

Review Article

Orthodontic treatment combined with periodontal tissue regeneration improves clinical symptoms and periodontal function in patients with periodontitis

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Abstract: Periodontal tissue regeneration (PTR) is a technique commonly used in treating periodontitis; but severe periodontitis often leads to tooth migration, so the combined orthodontic treatment (OT), which is of favorable effect, is also a matter worth attention. This study aims to explore the effect of OT combined with PTR on patients with periodontitis and related inflammatory factors, and to investigate the adverse reactions. Seventy-seven patients with periodontitis treated in our hospital from February 2018 to September 2019 were divided into two groups: group A (n=40) and group B (n=37). Patients in group A received PTR surgery, while those in group B were treated with OT combined with PTR. The curative effect, adverse reactions and the effect on inflammatory factors were observed. Compared with group A, group B presented lower inflammatory factors, lower incidence of adverse reactions and better curative effects. OT combined with PTR can effectively improve the clinical symptoms of periodontitis.

Keywords: Orthodontic treatment, periodontal tissue regeneration, periodontitis, clinical symptoms, periodontal function

Introduction

Periodontitis is a chronic inflammatory disease [1], which involves the degeneration of the periodontal ligament, the formation of periodontal pockets and the absorption of alveolar bone; leading to the destruction of the supporting structure of the teeth. According to the World Health Organization, 10-15% of the global population suffers from severe periodontitis [2, 3]. Poor oral health can exert a major impact, leading to tooth loss, pain and discomfort; and may prevent the elderly from chewing food properly, often resulting in malnutrition and thus is a hazard to patients' quality of life [4]. The burden of periodontal disease and its impact on overall health and the patients' quality of life call for effective treatment of this disease in the clinic [5]. Currently, periodontal tissue regeneration (PTR) is a common treatment for periodontitis, in which new cementum, alveolar bone and functional periodontal membranes are formed [6], thus reducing the progression of the disease and subsequent periodontal tissue rup-

ture. However, this treatment can only clean necrotic tissue and control inflammation, which limits the recovery of periodontal tissue [7]. Severe periodontitis usually leads to pathological tooth migration, in which case orthodontic rearrangement is an essential complement to periodontal management [8]. Orthodontic treatment (OT) can successfully align pathologically migrated teeth and improve periodontal stability in patients with periodontitis [9] while improving facial appearance and chewing by adjusting the teeth [10]. Therefore, this study explored the effect of OT combined with PTR on periodontitis, so as to provide better references in treating this disease.

Materials and methods

General information

A total of 77 patients with dental periodontitis treated in our hospital from February 2018 to September 2019 were selected and divided into groups A and B. In group A, 40 patients

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Table 1. General information of patients in the two groups (x ± sd) [n (%)]

Categories	Group A (n=40)	Group B (n=37)	t/ χ^2 value	P value
Gender			0.293	0.588
Male	23 (57.50)	19 (51.35)		
Female	17 (42.50)	18 (48.65)		
Age (years old)	36.28±7.49	37.42±7.69	0.658	0.512
Height (cm)	168.34±8.24	169.50±8.43	0.610	0.543
Weight (kg)	66.28±4.29	65.29±4.58	0.979	0.330
Residence			0.000	0.975
Rural	15 (37.50)	14 (37.84)		
Urban	25 (62.50)	23 (62.16)		
Educational background			0.000	0.979
Below high school	12 (30.00)	11 (29.73)		
High school or above	28 (70.00)	26 (70.27)		
Ethnicity			0.657	0.417
Han	36 (90.00)	31 (83.78)		
Ethnic minorities	4 (10.00)	6 (16.22)		
Economic level			0.624	0.732
Poor	9 (22.50)	11 (29.73)		
Comparatively well-off	18 (45.00)	14 (37.84)		
Well-off	13 (32.50)	12 (32.43)		
Staying up late			0.251	0.616
Yes	26 (65.00)	22 (59.46)		
No	14 (35.00)	15 (40.54)		
Exercise			0.583	0.445
Yes	24 (60.00)	19 (51.35)		
No	16 (40.00)	18 (48.65)		
Obesity			0.006	0.933
Yes	18 (45.00)	17 (45.95)		
No	22 (55.00)	20 (54.05)		
Diabetes			0.010	0.919
Yes	21 (52.50)	19 (51.35)		
No	19 (47.50)	18 (48.65)		
Hypertension			0.829	0.362
Yes	17 (42.50)	12 (32.43)		
No	23 (57.50)	25 (67.57)		
Smoking			0.000	0.990
Yes	26 (65.00)	24 (64.86)		
No	14 (35.00)	13 (35.14)		
Drinking			0.528	0.467
Yes	28 (70.00)	23 (62.16)		
No	12 (30.00)	14 (37.84)		

