wear in an ageing population, Br. Dent. J. 223 (2017) 293–297, https://doi.org/10.1038/sj.bdj.2017.715.

[21] J. Seong, D. Bartlett, R.G. Newcombe, N.C.A. Claydon, N. Hellin, N.X. West, Prevalence of gingival recession and study of associated related factors in young UK adults, J. Dent. 76 (2018) 58–67, https://doi.org/10.1016/j.jdent.2018.06.005.

[22] M. Brannstrom, A hydrodynamic mechanism in the transmission of pain-produced stimuli through the dentine, in: D.J. Anderson (Ed.), Sensory Mechanisms in Dentine, Pergamon Press, New York, 1963, pp. 73–79.

[23] N.X. West, J. Seong, M. Davies, Management of dentine hypersensitivity: efficacy of professionally and self-administered agents, J. Clin. Periodontol. 42 (Suppl 16) (2015) S256–302, https://doi.org/10.1111/jcpe.12336.

[24] R. Davies, C. Scully, A.J. Preston, Dentifrices–an update, Med. Oral Patol. Oral Cir. Bucal 15 (2010) e976–82, https://doi.org/10.4317/medoral.15.e976.

[25] M. Mantzourani, D. Sharma, Dentine sensitivity: past, present and future, J. Dent. 41 (Suppl 4) (2013) S3–S17, https://doi.org/10.1016/S0300-5712(13)70002-2.

[26] S. Mason, N. Hughes, F. Sufi, L. Bannon, B. Maggio, M. North, J. Holt, A comparative clinical study investigating the efficacy of a dentifrice containing 8% strontium acetate and 1040 ppm fluoride in a silica base and a control dentifrice containing 1450 ppm fluoride in a silica base to provide immediate relief of dentin hypersensitivity, J. Clin. Dent. 21 (2010) 42–48.

[27] T. He, R. Cheng, A.R. Biesbrock, A. Chang, L. Sun, Rapid desensitizing efficacy of a stannous-containing sodium fluoride dentifrice, J. Clin. Dent. 22 (2011) 40–45.

[28] J.H. Bae, Y.K. Kim, S.K. Myung, Desensitizing toothpaste versus placebo for dentin hypersensitivity: a systematic review and meta-analysis, J. Clin. Periodontol. 42 (2015) 131–141, https://doi.org/10.1111/jcpe.12347.

[29] M.L. Hu, G. Zheng, Y.D. Zhang, X. Yan, X.C. Li, H. Lin, Effect of desensitizing toothpastes on dentine hypersensitivity: a systematic review and meta-analysis, J. Dent. 75 (2018) 12–21, https://doi.org/10.1016/j.jdent.2018.05.012.

[30] J.C. Pereira, A.D. Segala, D.G. Gillam, Effect of desensitizing agents on the hydraulic conductance of human dentin subjected to different surface pre-treatments–an in vitro study, Dent. Mater. 21 (2005) 129–138, https://doi.org/10.1016/j.dental.2004.02.007.

[31] T.C. Hare, M. Zsiska, Y. Boissy, T.E. Dufresne, J.H. Nurre, P.A. Chmielewski, P.A. Drake, Immediate and Durable Effects of an Oxalate Strip on Human Dentine In Vitro, Compend, Cont. Educ. Dent 37 (2016) 6–12 https://www.aegisdentalnetwork.com/cced/special-issues/2016/05/immediate-and-durable-effects-of-an-oxalate-strip-on-human-dentin-in-vitro.

[32] J. Cunha-Cruz, J.R. Stout, L.J. Heaton, J.C. Wataha, Northwest PRECEDENT, Dentin hypersensitivity and oxalates: a systematic review, J. Dent. Res. 90 (2011) 304–310, https://doi.org/10.1177/0022034510389179.

