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A randomised controlled trial to compare the efficacy of an aluminium lactate/potassium nitrate/hydroxylapatite toothpaste with a control toothpaste for the prevention of dentine hypersensitivity.

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Short title: Aluminium lactate toothpaste for dentine hypersensitivity

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A randomised controlled trial to compare the efficacy of an aluminium lactate/potassium nitrate/hydroxylapatite toothpaste with a control toothpaste for the prevention of dentine hypersensitivity.

Abstract

Objectives

To determine the efficacy of a cosmetic aluminium lactate/potassium nitrate/hydroxylapatite toothpaste for the reduction of dentine hypersensitivity (DH) pain as compared to a control toothpaste containing potassium nitrate.

Methods

The study was a randomised, examiner-blind, two treatment arm, parallel controlled trial in healthy adults with at least 2 sensitive teeth (Schiff $\geq$2). At baseline, immediately after treatment and at 7 and 14 days of twice-daily brushing of the test or control toothpaste the sensitivity of 2 test teeth was measured following iced-water (Schiff and VAS) and tactile (Yeaple probe) stimuli, and a whole mouth plaque score was obtained. Participants also completed a whole-mouth VAS and DHEQ15 quality of life questionnaire at baseline, 7 and 14 days.

Results

Both toothpastes reduced DH in test teeth, but pain reduction in the test group was significantly better at all timepoints and by all measures ($p=0.005$, tooth-level VAS immediately after brushing; $p<0.001$ all other comparisons). There was a relative risk reduction of Schiff sensitivity of 55% immediately after brushing which rose to 81% after 7 and 88.6% after 14 days (all $p<0.001$). There were no differences in plaque, whole mouth VAS or DHEQ15 scores at any time point.

Conclusion

This study demonstrated the efficacy of an aluminium lactate/potassium nitrate/hydroxylapatite toothpaste compared to a potassium nitrate control toothpaste for the prevention of dentine hypersensitivity both immediately and over a 2 week period. This agent appears to have potential for pain alleviation from the common oral pain condition of DH and further research is warranted.

Clinical Significance

DH pain, whilst transient in nature, is arresting in magnitude, affecting quality of life. Daily application of efficacious toothpastes can relieve DH pain however, as yet, there is no gold standard treatment. The results of this study support further investigation of an aluminium lactate/potassium nitrate/hydroxylapatite toothpaste for DH management.

Introduction

Dentine hypersensitivity (DH) is a common oral condition, a recent systematic review reporting an average prevalence of 33.5% for the 65 studies that fit study inclusion and exclusion criteria, a figure which rose to 43.9% when only studies limited to young adults were analysed [1]. In a healthy mouth DH arises when dentine is exposed usually by tooth wear or gingival recession and the dentine tubules are opened such that they are patent from the tooth surface to the pulp [2]. When patent dentine tubules are exposed to a stimulus such as cold air or water, pressure or osmotic, fluid within dentine tubules transmits this stimulus to the pulpal nerves resulting in a short sharp pain response [2,3]. Although pain is usually transient it can be intense and can have a demonstrable negative impact on quality of life [4,5].

Treatments for dentine hypersensitivity may be professionally administered or supplied over the counter for home use. They contain agents that act to depolarise the nerves or block the dentine tubules so that no pain response is triggered [2,3]. Whilst there is some evidence to support the efficacy of professionally administered treatments for DH [6], home use products such as toothpastes are convenient, simple to use and generally the first line of treatment [7,8]. Further, research has demonstrated a number of active agents in toothpastes can be effective at pain alleviation having the additional advantage of a cost benefit over professionally applied products. A number of systematic reviews have evaluated the efficacy of toothpastes for the reduction of DH pain [6,9,10]. However, due to the heterogeneity of study designs such as the use of different DH triggers, assessments and time periods, direct comparisons between studies are difficult [6,9,10]. A recent review does present evidence to suggest that compared to a negative control most DH toothpastes have some effect [10,11], but there is insufficient evidence to signal one formulation as better than the others particularly as different formulations appear to work better at different timepoints post treatment [6,12], such as potassium taking a couple of weeks to show efficacy compared to an occluding agent which can had a strong immediate effect [9].

