

Application of Cefaclor in Orthodontics through Micro-Implant Anchorage in Patients with Periodontitis

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Fengxing Xu¹

¹Department of Stomatology, First People's Hospital of Yongkang City, 321300 Yongkang, Zhejiang, China

AIM: Chronic periodontitis leads to gingival swelling, hyperplasia, and tooth mobility, which affects orthodontic treatment. The aim of this study was to investigate the application of cefaclor in orthodontics through micro-implant anchorage in patients with periodontitis.

METHODS: A retrospective study was conducted on patients with periodontitis who received micro-implant anchorage treatment in the department of orthodontics at the First People's Hospital of Yongkang City from July 2019 to January 2022. According to different treatment regimens, these patients were divided into the test group (patients receiving cefaclor and micro-implant anchorage treatment) and the control group (patients receiving micro-implant anchorage treatment only). The plaque index (PLI), gingival index (GI), sulcus bleeding index (SBI), and serum inflammatory factor levels were compared between the two groups after treatment.

RESULTS: One hundred and five patients were included in the study, (44 males and 61 females, median age 21 [15–25] years), 51 in the cefaclor group and 54 in the no cefaclor group. After treatment, the PLI, GI, and SBI scores in the two groups were higher than those before treatment, and the levels of serum inflammatory markers significantly increased ($p < 0.05$). After treatment, the PLI, GI, and SBI scores in the test group were significantly lower than those in the control group ($p < 0.001$). The levels of serum interleukin-1 β , interleukin-6, interleukin-8, and tumor necrosis factor- α were significantly lower in the test group, and the interleukin-2 level was higher in the test group ($p < 0.001$). There was no significant difference in the incidence of complications between the two groups ($p > 0.05$).

CONCLUSIONS: Cefaclor and micro-implant anchorage have a good clinical effect on orthodontics in patients with periodontitis, improving periodontal health and reducing inflammatory response.

Keywords: orthodontics; cefaclor; micro-implant anchorage

Introduction

Malocclusion is a common developmental deformity in clinical practice, which is closely related to genetics, environment, bad habits, and other factors [1]. An earlier study has shown that the incidence of teeth hypoplasia is high in orthodontic patients, reaching approximately 4.6%, which is more common in females [2]. Oral diseases lead to severe functional and verbal impairments, as well as tooth loss in adults [3]. The conventional anchorage devices include the trans palatal arch, fixed lingual arch, extraoral arch, Nance arch, and lip bumper, which require patient compliance. However, the conventional devices lack stability, they are not comfortable, and their clinical effect is less than ideal [4, 5].

In 2015, the First People's Hospital of Yongkang City introduced micro-implant anchorage. This method relies on an embedding force applied to bone tissues for orthodontic treatment [6]. Micro-implant anchorage is safe, and it offers comfortable treatment that involves simple surgery, little

trauma, and high stability, which have been unanimously recognized by dentists and patients. Studies have shown that orthodontic treatments cause a stress response in the body, leading to an increase in the level of inflammatory factors and causing certain obstacles to the treatment and recovery of patients [7, 8]. After micro-implant anchorage treatment, patients are prone to periodontitis if they do not pay attention to their oral hygiene. Periodontitis leads to the destruction of the support tissues of teeth, reducing the effect of orthodontic treatments [9, 10]. Thus, the clinical program should be improved to prevent the occurrence of periodontitis.

Cefaclor, a semisynthetic cephalosporin, has the characteristics of good absorption and widespread distribution in the body, indicating that it can act on multiple organ systems within the human body [11]. Currently, cefaclor is common in the clinical treatment of respiratory tract infections, bacterial enteritis, periodontitis, and other diseases, with good anti-inflammatory and antibacterial effects [12]. However, there are few studies on the use of cefaclor in micro-implant anchorage. To assess the efficacy of this entity, this study collected the clinical data of 105 orthodontic patients in First People's Hospital of Yongkang City.

Correspondence to: Fengxing Xu, Department of Stomatology, First People's Hospital of Yongkang City, 321300 Yongkang, Zhejiang, China (e-mail: m15888912186@163.com).

