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SCIENTIFIC SECTION

White lesions after orthodontic treatment: does low fluoride make a difference?

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Objective: To compare and measure the changes in size of post-orthodontic demineralized white lesion enamel lesions treated with a low fluoride (50 ppm) versus a non-fluoride mouthrinse/toothpaste regime.

Study design: An experimental double-blind prospective randomized clinical controlled trial.

Setting: A university dental school orthodontic clinic (Sheffield, UK).

Participants: Twenty-six patients identified as having post-orthodontic demineralized white lesions on removal of their fixed appliance.

Method and interventions: The participants were randomly and blindly assigned to either a low fluoride mouthrinse/toothpaste treatment regime or an inactive control. Computerized image analysis of calibrated photographic images taken under polarized light were used to measure the lesions.

Outcome measures: Lesion size and proportion (DWL%t) and percentage reduction (ADPR) at debond, and at 12 and 26 weeks later.

Results: Five participants dropped out of the study, 12 had the low fluoride regime and 9 did not. As a percentage of the total labial tooth area (DWL%t) the mean size of the lesions at debond was 8.1% (SD 3.7). After 12 weeks the mean size of lesion had reduced to 4.6% (SD 2.6), which was a significant reduction ($p=0.03$). After 26 weeks the mean size was 3.5% (SD 2.1), which was a very significant reduction ($p<0.003$). This confirmed statistically that post-orthodontic demineralized white lesions do reduce in size with time reflecting remineralization or other enamel surface changes. Intervention using a test low fluoride mouthrinse/toothpaste combination at 26 weeks showed an average difference percentage reduction (ADPR) of 54.3% (Upper 95% CI=62.08, Lower 95% CI=46.44%) compared with a non-active control combination, which showed an ADPR of 66.1% (Upper 95% CI=77.74, Lower 95% CI=54.51%). This failed to show any differences or therapeutic affect.

Conclusions: Post-orthodontic demineralized white lesions reduced in size during the 6 months following treatment by approximately half the original size. There was no clinical advantage in using the low fluoride formulation of mouthrinse/toothpaste in this study.

Key words: *White spots, demineralization, fluoride mouthrinse*

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Introduction

Enamel demineralization and white lesions occur during and sometimes remain after orthodontic treatment.[1,2] This phenomenon has become a particular clinical problem since directly bonded orthodontic brackets were introduced.[3] O'Reilly and Featherstone[4] and Ogaard[5,6] have shown that visible white lesions can develop within 4 weeks of the fitting of a fixed bonded orthodontic appliance. Melrose *et al.*[7] have shown that similarly early enamel carious lesions can form associated with orthodontic bands in periods as short as 4 weeks. Clearly, the best approach during orthodontic treatment is to prevent lesions occurring. It has been concluded that fluoride preparations, oral hygiene instruction and dietary control have the greatest effect on reducing demineralization.[8] Once formed, many of these early lesions appeared to be surface demineralization, rather than a sub-surface lesion with an intact surface zone. Remineralization of these white lesions is a natural phenomenon resulting in the partial reversal of what is an early caries lesion. The factors involved are discussed

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in the proceedings of a workshop by Leach.[9] The mineral of the dental enamel is in equilibrium with its environment and saliva contains all the necessary elements for hydroxyapatite crystal growth. In the natural state there is natural demineralization and remineralization continually taking place. An excellent example of this is the maturation of tooth enamel that occurs shortly after a tooth erupts.[10] This study examined a group of 9 year old children revealed 72 carious white lesions, which were carefully recorded. Six years later 50% of those lesions had disappeared, inferring that remineralization had taken place. Melrose *et al.*[7] commented that the superficial lesions seen after orthodontic treatment will tend to remineralize more rapidly and completely than deeper lesions on removal of the cariogenic challenge. Remineralization varies considerably from subject to subject and from site to site in the mouth.[11] These studies have shown an average remineralization of 20–30% over 2 weeks (measured as a percentage mineral change). Sometimes the amount of remineralization cannot totally overcome the amount of demineralization even with an effective agent present. Following removal of the appliance, some regression of post-orthodontic lesions is known to occur provided other aetiological factors are favorable. Ogaard *et al.*[6] warned against treating visible white lesions on labial surfaces with concentrated fluoride agents, since this arrests the lesion (hypermineralization). Instead, they advocated allowing remineralization by saliva, as this results in greater repair and a less visible lesion.

