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Review Article

Periodontal tissue regeneration combined with orthodontics can restore periodontal function and improve quality of life in patients with periodontitis

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Abstract: Objective: This study aimed to explore the effectiveness of periodontal tissue regeneration combined with orthodontics for treating periodontitis and related contributing factors. Methods: We randomly assigned 185 patients with periodontitis admitted in our Hospitals to receive periodontal tissue regeneration (the control group, CG, n=85) or to receive periodontal tissue regeneration combined with orthodontics (the intervention group, IG, n=100). The clinical efficacy, recovery of periodontal function, and incidence of adverse reactions in both groups were monitored. Serum levels of interleukin-10 (IL-10) and interleukin-6 (IL-6) before and after treatment were measured by enzyme-linked immunosorbent assay (ELISA). The pain intensity was assessed by the visual analog scale (VAS) and the quality of life by the oral health-related quality of life (OHRQOL) scale. Risk factors affecting the treatment effectiveness of patients were explored by the logistic multivariate regression analysis. Results: The two groups were not different in the incidence of adverse reactions. Patients from IG showed superior clinical efficacy and recovery of periodontal function as compared with those from CG. IG had markedly lower VAS score and higher QHRQOL score than CG. Serum levels of IL-10 and IL-6 were markedly lower in IG than in CG. According to the logistic multivariate regression analysis, risk factors affecting the treatment effectiveness of patients included course of disease, smoking, treatment method, IL-10, and IL-6. Conclusion: Periodontal tissue regeneration combined with orthodontics can improve the clinical efficacy for treating periodontitis, suppress the inflammatory response, and enhance the quality of life.

Keywords: Periodontal tissue regeneration combined with orthodontics, periodontitis, periodontal function, quality of life

Introduction

Periodontitis is an inflammatory disease caused by immune destruction induced by oral bacteria, manifesting as pathological loss of periodontal ligaments and alveolar bone [1, 2]. Nearly 50% of adults in the United States suffer from periodontitis, those with severe periodontitis accounting for about 10% [3]. Severe periodontitis will damage the physical health and quality of life of patients, but effective treatment methods can help improve the quality of life [4]. Existing treatments for periodontitis are diversified, from daily interventions like smoking cessation and diet changes to treatment regimens such as drugs, surgery, and instrumental cleaning, but none of them shows superiority [5]. Here, we conducted a comparative study of surgical treatment alone or combined with instrumental cleaning for periodontitis, hoping to provide new ideas for improving the quality of life of patients with periodontitis.

Periodontal tissue regeneration can address the deficiencies of conventional treatments for periodontitis such as open flap debridement and shows advantages in improving adhesion, reducing the depth of periodontal pockets, and relieving gingival recession [6]. Periodontal tissue regeneration is as effective as routine therapies for treating severe periodontitis such as aggressive periodontitis [7]. It also shows good clinical efficacy in the treatment of gingival recession in terms of probing depth reduction

and aesthetic effect [8]. Orthodontics, another option for periodontitis treatment, can improve the dentition of patients and can be combined with periodontal surgeries to treat patients with periodontitis [9]. Periodontal tissue regeneration combined with orthodontics can reduce alveolar bone density and improve periodontal conditions at bone defect sites [10, 11].

So far few studies have been reported on the efficacy and related contributing factors of the above two treatments in patients with periodontitis. Therefore, we conducted this study to compare the efficacy of periodontal tissue regeneration with orthodontics and periodontal tissue regeneration alone for treating patients with periodontitis, to provide guidance on choosing treatment regimens for patients with periodontitis.

