Original Article

Comparison of single-visit versus multiple-visit root canal therapy for chronic anterior apical periodontitis

Bogang Xiong^{1*}, Xiujuan Hou^{2*}, Tianyong Xia³, Yuna Liu⁴

¹Department of Stomatology, Beijing Hospital of Integrated Traditional Chinese and Western Medicine, Beijing, China; ²Department of Repair, Affiliated Yantai Stomatological Hospital, Binzhou Medical University, Yantai, Shandong, China; ³Weifang Stomatological Hospital, Weifang, Shandong, China; ⁴Department of Clinical Laboratory, Beijing Hospital of Integrated Traditional Chinese and Western Medicine, Beijing, China. *Equal contributors and co-first authors.

Received July 26, 2024; Accepted October 8, 2024; Epub November 15, 2024; Published November 30, 2024

Abstract: Objective: To compare the efficacy of single-visit root canal therapy (RCT) and traditional multi-visit RCT for chronic apical periodontitis in anterior teeth. Methods: A retrospective analysis was conducted on 106 patients with sinus-type anterior chronic apical periodontitis who underwent root canal treatment during March 2020 and April 2023 at Beijing Hospital of Integrated traditional Chinese and Western Medicine. The patients were divided into an observation group (55 cases, single-visit RCT) and a control group (51 cases, traditional multi-visit RCT) according to different treatment methods. Results: There were no significant differences in the sinus tract healing at post-treatment 2 weeks, the pain incidence at post-treatment one month, or clinical composite efficacy at posttreatment 6 months between the two groups (all P>0.05). However, after 3 and 6 months of treatment, the apical projection zone was significantly reduced in both groups compared to pre-treatment areas (P<0.05), though the difference between groups was not significant (P>0.05). The levels of tumor necrosis factor- α (TNF- α) and interleukin-6 (IL-6) in gingival fluid were significantly lower (P<0.05) while interleukin-10 (IL-10) levels were significantly higher (all P<0.05) in both groups after 6 months of treatment compared to the pre-treatment levels. Again, no significant differences were found between the two groups (all P>0.05). The operation time and treatment cost of observation group were remarkably lower than those in control group (P<0.05). Conclusion: For patients with chronic sinus-type anterior apical periodontitis, a single-visit RCT can achieve similar results as traditional multiple-visit RCT, but with significantly shorter operation time and less medical cost. This approach is recommended for clinical practice.

Keywords: Single-visit RCT, multiple-visit RCT, chronic periapical inflammation, clinical efficacy

Introduction

Dental diseases such as deep caries, trauma, and hidden cracks that are not promptly treated or filled, or where bacteria have invaded the pulp without root canal treatment, can lead to pulp necrosis, crown discoloration, and the spread of pathogenic microorganisms to the tissues surrounding the root tip through the canal system [1, 2]. Sinus-type chronic periapical periodontitis arises from bacteria and microbial abscesses in the root canal system that are left untreated for an extended period [3]. The disease is likely to become a chronic and difficult-to-treat periapical periodontitis due to long duration of the lesion, tortuous sinus tract, and recurrent exacerbations of the

patient's condition, which may result in the formation of ciliated columnar epithelium [4, 5].

Currently, the most effective and common clinical treatment method is root canal therapy (RCT). Traditional multiple-visit RCT offers advantages of stable curative effect, effective root canal disinfection, and less pain. However, the traditional method has its drawbacks, including a long treatment time, requiring patients to visit multiple times, and higher treatment costs, contributing to a heavier medical burden [6, 7]. In response to these challenges, an increasing number of scholars advocate for single-visit RCT, which aims to reduce patient discomfort and economic burden. But some studies suggest that the treatment effect of

one-time RCT is not as good as traditional multiple RCT [8]. In order to improve the therapeutic efficacy of chronic periapical periodontitis in the patients with sinus tract, enhance their quality of life, and reduce their medical burden at the same time, this study conducted a comparative analysis of the efficacy of one-time RCT and traditional multiple RCT for chronic periapical periodontitis in anterior teeth.

