J Clin Periodontol 2004; 31: 885–889 doi: 10.1111/j.1600-051X.2004.00581.x
Printed in Denmark. All rights reserved

Journal of Clinical Periodontology

Dentine hypersensitivity: a randomised, double-blind placebo-controlled study of the efficacy of a fluoride-sensitive teeth mouthrinse

R. J. Yates[1], R. G. Newcombe[2] and M. Addy[1]

[1]Division of Restorative Dentistry, Dental School, Bristol, UK; [2]Department of Epidemiology, Statistics and Public Health, University of Wales College of Medicine, Cardiff, UK

Yates RJ, Newcombe RG, Addy M: Dentine hypersensitivity: a randomised, double-blind placebo-controlled study of the efficacy of a fluoride-sensitive teeth mouthrinse. J Clin Periodontol 2004; 31: 885–889. doi: 10.1111/j.1600-051X.2004.00581.x. © Blackwell Munksgaard, 2004.

Abstract

Objectives: Potassium and fluoride salts have been used in the treatment of dentine hypersensitivity (DH). The primary aim of this study was to compare a fluoride-containing mouthrinse product with a placebo rinse for the treatment of DH. A secondary aim was to compare effects on plaque index (PI) and gingivitis index (GI).

Material and Methods: The study was a double-blind, randomised, two-treatment parallel design involving 91 subjects with DH. At screening, an air evaporative stimulus (AES) was used for selection. Approximately 4 weeks later, at the baseline visit, DH was recorded, using a response-based visual analogue scale (VAS) from upper and lower incisors, canines, premolars and first molars in response to AES and from two to six teeth in response to a cold water stimulus (CWS). PI and GI were also recorded. Subjects were then allocated the test or placebo rinse. On days 28 and 56, VAS scores were again recorded for AES and CWS, with PI and GI recorded at day 56.

Results: Both groups improved symptoms to day 28 and again to day 56. The majority of the data favoured the test rinse as more effective but there was no clear evidence for a statistically significant difference between test and placebo. PI at lingual sites approached significance for the test rinse.

Conclusions: The placebo response has again been shown to play a significant role in DH clinical trials and narrows the range over which to detect treatment differences. Study designs to minimise or prevent the placebo response in DH seem worthy of consideration.

Key words: amine fluoride; dentine hypersensitivity; fluoride; mouthrinse study; potassium

Accepted for publication 8 January 2004

Dentine hypersensitivity (DH) has been the subject of a number of relatively recent reviews (Dababneh et al. 1999, Addy 2000, 2002, Canadian Advisory Board on Dentine Hypersensitivity 2003). These reviews all allude to the problems of management and, more specifically, the treatment of the condition. These difficulties essentially arise for a number of reasons: the aetiology of the condition is ill understood; the number of apparently efficacious treatment agents is large and peculiarly varied; the actual effects of treatment formulations on teeth are, for the most, unknown. Management strategies, which take into account possible aetiological factors, have been propounded (Addy 2002, Canadian Advisory Board on Dentine Hypersensitivity 2003) but whilst eminently sensible, these strategies have not been submitted to classical research protocols such as randomised clinical trials. Treatments for DH, on the other hand, have been subjected to such randomised clinical trials and over many decades (for reviews see Jackson 2000, Pashley 2000). More recently, despite the publication of guidelines for the design of

trials of treatments in DH (Holland et al. 1997), there remain problems, which could or do compound study outcomes, particularly for home-use studies. Perhaps, of greatest significance are the phenomena of regression to the mode, which is the tendency for painful conditions to naturally improve, and the placebo response of the subject knowingly participating in a sensitivity study and using a possibly efficacious product (for reviews see Curro et al. 2000, Addy 2002). The latter placebo response is difficult to quantify, primarily because the majority of desensitising formulations are toothpastes and there is not a truly placebo toothpaste.

The studies could be compromised by the population chosen for investigation. The internationally accepted definition of DH includes the exclusion of other forms of dental defect or disease, which may have similar symptoms. One obvious condition is the sensitivity associated with periodontal disease and periodontal treatments where the prevalence of sensitivity is disproportionately high (Chabanski et al. 1996, Chabanski & Gillam 1997). Acknowledging that this may be a distinct entity and different from DH, particularly since micro-organisms penetrate dentinal tubules in periodontal disease (Adriaens et al. 1988), the most recent European Federation of Periodontology Workshop recommended the term ''root sensitivity'' (Sanz & Addy 2002, von Troil et al. 2002). As stated, numerous ''actives'' have been used to treat DH, mostly incorporated in toothpastes: more recently perhaps, the most common are potassium salts (for review see Jackson 2000).