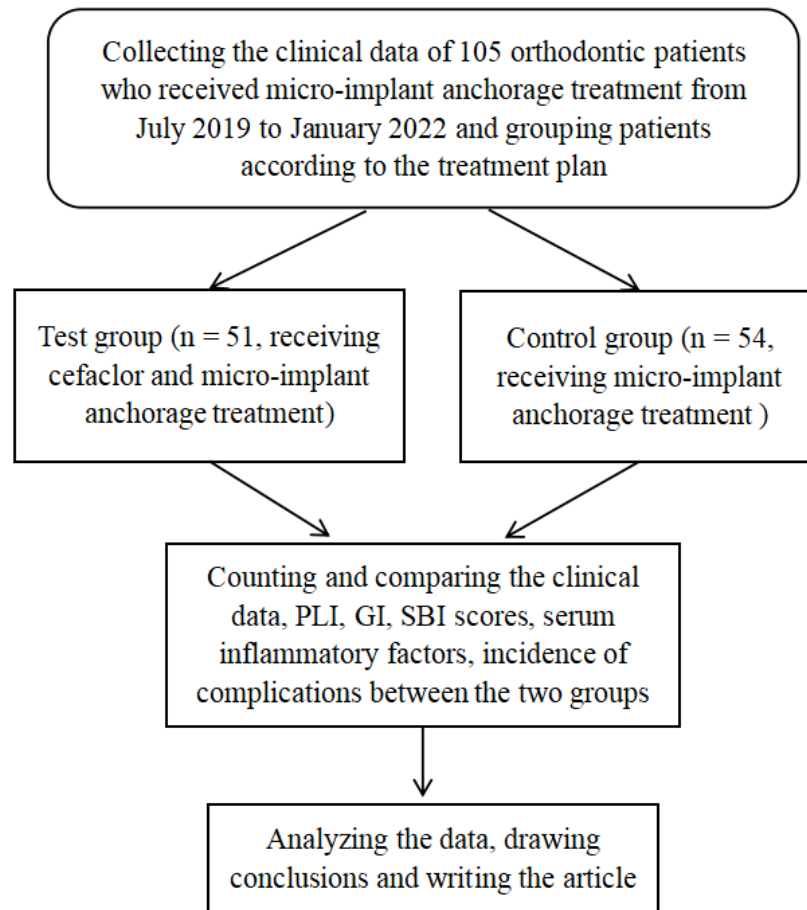


Fig. 1. Flowchart of study design. PLI, plaque index; GI, gingival index; SBI, sulcus bleeding index.

Materials and Methods

General Data

Orthodontic patients who underwent micro-implant anchorage in First People's Hospital of Yongkang City from July 2019 to January 2022 were selected as the research subjects. This study retrospectively selected 105 orthodontic patients who underwent microimplant anchorage. Patients were categorized into test and control groups based on the treatment available in the case system. This study was in line with the Declaration of Helsinki (2013) [13]. This study has been approved by the institutional ethics committee of First People's Hospital of Yongkang City (approval No.: 20190503), and all patients provided written informed consent. The inclusion criteria were as follows: (1) patients were diagnosed by oral assessment and imaging examination and underwent micro-implant anchorage; (2) patients had a positive spirit and volunteered to cooperate for the duration of the study; and (3) patients had good oral hygiene, without oral ulcer. The exclusion criteria were as follows: (1) patients with a history of orthodontics; (2) patients with heart, lung, and other important organ diseases; and (3) patients with blood and endocrine system diseases. The flow chart of the study design is shown in Fig. 1.

Surgical Technique

Patients in both groups underwent micro-implant anchorage using the Vector TAS™ Mini-Screw implant anchorage device [model: 8 mm × 1.4 mm; National Medical Products Administration [NMPA] (I) approval No.: 20173631800, Ormco, Brea, CA, USA]. All patients were treated by dentists within the same group of practitioners, and the surgical procedure was as follows. (1) For oral cleaning, 0.1% cetylpyridinium chloride (NMPA approval No.: H20010753; specification: 200 mL/bottle; manufacturer: Hangzhou Minsheng Pharmaceutical Co., Ltd., Hangzhou, China) was used for gargling, and lidocaine (NMPA approval No.: H34020932; specification: 5 mL:0.1 g/branch; manufacturer: Anhui Changjiang Pharmaceutical Co., Ltd., Wuhu, China) was used for local infiltration anesthesia inside the oral cavity. (2) The specific position and shape of each patient's tooth root were examined, and the tooth to be implanted with the micro-implant was separated by brass wire. The implanting angle and depth were evaluated, and the implantation site was marked to ensure the normal structure of the adjacent teeth at this site. (3) After cutting the mucosa of each patient's alveolar membrane, the micro-implant was implanted. Dentists avoided causing damage to alveolar soft tissues during this process. If

Table 1. Comparison of clinical data in both groups.