Remineralization also produces a greater resistance to further dissolution and this is due to the fact that during remineralization, components are replaced with less soluble substance that may have larger crystals.[12] This has been reported[4] as plugging of diffusion pathways of enamel by hydroxyapatite crystals as hyper-remineralization. Workers in this field have, however, recommended the remineralization of small lesions with low fluoride preparations.[13,14] They have shown that lesions smaller then 60 μm deep can be remineralized using these preparations. In order to avoid arresting the lesion and obtunding the surface layer several workers have recommended low dose fluoride applications to enhance sub-surface remineralization. Lee Linton[13] showed that a 50 ppm F mouthrinse had a higher efficiency for remineralization than a control solution or a regular mouthrinse containing 250 ppm. For lesions on surfaces other than on the visible labial surface, application of concen-trated fluoride was suggested to prevent further progression. It has been suggested that acid etching of fluoride-treated lesions could facilitate remineralization of the lesion by oral fluids of synthetic remineralizing fluids.[15]

The purpose of the study was to examine and measure, in a randomized longitudinal prospective clinical study of post-orthodontic demineralized white lesions, the changes in size, and subsequent prognosis and fate of these lesions. In addition to compare the fate of post-orthodontic demineralized white lesions when subjected to intervention with a rinsing/toothpaste regime of either a specially formulated low fluoride mouthrinse/toothpaste test combination or a control fluoride-free mouthrinse/toothpaste combination, using an experimental double blind prospective randomized controlled trial.

The study was designed to test the following hypotheses:

- that post-orthodontic white enamel demineralized lesions reduce in size in the post-treatment period.
- that a low fluoride remineralizing mouthwash leads to a greater reduction in size of visible post-orthodontic white lesions compared with a no fluoride mouthrinse.

Participants and methods

Study design

The study was an experimental double blind prospective randomized clinical controlled trial with 2 parallel groups. Participants who had suffered post-orthodontic demineralized white lesions following comprehensive fixed appliance therapy were offered the opportunity to enroll into the trial and if in agreement provided with either a test (low-fluoride) or a control (fluoride-free) mouthrinse/toothpaste combination for use on a daily basis according to a specified regime. The trial was double blind and the test and control interventions were randomized, the contents being unknown to the researcher at the time of both imaging and measurement. Ethical approval was obtained from South Sheffield Research Ethics Committee (reference no. SSR 98\002) All patients were treated according to the declaration of Helsinki.[16]

Inclusion criteria

To be accepted into the study the participants must have had:

- at least 12 months fixed appliance therapy;
- at debond post-orthodontic demineralized white lesions identified by the debonding clinician;
- lesions were not present at start of treatment when compared with pre-treatment clinical photographs;

- be possible to acquire the first images close to the date of debond;
- demineralized white lesions present on at least one of the anterior 8 upper or lower teeth including the most anterior remaining premolar.

Agreement that participants would undertake to use interventions provided by the researchers and would be content with the structure of the clinical trial.

Sample

Sample size calculations were carried out. Using the data from a previous study of demineralized white lesions, assuming a significance level of 0.05 and a 2-sided *t*-test, statistical advice from the Statistical Services Unit, University of Sheffield, UK, using nQuery software gave the opinion that with an expected reduction in lesion area of 40% in the control group and 70% in the test group (i.e. a 30% difference) this could be detected with $n=11$ in each group.

Recruitment of participants

Participants in the randomized controlled clinical trial were recruited from patients consecutively completing comprehensive fixed appliance therapy in the Orthodontic Clinic at the Charles Clifford Dental Hospital, Sheffield. At debond patients were referred to a regular research clinic when the orthodontist completing orthodontic treatment suspected post-orthodontic demineralized white lesions. Patients attending this clinic agreed to attend the research clinic regularly, and were prepared to enter the clinical trial and have their teeth imaged by photography. Participants were given an appropriate explanation of the study and informed consent obtained by the principal researcher. They were issued with an information sheet and clear instructions on how to use the mouthrinse/toothpaste combination.

