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Efficacy of glycine powder air-polishing in supportive periodontal therapy: a systematic review and meta-analysis

Mengyuan Zhu †, **Meilin Zhao** †, **Bo Hu**, **Yunji Wang**, **Yao Li**, **Jinlin Song** *

College of Stomatology, Chongqing Medical University, Chongqing Key Laboratory of Oral Diseases and Biomedical Sciences, Chongqing Municipal Key Laboratory of Oral Biomedical Engineering of Higher Education, Chongqing, China

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***Correspondence:**
Jinlin Song
College of Stomatology, Chongqing Medical University, Chongqing Key Laboratory for Oral Diseases and Biomedical Sciences, Chongqing Municipal Key Laboratory of Oral Biomedical Engineering of Higher Education, #426 Songshibei Road, Yubei District, Chongqing 401147, China.
E-mail: songjinlin@hospital.cqmu.edu.cn
Tel: +86-23-8886-0026
Fax: +86-23-8886-0026

†Mengyuan Zhu and Meilin Zhao equally contributed to this study.

ORCID iDs
Mengyuan Zhu
https://orcid.org/0000-0003-4825-4168
Meilin Zhao
https://orcid.org/0000-0002-3823-5118
Bo Hu
https://orcid.org/0000-0002-2125-6967
Yunji Wang
https://orcid.org/0000-0002-2691-8042
Yao Li
https://orcid.org/0000-0002-4741-6279
Jinlin Song
https://orcid.org/0000-0002-0224-6640

ABSTRACT

Purpose: This systematic review and meta-analysis was conducted to assess the effects of glycine powder air-polishing (GPAP) in patients during supportive periodontal therapy (SPT) compared to hand instrumentation and ultrasonic scaling.
Methods: The authors searched for randomized clinical trials in 8 electronic databases for relevant studies through November 15, 2019. The eligibility criteria were as follows: population, patients with chronic periodontitis undergoing SPT; intervention and comparison, patients treated by GPAP with a standard/nozzle type jet or mechanical instrumentation; and outcomes, bleeding on probing (BOP), patient discomfort/pain (assessed by a visual analogue scale [VAS]), probing depth (PD), gingival recession (Rec), plaque index (PI), clinical attachment level (CAL), gingival epithelium score, and subgingival bacteria count. After extracting the data and assessing the risk of bias, the authors performed the meta-analysis.
Results: In total, 17 studies were included in this study. The difference of means for BOP in patients who received GPAP was lower (difference of means: −8.02%; 95% confidence interval [CI], −12.10% to −3.95%; $P<0.00001$; $I^2=10\%$) than that in patients treated with hand instrumentation. The results of patient discomfort/pain measured by a VAS (difference of means: −1.48, 95% CI, −1.90 to −1.06; $P<0.001$; $I^2=83\%$) indicated that treatment with GPAP might be less painful than ultrasonic scaling. The results of PD, Rec, PI, and CAL showed that GPAP had no advantage over hand instrumentation or ultrasonic scaling.
Conclusions: The findings of this study suggest that GPAP may alleviate gingival inflammation more effectively and be less painful than traditional methods, which makes it a promising alternative for dental clinical use. With regards to PD, Rec, PI, and CAL, there was insufficient evidence to support a difference among GPAP, hand instrumentation, and ultrasonic scaling. Higher-quality studies are still needed to assess the effects of GPAP.

Keywords: Glycine; Meta-analysis; Periodontitis; Systematic review; Ultrasonics

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Author Contributions

Conceptualization: Meilin Zhao, Jinlin Song; Data curation: Mengyuan Zhu; Formal analysis: Mengyuan Zhu, Meilin Zhao, Bo Hu; Funding acquisition: Meilin Zhao, Jinlin Song; Investigation: Mengyuan Zhu, Bo Hu; Methodology: Mengyuan Zhu, Meilin Zhao, Jinlin Song; Project administration: Meilin Zhao, Bo Hu; Resources: Meilin Zhao; Software: Mengyuan Zhu, Bo Hu, Yao Li; Supervision: Yunji Wang, Yao Li; Validation: Mengyuan Zhu, Yao Li; Visualization: Mengyuan Zhu, Meilin Zhao, Bo Hu, Yunji Wang, Jinlin Song; Writing - original draft: Mengyuan Zhu, Meilin Zhao; Writing - review & editing: Mengyuan Zhu, Meilin Zhao, Bo Hu, Yunji Wang, Yao Li, Jinlin Song.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

