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Prognostic factors in the treatment of generalized aggressive periodontitis: II. Effects of smoking on initial outcome

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Abstract

Aims: The aim of this study was to investigate the effects of smoking on the response to non-surgical treatment for aggressive periodontitis.

Methods: Seventy-nine patients with generalized aggressive periodontitis were included in the study; 20 were smokers. All patients received a course of non-surgical periodontal therapy and outcomes assessed 10 weeks post-operatively. Non-responding patients were designated if they had 30% or more non-responding deep sites.

Results: At baseline, bleeding scores were lower in smokers. There was no difference in baseline plaque, pocket depth (PD), recession or clinical attachment levels (CALs); when sites were selected by equal levels of CAL, increased recession was seen in smokers. Outcomes were poorer in smokers (mean PD change 1.75 ± 0.56 *versus* 2.23 ± 0.87 mm). The odds ratio for 30% of sites not responding in smokers was 2.9; for 40% non-responding it was 5.9. Smoking altered the distribution of site-specific responses to increase specifically the number of non-responding sites. There was no significant difference in responses between ex-smokers and never-smokers.

Conclusions: The results demonstrate that smoking is a major risk factor for poor response to initial treatment and emphasize the importance of smoking cessation in periodontal therapy.

Key words: aggressive periodontitis; prognosis; smoking; treatment

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In recent years it has been clearly established that tobacco smoking is a major risk factor in the aetiology of periodontitis. Studies suggest that in moderate to heavy smokers there is a relative risk of at least five times for the development of periodontitis (Tonetti 1998, Bergstrom 2004). In addition, there is considerable evidence demonstrating that continued tobacco smoking impairs response to periodontal treatment. The evidence suggests that smoking is a major deleterious factor in responses to non-surgical, surgical and regenerative periodontal therapies and is also known to increase risk of implant failure (Ryder et al. 1999, Meinberg et al. 2001, Kamma & Baehni 2003, Trombelli et al. 2003, Cortellini & Tonetti 2004, Fardal et al. 2004, Papantonopoulos 2004, D'Aiuto et al. 2005, Labriola et al. 2005, Preshaw et al. 2005, Heasman et al. 2006).

In a recent study of prognostic factors in the treatment of aggressive periodontitis we have reported a wide range of variations in initial outcome following non-surgical treatment of a group of 79 patients with aggressive periodontitis (Hughes et al. 2006). In that study, we found that clinical parameters such as plaque, bleeding and initial pocket depth (PD) were poor predictors of treatment outcome at both the site-specific and individual patient level. In addition, we found that smoking is significantly associated with a poor response to treatment. In the present report here we have analysed the effects of smoking on

treatment outcome in this patient cohort in some depth.

Material and Methods

Details of the study design have been described fully in a previous report (Hughes et al. 2006). Briefly, patients with a clinical diagnosis of generalized aggressive periodontitis with attachment loss of greater than 6 mm affecting a minimum of six teeth under the age of 40 years old were recruited to this study. Following full clinical assessment and examination including recording of probing depths and attachment levels with an electronic probe (Florida probe™ Florida Probe, Gainesville, FL, USA) all patients received a standardized course of non-surgical periodontal treatment consisting of oral hygiene instruction and full-mouth debridement over four visits. Initial responses to this therapy were assessed 10 weeks following the last treatment visit where clinical parameters were reassessed fully. Protocols for this study were approved by the East London and City Health Authority Local Research Ethics Committee. All participants signed a written consent form.

Smoking history

A full smoking history was obtained by questionnaire from each patient at baseline and at post-operative review appointments. The details of the questionnaire are given in Table 1. In addition, the smoking history was supplemented with a measurement of carbon monoxide in expired air by smokerlyzer metre. Patients were classified as current smokers either if they were self-reported current smokers, or had a smokerlyzer reading of >7. All smokers received a ''level 1'' brief smoking cessation intervention which consisted of brief advice on the significance of smoking and the aetiology and prognosis of periodontal disease and the benefits of quitting smoking to periodontal and general health.

Table 1. Smoking history questionnaire used in the study

(a) Do you smoke cigarettes now? (i.e., not cigars/pipe)	
if Yes:	
(b) What kind of cigarettes do you smoke? (Circle all that apply)	Manufactured with filters Manufactured without filters Hand-rolled
(c) How many manufactured cigarettes do you smoke in a day?	
And/or	
(d) About how many ounces of tobacco do you use per week for hand-rolled cigarettes?	Ounces
(e) If not a present cigarette smoker did you smoke in the past?	
(f) If Yes, how many manufactured cigarettes did you smoke in a day	
And/or	
(g) How many ounces of tobacco did you use per week for hand-rolled cigarettes?	
(h) How old were you when you stopped smoking?	
(i) How old were you when you started smoking cigarettes?	
(j) Do you smoke cigars?	
(k) If Yes, how many cigars per week?	
(l) Do you smoke a pipe?	
(m) If Yes, how many ounces of tobacco do you smoke per week?	

