Interleukin-1 Gene Polymorphisms and Long-Term Stability Following Guided Tissue Regeneration Therapy*

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Background: Specific interleukin (IL)-1 gene polymorphisms are associated with an increased susceptibility to severe periodontitis, increased inflammation, and increased likelihood of tooth loss during the maintenance phase after conventional periodontal therapy. The aim of the present study was to evaluate the impact of genotype on the maintenance of gained clinical attachment obtained after guided tissue regeneration (GTR) surgical therapy in deep intrabony defects.

Methods: Forty deep (≥4 mm) interproximal angular bony defects with presurgical clinical attachment loss of >8 mm were treated by GTR using a non-absorbable expanded polytetrafluoroethylene (ePTFE) membrane. Membranes were surgically removed 4 to 6 weeks after surgery. Afterwards patients were placed on monthly recall for the first year and every 3 months for the following 3 years. At the 4-year re-evaluation, a IL-1 genetic susceptibility test was performed on all patients.

Results: Fourteen (35% of the 40 patients) were genotype-positive (+). At baseline no statistically significant differences were found between patients with different genotypes in full mouth plaque score (FMPS), full mouth bleeding score (FMBS), clinical attachment level (CAL), probing depth (PD), or gingival recession. At year 1 follow up visit, no statistically significant differences were noted between genotype + and genotype – patients in FMPS, FMBS, amount of CAL gain, decrease in PD, or increase in gingival recession. Sixteen patients had membrane exposure after the GTR procedures. In these patients, the amount of CAL gain (P <0.001) and PD reduction (P <0.01) 1 year after surgery was significantly lower than those observed in patients without membrane exposure. At the year 4 follow-up visit, no significant differences were found between genotype negative and positive patients in FMPS or FMBS and both groups showed a significant loss in CAL (P <0.001) and increase in PD (P <0.001) when compared to year 1 visit. No change in gingival recession was noted. Genotype + patients showed significantly more CAL loss (P <0.002) and increase in PD (P <0.001) between the years 1 and 4 when compared to genotype – patients. A significant association between genotype and stability of the regenerated attachment was also demonstrated.

Conclusions: The results of this study demonstrate that genotype expression did not effect GTR treatment response at 1 year, but had a great impact on long-term stability (year 4). In a 3-year period, patients with positive IL-1 genotype lost about 50% of the first year gained CAL and were about 10 times more likely of experiencing ≥2 mm CAL loss when compared to oral hygiene matched genotype-negative patients. *J Periodontol 2000;71:606-613.*

KEY WORDS

Periodontal attachment loss/prevention and control; genotype; periodontitis/etiology; tooth loss/prevention and control; polymorphism, gene.

The ultimate goal in periodontal therapy is to regenerate the attachment apparatus lost to periodontal disease. Application of the principles of guided tissue regeneration (GTR) in the treatment of vertical bony defects has been shown to result in significant and predictable gain of clinical attachment and bone fill.[1-7] It has been demonstrated that these clinical improvements can be maintained over time in patients enrolled in periodontal maintenance programs.[8-10] Furthermore, high plaque and bleeding on probing scores,[6,9] cigarette smoking,[11] and lack of compliance[9,12] are frequently associated with clinical attachment loss. Among inherent patient factors, genetic characteristics have not yet been evaluated in relation to the response to GTR therapy or to the long-term results. With the discovery of a specific genetic marker for susceptibility to periodontitis and the availability of a laboratory test† for identifying this marker, it has now become possible to assess the patient's genetic risk.