Exclusion and inclusion criteria

Inclusion criteria: Patients confirmed with periodontitis [11] from available clinical data. This study was carried out under the approval of the Medical Ethics Committee of our hospital, and written informed consent was obtained from patients and their families after informing them of the details of this study.

Exclusion criteria: Patients with communication disorders; Patients during pregnancy or lactation; Patients who had dental treatment prior to this study; Patients during their menstrual period.

Treatment methods in the two groups

Patients in group A underwent PTR. After cleaning the gingiva, the purulent part was scraped, and the root of the tooth was leveled to inhibit plaque. Then artificial bone was placed, the mucoperiosteal flap was sutured, and the damaged part around the gingiva was removed.

In group B, OT was supplemented in addition to treatment of group A. Having fixed the mouth, the teeth were corrected to shorten or close the gap, and the teeth were arranged neatly. The orthodontic device needs to be maintained regularly during the treatment.

Outcome measures

with an average age of 36.28±7.49 years, were treated with PTR. While the remaining 37 patients in group B were treated with OT combined with PTR, with an average age of 37.42±7.69 years.

(1) Visual Analogue Scale/Score (VAS) [12] was employed to compare the pain degree between the two groups before and after treatment. On a scale of 10 points, the score was proportional to the level of pain.

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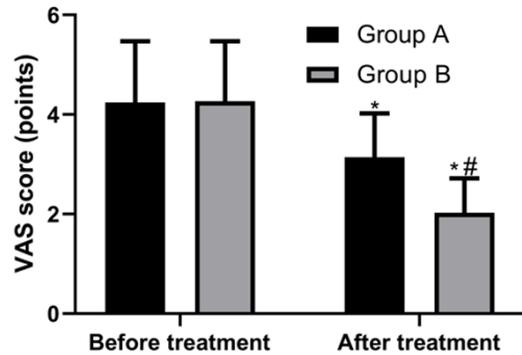


Figure 1. Pain before and after treatment in the two groups. Compared within the same group, the VAS score after treatment decreased in both groups ($P < 0.05$). Inter-group comparison exhibited that there was no difference in VAS score between the two groups before treatment ($P > 0.05$), but the post-treatment VAS score in group B was notably lower than that in group A ($P < 0.05$). Note: * indicates $P < 0.05$ compared with the same group before treatment; # indicates $P < 0.05$ compared with group A.

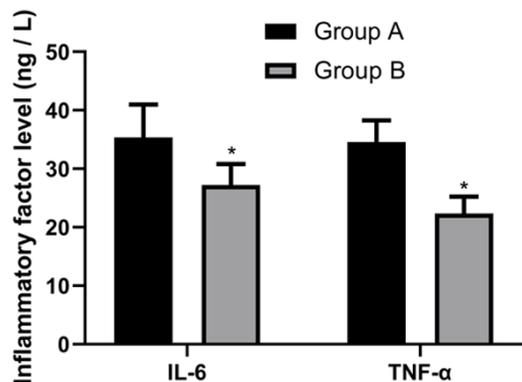


Figure 2. Inflammatory factor levels after treatment in the two groups. Group B presented remarkably lower IL-6 and TNF- α levels than group A after treatment ($P < 0.05$). Note: * indicates $P < 0.05$ compared with group A.