Materials and methods

Basic information

We randomly assigned 185 patients with periodontitis admitted in Stomatological Hospital of Southern Medical University and The Affiliated Stomatological Hospital of Nanchang University from June 2014 to August 2017 to receive periodontal tissue regeneration (the control group, CG, n=85) or to receive periodontal tissue regeneration combined with orthodontics (the intervention group, IG, n=100). CG comprised 48 males and 37 females who were aged 22-59 years, with a mean age of 54.96±6.84 years, while IG comprised 50 males and 50 females who were aged 24-62 years, with a mean age of 56.67±7.90 years. This study was approved by the ethics committee of Stomatological Hospital of Southern Medical University and The Affiliated Stomatological Hospital of Nanchang University. All the research subjects and their guardians signed the informed consent form with full knowledge of this study. Inclusion criteria: Patients diagnosed with periodontitis [12]; patients with no contraindications for periodontal tissue regeneration or orthodontics; patients in compliance with the criteria proposed by Armitage [13]; patients with at least 16 teeth located on 4 different dental hemi-arches; patients with no more than 2 years of course of disease. Exclusion criteria: Those under the age of 18 or over 65 years; those with a history of periodontal tissue regeneration or orthodontics treatment; those who had taken drugs that may affect the indicators of this study within the past six months; those with malignant tumors or other types of oral diseases. The inclusion criteria were applicable to both groups of patients.

Treatment methods

Periodontal tissue regeneration: We cleaned the patient's gums first, followed by subgingival scaling of the suppurative tissue and root planning. We performed a periodontal flap surgery on patients with severe dental bone damage and deep periodontal pockets, implanted artificial bone in the bone defect area near the margin of the alveolar ridge, and then sutured the mucoperiosteal flap. Finally, we cleaned the damaged gum tissue.

Orthodontics: We fixed the patient's mouth with a molar-bonded buccal tube, applied the straight wire appliance to the displaced tooth section, and aligned the teeth with 0.25 mm nickel-titanium wire. Then we moved the nickel-titanium wire to close the diastema or to leave 2-3 mm space between teeth for repair. After orthodontic treatment, we used the lingual retaining appliance for fixation. We also guided patients on how to properly clean and maintain the oral appliance. We stopped fastening the screw right away if inflammation occurred. Patients were scheduled to receive periodontal maintenance every 3 months.

Patients from CG were treated with periodontal tissue regeneration alone, while patients from IG were treated with periodontal tissue regeneration combined with orthodontics. Both groups received basic oral treatment and oral hygiene education before treatment.

Efficacy evaluation

A complete response referred to a complete disappearance of periodontal redness, swelling, and pain, a marked decrease in the gingival index (GI), plaque index (PLI), sulcus bleeding index (SBI), probing depth (PD), clinical attachment loss (CAL), and a normal periodontal appearance. A moderate response referred to relief of periodontal redness, swelling, and pain, a moderate decrease in GI, PLI, SBI, PD, CAL, and an improved periodontal appearance. No response referred to no improvement of periodontal redness, swelling, and pain and periodontal appearance, and unchanged or

even higher GI, PLI, SBI, PD, and CAL. Total effective rate = (case number of complete response + case number of moderate response)/ total number of cases × 100%.

Outcome measures

The two groups were compared in clinical efficacy, adverse reactions, and the oral health-related quality of life (QHRQOL) score [14] after treatment, and in levels of periodontal indexes that reflect the periodontal function (GI, PLI, SBI, PD, CAL), visual analog scale (VAS) score [15], interleukin-10 (IL-10) concentration, and interleukin-6 (IL-6) concentration 3 months before or after the treatment. The OHRQOL score was measured by the Oral Health Impact Profile (OHIP-14), with scores ranging from 0 to 56 points (the score is proportional to the quality of life). VAS scores range from 0 to 10 points and the score is proportional to the pain intensity. GI (0-5 points) was used to assess the gum color, gum quality, and bleeding tendency, PLI (0-3 points) to assess the area and thickness of dental plaque, SBI (0-5 points) to assess the status, bleeding, color, and shape of the gum, PD to assess the depth of the gingival and periodontal pocket, which is the distance from the gingival margin to the bottom of the pocket or sulcus, and CAL to assess the distance from the cemento-enamel junction to the bottom of the pocket or sulcus. Serum levels of IL-10 and IL-6 were measured by the enzyme-linked immunosorbent assay (ELISA) [16], in strict accordance with the instructions of human IL-10 ELISA and human IL-6 ELISA kits (Fanke Biotechnology Co., Ltd., Shanghai, China, FK-R0066, FK-R0049).