Patients and methods

Clinical data

A retrospective analysis was conducted on 106 patients with sinus-type anterior chronic apical periodontitis who underwent root canal treatment from Mar. 2020 to Apr. 2023 at Beijing Hospital of Integrated traditional Chinese and Western Medicine. The patients were divided into an observation group (55 cases) and a control group (51 cases) according to different treatment methods. The research was approved by the Ethics Committee of Beijing Hospital of Integrated traditional Chinese and Western Medicine. The sample size for each group is determined based on the formula $n = C^2\sigma^2/p^2,$ while taking into account the actual treatment plan for the patients.

Inclusion criteria

(1) Patients with swollen and painful affected teeth, along with a history of recurrent gum swelling. The sinus tract was detectable using a probe, pulp vitality tests were negative, and apical radiography showed a clear projection area around the apical tip (diameter <5 mm), meeting the diagnostic criteria for chronic periapical inflammation. (2) All the affected teeth were single-rooted and without any periodontal disease. (3) Patients ranged from 18 to 60 years old. (4) Patients with good adherence to treatment. (5) Patients with complete clinical data.

Exclusion criteria

(1) Patients with other periodontal or endodontic lesions; (2) Patients allergic to the drugs used in this study; (3) Patients in pregnancy, lactation or those planning pregnancy in the near future; (4) Patients with severe dysfunction of the heart, liver, kidneys and other vital organs; (5) Patients with concurrent malignant

tumors; (6) Patients with comorbid immune system disorders.

Methods

The control group underwent conventional multiple-visit root canal therapy, involving routine pulp opening, extraction and radiographic examination. Strict aseptic protocols were followed, and the working length of root canal was measured using an apical locator. Root canal preparation was performed using a gradual step-back technique, alternating between irrigation with rinsing solution and the use of 15to 40-gauge enlarging needles and root canal files to clean and lubricate the canal walls. During the process, attention should be paid to avoiding mechanical damage to the apical tissue. The root canals were dried with sterilized paper points and temporarily sealed with a formaldehyde-cresol mixture. Patients were scheduled for follow-up visit one week later. If symptoms persisted, additional closures with formaldehyde-cresol were applied. Once the patient's symptoms alleviated, cold filling was applied to the affected teeth using the vertical pressurization method. X-rays were taken 30 min after filling to assess the quality of the filling.

The observation group underwent a single-visit RCT procedure. Root canal preparation was performed in the same way as in control group. The root canal was then filled with a solid guttapercha tip and iodoform zinc oxide paste. Zinc phosphate cement was used as the conventional base, and occlusion was adjusted using the lateral pressure method.

Both groups received the same fistula management. A periodontal probe was used to probe the patient's apical lesion area, and hydrogen peroxide and saline were injected through the fistula tract. The periapical and fistula tracts were repeatedly rinsed until the mucosa became slightly whitish, and the fistula tract was cauterized after purulent discharge was cleared.

Observation of indicators

(1) Comparison of pain conditions. The pain status of the patients was evaluated 1 week after treatment. The degree of pain was classified into four grades: no pain; mild pain (mild pain reaction that did not affect biting or eat-