INTRODUCTION

Supportive periodontal therapy (SPT) is considered an essential part of the 4 phases of contemporary periodontal therapy in maintaining periodontal health by removing both supragingival and subgingival biofilm, thereby reducing the risk of periodontal inflammation [1-3]. This kind of therapy includes debridement, removal of bacterial biofilm from sulcular and pocket areas, and oral hygiene instruction [4]. The most significant step is debridement, which can effectively remove supragingival and subgingival biofilm, as well as maintaining the clinical attachment level (CAL). Debridement by hand and ultrasonic instruments is generally used to remove biofilm during the maintenance phase [3]. However, removing biofilm using hand instruments has limited efficiency, as there is only point-line contact during the procedure, and simultaneously, hard tissue is damaged to some extent [5]. Ultrasonic scaling is considered to have advantages over hand instrumentation since it is less time-consuming and more ergonomic [6]. However, the high-frequency oscillation of ultrasonic scaling may cause some damage to the cementum, similar to the damage caused by hand instruments [5]. Since SPT is a long process, repeated root planing and hard tissue damage during the process can cause tooth sensitivity and even pain, resulting in patient discomfort [7-9]. Furthermore, the above 2 methods are labour-intensive [10,11]. Therefore, it is necessary to develop a new technology that is both effective and comfortable.

Air-polishing devices (APDs) were introduced for clinical use as an alternative to conventional techniques of biofilm removal, and are considered to be less time-consuming and capable of removing supragingival and subgingival biofilm effectively. Furthermore, APDs can reach and polish areas that are difficult for hand instrumentation and ultrasonic scaling [8,12]. The original material used in air-polishing was sodium bicarbonate, which is an efficient agent to remove supragingival biofilm, and air-polishing appeared to be less time-consuming compared to conventional methods [13,14]. However, the mean particle size, hardness, and shape of the sodium bicarbonate powders used in APDs made the powders very abrasive, leading to tooth (especially dentin) substance removal and sometimes also causing soft tissue injury [15,16]. Recently, the indications of APDs have expanded from supragingival applications, utilizing highly abrasive sodium bicarbonate powders, to subgingival applications. A special nozzle was designed to be placed subgingivally, deep in a periodontal pocket, with 3 outlets that direct 1 air-polishing jet toward the root surface, 1 toward the pocket epithelium, and 1 tangential to the periodontal pocket. The water outlet is located at the tip of the nozzle. The use of this specially designed nozzle effectively reduced the working pressure in comparison with supragingival air-polishing. In order to facilitate the removal of biofilm from root surfaces while minimizing trauma, a minimally abrasive air-polishing powder, consisting of an amino acid glycine salt, was introduced [16]. Compared to sodium bicarbonate, glycine is less abrasive and highly water-soluble [17]. In addition, glycine has been proven to have immunomodulatory, anti-inflammatory, and cytoprotective effects on periodontal tissue, making it an ideal material for periodontal air-polishing [18].

Air-polishing using a powder formulation of the amino acid glycine is referred to as glycine powder air-polishing (GPAP). Several investigators have proven the efficacy of GPAP in reducing subgingival biofilm and microbial load and showed that it was more acceptable to patients than other forms of air-polishing [16,19]. However, others have found no statistically significant differences between GPAP and hand instrumentation or ultrasonic scaling after treatment. This inconsistency has hindered the clinical adoption of GPAP [20,21]. A previous meta-analysis investigated whether air-polishing was equally effective or superior compared

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with conventional methods [22]. The preliminary findings of their study provided some evidence that air-polishing could be an alternative to conventional debridement during SPT, and that air-polishing seemed to be as effective as conventional treatments. However, they did not conduct a meta-analysis of patient discomfort/pain level, the plaque index (PI), or gingival recession (Rec) due to the limited number of studies they included. Besides, they compared the efficacy of air-polishing and conventional methods without making a distinction among various powders, while we only studied the efficacy of glycine powder for air-polishing as compared to conventional methods. Therefore, the objective of this study was to conduct a meta-analysis of randomized controlled trials (RCTs) to evaluate the effectiveness of GPAP for patients undergoing SPT compared to hand instrumentation and ultrasonic scaling using a broad range of clinical parameters and treatment discomfort/pain levels.

