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Local delivery of chlorhexidine gluconate (PerioChip™) in periodontal maintenance patients

P. A. Heasman, L. Heasman, F. Stacey and G. I. McCracken
Restorative Dentistry, Dental School, University of Newcastle upon Tyne, UK

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Abstract
Aim: The aim of this randomised, split-mouth, single-blind study was to determine the efficacy of controlled-release delivery of chlorhexidine gluconate 2.5 mg (PerioChip™) in patients with residual bleeding pockets (>5 mm) at least 3 months following oral hygiene and root debridement phase therapy.
Material and Methods: 26 patients (non-smokers) were screened and potential study sites identified. Clinical parameters recorded at baseline and all subsequent visits were plaque index (PI), pocket probing depth (PPD), bleeding index (BI) and clinical attachment level (CAL). All study sites were debrided using ultrasonic instrumentation. PerioChips (PC) were placed in the selected sites of two quadrants (left or right) whilst identified sites in the remaining quadrants were left without adjunctive antimicrobial treatment. Clinical measurements were made at follow-up visits after 1, 3 and 6 months. Mean changes from baseline in PPD, BI and CAL were calculated with the patient as the experimental unit and comparability between the treatments was determined using *t*-tests.
Results: At baseline there were no significant differences between PC and control sites for mean PI, PD, BI or CAL. The mean (SE) reductions in PPD for PC and control treatments were: 0.47 (0.1), 0.46 (0.1); 0.76 (0.1), 0.55 (0.1); 0.78 (0.1), 0.45 (0.1) for months 1, 3 and 6 respectively. Only at month 6 did the difference between treatments approach statistical significance ($p=0.06$). Mean (SE) reductions in CAL over the same periods were: 0.17 (0.1), 0.04 (0.08); 0.38 (0.1), 0.21 (0.1); 0.43 (0.1), 0.15 (0.09) $p=0.048$. Mean (SE) reduction in BI between PC and control treatments only reached statistical significance at 6 months: 1.08 (0.1), 0.59 (0.1) $p=0.05$.
Conclusion: These data suggest that PerioChip™ is beneficial for patients on maintenance therapy although the benefit is not apparent until 6 months after placement.

Key words: chlorhexidine gluconate; controlled delivery; periodontal maintenance

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The 1990s has seen the emergence of a range of controlled-delivery (slow-release) devices for antimicrobials to be introduced directly to periodontal pockets. This direct route of administration establishes and maintains an effective concentration of the active agent at the site of infection without the risk of incurring many of the side effects that can accompany systemic administration.

One such product, PerioChip™, is a biodegradable, local delivery system that contains 2.5 mg of chlorhexidine gluconate in a cross-linked, hydrolysed gelatin vehicle. When in situ, there is an initial peak concentration of 2000 μg/ml chlorhexidine in crevicular fluid (Soskolne et al. 1998). Concentrations of the drug remains above the minimum inhibitory concentration for more than 99% of periodontal pocket flora for up to 9 days (Stanley et al. 1989).

Clinical efficacy of PerioChip has been proven unequivocally in multicentre phase III trials in Europe (Soskolne et al. 1997) and the United States (Jeffcoat et al. 1998). In these studies, the product was used as an adjunct to, and immediately following the initial treatment phase (scaling and root planing) in patients with moderately advanced chronic periodontitis. As yet, there have been no studies to determine the potential value of PerioChip for patients on a periodontal maintenance programme. The aim of this trial, therefore, was to evaluate the efficacy of PerioChip in a cohort of recall patients

who had previously been treated non-surgically for moderate to advanced periodontal disease.

Material and Methods

This was a randomised, split-mouth design for comparison of 2 treatments; scaling and root planing alone (SRP) versus SRP plus PerioChip. The trial was undertaken on the Department of Periodontology of Newcastle Dental School and Hospital (UK), received ethical (IRB) approval from the Joint Ethics Committee of Newcastle and North Tyneside and fulfilled directives of Good Clinical Practice (EC Directive, 1991).