- ing); Moderate pain (pain that interfered with the ability to bite and eat); and severe pain (Intense pain that prevented biting and eating, possibly accompanied by significant swelling). Pain incidence = (mild pain + moderate pain + severe pain)/total number of cases × 100%.
- (2) Comprehensive efficacy. Six months after treatment, the efficacy of patients' comprehensive treatment was assessed based on their symptoms, clinical signs, and X-ray findings. Significantly effective: the patient's symptoms, such as percussion pain, spontaneous pain, and swelling in the affected area, disappeared. There was no redness or swelling in the gingiva at the apical area. The sinus opening healed, and X-ray showed that the periapical lesion had disappeared, the sclerotic plate was intact, and the periodontal space was normal. Effective: no obvious symptoms of discomfort such as percussion pain, limitation of mastication or spontaneous pain in the affected area, no redness and swelling of the gingiva at the apical area, the sinus opening had healed, and the X-ray examination showed a significant reduction in the periapical low-density shadow, although it had not completely disappeared. Failure: The patient still experienced significant percussion pain in the affected tooth area, which may have been accompanied by swelling. X-ray examination showed no significant improvement in the low-density shadow around the root apex. Overall effective rate = (significantly effective cases + effective cases)/total number of cases × 100%.
- (3) Sinus healing. Sinus healing was evaluated 2 weeks after treatment and categorized into three levels. Sinus healing: The sinus opening showed no oozing, redness, swelling, or tenderness, and a probe could not penetrate the tract. Sinus improvement: the sinus opening appeared slightly red and swollen with mild tenderness and a small amount of exudation. The probe could be inserted but at a shallower depth. No improvement: the sinus opening is red, swollen, and purulent with obvious tenderness, and the probe could be inserted into the root apex. Total improvement rate = (sinus healing cases + sinus improvement cases)/total number of cases × 100%.
- (4) Condition of root tip healing. Patients were examined by X-ray before treatment, and at 3 and 6 months post-treatment. The periapical areas of the teeth were fully exposed, and the

- x-ray images were imported into Image-Pro Plus 6.0 biological image processing system to record changes of periapical projection area.
- (5) Inflammatory factors in periodontics. The levels of periodontal inflammatory factors were measured before and after 6 months of treatment. After rinsing the mouth with warm water and blow-drying the tooth surface, gingival sulcus fluid was collected from the affected teeth using filter paper strips. The levels of interleukin-6 (IL-6), interleukin-10 (IL-10), and tumor necrosis factor-alpha (TNF- α) were measured using enzyme-linked immunosorbent assay (ELISA). Meanwhile, 50 healthy individuals were selected as the healthy control group, and their gingival fluid was tested for the same inflammatory markers.
- (6) Operation time-consuming and cost. The duration of surgery and the cost of surgical treatment were compared between the two groups of patients.

Statistical analysis

SPSS 27.0 was used for statistical analysis. The measured data were expressed as mean \pm SD and compared between groups by t-test. The counted data were expressed as number (%) and compared using chi-square test. Tank data were compared by rank-sum test. The difference was considered significant when P<0.05.

Results

Clinical information

There was no significant difference between the two groups in terms of gender, age and disease duration (all *P*>0.05) (**Table 1**).

Comparison of pain response levels

At 1 week postoperatively, 37 (76.27%) patients in the observation group reported no pain, 14 (25.45%) reported mild pain, 4 (7.27%) reported moderate pain, and no patients (0.00%) experienced severe pain. The incidence of pain in the observation group was 32.73%. In the control group, 30 patients (58.82%) reported no pain, 15 patients (29.41%) reported mild pain, 6 patients (11.76%) reported moderate pain, and no patients (0.00%) experienced

Table 1. Comparison of clinical data between the two groups

0.42	NI	Gender		Age(years	Disease duration (months, $\bar{x}\pm s$)	
Group	N	Male Female old, $\overline{x} \pm s$)		old, $\overline{x} \pm s$)		
Observation Group	55	30	25	43.82±5.30	7.95±1.83	
Control Group	51	29	22	44.17±6.34	8.06±1.77	
t/x²	-	0.0	058	0.785	0.314	
Р	-	>0	0.05	>0.05	>0.05	

Table 2. Comparison of pain degree between the two groups [n (%)]

Group	N	No pain	Mild pain	Moderate pain	Severe pain	Pain incidence (%)
Observation Group	55	37 (67.27)	14 (25.45)	4 (7.27)	0 (0.000)	32.73
Control Group	51	30 (58.82)	15 (29.41)	6 (11.76)	0 (0.000)	41.18
Z/x^2	-			0.968		0.812
Р	-			0.333		0.367