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Although there is a growing body of evidence demonstrating family history has an impact on disease susceptibility,[13-15] only recently has a specific genetic marker for identifying an individual's predisposition to adult periodontitis been reported.[16] Patients positive for this genotype consistently produced 2 to 4 times more IL-1 in gingival crevicular fluid and tissue biopsies, in response to the same bacterial challenge as the negative controls.[17-19] In addition, genotype-positive subjects showed increased inflammation and more bleeding on probing than genotype-negative patients.[16,20] Furthermore, it has been shown that IL-1 genotype is associated with an increased likelihood of tooth loss during the maintenance phase after conventional periodontal therapy.[21,22] Genotype-positive patients were 2.7 (odds ratio) times more likely to lose teeth during the 4-year follow up than genotype-negative patients, while smoking patients were 2.9 times more likely to lose teeth than non-smoking patients. When genotype and smoking were considered together, the odds ratio further increased with genotype-positive, smoking patients showing a 7.7 times greater likelihood of tooth loss when compared to genotype-negative, non-smoking patients.[21,22]

Furthermore, it has been shown in other long-term studies, that the results of mucogingival surgery[23] and conventional periodontal therapy[24] can be maintained, even in genotype-positive patients, provided that an aggressive maintenance program is instituted. No attempt has been made to correlate the IL-1 genotype to the long-term stability of the clinical outcomes achieved with GTR therapy.

The aim of the present study was to evaluate the impact of genotype on the maintenance of gained clinical attachment obtained after GTR surgery in deep intrabony defects.

MATERIALS AND METHODS

Study Population and Experimental Design

The study population consisted of 40 systemically healthy subjects (19 male and 21 female; 35 to 65 years of age; mean age, 48.2 years) affected by chronic adult periodontitis, treated in the Department of Periodontology, University of Bologna, and in maintenance for 4 years. Following completion of the initial cause-related therapy including oral hygiene instruction and full-mouth scaling and root planing, one isolated deep (≥4 mm) interproximal angular bony defect with presurgical clinical attachment loss of >8 mm in each patient was treated by guided tissue regeneration procedure using a non-absorbable ePTFE membrane.‡ Eleven incisors, 8 cuspids, 5 premolars and 6 molars were treated; 24 teeth were located in the maxillary arch. Defects did not extend into a furcation area. Baseline full-mouth plaque score and full-mouth bleeding scores were 10.2 ± 2.3 and 9.1 ± 2.2, respectively. Seven subjects smoked more than 10 cigarettes/day; one patient smoked 6 cigarettes/day; and the remaining did not smoke. None of the patients had been previously treated for periodontal disease.

Membranes were surgically removed 4 to 6 weeks after surgery. Afterwards patients were placed on monthly recall for the first year and every 3 months for the following 3 years. At the 4-year re-evaluation, the IL-1 genetic susceptibility test was performed on all patients.

Clinical Characterization of Patients and Selected Sites

Local and full mouth and plaque scores (FMPS) were recorded as the percentage of total surfaces (4 aspects per tooth) which revealed the presence of plaque.[25] Bleeding on probing was assessed dichotomously at a force of 0.3 N with a manual pressure-sensitive probe. Local and full mouth bleeding scores (FMBS) were recorded as the percentage of total surfaces (4 aspects per tooth) which revealed the presence of bleeding upon probing.

The following clinical measurements were taken 1 week before the surgery and at the 1 and 4 year follow-up: clinical attachment level (CAL), measured from the cemento-enamel junction (CEJ); probing depth (PD), measured from the gingival margin; and marginal gingival recession (REC), measured from the CEJ to the gingival margin. A single investigator performed the clinical measurements at baseline and at 1 and 4 years and was blinded to the results of the genetic testing. Measurements were performed at 6 sites around all teeth; the study, however, reports only local measurements at the deepest interproximal point of the selected defect. All measurements were performed by means of a manual pressure sensitive probe and were recorded to the nearest millimeter.

Surgical Procedure

The intrabony defects of the selected sites were treated according to the principles of guided tissue regeneration with the application of non-resorbable barrier membranes. In brief, full thickness flaps were elevated trying to preserve the marginal and the interdental tissues at the maximum possible extent. Following careful debridement and root planing, non-resorbable ePTFE membranes were positioned to completely cover the defects and overlapping 2 to 3 mm of the residual bone. Membranes were secured and stabilized to the neighboring teeth with Teflon sutures. Flap elevation was continued with a split thickness to permit coronal displacement of the flap and thus complete coverage of the membrane. Sutures were placed in the interproximal areas in order to achieve primary closure of the interdental tissues over the membranes.