The interventions under test and randomization

The mouthrinse/toothpaste combinations comprised of a low sodium fluoride test mouthrinse or an identical control mouthrinse with no sodium fluoride, plus a fluoride-free toothpaste. Sodium fluoride was present in the test mouthrinses in very low concentrations as recommended by various authorities[13,5] to promote remineralization. The mouthrinse had an effective NaF content of 50 ppm. The control mouthrinse contained all the same ingredients except sodium fluoride. All participants in the study were given a fluoride free toothpaste and were instructed to use this toothpaste throughout the study and not their regular toothpaste. Packs of mouthrinse and toothpaste were prepared by a dental products company (Boots Contract Manufacturing, Beeston, Nottingham NG2 3AA, UK). The participants were issued with 3–4 months supply in packs of 3×200 g tubes of paste and 3×1 litre of mouthrinse. Packs were numbered 1 onwards by the pharmaceutical company and the test/control packs were randomized by that company according to a table of random numbers held by the company. The code was placed in a sealed envelope until the conclusion of both the trial and measurements. Participants were instructed to keep all empty bottles and tubes, and return them to the researcher at their next visit. Participants and the researcher were unaware as to whether an intervention or control mouthrinse was being supplied. Clear written instructions were given to each participant on how to use the interventions and also about the clinical trial procedure in general as requested by the Ethics committee. Participants were instructed to use the mouthrinse twice a day after brushing their teeth in the morning and in the evening before bed. They were instructed to swish the mouthrinse around their teeth for 30 seconds.

Image acquisition

Images were acquired in a darkened dental surgery using polarized light from flashlights and polarizing lenses attached to a 35-mm system.[17] Previous work has shown the techniques of image acquisition is repeatable and enables the distinction of dimensional changes in lesions.[18] Images were acquired within a few days of debonding and at approximately monthly intervals up to and beyond 26 weeks in some cases.

Selection of lesions

For each subject included in the clinical trial, all 8 upper anterior teeth and all 8 lower anterior teeth were examined for discreet white lesions. They were known not to be pre-existing when compared with pre-treatment clinical photographs and they were associated with the position of the previously placed fixed appliances. Depending upon the remaining lesions, up to a maximum of 4 lesions were selected from each patient, representing a range of different teeth. Each lesion was measured independently for each image, which had been previously calibrated as part of the following protocol.

Processing protocol

The images were processed on a Pentium II PC (300 mHz) with a 64 MB RAM. Initially, the 35-mm

colour slides were scanned by a Fotovix converter (Fotovix IIIS, Model TF-156WE, Tamron Co., Japan) set to standard repeatable settings and converted into TIFF files as colour (RGB) images. The TIFF files were then processed using Image Pro-Plus (Version 4, Media Cybernetics, Ca., USA) as color images. The image was opened and, if necessary, adjusted for brightness using a contrast enhancement process. A processing procedure of 'sharpen' filter (set at minimum 3×3, one pass) was used to improve margin integrity of the teeth and lesions. Calibration (spatial) was via a modified plastic bite gauge held between the subject's teeth. All data was collected via the clipboard to a Microsoft Excel spreadsheet for storage and processing. At each visit made by the patient during the months following debond the area of demineralized white lesion (ws) and the area of the labial surface of the tooth under study (t) were measured.

Statistical analysis and outcome measures

In order to make understandable comparisons between groups, it is necessary to have a key number for each subject for any one parameter. Variation of enamel response between participants, rather than between teeth was the aim of this study. There are advantages in measuring more than one demineralized white lesion per subject and calculating the average per subject. We can then compare that figure for the whole subject with other participants in the clinical trial in order to compare test and control groups. Following examination of the curves and data seen in the earlier clinical longitudinal studies,[17,18] difference in lesion as a proportion of total tooth area (DWL%t) for A–B (where A=start and B=end) expressed as a percentage reduction (DPR), would a good measure. For participants with multiple lesions, the differences for up to four lesions were measured and averaged to give the average difference in percentage reduction (ADPR). For participants with only one tooth with a lesion, a single measurement was used. The average difference in percentage reduction (ADPR) thus calculated was compared between groups at defined points of time calculated from XY plots. For this study the ADPR at 12 and 26 weeks were agreed as outcome measures. If ADPR is normally distributed within a group, then 2-group t-tests could be used. If the data is not normally distributed, then a Mann-Whitney test should be used.

