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Original Article

Xianling Gubao capsules improve oral health, alveolar bone defects, and bone density in patients with periodontitis

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Abstract: Objective: To evaluate the effects of Xianling Gubao Capsules (XGC) on alveolar bone and inflammatory mediators in the gingival crevicular fluid in patients with periodontitis. Methods: A retrospective analysis was conducted on 90 periodontitis patients who received medication treatment at Daqing Longnan Hospital from September 2022 to June 2023. Patients were categorized into three groups: a control group (n=30, receiving basic periodontal treatment), a Caltrate group (n=30, receiving basic treatment plus Caltrate), and an XGC group (n=30, receiving basic treatment plus Xianling Gubao Capsules). Changes in alveolar bone defect height, alveolar bone density, plaque index (PI), probing depth (PD), gingival index (GI), gingival crevicular fluid volume, and inflammatory mediator levels were compared before and after treatment. Results: After 3 and 6 months of treatment, the XGC group exhibited significantly reduced alveolar bone defect height in incisors, canines, premolars, and molars and significantly increased alveolar bone density compared with the other two groups (all $P<0.05$). The XGC group also exhibited lower tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6) levels and higher interleukin-17 (IL-17) levels than the Caltrate and control groups (all $P<0.05$). Additionally, PI, PD, GI, and gingival crevicular fluid volume were significantly lower in the XGC group at both time points (all $P<0.05$). The incidence of adverse reactions did not differ significantly among the three groups ($P>0.05$). Conclusion: Xianling Gubao Capsules, when combined with conventional periodontal treatment, may enhance alveolar bone density, reduce alveolar bone defects, alleviate periodontal inflammation, and modulate inflammatory mediator levels in the gingival crevicular fluid. These findings suggest clinical benefits for periodontitis management.

Keywords: Xianling Gubao capsules, periodontitis, alveolar bone, gingival crevicular fluid, inflammatory factors, safety

Introduction

Periodontitis is a chronic inflammatory condition affecting the periodontal supporting tissues, primarily triggered by localized factors [1]. It is highly prevalent among individuals aged 35 and older, with plaque microorganisms serving as the primary etiological factor. As local inflammation progresses, the supporting structures of the teeth undergo gradual destruction, leading to attachment loss, tooth mobility, and ultimately, tooth loss [2, 3]. In China, the prevalence of periodontitis is alarmingly high, ranging from 70% to 85% [4]. Beyond its impact on oral health, periodontitis has been linked to over 50 systemic diseases, including diabetes, cardiovascular diseases, immune disorders, and cognitive impairments [5, 6]. Given these implications, active intervention is recommended for patients with periodontitis.

As a chronic infectious oral disease, periodontitis is managed through various treatment modalities, which continue to evolve with advancements in medical technology. Current treatment approaches include non-surgical interventions (such as scaling and root planing, ultrasonic debridement, laser therapy, and endoscopic treatment), pharmacological therapies (topical or systemic drug administration), stem cell therapy (using dental pulp stem cells to regenerate periodontal tissues), and tissue engineering and regenerative medicine (lever-

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aging tissue engineering techniques to promote periodontal regeneration). However, each method has its advantages and limitations. Non-surgical therapy remains the first-line treatment but may increase root sensitivity. Stem cell therapy, while promising, is costly and difficult to implement on a large scale. Tissue engineering and regenerative medicine, though showing potential in animal studies, have yet to reach clinical application. Pharmacological treatment, despite potential side effects and extended treatment duration, offers higher patient compliance and requires fewer medical resources, making it more feasible for widespread use [7].

Xianling Gubao Capsules (XGC), a proprietary Chinese medicine, are composed of herbal ingredients including Herba Epimedii, Radix Dipsaci, Salvia miltiorrhiza, Rhizoma Anemarrhenae, Fructus Psoraleae, and Radix Rehmanniae. These capsules are traditionally used to nourish the liver and kidneys, promote blood circulation, alleviate meridian obstruction, and strengthen tendons and bones. XGC have been shown to regulate metabolism, stimulate bone formation, enhance bone density, and increase bone mineral content while inhibiting osteoclast activity and promoting bone remodeling, thereby improving overall bone mass and quality. Additionally, they facilitate callus and osteoid formation at fracture sites, accelerate trabecular bone maturation and osteoblast proliferation, and promote chondrocyte differentiation and maturation [8, 9]. Clinically, XGC are widely used for conditions such as osteoporosis and arthritis. However, research on their application in periodontitis treatment remains limited.

This study retrospectively analyzed the efficacy and safety of XGC in alleviating inflammation and mitigating alveolar bone resorption in patients with periodontitis, providing new insights into potential treatment strategies for the disease.

Materials and methods

Case selection

This retrospective study was approved by the Ethics Committee of Daqing Longnan Hospital. The study design is illustrated in **Figure 1**. Using the hospital's electronic medical record system, the research period spanned from September 2022 to June 2023, with a follow-up duration of 6 months for each patient. The final patient follow-up was completed in December 2023.

Patient selection was based on the following inclusion criteria: (1) Diagnosed with periodontitis [10] and received comprehensive treatment at Daqing Longnan Hospital. (2) Aged ≥18 years. (3) Retained ≥6 single-rooted anterior teeth. (4) No history of periodontal treatment or use of bone metabolism-affecting drugs (e.g., hormonal medications) in the past 6 months. (5) No use of immunosuppressants in the past 3 months. (6) Complete medical records available.