Projects	Test group (n = 51)	Control group (n = 54)	χ^2/Z	<i>p</i>
Age, years, median (IQR)	21.00 (19.00–23.00)	21.00 (16.00–23.00)	-0.487	0.626
BMI, kg/m ² , median (IQR)	22.24 (20.12–23.31)	21.59 (20.21–23.57)	-0.899	0.368
Sex, n (%)			0.062	0.804
Males	22 (43.14)	22 (40.74)		
Females	29 (56.86)	32 (59.26)		
Types, n (%)			0.070	0.966
Insufficient gap	20 (39.22)	20 (37.04)		
Supplemental teeth	16 (31.37)	17 (31.48)		
Anomalies of eruption	15 (29.41)	17 (31.48)		
Clinical manifestations, n (%)			0.151	0.928
Anterior protrusion of arch	32 (62.75)	32 (59.26)		
Teeth not covered by lips	15 (29.41)	17 (31.48)		
Others	4 (7.84)	5 (9.26)		
Educational level, n (%)			4.217	0.377
College and above	13 (25.49)	15 (27.78)		
Senior high school	22 (43.14)	21 (38.89)		
Junior high school	15 (29.41)	12 (22.22)		
Primary school	1 (1.96)	4 (7.41)		
Illiteracy	0 (0.00)	2 (3.70)		
Residence, n (%)			0.006	0.938
City	24 (47.06)	25 (46.30)		
Countryside	27 (52.94)	29 (53.70)		

BMI, body mass index; IQR, interquartile range.

the implant could be attached to the gingiva, there was no need for a mucoperiosteal flap. (4) After completing these steps, the tooth tip was photographed (instrument: Digital dental panoramic X-ray system; model: Cranex-DPPI; manufacturer: Finland Soredex Company; address: Tuusula, Finland) to determine the relationship between the implant anchorage and the tooth root. Routine anti-infection treatment was performed in the absence of abnormalities. Patients orally took amoxicillin capsules [NMPA approval No.: H51021734; specification: 0.25 g (counted by C16H19N3O5S), manufacturer: Sichuan Pharmaceutical Inc.; Chengdu, China] for 5 days, tid, at 0.5 g/dose. At the end of treatment, patients were advised to revisit the hospital once a month, replace the chain-shaped elastics in a timely manner, and take them out after 2 years of continuous treatment.

In this study, patients in the test group were treated by oral administration of cefaclor (NMPA approval No.: H20033599; specification: 0.25 g × 12 tablets; Suzhou Chung-HUA Chemical & Pharmaceutical Industrial Co., Ltd., Suzhou, China) for 7 days, tid, at 0.25 g/dose.

Observation Indices

Clinical Data

Clinical data of patients in both groups were collected and compared, namely age, body mass index, sex, types of disease, clinical manifestations, educational level, and residence.

Related Index of Periodontium

The plaque index (PLI), gingival index (GI), and sulcus bleeding index (SBI) in both groups were collected 1 day before treatment and 1 week after treatment. (1) PLI is defined as the mean value of the orthodontic plaque index and lingual plaque index in the patient's labial (buccal) surface [14]. PLI was calculated as the sum of scores of each tooth/number of teeth examined per person. Scoring standards were as follows: complete removal of plaque in the detection area was recorded as 0 points; the coverage area of plaque in the detection area <1/3 was recorded as 1 point; 1/3 to 2/3 was recorded as 2 points; >2/3 was recorded as 3 points; and complete coverage of plaque in the detection area was recorded as 4 points. A lower score indicated a better clearance of plaque than a higher score. (2) GI is defined as a gingival condition observed by a blunt-headed periodontal probe combined with visual inspection. In patients with GI, the change in the color and quality of gingiva and the tendency of bleeding were examined [15]. The mean values of four tooth surfaces, namely the middle labial (buccal) papilla, distal middle labial (buccal) papilla, median labial (buccal) margin, and lingual gingival margin of each tooth were calculated. Scoring standards were as follows: gingival health was recorded as 0 points; mild gingival inflammation, showing mild changes in gingival color and mild edema with no bleeding on probing, was recorded as 1 point; moderate gingival inflammation, showing red gingiva, edema, bright, and bleeding on probing, was recorded

Table 2. Comparison of PLI, GI, and SBI scores between the two groups after treatment.