Aluminium lactate-based toothpastes are known to help plaque reduction and promote healthy gums when used twice daily [13]. There is also limited evidence that a mouthrinse formulation containing aluminium lactate may reduce DH pain [14], although a systematic review and meta-analysis of mouthrinses only demonstrated efficacy above control for patient reported DH [15]. More recently a study demonstrated that following use of a toothpaste containing both potassium nitrate and aluminium lactate, DH pain scores improved significantly from baseline to 4 weeks [16]. Improvements were also recorded in the group using the control standard fluoride toothpaste, however significant pain reduction by all measures was achieved earlier in the group using the test toothpaste at 2 weeks

for cold and evaporative stimuli [16]. Although it is possible that the DH improvements observed were due solely to the presence of potassium nitrate in the toothpaste, systematic reviews suggest that the effects of potassium take between two to four weeks to manifest [6,9], and it may be the case that in the study by Lee et al [16] significant improvements in DH are as a result of the aluminium lactate contributing to the desensitising effects recorded.

Aluminium nanoparticles in the form of a fluoride containing alumino-calcium-silicate based tooth-coating material (Nanoseal) have been shown in vitro to occlude dentine tubules [17] and to occlude more rapidly than a diamine silver fluoride sealant [17,18]. In toothpaste formulations, it is thought that aluminium particles could block dentine tubules as a result of their interaction with phosphate ions in saliva and the formation of aluminium phosphate [19]. Aluminum ions easily associate with hydroxide ions and phosphate ions, and there is a well recognised process in which such associations are crystallized depending on solution conditions such as pH and coexisting ions. It is assumed that the addition of phosphate ions further accelerates this process even at pH 6.0 or 7.0 and it is considered that such aggregates and crystals are deposited on the surface of the dentinal tubules and hence narrow or occlude the dentinal tubules. The toothpaste additive amorphous hydroxylapatite has also been reported to have the capability to occlude dentinal tubules [20,21] and reduce DH pain [22]. Further, in a pilot study (Nov 2020) a toothpaste containing hydroxylapatite, aluminium lactate and potassium reduced tactile stimulated DH pain as measured by VAS significantly more after 7 days, than the control paste containing aluminium lactate and potassium nitrate [23].

The aim of the present study was to test the efficacy of a cosmetic toothpaste containing, aluminium lactate, potassium nitrate and hydroxylapatite compared to a benchmark cosmetic toothpaste control which also contains potassium for the reduction of dentine hypersensitivity pain. The study hypothesis was that after 7 days pain would be improved significantly more in the group using the test toothpaste.

Methods

Study Design

This was a randomised, examiner blind, two treatment arm, parallel, controlled trial. The study was given a favourable ethics opinion by the South-West-Frenchay Research Ethics Committee Reference 20/SW/0036, IRAS ID: 266661 and conducted in accordance with Good Clinical Practice. At screening participants with a history of DH who gave informed consent and were eligible for study entry, were supplied with a wash-in toothpaste to use twice daily for a minimum of 7 days before returning for their baseline visit. At baseline following a whole mouth plaque score and DH measurements for 2

teeth identified as sensitive, participants were randomised to test or control toothpaste and were asked to brush with their allocated toothpaste under supervision. DH scores were repeated post toothbrushing, and participants were asked to complete a quality of life questionnaire. After 7 and 14 days of twice-daily brushing with their allocated toothpaste participants returned to the study site and plaque scores, DH scores and the quality of life questionnaire were repeated.

Participant recruitment

Healthy participants were recruited from a Clinical Trials Unit database of individuals who had expressed an interest in taking part in healthy participant trials. Potential participants were sent the participant information sheet, and a screening appointment for those who responded positively was made. The study was carried out in a UK dental School. As this study took place from 3 August and 7 October 2020 during the Covid-19 pandemic the participant information sheet contained additional information to explain how study appointments would work and the measures in place to ensure participant safety while visiting the study site. In addition, every participant was contacted 24-48 hours prior to their appointment to assess their current Covid-19 status so that no one with known disease/symptoms attended the study site.

Screening visit

Participants who gave written informed consent were assessed for eligibility to take part in the study. Assessments conducted by the study dentist comprised a medical history, an oral hard and soft tissue examination and an assessment of DH in response to a cold stimulus. Eligible participants were healthy adults aged 18-65 with no condition that would impact on their safety or wellbeing if enrolled on the study, with at least 20 natural teeth and at least 2 sensitive teeth with a Schiff score $\geq$2 following exposure to a drop of water at 0^{o}C [24]. Participants were excluded if they had an allergy or known intolerance to study products, a condition causing reduced saliva flow or similar that could affect study outcomes or were taking daily doses of medication that could affect pain perception. Additional dental exclusions were dental prophylaxis within 4 weeks of screening, tongue or lip piercing, clinical caries anywhere in the mouth, desensitizing treatment within 2 weeks of screening, active periodontal diseases, and tooth bleaching within 8 weeks of screening. Participants meeting all eligibility criteria were enrolled in the study and given a standard fluoride toothpaste (Signal Toothpaste, Unilever) and toothbrush to use until their baseline study appointment a minimum of 7 days later. Participants were asked to refrain from all oral hygiene procedures and eating and drinking for an hour prior to their baseline appointment.