‡ Gore-Tex Regeneration Material, W.L. Gore & Associates, Inc., Flagstaff, AZ.

Clinically exposed membranes were surgically removed at 4 weeks; in the case of unexposed barrier material, the re-entry procedure was performed at 6 weeks.

Postsurgical Anti-Infection Treatment

Patients received systemic amoxicillin plus clavulanic acid, 1g per day, for 8 days and were instructed to rinse the mouth with a 0.12% solution of chlorhexidine twice a day up to the time of membrane removal (4 to 6 weeks). During this period, patients were recalled once a week for professional tooth cleaning. Following membrane removal, the patients continued with the daily rinses of chlorhexidine for an additional 5 weeks. Mechanical tooth cleaning in the surgically treated area was reinstituted 4 weeks after membrane removal.

Periodontal Maintenance

All patients were recalled for professional tooth cleaning and reinforcement of self-performed oral hygiene measures at 1 month intervals up to the 1-year examination. Afterwards patients received hygiene re-instruction, mechanical tooth cleaning, and subgingival instrumentation in sites with bleeding on probing at 3-month intervals between the 1- and the 4-year examination.

IL-1 Genetic Test

At the time of the 4-year examination, all patients were tested for the IL-1 genotype. A finger stick blood sample was collected for each patient using a specially provided DNA filter paper and the dried specimen was sent to a centralized laboratory for DNA analysis. The results are reported as "positive" or "negative" for the IL-1 genetic polymorphism depending on the presence of allele 2 in both IL-1α and IL-1β genes.

Data Analysis

The significance of changes in CAL, PD, and gingival recession over the 4-year follow-up visits were determined using non-parametric Wilcoxon rank test. The following comparisons were made using Wilcoxon-Mann-Whitney test: all the variables between genotype positive and negative patients; changes of CAL, PD, and gingival recession from the baseline to first year follow up visit; from 1 year to 4 years after surgery between patients with different genotypes; and CAL, PD, and gingival recession between patients with or without membrane exposure after surgery. Multivariate linear regression models were fitted to determine effects of variables on 1-year CAL gain and 4-year CAL loss after adjusting for other confounding variables. A multivariate logistic regression model was fitted to determine the association between IL-1 genotype and the stability of the regenerated CAL between 1 and 4 years after surgery. The significance level took into account correction for multiple comparisons.

RESULTS

Forty patients were treated with GTR procedures. Clinical measurements were taken at baseline and at 1 and 4-year follow up visits. Among the 40 patients, 14 (35%) were genotype-positive; i.e., had allele 2 for both IL-1A (+4845) and IL-1B (+3953). There were 21 females and 19 males in the study. Sixteen females and 10 males were genotype negative, and 5 females and 9 males were genotype positive. Five patients in the genotype negative group were smokers (more than 10 cigarette/day) and 3 smokers (2 smoked more than 10 cigarette/day and one, 6 cigarettes /day) belonged to the genotype positive group. The mean age of the 40 patients was 45 ± 9 years old, 45 ± 8 years old for genotype negative and 46 ± 10 years old for genotype positive patients.

BASELINE MEASUREMENTS

Table 1 showed the comparison of clinical measurements between genotype positive and genotype negative patients at baseline. No statistically significant differences were noted between patients with different genotypes at baseline in FMPS, FMBS, CAL, PD, or gingival recession.

1-Year Follow Up

At the year 1 follow up visit, genotype negative patients had FMPS of 8.6 ± 1.6 and FMBS of 6.2 ± 1.2 and genotype positive patients had FMPS of 8.4 ± 1.9 and FMBS of 5.9 ± 1.5. No significant difference between genotype positive and negative groups in FMPS and FMBS were noted. Both genotype patients showed a significant gain in CAL, decrease in PD, and increase in gingival recession at the one year follow-up (Table 2).