Study cohort

26 adults with moderate to severe chronic periodontitis were randomly selected from the pool of recall (maintenance) patients on the Department. Inclusion criteria were: signed informed consent; a minimum of 10 natural uncrowned teeth; a minimum of one pocket per quadrant with a pocket probing depth (PPD) of at least 5 mm with persistent bleeding on probing; non-surgical phase of therapy completed at least 3 months prior to baseline. Exclusion criteria were: early onset periodontitis; any teeth with furcation involvement; systemic antimicrobial therapy within 2 months prior to entry; history of allergy to chlorhexidine; smoking; history of periodontal surgery; periodontal treatment undertaken less than 3 months prior to the baseline visit.

Power and sample size
Calculations were based on published data from a previous study of PerioChip efficacy (Soskolne et al. 1997) and a proposed comparison of 2 means using a 2-sample *t*-test. We set the clinically relevant difference for reduction in the primary outcome variable (PPD) between treatments as 0.5 mm. Thus standardised difference=0.8, $(1\text{-}\beta)=0.8$ and $\alpha=0.05$ gave a sample size of 26 patients to receive each treatment.

Design and treatments

Suitability for recruitment was assessed at a screening visit. Potential target sites were identified and informed consent was given. At baseline (2–4 weeks later) clinical measurements were recorded, a supragingival ultrasonic scaling and a prophylaxis of all teeth were performed and all target sites were root planed under local anaesthesia for a maximum of 5 min for each tooth. Target sites were randomised at split mouth level (left side/right side) to one of the 2 treatment groups; SRP alone, SRP + PerioChip. Following debridement, target sites were irrigated gently with cold saline and then left for 10 min to achieve haemostasis prior to placement of PerioChips.

Patients were re-examined at 1, 3 and 6 months to assess safety and efficacy but no further PerioChips were placed irrespective of pocket depth. A supragingival scaling and prophylaxis were performed at exit from the study at the month 6 visit. For each patient, the same hygienist carried out clinical measurements and instrumentation throughout the study and one clinician (PAH) placed all PerioChips, always in the absence of that hygienist.

Clinical measurements

The following clinical measurements were recorded for the target sites only.

Plaque examination
Plaque was recorded using the Silness & Löe plaque index (PI) (Silness & Löe 1964).

Pocket probing depth (PPD)
Probing depths were to the nearest 0.5 mm using a manual University of North Carolina periodontal probe. Each pocket was probed 2× to provide replicate measurements. A third measurement was made if there was a ⩾0.5 mm difference between the first 2 recordings. The median of the 2 (or 3) recordings was used in the data analysis.

Bleeding index (BI)
Bleeding from each site was assessed 25 seconds after probing pocket depth using the Bleeding Index of Muhlemann (1977).

Clinical attachment level (CAL)
Measurements were recorded using the Florida Probe (Florida Probe Corporation, Gainesville, FL) clinical attachment disc probe set at a resolution of 0.1 mm and a probing force of 20 g. Again, a first pass of all sites was performed and then a second reading obtained (double pass technique). The median of the 2 scores was recorded. If these varied by ⩾0.5 mm a third reading was taken and the median of the 3 scores used for the analysis (Namgung & Yang 1994, Yang et al. 1998).

Calibration of examiners

2 experienced research hygienists (LH, FS) were calibrated for SRP procedures and recording clinical data to ensure that all clinical procedures were standardised according to the study protocol and to minimise both intra- and inter-examiner variability across the time points. The 2 clinical examiners were calibrated initially for PPD and CAL according to the method of Jeffcoat et al. (1998). Briefly, as part of the calibration exercise, each of the 2 examiners measured PPD and CAL 2× at 10 sites (PPD⩾5 mm) in each of 5 patients. For both examiners and all 25 sites, the mean absolute difference between the 1st and 2nd measurements was ⩽0.5 mm for both parameters. With these criteria in place, the observed inter-examiner agreement (±0.5 mm) was 85% for PPD and 88% for CAL. With respect to PI and BI, both examiners scored independently 200 sites in 5 subjects who were not in the clinical trial. Intra- and inter-examiner weighted kappa scores for both indices were ⩾0.75.

