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Combined posterior superior alveolar and anterior middle superior alveolar nerve blocks with labial infiltration versus nerve blocks alone for pain management in minimally invasive non-surgical periodontal therapy: a split-mouth randomized controlled trial

Ting-Ting Cai¹, Jia-Qi Zhang², Meng-Ran Han¹ and Yong-Wei Fu^{2*}

Abstract

Background To compare the efficacy of combining posterior superior alveolar (PSA) block, anterior middle superior alveolar (AMSA) block, and labial infiltration of the maxillary central incisor versus PSA + AMSA alone for pain control during minimally invasive nonsurgical periodontal therapy (MINST).

Methods Twenty-four patients with stage II-III periodontitis were enrolled in the single-center, single-blind, split-mouth randomized controlled trial. The maxillary right and left quadrants were randomized to receive either PSA + AMSA blocks and labial infiltration (test group) or PSA + AMSA alone (control group) during subgingival instrumentation. Pain levels during injection and treatment were assessed using a 100 mm visual analog scale (VAS). Primary outcomes included intraoperative and injection-related pain scores, while secondary outcomes comprised treatment duration, injection time, patient satisfaction, and adverse events. Data were analyzed using GraphPad Prism 9.

Results Twenty-one subjects completed the study. No significant difference in injection pain was observed between groups (test: 22.74 ± 14.10 mm vs. control: 20.21 ± 12.27 mm; P = 0.248). However, the test group exhibited a statistically significant reduction in intraoperative pain (test: 11.07 ± 10.36 mm vs. control: 16.43 ± 11.55 mm; P = 0.021). Patient satisfaction was significantly higher in the test group [test: 90 (IQR 90 - 100) vs. control: 90 (80 - 90); P = 0.004]. No clinically meaningful differences were detected in treatment duration or adverse event rates (P > 0.05).

*Correspondence: Yong-Wei Fu fuyongweivip@sina.com

Full list of author information is available at the end of the article



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Conclusions The combined PSA + AMSA blocks and labial infiltration protocol reduced intraoperative pain and improved satisfaction versus PSA + AMSA blocks, without prolonging treatment. Despite clinical promise, the small sample size limits generalizability, necessitating multicenter trials to validate efficacy and broader applicability.

Trial registration The trial protocol was retrospectively registered in the Chinese Clinical Trial Registry (ChiCTR2400086566) on 05-07-2024.

Keywords Anterior middle superior alveolar nerve block, Local anesthesia, Periodontitis, Minimally invasive non-surgical periodontal therapy, Subgingival instrumentation

Background

Subgingival instrumentation represents the fundamental mechanical treatment for periodontitis; however, procedural discomfort often reduces treatment compliance by increasing dental anxiety [1, 2, 3]. Local anesthesia, mainly administered via infiltration or nerve block techniques, is commonly used during subgingival instrumentation for stages II-IV periodontitis [4, 5, 6]. Compared to infiltration anesthesia, which requires multiple injections and causes transient discomfort, nerve block anesthesia shows greater clinical efficacy due to fewer required punctures and improved patient tolerance.

For nonsurgical periodontal therapy in the maxillary quadrant, two primary nerve block techniques are commonly employed: (1) the combined blockade of posterior superior alveolar (PSA), middle superior alveolar, anterior superior alveolar, nasopalatine, and greater palatine nerves, and (2) the PSA combined with anterior middle superior alveolar (AMSA) approach through palatal injection [7, 8]. The AMSA approach offers distinct clinical advantages, including reduced injection frequency and anesthetic volume [8, 9], showing promising potential in periodontal therapy. However, AMSA presents a notable limitation in achieving adequate anesthesia of maxillary central incisors [10, 11], which may be attributed to cross-innervation from the contralateral anterior superior alveolar nerve fibers [10], often requiring supplemental infiltration [8].