Statistical analysis

Count data were expressed by the case number/percentage (n/%) and its intergroup comparison was analyzed by the chi-square test. The correction for continuity was used when the theoretical frequency in the chi-square test was less than 5. Measurement data were expressed by the mean ± SD. Its intergroup comparison was analyzed by the independent sample t-test and its intragroup comparison by the paired t-test. GraphPad Prism 6 (GraphPad Software, San Diego, USA) was used to analyze and visualize those data. Risk factors affecting the treatment efficacy in periodontitis patients were subjected to the multivariate logistic regression analysis and the data were analyzed on SPSS22.0 (Beijing Baiao Yijie Technology Co., Ltd., China). The difference was statistically significant when $P<0.05$.

Results

Baseline data

Patients from the two groups were not markedly different in sex ratio, age, average age, body mass index (BMI), course of disease, degree of tooth mobility, bad breath, diabetes, drinking, smoking, marital status, high-density lipoprotein-cholesterol (HDL-C), and low-density lipoprotein-cholesterol (LDL-C) ($P<0.05$). More details are shown in **Table 1**.

Comparison of clinical efficacy

IG had a markedly higher total effective rate than CG (92.00% vs. 77.65%, $P<0.05$). More details are shown in **Table 2**.

Recovery of periodontal function and the VAS score

The two groups were not different in GI, PLI, SBI, PD, CAL and the VAS score before treatment ($P>0.05$). The expression levels of those periodontal indexes and the VAS score were reduced in both groups after treatment, with a sharper reduction in IG than in CG, and the differences were statistically significant ($P<0.05$). More details are shown in **Figure 1**.

Adverse reactions

There was no significant difference between CG and IG in the incidence of adverse reactions including facial swelling, dizziness, and vomiting (11.76% vs. 6.00%, $P>0.05$). More details are shown in **Table 3**.

Serum levels of IL-10 and IL-6

CG and IG were not significantly different in serum levels of IL-10 and IL-6 before treatment ($P>0.05$). Serum IL-10 showed a marked increase after treatment, while serum IL-6 showed a marked decrease. IG had notably higher serum IL-10 level and lower serum IL-6 level than CG after treatment ($P<0.05$). More details are shown in **Figure 2**.

The OHRQOL scores

The overall score, physical, mental, and social well-being scores of the OHRQOL scale were

Table 1. Baseline data of patients [n (%), mean ± SD]

Factors	n	Control group (n=85)	Intervention group (n=100)	χ^2/t	P
Sex				0.772	0.380
Male	98	48 (56.47)	50 (50.00)		
Female	87	37 (43.53)	50 (50.00)		
Age (year)				0.023	0.879
<55	86	39 (45.88)	47 (47.00)		
≥55	99	46 (54.12)	53 (53.00)		
Average age (year)	185	54.96±6.84	56.67±7.90	1.560	0.121
BMI (kg/m^2)	185	23.71±2.29	23.90±2.48	0.538	0.591
Course of disease (month)	185	8.85±4.31	8.97±4.45	0.185	0.853
Degree of tooth mobility				0.722	0.395
I	83	41 (48.24)	42 (42.00)		
II	102	44 (51.76)	58 (58.00)		
Bad breath				0.816	0.366
No	111	54 (63.53)	57 (57.00)		
Yes	74	31 (36.47)	43 (43.00)		
Diabetes				1.283	0.257
No	142	62 (72.94)	80 (80.00)		
Yes	43	23 (27.06)	20 (20.00)		
Drinking				0.491	0.483
No	116	51 (62.20)	65 (65.00)		
Yes	69	34 (37.80)	35 (35.00)		
Smoking				0.383	0.536
No	124	55 (64.71)	69 (69.00)		
Yes	61	30 (35.29)	31 (31.00)		
Marital status				1.427	0.232
Unmarried	65	26 (30.59)	39 (39.00)		
Married	120	59 (69.41)	61 (61.00)		
HDL-C (mM)	185	0.91±0.38	1.02±0.46	1.754	0.081
LDL-C (mM)	185	2.97±1.06	2.88±0.85	0.641	0.523

Table 2. Comparison of clinical efficacy [n (%)]

Group	n	Complete response	Moderate response	No response	Total effective rate
Control group	85	37 (43.53)	29 (34.12)	19 (22.35)	77.65
Intervention group	100	62 (62.00)	30 (30.00)	8 (8.00)	92.00
χ^2	-	-	-	-	7.594
P	-	-	-	-	0.006

statistically higher in IG than in CG (P<0.05). More details are shown in **Figure 3**.