Outcome measures

The following measurements were calculated to be used as outcome measures:

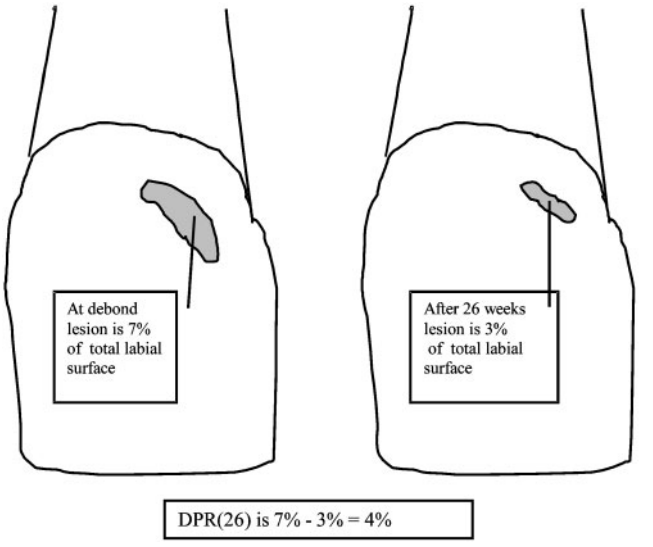

Figure 1 Illustrates the calculation of the difference of the demineralized white lesion as a percentage of area of the labial surface of the tooth (t) which in this hypothetical case is 7−3%=4% at 26 weeks [(DWL%t(0) − DWL%t(26)=DPR(26)]

- *DWL%t*—The demineralized white lesion as a percentage area of the visible labial surface of the tooth calculated by:

$$\text{DWL\%t} = \frac{\text{Area of white lesion (ws)}}{\text{Area of labial surface of tooth (t)}} \times \frac{100}{1}$$

- *DPR(x)*—The difference in percentage reduction at x weeks for each tooth. The difference of DWL%t for A–B, where A=Start and B=End (x weeks). This parameter was calculated for each tooth at 12 and 26 weeks; Figure 1 illustrates the methodology of this calculation.
- *ADPR(x)*—The average difference in percentage reduction for each subject at between debond and x weeks. Calculated from the mean of XY plots for each tooth against time of DWL%t. This was calculated for 12 and 26 weeks for each subject.

Figure 2 shows the method of calculation for one subject in the study.

Results

Participants studied and drop out

Twenty-six participants were recruited to the clinical trial, and issued blindly and randomly with the mouthrinse/toothpaste combination. The participants were numbered 1–26 in the order that they were recruited to the trial. Five participants (numbers 5, 10, 13, 18 and 25) subsequently failed to attend for any further appointments after their initial visit despite

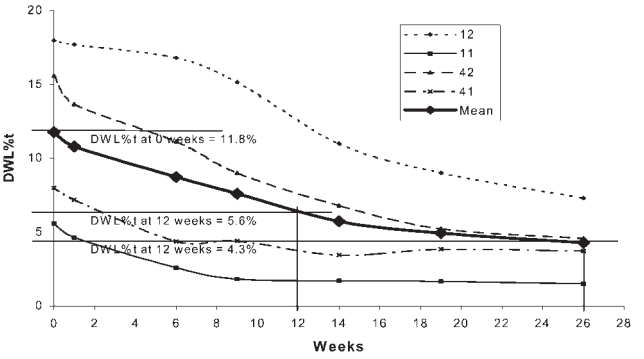

Figure 2 A typical graph of change in DWL%t with time for four teeth in one subject. The thick black plot shows the change in DWL%t with time as the mean of the lesions on the four teeth 12, 11, 42 and 41. From the mean curve the DWL%t at 0, 12 and 26 weeks has been identified. The difference between 0–12 and 0–26 weeks can then be calculated. For this case ADPR(12) was 11.8−5.6=6.2% and ADPR(26) was 11.8−4.3=7.5%

diligent follow-up. The detailed flow of participants is shown in Figure 3. All other participants (n=21) returned for a minimum of three visits. The number of visits per subject ranged from 3 to 7. The intervals between the visits were variable depending upon clinic and subject availability. Ten patients out of the 21 (47.6%) returned empty bottles and toothpaste tubes, 11 did not. It was felt that analysing this data as a measure of co-operation was unrealistic in view of the low numbers involved. All of the participants were observed longitudinally for a period of greater than 26 weeks, and on 4 occasions up to and beyond 40 weeks. No adverse events were reported.

