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Original Article

Clinical efficacy and safety of photodynamic therapy combined with tea polyphenols in treating peri-implantitis

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Abstract: Objective: To evaluate the clinical efficacy and safety of photodynamic therapy (PDT) plus tea polyphenols (TP) in treating peri-implantitis. Methods: The clinical records of 91 peri-implantitis patients treated at the North China University of Science and Technology Affiliated Hospital and Tangshan Hongci Hospital were analyzed retrospectively. Forty-one patients who received PDT alone were assigned to the control group, while the other 50 patients receiving both PDT and TP were allocated to the study group. Periodontal indices, inflammatory factors, swallowing function, pain, MOS 36-Item Short-Form Health Survey (SF-36) scores, therapeutic effect and adverse reactions were compared between the two groups. Results: Post therapy, significant reductions in the modified plaque index (mPLI), modified sulcus bleeding index (mSBI), probing depth (PD), and clinical attachment level (CAL) were observed in both groups ($P<0.05$), with more notable decreases in the study group ($P<0.05$). Besides, the levels of tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6) as well as interleukin-1β (IL-1β) also decreased notably in both groups ($P<0.05$), with notably lower levels in the study group ($P<0.05$). SF-36 scores across all dimensions significantly improved in both groups ($P<0.05$), with the study group demonstrating more substantial improvements ($P<0.05$). Swallowing function scores significantly decreased in both groups ($P<0.05$), with a more marked improvement in the study group ($P<0.05$). Similarly, the VAS scores of both groups significantly decreased post-treatment ($P<0.05$), especially the study group ($P<0.05$). In contrast to the control group, a notably higher overall response rate was observed in the study group ($P=0.020$), while no significant inter-group difference was observed in the total incidence of adverse reactions ($P=0.683$). Conclusion: PDT plus TP is more effective than PDT alone in treating peri-implantitis. This combined approach significantly reduces inflammation, improves periodontal health, and enhances quality of life, without increasing the incidence of adverse reactions. These findings suggest its potential for broader clinical application.

Keywords: Photodynamic therapy, tea polyphenols, peri-implantitis, clinical efficacy, safety

Introduction

As dental implant technology advances rapidly, a growing number of patients are undergoing dental implant restoration, leading to a corresponding rise in peri-implant complications [1]. Peri-implantitis, one of the most common complications following implant procedures, has an incidence of 1%-47% [2]. Peri-implantitis can provoke localized redness and swelling, along with suppuration and halitosis, significantly compromising patients' quality of life [3].

Traditional methods to treat peri-implantitis, such as mechanical debridement, chemotherapy and antibiotic therapy, often fail to completely eliminate the pathogenic factors and can result in irreversible tissue damage, along with toxic side effects [4, 5]. In recent years, photodynamic therapy (PDT) has emerged as a promising treatment for peri-implantitis, yielding significant and noteworthy outcomes [4]. PDT is effective in targeting periodontal pathogens and can penetrate deep into periodontal pockets, root furcation, and other difficult-to-reach areas, without causing problems such as antibiotic resistance [6]. However, the depth of action of photosensitizers used in PDT is limited. Tea polyphenols (TP), active substances extracted from tea, have been shown to prevent and treat

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periodontitis through their antioxidant, bacteriostatic, and anti-pathogenic properties [7]. Despite this, the combined use of PDT and TP for treating peri-implantitis has been infrequently studied. This study aims to evaluate the clinical efficacy and safety of PDT plus TP in treating peri-implantitis, with the goal of providing reliable guidance for future peri-implantitis therapies. The innovation of this study lies in the utilization of combined therapy involving PDT and TP, which may offer more significant treatment effects.

Methods and materials

Sample data

In this retrospective study, the clinical records of 120 peri-implantitis patients treated at the North China University of Science and Technology Affiliated Hospital and Tangshan Hongci Hospital were analyzed. This study was approved by the Ethics Committee of North China University of Science and Technology Affiliated Hospital.

Inclusion and exclusion criteria

Inclusion criteria: Cases meeting the diagnostic criteria for peri-implantitis as outlined in the *Diagnosis of Peri-implantitis,* confirmed by exploration probing and X-ray imaging [8]; Patients over 18 years old; Patients with no fewer than 18 remaining teeth and at least one implant that was not loose; Patients with available and complete clinical records.