A total of 123 patients were initially screened, followed by secondary selection based on the following exclusion criteria: (1) Presence of surgical contraindications, including severe cardiovascular or cerebrovascular diseases, diabetes, or mental disorders. (2) Concurrent oral conditions (e.g., periapical abscess, impacted teeth, malocclusion) or acute local inflammatory reactions. (3) Malignant oral lesions. (4) Autoimmune diseases or multiple organ dysfunction. (5) Long-term medication use or smoking (≥10 cigarettes per day). (6) Self-discontinuation of medication during the study period. (7) History of maxillofacial trauma.

After applying the exclusion criteria, 90 patients were included in the study. They were assigned to three groups based on the interventions received: a control group (n=30), a Caltrate group (n=30), and an XGC group (n=30).

Intervening methods

The control group received standard periodontal treatment, including oral hygiene education, instruction on proper brushing techniques, supragingival scaling, subgingival scaling, and root planing to remove plaque and calculus. Treatment was administered once every 3 months for a total of two sessions.

The Caltrate group received the same standard periodontal treatment along with Caltrate (Wyeth Pharmaceuticals, 600 mg/tablet, No. H10950029), taken as one tablet daily for 6 months.

The XGC group received the standard periodontal treatment supplemented with XGC (Guizhou

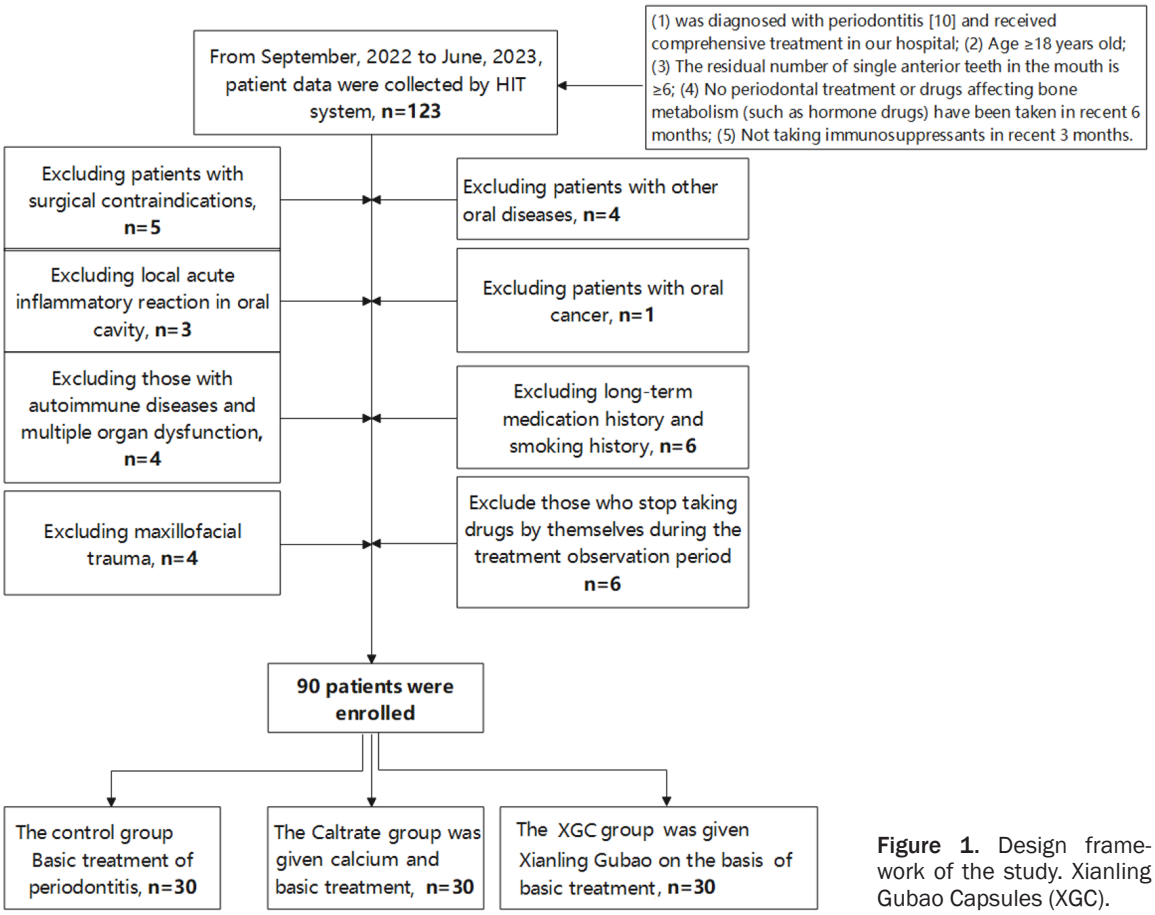

Figure 1. Design framework of the study. Xianling Gubao Capsules (XGC).

Tongjitang Pharmaceuticals Co. Ltd., 0.5 g/capsule, No. Z20025337), taken at 1.0 g three times daily for 6 months.

Data collection and outcome measurement

A designated data collector used the Healthcare Information Technology (HIT) system to automatically import or manually input patient information, ensuring data source verification and defining the collection scope in advance. Another data collector supervised data usage to protect patient privacy and data security. The principal investigator reviewed the data upon completion of the collection process.

Primary outcomes: Alveolar bone defect height and alveolar bone density were assessed at three time points: baseline (before treatment initiation), the 3-month follow-up, and the 6-month follow-up.