MATERIALS AND METHODS

The study was conducted and reported in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines.

Search strategy

Searches for randomized controlled trials were conducted in the following electronic databases: PubMed, Embase, Cochrane CENTRAL, Web of Science, Science Direct, China National Knowledge Infrastructure (CNKI), Chinese Medicine Premier's Wanfang database, and the Chinese Scientific Journals database (VIP). The last search was updated on November 15, 2019. The main MeSH terms included “dental polishing” and “glycine.” For example, when searching in PubMed, the search strategy used (air polishing) AND (“glycine” OR “Aminoacetic Acid” OR “Glycine, Copper Salt” OR “Copper Salt Glycine” OR “Glycine, Monosodium Salt” OR “Monosodium Salt Glycine” OR “Salt Glycine, Monosodium”). The strategy was modified appropriately, considering differences in controlled vocabulary and syntax rules in each database. Additionally, the reference lists of the relevant studies were also scanned without language restriction, in case any studies could have been missed. Two review authors (Zhu M Y and Zhao M L) searched and checked the electronic databases separately. If there was any disagreement, those 2 authors turned to a third author (Song J L) for consensus.

Inclusion and exclusion criteria

The inclusion criteria of this study were as follows: 1) population: patients with chronic periodontitis, having completed comprehensive periodontal therapy; 2) intervention: patients undergoing SPT with APDs; 3) comparison: patients undergoing SPT with hand instruments or ultrasonic scalers; 4) outcomes: bleeding on probing (BOP), patient discomfort/pain, probing depth (PD), Rec, PI, CAL, gingival epithelium (GE) score and subgingival bacteria count; and 5) study type: RCTs.

Studies were excluded if: 1) they included patients who were pregnant women or lactating mothers, who had taken antibiotics or anti-inflammatory medication in the past 6 months, who were allergic to glycine, and who had diabetes mellitus, cancer, or HIV; or 2) they were not RCTs.

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Study selection

Two reviewers (Zhu MY and Zhao ML) selected the titles and abstracts of the articles in the electronic databases to choose suitable studies. Duplicates were then removed from the resulting list. After carefully reading the full text of each remaining study, reviewers removed articles that were not RCTs or *in vivo* experiments. Seventeen studies were eventually included. If there was any disagreement, the 2 primary reviewers discussed the issue with a third author (Song JL) for consensus.

Data extraction and risk of bias assessment

Data from each study were extracted by 2 independent investigators (Zhu MY and Zhao ML), and included: name of the first author and year of publication, study design, characteristics of patients, number, sex, age, country, treatment type, outcome measures, and follow-up. The investigators discussed any disagreements within the group until they reached consensus.

The risk of bias assessment was independently performed by 2 investigators (Zhu MY and Zhao ML) according to the Cochrane handbook [23], which included the following items: 1) random sequence generation (selection bias); 2) allocation concealment (selection bias); 3) blinding of participants and personnel (performance bias); 4) blinding of outcome assessment (detection bias); 5) incomplete outcome data (attrition bias); 6) selective reporting (reporting bias); and 7) other bias.

The authors evaluated all the included studies according to the above items and estimated the risk of bias: 1) low risk of bias if 6 domains were deemed to have a low risk of bias; 2) moderate risk of bias if 1 or more domains were considered to have a unclear risk of bias; and 3) high risk of bias if 1 or more domains were determined to have a high risk of bias.

Statistical analysis

Zhu MY and Zhao ML performed a meta-analysis using RevMan 5.3 (the Nordic Cochrane Centre, the Cochrane Collaboration, Copenhagen, Denmark) when at least 2 studies shared the same index. Mean and standard deviation (SD) values were extracted to report the results of continuous outcomes with 95% confidence intervals (CIs). A random-effects model was selected to calculate the outcomes of the pooled data [24]. Heterogeneity was analysed using I^2, and the level of significance was set at $\alpha=0.1$. $I^2<50\%$ was defined as low heterogeneity, and $I^2>50\%$ as high heterogeneity [25]. A subgroup analysis was performed according to specific time points, smoking status and PD before treatment (initial PD) if high heterogeneity existed. The statistical significance level was set at $P<0.05$.