(2) After treatment, 5 ml of venous blood was drawn from patients in both groups and left for 20 min. The serum was then separated by centrifuge ($10 \times g$ at 4°C for 15 minutes, BMH Instrument Co., Ltd., Beijing, China) and then quick-frozen with liquid nitrogen and stored at -80°C for later use. ELISA (Elisa Biotechnology Co., Ltd., Suzhou, China) was adopted to detect IL-6 (interleukin 6) and TNF- α (tumor necrosis factor).

(3) Gingival index (GI), plaque index (PLI), clinical attachment loss (CAL) and periodontal

probing depth (PD) were observed 2 months after treatment.

(4) X-ray cephalometry was applied to measure the angle of the nasion, alveolar and lower alveolar seats (SNB angle), the angle of nasion, sella center and alveolar seat (SNA angle), as well as the angle of the nasion, upper and lower alveolar seats (ANB angle) after treatment.

(5) Efficacy evaluation of periodontitis symptoms [13]: Markedly effective: pain and redness and swelling were eliminated; Effective: pain and redness and swelling were improved; Ineffective: pain and redness and swelling did not change.

(6) The subjective satisfaction of patients, including masticatory function, aesthetic degree, dental health and overall satisfaction, was observed 5 months after treatment. With a total score of 100 points, the satisfaction was in direct proportion to the score.

Statistical analysis

Statistical analysis was performed using SPSS 21.0 (SPSS, Inc., Chicago, IL, USA). The measurement data were expressed as mean \pm standard deviation ($\bar{x} \pm \text{sd}$), and the comparison between groups was conducted by t test. While the counting data were expressed in the form of cases/percentages [n (%)], and the inter-group comparison was analyzed by the Chi-square test. $P < 0.05$ indicated a statistically significant difference.

Results

There was no significant difference in general information between the two groups

The general information did not identify any significant difference between the two groups before intervention ($P > 0.05$) (**Table 1**).

OT combined with PTR resulted in less pain

The VAS scores before and after treatment in group A were (4.24 ± 1.23) points and (3.14 ± 0.88) points; and the VAS scores in group B before and after treatment were (4.27 ± 1.20) points and (2.03 ± 0.69) points, respectively. Intra-group comparison revealed that the post-treatment VAS score dropped significantly in both groups ($P < 0.05$). Inter-group

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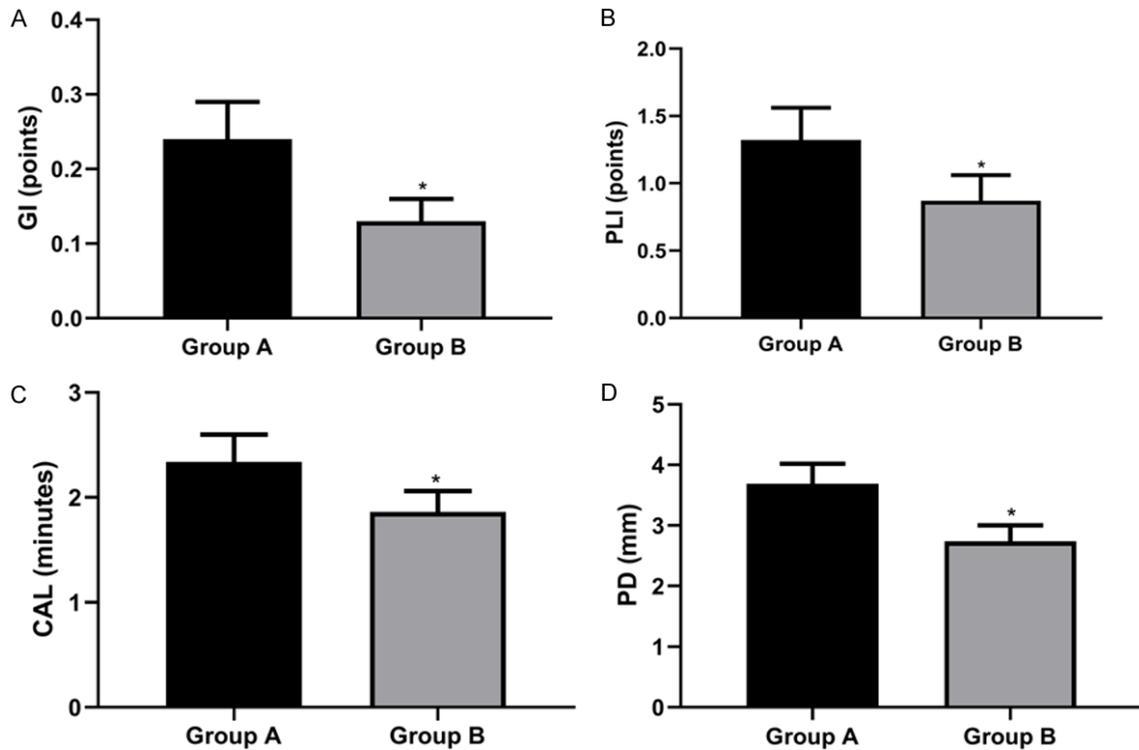