Plaque index (PI), probing depth (PD), gingival index (GI), and gingival crevicular fluid volume were measured at baseline, 3 months, and 6 months.

PI was assessed using a plaque-disclosing agent applied to the tooth surface near the gingival margin. Stained areas indicated plaque presence.

PD was measured using a periodontal probe with a standardized probing force of approximately 20-25 g, recording the distance from the gingival margin to the base of the pocket or sulcus.

GI was evaluated using a blunt-tipped periodontal probe in combination with visual inspection and probing to determine bleeding presence in the gingival sulcus.

Gingival crevicular fluid volume was quantified using the filter strip method.

Secondary outcomes: Baseline clinical data, including sex, age, and disease duration, were collected.

Inflammatory factor levels in gingival crevicular fluid (TNF-α, IL-6, and IL-17) were measured at baseline, 3 months, and 6 months.

Table 1. Comparison of baseline clinical data

Data		Caltrate group (n=30)	XGC group (n=30)	Control group (n=30)	F/X^2	P
Sex	Male	13	15	15	0.356	0.827
	Female	17	15	15		
Average age (years)		51.29±5.11	52.03±4.23	51.34±5.18	1.549	0.125
Average BMI (kg/m^2)		23.01±3.39	22.89±3.56	22.98±3.21	0.444	0.661
Average course of disease (years)		5.03±0.51	4.98±0.62	4.98±0.49	0.223	0.569

BMI, Body mass index; XGC, Xianling Gubao Capsules.

Before sample collection, patients rinsed their mouths to remove food debris. Saliva was isolated using sterile cotton.

A collection strip was inserted into the periodontal pocket until resistance was felt and remained in place for 30 seconds. The strip was then transferred to a sterile centrifuge tube. Enzyme-linked immunosorbent assay (ELISA) was performed using a reagent kit (Shanghai Keaibo Biological Co., Ltd.) with a microplate reader and micropipettor.

Incidence of adverse reactions, including diarrhea, rash, nausea, and vomiting, was recorded during treatment.

Statistical methods

Statistical analysis was conducted using SPSS 26.0. Measured data were tested for normality and expressed as mean ± standard deviation (mean ± SD). Group differences were first assessed using a homogeneity test of variance, followed by one-way analysis of variance (ANOVA). Post hoc pairwise comparisons were performed using the Least Significant Difference (LSD) test. Categorical data were expressed as percentages, and differences between groups were analyzed using chi-square or Fisher's exact test. A *P*-value <0.05 was considered significant.

Results

Comparison of baseline clinical data

Baseline clinical data, including sex, mean age, mean body mass index (BMI), mean disease duration, and underlying conditions, were collected and compared among the three groups. No significant differences were observed (all P>0.05) (**Table 1**).

Comparison of alveolar bone defect height and alveolar bone density before and after treatment

No significant differences were found in the alveolar bone defect height of incisors, canines, premolars, and molars among the three groups before treatment (all P>0.05, **Figure 2**). However, at 3 and 6 months, the XGC group exhibited significantly lower alveolar bone defect height compared with the other two groups (P<0.05).

Similarly, no significant differences in alveolar bone density of incisors, canines, premolars, and molars were observed before treatment (all P>0.05, **Figure 3**). However, at 3 and 6 months, alveolar bone density in the XGC group was significantly higher than in the other two groups (P<0.05).

Comparison of inflammatory factor levels in gingival crevicular fluid before and after

Before treatment, no significant differences were found in the levels of TNF-α (**Figure 4**), IL-6 (**Figure 5**), or IL-17 (**Figure 6**) among the three groups (all P>0.05). However, at 3 and 6 months, the XGC group exhibited significantly lower TNF-α and IL-6 levels and higher IL-17 levels compared with the Caltrate and control groups (all P<0.05).

Comparison of periodontal condition before and after treatment

Before treatment, there were no significant differences in PI, PD, GI, and gingival crevicular fluid volume among the three groups (all P>0.05, **Figure 7**). However, at 3 and 6 months, significant differences were observed among the groups (all P<0.05), with the XGC group showing the lowest PI, PD, GI values, and gingival crevicular fluid volume compared to the other two groups (all P<0.05).