Risk factors affecting the treatment efficacy of periodontitis patients

In this study, 158 patients had a complete or moderate response to treatment, and 27 patients had no response. We compared clinical parameters and related indicators between those with a complete or moderate response and those with no response. The comparison between patients with a complete or moderate response and those with no response showed no significant difference in sex ratio, age, average age, BMI, degree of tooth mobility, bad breath, diabetes, drinking, marital status, HDL-C, and LDL-C (P>0.05), but revealed marked differences in the course of disease, smoking, the treatment method, IL-10 level, and IL-6 level (P<0.05). Factors showing differences were subjected to multivariate logistic regression analysis. The course of disease (P=0.003), smoking (P=0.015), treatment method (P=0.005), IL-10 level (P=0.038), IL-6 level (P=0.001) were independent risk factors affecting the treatment efficacy of patients with periodontitis. Periodontitis patients who were treated with periodontal tissue regeneration alone and who had a longer course of disease, a smoking history, a lower IL-10 level, and a higher IL-6 level were vulnerable to a higher risk of showing no response to treatment. More details are shown in **Tables 4**-**6**.

Discussion

Periodontitis is a chronic inflammatory oral disease related to the infectious destruction of alveolar cortical bone, and its risk factors include genetic inheritance, smoking, and malnutrition [17, 18]. Existing treatments for periodontitis include surgical treatment and non-surgical treatment. Surgeries show superior clinical efficacy in patients with advanced peri-