Figure 3. Post-treatment periodontal indicators in the two groups. A. Comparison of GI values between the two groups after treatment: The GI value in group B was dramatically lower than that in group A ($P < 0.05$). Note: * indicates $P < 0.05$ compared with group A. B. Comparison of PLI values between the two groups after treatment: The PLI value in group B was remarkably lower than that in group A ($P < 0.05$). Note: * indicates $P < 0.05$ compared with group A. C. Comparison of CAL values between the two groups after treatment: The post-treatment CAL value in group B was markedly lower than that in group A ($P < 0.05$). Note: * indicates $P < 0.05$ compared with group A. D. Comparison of PD values between the two groups after treatment: The post-treatment PD value in group B was obviously lower than that in group A ($P < 0.05$). Note: * indicates $P < 0.05$ compared with group A.

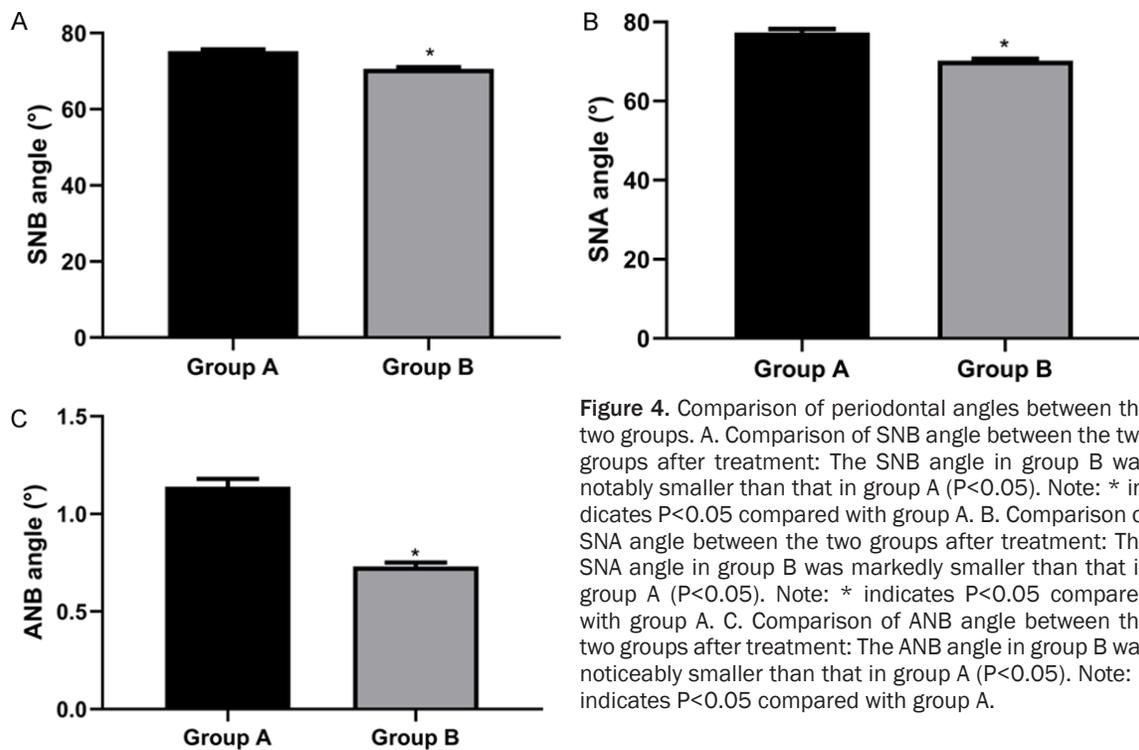


Figure 4. Comparison of periodontal angles between the two groups. A. Comparison of SNB angle between the two groups after treatment: The SNB angle in group B was notably smaller than that in group A ($P < 0.05$). Note: * indicates $P < 0.05$ compared with group A. B. Comparison of SNA angle between the two groups after treatment: The SNA angle in group B was markedly smaller than that in group A ($P < 0.05$). Note: * indicates $P < 0.05$ compared with group A. C. Comparison of ANB angle between the two groups after treatment: The ANB angle in group B was noticeably smaller than that in group A ($P < 0.05$). Note: * indicates $P < 0.05$ compared with group A.

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Table 2. Comparison of adverse reactions between the two groups [n (%)]

Adverse reactions	Group A (n=40)	Group B (n=37)	X ²	P
Peripyema	2 (5.00)	1 (2.70)	-	-
Periodontal redness	3 (7.50)	0 (0.00)	-	-
Gomphiasis	2 (5.00)	1 (2.70)	-	-
Gingival bleeding	1 (2.50)	1 (2.70)	-	-
Facial swelling	1 (2.50)	1 (2.70)	-	-
Nausea	1 (2.50)	0 (0.00)	-	-
Vomiting	2 (5.00)	0 (0.00)	-	-
Dizziness	1 (2.50)	0 (0.00)	-	-
Fever	2 (5.00)	1 (2.70)	-	-
Total incidence	15 (37.50)	5 (13.51)	5.751	0.016