The AMSA technique was first introduced by Friedman and Hochman in 1997 [12]. This computer-controlled local anesthetic delivery method involves needle insertion at the hard palate, specifically at the midpoint between the free gingival margin of the first and second premolars and the mid-palatal suture. During administration, patients maintain maximal mouth opening while the needle is inserted at a 45° angle to the palatal surface, with the bevel oriented toward the palatal tissue. The injection protocol combines low-flow delivery during needle advancement with slow deposition of 0.6-0.9 mL anesthetic over 60-90 s upon bone contact. This singleinjection technique achieves simultaneous anesthesia of the anterior and middle superior alveolar nerves, providing effective anesthesia from the ipsilateral central incisor to the second premolar, including both buccal and palatal gingival tissues, while preserving extraoral sensation [7, 13]. Subsequent studies have demonstrated its clinical applications in endodontic therapy, tooth preparation, nonsurgical periodontal treatment, and periodontal surgery [8, 11, 14, 15, 16, 17].

Current evidence regarding the application of AMSA in nonsurgical periodontal therapy remains limited, with no established consensus [5, 8, 18]. Previous studies have demonstrated that the combined use of AMSA and PSA in periodontal therapy significantly reduces injection sites, offering distinct clinical advantages [5]. Most studies confirm that AMSA's anesthetic coverage includes ipsilateral incisors, canines, premolars, and palatal tissues from the midline to molars, along with the buccal attached gingiva of corresponding teeth [13, 15, 18]. While AMSA offers advantages in reducing injection sites and anesthetic volume, its efficacy in anesthetizing labial and buccal periodontal tissues remains unpredictable [8].

In summary, the application of AMSA alone in maxillary quadrant nonsurgical periodontal therapy presents limitations in achieving adequate anesthesia for the labial aspect of maxillary central incisors and the buccal aspect of maxillary molars. The combined PSA-AMSA approach may improve anesthetic success rates. To address the persistent challenge of incomplete labial anesthesia in maxillary central incisors during AMSA application, we propose a novel anesthetic protocol combining PSA, AMSA, and labial infiltration anesthesia for maxillary central incisors. To our knowledge, no previous studies have reported the application of this combined anesthetic protocol in nonsurgical periodontal therapy prior to this submission. This study aims to compare the efficacy of combined PSA + AMSA with labial infiltration versus PSA + AMSA alone for pain control during minimally invasive nonsurgical periodontal therapy (MINST) through a split-mouth randomized controlled clinical trial. We hypothesized that the combined PSA + AMSA with labial infiltration protocol would improve pain control compared to PSA + AMSA alone.

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Methods

This single-center, randomized controlled trial utilized a prospective split-mouth design with participant masking. The protocol received ethical approval from the Ethical Committee of the First People's Hospital of Lianyungang (Approval No. KY-20240102001-01). This study was conducted in accordance with the ethical principles of the Declaration of Helsinki and its later amendments. It was retrospectively registered with the Chinese Clinical Trial Registry (ChiCTR2400086566) and adhered to the Consolidated Standards of Reporting Trials (CONSORT) guidelines. All participants provided written informed consent after detailed study explanation.

Sample size calculation

An a priori power analysis was conducted using PASS 11 (NCSS, LLC) for two independent sample means comparison. Pilot data from 7 participants per group revealed differential intraoperative pain intensity measured by a 100-mm visual analog scale (VAS) during subgingival instrumentation, with mean scores of 17.50 ± 12.58 mm in the test group (PSA+AMSA+labial infiltration) versus 27.14 ± 10.75 mm in the control group (PSA+AMSA). With a one-tailed significance level (α =0.05) and 80% power (β =0.2), the calculated minimum sample size was 19 participants per arm. To account for potential dropouts, the final target enrollment was increased to 24 participants.

Participants

Patients with periodontitis were recruited from the Department of Periodontology at the First People's Hospital of Lianyungang between January 2024 and June 2024. Twenty-four participants meeting the inclusion criteria and diagnosed with generalized periodontitis (Stage II-III, Grade A-C) based on the 2018 Classification of Periodontal Diseases were enrolled.

Inclusion criteria

- (1) Aged 18–70 years.
- (2) Clinically diagnosed with Stage II-III periodontitis (Grade A-C) [19].
- $(3) \ge 20$ natural teeth (excluding third molars).
- (4) No systemic diseases.
- (5) Willing to participate and provide written informed consent after understanding the study objectives and procedures.