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

Group	N	Significantly effective	Effective	Failure	Overall effective rate (%)
Observation Group	55	39 (70.91)	13 (23.64)	3 (5.45)	94.55
Control Group	51	41 (80.39)	9 (17.65)	1 (1.96)	98.04
Z/x^2	-		1.182		0.188
P	-	0.238			0.665

Table 4. Comparison of sinus tract healing between the two groups [n (%)]

Group	N	Healing of sinus tract	Sinus improvement	No improvement in sinus tract	Total improvement rate (%)
Observation Group	55	42 (76.36)	8 (14.55)	5 (9.09)	90.91
Control Group	51	43 (84.31)	6 (11.76)	2 (3.92)	96.08
Z/x^2	-		1.080		0.462
Р	-		0.281		0.497

severe pain, yielding a pain incidence of 41.183%. The difference in the pain incidence between the two groups was not statistically significant (*P*>0.05) (**Table 2**).

Evaluation of comprehensive efficacy

Six months after treatment, 39 cases (70.91%) in the observation group showed obvious effects, 13 cases (23.64%) showed effective results, and 3 cases (5.45%) were ineffective, demonstrating a total effective rate of 94.55%. In the control group, 41 cases showed significant improvement (80.39%), 9 cases showed effective results (17.65%), and 1 case (1.96%) had no improvement, with a total effective rate of 98.04%. The difference in comprehensive clinical efficacy between the two groups was not statistically significant (*P*>0.05) (**Table 3**).

Comparison of sinus tract healing

In the observation group two weeks after treatment, there were 42 cases (76.36%) with sinus healing, 8 cases (14.55%) with sinus improvement, and 5 cases (9.09%) with no improvement in the sinus. The total sinus improvement rate was 90.91%. In the control group, sinus healing occurred in 43 cases (84.31%), sinus improvement in 6 cases (11.76%) and no sinus improvement in 2 cases (3.92%). The total sinus improvement rate was 94.23%. The difference in sinus tract healing between the two groups was not statistically significant (*P*>0.05) (Table 4).

Comparison of apical healing

After 3 and 6 months of treatment, the area of the apical projection zone was significantly

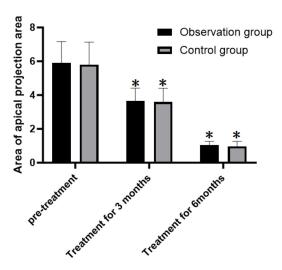


Figure 1. Comparison of the area of apical projection zone between the two groups. Note: *P<0.05 compared to pre-treatment level in the same group.

reduced in both groups compared to the pretreatment area (P<0.05). However, there was no significant difference in the reduction of the apical projection zone between the two groups (P>0.05) (**Figure 1**).

Inflammatory factor levels in the periodontium

After 6 months of treatment, the levels of IL-6 and TNF- α levels in the gingival fluid were significantly lower (all P<0.05) while the levels of IL-10 were significantly higher (P<0.05) in both groups compared to the pre-treatment levels. However, there was no significant difference in the levels of IL-6, IL-10, or TNF- α between the two groups at the same time points (all P>0.05). Furthermore, before and 6 months after treatment, the levels of IL-6, IL-10, and TNF- α in both groups were significantly higher than those of the healthy control group (all P<0.05) (**Table 5**).

Duration of surgery and cost of treatment

The operation time and treatment cost for the observation group were remarkably lower than those in control group (all *P*<0.05) (**Table 6**).

Discussion

Chronic apical periodontitis is a common condition in clinical stomatology, characterized by a chronic inflammatory reaction that occurs when the inflammation in the dental pulp extends to the periapical tissues. When inflammation per-

sists and recurs, granulation tissue forms at the root apex, leading to gradual resorption of the alveolar bone and formation of a gingival fistula, which results in recurrent periodontal swelling and pus drainage. This significantly affects the longevity and function of the affected tooth [9, 10]. In patients with fistula-type anterior chronic periapical inflammation, treatment becomes more challenging due to the unique structural characteristics of the condition [11].