Table 2. Clinical features of smokers and non-smokers at baseline (mean ± standard deviation)

	Smokers	Non-smokers	Significance level
Age	35.30 ± 4.19	33.68 ± 5.33	$p = 0.18$
Mean baseline CAL	6.69 ± 0.66	6.53 ± 0.83	$p = 0.41$
Mean baseline pocket depth	6.20 ± 0.38	6.28 ± 0.57	$p = 0.57$
Mean baseline recession	0.18 ± 0.20	0.24 ± 0.17	$p = 0.27$
Number of deep sites at baseline	21.00 ± 14.88	24.97 ± 20.92	$p = 0.38$
Baseline plaque score (%)	50 ± 15%	49 ± 15 %	$p = 0.66$
Baseline bleeding score (%)	43 ± 33%	61 ± 27 %	$p < 0.05$*

CAL, pocket depth and recession for deep sites only; plaque and bleeding scores are whole mouth percentages. Differences tested by Mann–Whitney *U* test except for plaque and bleeding which were tested by χ^2 test; *, significantly different.
CAL, clinical attachment level.

Data analysis

Patient full-mouth bleeding and plaque scores were expressed as a percentage of all sites. PD and recession was measured on deep sites only, i.e. those that exhibited a minimum of 5 mm at baseline. In order to measure patient-level outcomes patients were classified as ''responders'' or ''non-responders'' on the basis of the percentage of their deep sites that showed no response to therapy, as previously described (Hughes et al. 2006). Non-responders were classified as those in whom 30% or more of their deep sites showed no reduction in PD following treatment.

In addition to the analyses on deep sites (those with 5 mm+ pocketing), data from all sites that exhibited 6 mm or greater loss of clinical attachment were separately analysed.

Results

Seventy-nine patients completed the study protocol as outlined. The basic demographic details of the patient cohort have been previously described. Twenty of the recruited patients were smokers and 59 were non-smokers (never-smokers or ex-smokers). The baseline demographic and clinical details for smokers and non-smokers are shown in Table 2. There was no difference in mean age, number of affected sites, or baseline plaque levels between smokers and non-smokers. Non-smokers had significantly higher bleeding scores than smokers. There was no difference between smokers and non-smokers in PDs, recession and clinical attachment levels (CALs) levels. Table 3 shows the clinical outcomes post-operatively of smokers and non-smokers. There was no significant difference in plaque scores, both groups showing a marked improvement in scores over baseline. The mean reduction in PD was markedly less in smokers.

The percentage of sites in each patient that did not respond to therapy is shown in Fig. 1. Fifty per cent of smokers were classified as non-responders whereas 25.4% of non-smokers were non-responders ($p = 0.04$, odds ratio of 2.93%, 95% confidence interval (CI) 1.02–8.42 by χ^2 analysis). Forty per cent of smokers had 40% or more sites not responding whereas only 10.2% of non-smokers had a similarly poor response ($p = 0.0025$, odds ratio 5.889%, 95% CI 1.72–20.15 by χ^2 analysis).

Table 3. Clinical features of smokers and non-smokers 10 weeks post-operatively

	Smokers	Non-smokers	Significance level
Plaque score	21 ± 14%	18 ± 12%	$p = 0.28$
Bleeding score	18 ± 20%	24 ± 17%	$p = 0.26$
PD change	1.75 ± 0.56 mm	2.23 ± 0.87 mm	$p = 0.03$*
Post –operative recession	0.11 ± 0.39 mm	0.24 ± 0.56 mm	$p = 0.24$
CAL change	1.67 ± 0.73 mm	1.99 ± 0.74 mm	$p = 0.04$*
Per cent non-responding sites	28.60 ± 23.71%	17.45 ± 13.77%	$p = 0.01$*

CAL, clinical attachment level; PD, pocket depth; *, significantly different.