Data and statistical analysis

Data were analysed on an intention-to-treat basis with the subject as the unit of statistical analysis. The protocol-defined primary outcome variable was the reduction of PPD from baseline. At the 1, 3 and 6 month visits, the change from baseline for PPD, BI and CAL for each site was calculated. A mean value was calculated for each treatment (split-mouth) and an overall mean of the differences from baseline was calculated for each treatment. Summary statistics were determined and 2 sample *t*-tests undertaken to identify statistically significant differences between the treatments (at $p=0.05$). In addition, the proportion of sites within a patient showing an improvement from baseline of PPD of >1 and >2 mm were recorded. The distribution of the scores at the 6 month visit was compared across the treatments using nonparametric, Cochran-Mantel-Haenszel row means test. Mean PI scores were calculated for treatment and control sites on a subject-wise basis and group means were

Table 1. Baseline clinical data. Mean (SE) pocket probing depths (mm) (PPD), clinical attachment level (mm) (CAL), bleeding index (BI) and plaque index (PI) for Periochip +SRP and SRP alone groups

	PC+SRP	SRP
PPD	6.64 (0.12)	6.47 (0.11)
CAL	14.23 (0.19)	14.14 (0.16)
BI	2.56 (0.10)	2.51 (0.10)
PI	1.03 (0.15)	1.22 (0.24)

Table 2. Means (SE) of the differences (△) from baseline for pocket probing depth (PPD), clinical attachment (CAL) and bleeding index (BI) for PerioChip+scaling/root planing (PC+S/RP) and scaling/root planing only (S/RP) groups

	Month 1		Month 3		Month 6	
	PC+S/RP	S/RP	PC+S/RP	S/RP	PC+S/RP	S/RP
△ PPD	0.47 (0.10)	0.46 (0.11)	0.76 (0.11)	0.55 (0.10)	0.78 (0.12)	0.45 (0.13)
					$p=0.05$	
△ CAL	0.17 (0.12)	0.04 (0.08)	0.38 (0.11)	0.21 (0.10)	0.43 (0.15)	0.15 (0.09)
					$*p=0.048$	
△ BI	0.88 (0.10)	0.61 (0.20)	1.01 (0.2)	0.70 (0.10)	1.08 (0.10)	0.59 (0.10)
					$*p=0.05$	

determined at baseline, 1, 3 and 6 months. Differences between the means were tested using a 2 sample *t*-test.

Results

24 of the recruited 26 subjects completed the study. 2 subjects withdrew following the 3 month visit for non-treatment related reasons. The mean (sd) of the recruited cohort was 42.6 (12.6) years; range 34–59 years. The ratio of males:females was 8:18 and all subjects were white caucasians. A total of 135 PerioChips were placed (87 at molar sites) and 165 control sites (102 molar sites) were identified.

Only 1 subject reported any oral symptoms at any time during the trial. Clinical examination revealed non-treatment related aphthae of the buccal mucosa at the month-3-visit. These had resolved completely after 1 week.

Baseline data for PerioChip + S/RP and S/RP alone sites, analysed on a subject-wise basis, are given in Table 1. These data confirm that the target sites in the 'test' and 'control' quadrants were very similar with respect to PPD, CAL, BI and PI at baseline.

At successive visits (months 1, 3 and 6), the respective mean (se) PI scores (test sites/control sites) were: 0.56 (0.12)/0.64 (0.13); 0.62 (0.12)/0.67 (0.13); 0.73 (0.15)/0.77 (0.16).