Conventional multiple-visit root canal therapy requires patients to attend multiple follow-up sessions, increasing the risk of secondary periapical infections, which can even lead to further destruction of periapical tissues and deterioration of the patient's condition [12-14]. Research indicates that in most cases of chronic periapical infection, which often involves single-canal teeth with indistinct boundaries between the root canal and pulp cavity, the key to the successful endodontic treatment lies in thorough cleaning and disinfection of the root canal, preventing recurrence of inflammation. and ensuring proper three-dimensional obturation of the canal [15-17]. Conventional multiple-visit endodontic procedures are prone to provoke a localized inflammatory response in the periapical area due to repeated anti-inflammatory seals, triggering re-infections in the root canal, thus affecting treatment outcome [18-20]. In recent years, with the continuous development and advancement of medical technology, single-visit endodontics has been increasingly used for clinical work.

However, in the selection of patients for singlevisit RCT, studies suggest that patients should be free of clinical symptoms such as pain, swelling, and fistulae to be considered suitable candidates [21]. However, it has also been suggested that single-visit RCT can be equally effective in treating patients with fistula-type chronic periapical infections [22]. In the present study, we developed strict inclusion criteria to explore the efficacy of single-visit endodontics in patients with anterior fistula-type chronic periapical periodontitis, ensuring that the selected patients did not have systemic diseases that could interfere with root canal treatment. Teeth with chronic apical periodontitis typically harbor a complex bacterial infection in the root canal system, compared to affected teeth with viable pulp [23, 24]. The microorganisms infect-

Table 5. Comparison of the levels of periodontal inflammatory factors among groups before and after treatment ($\bar{x}\pm s$)

Group	Number of Cases	IL-6 (ng/ml)	IL-10 (pg/ml)	TNF-α (ng/ml)
Observation group (n = 55)	Pre-treatment	6.12±0.67*	9.15±0.73*	1.97±0.31*
	Six months after treatment	3.07±0.51*	10.62±0.81*	1.04±0.22*
	t	26.863	9.998	18.144
	Р	<0.0001	< 0.0001	<0.0001
Control group (n = 51)	Pre-treatment	6.07±0.59*	9.08±0.80*	1.89±0.30*
	Six months after treatment	3.13±0.62*	10.74±0.93*	1.09±0.27*
	t	24.532	9.664	14.155
	Р	<0.0001	< 0.0001	< 0.0001
Healthy control group $(n = 50)$	-	1.76±0.51	5.83±1.58	0.71±0.15

Note: Compared to the healthy control group, *P<0.05. IL-6, Interleukin-6; IL-10, Interleukin-10; TNF-α, Tumor necrosis factor-α.

Table 6. Comparison of surgery duration and treatment cost between the two groups $(\bar{x}\pm s)$

Group	Ν	Duration of surgery (min)	Expense (Yuan)
Observation Group	55	30.19±7.30	583.41±48.39
Control Group	51	57.58±6.15	910.35±64.52
t	-	20.807	29.651
P	-	< 0.0001	<0.0001

ing the root canal are predominantly anaerobic, with melanin-producing anaerobes (e.g., Prevotella, Porphyromonas) being the most frequently detected, followed by parthenogenetic anaerobes (e.g., Streptococcus spp., Enterococcus spp.) [25-27]. These microorganisms often from biofilms within the root canals of affected teeth, colonizing the dentin surface and invading dentinal tubules or distributing on the apical dentin surface, particularly around the apical foramen and in resorption cavities of varying diameters [28-30]. These hidden bacteria may become a cause of infection or reinfection during or after RCT. Thus, effective removal of as many bacteria as possible from the infected root canals using various pharmaceutical materials and techniques is the key to successful root canal treatment [31, 32].