Exclusion criteria

- (1) Pregnancy or lactation.
- (2) Current or former smoker within the past 5 years.
- (3) Presence of systemic diseases.

- (4) Periodontal treatment within the past year.
- (5) Allergy to articaine hydrochloride with epinephrine.
- (6) Use of central nervous system depressants (including alcohol or analgesics) within 48 h prior to the study.

Randomization and blinding

A statistician generated a sequence of 24 random numbers using randomization software, which were divided into two equal groups (A and B) by the study designer based on parity (odd numbers: Group A; even numbers: Group B). Sealed randomization cards documenting sequence numbers, random numbers, and group assignments were prepared in duplicate and securely stored. Neither the statistician nor the study designer participated in clinical procedures.

The clinical investigator enrolled participants, assigned sequential numbers, and randomized 24 participants into Group A (n = 12) and Group B (n = 12). During the initial subgingival instrumentation session, the right maxillary quadrant of Group A was the test group, and Group B's right quadrant was the control. During the second subgingival instrumentation session, Group A's left quadrant served as the control, and Group B's left quadrant as the test group.

To maintain blinding integrity, participants received identical standardized instructions for both quadrants, while outcome assessments (including questionnaire data) were systematically collected by nurses masked to group allocation. The clinical operator remained unblinded to implement protocol-specific interventions. The statistician conducted analyses using coded datasets without access to group identifiers. Participants, nurse assessors, and the statistician were blinded to group allocation.

Procedures

At the first visit, potential participants were screened based on the inclusion and exclusion criteria. Eligible individuals provided written informed consent and completed baseline assessments, including demographic data collection, periodontal examination with measurements of full-mouth plaque score (FMPS), bleeding on probing (BOP), probing depth (PD), gingival margin level (GML), and clinical attachment level (CAL) [20], radiographic evaluation, and oral hygiene instruction using videos, models, and intraoral demonstrations, followed by supragingival scaling and polishing.

During the second visit, participants were assigned sequential numbers based on enrollment order, with the right maxillary quadrant designated as either the test or control group for subgingival instrumentation under local anesthesia. The test group received articaine hydrochloride with epinephrine (Septanest, France) using a computer-controlled local anesthetic delivery system

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(TMY-II, Tianjin Yiteng Shengjie Medical Devices Co., Ltd.), including PSA (0.6 mL, 1/3 ampule), AMSA (0.8 mL, 1/2 ampule), and labial infiltration of the maxillary central incisor (0.3 mL, 1/6 ampule). The control group received PSA (0.6 mL, 1/3 ampule) and AMSA (0.8 mL, 1/2 ampule) only. Anesthetic administration time was recorded, and injection pain was assessed using a VAS (0–100 mm). Subgingival instrumentation was performed using ultrasonic subgingival tips (H3, H4R, H4L, Satelec, France) under $3.5\times$ dental magnification, with tips positioned below the gingival papilla to avoid coronal contact. No subgingival irrigation was performed postinstrumentation to allow natural blood clot formation [21, 22]. Total procedure time and intraoperative pain (VAS, 0–100 mm) were recorded.

At the third visit (7 days after the second visit), the left maxillary quadrant in each participant received subgingival instrumentation according to group-specific anesthetic protocols. Following subgingival instrumentation of the left or right maxillary quadrant, participants were instructed to document postoperative pain, bleeding, and swelling daily for 7 consecutive days using a 100 mm VAS in standardized diaries, with parallel documentation of fever occurrence through a binary checklist (present/absent). At the 1-week follow-up visit, clinicians verified diary completeness, clinically assessed periodontal abscess formation, and evaluated patient satisfaction using clinician-administered VAS questionnaires (0–100 mm).

In the subsequent weeks, subgingival instrumentation of the left and right mandibular quadrants was performed in two separate sessions under inferior alveolar, lingual, and buccal nerve block anesthesia, with visits scheduled at approximately one-week intervals.

Outcome measures

The primary outcome measures included intraoperative and injection-related pain scores. Secondary endpoints comprised treatment duration, injection time, patient satisfaction, and the incidence of adverse events.