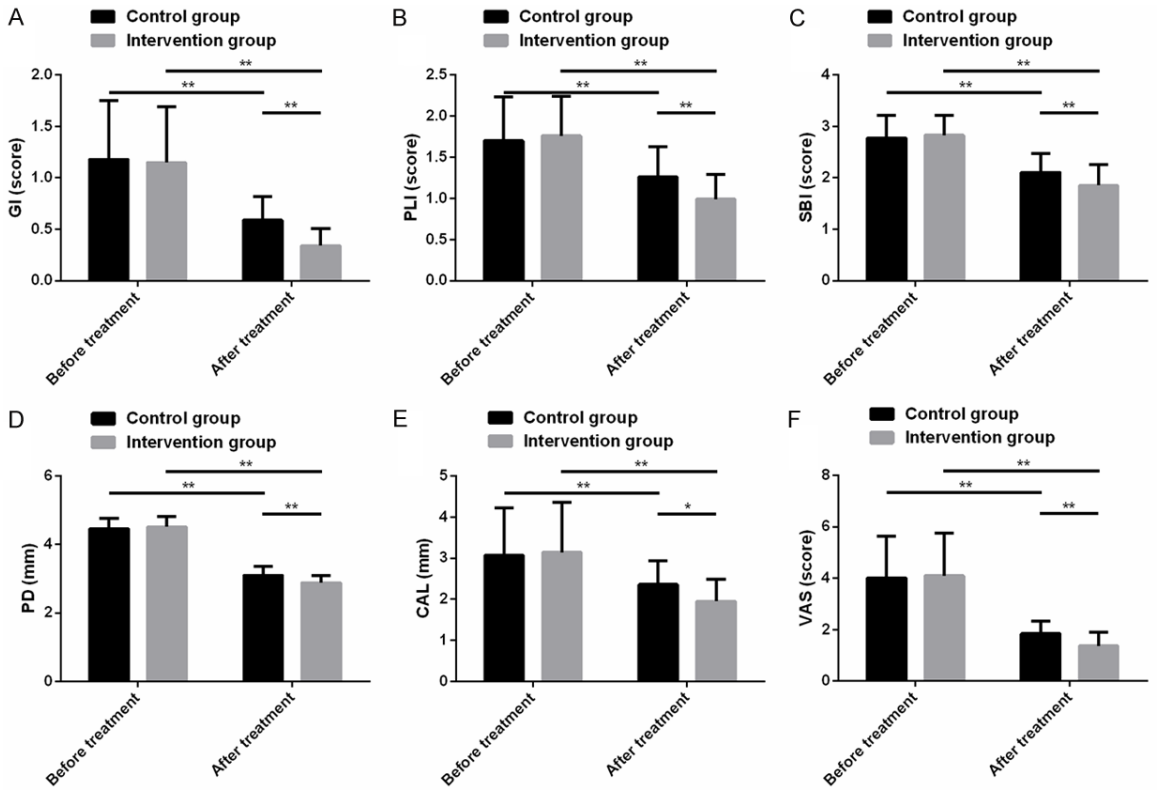

Figure 1. Recovery of periodontal function and the VAS score. A: GI level was reduced after treatment in IG, markedly lower than that in CG. B: PLI level was reduced after treatment in IG, markedly lower than that in CG. C: SBI level was reduced after treatment in IG, markedly lower than that in CG. D: PD level was reduced after treatment in IG, markedly lower than that in CG. E: CAL level was reduced after treatment in IG, markedly lower than that in CG. F: VAS score was reduced after treatment in IG, markedly lower than that in CG. Note: *P<0.05, **P<0.01.

Table 3. Comparison of adverse reactions [n (%)]

Factors	Control group (n=85)	Intervention group (n=100)	χ^2	P
Facial swelling	4 (4.71)	3 (3.00)	-	-
Dizziness	3 (3.53)	3 (3.00)	-	-
Vomiting	3 (3.53)	0 (0.00)	-	-
Total	10 (11.76)	6 (6.00)	1.933	0.165

odontal disease, which can significantly shrink the short-term and long-term periodontal and reduce patients' need for additional adjuvant therapy [19]. Periodontal tissue regeneration and orthodontics are surgical treatment options for patients with periodontitis. Here we explored the efficacy of these two treatments and related factors, aiming to provide guidance for the treatment choices of periodontitis.

There are abundant studies that investigate the treatment effectiveness and underlying mechanisms of periodontal tissue regeneration or orthodontics treatment for patients with periodontitis. In the study by Jepsen [20], periodontal tissue regeneration showed significant advantages in improving bifurcation defects in patients with periodontitis over surgical debridement. The study by Bollen et al. [21] demonstrated that orthodontics could improve the periodontal condition by reducing the difficulty in plaque removal and controlling the incidence of occlusal trauma. This study made a comparison between periodontal tissue regeneration combined with orthodontics and periodontal tissue regeneration alone in treating periodontitis. Patients from IG showed stronger responses to treatment and better recovery of periodontal indexes (GI, PLI, SBI, PD, and CAL), suggesting that periodontal tissue regeneration combined with orthodontics has superior efficacy in the treatment of periodontitis.

VAS is a tool to quantify the pain intensity of patients with periodontitis, while OHRQOL works to assess the quality of life of patients with periodontitis [22, 23]. Here we employed VAS

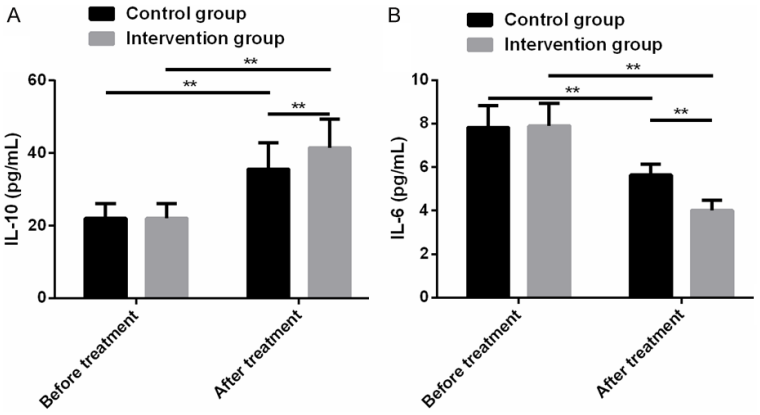

Figure 2. Serum levels of IL-10 and IL-6. A: Serum IL-10 level was notably increased in IG after treatment, markedly higher than that in CG. B: Serum IL-16 level was notably reduced in IG after treatment, markedly higher than that in CG. Note: **P<0.01.