In this study, we compared the efficacy of single-visit RCT and traditional multiple-visit RCT in treating chronic apical periodontitis in anterior teeth, specifically focusing on patients with fistula-type anterior chronic apical periodontitis. Our analysis revealed that the postoperative outcomes, including pain reduction, sinus healing, apical healing, and overall clinical efficacy, were comparable between the two groups. Additionally, inflammatory markers in gin-

gival sulcus fluid were significantly reduced in both groups, with no significant difference between them, which aligns with the findings reported by others [33, 34]. This suggests that single-visit RCT can achieve similar effects as traditional multiple-visit RCT for patients with sinus-type ante-

rior chronic periapical periodontitis. However, it is necessary to remove as many microorganisms as possible from the root canal to reduce infections during surgery, while minimizing irritation to the periapical tissue. In addition, the operation time and treatment cost for patients in the observation group (single-visit RCT) were significantly lower than those in the control group (multiple-visit RCT). This suggests that compared to the traditional multiple-visit endodontic procedures, single-visit RCT can effectively reduce both the operation time and the surgical burden on patients [35, 36].

However, due to the relatively small sample size and relatively short follow-up period in this study, further studies with a larger sample size and extended follow-up is necessary to observe the long-term outcome of patients treated with different regimens.

Conclusion

For patients with fistula-type anterior chronic apical periodontitis, a single-visit RCT can achieve similar results as traditional multiple-visit RCT. Additionally, single-visit RCT significantly reduces operation time and lowers the surgical burden on patients, making it a sound treatment option.

Acknowledgements

This work was supported by Science and Technology Innovation Project of China Academy of Traditional Chinese Medicine (CI2021A02808).

Disclosure of conflict of interest

None.

Address correspondence to: Yuna Liu, Department of Clinical Laboratory, Beijing Hospital of Integrated Traditional Chinese and Western Medicine, No. 3 Yongding Road East Street, Haidian District, Beijing, China. Tel: +86-13439007710; E-mail: bogangxiong@163.com

References

- [1] Ribeiro DM, Réus JC, Felippe WT, Pacheco-Pereira C, Dutra KL, Santos JN, Porporatti AL and De Luca Canto G. Technical quality of root canal treatment performed by undergraduate students using hand instrumentation: a metaanalysis. Int Endod J 2018; 51: 269-283.
- [2] Abbott PV. Indications for root canal treatment following traumatic dental injuries to permanent teeth. Aust Dent J 2023; 68 Suppl 1: \$123-\$140.
- [3] Huynh R, Peters CI, Zafar S and Peters OA. Evaluating the stress of root canal treatment in patients and dentists compared to other dental treatments: a systematic review and meta-analysis. Eur J Oral Sci 2023; 131: e12941.
- [4] Farias ZBBM, Silva LPD, de Arruda JAA, Cavalcante JS, Almeida HCR, Oliveira MCV, Souza LB and Sobral APV. ALDH1 expression and potential clinical implications in chronic inflammatory periapical lesions. Braz Oral Res 2022; 36: e019.
- [5] Huang Y, Zhou P, Liu S, Duan W, Zhang Q, Lu Y and Wei X. Metabolome and microbiome of chronic periapical periodontitis in permanent anterior teeth: a pilot study. BMC Oral Health 2021; 21: 599.
- [6] Ahmad MZ, Sadaf D, Merdad KA, Almohaimeed A and Onakpoya IJ. Calcium hydroxide as an intracanal medication for postoperative pain during primary root canal therapy: a systematic review and meta-analysis with trial sequential analysis of randomised controlled trials. J Evid Based Dent Pract 2022; 22: 101680.
- [7] Asgary S, Eghbal MJ, Shahravan A, Saberi E, Baghban AA and Parhizkar A. Outcomes of root canal therapy or full pulpotomy using two endodontic biomaterials in mature permanent teeth: a randomized controlled trial. Clin Oral Investig 2022; 26: 3287-3297.