Parameter		Test group (n = 51) ^o	Control group (n = 54) ^o	Z	p
PLI	Before treatment	1.38 (1.26–1.58)	1.42 (1.30–1.56)	-0.378	0.705
	After treatment	1.47 (1.31–1.47)*	1.68 (1.47–1.86)*	-4.630	<0.001
GI	Before treatment	1.09 (0.99–1.17)	1.11 (0.98–1.20)	-0.443	0.658
	After treatment	1.15 (1.02–1.24)*	1.32 (1.14–1.51)*	-4.922	<0.001
SBI	Before treatment	1.54 (1.44–1.86)	1.65 (1.43–1.84)	-0.266	0.790
	After treatment	1.68 (1.63–1.76)*	2.05 (1.99–2.09)*	-8.833	<0.001

^oAll values are expressed as median (IQR) points.

Compared with the same group before treatment. * indicates a significant difference, $p < 0.05$.

PLI, plaque index; GI, gingival index; SBI, sulcus bleeding index.

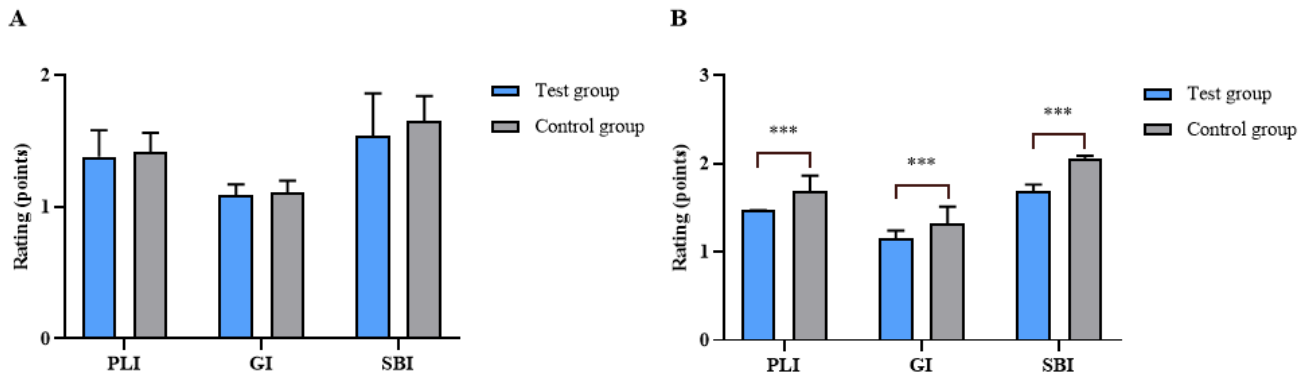


Fig. 2. Comparison of PLI, GI, and SBI scores in both groups before and after treatment (median [IQR] points). (A) Comparison of PLI, GI, and SBI scores in both groups before treatment. (B) Comparison of PLI, GI, and SBI scores in both groups after treatment. *** indicates a significant difference, $p < 0.001$. PLI, plaque index; GI, gingival index; SBI, sulcus bleeding index.

as 1 point; and severe gingival inflammation, manifested as obvious redness and swelling of gums or ulcers, and the tendency of automatic bleeding, was recorded as 3 points. A lower score indicated that patients had better gingival health than those with a higher score. (3) SBI is defined as the bleeding of the gingival sulcus by a blunt-headed periodontal probe [16]. The scoring standards of SBI were identical to those of GI, ranging from 0 points to 3 points. A lower score indicated that patients had less gingival sulcus bleeding than those with a higher score.