Statistical analysis

Statistical analyses were performed using GraphPad Prism 9 (v9.0.0, GraphPad Software). Data are expressed as mean±standard deviation (SD) for normally distributed variables, median (interquartile range, IQR) for nonparametric data, and frequencies with percentages for categorical variables. Normality was assessed using the Shapiro-Wilk test. Paired comparisons were analyzed with Student's *t*-tests for parametric data and Wilcoxon signed-rank tests for nonparametric data. For three-group comparisons of repeated measures, the Friedman test was applied, followed by post hoc pairwise Wilcoxon signed-rank tests. Categorical outcomes were evaluated

using Fisher's exact test. Statistical significance was defined as two-tailed P < 0.05.

Results

Participant characteristics

Between January 2024 and June 2024, 109 patients with periodontitis were screened at the Department of Periodontology, First People's Hospital of Lianyungang. Of these, 24 met the inclusion criteria and were enrolled. During the study, one participant withdrew, and two were lost to follow-up, yielding 21 participants who completed the trial. The study flowchart is shown in Fig. 1.

Participant demographics and clinical characteristics are summarized in Table 1. Baseline periodontal parameters for the unilateral maxillary quadrant, including FMPS, BOP, PD, GML, CAL, and the number of sites with PD \geq 4 mm and PD \geq 6 mm, are presented in Table 2. No significant differences in these parameters were observed between the test and control groups (all P>0.05).

Injection and treatment-related outcomes

The test group demonstrated slightly higher injection pain scores than the control group, though this difference was not statistically significant. In contrast, intraoperative pain scores were significantly lower in the test group (P<0.05). Injection time was significantly longer in the test group (P<0.05), while treatment duration showed no significant difference between the groups. Patient satisfaction was significantly higher in the test group compared to the control group (P<0.05) (Table 3).

Significant differences in injection pain scores were observed among the three anesthetic techniques (PSA, AMSA, and labial infiltration) in the test group (P<0.001). The PSA block exhibited the lowest median pain scores (Table 4), followed by AMSA block and labial infiltration. Post hoc pairwise comparisons demonstrated statistically lower pain levels with PSA compared to both AMSA (P<0.001) and labial infiltration (P<0.001), whereas no significant difference was detected between AMSA and labial infiltration (P=0.906).

Adverse events

Adverse events in this study primarily occurred within 2 days post-treatment. No statistically significant difference in the incidence of adverse events was observed between the test and control groups (Table 5).

Discussion

This split-mouth randomized controlled trial assessed the efficacy of the combined PSA-AMSA with labial infiltration in MINST. The findings indicate that this combined PSA+AMSA blocks and labial infiltration protocol reduces intraoperative pain and enhances patient Cai et al. BMC Oral Health (2025) 25:746 Page 5 of 9