Baseline visit

Following an oral hard and soft tissue examination the study dentist undertook a whole mouth Quigley-Hein modified Turesky plaque score [25]. Two non-adjacent accessible teeth (incisors, canines or pre-molars), that demonstrated tactile sensitivity (Yeaple ≤20g) [26] and a Schiff score ≥2 [24] following the application of a drop of water at 0^{o}C were identified. Teeth with exposed dentine used as abutments for fixed or removable partial dentures, teeth with crowns or veneers, orthodontic bands or cracked enamel or teeth with evidence of caries were excluded from being test teeth. Participants were also asked to rate their DH on a 100mm VAS scale from 'no tooth pain' to 'the worst tooth pain ever experienced'.

Participants with ongoing eligibility were randomised to either the test (potassium nitrate/aluminium lactate/hydroxyapatite/sodium monofluorophosphate; RDA, 11; Sunstar, Switzerland) or control (potassium nitrate/sodium fluoride; Sensodyne daily, GSK Consumer Healthcare, UK) toothpaste according to the randomisation schedule generated by the study statistician. Randomisation was undertaken in a separate area by non-blinded study staff, each participant being allocated the randomisation number next on the schedule in the order that their continued eligibility at baseline was confirmed. Participants were asked to complete the DHEQ15 the DH quality of life (DH-QoL) questionnaire [27] supplemented with 7 additional questions, and provided with a new toothbrush, their study toothpaste and dosing instructions for home use twice daily. Participants were then asked to brush their teeth with their allocated product for a timed minute under supervision prior to returning to the study dentist who was blinded to the treatment that they had been randomised to for a second assessment of DH of the test teeth by all three measures. A visit 3 study appointment was made and participants were reminded they should refrain from all oral hygiene procedures and eating and drinking for an hour prior to this appointment.

Study visits 3 and 4

At both visits, following an oral hard and soft tissue examination, the study dentist blinded to the participants allocated toothpaste undertook a whole mouth Quigley Hein modified Turesky plaque score and assessed the test teeth for DH by Yeaple probe and Schiff score following a 0^{o}C water stimulus. Participants were asked to rate their DH by VAS and to complete the quality of life questionnaire again. At visit 3 a final study visit appointment was made and participants were reminded they should refrain from all oral hygiene procedures and eating and drinking for an hour prior to this appointment. At visit 4 participants returned all unused toothpaste and their toothbrush.

Examiner scored tooth assessments

Plaque was scored at 2 sites per tooth (buccal and lingual/palatal surface) of all scorable teeth excluding 3rd molars, following plaque disclosure using the Quigley-Hein modified Turesky plaque index (0 = no plaque; 1 = separate flecks or discontinuous band of plaque at the gingival (cervical) margin;2 = thin (up to 1 mm), continuous band of plaque at the gingival margin; 3 = band of plaque wider than 1 mm, but less than one-third of surface; 4 = plaque covering one-third or more, but less than two-thirds of surface; 5 = plaque covering two-thirds or more of surface) [25].

DH in response to tactile stimulus was determined by Yeaple probe which was calibrated at the start of every study day. Starting at a force of 10g and increasing in 10g increments the Yeaple probe tip was passed over the exposed dentine on the buccal surface of the selected teeth, apical to the cement-enamel junction until the participant indicated that they were experiencing discomfort by providing a "yes" response. The force setting which elicited the “yes” response was repeated, and if a second "yes" was not obtained, the force setting was increased by 10g. Sensitivity was assessed until a force which elicited two consecutive "yes" responses was identified.

DH response to the cold stimulus followed the tactile assessment, with a minimum of five minutes in between each assessment type to allow recovery. The cold stimulus was applied as a drop of 0^{o}C to the exposed dentine at the buccal cervical region of the identified teeth. Appropriate measures to isolate the test tooth surface in order to prevent stimulus exposure to adjacent tooth or surrounding soft tissue were taken and the participant response recorded using the examiner scored Schiff index (0 = Subject does not respond to stimulus; 1 = Subject responds to stimulus but does not request discontinuation of stimulus; 2 = Subject responds to stimulus and requests discontinuation or moves from stimulus; 3= Subject responds to stimulus, considers stimulus to be painful, and requests discontinuation of the stimulus) [24].