The means (se) of the differences from baseline for PPD, CAL and BI at months 1, 3 and 6 are given in Table 2. Only the improvement in CAL and the reduction in BI at 6 months were significant at $p=0.05$. The mean %s of sites/subject for each treatment showing no change or reductions of ≥ 1 mm, ≥ 2 mm at month 6 only are given in Fig. 1. At this time point, the mean proportion of sites with a reduction of PPD ≥ 2 mm was significantly greater for the PerioChips + S/RP treatment than with S/RP alone.

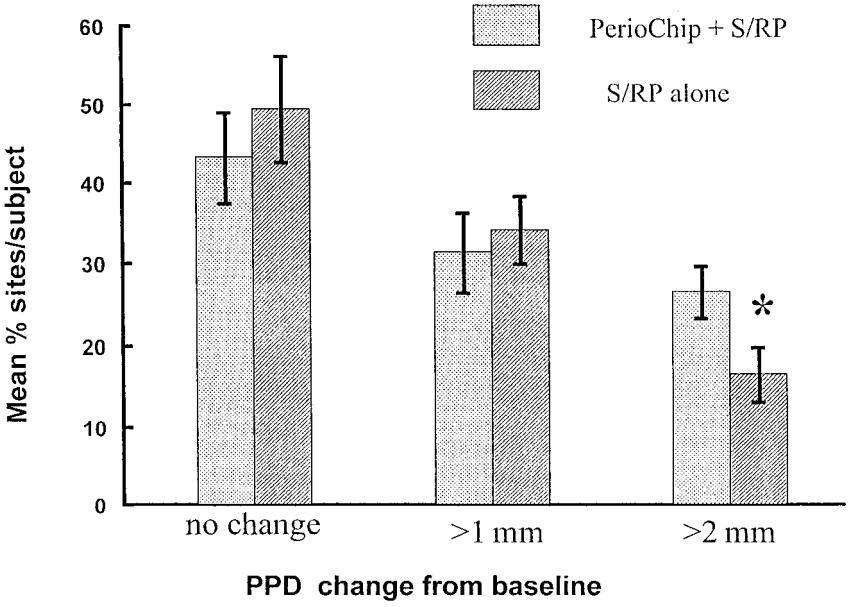

Fig. 1. Mean % (SE) sites per subject with reduction of pocket probing depth of 0, >1 (less than 2) and >2 mm at 6 months (ns – not significant; $*p<0.02$).

Discussion

Previous multi-centre studies have shown that PerioChip is an efficacious, adjunctive treatment to S/RP in the management of patients with chronic periodontitis. The adjunctive treatments provided significantly greater reductions of PPD at both 6 (Soskolne et al. 1997, Jeffcoat et al. 1998) and 9 months (Jeffcoat et al. 1998) post-treatment. The magnitude of this superiority was 0.2–0.5 mm. The patients recruited to our present study were on a recall programme and had a history of moderate – advanced chronic periodontitis, the treatment phase having been completed at least 3 months prior to baseline. Furthermore, none of the selected target sites had demonstrated any reduction in PPD following the non-surgical treatment. Many other sites in these patients had shown marked improvement in PPD and BI prior to recruitment (CAL not measured). Consequently, we do not consider our patients to have refractory periodontitis but rather a number of non-responding sites as a result of inadequate debridement during the treatment phase. Support for this hypothesis is provided by the remarkable consistency between our month 1 and month 3 PPD data and those of Soskolne and co-workers (1997) at similar times. This indicates that the rate of resolution of inflammation at the target sites (for both PC+S/RP and S/RP treatments) is virtually identical in the 2 studies, thus confirming that our non-responding sites were almost certainly managed inadequately during the initial phase of mechanical debridement. Nevertheless, our data indicate that PerioChip is efficacious as an adjunctive treatment to additional root planing at previously non-responding sites.