Genotype negative patients showed a gain in CAL of 5.3 ± 1.7 mm, reduction of 6.4 ± 1.6 mm in PD, and increase of 1.2 ± 1.0 mm in gingival recession. Genotype positive patients had a gain of 5.1 ± 1.5 mm in CAL, reduction of 6.4 ± 1.1 mm in PD, and increase

Table 1.

Comparison of Oral Hygiene and Clinical Variables Between Genotypes at Baseline (mean values ± SD)

Genotype	N	FMPS (%)	FMBS (%)	CAL (mm)	PD (mm)	REC (mm)
Negative	26	10.3 ± 2.5	9.1 ± 2.1	10.6 ± 1.9	9.1 ± 1.8	1.5 ± 1.0
Positive	14	10.0 ± 2.7	8.9 ± 1.9	9.7 ± 1.0	8.7 ± 1.0	1.0 ± 0.5
P		0.32 (NS)*	0.50 (NS)	0.12 (NS)	0.48 (NS)	0.10 (NS)

* Not significant.

Table 2.

Comparison of Clinical Variables Between Year 1 Follow-Up and Baseline, Between Year 1 and 4 Follow-Up and Between Year 4 Follow-Up and Baseline (mean values ± SD)

Clinical Attachment Level		
Genotype	Negative	Positive
Baseline	10.6±1.9	9.7±1.0
1 year	5.4±1.5	4.6±1.2
4 year	6.4±1.6	6.9±2.0
P		
1 year vs. baseline	0.0001	0.0001
4 year vs. 1 year	0.0001	0.0001
4 year vs. baseline	0.0001	0.0005
Probing Depth		
Genotype	Negative	Positive
Baseline	9.1±1.8	8.7±1.0
1 year	2.7±0.7	2.4±0.5
4 year	3.5±1.1	4.6±1.5
P		
1 year vs. baseline	0.0001	0.0001
4 year vs. 1 year	0.0001	0.0001
4 year vs. baseline	0.0001	0.0001
Gingival Recession		
Genotype	Negative	Positive
Baseline	1.5±1.0	1.0±0.6
1 year	2.7±1.4	2.2±0.9
4 year	2.9±1.3	2.3±0.9
P		
1 year vs. baseline	0.0001	0.0005
4 year vs. 1 year	0.13 NS*	1 NS
4 year vs. baseline	0.0001	0.0001

* Not significant.

of 1.2 ± 0.9 mm in gingival recession. No statistically significant differences were noted between genotype positive and genotype negative patients in the amount of CAL gain, decrease in PD, and increase in gingival recession one year after the surgery.

Sixteen patients had membrane exposure after GTR surgery; 9 (56%) were genotype-negative and 7 (44%) genotype-positive. This difference was not statistically significant ($P = 0.4$).

The amount of CAL gain for patients with membrane exposure (4.2 ± 1.0 mm) was significantly lower than those without membrane exposure (5.9 ± 1.5 mm) ($P < 0.001$) 1 year after surgery. The amount of PD reduction was also significantly lower in patients with membrane exposure than those in patients without membrane exposure ($P < 0.005$). No significant difference in gingival recession was noted between patients with or without membrane exposure (Table 3).

The associations between the amount of CAL gain one year after surgery and other variables were also determined. These variables included baseline CAL, PD, gingival recession, first year FMPS and FMBS, and patient age and smoking habit. Patients with higher baseline CAL loss and deeper PD were found to have significantly more CAL gain for the first year after the surgery ($P < 0.0001$). Patients with higher FMPS ($P < 0.0001$) were shown to have less CAL gain for the first year. No associations of 1-year CAL gain with age and smoking were found.