Quality of life questionnaire

The DHEQ15 quality of life questionnaire [27] was supplemented with the following questions; (16) My sensitive teeth make me anxious in social situations that involve eating, (17) I have stopped eating food that cause my teeth to feel sensitive, (18) I have stopped eating or drinking certain things because of these sensations, (19) I worry that eventually with age all my teeth will get more sensitive, (20) The anticipation of sensitivity pain affects what I eat/drink in my daily life (21) I wish to go back to a time when I didn’t have sensitive teeth, (22) Having these sensations makes me feel like I can’t enjoy life as much, (23) Thinking of these sensations is a source of stress or anxiety. All were scored on a 7-point Likert scale from strongly disagree to strongly agree. In addition, participants rated their quality of life on a global VAS scale.

Statistical analysis

With 40 participants planned per group, the detectable difference between the two formulations is 0.626 times the estimated within-groups standard deviation (SD).

Schiff, tactile and tooth level VAS sensitivity scores were characterised at each assessment by the average of the scores for the two designated study teeth. Plaque was characterised at each scoring assessment by the average of the scores for all teeth scored. Means and SDs for all measures for each treatment group were calculated.

The primary analysis of efficacy was analysis of covariance to compare the groups allocated to the two toothpastes, with the corresponding baseline pre product use value as covariate. This was performed for each outcome measure at each response time point. In each analysis, adjusted mean treatment differences are reported with 95% confidence intervals, as well as p-values. Means and SDs were also reported for changes from baseline in each treatment group.

At each follow-up time point, the analysis also determined how many (2, 1 or 0) of the designated teeth remained sensitive (Schiff score 3 or 2). The corresponding proportions were calculated in each group, together with the relative risk reduction for the test paste relative to the control paste, all with 95% confidence intervals [28,29].

The primary outcome was difference in dentine hypersensitivity as measured by examiner Schiff score after 7 days, adjusted for the baseline Schiff score (co-variate).

Results

The study was conducted between 3 August and 7th October 2020 and recruited 83 participants, 82 of whom were randomised. Randomised participants had an average age of 39 years (range 18-77), 49 were female and 33 were male, 72 were White, 9 Asian and 1 Black. A higher proportion of women than men were allocated to the test product (67% vs 36%) and the test group was slightly older (41 vs 37 years). Participant flow through the study is shown in Figure 1. There were no adverse events recorded for the study.

Plaque scores

Changes in whole mouth mean Turesky plaque index from baseline to 14 days were small (Table 1).

Table 1 Mean (SD) whole mouth mean Turesky plaque scores and change in plaque scores from baseline.

	Test (n=42)		**Control (n=40)**	
Timepoint	Plaque Score	Change from baseline	Plaque Score	Change from baseline

baseline	1.37 (0.69)	-	1.43 (0.60)	-
7 days	1.29 (0.67)	-0.08 (0.23)	1.44 (0.66)	+0.02 (0.32)
14 days	1.31 (0.60)	-0.06 (0.28)	1.35 (0.59)	-0.07 (0.36)

Plaque scores showed some evidence of improvement in both groups by 14 days. There was no evidence of any difference between the two products. After adjusting for baseline scores (ANCOVA) the estimated mean differences between plaque scores after 7 and 14 days were -0.102 (95% confidence interval -0.224 to +0.020, p=0.10) and +0.001 (-0.130 to + 0.133, p=0.98), respectively. Results for buccal and palatal/lingual plaque scores were similar.

Dentine Hypersensitivity scores

DH pain scores at each study assessment are shown in Table 2 and changes in theses scores from baseline values pre toothbrushing are shown in Table 3. There was an improvement in DH pain scores for both treatment groups for all measures, but improvements were much greater in the group using the test toothpaste. The differences in pain scores were significant in favour of the test toothpaste at all study time points for both examiner Schiff and Yeaple scores and participant reported VAS (Table 4).