[33] A.S. Altuve, R.W. Gerlach, Innovations in dentin hypersensitivity: a unique oxalate based strip technology, Compend. Cont. Educ. Dent. 37 (2016) 2–5 https://www.aegisdentalnetwork.com/cced/special-issues/2016/05/innovations-in-dentin-hypersensitivity-a-unique-oxalate-based-strip-technology.

[34] C.J. Anderson, R.W. Gerlach, K. Gerard, M. Ferrari, Use of oxalate strips in dentistry: overall response and case studies with recent and longstanding sensitivity, Compend. Cont. Educ. Dent. 37 (2016) 32–37 https://www.aegisdentalnetwork.com/cced/special-issues/2016/05/use-of-oxalate-strips-in-dentistry-overall-response-and-case-studies-with-recent-and-longstanding-sensitivity.

[35] P. Amini, M. Miner, P.A. Sagel, R.W. Gerlach, Effects of 1.5% oxalate stripes versus 5% potassium nitrate dentifrice on dentin hypersensitivity, Compend. Cont. Educ. Dent. 37 (2016) 21–25 https://www.aegisdentalnetwork.com/cced/special-issues/2016/05/comparative-effects-of-one-point-five-percent-oxalate-strips-versus-five-percent-potassium-nitrate-dentifrice-on-dentin-hypersensitivity.

[36] A. Papas, M. Singh, M. Magnuson, M. Miner, P. Sagel, R. Gerlach, Randomised controlled trial evaluating use of two different oxalate products in adults with recession-associated dentin hypersensitivity, Compend. Cont. Educ. Dent. 37 (2016) 26–31 https://www.aegisdentalnetwork.com/cced/special-issues/2016/05/randomized-controlled-trial-evaluating-use-of-two-different-oxalate-products-in-adults-with-recession-associated-dentin-hypersensitivity.

[37] N. West, R.G. Newcombe, N. Hughes, S. Mason, B. Maggio, F. Sufi, N. Claydon, A 3-day randomised clinical study investigating the efficacy of two toothpastes, designed to occlude dentine tubules, for the treatment of dentine hypersensitivity, J. Dent. 41 (2013) 187–194, https://doi.org/10.1016/j.jdent.2012.11.007.

[38] T. Schiff, M. Dotson, S. Cohen, W. De Vizio, J. McCool, A. Volpe, Efficacy of a dentifrice containing potassium nitrate, soluble pyrophosphate, PVM/MA copolymer, and sodium fluoride on dentinal hypersensitivity: a twelve-week clinical study, J. Clin. Dent. 5 (1994) Spec No, 87-92.

[39] A.M. Polson, J.G. Caton, R.N. Yeaple, H.A. Zander, Histological determination of probe tip penetration into gingival sulcus of humans using an electronic pressure-sensitive probe, J. Clin. Periodontol. 7 (1980) 479–488, https://doi.org/10.1111/j.1600-051X.1980.tb02154.x.

[40] T. He, J. Chang, R. Cheng, X. Li, L. Sun, A.R. Biesbrock, Clinical evaluation of the fast onset and sustained sensitivity relief of a 0.454% stannous fluoride dentifrice compared to an 8.0% arginine-calcium carbonate-sodium monofluorophosphate dentifrice, Am. J. Dent. 24 (2011) 336–340.

[41] Z.Y. Yang, Wang F, K. Lu, Y.H. Li, Z. Zhou, Arginine-containing desensitizing toothpaste for the treatment of dentin hypersensitivity: a meta-analysis, Clin. Cosmet. Investig. Dent. 8 (2016) 1–14, https://doi.org/10.2147/CCIDE.S95660.

[42] T. Pamir, H. Dalgar, B. Onal, Clinical evaluation of three desensitizing agents in relieving dentin hypersensitivity, Oper. Dent. 32 (2007) 544–548, https://doi.org/10.2341/07-5.

[43] V. Camilotti, J. Zilly, M. Busato Pdo, C.A. Nassar, P.O. Nassar, Desensitizing treatments for dentin hypersensitivity: a randomized, split-mouth clinical trial, Braz. Oral Res. 26 (2012) 263–268, https://doi.org/10.1590/S1806-83242012000300013.