Exclusion criteria: Cases with comorbid systemic immune system diseases; Cases with comorbid malignant tumors; Cases with infections in other body parts; Cases with prior antibiotic use before admission; Patients allergic to any medications used in this study; Pregnant or lactating women.

Sample screening

Based on the above-mentioned criteria, 120 patients were initially screened, and 91 participants were selected based on the study's inclusion criteria. Of these, 41 patients treated solely with PDT were assigned to the control group, while the remaining 50 who received both PDT and TP were assigned to the study group.

Therapeutic regimen

The control group received PDT as follows: The oral cavity of the patient was thoroughly cleaned, focusing on the teeth and implants. A manual carbon fiber scraper was adopted to fully clean the periphery of the implants and the adjacent teeth, while the root and periodontal tissues were smoothed. Hemostatic treatment was administered to any gingival bleeding sites, and excess water from the teeth was eliminated. Until the teeth were completely dry, toluidine blue photosensitizer was applied to the bottom of the implants, ensuring complete staining of the surfaces. Excess toluidine blue was then removed. Afterwards, a PAD Plus photo-combination disinfector was used to treat the patient's peri-implantitis. The parameters were set as follows: Power: 750 mW; wavelength: 635 nm. The implants coated with toluidine blue were fully irradiated for about 1 min at a single angle. After irradiation, the patient's oral cavity was rinsed with 0.9% sodium chloride solution to remove the remaining photosensitizer. During PDT, medical staff ensured eye protection for patients to prevent accidental exposure to splashed medication that could cause eye damage. The treatment was conducted over a 3-month period.

The observation group received PDT plus TP. The PDT treatment followed the same procedure as in the control group. Additionally, compound TP gargle (Yunnan Zipeng Technology Co., Ltd., production batch number: 120017; Specification 200 mL) was adopted for adjuvant treatment. Specifically, 20 mL gargle was adopted to clean the mouth 2-3 times a day, with the patient instructed not to eat after the night gargle to maintain oral hygiene. The treatment duration was the same as PDT, lasting for 3 months.

Outcome measures

Primary outcome measures: (1) Clinical efficacy [9]: Cured was defined as clinical symptoms that completely disappeared such as pyorrhea and swelling, and normal periodontal color; Markedly effective was defined as greatly improved periodontal status with disease symptoms that basically disappeared, or with occasional discomfort; Effective was defined as greatly improved periodontal indexes and alleviated disease symptoms; Ineffective was defined as unimproved or even worsened condition. Overall response rate = (cured cases + markedly effective cases + effective cases)/ total cases × 100%. (2) Periodontal indexes [10, 11]: Before and after treatment, the

Table 1. Comparison of baseline data between the two groups

Factors	Study group (n=51)	Control group (n=40)	χ^2	*P* value
Age			0.020	0.888
≥30 years old	16	12		
<30 years old	35	28		
Gender			0.361	0.548
Male	30	26		
Female	21	14		
BMI			0.109	0.742
≥23 kg/m^2	26	19		
<23 kg/m^2	25	21		
Course of disease			0.322	0.570
≥1 month	15	14		
<1 month	36	26		
History of alcoholism			0.033	0.8550
Yes	11	8		
No	40	32		
History of smoking			0.071	0.789
Yes	14	12		
No	37	28		
Place of residence			0.187	0.665
Rural areas	39	29		
Urban areas	12	11		

BMI: body mass index.

patient's teeth and gums were probed to assess the periodontal indices, which were compared between the two groups, including modified sulcus bleeding index (mSBI), modified plaque index (mPLI), probing depth (PD), as well as clinical attachment level (CAL).

mSBI evaluates gingival bleeding around the implant on a scale of 0 to 3 points [12]: 0 points indicate no bleeding, 1 point indicates scattered bleeding spots, 2 points indicate a line of bleeding, and 3 points indicate bleeding overflowing the gingival sulcus. mPLI assesses plaque around the implant on a scale of 0 to 3 points [13]: 0 points indicate no plaque, 1 point indicates few visible plaque deposits, 2 points indicate visible plaque, and 3 points indicate significant plaque formation resembling soft deposits. PD is the vertical distance from the gingival margin to the bottom of the gingival sulcus around the implant [12], with normal values ranging from 2 to 3 mm. CAL is the distance from the bottom of the pocket to the cementoenamel junction, with a normal value ranging from 1 to 3 mm [13]. In a healthy individual, the attachment level is generally at or near the cementoenamel junction of the tooth, indicating good periodontal health and stability.