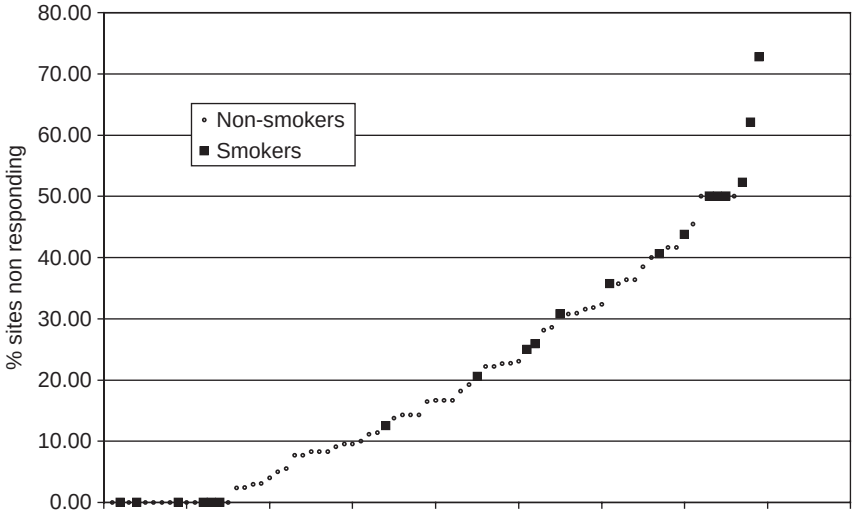

Fig. 1. Treatment outcomes for all patients expressed as number of deep sites which did not respond to treatment.

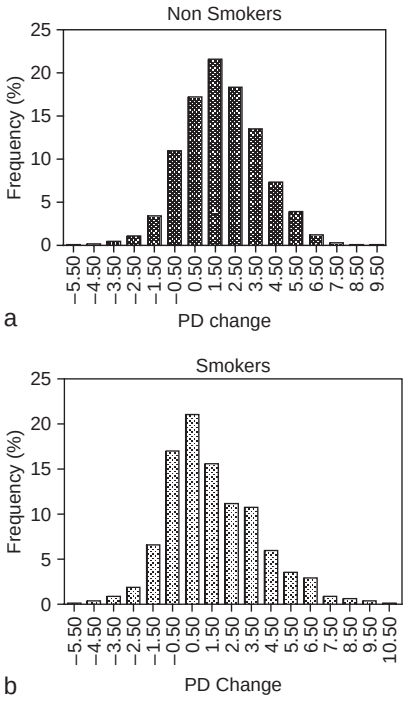

Fig. 2. Frequency distribution of the change in pocket depth of all deep sites in smokers and non-smokers. The distribution of responses in non-smokers was normally distributed; responses in smokers departed significantly from normal distribution (Skewness 0.617, $p < 0.0001$ by Kolmogorov–Smirnov test).

Figure 2 shows the distribution of changes in PD on deep sites following treatment for smokers and non-smokers. The distribution of responses in non-smokers was normally distributed; however responses in smokers departed significantly from normal distribution (Skewness 0.617, $p < 0.0001$ by Kolmogorov–Smirnov test) and was skewed towards increased numbers of poorly responding sites.

Nineteen of the non-smokers were self-reported ex-smokers who had stopped smoking for between 0 and 15 years (mean 5.3 years). Figure 3 shows the responses of ex-smokers against never-smokers. There was no significant difference in treatment response between ex-smokers and never-smokers ($p = 0.49$, χ^2 test). Mean change in PD for ex-smokers was 2.1 ± 0.84 mm, for never-smokers it was 2.3 ± 0.89 mm.

There was a good correlation between self-reported smoking and smokerlyzer reading ($R^2 = 0.65$, $p < 0.0001$) although there were consistently high smokerlyzer readings in three patients who self-reported to be non-smokers. These patients were treated as smokers for the purpose of the data analysis. Figure 4 shows the distribution of percentage of non-responding sites in each patient compared with their smokerlyzer readings. There was a weak but significant correlation between level of smokerlyzer reading and the percentage of non-responding sites in smokers ($R^2 = 0.2$, $p = 0.03$).

The results obtained when all sites with CAL of 6 mm or more were included in the analysis are shown in Table 4. There was no difference in CAL levels between smokers and non-smokers, but there was markedly more recession (and concomitantly less mean PD) in smokers at baseline. In addition not only was the overall response to treatment again poorer in smokers, but more further gingival recession was seen post-operatively.

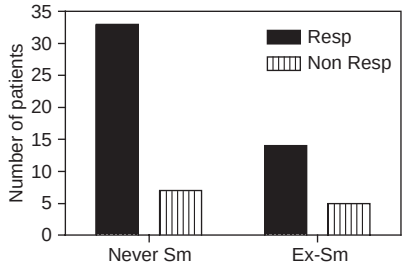

Fig. 3. Outcomes of ex-smokers *versus* never-smokers dichotomized into responding patients and non-responding patients.