Serum Inflammatory Markers

In brief, 1 day before treatment and 1 week after treatment, 4 mL of peripheral venous blood was collected from patients in both groups, placed in the BIOBASE centrifuge (model: TGL-16M; manufacturer: BIOBASE Group; Jinan, China), and centrifugated at 3500 r/min for 10 min. The supernatant was obtained and stored in a freezer at -80°C . The levels of interleukin- 1β (IL- 1β), interleukin-6 (IL-6), interleukin-8 (IL-8), interleukin-2 (IL-2), and tumor necrosis factor- α (TNF- α) were measured by enzyme-linked immunosorbent assays. The reagent kits of IL- 1β , IL-6, IL-8, and IL-2 (serial No.: LM19773, LM33910, LM43272, LM65145) were purchased from Shanghai Lianzu Biotechnology Co., Ltd. (address: Shanghai, China), and the TNF- α reagent kit (se-

rial No.: RJ23641) was procured from Shanghai Ren Jie Biotechnology Co., Ltd. (address: Shanghai, China). The assays were carried out according to the manufacturers' instructions.

Complications

The adverse reactions of both groups were recorded during the treatment, and they included oral inflammation, oral infection, oral discomfort, tooth mobility, gastrointestinal system damage, and soft tissue edema.

Statistical Analysis

The SPSS 26.0 statistical software (IBM, Armonk, NY, USA) was used to process the data in this study, and GraphPad Prism 7 (GraphPad Software, San Diego, CA, USA) was adopted to generate the graphs. The categorical variables were detected by χ^2 test, indicated by [n (%)]. The normal distribution of continuous variables was detected by the Shapiro–Wilk test. Mann–Whitney U test was used to compare the data between groups that did not conform to the normal distribution, and Wilcoxon signed rank test was adopted for intra-group comparisons. Those not conforming to the normal distribution were indicated by M (P_{25} , P_{75}). The difference was statistically significant when $p < 0.05$.

Table 3. Comparison of serum inflammatory factor levels before and after treatment in both groups.

Parameter		Test group (n = 51) ^o	Control group (n = 54) ^o	Z	p
IL-1 β (pg/mL)	Before treatment	8.92 (6.57–10.34)	8.15 (5.65–10.49)	-0.587	0.557
	After treatment	1.40 (1.25–1.53)*	1.94 (1.78–2.20)*	-8.804	<0.001
IL-6 (pg/mL)	Before treatment	8.96 (6.52–11.12)	8.56 (7.01–10.36)	-0.154	0.878
	After treatment	1.55 (1.45–1.65)*	3.16 (2.94–3.34)*	-8.830	<0.001
IL-8 (pg/mL)	Before treatment	17.25 (15.25–20.35)	17.10 (14.82–19.44)	-0.660	0.509
	After treatment	7.05 (6.78–7.31)*	8.80 (8.26–9.15)*	-8.829	<0.001
IL-2 (μ g/L)	Before treatment	1.63 (1.34–1.81)	1.53 (1.35–1.81)	-0.308	0.758
	After treatment	4.71 (4.37–5.03)*	4.02 (3.84–4.13)*	-8.384	<0.001
TNF- α (μ g/L)	Before treatment	6.10 (5.75–6.27)	6.03 (5.85–6.25)	-0.741	0.459
	After treatment	3.67 (3.21–4.33)*	5.12 (4.79–5.37)*	-8.746	<0.001

^oAll values are expressed as median (IQR).

Compared with the same group before treatment. * indicates a significant difference, $p < 0.05$. IL-1 β , interleukin-1 β ; IL-6, interleukin-6; IL-8, interleukin-8; IL-2, interleukin-2; TNF- α , tumor necrosis factor- α .

Table 4. Comparison of patients' complications in both groups.

Complications	Test group (n = 51)	Control group (n = 54)	χ^2	p
Oral inflammation	1 (1.96)	1 (1.85)	-	-
Oral infection	1 (1.96)	2 (3.70)	-	-
Oral discomfort	2 (3.92)	3 (5.56)	-	-
Tooth mobility	1 (1.96)	1 (1.85)	-	-
Gastrointestinal system damage	1 (1.96)	0 (0.00)	-	-
Soft tissue edema	0 (0.00)	2 (3.70)	-	-
Others	3 (5.88)	1 (1.85)	-	-
Total	9 (17.65)	10 (18.52)	0.013	0.908

All values are expressed as n (%).