- [8] Lu Y, Liu Z, Huang J and Liu C. Therapeutic effect of one-time root canal treatment for irreversible pulpitis. J Int Med Res 2020; 48: 300060519879287.
- [9] Munoz-Sanchez ML, Linas N, Decerle N, Nicolas E, Hennequin M and Cousson PY. A combination of full pulpotomy and chairside CAD/ CAM endocrown to treat teeth with deep carious lesions and pulpitis in a single session: a preliminary study. Int J Environ Res Public Health 2020; 17: 6340.
- [10] Aldeen RZ, Aljabban O, Almanadili A, Alkurdi S, Eid A, Mancino D, Haikel Y and Kharouf N. The influence of carious lesion and bleeding time on the success of partial pulpotomy in permanent molars with irreversible pulpitis: a prospective study. Bioengineering (Basel) 2023; 10: 700.
- [11] Myciński P, Dobroś K, Kaczmarzyk T and Zarzecka J. Assessment of conformity between clinical (radiological) and histopathological diagnoses of chronic inflammatory periapical lesions treated with apicoectomy. Clinical and histopathological diagnoses of periapical lesions. Research article. Folia Med Cracov 2020; 60: 103-111.
- [12] Di Spirito F, Scelza G, Fornara R, Giordano F, Rosa D and Amato A. Post-operative endodontic pain management: an overview of systematic reviews on post-operatively administered oral medications and integrated evidencebased clinical recommendations. Healthcare (Basel) 2022; 10: 760.
- [13] Ishii K, Tamura T, Hatori K, Himi K, Nakamura T, Toyama Y, Miyata T and Takeichi O. Elevated Foxo3a and Fas-ligand expression in human periapical granulomas as a potential treatment target. Oral Dis 2023; 29: 1128-1136.
- [14] Krenn S, Gutwald R, Bönigk M and Krenn V. Dental apical inflammation score (DAIS): histopathological scoring for the evaluation of the apical inflammatory activity and local bone destruction. Pathol Res Pract 2020; 216: 153223.
- [15] Georgiou AC, Cornejo Ulloa P, Van Kessel GMH, Crielaard W and Van der Waal SV. Reactive oxygen species can be traced locally and systemically in apical periodontitis: a systematic review. Arch Oral Biol 2021; 129: 105167.
- [16] Wan CY, Li L, Liu LS, Jiang CM, Zhang HZ and Wang JX. Expression of matrix metalloproteinases and tissue inhibitor of matrix metalloproteinases during apical periodontitis development. J Endod 2021; 47: 1118-1125.
- [17] Keranmu D, Ainiwaer A, Nuermuhanmode N and Ling W. Application of concentrated growth factor to autotransplantation with inflammation in recipient area. BMC Oral Health 2021; 21: 556.