The present study was commissioned to evaluate a mouthrinse, based on fluoride salts (potassium fluoride, amine fluoride), as well as a film-building polymer, used alongside tooth brushing with toothpaste for the treatment of DH. Using a mouthrinse offered the opportunity at least to take into account some of the potentially confounding influences in studies on DH alluded to above, in particular, the placebo response.

Material and Methods

The study was a single-centre, placebo-controlled, randomised, double-blind, parallel-group design, planned to involve at least 45 subjects each to the two mouthrinse groups. The protocol was reviewed and accepted by the United Bristol Healthcare Trust Ethics Committee and a Clinical Trial Exemption Certificate obtained from the UK Medical Controls Agency, London. The study was designed, conducted, monitored, analysed and reported according to the Guidelines for Good Clinical Practice. Subjects were given verbal and written information on the study and signed consent forms to participate. Subjects were screened by a single study Clinical Investigator (R. J. Y.) who completed the clinical record forms (CRFs) and performed all clinical examinations, indices and sensitivity tests. Subjects of both genders and 18–70 years were recruited if they were medically fit with no medical or pharmacotherapy histories, which might influence the conduct of the study. Other than symptoms of DH, subjects had to be dentally fit with no dental conditions or disease, which might explain tooth sensitivity and including active periodontitis. DH was diagnosed by firstly asking subjects to rate their perception of sensitivity to hot and cold food and drink, sweet and sour food, tooth brushing, etc. Sensitive teeth were identified by the response to an evaporative stimulus, which was a 1 s blast of air from a dental unit syringe at 40–65 psi and $19 \pm 5^{\circ}$C directed perpendicular and at a distance of 1–3 mm to the exposed buccal cervical areas of exposed dentine. Adjacent teeth were protected by the clinician's fingers. Subjects were asked to grade the painful response using a 10 cm visual analogue scale (VAS) where 0 cm = no pain and 10 cm = extreme pain. Subjects were accepted into the study if they had two or more teeth with a VAS score of $\geqslant 5$ cm.

Once recruited, the subjects returned within 4 weeks to the study centre, where baseline measures were carried out as follows:

1. Evaporative stimulus as above applied to all scorable incisors, canines, premolars and first molars (maximum 24 teeth) and VAS scores recorded. Non-scorable teeth were those that had restorations at or encroaching upon the buccal cervical area of exposed dentine and included teeth with full coverage restorations. A minimum of two teeth and a maximum of six teeth with $\geqslant 5$ cm VAS score were designated as investigational teeth and subjected to:
2. Cold water stimulus (cws) applied as a 5 ptl of water taken from ice and applied immediately to the buccal cervical exposed dentine using an Eppendorf micropipette.
3. Gingival index (GI) (Loe & Silness 1963) from mesio- and mid-buccal and lingual sites of the Ramfjord (Ramfjord 1967) teeth.
4. Plaque index (PI) (Silness & Loe 1964) from the buccal and lingual surfaces of the Ramfjord teeth. (NB: GI and PI were scored after drawing a Williams pattern periodontal probe within the gingival crevice from the distal to mesial aspect of the GI and PI designated teeth).
5. A soft-tissue examination was visually performed and any pre-study anomaly noted.

After collection of the baseline data, the subjects were allocated to either the test or placebo control mouth rinses. The test mouthrinse was a marketed product (elmex SENSITIVE PLUS dental rinse, GABA International, Switzerland) for the treatment of DH and containing the actives, potassium fluoride, amine fluoride and a film-building polymer (Polyvinyl pyrrolidone/dimethylaminoethylmathacrylate polycarbamyl polyglycol ester). The placebo control mouthrinse (GABA International, Switzerland) was an aqueous alcohol flavoured solution of the same appearance as the test mouthrinse and containing no ingredients, which might be effective in the treatment of DH. The mouthrinses were in identical bottles with identical labelling except for individual subjects study numbers. A sealed code breaker was kept in the study file in case of adverse events thought to arise from the formulations. The mouthrinses were to be used as 10 ml volumes twice a day for a minimum of 30 s. Subjects were also given a standard fluoride toothpaste (Macleans Aquafresh, GlaxoSmithKline, Weybridge, UK) and toothbrush (Elmex Super Soft, GABA International) with instructions to brush for at least 1 min morning and evening using 2 cm (1 in) of toothpaste on the brush head. Tooth brushing with toothpaste and water rinsing was to be immediately before mouth rinsing with the study rinse. A diary to record study product use was provided to all subjects. On day 28 after baseline, subjects returned to

