Influence of Smoking on Long-Term Clinical Results of Intrabony Defects Treated With Regenerative Therapy

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This retrospective study compares the short-term (1 year) and long-term (2 to 5 year) clinical results of regenerative therapy in clinical private practice using a bone allograft for the treatment of intrabony defects in smokers and non-smokers. A total of 110 intrabony lesions were treated with demineralized freeze-dried bone allograft (DFDBA) following thorough defect debridement and root preparation in 53 patients (15 cigarette smokers and 38 non-smokers). Assessments of clinical attachment level (CAL) and probing depth (PD) were recorded at pre-treatment, 1 year post-treatment, and 2 to 5 years post-treatment. At 1 year post-treatment, significant gains in mean CAL were maintained for both smokers (2.7 mm) and non-smokers (3.4 mm). Similarly, significant reductions in mean PD were observed for smokers (3.0 mm) and non-smokers (3.8 mm) at the 1-year follow-up. However, when comparing relative improvements in clinical measures, smokers were found to exhibit significantly poorer treatment results (i.e., sites exhibited less CAL gain) at 1 year and 2 to 5 years follow-up. Relative to pre-treatment scores, differences in improvements observed for CAL at the 1-year evaluation (29.2% for smokers and 42.5% for non-smokers) were sustained in the subgroup of patients at 2 to 5 years follow-up (31.3% for smokers and 41.8% for non-smokers). Similar but non-significant trends were observed for relative reductions in probing depth for smokers and non-smokers at 1 year (41.9% for smokers and 49.3% for non-smokers) and 2 to 5 years follow-up (43.9% for smokers and 48.3% for non-smokers) for the subgroup of patients followed beyond 1 year. These results suggest that smoking adversely affects treatment outcome, as measured by gains in clinical attachment levels of intrabony defects treated by regenerative therapy using DFDBA. J Periodontol 1996;67:1159–1163.

Key Words: Bone, demineralized; bone, freeze-dried; bone grafts; follow-up studies; periodontal diseases/surgery; periodontal diseases/therapy; smoking/adverse effects; bone regeneration.

The use of demineralized freeze-dried bone allograft (DFDBA) in regenerative therapy has provided a clinically successful approach for the treatment of intrabony defects. DFDBA placement has shown the potential to enhance the formation of a new attachment apparatus, including new bone, cementum, and periodontal ligament.1 Although the formation of a new attachment apparatus can only be verified histologically, the clinical benefits include pocket reduction, bone repair, and a gain or stabilization of the clinical attachment level.23

Like any other periodontal procedure, however, predictability is based in part on the identification and management of factors associated with its success or failure. Melloni,4 for example, reviewed periodontal bone grafting techniques and identified the following factors as important for treatment success: 1) patient selection; 2) defect selection; 3) anesthesia; 4) flap design and reflection; 5) soft tissue debridement; 6) root planing; 7) intramarrow penetration; 8) graft procurement; 9) graft insertion; 10) flap closure; 11) suturing; 12) periodontal dressing; 13) postoperative management; 14) maintenance; and 15) re-evaluation. Other factors also considered important included good physical health, positive attitude towards therapy, acceptable level of plaque control, and commitment to a maintenance program.4
Recent studies have shown that smoking can diminish the results of periodontal surgery,\(^9\) including improvements in regenerative outcome following guided tissue regeneration procedures using barrier membranes.\(^4\) Little information, however, is available on the effects of smoking on clinical outcome following regenerative procedures using bone grafts. The purpose of this retrospective study from a private practice was to compare the short-term (1 year) and long-term (2 to 5 year) clinical results of regenerative therapy using DFDBA for the treatment of intrabony defects in smokers and non-smokers.

**MATERIALS AND METHODS**

Fifty-three patients (31 female and 22 male), ranging in age from 28 to 69 years (average 46.3 years), who had been diagnosed with moderate to advanced adult periodontitis and followed for a minimum of 1 year after treatment, were identified for the analysis. Fifteen of the patients were smokers (14 caucasian; 7 male and 8 female; mean age 45.0) and 38 were non-smokers (36 caucasian; 15 male and 23 female; mean age 46.7). All smokers reported a history of smoking \(\leq 1\) pack of cigarettes per day for over 10 years, with nine patients smoking approximately one-half pack or less and five smoking approximately one pack per day. Patients were treated in a private practice limited to periodontics.