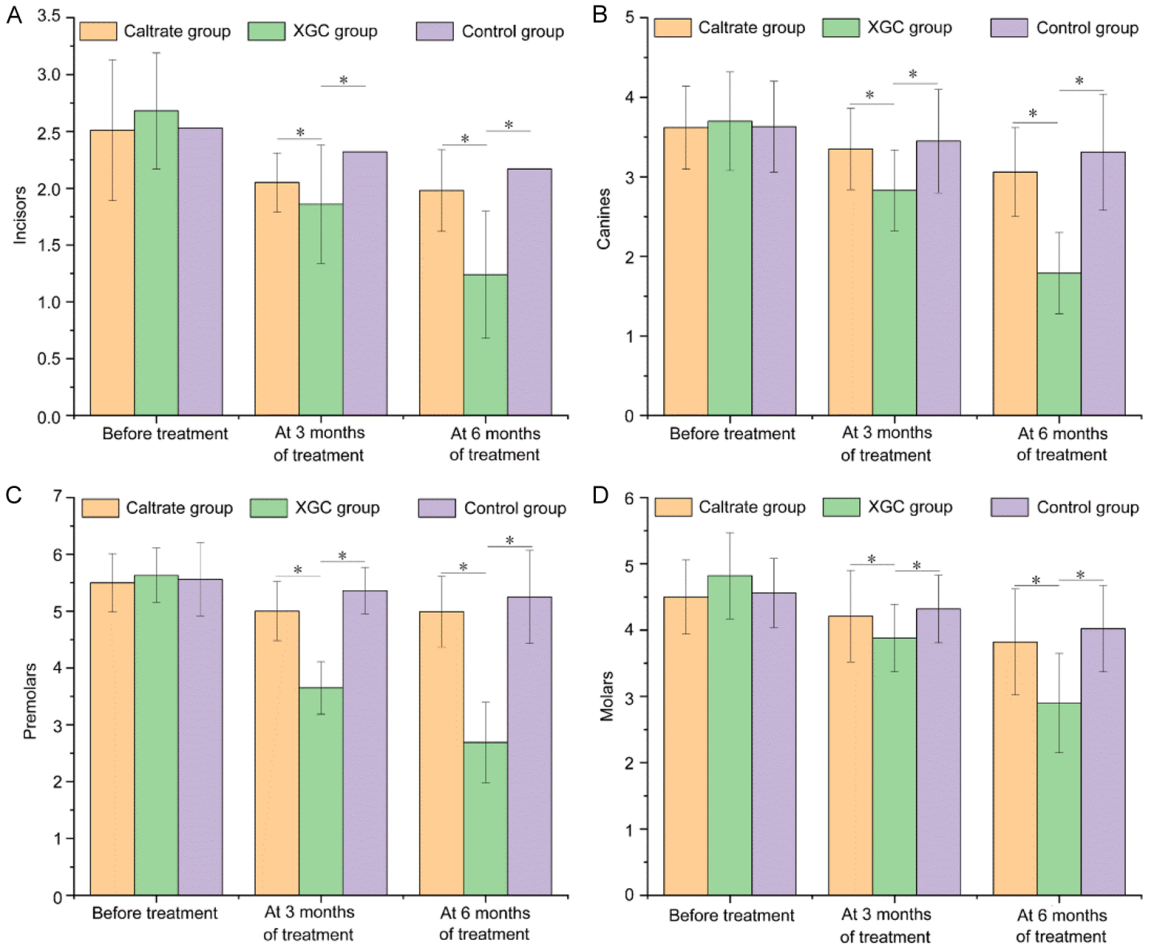

Figure 2. Comparison of the height of alveolar bone defects before and after treatment. At 3 and 6 months of treatment, the XGC group exhibited significantly lower height of alveolar bone defects of incisors (A), canines (B), premolars (C), and molars (D) compared to the other two groups ($P<0.05$). XGC: Xianling Gubao capsules. * represents a significant difference between groups.

Comparison of incidence of adverse reactions

Adverse reactions included: Caltrate group: 1 case of nausea, 1 case of rash, and 1 case of diarrhea, with a total incidence of 10.00% (3/30). XGC group: 2 cases of nausea, 1 case of vomiting, and 1 case of diarrhea, with a total incidence of 13.33% (4/30). Control group: 1 case of nausea and 1 case of diarrhea, with a total incidence of 6.67% (2/30).

There was no significant difference in the total incidence of adverse reactions among the three groups (P>0.05) (**Table 2**).

Images of a typical case

A representative case involved a 46-year-old female patient. Before treatment, extensive plaque and calculus were present, along with attachment loss (**Figure 8A**). Following basic treatment, oral hygiene improved, and gingival color was enhanced; however, attachment loss persisted (**Figure 8B**). After treatment with XGC, further improvement in oral hygiene was observed, and bleeding on probing (BOP) was negative (**Figure 8C**).

Discussion

The results of this study demonstrated that, compared to the control group receiving conventional periodontal treatment, patients in the Caltrate group (supplemented with Caltrate) and the XGC group (supplemented with XGC) exhibited a significant reduction in alveolar bone defect height and a notable increase in alveolar bone density. This suggests that phar-