the study clinic where Evaporative and Cold Water VAS scores were recorded together with an oral soft-tissue examination and the use of non-leading questions on general and oral health changes or adverse events. At the visit all unused study materials were returned and new supplies of mouthrinse, toothpaste and toothbrush were provided. At day 56, the same criteria were followed together with the scoring of GI and PI. During the study period, the following were not permitted: the use of other oral hygiene products, dental treatment to investigational teeth, antiseptic mouth rinses, lozenges or sprays and any other drugs, notably analgesics, which might influence pain perception within 24 h of assessment days.

Statistical methods

The sample size of 45 per group was chosen to provide an 80% chance of showing a standard deviation of 0.59 difference in VAS scores significant at the 5% level ($p<0.05$). In the event, complete data sets for 91 subjects (46 test and 45 placebo) were available at baseline and days 28 and 56. Mean mouth scores were calculated for each subject in each treatment group for evaporative and cold water stimuli VAS scores, GI and PI at the appropriate time points. Analysis of co-variance (ANCOVA) was used to determine the significance of differences between the two treatment groups for each measurement parameter using the baseline data as co-variate. A preliminary assessment of the data distribution showed that the VAS scores had some positive skewness and confirmatory non-parametric tests (Mann-Whitney) were performed. Two-way analysis of variance (ANOVA) was performed on evaporative stimulus VAS scores at baseline modelled on subject and tooth position.

Results

A total of 91 subjects participated and all completed the study satisfactorily. There were 46 subjects in the test group (10 male, 36 female, average age: 35.2 ± 11.2 years) and 45 subjects in the placebo group (six males, 39 females, average age: 36.3 ± 11.0 years). The means (standard deviation) of the VAS scores for the air evaporative stimulus (AES) for the two rinse groups for all teeth at Screening, Baseline, Day 28 and Day 56 are shown in Table 1. In mean terms there was an improvement in symptoms from baseline of approximately 6 mm by Day 28 and a further 6 mm by Day 56 in both groups. ANCOVA revealed no significant differences at either time point between the two treatment groups ($p>0.05$). The means (standard deviation) of the VAS scores for the AES for the two groups for teeth chosen for the CWS acceptance VAS score (minimum 50 mm) at Screening, Baseline, Day 28 and Day 56 are shown in Table 1. In mean terms, both treatment groups improved to Day 28 and then further to Day 56. The improvements were in mean terms greater with the test than the placebo rinse but these differences did not reach statistical significance ($p>0.05$). The means (standard deviation) of the VAS scores for the AES for the two rinse groups for all teeth scoring >50 mm at Screening, Baseline, Day 28 and Day 56 are shown in Table 1. Again, numerically the improvements from baseline favoured the test rinse but differences did not reach statistical significance ($p>0.05$). The means (standard deviation) for the VAS scores for the CWS for the two groups at Baseline, Day 28 and Day 56 are shown in Table 1. There was quite a large baseline difference between the groups with less mean pain in the test group and changes from Baseline to Day 28 and Day 56 favoured the placebo rinse. ANCOVA, however, showed no statistically significant differences between the treatment groups. The supplemental analysis to determine the significance of differences, at Baseline, by subject and the 12 tooth types/sites (upper/lower; incisors/canines/premolars/first molar), using two-way ANOVA revealed highly significant differences for both (Table 2).

The mean GI based on all sites at Baseline and Day 56 are shown in Table 3. Small mean improvements are apparent in both groups but differences between treatments did not reach significance. The mean PI at baseline and Day 56 for both treatment groups for all surfaces and buccal and lingual separately also are given in Table 3. Small improvements in baseline plaque scores were seen in both groups. Greater reductions were seen for all scores in the active group but differences were not significant except for lingual plaque where significance was approached ($p=0.07$).