All patients underwent initial therapy in either the office of their general dentist or periodontist. Plaque control orientation was performed in the periodontal practice until an excellent level was achieved, with deposits being absent or light. This consisted of a minimum of two visits outside the dental operatory environment where plaque disclosure, technique demonstration, and performance were reinforced. Occlusal therapy consisted of bite adjustment or splinting of teeth to reduce excessive mobility or fremitus patterns. Examinations included assessments of periodontal probing depth (PD) and clinical attachment level (CAL). The PD represented the greatest distance from the gingival margin to the base of the pocket, whereas the CAL measured the distance from the cemento-enamel junction, crown, or restoration margin to the base of the pocket.

Following the presurgical examination, a total of 110 intrabony defects were treated with DFDBA (67 in non-smokers, 43 in smokers).

Patients rinsed presurgically with a chlorhexidine mouthrinse.\(^4\) All surgeries and measurements were performed by one individual (P.S.R.). A sulcular incision, full-thickness flap was employed except in those teeth where an inverse bevel was used to achieve a more favorable architecture. The defects were thoroughly debrided and the roots scaled and planed with ultrasonic and hand instruments. Rotary high-speed instrumentation with flame-shaped finishing burs\(^6\) was used for additional root debridement. Citric acid (pH 1) was used in the majority of sites for further debridement of the root (smokers: 68% of sites; non-smokers: 79% of sites). Intrabony defects were categorized according to the defect morphology.\(^8\) Intramarrow penetration was performed to increase the communication directly to the marrow vascular spaces. If large ledges or exostoses were present in the surgical area, they were removed/reduced through osteoplasty which also helped ensure primary closure. Defects were treated with either DFDBA\(^4\) alone (smokers: 37% of sites; non-smokers: 34% of sites) or in combination with tetracycline hydrochloride mixed in a ratio of less than 4:1.\(^10\) Defects were filled at least to the level of the existing bony walls or slightly overfilled. Grafts were placed incrementally with light pressure. Flaps were sutured with #5-0 monofilament sutures\(^4\) with emphasis on primary closure. A periodontal dressing\(^**\) was placed for 7 to 10 days. Patients were prescribed penicillin, erythromycin, or doxycycline for the first 10 days followed by doxycycline for an additional 10 to 14 days.

Patients were seen every 7 to 10 days for post-operative treatment at which time sutures were removed at either the first or second visit. They were then seen every other week for the second month and every 3 months thereafter, with some of the latter visits alternated with the general dentist’s office. Post-operative visits included plaque debridement, selective stain polishing, and reinforcement of oral hygiene. Patients utilized either an essential oil\(^11\) or chlorhexidine\(^4\) post-operative oral rinse. Re-examination of PD and CAL was performed at 12 months post-surgery and each subsequent 12-month visit.

**Data Analysis**

Data for sites within patients were averaged to yield a mean score per patient for each clinical measure. Pre-treatment and post-treatment probing depths and attachment levels for smokers and non-smokers were compared using the Wilcoxon ranked sum tests. Changes from pretreatment to post-treatment were compared within groups using the Wilcoxon matched pairs test. Between-group comparisons of the proportional changes in probing depths and attachment level scores relative to pre-treatment values were calculated and submitted to statistical analysis using an analysis of variance (ANOVA). In addition, to verify that relative differences in treatment response could not be accounted for by differences at pre-treatment, the data were submitted to an analysis of covariance (ANCOVA). Proportional changes in clinical

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1. Peridex, Procter & Gamble, Cincinnati, OH.
2. Brassoc USA, Savannah, GA.
3. LifeNet, Virginia Beach, VA.
4. Ethicon, Inc., Somerville, NJ.
5. *Coe-Pak, G.C. America, Inc., Chicago, IL.
measures were adjusted using pre-treatment scores in the ANCOVA, which yielded the same statistical results. Comparisons involving the 2–5 year data were based on a subgroup analysis of 68 sites from 43 patients. In the analysis of these data, the number of years to follow-up also was included as a covariate in the ANCOVA. In all parametric tests, scores were weighted to take into account differences in the number of sites contributing to a patient's mean score. All tests were performed at a level of $P \leq 0.05$.

**RESULTS**

A comparison of pre-treatment PD scores at graft sites indicated significantly greater pocket formation for non-smokers than smokers ($7.1 \pm 1.1$ versus $6.4 \pm 0.7$, $P \leq 0.001$). A similar comparison of pre-treatment CAL scores revealed a significantly greater mean clinical attachment loss at sites among non-smokers than smokers ($7.4 \pm 1.3$ versus $6.9 \pm 1.4$, $P \leq 0.001$). As seen in Tables 1 and 2, significant reductions in PD and increases in CAL were observed for non-smokers and smokers at both 1 year and 2 to 5 years post-treatment.