Secondary outcome measures: (1) Inflammatory factors [14]: Gingival crevicular fluid samples were collected from every patient prior to and post therapy. Tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), and interleukin-1β (IL-1β) levels were measured using enzyme-linked immunosorbent assay (ELISA). Corresponding kits were provided by MultiSciences (Lianke) Biotech Co., Ltd. The clinical data for these inflammatory factors in gingival crevicular fluid were compared between the two groups. (2) Adverse reactions: Adverse reactions were recorded and analyzed for both groups, including pain, nausea and vomiting, and redness and swelling. (3) Swallowing function: The function was evaluated using the Wakita drinking test, where patients were asked to drink 30 mL of warm water without assistance [15]. Lower scores indicated better swallowing function recovery. (4) Visual Analogue Score (VAS): Pain levels were evaluated using the VAS [16], with higher scores indicating more intense pain. (5) Quality of life (QoL): QoL before and after treatment was assessed using the MOS 36-Item Short-Form Health Survey (SF-36) [17]. The total score ranges from 0 to 100, with higher scores indicating better QoL.

Statistical analyses

Statistical analyses were performed using SPSS 20.0, and data illustration was performed with GraphPad 8. Measurement data were normally distributed and presented as Mean ± SD. Inter-group and intra-group comparisons were performed using the independent-samples T test and paired t test, respectively. Counting data (percentage) were analyzed using the chi-square test and presented by χ^2. P<0.05 was considered statistically significant.

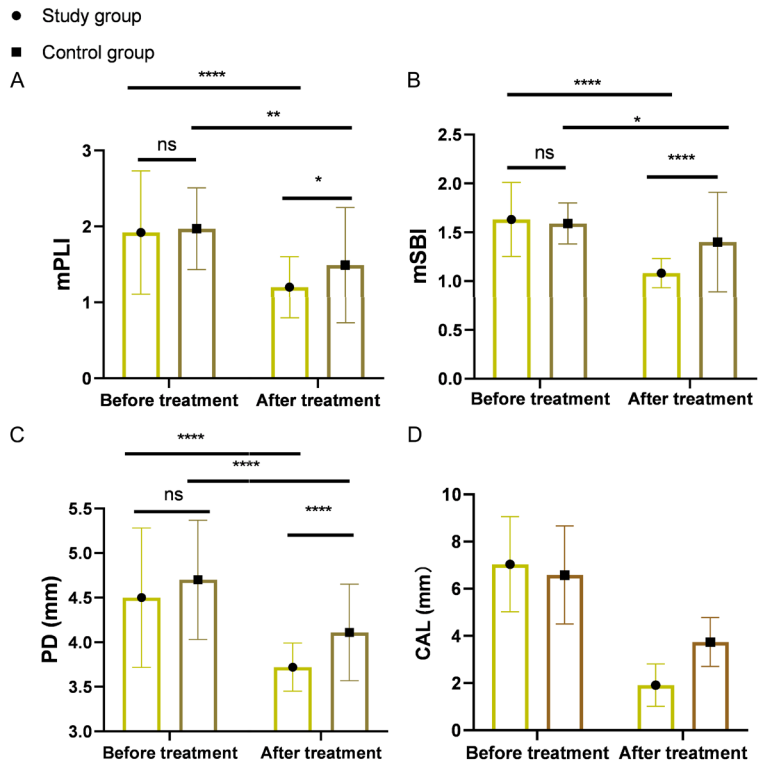

Figure 1. Comparison of mPLI (A), mSBI (B), PD (C) and CAL (D) between the two groups before and after treatment. Notes: mPLI: Modified plaque index; mSBI: Modified sulcus bleeding index; PD: Probing depth; CAL: clinical attachment level. nsP>0.05; *P<0.05; **P<0.01; ****P<0.0001.

Results

Baseline data

An inter-group comparison of baseline data revealed no significant differences between the study and control groups in terms of age, sex, history of smoking, body mass index (BMI), course of disease, history of alcoholism, or place of residence (all P>0.05, **Table 1**).