The periodontal index of OT combined with PTR was better

The GI value of group A and group B was (0.24±0.05) and (0.13±0.03), respectively. The PLI value of group A and group B was (1.32±0.24) and (0.87±0.19), respectively. The CAL value of group A and group B was (2.34±0.26) points and (1.86±0.20) points, and the PD value of group A and group B was (3.69±0.33) mm and (2.74±0.26) mm, respectively. It was clear that the relevant indexes in group B were significantly lower than those in group A (P<0.05) (Figure 3).

OT combined with PTR better improved periodontal angles

OT combined with PTR resulted in less adverse reactions

The SNB angles of group A and group B were (75.28±0.45)° and (70.64±0.38)°, respectively; and the SNA angles of group A and group B were (77.39±0.85)° and (70.24±0.46)°; while the ANB angles of groups A and B were (1.14±0.04)° and (0.73±0.02)°, respectively. The relevant periodontal angles in group B were significantly smaller than those in group A (P<0.05) (Figure 4).

OT and PTR resolved periodontitis faster

The total incidence of adverse reactions in group B (13.51%) was significantly lower than that in group A (37.5%) (P<0.05) (Table 2).

OT combined with PTR was more effective

The resolution time of periodontitis in group A and group B was (25.35±2.68) d and (16.79±2.13) d, respectively (P<0.05). The resolution time of periodontitis in group B was significantly shorter than that in group A (P<0.05) (Figure 5).

OT combined with PTR was more satisfactory

The mastication function scores of group A and group B were (80.43±4.35) and (89.52±5.23),

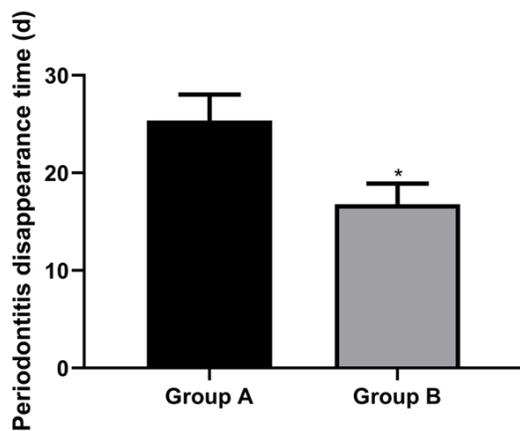


Figure 5. Comparison of periodontitis resolution time between the two groups. The resolution time of periodontitis in group B was shorter than that in group A (P<0.05). Note: * indicates P<0.05 compared with group A.

comparison demonstrated that there was no significant difference in the VAS score between the two groups before treatment (P>0.05), but the post-treatment VAS score in group B was significantly lower than that in group A (P<0.05) (Figure 1).