General results

As part of the double blind technique the curves for the study were calculated and produced before the randomization code was unlocked. Figure 2 shows typical readings for a subject in the study. For all participants the mean lesion area at debond was 3.06 mm^2 (SD=1.45) and at the end of reading was 1.32 mm^2 (SD=0.87). Table 1 shows the baseline characteristics of the treatment and control groups.

Comparing lesion size at 0, 12 and 26 weeks for all participants

Table 2 summarizes the descriptive statistics for the combined group. The data were found to be normally distributed by plotting distribution graphs consequentially 2-group t-tests were used. The mean percentage of total tooth area (DWL%t) at debond was 8.1% (Upper 95% CI=9.80, Lower 95% CI=6.45%). After 12 weeks the mean percentage had reduced to 4.6% (Upper 95% CI=5.74, Lower 95% CI=3.36), which was a significant

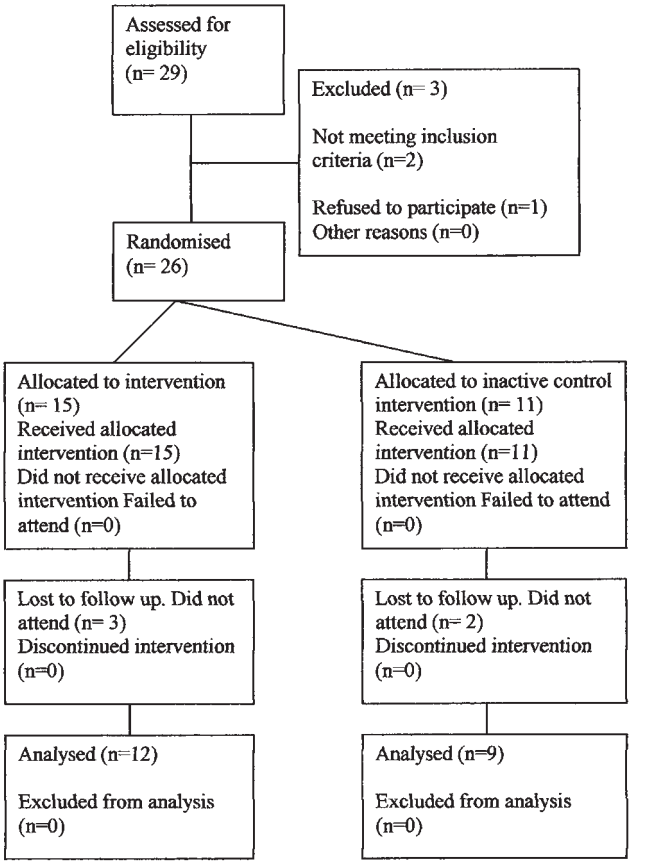

Figure 3 CONSORT diagram to show flow of participants through each stage of the randomized trial

reduction (p=0.03). After 26 weeks the mean was 3.5% (Upper 95% CI=4.43, Lower 95% CI=2.52), which was a very significant reduction (p<0.003). This confirmed statistically that post-orthodontic demineralized white lesions do reduce in size with time reflecting the remineralization of the enamel.

Comparing test and control intervention in the clinical trial

Figure 3 is a CONSORT[19] diagram that shows the flow of participants through the study. After unlocking the randomization code 12 participants had been exposed to the active low fluoride mouthwash/toothpaste regime and 9 participants had been exposed to the inactive control. Figure 4 shows graphically results for each case at 12 weeks in the clinical trial. At 12 weeks the average difference in percentage reduction (ADPR) for the participants who had blindly been subjected to a test remineralizing mouthrinse/toothpaste combination (n=12) was 40.0% (Upper 95% CI=49.30, Lower 95% CI=30.80) and for those participants who had been

Table 1 Baseline characteristics of the final treatment and control groups showing case number, gender, age, treatment or control, mean lesion area at debond and 26 weeks