[44] D. Sharma, J.A. McGuire, J.T. Gallob, P. Amini, Randomised clinical efficacy trial of potassium oxalate mouthrinse in relieving dentinal sensitivity, J. Dent. 41 (Suppl 4) (2013) S40–48, https://doi.org/10.1016/S0300-5712(13)70005-8.

[45] G.R. Burnett, J.T. Gallob, K.R. Milleman, S. Mason, A. Patil, C. Budhawant, J.L. Milleman, Potassium oxalate oral rinses for long-term relief from dentinal hypersensitivity: Three randomised controlled studies, J. Dent. 70 (2018) 23–30, https://doi.org/10.1016/j.jdent.2017.12.004.

[46] D. Sharma, C.X. Hong, P.S. Heipp, A novel potassium oxalate-containing tooth-desensitising mouthrinse: a comparative in vitro study, J. Dent. 41 (Suppl 4) (2013) S18–27, https://doi.org/10.1016/S0300-5712(13)70003-4.

[47] T.C. Hare, M. Zsiska, Y. Boissy, M.L. Barker, P.A. Drake, Relative performance of antisensitivity dentifrice, rinse and oxalate strips: an in vitro comparison of common global over-the-counter products, Compend. Contin. Educ. Dent. 37 (2016) 13–20 https://www.aegisdentalnetwork.com/cced/special-issues/2016/05/relative-performance-of-antisensitivity-dentifrice-rinse-and-oxalate-strips-an-in-vitro-comparison-of-common-global-over-the-counter-products.

[48] C.A. Arrais, D.C. Chan, M. Giannini, Effects of desensitizing agents on dentinal tubule occlusion, J. Appl. Oral Sci. 12 (2004) 144–148, https://doi.org/10.1590/S1678-77572004000200012.

[49] G. Eliades, M. Mantzourani, R. Labella, B. Mutti, D. Sharma, Interactions of dentine desensitisers with human dentine: morphology and composition, J. Dent. 41 (Suppl 4) (2013) S28–S39, https://doi.org/10.1016/S0300-5712(13)70004-6.

[50] I. Petrou, R. Heu, M. Stranick, S. Lavender, L. Zaidel, D. Cummins, R.J. Sullivan, C. Hsueh, J.K. Gimzewski, A breakthrough therapy for dentin hypersensitivity: how dental products containing 8% arginine and calcium carbonate work to deliver effective relief of sensitive teeth, J. Clin. Dent. 20 (2009) 23–31.

[51] D.G. Gillam, Current diagnosis of dentin hypersensitivity in the dental office: an overview, Clin. Oral Invest. 17 (Suppl 1) (2013) S21–29, https://doi.org/10.1007/s00784-012-0911-1.

[52] G.A. Hawker, S. Mian, T. Kendzerska, M. French, Measures of adult pain: visual analog scale for pain (VAS pain), numeric rating scale for pain (NRS pain), McGill pain questionnaire (MPQ), short-form McGill pain questionnaire (SF-MPQ), chronic pain grade scale (CPGS), short Form-36 bodily pain scale (SF-36 BPS), and measure of intermittent and constant osteoarthritis pain (ICOAP), Arthritis Care Res. (Hoboken) 63 (Suppl 11) (2011) S240–252, https://doi.org/10.1002/acr.20543.

[53] N.M. Freda, A. Veitz-Keenan, Calcium sodium phosphosilicate had some benefit on dentine hypersensitivity, Evid. Dent. 17 (2016), https://doi.org/10.1038/sj.ebd.6401148 12-a3.

[54] N. Pandis, Use of controls in clinical trials, Am. J. Orthod. Dentofacial Orthop. 141 (2012) 250–251, https://doi.org/10.1016/j.ajodo.2011.10.018.