OT combined with PTR showed lower levels of inflammatory factors

The levels of IL-6 in group A and group B after treatment were (35.35±5.64) ng/L and (27.24±3.56) ng/L, respectively. The levels of TNF-α after treatment in groups A and B were (34.58±3.69) ng/L and (22.36±2.86) ng/L, respectively. The above data indicated that the levels of IL-6 and TNF-α in group B were significantly lower than those in group A after treatment (P<0.05) (Figure 2).

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Table 3. Comparison of efficacy between the two groups [n (%)]

Efficacy evaluation	Group A (n=40)	Group B (n=37)	χ^2	P
Markedly effective	9 (22.50)	15 (40.54)	-	-
Effective	21 (52.50)	20 (54.05)	-	-
Ineffective	10 (25.00)	2 (5.41)	-	-
Total effective rate	30 (75.00)	35 (94.59)	5.610	0.017

Table 4. Comparison of subjective satisfaction of treatment between the two groups ($\bar{x} \pm \text{sd}$)

	Group A (n=40)	Group B (n=37)	t	P
Masticatory function	80.43±4.35	89.52±5.23	8.315	<0.001
Aesthetic degree	78.24±3.67	88.64±4.62	10.980	<0.001
Gingival health	76.65±4.24	87.36±5.65	9.453	<0.001
Overall satisfaction	74.75±4.39	90.17±5.24	14.040	<0.001

respectively. The aesthetic scores of group A and group B were (78.24±3.67) and (88.64±4.62), respectively. The gingival health scores of group A and group B were (76.65±4.24) and (87.36±5.65), respectively. The overall satisfaction scores of group A and group B were (74.75±4.39) and (90.17±5.24), respectively. From the above values, we can see that the subjective satisfaction in group B was significantly higher than that in group A ($P < 0.05$) (Table 4).

Discussion

Periodontitis is a complex, chronic, inflammatory, and noncommunicable disease caused by the formation of biofilms below the gingival margins. Although pathogenic biofilms are a "necessary cause" of periodontitis, they are not sufficient in themselves to cause periodontitis; while a destructive immune inflammatory response is the key to the formation of destructive events [14]. Periodontitis is a multifactorial disease characterized by an inflammatory response to elevated levels of subgingival pathogens, resulting in connective tissue destruction and alveolar bone loss [15]. IL-6 is a pleiotropic cytokine [16], which is also a powerful stimulant of osteoclast differentiation and bone resorption. Its production is regulated by polymorphism, and higher IL-6 levels have been found locally in patients with chronic periodontitis [17]. Also a cytokine, TNF- α is related to gingival tissue destruction and remodeling

[18]. Studies have shown that periodontitis is associated with the increase of serum pro-inflammatory states, such as increased TNF- α [19]. In periodontitis, up-regulated pro-inflammatory cytokines trigger periodontal tissue destruction [20]. In this study, the levels of related inflammatory factors in the serum of patients treated with combination therapy were lower than those treated with monotherapy, which may indicate that OT combined with PTR inhibited proinflammatory factors. Some studies have reported that IL-6 signal transduction can induce related cytokines to help explain the bone destructive phenotype of periodontal apical lesions, and ultimately elucidate its systemic complications [21]; suggesting that the less adverse effects of combined therapy in this study may be caused by a lower level of proinflammatory factors. Periodontal parameters are important indicators for the observation of periodontitis, which are subject to the control of periodontitis intensity [22]. The results of periodontal parameters showed that the combination of OT and PTR significantly relieved the severity of periodontitis. According to research, periodontal parameters of patients with periodontitis remain stable during OT under strict biofilm control [23]. Furthermore, we compared the periodontal angles and observed patients' facial correction, and the results indicated that the OT combined with PTR could correct the periodontal angles of the patients, and meanwhile ensured the aesthetics of the teeth. Finally, the comparison of the efficacy and satisfaction between the two groups revealed that OT combined with PTR permitted better efficacy. In short, OT combined with PTR is more effective and less risky. Studies have shown that the combination of periodontal therapy with orthodontic invasion seems to be a good way to improve periodontal conditions, as long as the biomechanical force system and oral hygiene are controlled at the same time [24]. Other studies have shown that for patients without lateral incisors, including first premolar invasion and canine extrusion, orthodontic space closure does not pose a long-term risk of periodontal tissue deterioration or temporomandibular joint disease [25].