Comparison of periodontal indices between the two groups

Before therapy, the levels of mPLI, mSBI, PD and CAL in the study group were 1.92±0.81, 1.63±0.38, 4.50±0.78 mm and 7.04±2.02 mm, respectively. The levels of these indices in the control group were 1.97±0.54, 1.59±0.21, and 4.70±0.67 mm, 6.58±2.08, respectively. After therapy, the levels of mPLI, mSBI, PD and CAL in the study group were 1.20±0.40, 1.08±0.15, 3.72±0.27 mm and 1.91±0.90, respectively, and those in the control group were 1.49±0.76, 1.40±0.51, 4.11±0.54 and 3.74±1.04 mm, respectively. Prior to therapy, the levels of mPLI, mSBI, PD and CAL were similar between the two groups (P>0.05); while post therapy, the levels in both groups dropped notably (P<0.05), with more pronounced reductions in the study group (P< 0.05, **Figure 1**).

Comparison of serum inflammatory factors between the two groups

Before therapy, the levels of TNF-α, IL-6 and IL-1β in the study group were 4.07±0.12 ng/L, 194.58±8.86 ng/mL, and 315.87±7.00 ng/L, respectively, and these levels in the control group were 4.13±0.19 ng/L, 192.90±7.98 ng/mL, and 317.07±6.00 ng/L, respectively. After therapy, the levels of TNF-α, IL-6 and IL-1β in the study group dropped to 1.59±0.31 ng/L, 143.48±6.24 ng/mL, 157.93±3.50 ng/L, respectively; and these levels in the control group were 3.11±0.44 ng/L, 159.43±8.57 ng/mL and 204.51±1.17 ng/L, respectively. Prior to therapy, the two groups were comparable regarding the levels of TNF-α, IL-6 and IL-1β (all P>0.05); whereas post therapy, the levels in both groups decreased greatly (all P<0.05), with the study group demonstrating more substantial decreases (all P<0.05, **Figure 2**).

Comparison of QoL between the two groups

Before therapy, the scores for physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional, and mental health scores of the control group were 56.91±5.69, 69.51±5.29, 40.02±6.46, 52.88±7.69, 59.13±5.64, 54.82±4.70, 63.37±7.34, and 57.35±7.14, while those of the study group were 57.69±4.40, 69.73±5.68, 40.26±6.52, 52.45±5.88, 59.18±4.61, 54.03±6.79, 64.50±7.01 and 56.97±6.24, respectively. After therapy, the physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional, and mental health

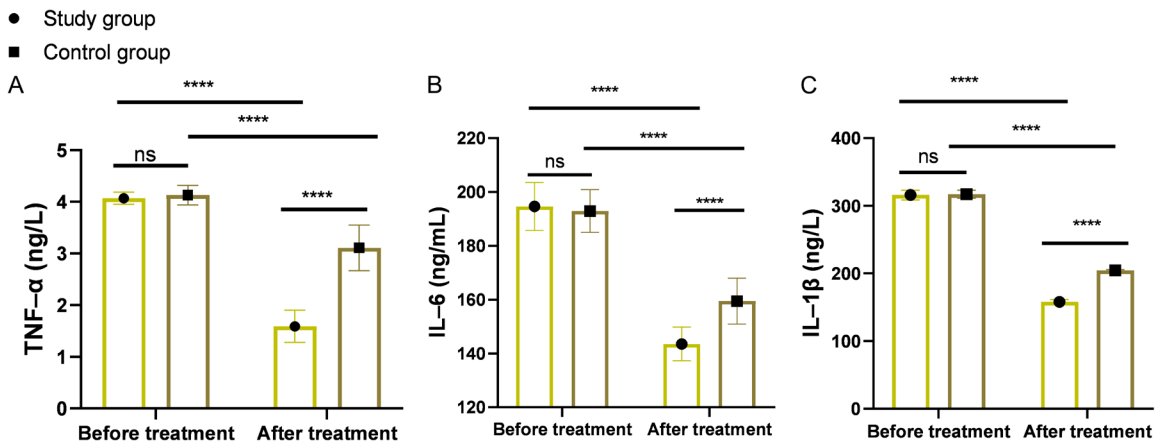

Figure 2. Comparison of TNF-α (A), IL-6 (B) and IL-1β (C) between the two groups before and after treatment. Notes: TNF-α: Tumor necrosis factor-α; IL-6: interleukin-6; IL-1β: Interleukin-1β. nsP>0.05; ****P<0.0001.

scores of the control group were 78.01±4.54, 79.34±4.73, 79.66±6.04, 82.16±7.71, 76.85±5.55, 79.46±6.43, 84.92±6.92, and 72.90±6.18, respectively; while those of the study group were 80.77±5.04, 81.69±4.97, 83.33±4.89, 85.19±5.36, 80.60±4.41, 87.33±5.68, 88.68±6.94 and 80.79±5.26, respectively. Before treatment, no significant difference was observed in SF-36 scores across all dimensions between the two groups (all P>0.05). However, after therapy, the SF-36 scores significantly improved in both groups (all P<0.05), with the study group showing greater improvements (all P<0.05, **Figure 3**).