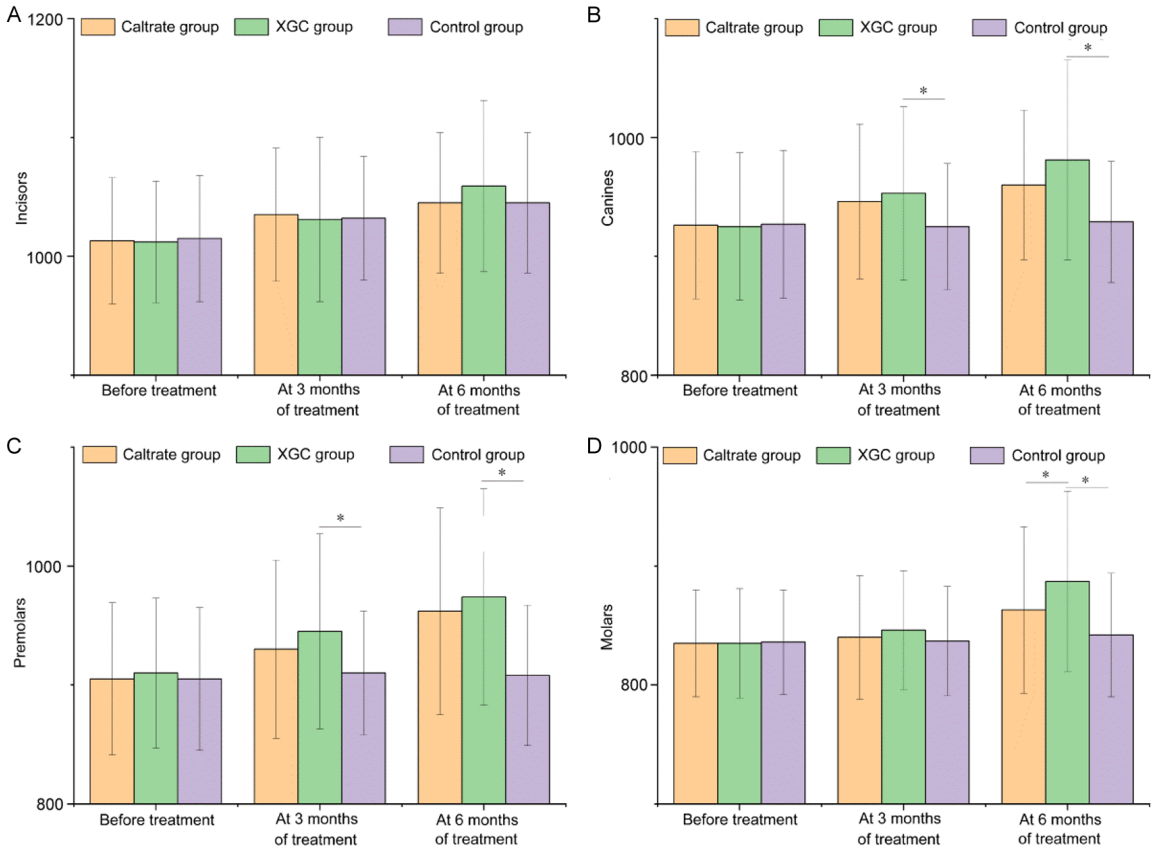

Figure 3. Comparison of alveolar bone density before and after treatment. At 3 and 6 months of treatment, the XGC group exhibited significantly higher alveolar bone density of incisors (A), canines (B), premolars (C), and molars (D) compared to the other two groups ($P<0.05$). XGC: Xianling Gubao capsules. * represents a significant difference between groups.

macological adjunctive therapy effectively improves alveolar bone defects associated with periodontitis.

Periodontitis is a chronic inflammatory disease and a leading cause of tooth loss in adults [11]. Due to factors such as root bifurcation lesions and deep periodontal pockets, conventional periodontal treatments often fail to completely eliminate the plaque microbiome. Consequently, pharmacologic interventions have emerged as an essential adjunctive measure in periodontitis management [12, 13], demonstrating proven efficacy in alleviating clinical symptoms. While Caltrate inhibits bone loss and enhances bone density, XGC showed superior efficacy in this study.

Periodontitis affects both the gingival and deep periodontal tissues, with its pathogenesis closely linked to plaque microorganisms [14]. Loos et al. [15] identified the typical clinical manifestations of periodontitis, including gingival swelling and redness, periodontal pocket formation, progressive attachment loss, and alveolar bone resorption. Without timely intervention, periodontitis can lead to tooth mobility and eventual loss. Zhang et al. [16] systematically demonstrated that periodontal tissue destruction occurs through two primary mechanisms: direct damage caused by periodontal pathogens and their products, and indirect destruction resulting from an excessive host immune response. Baeza et al. [17] further confirmed that the latter mechanism is the primary driver of periodontal tissue damage. Hajishengallis et al. [18] highlighted the critical role of inflammatory mediators in the host response, detailing key mediators such asIL-1, IL-6, IL-8, TNF, and prostaglandin E. These findings align with the results of this study, collectively confirming the strong association between inflammatory responses and periodontitis.

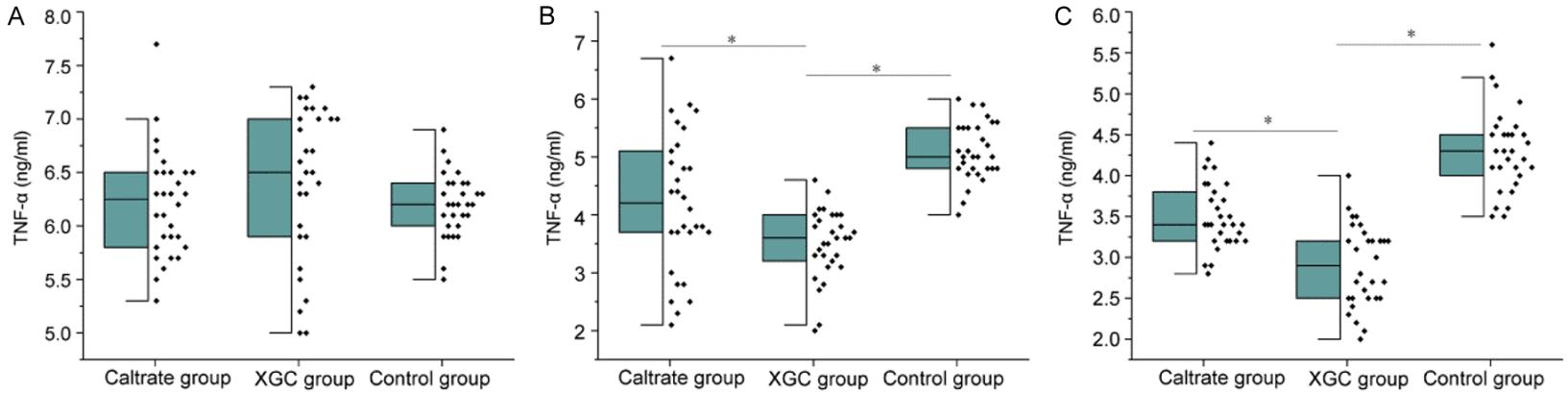

Figure 4. Comparison of TNF-α levels in gingival crevicular fluid before and after treatment. There was no significant difference in the levels of TNF-α in gingival crevicular fluid among the three groups before treatment ($P>0.05$) (A). At 3 months (B) and 6 months (C) of treatment, patients in the XGC group exhibited lower levels of TNF-α compared with the Caltrate group and the control group ($P<0.05$). TNF-α: tumor necrosis factor-α; XGC: Xianling Gubao capsules. * represents a significant difference between groups.