In the present study, the potential

Table 3. Pocket probing depth data at 6 months post-treatment in clinical trials of locally delivered antimicrobials placed at sites of ⩾5 mm

Study	Cohort	Treatment	Mean reduction in PPD from baseline (mm)
Heasman et al. (2000) (present study)	maintenance	PC&SRP	0.78
		SRP alone	**0.45**
Soskolne et al. (1997)	moderate periodontitis	PC&SRP	1.16
		SRP alone	**0.70**
Jeffcoat et al. (1998)	chronic adult periodontitis	PC&SRP	0.89
		SRP alone	**0.72**
Kinane & Radvar (1999)	chronic adult periodontitis	minocycline and SRP	1.10
		tetracycline and SRP	1.38
		metronidazole and SRP	0.93
		SRP alone	**0.71**
Ainamo et al. (1992)	chronic adult periodontitis	metronidazole alone	1.30
		SRP alone	**1.50**
Stelzel & Florés-de-Jacoby (1997)	maintenance	metronidazole alone	1.30
		SRP alone	**1.50**
Rudhart et al. (1998)	maintenance	metronidazole alone	1.60
		SRP alone	**1.60**

PC: PerioChip.
SRP: Scaling and root planing.

benefit of adjunctive use of PerioChip becomes apparent only after 6 months with respect to the 3 clinical outcomes; PPD, CAL and BI. The differences in clinical outcomes between treatments at months 1 and 3 were not statistically significant. Closer examination of the data in Table 2 however shows that for PC+S/RP sites, PPD, CAL and BI remain virtually unchanged between 3 and 6 months whereas the S/RP only sites appear to be showing the initial signs of deterioration. Statistically significant differences between the treatments observed at 6 months with respect to both CAL and BI are a result of stabilisation of the PerioChip-treated sites and some relapse of sites managed by S/RP alone. It might be argued therefore that the use of adjunctive PerioChip in a cohort of recall patients helps to maintain improvement in clinical outcomes which are seen at 3 months post S/RP. We must also note that PPD, CAL and BI should not be regarded as independent variables. If the Bonnferroni correction is applied to allow for multiple *t*-tests and to reduce the likelihood of Type I error, then for the 6 month data the level of significance is effectively lowered to $p=0.017$ and the significant differences between our treatment groups are no longer observed. It might be argued however that application of the correction factor is an overly rigorous and conservative approach when the *p*-values for all 3 comparisons (at 6 months) approximate to $p=0.05$ (prior to correction).

An alternative, and perhaps more clinically relevant, way of analysing PPD outcome data is to look at the average % of sites/subject that demonstrate reductions of <1, >1 and >2 mm. There were no significant differences between the treatments at either 1 or 3 months (data not shown) although at 6 months there were significantly more PerioChip-treated sites showing PPD reductions of >2 mm when compared to the S/RP alone sites ($p<0.05$). This observation may be interpreted as being of clinical significance as a pocket reduction of 2 mm is identified easily by the clinician at the chairside and as such, is likely to impact upon the treatment strategy and long-term treatment planning for the patient (Jeffcoat et al. 1998). When data are presented in this way the potential clinical benefit and perhaps cost-effectiveness of the treatment to an individual patient may be evaluated. Such an assessment is not always possible when means of differences in treatment outcomes (albeit statistically significant) between groups are of relatively small magnitude (Table 2).

Local delivery of antimicrobials has, hitherto, not been used widely in recall/maintenance patients. A metronidazole 25% gel in a semi-solid suspension was used in recall patients in 2 independent trials (Stelzel & Florès de Jacoby 1997, Rudhart et al. 1998) (Table 3). Both studies adopted a split-mouth design to compare the repeated application of metronidazole gel (days 0 and 7) against S/RP and showed the 2 treatments to be equivalent with reductions in PPD in the order of 1.32–1.6 mm after 175 days. These data have to be considered with some caution primarily because, in recall patients whose previous subgingival scaling was undertaken 10 months previously (Stelzel & Florès de Jacoby) it is difficult to blind an examiner to sites which have and have not been more recently debrided. Furthermore, it is questionable whether in clinical practice, the application of local antimicrobials can, or should be justified in the absence of subgingival instrumentation, if only to disrupt the microbiol biofilm on the root surface.