When post-treatment scores were compared for the subgroup of patients followed 2 to 5 years using ANCOVA, controlling for differences related to subjects and pre-treatment scores, a significant group difference was observed for the relative change in mean CAL, with PD showing a non-significant but similar trend (Table 3). The relative decrease in mean CAL observed for non-smokers was significantly greater than for smokers at 1 year (42.5% versus 29.2%) and at 2 to 5 years post-treatment (41.8% versus 31.3%) (Fig. 1). Similar trends of improvement in mean PD were observed for smokers and non-smokers at 1 year (49.3% versus 41.9%) and at 2 to 5 years post-treatment (48.3% versus 43.9%).

Clinical attachment level gains ≥ 2 mm were observed at 100 of the 110 sites at 1 year post-treatment. There were 12 sites which lost ≤ 1 mm during the 2 to 5 years post-treatment period; of these latter sites, eight were found in smokers.

**DISCUSSION**

Re-entry studies\(^3\) have shown that the use of DFDBA in grafting procedures can improve intrabony lesions and is a more effective technique than flap curettage.\(^4\) Case reports presented by Werbitt\(^5\) showed radiographic improvement of intrabony lesions for up to 9 months. The results of our retrospective study demonstrate that substantial improvements in CAL gains and PD reductions can be achieved using DFDBA. Moreover, these clinical improvements appear relatively stable over long periods of time (2 to 5 years; see Table 2).

Although significant clinical improvements were observed for smokers and non-smokers, smoking was significantly associated with the amount of CAL gain at follow-up while PD reduction followed a similar trend. In the subgroup of patients followed 2 to 5 years, a relative

### Table 1. Clinical Measures at Pre-Treatment and 1-Year Post-Treatment

<table>
<thead>
<tr>
<th>Measures</th>
<th>Non-Smokers</th>
<th>Smokers</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-Treatment</td>
<td>1-Year</td>
</tr>
<tr>
<td>CAL (mm)</td>
<td>$7.4 \pm 1.3^*$</td>
<td>$4.0 \pm 1.0$</td>
</tr>
<tr>
<td>PD (mm)</td>
<td>$7.1 \pm 1.1^*$</td>
<td>$3.3 \pm 0.7$</td>
</tr>
</tbody>
</table>

Values represent mean ± standard deviation. Percent change from pre-treatment is indicated in parentheses. N = 38 non-smokers; N = 15 smokers. CAL = Clinical attachment level. PD = Probing depth. $^*P \leq 0.001$ Wilcoxon matched pairs test (pre-treatment versus 1-year).

### Table 2. Clinical Measures at Pre-Treatment, 1-Year and 2–5 Years Post-Treatment for Patients Followed Beyond 1 Year

<table>
<thead>
<tr>
<th>Measures</th>
<th>Non-Smokers</th>
<th>Smokers</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-Treatment</td>
<td>1 Year</td>
</tr>
<tr>
<td>CAL (mm)</td>
<td>$7.6 \pm 1.2$</td>
<td>$4.1 \pm 1.0$</td>
</tr>
<tr>
<td>PD (mm)</td>
<td>$7.3 \pm 1.2$</td>
<td>$3.5 \pm 0.8$</td>
</tr>
</tbody>
</table>

Values represent mean ± standard deviation. N = 26 non-smokers; N = 8 smokers. All pre-treatment and post-treatment comparisons significant at $P \leq 0.001$ using a Wilcoxon matched pairs test. CAL = Clinical attachment level. PD = Probing depth.

### Table 3. Comparisons of Relative Changes in Clinical Measures at 1 Year and 2 to 5 Years Post-Treatment for Patients Followed Beyond 1 Year

<table>
<thead>
<tr>
<th>Measures</th>
<th>Non-Smokers</th>
<th>Smokers</th>
<th>Non-Smokers</th>
<th>Smokers</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1-Year Post-Treatment</td>
<td>2–5 Years Post-Treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAL (mm)</td>
<td>$42.5 \pm 0.13^*$</td>
<td>$29.2 \pm 0.13$</td>
<td>$41.8 \pm 0.16^*$</td>
<td>$31.3 \pm 0.14$</td>
</tr>
<tr>
<td>PD (mm)</td>
<td>$49.3 \pm 0.11$</td>
<td>$41.9 \pm 0.11$</td>
<td>$48.3 \pm 0.14$</td>
<td>$43.9 \pm 0.11$</td>
</tr>
</tbody>
</table>

Note: Values represent percentage change from pre-treatment value. N = 26 non-smokers; N = 8 smokers. CAL = Clinical attachment level. PD = Probing depth. $^*P \leq 0.05$ (non-smokers versus smokers).
Figure 1. Clinical attachment level changes in intrabony defects after regenerative therapy using demineralized freeze-dried bone allograft in patients followed over 2 to 5 years. Values represent clinical attachment level (mean ± S.D.) for the subgroup of patients followed over 2 to 5 years.