A multivariate linear regression model was fitted to determine the effects of these variables on 1-year CAL gain. After adjusting for other variables, membrane exposure ($P < 0.001$) and FMPS ($P < 0.001$) were significantly associated with the 1-year CAL gain. With same levels of full mouth plaque scores, patients with membrane exposure had a lower CAL gain of 1.36 mm when compared to those without membrane exposure.

Comparison of 1- and 4-Year Follow-Up Visits

No significant differences between genotype negative and positive groups in FMPS (8.9 ± 1.6 for negative and 9.1 ± 1.3 for positive patients) or FMBS (6.8 ± 1.4 for negative and 6.6 ± 1.4 for positive patients) were noted at the 4-year follow-up visit. Both groups of patients showed a significant loss in CAL ($P < 0.001$) and increase in PD ($P < 0.001$) at year 4 when compared to the year 1 visit. No change in gingival recession was noted. Additionally, all the clinical measurements taken at the year 4 visit still showed a significant difference from those of baseline (Table 2).

Genotype positive patients showed significantly more CAL loss (2.3 ± 1.1 mm) between the first and the fourth year after the surgery when compared to genotype negative patients (1.0 ± 1.1 mm) ($P < 0.002$). Genotype positive patients also had significantly more

Table 3.

Comparison of Changes in Clinical Variables at 1-Year Follow-Up Between Sites With and Without Membrane Exposure (in mm)

Membrane Exposure	N	CAL Gain	PD Reduction	REC Increase
No	24	5.9 ± 1.5	6.9 ± 1.3	1.0 ± 0.8
Yes	16	4.2 ± 1.0	5.7 ± 1.2	1.5 ± 0.8
P		0.0007	0.0046	0.37 (NS)*

* Not significant.

increase in PD (2.2 ± 1.1 mm) than genotype negative patients (0.9 ± 1.1 mm) (P<0.001). No difference was noted in the change of gingival recession between genotype groups over the follow-up period (Table 4).

The associations between other variables and the amount of CAL loss from 1 to 4 years after surgery were determined. The variables included the first and fourth year FMPS and FMBS, local plaque and bleeding scores at the year 4 visit, and patient age and smoking habit. Patients with high FMBS at year 1 visit showed significantly more CAL loss (P <0.0005). Patients with high FMBS (P<0.0001), high local plaque scores (P<0.002) and local bleeding scores (P<0.003) at the year 4 visit were shown to have more CAL loss between 1 and 4 years after the surgery.

A multiple linear regression model was fitted to determine the effects of these variables on CAL loss between 1 and 4 years after the GTR surgery. After adjusting for other variables, FMPS at the year 4 visit (P<0.0004) was significantly associated with CAL loss over the follow-up period. Genotype was an effect modifier as demonstrated by the statistically significant interaction between FMPS and IL-1 genotype (P <0.0003). From the multiple linear regression model, for each one score increase in FMPS, genotype-negative patients increased attachment loss by 0.44 mm, and genotype-positive patients had increased attachment loss by 0.56 mm.

Stability of the Regenerated Attachment

Patients with less than 2 mm regenerated CAL loss between the year 1 and 4 follow-up visits were considered having a stable GTR result. Those who lost 2 mm or more CAL during the same period were considered having true loss of the regenerated attachment. Significant association between IL-1 genotype and stability of the regenerated attachment was noted (OR = 9.95; 95% CL: 2.13-46.56) (Table 5). Patients with positive IL-1 genotype were significantly more likely to lose the regenerated attachment between the follow-up periods than patients with negative genotype.

Table 4.

Comparison of Clinical Parameter Changes Between Genotypes (4-year versus 1-year follow-up; in mm)

Genotype	N	CAL Loss	PD Increase	REC Increase
Negative	26	1.0 ± 1.1	0.9 ± 1.1	0.2 ± 0.4
Positive	14	2.3 ± 1.1	2.2 ± 1.1	0.1 ± 0.3
P		0.0015	0.0004	0.47 (NS*)

* Not significant

Table 5.