Discussion

The data presented in this study confirm and extend the observations that smoking is a major negative prognostic factor in the initial outcome of non-surgical treatment of aggressive periodontitis. These data are consistent with previous reports that have demonstrated a poorer response to periodontal treatment of various types in the wide range of different clinical cohorts (Ryder et al. 1999, Meinberg et al. 2001, Kamma & Baehni 2003, Trombelli et al. 2003, Cortellini & Tonetti 2004, Fardal et al. 2004, D'Aiuto et al. 2005, Labriola et al. 2005). In the present study there was no difference in age or severity of disease as judged by the number of deep sites (5 mm PDs or greater) between smokers and non-smokers and plaque levels were the same in both groups. Furthermore,

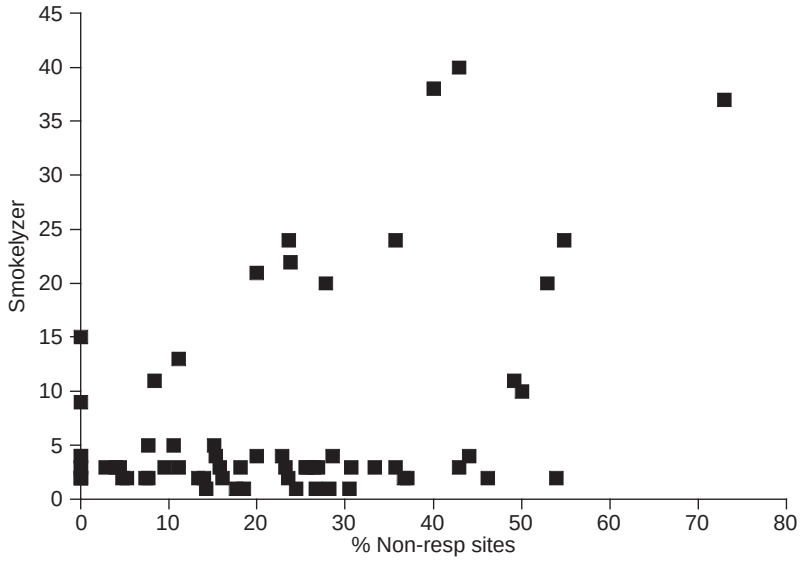

Fig. 4. Distribution of treatment outcomes as assessed by the percentage of non-responding sites compared with baseline smokerlyzer readings.

Table 4 Clinical features of smokers and non-smokers analysing all sites with 6 mm+CAL at baseline

	Smokers	Non-Smokers	Significant?
No of deep sites at baseline	39.65 ± 21.57	38.41 ± 10.26	$p = 0.87$
Baseline CAL	6.27 ± 0.49	6.30 ± 0.15	$p = 0.85$
Baseline pocket depth	4.95 ± 1.02	5.60 ± 0.66	$p = 0.010$*
Baseline recession	1.33 ± 1.00	0.69 ± 0.80	$p = 0.011$*
CAL change	1.75 ± 2.10	1.88 ± 0.51	$p = 0.58$
Pocket depth change	1.33 ± 1.11	1.86 ± 0.58	$p = 0.04$*
Recession change	0.42 ± 1.04	0.02 ± 0.08	$p = 0.05$*

CAL, clinical attachment level; *, significantly different.

post-operative plaque levels were the same in both groups. However, at baseline examination bleeding scores were significantly lower in smokers compared with non-smokers, which is consistent with clinical observations of reduced inflammation in patients who are current smokers (Nair et al. 2003, Dietrich et al. 2004). Despite this, the overall outcome in the smokers was significantly worse, with an overall smaller mean reduction in PD. The percentage of non-responding sites was much higher in smokers compared with non-smokers. Fifty per cent of smokers in our study cohort were classified as non-responders whereas only 25.4% of non-smokers were in this group, and risk of non-response in smokers had an odds ratio of 2.9. The significance of smoking as a factor associated with poor prognosis is illustrated by the data showing increased risk of 40% of sites not responding to treatment, the latter very poor response to periodontal treatment being greatly over represented in the smoking group with an odds ratio of 5.9.

Interestingly, analysis of the distribution of changes in PD for all sites suggested that the effects of smoking did not simply reduce the magnitude of response of all sites equally, but rather the effect was the result of smoking increasing the numbers of sites which did not respond at all to treatment. This observation was demonstrated by the skewed distribution of site-specific responses seen in smokers compared with non-smokers.