Table 1. The mean (standard deviation) of VAS scores for air evaporative and cold water stimuli at Screening, Baseline, Day 28 and Day 56

	Screening	Baseline	Day 28	Day 56
Air evaporative all teeth				
test	30.57 (11.30)	33.01 (11.11)	27.17 (13.69)	21.56 (13.88)
control	33.81 (14.01)	35.61 (15.16)	30.03 (15.95)	23.83 (13.69)
Air evaporative selected teeth for water				
test	54.84 (13.89)	66.67 (9.84)	46.02 (18.79)	37.10 (20.16)
control	56.62 (14.73)	68.96 (9.22)	51.38 (15.33)	43.33 (16.76)
Air evaporative VAS >50 mm teeth				
test	53.79 (13.92)	66.88 (9.65)	45.77 (18.55)	36.49 (19.66)
control	55.61 (14.97)	68.61 (8.64)	51.52 (16.65)	42.58 (15.66)
Cold water				
test		42.48 (31.47)	37.22 (28.03)	35.39 (28.60)
control		52.03 (28.40)	40.59 (28.38)	40.89 (29.05)

Table 2. The mean (standard deviation) VAS score for air evaporative stimulus at baseline by tooth type

Upper						Lower					
1	2	3	4	5	6	1	2	3	4	5	6
29.17 (25.12)	31.51 (23.85)	35.34 (26.72)	44.45 (26.26)	37.30 (26.78)	39.06 (28.45)	32.63 (25.92)	32.40 (24.15)	28.66 (21.64)	35.90 (22.85)	36.08 (25.83)	30.33 (27.66)

VAS, visual analogue scale.

Table 3. The mean (standard deviation) gingivitis index (GI) and plaque index (PI) scores at Baseline, and Day 56, for all teeth and buccal and lingual surfaces

	Baseline			Day 56		
	all	buccal	lingual	all	buccal	lingual
GI test	0.73 (0.27)	0.45 (0.30)	1.01 (0.32)	0.65 (0.28)	0.43 (0.26)	0.87 (0.35)
control	0.80 (0.30)	0.49 (0.33)	1.12 (0.36)	0.74 (0.27)	0.47 (0.25)	1.02 (0.35)
PI test	0.87 (0.52)	0.61 (0.53)	1.13 (0.59)	0.78 (0.43)	0.54 (0.44)	1.01 (0.47)
control	0.92 (0.43)	0.62 (0.47)	1.22 (0.48)	0.90 (0.34)	0.63 (0.40)	1.16 (0.41)

Discussion

As described in the title, this study had a randomised, double-blind, placebo-controlled design using a methodology that considered the recommendations of the Guidelines for the Design and Conduct of Clinical Trials on DH (Holland et al. 1997). The study was 8 weeks in duration, parallel in design and used subject inclusion/exclusion criteria cited in the guidelines publication. In particular, diagnosis was based on the internationally accepted definition of DH (Holland et al. 1997), which was proposed earlier (Dowell & Addy 1983) and with one minor change later agreed by the Canadian Advisory Board on Dentine Hypersensitivity (2003). A power calculation was used to recruit sufficient subjects to show whether an a priori decided difference in pain scores, if present, was significant. Two different stimuli were employed, air evaporative and cold water both of which are relevant to the everyday initiation of sensitivity in these subjects. The recommendation is to apply the lesser intense stimulus first (Holland et al. 1997). Since there was likely to be little difference between the two stimuli, and because the evaporative stimulus was used at the start of the study to select particular teeth for the CWS, the air evaporative was used first. The assessment methods were response based using a VAS score completed by the subject rather than a stimulus-based binary response using stimuli of increasing intensity (for review see Gillam et al. 2000). The guidelines are less prescriptive for which or how many teeth are selected. So all teeth up to the first molar were tested by the evaporative stimulus and at least two and up to six by cold water. A true run-in/wash-out period was not used between Screening and Baseline (approximately 4 weeks) because subjects still had to meet the screening criteria for inclusion at the baseline visit. As discussed, the study was able to use a placebo control, which as recommended (Holland et al. 1997), the present authors define as a formulation containing no ingredients expected to have, or proven to be of therapeutic value in DH.