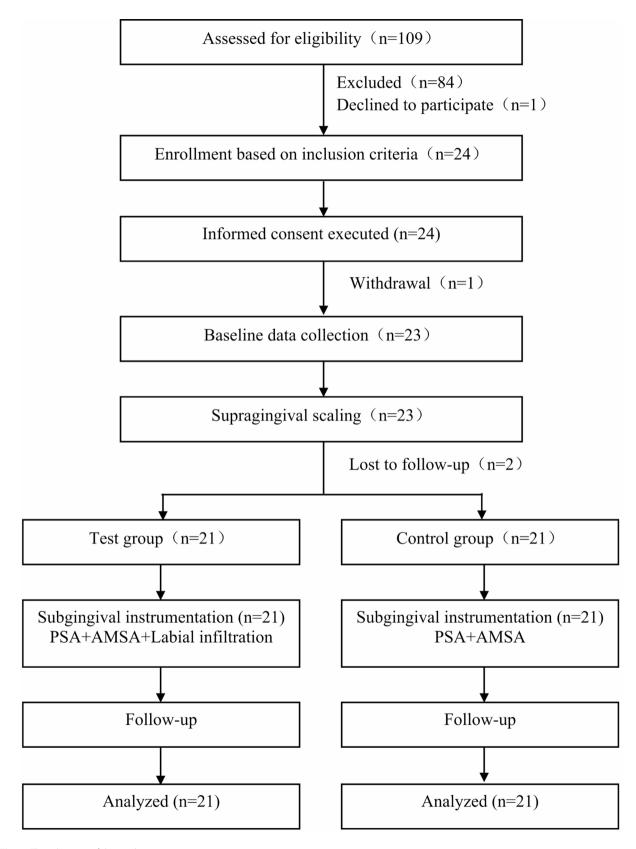


Fig. 1 Flow diagram of the study

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Table 1 Baseline characteristics of included subjects (n=21)

Parameters	Values
Sex [n(%)]	
Male	8 (38.09)
Female	13 (61.91)
Age (years, mean \pm SD)	40.33 ± 9.55
Education level [n(%)]	
<9 years	3 (14.29)
9–12 years	6 (28.57)
>12 years	12 (57.14)
Periodontitis stage [n(%)]	
Stage II	13 (61.90)
Stage III	8 (38.10)
Periodontitis grade [n(%)]	
Grade A	1 (4.76)
Grade B	9 (42.86)
Grade C	11 (52.38)
FMPS (%, mean \pm SD)	82.60 ± 9.91
BOP (%, mean \pm SD)	87.14 ± 11.28
PD (mm, mean \pm SD)	4.06 ± 0.71
GML(mm, Me (IQR))	0.76 (0.35-1.32)
CAL (mm, mean \pm SD)	4.62 ± 1.17

FMPS, full-mouth plaque score; BOP, bleeding on probing; PD, probing depth; GML, gingival margin level; CAL, clinical attachment level; SD, standard deviation; Me, median; IQR, interquartile range

satisfaction versus PSA+AMSA blocks. To our knowledge, this is the first study to report the application of PSA, AMSA, and labial infiltration anesthesia in MINST.

The test group demonstrated marginally elevated injection pain scores compared to the control group, although this difference lacked statistical significance (P > 0.05). Within the test group, maxillary central incisor labial

infiltration exhibited similar pain levels to the AMSA block (P=0.906), while both procedures produced significantly higher pain scores than the PSA block (P<0.001), with PSA demonstrating the lowest overall scores. This pattern suggests heightened nociceptive sensitivity in maxillary anterior labial mucosa, aligning with Loomer et al.'s findings that anterior alveolar nerve blocks induced greater discomfort than PSA injections under computer-controlled administration [5]. Based on these observations, we recommend pre-procedural application of topical anesthetic gel to mitigate injection-related discomfort.

The hypothesis of this study was that the combined PSA + AMSA with labial infiltration would improve pain control during MINST, compared to PSA + AMSA blocks alone. In the study, the test group showed significantly lower intraoperative pain scores and higher satisfaction scores than the control group, aligning with our hypothesis. These results demonstrate that combining PSA, AMSA, and labial infiltration provides optimal anesthesia for MINST in the maxillary quadrant. This protocol requires only three injections and one cartridge of articaine with epinephrine to anesthetize half of the maxilla, effectively addressing the inadequate buccal anesthesia of AMSA alone and the insufficient labial anesthesia of the maxillary central incisor with PSA-AMSA [8].

While the test group exhibited lower intraoperative pain scores versus controls $(11.07 \pm 10.36 \text{ mm vs.} 16.43 \pm 11.55 \text{ mm}, P = 0.021)$, interpretation of clinical relevance requires caution. Current evidence lacks established minimal clinically important differences (MCIDs)

Table 2 Periodontal parameters at baseline in test and control groups (referred to one maxillary quadrant)

Periodontal parameters	Test group $(n=21)$	Control group $(n=21)$	<i>P</i> -value
FMPS (%, mean ± SD)	78.66 ± 13.21	77.48 ± 13.33	0.535 ^a
BOP (%, mean \pm SD)	90.54 ± 10.93	89.90 ± 10.77	0.650 ^a
PD (mm, mean \pm SD)	4.26 ± 0.72	4.31 ± 0.77	0.667 ^a
GML (mm, Me (IQR))	0.54 (0.28-1.03)	0.61 (0.24–1.32)	0.763 ^b
CAL(mm, mean \pm SD)	4.64 ± 1.24	4.80 ± 1.52	0.192 ^a
No. of sites with PD \geq 4 mm (n, mean \pm SD)	27 ± 6.67	27.67 ± 7.8	0.428 ^a
No. of sites with PD \geq 6 mm (n, mean \pm SD)	9.14±6.27	10.52 ± 7.30	0.213 ^a