Case	Sex	Age (years)	Treatment =t/control =c	Debond area (mm^2)	26-week area (mm^2)
1	F	14	c	4.35	1.87
2	F	14	t	2.9	1.29
3	M	15	c	1.3	0.7
4	F	18	t	2.75	2.05
6	F	14	t	3.89	1.81
7	F	13	t	4.55	1.9
8	F	21	t	6.8	3.6
9	F	15	c	3.18	0.29
11	M	16	t	1.74	0.42
12	M	17	c	3.42	0.42
14	F	20	t	3.79	1.77
15	F	16	c	1.57	0.87
16	F	16	c	3.8	1.62
17	M	19	t	1.8	0.44
19	M	15	c	2.2	0.73
20	M	17	t	4.14	1.36
21	F	14	t	3.5	1.16
22	F	14	c	4.17	2.65
23	F	17	t	1.24	0.7
24	F	13	c	0.52	0.12
26	F	13	t	2.65	1.88

given a control combination (n=9) it was 51.5% (Upper 95% CI=61.76, Lower 95% CI=41.30). Table 3 shows these figures summarized. There was no statistically significant difference between the groups.

Figure 5 shows graphically the results for each case at 26 weeks. At 26 weeks the ADPR for the test group was 54.3% (Upper 95% CI=62.08, Lower 95% CI=46.44) and for the control group 66.1% (Upper 95% CI=77.74, Lower 95% CI=54.57). There was no statistical difference between these groups confirming that no demonstrable beneficial effect of the test interventions was seen using this outcome measure. Because of the sample size

Table 2 Summary descriptive statistics for lesion as a proportion of total tooth area and differences at 12 and 26 weeks

Cl'inical trial	Group results combined (n=21)			
	Mean	SD	Lower 95% CI	Upper 95% CI
DWL%t(0)	8.1	3.7	6.45	9.80
DWL%t(12)	4.6	2.6	3.36	5.74
DWL%t(26)	3.5	2.1	2.52	4.43
Difference 0–12	3.6	2.0	2.67	4.47
Difference 0–26	4.7	2.2	3.67	5.63

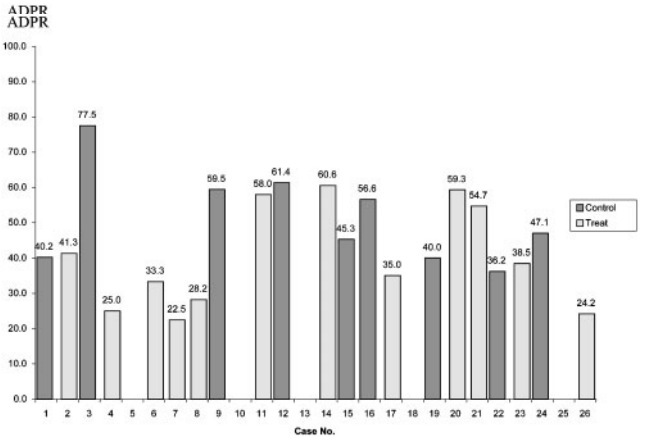

Figure 4 Average difference in percentage reduction (ADPR) at 12 weeks for all cases in the clinical trial. (The greater the value of ADPR the more the lesions have remineralized and reduced in size)

recruited it was possible to detect a difference of greater than 30% between test and control groups (*see* earlier). It remains possible that there was a smaller difference between the groups that may not be clinically relevant.

Discussion

This study has found that there was no significant difference in the size reduction of post-orthodontic white lesions when using a low fluoride mouthrinse compared with a no fluoride mouthrinse used as a control. This does not confirm the therapeutic affect of low fluoride (<50 ppm) preparations observed by other workers.[13,14] The sample size was sufficient to detect a 30% difference in lesion proportion, which was not detected. It was considered that recruiting further participants to this study would not be able to demonstrate a useful clinical effect. The mean size of the lesions under consideration was 3.06 mm^2 at debond and had reduced to 1.32 mm^2 at the end of recordings. A therapeutic effect of less than 30% would therefore be clinically and visually insignificant.