Comparison of swallowing function levels (Wakita drinking test) between the two groups

In the study group, the mean Wakita drinking test score before treatment was 21.01±2.06, which significantly decreased to 8.16±0.80 after treatment (P<0.0001). In the control group, the mean Wakita drinking test score before treatment was 20.91±2.04, which notably increased to 13.84±1.42 after treatment (P<0.0001). Before treatment, there was no significant difference in Wakita drinking test scores between the two groups (P>0.05). However, after treatment, the Wakita drinking test scores of both groups significantly decreased (P<0.05), with the study group exhibiting a greater decrease in scores, indicating better swallowing function levels (P<0.05, **Table 2**).

Comparison of pain levels between the two groups

In the study group, the pain level before treatment was 6.98±0.70 points, which decreased to 2.21±0.06 points after treatment. In the control group, the VAS score before treatment was 7.02±0.72 points, which decreased to 4.90±0.45 points after treatment. Before treatment, there was no significant difference in VAS scores between the two groups (P>0.05). After treatment, the VAS scores of both groups significantly decreased (P<0.05), with greater reduction observed in the study group (P<0.05, **Table 3**).

Comparison of treatment efficacy between the two groups

In the study group, 48 individuals (94.12%) responded to the treatment. Among them, 10 individuals (19.61%) were cured, 18 individuals (35.29%) showed marked effectiveness, 20 individuals (39.22%) were effective, and 3 individuals (5.88%) showed no response to the treatment. In the control group, 31 individuals (77.50%) responded to the treatment. Specifically, 5 individuals (12.50%) were cured, 10 individuals (25.00%) showed marked effectiveness, 16 individuals (40.00%) had effective treatment responses, and 9 individuals (22.50%) had no response to the treatment. Analysis of clinical efficacy revealed a notably lower overall response rate in the control group compared to the study group (P=0.020, **Table 4**).

Comparison of adverse reactions

In the study group, 5 individuals (9.80%) reported adverse reactions, including pain (2 individuals, 3.92%), nausea and vomiting (2 individuals, 3.92%), and redness and swelling (1 individual, 1.96%). In the control group, 5 indi-