Conclusion

OT combined with PTR can improve the clinical symptoms and periodontal function of patients with periodontitis, and reduce related risks.

Disclosure of conflict of interest

None.

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References

- [1] Hernandez-Monjaraz B, Santiago-Osorio E, Monroy-Garcia A, Ledesma-Martinez E and Mendoza-Nunez VM. Mesenchymal stem cells of dental origin for inducing tissue regeneration in periodontitis: a mini-review. *Int J Mol Sci* 2018; 19: 944.
- [2] Joshi D, Garg T, Goyal AK and Rath G. Advanced drug delivery approaches against periodontitis. *Drug Deliv* 2016; 23: 363-377.
- [3] Slots J. Periodontitis: facts, fallacies and the future. *Periodontol* 2000 2017; 75: 7-23.
- [4] Eke PI, Wei L, Borgnakke WS, Thornton-Evans G, Zhang X, Lu H, McGuire LC and Genco RJ. Periodontitis prevalence in adults \geq 65 years of age, in the USA. *Periodontol* 2000 2016; 72: 76-95.
- [5] Chen FM, Gao LN, Tian BM, Zhang XY, Zhang YJ, Dong GY, Lu H, Chu Q, Xu J, Yu Y, Wu RX, Yin Y, Shi S and Jin Y. Treatment of periodontal intrabony defects using autologous periodontal ligament stem cells: a randomized clinical trial. *Stem Cell Res Ther* 2016; 7: 33.
- [6] Venkataiah VS, Handa K, Njuguna MM, Hasegawa T, Maruyama K, Nemoto E, Yamada S, Sugawara S, Lu L, Takedachi M, Murakami S, Okura H, Matsuyama A and Saito M. Periodontal regeneration by allogeneic transplantation of adipose tissue derived multi-lineage progenitor stem cells in vivo. *Sci Rep* 2019; 9: 921.
- [7] Zhang H, Liu S, Zhu B, Xu Q, Ding Y and Jin Y. Composite cell sheet for periodontal regeneration: crosstalk between different types of MSCs in cell sheet facilitates complex periodontal-like tissue regeneration. *Stem Cell Res Ther* 2016; 7: 168.
- [8] Kruk H, Bensaid X, Chevalier G, Cherkaoui S, Fontanel F and Danan M. Severe periodontitis and orthodontics: how far should we go? *Int Orthod* 2018; 16: 450-462.
- [9] Hirschfeld J, Reichardt E, Sharma P, Hilber A, Meyer-Marcotty P, Stelzig-Eisenhauer A, Schlagenhaupt U and Sickel FE. Interest in orthodontic tooth alignment in adult patients affected by periodontitis: a questionnaire-based cross-sectional pilot study. *J Periodontol* 2019; 90: 957-965.
- [10] Sim HY, Kim HS, Jung DU, Lee H, Lee JW, Han K and Yun KI. Association between orthodontic treatment and periodontal diseases: results from a national survey. *Angle Orthod* 2017; 87: 651-657.
- [11] Ferreira MC, Dias-Pereira AC, Branco-de-Almeida LS, Martins CC and Paiva SM. Impact of periodontal disease on quality of life: a systematic review. *J Periodontol Res* 2017; 52: 651-665.
- [12] Pointer JS. A novel visual analogue scale (VAS) device: an instrument based on the VAS designed to quantify the subjective visual experience. *Ophthalmic Physiol Opt* 2004; 24: 181-185.
- [13] Papapanou PN, Sanz M, Buduneli N, Dietrich T, Feres M, Fine DH, Flemmig TF, Garcia R, Gianobile WV, Graziani F, Greenwell H, Herrera D, Kao RT, Kebschull M, Kinane DF, Kirkwood KL, Kocher T, Kornman KS, Kumar PS, Loos BG, Machtei E, Meng H, Mombelli A, Needleman I, Offenbacher S, Seymour GJ, Teles R and Tonetti MS. Periodontitis: consensus report of workgroup 2 of the 2017 world workshop on the classification of periodontal and peri-implant diseases and conditions. *J Clin Periodontol* 2018; 45 Suppl 20: S162-S170.
- [14] Dommisch H, Kuzmanova D, Jonsson D, Grant M and Chapple I. Effect of micronutrient malnutrition on periodontal disease and periodontal therapy. *Periodontol* 2000 2018; 78: 129-153.
- [15] Ratheesh V, Subramanian S, Prakash PSG and Victor DJ. Evaluation of association of vitamin d receptor genetic polymorphism with severe chronic periodontitis in an ethnic tamilian population. *Genet Test Mol Biomarkers* 2018; 22: 615-621.
- [16] Ekshyyan O, Khandelwal AR, Rong X, Moore-Medlin T, Ma X, Alexander JS and Nathan CO. Rapamycin targets Interleukin 6 (IL-6) expression and suppresses endothelial cell invasion stimulated by tumor cells. *Am J Transl Res* 2016; 8: 4822-4830.
- [17] Farhat SB, de Souza CM, Braosi AP, Kim SH, Tramontina VA, Papalexioiu V, Olandoski M, Mira MT, Luczyszyn SM and Trevisatto PC. Complete physical mapping of IL6 reveals a new marker associated with chronic periodontitis. *J Periodontol Res* 2017; 52: 255-261.
- [18] Majumder P, Thou K, Bhattacharya M, Nair V, Ghosh S and Dey SK. Association of tumor necrosis factor-alpha (TNF-alpha) gene promoter