The drop out rate of 19.2% was higher than desirable. A feature of trials on patients who have suffered

Table 3 A summary of the mean average difference in percentage reduction (ADPR) at 12 and 26 weeks for the intervention sub-groups

	Mean ADPR	SD	Lower 95%CI	Upper 95%CI
Test Low F (n=12)				
12 Weeks	40.0%	14.5	30.80	49.30
26 Weeks	54.3%	12.3	46.44	62.08
Control No F (n=9)				
12 Weeks	51.5%	13.3	41.30	61.76
26 Weeks	66.1%	15.5	54.57	77.74

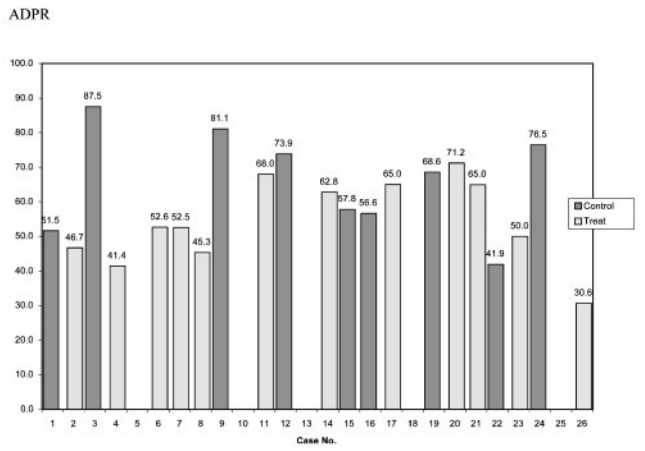

Figure 5 Average difference in percentage reduction (ADPR) at 26 weeks for all cases in the clinical trial. (The greater the value of ADPR the more the lesions have remineralized and reduced in size.)

post-orthodontic demineralization is a high drop out rate.[4,11] These participants may well have their lesions because of their lack of compliance and many of the participants may well have been 'burnt' after prolonged orthodontic treatment.

There was a wide variation in response between the participants in both groups. On the face of it the control group fared better than the test group, but these values were not significantly different when subjected to a 2-sample *t*-test. The fact that the control group appeared to actually fare better then the test group by a small amount indicates that there is unlikely to be any useful clinical difference (e.g. >30%) between the groups even in a larger multi-center study. There may be many factors influencing the wide variation in response. Failure to comply with the treatment regime may explain some of the variation. The lack of therapeutic effect seen with the treatment regime that has been reported as successful in previous studies[14] may reflect either this lack of compliance or, of course, a true lack of therapeutic effect of low dose fluoride.

The size reduction with time measured as a proportion plotted as graphs in the clinical trial showed the general exponential reduction in demineralized white lesion area seen in earlier longitudinal studies and reported in experimentally induced caries.[20] There was a wide variation in response. Consistently, all lesions reduced in size with time. Natural enamel remineralization and tooth wear seem the most likely cause. In 4 cases, after 6 months (26 weeks) very little further size reduction appeared to occur. On average, in all participants studied the difference in percentage reduction showed a reduction in lesion area of about a third after 12 weeks and a half after 26 weeks. The reductions are similar to those reported using the very different measurement technique of quantitative light induced fluorescence (QLF).[21] Benson *et al.*[22,23] in a comparative *in vitro* study that both methods would be applicable to a clinical trial, and this present work validates both methodologies and outcome. These reductions were statistically significant when comparing the demineralized white lesion as a percentage of labial tooth area (DWL%t) at both 0–12 weeks ($p=0.03$) and 0–26 weeks ($p=0.003$).

Conclusions

- This prospective randomized controlled clinical trial confirmed, using larger numbers and an improved methodology than in the previous longitudinal studies, that there was a general exponential reduction in demineralized white lesion area. There was a statistically significant reduction in lesion area measured proportionally at 12 weeks ($p=0.03$) and 26 weeks ($p=0.003$).
- In the period after removal of orthodontic appliances there was a wide variation in the response of post-orthodontic demineralized white lesions, but consistently lesions reduced in size with time. On average, in all participants studied the difference in percentage reduction showed a reduction in lesion area of about a third after 12 weeks and a half after 26 weeks.
- Numbers recruited to the study were sufficient to confirm any effect above 30% change in lesion area, if it did indeed exist.
- The fate the lesions subjected to intervention using a test low fluoride mouthrinse/toothpaste combination compared with a non-active control combination failed to show any differences or therapeutic affect.

Contributors

Derrick Willmot was responsible for study design, obtaining funding, logistics, administration, recruitment of participants, data interpretation, drafting, critical revision and final approval of the article. Darren Lath was responsible for technical support. Philip Benson was responsible for critical revision, and final approval of the article. Derrick Willmot is the guarantor.

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