Association Between Genotype and the Stability of CAL 1 and 4 Years After Surgery

Genotype	CAL loss	
	<2 mm	≥2 mm
Negative	19	7
Positive	3	11

OR = 9.95 (2.13–46.56)

A logistic regression model was fitted to evaluate the association of the IL-1 genotype to the stability of the regenerated attachment while adjusting for significant confounders. FMPS was significantly associated with the stability of the regenerated attachment (P <0.002). IL-1 genotype was a significant effect modifier as demonstrated by the statistically significant interaction between FMPS and IL-1 genotype (P <0.001). The stability of the regenerated attachment in genotype-negative patients was affected only by their FMPS. For each 1 score of FMPS increase, genotype-negative patients had increased odds of 2.8 to lose CAL ≥2 mm than those with lower FMPS, and genotype-positive patients had increased odds of 3.8 than those of lower FMPS. For each 2 scores of FMPS increase, genotype-negative patients had increased odds of 7.2 to lose CAL 2 mm or more than those with lower FMPS and genotype-positive patients had increased odds of 14.6 than those of lower FMPS.

DISCUSSION

The results of the IL-1 genetic test indicated that 14 out of the 40 patients in our study were genotype-positive. This gives a prevalence of 35% which is similar to approximately 30% reported for Northern European Caucasians[16] and for Hispanics.[23-24]

Significant CAL gain was evident at the year 1 follow up for all patients, indicating that both genotype-negative and -positive patients can be successfully treated with GTR. In fact, at year 1, the amount of clinical attachment gain, reduction in probing depth, and increase in gingival recession did not differ statistically between genotype-positive and genotype-negative patients. Results demonstrated both a clinically and statistically significant gain in clinical attachment and reduction in probing depth with no clinically significant increase in recession of the gingival margin.

Baseline CAL, PD, plaque scores, and membrane exposure were associated with the amount of CAL gain for the first year. These findings were in agreement with previous GTR studies,[12,26-28] which have indi-

cated that the amount of clinical attachment gained with the GTR surgical procedure is correlated positively with the initial depth of periodontal defects and negatively with patient level of plaque accumulation and gingival inflammation.[12]

Furthermore, bacterial plaque colonizing clinically exposed membrane materials has been indicated as one of the main factors in jeopardizing the healing process after GTR surgery.[26,27,29,30] A negative correlation between the amount of bacteria colonizing the barrier material and the amount of clinical attachment gain has been reported.[26-28,31]

Neither patient age or genotype had an effect on the CAL gain the first year after surgery. When all the variables were considered together with the multivariate analysis, only full-mouth plaque scores and membrane exposure incidence correlated with the amount of CAL gain. Higher plaque scores resulted in less CAL gain for the first year after surgery. In the present study, with the same levels of oral hygiene, patients with membrane exposure showed 1.36 mm lower in CAL gain than those without membrane exposure. This again demonstrates the importance of plaque control, primary closure of the membrane, and minimal stress of the surgical flaps.

The first year after GTR surgery was considered as a healing period of regeneration. After the first year, the effort was focused on the maintenance of the regenerated attachment. During the maintenance phase (between year 1 and year 4 follow-up) patients were provided with a regimen of periodontal maintenance consisting of professional oral hygiene recalls every 3 months.

The clinical measurements were taken again at the year 4 follow-up visit. All the patients demonstrated relative small, but significant, changes in CAL and PD over the 3 years. An overall average of 1.65 mm was lost during this 3 year maintenance period. This finding is similar to that reported in studies on the stability of the clinical outcomes 5 years following GTR therapy.[10]

Genotype-positive patients demonstrated significantly more CAL loss than the genotype-negative patients. There was no difference in FMPS and FMBS between patients with different genotypes. Without considering other variables, on average, genotype-negative patients lost 18.9% of their first year gained CAL (1.0 mm of 5.5 mm first year gain). However, genotype-positive patients lost 45.1% of their first year gain (2.3 mm of 5.1 mm). Therefore, the data indicate that although both genotype-positive and -negative patients demonstrated significant gain in CAL at 1 year, patients with a positive genotype lost almost half of their gained CAL during the 3-year maintenance period. In both genotype groups the loss of attachment was due to a deepening of the probing depth since the gingival margin remained stable between 1- and 4-year examinations.