Additional 6 month data showing mean reductions in probing depths from baseline in clinical trials of locally delivered antimicrobials are given in Table 3 (comparative data from the present study are also shown). All the studies used SRP alone as the positive control arm. Interestingly, the reductions in probing depths at 6 months in the SRP alone groups were almost identical (0.70–0.72) in the 3 studies in which the local antimicrobials were applied as an adjunct to SRP in patients with chronic periodontitis (Soskolne et al. 1997, Jeffcoat et al. 1998, Kinane & Radvar 1999). In comparison, our six month data for the SRP alone group shows a mean reduction in probing depths of only 0.45 mm. The patients in our study, however, were on a recall programme and all sites had previously been treated by SRP prior to enrolment in the clinical trial. The sites had been selected on the basis of having shown no clinical improvement

following the initial phase therapy and this may indicate sites that have been difficult to manage during the debridement phase (perhaps because of poor access or irregular local anatomy). A further observation is that the magnitude of resolution in probing depths is consistently two-fold greater for SRP treatments in those studies where metronidazole alone is the local antimicrobial treatment. This is irrespective of whether the study involved recall patients or patients receiving their first course of periodontal treatment (Ainamo et al. 1992, Steizel & Florès-de-Jacoby 1997, Rudhart et al. 1998). This discrepancy in the magnitude of response of patients to SRP is somewhat curious as all the data are taken from the same timepoint (6 months) and in each case the authors describe very similar protocols used for the scaling and root planing procedure.

In a more recent single-blind study local metronidazole therapy was used as an adjunct to S/RP in maintenance patients using the split-mouth design (Riep et al. 1999). Data were only collected up to 3 months post-treatment at which point there were no statistically significant differences between the treatments for either PPD reduction or CAL gain. Considering our previous argument, it is conceivable that differences between the treatments might only become apparent after 6 month data have been analysed. Riep et al. (1999) also demonstrated that, whereas *P. gingivalis* was reduced significantly and *A. actinomycetemcomitans* was unaffected by both treatments (gel+S/RP and S/RP alone), *P. intermedius* was reduced significantly only after S/RP alone. Whilst acknowledging that the analysis involved only a small number of pathogens this latter observation demonstrated eloquently the potential limitations of using antimicrobials in the absence of conventional therapy.

In conclusion, the results of this study show that PerioChip is a safe and effective adjunctive therapy to S/RP in the management of previously non-responding sites in recall/maintenance patients. Clinical improvement at these sites following S/RP alone tends to suggest that their failure to respond to the initial treatment phase resulted from incomplete debridement. No conclusions should therefore be made from our data regarding the potential value of local antimicrobials for the management of refractory periodontitis.

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Zusammenfassung

Lokale Freisetzung von Chlorhexidinglukonat (PerioChip™) bei Patienten in der Parodontalen Erhaltungstherapie

Ziel: Das Ziel dieser randomisierten, splitmouth, einfach Blindstudie war die Bestimmung der Effektivität einer kontrollierten Freisetzung von Chlorhexidinglukonat 2.5 mg (PerioChip™) bei Patienten mit restlichen blutenden Taschen (>5 mm) mindestens 3 Monate nach oraler Hygiene und Wurzelreinigung und -glättung.

Material und Methoden: 26 Patienten (Nichtraucher) wurden befundet und die potentiellen Studienflächen ausgewählt. Die klinischen Parameter wurden zur Basis und zu allen folgenden Visiten aufgezeichnet: Plaque-Index (PI), Sondierungstiefe (PPD), Blutungsindex (BI) und klinisches Attachmentniveau (CAL). Alle Studienflächen wurden mit Ultraschall gereinigt. Die PerioChips (PC) wurden in die ausgewählten Flächen von 2 Quadranten (links oder rechts) eingebracht, während die identifizierten Flächen in den verbleibenden Quadranten ohne adjunktive antimikrobielle Therapie blieben. Die klinischen Messungen wurden zu den folgenden Sitzungen nach 1, 3 und 6 Monaten durchgeführt. Die mittleren Veränderungen von der Ausgangsuntersuchung für PPD, BI und CAL wurden berechnet (Patient als statistische Einheit) und zwischen den Behandlungsterminen under Nutzung des *t*-Testes verglichen.