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- polymorphisms with aggressive and chronic periodontitis in the eastern Indian population. *Biosci Rep* 2018; 38: BSR20171212.
- [19] Ide M, Harris M, Stevens A, Sussams R, Hopkins V, Culliford D, Fuller J, Ibbett P, Raybould R, Thomas R, Puenter U, Teeling J, Perry VH and Holmes C. Periodontitis and cognitive decline in Alzheimer's disease. *PLoS One* 2016; 11: e0151081.
- [20] Hayashi J, Hasegawa A, Hayashi K, Suzuki T, Ishii M, Otsuka H, Yatabe K, Goto S, Tatsumi J and Shin K. Effects of periodontal treatment on the medical status of patients with type 2 diabetes mellitus: a pilot study. *BMC Oral Health* 2017; 17: 77.
- [21] Hernandez-Caldera A, Vernal R, Paredes R, Veloso-Matta P, Astorga J and Hernandez M. Human periodontal ligament fibroblasts synthesize C-reactive protein and Th-related cytokines in response to interleukin (IL)-6 transsignalling. *Int Endod J* 2018; 51: 632-640.
- [22] Javed F, Ahmed HB, Mehmood A, Mikami T, Malmstrom H and Romanos GE. Self-perceived oral health and periodontal parameters in chronic periodontitis patients with and without rheumatoid arthritis. *J Investig Clin Dent* 2016; 7: 53-58.
- [23] Carvalho CV, Saraiva L, Bauer FPF, Kimura RY, Souto MLS, Bernardo CC, Pannuti CM, Romito GA and Pustiglioni FE. Orthodontic treatment in patients with aggressive periodontitis. *Am J Orthod Dentofacial Orthop* 2018; 153: 550-557.
- [24] Melsen B, Agerbaek N, Eriksen J and Terp S. New attachment through periodontal treatment and orthodontic intrusion. *Am J Orthod Dentofacial Orthop* 1988; 94: 104-116.
- [25] Rosa M, Lucchi P, Ferrari S, Zachrisson BU and Caprioglio A. Congenitally missing maxillary lateral incisors: long-term periodontal and functional evaluation after orthodontic space closure with first premolar intrusion and canine extrusion. *Am J Orthod Dentofacial Orthop* 2016; 149: 339-348.