Perhaps, as expected, there was an improvement over time in both groups in VAS scores up to Day 28 and then further improvement to Day 56. Indeed, the further incremental improvement between Day 28 and Day 56 for some parameters was, in magnitude, similar to that recorded from baseline to Day 28, thereby almost doubling the improvement. Clearly, it would have been interesting to prolong the study to see if further incremental improvement occurred. Most, but not all, of the data for pain, were in favour of the test product but there was no clear evidence for a significant difference between the products. The data for a not inconsiderable improvement in the placebo group are consistent with other studies by this group where a true placebo agent had been used as control (Yates et al. 1997a, b). A related finding was seen also in a study with a wash-in period during which subjects used a proprietary fluoride toothpaste product, and in which one-third of subjects unknowingly continued with the same paste in the study proper (West et al. 1997). No improvement in sensitivity was seen in the total patient group during the wash-in period, but a significant and similar improvement to the test products was achieved with the wash-in paste in the subjects allocated to it during the study proper. These data again clearly indicate that a placebo response occurs in DH studies (for review see Curro et al. 2000). On the one hand, assuming that the test product, which has a product license for use in DH, is efficacious. It must be that the magnitude of the placebo response overshadowed any therapeutic action. On the other hand, as with most home-use desensitising products, the actual effects of the mouthrinse ingredients, on or in the tooth, are not known. It could be the result can be explained by the placebo response. This might be questioned, however, since most data were in favour of the test product. Whether regression to the mode influenced the outcome of the study cannot be assessed in this design and would require lengthy follow-up of subjects without interventions.

The results for plaque and gingivitis showed improvements in both groups favouring the test product particularly for plaque at lingual sites. These improvements in the placebo group can be explained by the Hawthorne phenomenon, whereby oral hygiene improves in subjects knowingly participating in an oral hygiene product study (for review wee Addy & Moran 1997). The sizes of the improvements were, however, small and less than usually noted. Several reasons may explain this, including the benefits of the test product to lingual sites. Firstly, the oral hygiene of DH subjects is known to be very good particularly at buccal surfaces (Addy et al. 1987). The scope for showing an improvement either by a chemical product and/or Hawthorne effect, therefore, is very small. Secondly, lingual sites in most individuals receive little attention during the brushing cycle (Rugg-Gunn & MacGregor 1978, MacGregor & Rugg-Gunn 1979) and, therefore, the Hawthorne effect may not occur here. As a result, therefore, chemical plaque inhibition is more likely to be revealed at sites receiving limited mechanical cleaning.

In conclusion and consistent with other studies, significant placebo responses can be expected in DH treatment studies and these may overshadow the treatment effects of known actives such as potassium and fluoride salts. This should not be used to undermine the value of desensitising products since it must be the perception of using an effective agent, even when not, that triggers the placebo response. It would be of value to develop protocols that avoid the perception that the formulation in use is a desensitising product: a task that certainly is not impossible.

Acknowledgments

This study was supported by GABA International AG, Muenchenstein, Switzerland.

References

Addy, M. (2000) Dentine hypersensitivity: definition, prevalence, distribution and aetiology. In: *Tooth Wear and Sensitivity*, eds. Addy, M., Embery, G., Edgar, W. M. & Orchardson, R., pp., 239–224. London: Martin Dunitz.

Addy, M. (2002) Dentine hypersensitivity: new perspectives on an old problem. *International Dental Journal* **52** Supplement 5/02, 367–375.

Addy, M. & Moran, J. M. (1997) Evaluation of oral hygiene products: science is true; don't be misled by the facts. *Periodontology 2000* **15**, 40–51.

Addy, M., Mostafa, P. & Newcombe, R. G. (1987) Dentine hypersensitivity: the distribution of recession, sensitivity and plaque. *Journal of Dentistry* **15**, 242–248.

Adriaens, P. A., DeBoever, J. A. & Loesche, W. J. (1988) Bacterial invasion in root, cementum and radicular dentine of periodontally diseased teeth in humans -a reservoir of periodontopathic bacteria. *Journal of Periodontology* **59**, 222–230.

Canadian Advisory Board on Dentine Hypersensitivity (2003) Consensus-based recommendations for the diagnosis and management of dentine hypersensitivity. *Journal of the Canadian Dental Association* **69**, 221–228.

Chabanski, M. B. & Gillam, D. G. (1997) Aetiology, prevalence and features of cervical dentine sensitivity. *Journal of Oral Rehabilitation* **24**, 15–19.

Chabanski, M. B., Gillam, D. G., Bulman, J. S. & Newman, H. N. (1996) Prevalence of cervical dentine sensitivity in a population of patients referred to a specialist periodontology department. *Journal of Clinical Periodontology* **23**, 989–992.