Ergebnisse: Zur Basis gab es keine signifikanten Differenzen zwischen PC und Kontrollflächen für die mittleren Werte für PI, PD, BI und CAL. Die mittlere (SE) Reduktion für PPD bei PC und Kontrollflächen nach Therapie war: 0.47 (0.1), 0.46 (0.1); 0.76 (0.1), 0.55 (0.1); 0.78 (0.1), 0.45 (0.1) für die Monate 1, 3 und 6. Nur zum Monat 6 erreichte die Differenz zwischen den Behandlungsmodalitäten statistische Signifikanz (p=0.06). Die mittlere (SE) Reduktion im CAL über die gleichen Perioden waren: 0.17 (0.1), 0.04 (0.08); 0.38 (0.1), 0.21 (0.1); 0.43 (0.1), 0.15 (0.09) (p=0.048). Die mittlere (SE) Reduktion im BI zwischen PC und Kontrollen erreichte nur zum 6. Monat statistische Signifikanz: 1.08 (0.1), 0.59 (0.1) (p=0.05).

Schlußfolgerungen: Die Daten der Studie zeigen, daß PerioChip™ einen günstigen Effekt in der Erhaltungstherapie für Patienten hat, obwohl der Nutzen bis zum 6. Monat nach Applikation nicht vorhanden ist.

Résumé

Libération locale de gluconate de chlorhexidine (Periochip™) chez des patients en maintenance parodontale

Le but de cette étude randomisée, en simple aveugle et bouche divisée, est de déterminer l'efficacité de la libération contrôlée de gluconate de chlorexidine à 2.5 mg (Periochip™), chez des patients avec des poches saignantes résiduelles (>5 mm) au moins 3 mois après instructions d'hygiène orale et débridement radiculaire. 26 patients, non-fumeurs, reçurent un bilan complet et les sites potentiel furent identifiés. Les paramètres cliniques enregistrés initialement et lors des visites suivantes étaient l'indice de plaque (PI), la profondeur de poche au sondage (PPD), l'indice de saignement (BI) et le niveau clinique d'attache (CAL). Tous les sites furent débridès à l'aide d'une instrumentation ultrasonique. Des copeaux de Périochip (PC) furent placés dans les sites selectionnés de 2 quadrants (droit ou gauche) alors que les sites selectionnés sur les quadrants restants furent laissés sans traitement antimicrobiens supplémentaires. Des mesures cliniques furent réalisées lors des visites de suivi, après 1, 3 et 6 mois. Les modifications moyennes par rapport à l'état initial et pour PPD, BI et CAL étaient calculées en considérant le patient comme unité expérimentale et la comparaison entre les patients fut déterminée par des tests *t*. Initialement, il n'y avait pas de différence significative entre les sites PC et les sites contrôles pour les PI, PD, BI ou CAL moyens. Les réductions moyennes (SE) de PPD pour les traitements PC et contrôles étaient respectivement de: 0.47 (0.1), 0.46 (0.1), 0.76 (0.1), 0.55 (0.1), 0.78 (0.1), 0.45 (0.1), à 1, 3, ou 6 mois. Seul, à 6 mois, les différences entre les traitements approchaient une signification statistique (p=0.06). Les réductions moyennes (SE) de CAL pour les mêmes périodes étaient de: 0.17 (0.1), 0.04 (0.08), 0.38 (0.1), 0.21 (0.1), 0.43 (0.1), 0.15 (0.09) (p=0.048). La réduction moyenne (SE) du BI entre les traitements PC et contrôles n'atteignaient des signification statistique qu'à 6 mois: 1.08 (0.1), 0.59 (0.1), (p=0.05). Ces données suggèrent que Periochip™ est bénéfique pour les patients en maintenance, bien que les bénéfices ne soient pas apparents avant 6 mois aprés placement.