Patients enrolled in the present study were divided into 2 groups on the basis of the amount of clinical attachment lost during the maintenance phase. Patients with <2 mm of CAL loss between the first and the fourth year visit were compared to those who had ≥2 mm of attachment loss. Overall, the need for a strong periodontal maintenance program was clearly confirmed, given that 45% of the patients demonstrated ≥2 mm loss of attachment. However, there was a clear distinction by genotype with 27% (7/26) of the genotype-negative and 79% (11/14) of the genotype-positive patients exhibiting ≥2 mm loss between the first and fourth year follow-up examinations. In the present data, genotype-positive patients were 9.95 times more likely to lose ≥2 mm or more of the gained CAL.

When all the variables are considered together, FMPS at the year 4 visit was significantly associated with the amount of CAL loss and the stability of the regenerated attachment. Genotype was a strong modifier. IL-1 genotype positive is a high IL-1 producer. The amplification effects of high IL-1 producers on plaque levels have been recently reported by Socransky et al.[32] They concluded that genotype-positive patients exhibit greater levels of harmful pathogens more frequently than those who are genotype-negative.[32] Since these pathogens are known to trigger the production of IL-1, and genotype-positive patients over produce IL-1, this interaction leads to greater tissue destruction more quickly in genotype-positive patients. Our findings appear to support this destructive interaction, thus indicating the need for more aggressive therapy and maintenance for these high risk individuals.

No association of smoking to GTR results is discussed, given the limited number of smokers (8) included in the present research. Substantial evidence exists demonstrating the negative impact of smoking on the breakdown of periodontal tissues, including the recent finding by McGuire and Nunn[21] of the mutliplicative effect of smoking and genotype. We believe that further research should be conducted on the interrelationship and impact of various risk factors; e.g., smoking and genotype, on maintenance of regenerated tissue.

In summary, GTR can be used to treat IL-1 genotype-positive patients, although a stronger plaque control regimen might be necessary for these patients in order to maintain the treatment outcomes achieved.

With the added patient information and risk factor assessment, we, as clinicians, can now focus our efforts by controlling the variables most dominant in influencing the treatment response to GTR therapy as well as those most critical in maintaining the positive treatment results achieved. This can lead to more predictable GTR treatment and cost-effective outcomes for the patient and for the clinician.

CONCLUSION

In conclusion, the results of the present study demonstrate that surgical techniques based upon the principles of GTR are an effective treatment modality for the management of deep intrabony defects. Furthermore, they indicate that, in addition to FMPS, membrane exposure has the greatest impact on treatment response (1 year) whereas, genotype expression has the greatest impact on long-term stability (4 years).

This study also indicates that the clinical outcomes achieved with the GTR cannot be fully sustained even if patients are maintained with a regular 3-month interval recall program. If one considers the 2 genotype groups separately, it becomes apparent that the genotype-positive group lost more than twice the amount of attachment than that lost by the genotype-negative group. This high risk group (IL-1 genotype-positive) demonstrated a 10 times greater likelihood of loosing ≥2 mm of CAL between the first and fourth year.

The findings from this study support the contention that genotype-positive patients are more prone to periodontal breakdown more quickly than genotype-negative patients and emphasizes the need for more aggressive supportive periodontal therapy in maintaining these patients.

If these data are confirmed, the IL-1 genetic test could become a useful tool in treatment planning before GTR surgery. The presence of a positive response will not be a contraindication to the GTR surgery, but might indicate a greater likelihood of experiencing CAL loss during the maintenance phase and thus the need to enroll the patients in a more aggressive maintenance protocol and a more accurate bacterial control than the one adopted in the present study.

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