Results

One hundred and five patients were included in the study, (44 males and 61 females (median age 21 [15–25] years), 51 in the cefaclor group and 54 in the no cefaclor group.

No Significant Differences were Observed in Clinical Data between the Two Groups

There were no significant differences in patients' clinical data between the test group and control group ($p > 0.05$; Table 1).

PLI, GI, and SBI Scores were Higher in Both Groups after Treatment

Before treatment, there were no significant differences in PLI, GI, and SBI scores between the two groups ($p > 0.05$). After treatment, the PLI, GI, and SBI scores of the two groups were higher than those before treatment ($p < 0.05$), but the scores were lower in the test group compared with the control group ($p < 0.001$; Table 2, Fig. 2).

Serum IL-1 β , IL-6, IL-8, and TNF- α Levels were Lower in Both Groups after Treatment

Before treatment, there were no significant differences in serum inflammatory marker levels between the two groups ($p > 0.05$). The levels of serum inflammatory factors in the two groups significantly improved after treatment ($p < 0.05$). After treatment, the levels of serum IL-1 β , IL-6, IL-8, and TNF- α were lower in the test group than those in the control group, and the IL-2 level was higher in the test group ($p < 0.001$; Table 3).

No Significant Difference in the Incidence of Complications was Observed between the Two Groups

The total incidences of complications in the test group and the control group were 17.65% and 18.52%, respectively, and there was no significant difference in the incidence of complications between the two groups ($p > 0.05$; Table 4).

Discussion

Orthodontics can treat insufficient tooth space, supernumerary teeth, and abnormal eruption, and can improve anterior protrusion of the arch, teeth not covered by lips, and other symptoms, thereby improving general facial features [17, 18]. In recent years, with the rapid development of economies and the increase in living standards, individuals have begun to focus on facial beauty and oral health [19]. However, conventional orthodontic treatments, with complex wearing processes, require high compliance, and most treatments are simply uncomfortable. Therefore, these methods do not meet the current needs of oral treatment [20, 21]. Continuous developments in materials science offer new treatment breakthroughs for orthodontics, one of which is micro-implant anchorage. Micro-implant anchorage reduces damage to patients' oral tissues, such as teeth and gums, and the flexible implanting area improves comfort and stability in those receiving orthodontic treatment. The micro-implant anchorage is recognized as an effective method by dentists, hygienists, and patients [22, 23]. In addition, previous studies have reported that conventional anchorage devices increase the difficulty of daily oral cleaning for patients, and they are prone to residue deposition which leads to bacterial growth and proliferation [24, 25]. In the long run, these residues damage the gums and even cause enamel decalcification. The micro-implant contributes to the maintenance of a healthy and clean oral environment, avoids damage of gums and enamel, protects masticatory function, and exerts a significant orthodontic effect. However, a previous study has found that the micro-implant anchorage can still damage a patient's gums and alveolar mucosa, resulting in increased levels of inflammatory factors [26]. Without effective intervention, micro-implant anchorage may cause infection, gingivitis, and periodontitis, resulting in poor efficacy. As a broad-spectrum and semisynthetic cephalosporin, cefaclor can inhibit the synthesis of the bacterial cell wall. After oral administration, cefaclor is rapidly absorbed from the intestinal tract and delivered to the tissues, thus playing antibacterial and anti-inflammatory roles.

Patients in the test group took cefaclor orally during treatment. The results of this study showed that PLI, GI, and SBI scores were lower in the test group after treatment than in the control group, suggesting that combined treatment can improve the periodontal health of patients. After measuring the inflammatory marker levels in all patients, this study found that the levels of serum IL-1 β , IL-6, IL-8, and TNF- α were lower in the test group than those in the control group, and the IL-2 level was higher in the test group, consistent with the findings of earlier studies. Furthermore, a series of protective responses are caused by trauma in the local tissues of orthodontic patients, including pain, fever, and other symptoms, which are not conducive to wound healing [27]. However, cefaclor can alleviate the inflammation of soft tissues and promote the recovery of patients.

In addition to improving masticatory function, orthodontic treatment can also improve facial attractiveness for most patients. The micro-implant anchorage technology can reduce the influence of patients' cooperation on the treatment effect and use the gap of tooth extraction to adduct teeth and improve facial appearance [28].