References

Ainamo, J., Lie, T., Ellingsen, B. H., Hansen, B. F., Johansson, L.-A., Karring, T., Kisch, J., Paunio, K. & Stoltze, K. (1992) Clinical responses to subgingival application of a metronidazole 25% gel compared to the effect of subgingival scaling in adult periodontitis. *Journal of Clinical Periodontology* **19**, 723–729.

European Community Directive. *91/507/EEC*, Brussels, July 1991.

Jeffcoat, M. K., Bray, K. S., Ciancio, S. G., Dentino, A. R., Fine, D. H., Gordon, J. M., Gunsolley, J. C., Killoy, W. J., Lowenguth, R. A., Magnusson, N. I., Offenbacher S., Palcanis, K. G., Proskin, H. M., Finkelman, R. D. & Flashner, M. (1998) Adjunctive use of a subgingival controlled-

release chlorhexidine chip reduces probing depth and improves attachment level compared with scaling and root planing. *Journal of Periodontology* **69**, 989–997.

Kinane, D. F. & Radvar, M. (1999) A six-month comparison of three periodontal local antimicrobial therapies in persistent periodontal pockets. *Journal of Periodontology* **70**, 1–7.

Muhlemann, H. R. (1977) Psychological and chemical mediators of gingival health. *Journal of Preventive Dentistry* **4**, 6–17.

Namgung, Y. Y. & Yang, M. C. K. (1994) Outlier reduction by an option-3 measurement scheme. *Biometrics* **50**, 173–182.

Riep, B., Purucker, P. & Bernimoulin, J.-P. (1999) Repeated local metronidazole therapy as adjunct to scaling and root planing in maintenance patients. *Journal of Clinical Periodontology* **26**, 710–715.

Rudhart, A., Purucker, P., Kage, A., Hopfenmuller, W. & Bernimoulin, J.-P. (1998) Local metronidazole application in maintenance patients. Clinical and microbiological evaluation. *Journal of Periodontology* **69**, 1148–1154.

Silness, J. & Löe, H. (1964) Periodontal disease in pregnancy (II). Correlation between oral hygiene and periodontal condition. *Acta Odontologica Scandinavica* **22**, 21–35.

Soskolne, W. A., Heasman, P. A., Stabholtz, A., Smart, G. J., Palmer, M., Flashner, M. & Newman, H. N. (1997) Sustained local delivery of chlorhexidine in the treatment of periodontitis. *Journal of Periodontology* **68**, 32–38.

Soskolne, W. A., Chajek, T., Flashner, M., Landau, I., Stabholtz, A., Kolatch, B. & Lerner, E. I. (1998) An in vivo study of the chlorhexidine release profile of the Periochip™ in the gingival crevicular fluid, plasma and urine. *Journal of Clinical Periodontology* **25**, 1017–1021.

Stanley, A., Wilson, M. & Newman, H. N. (1989) The in vitro effects of chlorhexidine on subgingival plaque bacteria. *Journal of Clinical Periodontology* **16**, 259–264.

Stelzel, M. & Florès-de-Jacoby, L. (1997) Topical metronidazole application in recall patients. *Journal of Clinical Periodontology* **24**, 914–919.

Yang, M. C. K., Namgung, Y. Y., Kang, T., Magnusson, I. & Hefti, A. (1998) Option-3 median measurement scheme in outlier reduction. In: *Statistics in medicine*, pp. 2607–215.

Address:

P. A. Heasman
Restorative Dentistry
Dental School
Framlington Place
Newcastle upon Tyne, NE2 4BW
UK

Fax: +44 191 232 5144
e-mail: p.a.heasman@newcastle.ac.uk