Table 2. Mean (SD) DH scores of 2 selected study teeth

	Schiff score		**Yeaple score**		**Participant reported VAS**	
Timepoint	Test (n=42)	Control (n=40)	Test (n=42)	Control (n=40)	Test (n=42)	Control (n=40)
Baseline pre brushing	2.310 (0.413)	2.225 (0.357)	16.4 (3.5)	17.5 (3.4)	58.0 (17.2)	52.6 (23.8)
Baseline post brushing	1.202 (0.530)	1.788 (0.505)	41.0 (9.0)	28.3 (7.3)	33.8 (20.6)	43.2 (25.7)
7 days	0.798 (0.507)	1.475 (0.493)	48.8 (7.6)	40.0 (5.2)	28.1 (22.7)	45.7 (24.1)
14 days	0.476 (0.427)	1.275 (0.566)	55.6 (6.7)	44.6 (5.8)	19.1 (20.7)	37.4 (26.2)

Table 3 Mean (SD) Change from baseline in DH scores of 2 test teeth

	Schiff score		**Yeaple score**		**Participant reported VAS**	
Timepoint	Test	Control	Test	Control	Test	Control
Baseline post brushing	-1.11 (0.62)	-0.44 (0.51)	+24.5 (9.9)	+10.8 (7.0)	-24.2 (22.5)	-9.4 (20.1)
7 days	-1.51 (0.61)	-0.75 (0.48)	+32.4 (7.8)	+22.5 (5.4)	-29.9 (28.8)	-6.9 (22.0)
14 days	-1.83 (0.55)	-0.95 (0.46)	+39.2 (8.1)	+27.1 (6.7)	-38.9 (27.5)	-15.2 (21.6)

Table 4 Estimated differences (test-control toothpaste) in averaged DH scores from the 2 test teeth, adjusted for pre-baseline brushing score using ANCOVA

	Assessment timepoint	Estimate	95% CI	p-value
Schiff	Baseline post brushing	-0.612	-0.836 to -0.388	<0.001
	7 days	-0.705	-0.920 to -0.489	<0.001
	14 days	-0.838	-1.046 to -0.631	<0.001
Yeaple	Baseline post brushing	+13.0	+9.3 to +16.6	<0.001
	7 days	+9.2	+6.3 to +12.1	<0.001
	14 days	+10.8	+8.0 to +13.6	<0.001
Participant reported VAS	Baseline post brushing	-12.6	-21.4 to -3.9	0.005
	7 days	-19.6	-29.5 to -9.7	<0.001
	14 days	-20.5	-30.3 to -10.8	<0.001

Furthermore, when Schiff scores were dichotomised and the proportion of study teeth that remained sensitive (Schiff score 2 or 3) was determined for each study timepoint there was a relative risk reduction (RRR) of DH pain of 55% immediately post supervised toothbrushing if teeth were brushed with the test as opposed to the control toothpaste (Table 5). This RRR rose to 81% after 7 and 88.6% after 14 days, the RRR achieved by using the test toothpaste in place of the control toothpaste was highly significant at all timepoints ($p<0.001$).

Table 5. Proportions of test teeth remaining sensitive (Schiff score 3 or 2) in the two treatment groups, and relative risk reduction by using the test instead of the control product.

	Test			**Control**			**Relative risk reduction[1]**		
		95% CI[2]			95% CI			95% CI	
Timepoint	Estimate	Lower	Upper	Estimate	Lower	Upper	Estimate	Lower	Upper
Baseline[3]	0.310	0.213	0.429	0.688	0.558	0.791	0.550	0.335	0.697
7 days	0.095	0.047	0.194	0.500	0.386	0.614	0.810	0.591	0.908
14 days	0.036	0.010	0.135	0.313	0.216	0.431	0.886	0.537	0.970

[1][25], [2][24], [3]Post supervised toothbrushing

Questionnaire variables

For both treatment groups, the mean quality of life scores as calculated from the questionnaire improved slightly overall from baseline pre-toothbrushing to visit 4. This applies to both the validated questionnaire and the additional 7 questions. However, there were no significant differences in the overall mean quality of life scores obtained from the questionnaire following use of the test as compared to the control toothpaste for 7 or 14 days (Table 6). Similarly, there were no significant differences following the use of test as compared to control toothpaste for the mean scores obtained from any individual question.

Table 6. Differences in composite 15-item DH-related quality of life score after 7 and 14 days toothpaste use between the test and control product (test – control), adjusted for corresponding baseline score.

Visit	Estimate	95% CI	p-value
7 days	-0.059	-0.145 to +0.027	0.174
14 days	-0.026	-0.133 to +0.081	0.631

When asked to rate their global DH VAS, pain scores improved following use of both toothpastes (Table 7), but no significant differences in global DH pain reported by the groups were detected, although scores favoured use of the test toothpaste. After adjusting for baseline scores (ANCOVA) the estimated mean differences between group global VAS after 7 and 14 days were -4.9 (95% CI -11.1 to +1.2, p=0.115) and -7.1 (-15.3 to + 1.1, p=0.089), respectively.