This study has some limitations. The study has a small sample size, and the observation indicators cited in this study lack objectivity, which may lead to biased results. As a retrospective study, this study cannot completely rule out the influence of confounding factors. Thus, the sample size should be expanded in future studies, and the experimental design should be improved. Prospective research will be conducted to control variables strictly, and more objective evaluation tools will be adopted to obtain accurate research data and to improve the clinical treatment plan of orthodontics.

Conclusions

Cefaclor and micro-implant anchorage have a good clinical effect on orthodontics in patients with periodontitis, improving periodontal health and reducing the inflammatory response.

Availability of Data and Materials

Data to support the findings of this study are available on reasonable request from the corresponding author.

Author Contributions

FXX designed the research study. FXX performed the research. FXX analyzed the data. FXX drafted the article and revised the manuscript critically for important intellectual content. The author read and approved the final manuscript and participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study has been approved by the institutional ethics committee of First People's Hospital of Yongkang City (approval No.: 20190503), and all patients provided written informed consent. The study is following the Declaration of Helsinki.

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This research received no external funding.

Conflict of Interest

The author declares no conflict of interest.

References

- [1] Wang Z, Feng J, Wang Q, Yang Y, Xiao J. Analysis of the correlation between malocclusion, bad oral habits, and the caries rate in adolescents. *Translational Pediatrics*. 2021; 10: 3291–3300.
- [2] De Santis D, Pancera P, Sinigaglia S, Faccioni P, Albanese M, Bertossi D, *et al.* Tooth agenesis: part 1. Incidence and diagnosis in orthodontics. *Journal of Biological Regulators and Homeostatic Agents*. 2019; 33: 19–22.
- [3] Isola G. The Impact of Diet, Nutrition and Nutraceuticals on Oral and Periodontal Health. *Nutrients*. 2020; 12: 2724.
- [4] Ahuja V, Thosar NR, Shrivastav S, Ahuja A. Effect of Lingual Arch Space Maintainer on the Position of Mandibular Molars and Incisors in the Vertical Direction during the Resolution of Mandibular Incisors Crowding: A Systematic Review of Clinical Trials in Humans. *International Journal of Clinical Pediatric Dentistry*. 2021; 14: S76–S81.
- [5] Roberts WE, Chang CH, Chen J, Brezniak N, Yadav S. Integrating skeletal anchorage into fixed and aligner biomechanics. *Journal of the World Federation of Orthodontists*. 2022; 11: 95–106.
- [6] Kaur H, Owen B, Tran B, Guan R, Luo J, Granley A, *et al.* The biomechanics of posterior maxillary arch expansion using fixed labial and lingual appliances. *The Angle Orthodontist*. 2020; 90: 688–694.
- [7] Martin C, Celis B, Ambrosio N, Bollain J, Antonoglou GN, Figuero E. Effect of orthodontic therapy in periodontitis and non-periodontitis patients: a systematic review with meta-analysis. *Journal of Clinical Periodontology*. 2022; 49: 72–101.
- [8] Yamaguchi M, Fukasawa S. Is Inflammation a Friend or Foe for Orthodontic Treatment?: Inflammation in Orthodontically Induced Inflammatory Root Resorption and Accelerating Tooth Movement. *International Journal of Molecular Sciences*. 2021; 22: 2388.
- [9] Lin H, Chen H, Zhao X, Ding T, Wang Y, Chen Z, *et al.* Advances of exosomes in periodontitis treatment. *Journal of Translational Medicine*. 2022; 20: 279.
- [10] Alsulaimani L, Alqarni H, Akel M, Khalifa F. The Orthodontics-Periodontics Challenges in Integrated Treatment: A Comprehensive Review. *Cureus*. 2023; 15: e38994.
- [11] Koytchev R, Ozalp Y, Erenmemisoglu A, Tyutyulkova N, Gatchev E, Alpan RS. Studies on the bioequivalence of second generation cephalosporins: cefaclor capsules and suspension. *Arzneimittel-Forschung*. 2004; 54: 583–587.