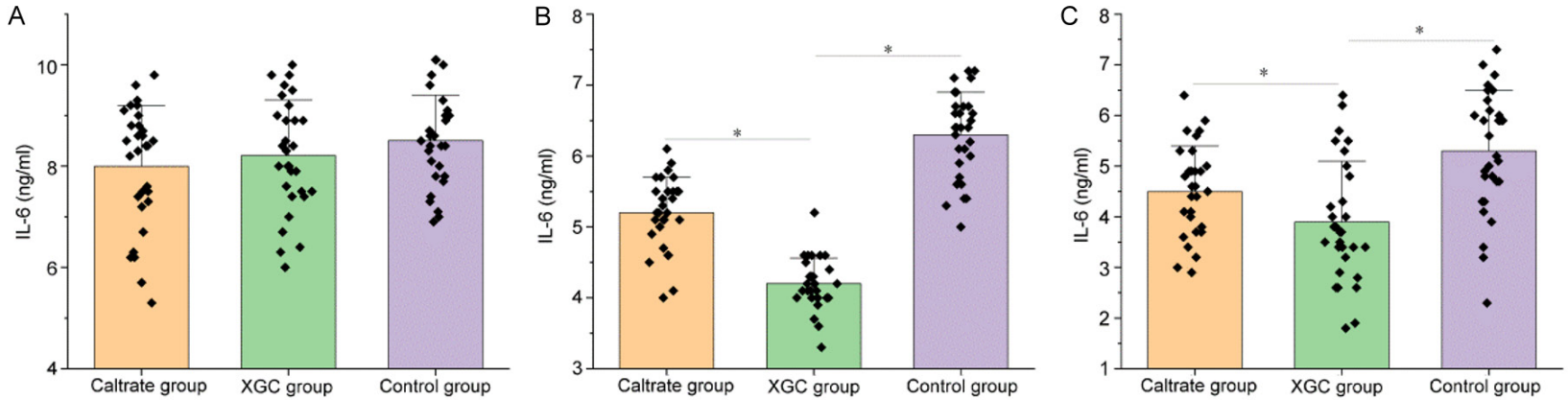

Figure 5. Comparison of IL-6 levels in gingival crevicular fluid before and after treatment. There was no significant difference in the levels of IL-6 in gingival crevicular fluid among the three groups before treatment ($P>0.05$) (A). At 3 months (B) and 6 months (C) of treatment, patients in the XGC group exhibited lower levels of IL-6 compared to the Caltrate group and the control group ($P<0.05$). IL-6: interleukin-6; XGC: Xianling Gubao capsules. * represents a significant difference between groups.

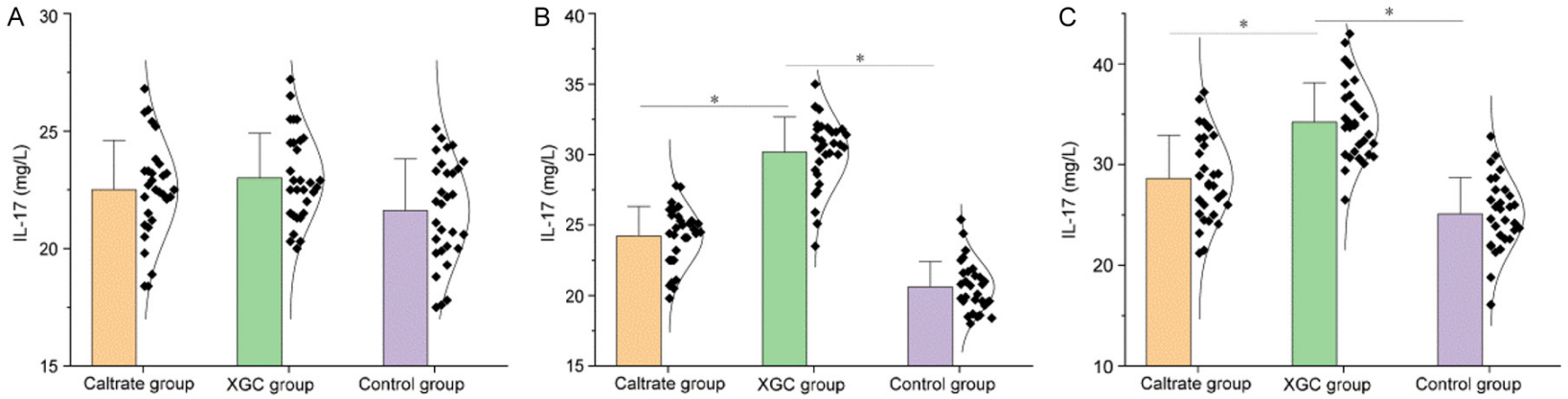

Figure 6. Comparison of IL-17 levels in gingival crevicular fluid before and after treatment. There was no significant difference in the levels of IL-17 in gingival crevicular fluid among the three groups before treatment ($P>0.05$) (A). At 3 months (B) and 6 months (C) of treatment, patients in the XGC group exhibited higher levels of IL-17 compared to the Caltrate group and the control group ($P<0.05$). IL-17: interleukin-17; XGC: Xianling Gubao capsules. * represents a significant difference between groups.