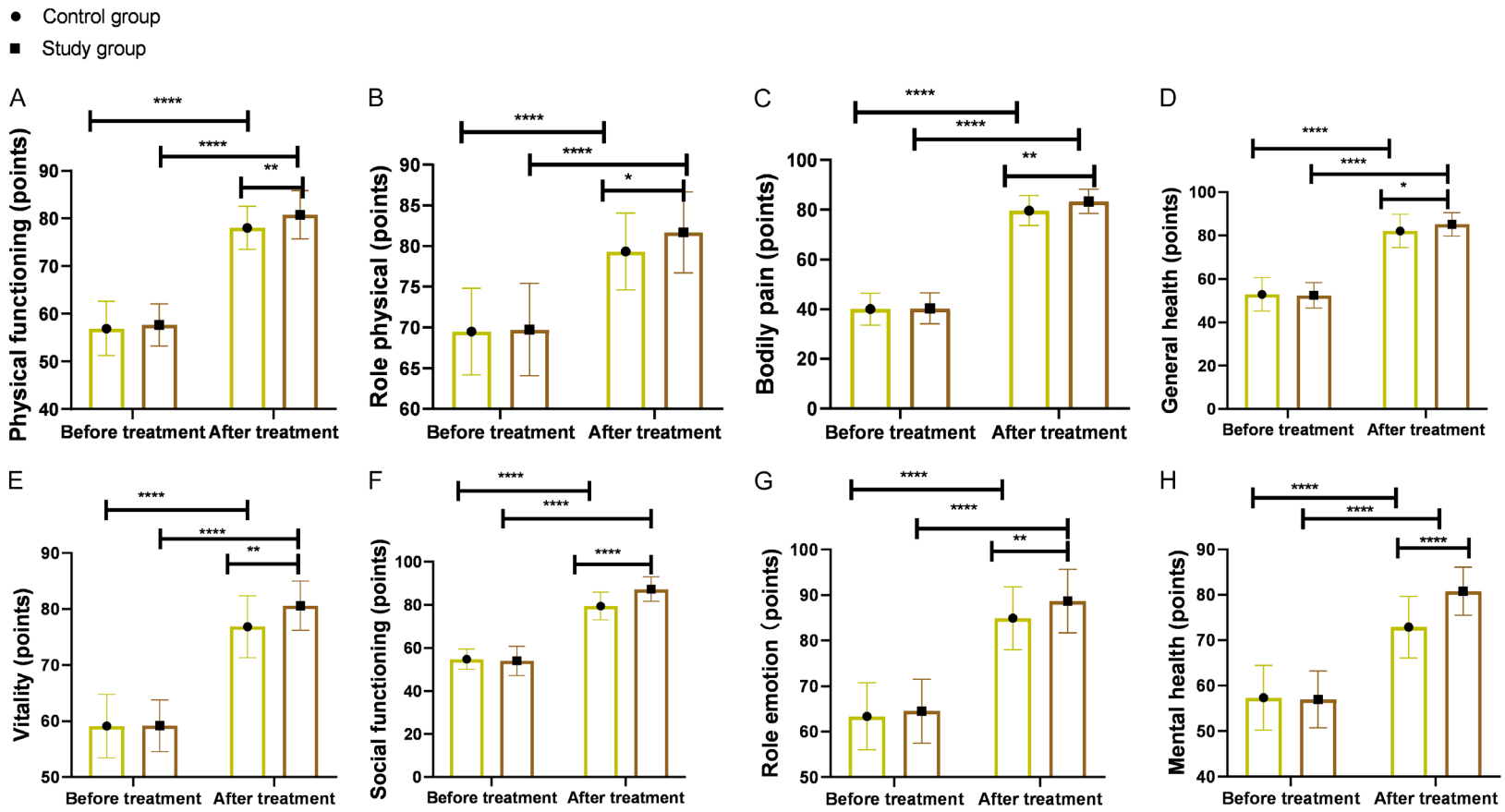

Figure 3. Comparison of SF-36 scores between the two groups. A. Physical functioning; B. Role physical; C. Bodily pain; D. General health; E. Vitality; F. Social functioning; G. Role emotional; H. Mental health. Notes: *P<0.05; **P<0.01; ****P<0.0001.

Table 2. Comparison of swallowing function levels between the two groups ($\bar{x}$±s, points)

Group	Before treatment	After treatment
Study group (n=50)	21.01±2.06	8.16±0.80#
Control group (n=41)	20.91±2.04	13.84±1.42#
T	1.689	22.31
P value	0.0930	<0.0001

Note: #P<0.05 vs. pre-treatment level.

Table 3. Comparison of pain levels between the two groups ($\bar{x}$±s, points)

Group	Before treatment	After treatment
Study group (n=50)	6.98±0.70	2.21±0.06#
Control group (n=41)	7.02±0.72	4.90±0.45#
T	0.6878	45.52
P value	0.4934	<0.0001

Note: #P<0.05 vs. pre-treatment level.

viduals (12.50%) reported adverse reactions, including pain (2 individuals, 5.00%), nausea and vomiting (1 individual, 2.50%), and redness and swelling (2 individuals, 5.00%). Analysis of adverse reactions uncovered no significant difference between the two groups regarding the total incidence (P=0.683, **Table 5**).

Discussion

Peri-implantitis is an inflammatory disease affecting both the soft and hard tissues around dental implants, and it is a leading cause of implant failure [18]. This condition can lead to gum swelling and pain, as well as implant loosening or dislocation [19]. However, traditional mechanical treatment may result in the recession of marginal ridge and compromise of the aesthetic area [20]. PDT, a new antibacterial therapy, has been widely adopted in clinical practice [21]. Previous studies have shown that PDT can effectively reduce bacteria on the implant surface without damaging the implants and surrounding tissues [22]. However, PDT alone cannot fully remove the plaque on teeth, resulting in recurrent oral infections and reducing treatment efficacy [23]. As a result, its therapeutic outcomes is not ideal for oral diseases in clinical practice. TP gargle, a natural plant-based oral gargle, contains active ingredients including TP, glycyrrhizin, DP300, glycerin, and vitamin E, which can help maintain oral cleanliness and inhibit the bacterial growth [24]. This study aims to evaluate the combined efficacy of PDT and TP gargle in treating peri-implantitis.