- [18] Ferreira NS, Gollo EKF, Boscato N, Arias A and Silva EJNLD. Postoperative pain after root canal filling with different endodontic sealers: a randomized clinical trial. Braz Oral Res 2020; 34; e069.
- [19] Sadaf D, Ahmad MZ and Onakpoya IJ. Effectiveness of intracanal cryotherapy in root canal therapy: a systematic review and meta-analysis of randomized clinical trials. J Endod 2020; 46: 1811-1823, e1.
- [20] Karatas E, Hadis M, Palin WM, Milward MR, Kuehne SA and Camilleri J. Minimally invasive management of vital teeth requiring root canal therapy. Sci Rep 2023; 13: 20389.
- [21] Gulabivala K and Ng YL. Factors that affect the outcomes of root canal treatment and retreatment-A reframing of the principles. Int Endod J 2023; 56 Suppl 2: 82-115.
- [22] Yu Q and Fan M. Impacts of multiple and onetime root canal therapy on immune and inflammatory response in endodontic patients. Altern Ther Health Med 2024: AT10253.
- [23] Al-Abdulla N, Bakhsh A, Mannocci F, Proctor G, Moyes D and Niazi SA. Successful endodontic treatment reduces serum levels of cardiovascular disease risk biomarkers-high-sensitivity C-reactive protein, asymmetric dimethylarginine, and matrix metalloprotease-2. Int Endod J 2023: 56: 1499-1516.
- [24] Budreikaitė K, Varoneckaitė M, Oleinikaitė D and Žilinskas J. Association between apical periodontitis and root canal treatment in patients with type II diabetes. A systematic review. Stomatologija 2022; 24: 100-103.
- [25] Webb K, Zain NMM, Stewart I, Fogarty A, Nash EF, Whitehouse JL, Smyth AR, Lilley AK, Knox A, Williams P, Cámara M, Bruce K and Barr HL. Porphyromonas pasteri and Prevotella nanceiensis in the sputum microbiota are associated with increased decline in lung function in individuals with cystic fibrosis. J Med Microbiol 2022; 71: 001481.
- [26] Beydoun MA, Beydoun HA, Hossain S, El-Hajj ZW, Weiss J and Zonderman AB. Clinical and bacterial markers of periodontitis and their association with incident all-cause and Alzheimer's disease dementia in a large national survey. J Alzheimers Dis 2020; 75: 157-172.
- [27] Mendoza R, Alvitez-Temoche D, Chiong L, Silva H, Mauricio F and Mayta-Tovalino F. Antibacterial efficacy of Matricaria recutita essential oil against Porphyromonas gingivalis and Prevotella intermedia: in vitro study. J Contemp Dent Pract 2023; 24: 551-555.

- [28] Meire MA and van der Waal SV. A critical analysis of research methods and experimental models to study intracanal medicaments. Int Endod J 2022; 55: 330-345.
- [29] González Sánchez JA, Munill Ferrer M, Suresh N, Nagendrababu V, Dummer PMH, Garcia-Font M and Abella Sans F. Successful root canal treatment of an atypical mandibular canine with a boomerang-shaped root and canal system with a large periapical lesion-a case report with 9-year follow-up. J Endod 2023; 49: 1369-1375.
- [30] Hall A, Baerts E and Edwards D. Root canal retreatment with gutta percha which techniques influence success? Evid Based Dent 2024; 25: 104-105.
- [31] Sobieszczański J, Mertowski S, Sarna-Boś K, Stachurski P, Grywalska E and Chałas R. Root canal infection and its impact on the oral cavity microenvironment in the context of immune system disorders in selected diseases: a narrative review. J Clin Med 2023; 12: 4102.
- [32] Iranmanesh P, Torabinejad M, Saatchi M, Toghraie D, Razavi SM and Khademi A. Effect of duration of root canal infection on the ability of dentin-pulp complex regeneration of immature permanent teeth: an animal study. J Endod 2022; 48: 1301-1307, e2.
- [33] Sánchez Aleman JA, Jiménez Prieto DI and García Guerrero CC. Post-treatment apical periodontitis in primary non-surgical root canal treatment: a multiple correspondence analysis. Iran Endod J 2023; 18: 233-240.
- [34] Agrawal R, Bhardwaj M, Doley B, Manas A, Ismail PMS, Patil PB and Singh KK. Expression of IL-6, TNF-alpha, and hs-CRP in the serum of patients undergoing single-sitting and multiple-sitting root canal treatment: a comparative study. J Family Med Prim Care 2022; 11: 1918-1922.
- [35] Liang YH and Yue L. Root canal treatment: key steps in root canal irrigation and medicaments. Zhonghua Kou Qiang Yi Xue Za Zhi 2019; 54: 788-792.
- [36] Goulart TS, Hawerroth T, da Silveira Teixeira C, Cesca K, Silva RR, de Moraes RR, Minamisako MC, Umeda Takashima MT, Cábia NC, Bortoluzzi EA, Mazzon RR, de Almeida J and da Fonseca Roberti Garcia L. Assessment of multispecies biofilm growth on root canal dentin under different radiation therapy regimens. Clin Oral Investig 2024; 28: 324.