Table 7 Mean (SD) Global DH VAS pain and change in VAS from baseline.

	Test			Control		
Timepoint	n	VAS score	Change from baseline	n	VAS score	Change from baseline
baseline	42	57.3 (16.0)		39	54.7 (22.4)	-
7 days	42	47.7 (16.9)	-9.5 (16.3)	39	51.0 (18.4)	-3.5 (15.5)
14 days	41	35.8 (19.4)	-21.7 (20.1)	39	40.4 (22.2)	-13.1 (21.1)

Discussion

This study tested whether there was a difference in the efficacy of 2 toothpastes to deliver DH pain relief. DH pain scores in those using the test toothpaste containing aluminium lactate, potassium nitrate and hydroxylapatite were significantly lower immediately after use and after use twice daily for 7 and 14 days than scores obtained from those using the control toothpaste containing potassium nitrate.

As might be expected using a toothpaste containing a known desensitising agent potassium nitrate as a control, there were improvements in DH pain scores, however these were immediately and after 7 days as well as at the 14 day time point. Systematic reviews suggest that the improvements in DH pain afforded by use of a potassium based desensitising toothpaste are not generally seen until after a minimum of 2 weeks twice-daily treatment [12], with other reviews suggesting that the timeframe is longer, 4 weeks and more [6]. However, although the control toothpaste contained potassium nitrate, a proven desensitising agent [30], this particular formulation does not have a licence for pain reduction claims in the UK, and is marketed as a cosmetic as is the test product.

The greatest efficacy for the control toothpaste in the present study was observed at 2 weeks for all measures and may be due to a true de-sensitising effect conferred by potassium, but earlier improvements are more likely due to regression towards the mean [31] which occurs in sensitivity studies due to fluctuations in the severity of DH experienced by sufferers as dentine tubules are opened or blocked by oral debris [32]. In DH studies such as this one, participants must score relatively highly in DH pain assessments to be eligible for entry into the study, and for some this level may be towards the maximum DH pain that they experience, therefore their scores are likely to decline naturally during the study. Participants in the present study may have also reported reduced pain due to the placebo effect [33,34].

Although improvements in DH pain from baseline were observed in those brushing with the control toothpaste, at every time point post baseline and by every DH measure, pain scores on test teeth recorded in the test group were significantly lower than those recorded in the control group. Furthermore, there was also a significant relative risk reduction of DH in the test teeth of those receiving the aluminium/hydroxylapatite containing toothpaste as compared to the control toothpaste. Prior to this study literature on aluminium containing over the counter DH treatments was limited. One study of a mouthrinse containing aluminium lactate indicated it reduced pain significantly more than a control mouthrinse ($p<0.05$) at 4 and 6 weeks [14] and one study of a toothpaste containing aluminium lactate and potassium nitrate demonstrated it reduced DH pain more rapidly than a control toothpaste but did not compare efficacy between test and control at each study time point [16]. This is the first study to demonstrate significantly superior efficacy of an experimental toothpaste containing aluminium lactate, potassium nitrate and hydroxylapatite compared to a control toothpaste. It is hypothesized that the aluminium ions react with phosphate ions in the saliva to form a precipitate which can block dentine tubules [19], together with the hydroxylapatite occluding the dentine tubules, facilitating a dual action of occlusion. Therefore, with the presence of potassium delivering a toothpaste that can target DH by both depolarisation of nerves combined with dentine tubule occlusion, this satisfies both methods of treatment modality for this condition. As indicated previously, while there are many toothpastes that have shown efficacy for the treatment of DH as compared to control there is insufficient evidence to identify one product as superior to the others [6,12]. To support the findings of the present study and be able to draw comparisons between this toothpaste and other lead products further randomised controlled studies are needed which include positive and negative DH controls.

Somewhat surprisingly, although whole-mouth VAS improved in both groups following treatment there were no significant differences between the groups at either timepoint although scores slightly

favoured the test group. Similarly, DH-QoL questionnaire scores improved in both groups following treatment but yielded no significant differences between them although the combined scores also slightly favoured the test group. DH-QoL is a quality of life tool designed specifically for evaluating the tangible and frequent discomfort of DH pain, and as such no other QoL was considered although additional questions were included. These findings are similar to those of a previous study which showed that test teeth treated with a calcium silicate sodium phosphate toothpaste had significantly lower VAS that those treated with a control toothpaste, but that differences between treatment groups for whole-mouth VAS and DH-QoL failed to reach significance [35]. The difference between VAS data obtained from specific teeth and that obtained from the whole mouth may reflect the subjective nature of pain, the perception of which is the result of a number of different factors [36,37]. Scales such as VAS measure pain by rating its intensity only which when a participant is being asked about a specific test tooth in isolation appears to work well, VAS being recognised as a standard scale for diagnosing and measuring DH pain in clinical trials [38]. However, as many factors contribute to pain perception, when asked in the context of the whole mouth rather than following direct stimulation of specific teeth the VAS score given by participants may be influenced by other factors. It is also possible that whole mouth VAS is not a sensitive enough measure to distinguish between DH treatments as not all teeth are sensitive.