^a Analysis by Paired- sample t test. ^b Analysis by Wilcoxon signed-rank tests. FMPS, full-mouth plaque score; BOP, bleeding on probing; PD, probing depth; GML, gingival margin level; CAL, clinical attachment level; SD, standard deviation; Me, median; IQR, interquartile range

Table 3 Comparison of VAS pain scores, procedural time metrics, and patient satisfaction between test and control groups

Parameters	Test group	Control group	<i>P</i> -value
	(n=21)	(n=21)	
Injection pain (mm, mean $\pm SD$) ^a	22.74 ± 14.10	20.21 ± 12.27	0.248 ^b
Intraoperative pain (mm, mean $\pm SD$)	11.07 ± 10.36	16.43 ± 11.55	0.021 ^{b,} *
Injection time (min, Me (IQR))	5 (4–5)	4 (3–4)	0.001 ^{c,} *
Treatment duration (min, Me (IQR))	28 (25–31)	26 (25-30.5)	0.945 ^c
Patient satisfaction (mm, Me (IQR))	90 (90–100)	90 (80–90)	0.004 ^c

^a Injection pain scores were derived from the mean of posterior superior alveolar (PSA), anterior middle superior alveolar (AMSA), and labial infiltration procedures in the test group, whereas the control group scores comprised PSA and AMSA measurements only. ^b Analysis by Paired-sample t test. ^c Analysis by Wilcoxon signed-rank tests. *Statistically significant difference at 0.05 level. *SD*, standard deviation; Me, median; IQR, interquartile range

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Table 4 Comparison of injection pain scores among three anesthetic techniques in test group (n=21)

	PSA block	AMSA block	Labial infiltration	<i>P</i> -value
Injection pain (mm, Me (IQR))	10 (0-12.5)	20 (10-37.5)	20 (17.5–35)	< 0.001 ^{a, *}
Post hoc analyses <i>P</i> -value				
PSA vs. AMSA	_	< 0.001 ^{b, *}	_	
PSA vs. Labial	_	_	< 0.001 ^{b,} *	
AMSA vs. Labial	_	0.906 ^b	_	

^a Analysis by Friedman test. ^b Analysis by post hoc Wilcoxon signed-rank tests. *Statistically significant difference at 0.05 level. PSA, posterior superior alveolar; AMSA, anterior middle superior alveolar; Me, median; IQR, interquartile range

Table 5 Adverse event incidence

Parameters	Test group $(n=21)$	Control group $(n=21)$	P-value
Post-operative pain [n (%)]	3 (14.29)	6 (28.57)	0.702
Post-operative swelling [n (%)]	4 (19.05)	3 (14.29)	>0.999
Post-operative bleeding [n (%)]	4 (19.05)	4 (19.05)	>0.999
Post-operative periodontal abscess [n (%)]	1 (4.76)	0 (0)	>0.999
Post-operative fever [n (%)]	1 (4.76)	0 (0)	>0.999

Intergroup differences in adverse event incidence rates were analyzed using Fisher's exact test

for intraoperative pain during subgingival instrumentation. Thus, we referenced the MCID for acute pain (10–13 mm reduction on a 100 mm VAS) [23, 24, 25]. Although the observed 5.36 mm reduction fell below this threshold, it may still benefit pain-sensitive patients, particularly in mitigating procedural anxiety [26]. This result is consistent with higher patient satisfaction in the test group (median 90 [IQR 90–100]) compared with the control group (median 90 [IQR 80–90]) (P=0.004). Future studies with larger cohorts and patient-reported outcomes are needed to define context-specific MCIDs and validate these findings.