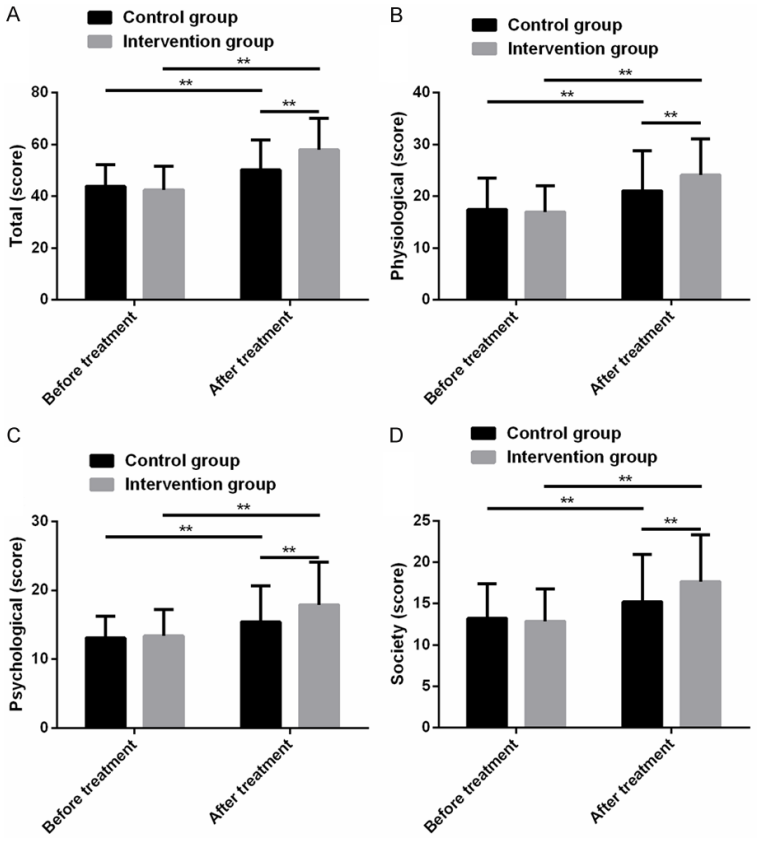

Figure 3. The OHRQOL scores. A: The overall score of the OHRQOL scale was higher in IG than in CG. B: The physical well-being score of the OHRQOL scale was higher in IG than in CG. C: The mental well-being score of the OHRQOL scale was higher in IG than in CG. D: The social well-being score of the OHRQOL scale was higher in IG than in CG.

and OHRQOL to assess the pain intensity and quality of life of patients with periodontitis under the two treatments. Patients from IG had lower pain intensity and higher quality of life after treatment, indicating that periodontal tissue regeneration combined with orthodontics does better in relieving pain and improving the quality of life of patients with periodontitis. Patients from both IG and CG suffered from adverse reactions such as facial swelling, dizziness, and vomiting. The incidence of adverse reactions was slightly lower in IG than in CG, but the difference was not significant, suggesting an approximate safety of these two treatments. The pathological mechanism of periodontitis involves the stress inflammatory response of host and biofilm structure to microbial invasion and is related to inflammation-related serological indicators including IL-10 and IL-6 [24, 25]. The genetic polymorphisms of IL-10 and IL-6 are in close relationship with aggressive periodontitis [26]. We studied the effects of two treatments on serum IL-10 and IL-6. IG had increased IL-10 level and decreased IL-6 level, implying that periodontal tissue regeneration combined with orthodontics can greatly suppress excessive inflammation in patients with periodontitis. We finally analyzed the risk factors that sway the efficacy of patients with periodontitis and identified the course of disease, smoking, the treatment method, IL-10, and IL-6. The results demonstrated that periodontitis patients who were treated with periodontal tissue regeneration alone and who had a longer course of disease, a smoking history, a lower IL-10 level, and a higher IL-6 level had a higher risk of showing no response to treatment. The study by Papantonopoulos et al. [27] concluded that smoking can compromise