Similarly, the DHEQ15 [27] may not be a sensitive enough measure for determining differences between treatment groups in DH-QoL in the timeframe of the present study particularly as both toothpastes resulted in improvements in DH pain. Perception that DH-QoL has improved is likely to be gradual and increase over time as participants realise that their DH is not affecting their daily life to the same extent as it was pre-treatment. Some study participants may routinely avoid situations that trigger their DH and thus not realise that their DH has improved until they accidentally, or subconsciously allow themselves to be exposed to their DH trigger.

This study was designed principally to determine whether a cosmetic toothpaste was also able to deliver relief from DH over the short term. As a result of this, participants were selected for DH rather than gingival health and plaque score, and it was not appropriate to undertake a dental prophylaxis at the baseline visit which would have enabled plaque accumulation to be determined, as this would affect DH measurements. Thus, it was unsurprising that there were no significant differences between the test and control toothpaste with respect to plaque score, however recording this measure confirmed that use of either toothpaste resulted in healthy plaque levels being maintained. There is some evidence that the aetiology of DH could be due to plaque bacteria in the dentine tubules [39,40], however this study, like many others confirms that the dentine hypersensitivity sufferer has excellent

oral hygiene and this aetiology hypothesis is very unlikely for the majority of individuals with this condition. A different study design would be necessary to compare the efficacy of these toothpastes for plaque control.

The study was sufficiently powered, blinded to DH assessors and study participants and included an acclimatisation period to minimise differences in treatment groups prior to the administration of the intervention. The control toothpaste selected for this study was an appropriate choice being a comparable cosmetic toothpaste containing potassium. As is indicated for DH studies 2 DH stimuli (thermal cold and tactile) and three measures of assessment Schiff score, Yeaple probe force eliciting 2 pain responses and VAS were used on test teeth [41]. Examiner Schiff score has recently been shown to be the most reliable pain scoring system and indicator of sensitivity when compared to other pain measures, with VAS also scoring highly for sensitivity and specificity [42], confirming their suitability for use in this study.

When evaluating all stimuli types, the ideal stimulus is one which is realistic and as close as possible to the natural stimulus. Electrical stimuli are thought to be inappropriate as there is no correlation between the electrical threshold and VAS pain rating to measure sensitivity [43], these stimuli are therefore not preferred. Tactile is a reasonable stimulus, for example using a toothbrush however, measuring the tactile stimulus force using the Yeaple probe is extremely time consuming for both the investigator and participant, needing a highly skilled operator. The probe design allows for adjustable force from 10 to 100 grams and is accurate to plus or minus 1 gram, it is battery-powered for safety and convenience and any probe tip can be fitted to the instrument. The Yeaple Probe has been used for periodontal pocket probing and dentine sensitivity testing in dental research for more than 18 years and has become the worldwide industry standard and thus selected for use in this study. However, one major drawback of the probe is that following calibration the probe is set to a microampere reading to correspond to the force chosen to be measured eg 20g. However, the operator does not know if they are exerting this force or more from the feedback light on the probe, and needs to touch the probe on the dentine surface in an oscillating motion around the correct force to ensure the light indicator flickers indicating they are reaching but not significantly exceeding the force selected, which takes skill.

The thermal cold stimulus is probably the most valid for DH [43] as it corresponds to natural stimuli for example cold drinks and food stuffs. The air blast that is used in many studies and may be considered a cold thermal stimulus is also, and more importantly, an evaporative stimulus, drawing cold air over the open dentine tubules. Even taking precautions to isolate test teeth, airblasts tend to affect a larger tooth area and are more difficult to control [43]. The evaporative stimulus also tends

to lead to an overrating of pain due to the anticipation of the cold air blast [44]. It was not possible to use an air blast stimulus in the present study conducted in the COVID – 19 period, without additional PPE and this was substituted with an ice-cold crop of water. Scores obtained from the ice-cold water stimulus correlated well with those obtained following the tactile stimulus and the ability to better control the application of this stimulus together with negating the elevated pain scores due to anticipation of the air blast indicate a pure thermal stimulus is highly suitable for DH studies.