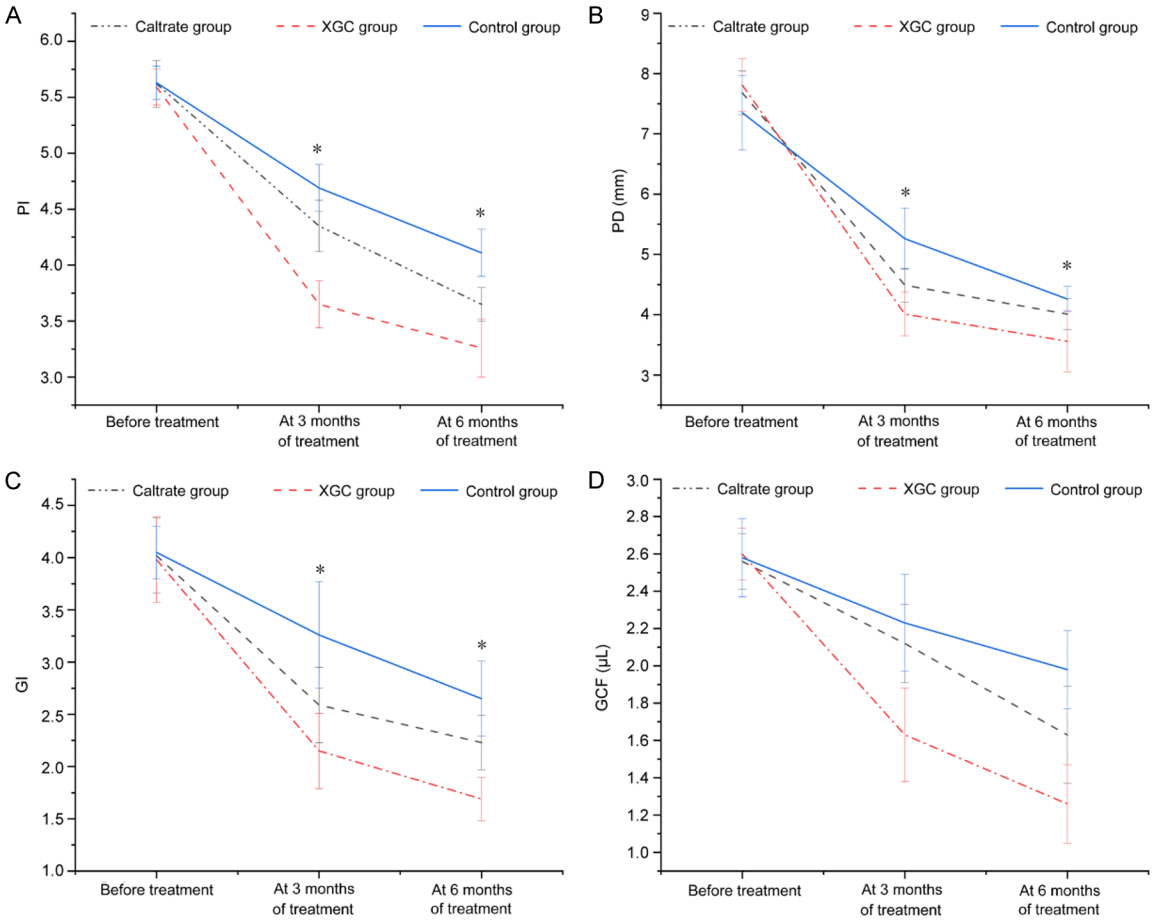

Figure 7. Comparison of periodontal condition before and after treatment. At 3 and 6 months of treatment, the XGC group showed reduced PI (A), PD (B), GI values (C), and gingival crevicular fluid volume (D) compared to the other two groups ($P<0.05$). PI: plaque index; PD: probing depth; GI: gingival index; XGC: Xianling Gubao capsules. * represents a significant difference between groups.

Table 2. Comparison of incidence of adverse reactions

Group	Number of cases	Nausea	Vomiting	Rash	Diarrhea	Incidence
Caltrate group	30	1	0	1	1	3 (10.00%)
XGC group	30	2	1	0	1	4 (13.33%)
Control group	30	1	0	0	1	2 (6.67%)
Fisher	-	-	-	-	-	0.365
P	-	-	-	-	-	0.716

XGC, Xianling Gubao Capsules.

To further evaluate the role of XGC in modulating the inflammatory state in periodontitis, inflammatory factor levels in gingival crevicular fluid were assessed. Compared to the control and Caltrate groups, the XGC group exhibited significant improvements at 3 and 6 months, as evidenced by lower IL-6 and TNF-α levels and higher IL-17 levels. XGC, selected for the XGC group, are a traditional Chinese medicine formulation developed in recent years to warm Yang and tonify the kidneys. While its application in dentistry remains limited, prior research [9] suggests that this formulation enhances trabecular bone quantity and density, thereby improving bone microstructure, which provided the rationale for this study. However, further validation is required to confirm its efficacy for periodontitis treatment.