Table 4. Univariate analysis of factors affecting the efficacy of periodontitis patients [n (%), mean ± SD]

Factors	n	Complete or moderate response (n=158)	No response (n=27)	χ^2/t	P
Sex				0.085	0.771
Male	98	83 (52.53)	15 (55.56)		
Female	87	75 (47.47)	12 (44.44)		
Age (year)				0.420	0.517
<55	86	75 (47.47)	11 (40.74)		
≥55	99	83 (52.53)	16 (59.26)		
Average age (year)	185	55.81±7.19	56.72±7.96	0.598	0.550
BMI (kg/m^2)	185	23.68±2.24	24.07±2.53	0.820	0.413
Course of disease (month)	185	7.56±3.74	9.31±4.87	2.144	0.033
Degree of tooth mobility				0.002	0.962
I	83	71 (44.94)	12 (44.44)		
II	102	87 (55.06)	15 (55.56)		
Bad breath				0.875	0.350
No	111	97 (61.39)	14 (51.85)		
Yes	74	61 (38.61)	13 (48.15)		
Diabetes				0.128	0.721
No	142	122 (77.22)	20 (74.07)		
Yes	43	36 (22.78)	7 (25.93)		
Drinking				0.212	0.645
No	116	98 (62.03)	18 (66.67)		
Yes	69	60 (37.97)	9 (33.33)		
Smoking				9.884	0.002
No	124	113 (68.35)	11 (59.26)		
Yes	61	45 (31.65)	16 (40.74)		
Marital status				0.050	0.823
Unmarried	65	55 (34.81)	10 (37.04)		
Married	120	103 (65.19)	17 (62.96)		
HDL-C (mM)	185	0.95±0.40	1.04±0.47	1.052	0.294
LDL-C (mM)	185	3.08±1.14	2.79±0.83	1.265	0.208
Treatment method				7.594	0.006
Combined treatment	100	92 (58.23)	8 (29.63)		
Single treatment	85	66 (41.77)	19 (70.37)		
IL-10 (pg/ml)	185	39.14±7.37	27.81±5.63	7.611	<0.001
IL-6 (pg/ml)	185	5.13±0.68	7.50±0.94	15.748	<0.001

Table 5. Assignment for multivariate logistic regression analysis

Factors	Variables	Assignment
Course of disease	X1	Continuous variable
Smoking	X2	No =0, yes =1
Treatment method	X3	Combined treatement =0, single treatment =1
IL-10 (pg/ml)	X4	Continuous variable
IL-6 (pg/ml)	X5	Continuous variable

the efficacy of non-surgical treatment for treating periodontitis, which is similar to the results of this study. Smoking patients have a higher risk of inflammation around the implant, so the treatment efficacy of smoking patients is weakened [28].

Conclusion

Periodontal tissue regeneration combined with orthodontic treatment of patients with periodontitis has better efficacy and is superior in relieving the inflammatory response and

Table 6. Multivariate logistic regression analysis of factors affecting the efficacy of periodontitis patients

Variables	B	S.E	Wals	P	OR	95% CI
Course of disease	0.332	0.018	8.942	0.003	1.321	1.062-1.158
Smoking	1.785	0.547	5.213	0.015	2.648	1.240-6.348
Treatment method	1.349	0.462	8.571	0.005	3.996	1.598-10.287
IL-10	1.051	0.534	5.396	0.038	2.435	1.196-6.590
IL-6	0.118	0.041	12.973	0.001	1.123	1.051-1.164

improving the quality of life. The innovation of this study lies in the comprehensive analysis of effects of the two treatment methods on patients in all aspects and in the assessment of risk factors affecting the treatment efficacy in periodontitis patients. There is still room for improvement in this study. For example, we should group patients according to the age to analyze the efficacy of treatment options for patients of different ages. In addition, we should design an aesthetic assessment after treatment to identify the treatment regimen with better aesthetic effects. We will address such deficiencies in the future to perfect this study.

Disclosure of conflict of interest

None.

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