Curro, F. A., Friedman, M. & Leight, R. S. (2000) Design and conduct of clinical trials on dentine hypersensitivity. In: *Tooth Wear and Sensitivity*, eds. Addy, M., Embery, G., Edgar, W. M. & Orchardson, R., pp. 299–314. London: Martin Dunitz.

Dababneh, R. H., Khouri, A. T. & Addy, M. (1999) Dentine hypersensitivity-an enigma? A review of terminology, epidemiology, mechanisms, aetiology and management. *British Dental Journal* **187**, 606–611.

Dowell, P. & Addy, M. (1983) Dentine hypersensitivity - A review, aetiology, symptoms and theories of pain production. *Journal of Clinical Periodontology* **10**, 341–350.

Gillam, D. G., Orchardson, R., Narhi, M. V. O. & Kontturi-Narhi, V. (2000) Present and future methods for the evaluation of pain associated with dentine hypersensitivity. In: *Tooth wear and sensitivity*, eds. Addy, M., Embery, G., Edgar, W. M. & Orchardson, R., pp. 283–298. London: Martin Dunitz.

Holland, G. R., Narhi, M. N., Addy, M., Gangarosa, L. & Orchardson, R. (1997) Guidelines for the design and conduct of clinical trials on dentine hypersensitivity. *Journal of Clinical Periodontology* **24**, 808–813.

Jackson, R. J. (2000) Potential treatment modalities for dentine hypersensitivity: home use products. In: *Tooth wear and sensitivity*, eds. Addy, M., Embery, G., Edgar, W. M. & Orchardson, R., pp. 327–338. London: Martin Dunitz.

Loe, H. & Silness, J. (1963) Periodontal disease in pregnancy. 1. Prevalence and severity. *Acta Odontologica Scandinavica* **21**, 532–551.

MacGregor, I. D. M. & Rugg-Gunn, A. J. (1979) A survey of toothbrushing sequence in children and young adults. *Journal of Periodontal Research* **14**, 225–230.

Pashley, D. (2000) Potential treatment modalities for dentine hypersensitivity: in-office products. In: *Tooth Wear and Sensitivity*, eds. Addy, M., Embery, G., Edgar, W. M. & Orchardson, R., pp. 351–366. London: Martin Dunitz.

Ramfjord, S. (1967) The Periodontal Index. *Journal of Periodontology* **38**, 602–610.

Rugg-Gunn, A. J. & MacGregor, I. D. M. (1978) A survey of toothbrushing behaviour in children and young adults. *Journal of Periodontal Research* **13**, 382–388.

Sanz, M. & Addy, M. (2002) Group D Summary. *Journal of Clinical Periodontology* **29** (Supplement 3), 195–196.

Silness, J. & Loe, H. (1964) Periodontal disease in pregnancy II. Correlation between oral hygiene and periodontal condition. *Acta Odontologica Scandinavica* **22**, 121–135.

Von Troil, B., Needleman, I. & Sanz, M. (2002) A systematic review of the prevalence of root sensitivity following periodontal therapy. *Journal of Clinical Periodontology* **29** (Supplement 3), 173–177.

West, N. X., Addy, M., Jackson, R. J. & Ridge, B. D. (1997) Dentine hypersensitivity: review and discussion of controls and the placebo response. A comparison of the effect of strontium acetate and potassium nitrate toothpastes on dentine hypersensitivity. *Journal of Clinical Periodontology* **24**, 209–215.

Yates, R., Owens, J., Jackson, R., Newcombe, R. G. & Addy, M. (1997a) A split mouth placebo controlled study to determine the effect of amorphous calcium phosphate in the treatment of dentine hypersensitivity. *Journal of Clinical Periodontology* **25**, 687–692.

Yates, R., West, N., Addy, M. & Marlow, I. (1997b) The effects of a potassium citrate, cetylpyridinium chloride, sodium fluoride mouthrinse on dentine hypersensitivity, plaque and gingivitis. A placebo controlled study. *Journal of Clinical Periodontology* **25**, 813–820.

Address:
Martin Addy
Division of Restorative Dentistry
Dental School
Lower Maudlin Street
Bristol BS1 2LY
UK
Fax: 0044-1179284100
E-mail: Martin.Addy@bristol.ac.uk