The comparison of clinical responses to treatment between smokers and non-smokers may be complicated methodologically, firstly because gingival recession may be greater in smokers than non-smokers. Thus, in this study we selected deep sites for analysis according to their PDs, as change in PD was a primary outcome measure. However, when we additionally examined sites according to the amount of clinical attachment loss, smokers had increased recession, suggesting that for an equivalent CAL, recession was increased in smokers. Furthermore, they also showed additional recession in response to treatment when compared with non-smokers. Secondly, reports also suggest that the measured level of clinical attachment using a probe may be underestimated in smokers when compared with non-smokers because of a reduction in the degree of probe penetration in relation to the actual anatomical level of the coronal attachment (Biddle et al. 2001).

The mechanisms by which smoking may exert its deleterious effects on treatment outcome are not fully understood. However, the data here support the idea that this is a direct effect on periodontal healing rather than acting through, for example, altered levels of plaque. Interestingly, when the distribution of treatment responses for all deep sites was examined the departure from a Gaussian distribution of responses in smokers suggests that rather than all sites being equally affected by smoking the overall effect is to increase the number of non-responding sites.

Although all smokers received brief advice about the benefits of quitting smoking, it was disappointing to note that none of the patients in the group managed to quit smoking during the study period. This result may emphasize the need for a more sophisticated and carefully planned strategy of smoking cessation advice for patients about to receive periodontal care. There was no significant difference in outcome seen between patients who had never smoked and those who were ex-smokers who had previously quit, although some of these had reportedly only quit within the last few months before diagnosis. These data suggest the immediate beneficial effects of quitting smoking on potential treatment outcome, although further studies of this question with larger subject numbers specifically designed to address this issue would be valuable (Tonetti 1998, Labriola et al. 2005).

The approach adopted within the study followed current smoking cessation guidelines for health professionals that opportunistic advice should be made available to all smokers to stop (West et al. 2000). These guidelines also indicate that clinicians should be adequately trained to discuss smoking and offer further support for current smokers through a referral to specialist support. A recent systematic review has concluded that this activity, carried out by oral health professionals in the surgery and incorporating an oral examination

component, may increase tobacco abstinence rates (Carr & Ebbert 2006).

Reflecting current practice, exhaled carbon monoxide was measured using a CO monitor (Smokerlyzer™, Bedfont Scientific, Rochester, UK) This offers an easy and immediate method of assessing smoking status with a specificity in excess of 95% (Deveci et al. 2004). As is current practice the cut-off level of 10 p.p.m. was reduced to >7 (Christensen et al. 2004, Pearce & Hayes 2005).

In general, there was a good correlation between the smokerlyzer readings and self-reported current smoking status. However, three patients had consistently high smokerlyzer readings who were self reported non-smokers. Unfortunately this inconsistency only came to light during data analysis when it was not possible to question these patients directly about this inconsistency. However, given that the smokerlyzer readings were high (between 17 and 24) these patients were classified as smokers in the analysis.

The distribution of the treatment responses as determined by the percentage of non-responding sites in each subject showed a weak correlation with smokerlyzer readings in smokers, although a number of non-smokers also showed poor response to treatment. These results suggest that prognosis may be determined by a range of factors in addition to smoking which might include genetic and microbiological parameters.

Overall the results suggest an important message for current smokers requiring periodontal treatment. The overall treatment responses in smokers were considerably worse than those of non-smokers, there is a greatly increased relative risk of poor site-specific responses to periodontal treatment and increased risk of clinically significant post-operative gingival recession. The data further serve to emphasize the importance of consideration of smoking cessation in periodontal treatment and suggest a rapid beneficial effect of quitting smoking on future treatment outcomes. When taken with the data from our previously reported findings the results suggest that smoking is a markedly more important prognostic indicator of treatment outcome in aggressive periodontitis than clinical parameters such as plaque, bleeding and initial PDs.

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Clinical Relevance

In this study, we examined in depth the effects of smoking on initial outcome of non-surgical treatment in patients with generalized aggressive periodontitis. Smokers had more recession, less bleeding but equal plaque levels. Their responses to treatment were poorer than in non-smokers, on average by about 0.5 mm, and they had a greatly increased risk of over 30% of their deep pockets not responding to treatment at all. There was no difference between responses to treatment in ex-smokers compared with those who had never-smoked. The results underline the potential importance of smoking cessation for periodontal patients.