The difference of 13.3% in CAL gain was found between smokers and non-smokers at 1 year re-examination; however, this difference showed a slight regression, decreasing to 10.5% at 2 to 5 years follow-up. Similar group trends were observed for PD on re-examination, both at 1 year (7.4%) and 2 to 5 years (4.4%).

The results of this retrospective study are consistent with the findings of Tonetti et al.\textsuperscript{6} and Rosenberg and Cutler\textsuperscript{3} who demonstrated that smoking adversely affects regenerative outcome. The present findings suggest that smoking also compromises the regenerative outcome achievable by using DFDBA as part of grafting procedures in the treatment of intrabony defects.

Because this retrospective analysis is based on clinical data obtained from a private practice, there are certain limitations that must be considered. First, the number of patients and sites in the smoking and non-smoking groups could not be controlled. Data were collected on all available patients. Second, probing forces could not be calibrated and annual re-examinations of sites were made as close to the anniversary dates as could be reasonably expected. Third, a variety of treatment procedures were used, including flap designs, citric acid, tetracycline incorporation into the graft, osteoplasty, post-operative antibiotic coverage, and post-operative rinses. The choice of treatment procedures was influenced by many considerations, including surgical judgment, medication history (e.g., whether a patient was taking an antibiotic for pre-medication), and other information that developed which might enhance results of treatment. Smoking behavior, however, was not a consideration in selecting patient treatment.

From a clinician's standpoint, the observed clinical differences may appear relatively modest, given the limitations of manual probing.\textsuperscript{14} One explanation for why greater differences were not seen is that many of the patients (9 out of the 14) smoked about one-half pack (10 cigarettes) per day. Rosenberg and Cutler\textsuperscript{3} attributed 80% of their 42% overall failure rate to smokers, the majority of whom smoked over 10 cigarettes per day. Tonetti et al.\textsuperscript{6} also included individuals who smoked 10 cigarettes or more daily in their smokers group; in their study, smokers gained significantly less clinical attachment level than non-smokers (2.1 ± 1.2 mm for smokers compared with 5.2 ± 1.9 mm for non-smokers). It is interesting to note, both in our study and that reported by Tonetti et al.,\textsuperscript{6} that attachment loss and probing depth scores for the non-smokers were greater than those of the smokers at pre-treatment.

The negative impact of smoking on the healing surgical wound may be related to the deleterious cellular effects of nicotine on fibroblasts\textsuperscript{15} and polymorphonuclear leukocytes.\textsuperscript{16} Cotinine, a destructive by-product of nicotine, has been detected in the bloodstream and in the gingival crevicular fluid.\textsuperscript{17} Smoking may also cause vasoconstriction of the gingival blood vessels,\textsuperscript{18} diminishing the healing response. Tobacco smoking reduces the short-term oxidation-reduction potential of dental plaque, which can enhance the proportion of anaerobic bacteria.\textsuperscript{19} The latter observation is of particular interest, since smokers have frequently been shown to have a poorer level of plaque control in comparison to non-smokers. In regenerative therapy, the level of plaque control has been associated with the degree of treatment success.\textsuperscript{5,20} Prior to surgery, all patients received instruction in plaque control for a minimum of one to two visits and had to demonstrate an excellent level of oral hygiene before undergoing treatment. Patients followed in this study were seen weekly during the first month, every other week for the second month, and every 3 months after surgery to enhance plaque control. Westfelt and others\textsuperscript{21} have shown that attachment levels following surgery are enhanced by a more frequent post-operative interval during the early stages of healing.

The impact of smoking, therefore, may be the result of many possible local or systemic effects, including alterations in osteoblast and fibroblast function, immune surveillance, or local bacterial ecology. Regardless, the clinical outcome appears to be one of less favorable wound healing. Moreover, smoking has recently been implicated as the greatest environmental risk factor for periodontal disease.\textsuperscript{22} Grossi et al.\textsuperscript{23} also showed that smokers had greater odds for more severe bone loss compared to non-smokers, and that the severity of bone loss was directly
and proportionally accounted for by increasing amounts of smoking.

In conclusion, these data provide evidence that cigarette smoking adversely affects the clinical outcome of intrabony defects treated with DFDBA. In this study, cigarette smoking was significantly associated with relative gains in clinical attachment levels and reductions in probing depths following treatment of intrabony defects with DFDBA. Further investigations are needed to determine whether the association of smoking to regenerative outcome represents a causal relationship.

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REFERENCES

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