Periodontal index is an effective measure of oral health [25]. In this study, the post-treatment levels of mPLI, mSBI, PD and CAL in the two groups decreased significantly, with more notable reductions observed in the study group. This suggests that TP combined with PDT can improve oral health more effectively than PDT alone. The oral cavity is a complex microbial environment, where diverse bacteria and microorganisms interact, forming intricate plaque biofilms. Pro-inflammatory factors and inflammatory cells exacerbate inflammatory responsex around the implant [26-28]. This study found notable decreases in TNF-α, IL-6 and IL-1β levels in both groups, with the study group showing more pronounced reductions. The result implies that the combined therapy can effectively reduce inflammatory factors in gingival crevicular fluid, alleviating the inflammatory reaction.

The SF-36 questionnaire is widely recognized as an effective instrument for assessing patients' health status and quality of life, providing an essential reference for clinical research and practice [29]. In this study, post-treatment SF-36 scores across all dimensions significantly improved in both groups (P<0.05), with notably higher scores observed in the study group. These findings strongly support the effectiveness of PTD combined with TP in enhancing the quality of life for patients with peri-implantitis.

In this study, there were no significant differences in swallowing function scores and pain levels between the two groups before treatment. However, post-treatment, both groups showed significant improvements in swallowing function and pain levels, with the study group demonstrating notably greater improvements compared to the control group. Additionally, the study group showed a significantly higher overall response rate compared to the control group, without increasing the total incidence of adverse reactions. The above results suggest that compared with PDT alone, TP combined

Table 4. Comparison of treatment efficacy between the two groups [n (%)]

Group	Cured	Markedly effective	Effective	Ineffective	Overall response
Study group (n=51)	10 (19.61)	18 (35.29)	20 (39.22)	3 (5.88)	48 (94.12)
Control group (n=40)	5 (12.50)	10 (25.00)	16 (40.00)	9 (22.50)	31 (77.50)
χ^2	0.823	1.115	0.006	5.408	5.408
P value	0.364	0.291	0.940	0.020	0.020

Table 5. Comparison of incidence of adverse reactions between the two groups [n (%)]

Group	Pain	Nausea and vomiting	Redness and swelling	Total adverse reaction
Study group (n=51)	2 (3.92)	2 (3.92)	1 (1.96)	5 (9.80)
Control group (n=40)	2 (5.00)	1 (2.50)	2 (5.00)	5 (12.50)
χ^2	0.062	0.130	0.650	0.167
P value	0.803	0.719	0.420	0.683

with PDT can effectively treat peri-implantitis and improve the periodontal condition of patients, without bringing more adverse reactions. Hui et al. [30] also reported significantly reduced mPLI, PPD, mSBI, and BOP levels, as well as lower CRP, TNF-α and IL-6 levels in early peri-implantitis patients treated with TP plus PDT. Their findings, which verified improved clinical efficacy and reduced inflammation, support the results of this study. The underlying mechanisms may include PDT's ability to remove bacteria from infected tissues, providing relief from pain, while TP suppresses bacterial growth in the mouth, effectively controlling early peri-implant diseases and preventing disease progression. The synergistic effect of combining both treatments contributes to their enhanced clinical efficacy.

This study still has certain limitations. Firstly, the relatively small sample size may introduce some degree of deviation, potentially affecting the generalizability of the findings. Additionally, the investigation did not explore the long-term prognosis of the patients in both groups. This underscores the need for further exploration into the impact of combining PDT with TP on the long-term outcomes of peri-implantitis. Hence, we aim to conduct a more comprehensive analysis to evaluate the combined use of PDT and TP for treating peri-implantitis, which will help generate more robust definitive conclusions.

Conclusion

In conclusion, the combination of PDT and TP is more effective than PDT alone in managing peri-implantitis. This integrated approach not only significantly reduces inflammation but also improves periodontal health and patients' quality of life. Importantly, these advantages are attained without increasing adverse reactions, demonstrating the potential for broad clinical utilization.

Disclosure of conflict of interest

None.

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