In this study, although the injection time was significantly longer in the test group compared to the control group (P=0.001), there was no significant difference in treatment duration between the two groups (P=0.945). These findings suggest that treatment duration, influenced by anesthetic administration time, data collection procedures, and calculus burden, did not differ significantly between the two anesthetic protocols, consistent with previous reports [5]. Notably, time variability was primarily attributed to differences in calculus removal complexity rather than anesthetic techniques.

In the present study, no statistically significant difference in the incidence of adverse events was observed between the test and control groups. Previous studies have reported that common complications of AMSA, such as localized ulcers in the palatal injection area, may be associated with the thin palatal mucosa, larger anesthetic volumes, and the presence of epinephrine in the anesthetic solution [7, 27]. In this study, no palatal ulcers occurred, potentially due to the relatively smaller AMSA anesthetic volume used (0.8 mL, half an ampule). These findings suggest that administering 0.8 mL of articaine with epinephrine via AMSA provides effective anesthesia while minimizing the risk of palatal ulcers.

This study has several limitations. First, the limited sample size (n = 21, calculated from a pilot study with 7 participants) compromises statistical power and generalizability. Although significant pain reduction was observed, this scale cannot fully represent population variations in pain sensitivity, anatomy, or disease severity. While preliminary power calculations aligned with hypothesized effects, the limited sample size may overestimate efficacy and obscure subgroup variations [28]. Multicenter trials with larger populations are critical to validate findings, address confounders, and confirm broader applicability. These results require cautious interpretation and replication in rigorously designed studies. Second, the unblinded clinical operator design introduces potential performance bias through operator-dependent technical variations, despite standardized protocols and blinded outcome assessment. Future investigations could implement sham infiltrations (needle placement without injection) to strengthen validity, though ethical concerns regarding simulated tissue penetration require resolution. Third, this trial was retrospectively registered (5 July 2024; ChiCTR2400086566) following administrative delays. All predefined outcomes, eligibility criteria, and statistical methods remained unmodified. Protocol adherence underwent independent audit, ensuring compliance despite deviation from prospective registration standards. Fourth, the absence of Gracey mini subgingival curettes during MINST may have influenced pain scores and treatment duration. Fifth, the use of articaine epinephrine injection, which contains epinephrine, could have affected treatment outcomes. Previous studies recommend the use of epinephrine-free local anesthetics during MINST [21, 22]. Finally, the lack of topical anesthesia prior to injections might have exacerbated procedural discomfort, potentially affecting satisfaction scores.

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Conclusions

The combined PSA + AMSA blocks and labial infiltration protocol significantly reduced intraoperative pain and improved patient satisfaction versus PSA + AMSA blocks, without prolonging treatment. Despite clinical promise, the limited sample size constrains generalizability, necessitating multicenter trials to validate efficacy and broader applicability.

Abbreviations

PSA Posterior superior alveolar AMSA Anterior middle superior alveolar

MINST Minimally invasive nonsurgical periodontal therapy

VAS Visual analog scale
IQR Interquartile range
FMPS Full-mouth plaque score
BOP Bleeding on probing
PD Probing depth
GML Gingival margin level
CAL Clinical attachment level

MCID Minimal clinically important difference

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12903-025-06175-z.

Supplementary Material 1

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Author contributions

Ting-Ting Cai drafted the manuscript. Jia-Qi Zhang conducted the research. Meng-Ran Han performed data analysis. Yong-Wei Fu designed the study, supervised the work, and critically revised the manuscript.

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Data availability

Data sets generated during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The protocol received ethical approval from the Ethical Committee of the First People's Hospital of Lianyungang (Approval No. KY-20240102001-01). This study was conducted in accordance with the ethical principles of the Declaration of Helsinki and its later amendments.

Informed consent

All participants provided written informed consent after detailed study explanation.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

¹ Jinzhou Medical University Graduate Training Base (The First People's Hospital of Lianyungang), Lianyungang 222000, Jiangsu Province, China

²Department of Stomatology, The First People's Hospital of Lianyungang, 6 East Zhenhua Road, Haizhou District, Lianyungang 222000, Jiangsu Province, China

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