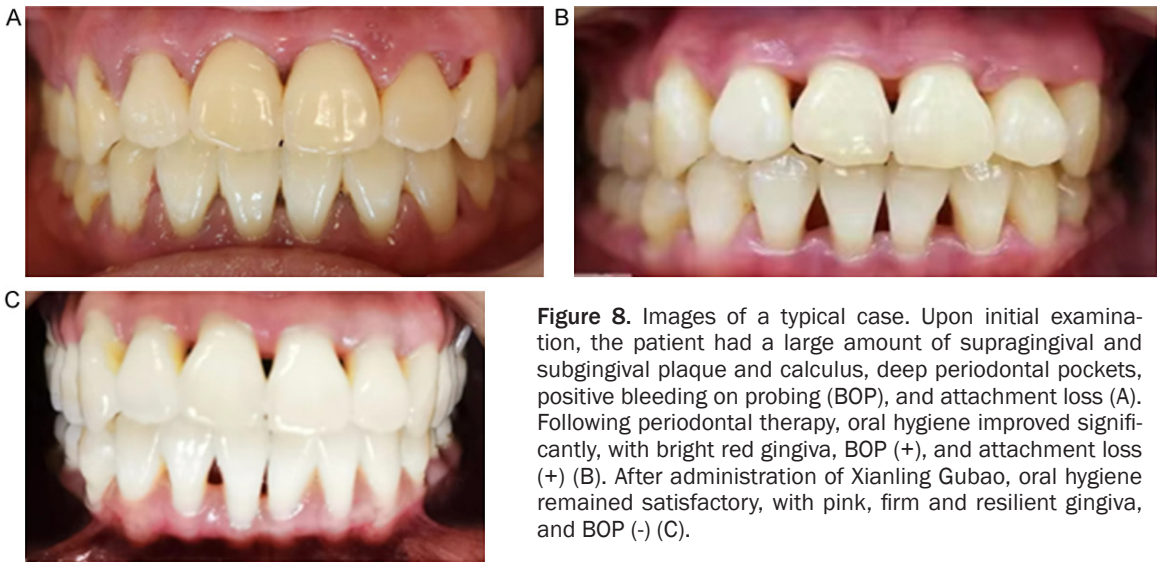

Figure 8. Images of a typical case. Upon initial examination, the patient had a large amount of supragingival and subgingival plaque and calculus, deep periodontal pockets, positive bleeding on probing (BOP), and attachment loss (A). Following periodontal therapy, oral hygiene improved significantly, with bright red gingiva, BOP (+), and attachment loss (+) (B). After administration of Xianling Gubao, oral hygiene remained satisfactory, with pink, firm and resilient gingiva, and BOP (-) (C).

Traditional Chinese medicine (TCM) theory suggests that tooth mobility is often associated with kidney Yang deficiency. Since the kidneys are believed to govern bone health, warming Yang and tonifying the kidneys is considered an appropriate therapeutic approach [19]. However, experimental research on the use of TCM-based kidney tonification for periodontitis remains scarce. According to TCM principles, kidney essence is intrinsically linked to dental health-when kidney essence is abundant, teeth remain strong, whereas deficiency leads to tooth loosening and potential loss. Thus, TCM advocates for treating periodontal disease by tonifying kidney essence [20]. Improving the inflammatory state in periodontitis patients through warming Yang and tonifying the kidneys may offer a viable strategy for alleviating periodontal disease.

XGC are a traditional Chinese medicine formulation that nourishes the liver and kidneys, promotes blood circulation, and strengthens tendons and bones. Existing research has confirmed that this medication increases trabecular bone formation and enhances bone density, thereby improving bone microstructure [21]. XGCs are derived from traditional Chinese medicinal herbs, including Herba Epimedii, Radix Dipsaci, Salvia miltiorrhiza, and Fructus Psoraleae.

Modern pharmacologic studies have shown that Herba Epimedii contains icariin, which upregulates the mRNA expression of alkaline phosphatase, osteocalcin, and osteoprotegerin in osteoblasts, thereby inducing bone marrow mesenchymal stem cell differentiation into osteoblasts and promoting fracture healing [22]. Fructus Psoraleae exhibits estrogen-like properties; in vitro studies suggest that it inhibits osteoclast differentiation, while animal studies indicate that it suppresses osteoclastic bone resorption, activates bone remodeling, and restores normal bone metabolic balance in osteoporotic rats [23]. Salvia miltiorrhiza has been shown to protect renal function and enhance renal blood flow perfusion, thereby accelerating renal function recovery and improving the efficacy of other medications [24].

Animal experiments [25] have demonstrated that XGCs increase IL-1α, IL-1β, IL-10, and IL-17 levels in canine gingival crevicular fluid, findings that are consistent with the results of this study. These results suggest that XGCs may improve periodontitis by alleviating inflammation.

This study also assessed the safety of XGCs in patients with periodontitis. Compared to the control and Caltrate groups, the incidence of adverse reactions in the XGC group was slightly higher, but the difference was not statistically significant, confirming that XGCs have a favorable safety profile.

However, this study has certain limitations, including its retrospective design, relatively small and homogeneous sample size, and short

follow-up period. Future large-scale, multicenter, prospective randomized controlled trials are needed to further validate these findings.

In conclusion, the addition of XGCs to conventional treatment may reduce alveolar bone defect height, improve alveolar bone density, alleviate periodontal inflammation, and decrease inflammatory factor levels in gingival crevicular fluid in patients with periodontitis. Furthermore, XGC demonstrate a high level of safety and substantial clinical application value.

Disclosure of conflict of interest

None.

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