Conclusion

This study demonstrated the efficacy of an aluminium lactate/potassium nitrate/hydroxylapatite toothpaste compared to a potassium nitrate control toothpaste for the prevention of dentine hypersensitivity both immediately and over 7 and 14 day time points when assessed with cold and tactile stimuli. This agent appears to have potential for pain alleviation from the common oral pain condition of DH and further research is warranted.

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Figure:

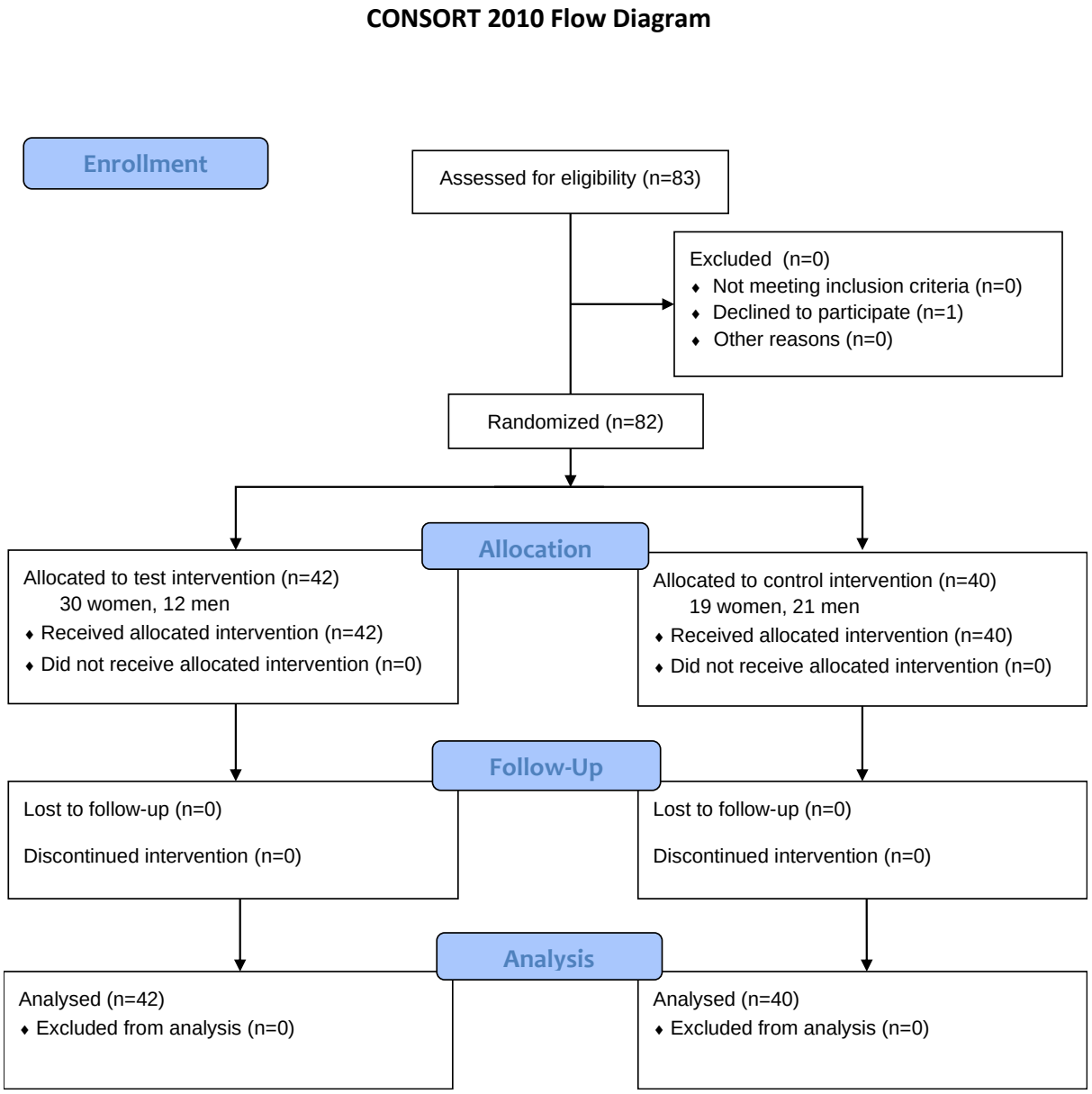

Figure 1. Participant flow through the study