- [12] Wang JF, Shi CY, Ying HZ. Cephalosporins-induced intestinal dysbiosis exacerbated pulmonary endothelial barrier disruption in streptococcus pneumoniae-infected mice. *Frontiers in Cellular and Infection Microbiology*. 2022; 12: 997368.
- [13] World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA*. 2013; 310: 2191–2194.
- [14] Azevedo CL, Henriques PSG, Pannuti CM, Michel-Crosato E. Selfie Dental Plaque Index: A New Tool for Dental Plaque Assessment. *Journal of Clinical and Experimental Dentistry*. 2022; 14: e926–e931.
- [15] Chiu S, Lee Y, Liu M, Chen H, Ye H, Liu Y. Evaluation of the marginal adaptation and gingival status of full-crown restorations using an intraoral camera. *BMC Oral Health*. 2022; 22: 517.
- [16] Newbrun E. Indices to measure gingival bleeding. *Journal of Periodontology*. 1996; 67: 555–561.
- [17] Yabe A, Ikoma M, Arai K. Evaluations of the facial attractiveness of young women with severe maxillary anterior crowding by orthodontists and laypeople with and without orthodontic treatment experience in Japan. *American Journal of Orthodontics and Dentofacial Orthopedics: Official Publication of the American Association of Orthodontists, its Constituent Societies, and the American Board of Orthodontics*. 2021; 159: 750–757.
- [18] Saini R, Thakur N, Jindal Goyal R, Sharma Rai K, Bagde H, Dhopte A. Analysis of Smile Aesthetic Changes With Fixed Orthodontic Treatment. *Cureus*. 2022; 14: e32612.
- [19] Kim YJ, Lee BK. Recent Trends in Orthognathic Surgery in Asia. *Facial Plastic Surgery Clinics of North America*. 2021; 29: 549–566.
- [20] Rask H, English JD, Colville C, Kasper FK, Gallerano R, Jacob HB. Cephalometric evaluation of changes in vertical dimension and molar position in adult non-extraction treatment with clear aligners and traditional fixed appliances. *Dental Press Journal of Orthodontics*. 2021; 26: e2119360.
- [21] Ke Y, Zhu Y, Zhu M. A comparison of treatment effectiveness between clear aligner and fixed appliance therapies. *BMC Oral Health*. 2019; 19: 24.
- [22] Choi SH, Jeon JY, Lee KJ, Hwang CJ. Clinical applications of miniscrews that broaden the scope of non-surgical orthodontic treatment. *Orthodontics & Craniofacial Research*. 2021; 24: 48–58.
- [23] Wang K, Fan H, Yang H, Li J, Xie W. Efficacy and safety of micro-implant anchorage in Angle class II malocclusion orthodontic treatment: A protocol for systematic review and meta-analysis. *Medicine*. 2020; 99: e23221.
- [24] Albhaisi Z, Al-Khateeb SN, Abu Alhaja ES. Enamel demineralization during clear aligner orthodontic treatment compared with fixed appliance therapy, evaluated with quantitative light-induced fluorescence: A randomized clinical trial. *American Journal of Orthodontics and Dentofacial Orthopedics: Official Publication of the American Association of Orthodontists, its Constituent Societies, and the American Board of Orthodontics*. 2020; 157: 594–601.
- [25] Nguyen H, Shin JW, Giap HV, Kim KB, Chae HS, Kim YH, *et al.* Midfacial soft tissue changes after maxillary expansion using micro-implant-supported maxillary skeletal

expanders in young adults: A retrospective study. *Korean Journal of Orthodontics*. 2021; 51: 145–156.

[26] AlMaghlouth B, AlMubarak A, Almaghlouth I, AlKhalifah R, Alsadah A, Hassan A. Orthodontic Intrusion Using Temporary Anchorage Devices Compared to Other Orthodontic Intrusion Methods: A Systematic Review. *Clinical, Cosmetic and Investigational Dentistry*. 2021; 13: 11–19.

[27] Li Y, Wang Y, Yin Y, Liu P. Simple periodontal therapy combined with periodontal orthodontics improves the

curative effect and reduces the inflammatory response in the treatment of PD. *American Journal of Translational Research*. 2022; 14: 6332–6340.

[28] Baxi S, Shadani K, Kesri R, Ukey A, Joshi C, Hardiya H. Recent Advanced Diagnostic Aids in Orthodontics. *Cureus*. 2022; 14: e31921.

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