RESULTS

Search selection

After a comprehensive search of PubMed, Embase, Cochrane CENTRAL, Web of Science, Science Direct, China National Knowledge Infrastructure (CNKI), Chinese Medicine Premier's Wanfang, and Chinese Scientific Journals database (VIP), 371 articles were initially selected. After removing the duplicates using Endnote X8, 218 articles remained. Thirty-seven articles were qualified for full-text scanning after screening the titles and abstracts. Since 20 articles were not RCTs or *in vivo* experiments, a total of 17 articles [5,8,9,20,21,26-37] were identified as meeting the inclusion criteria. Figure 1 shows the flowchart for the inclusion process. Table 1 specifies the main characteristics of the 17 included articles.

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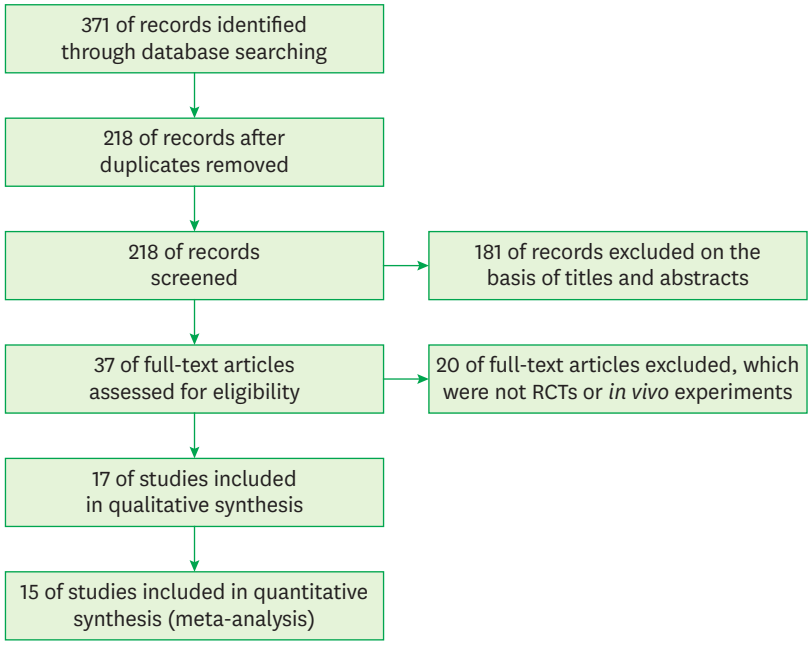

Figure 1. Study selection flow diagram.

Characteristics and risk of bias assessment of included studies

The characteristics of the 17 included studies [5,8,9,20,21,26-37] are presented in Table 1. All included RCTs were conducted among adults, from 18 to 72 years old. The investigators in 9 studies [5,9,20,21,28-30,33,36] chose BOP as an outcome measure, 9 studies [8,9,20,21,26,29,31,33,34] used a visual analogue scale (VAS) to evaluate the patients' discomfort/pain during treatment, ranging from 0 (very comfortable) to 10 (extremely painful), 16 studies [5,8,9,20,21,26-31,33-37] analysed PD, 4 studies [20,27,29,33] measured Rec, 12 studies [9,20,26-30,32-35,37] studied PI, and 5 studies [8,9,21,27,35] analysed CAL, 5 studies [20,21,27-29] reported viable bacteria counts, and only 1 study [30] conducted a histological analysis (GE scores). The follow-up period in the 17 studies [5,8,9,20,21,26-37] varied. A follow-up period of less than 6 months was defined as short-term. Fourteen studies [5,8,9,21,26-28,30-34,36,37] used a split-mouth design, 2 studies [20,29] used a parallel design, and 1 study [35] did not mention the study design.

Figure 2 shows the results for the risk of bias across all studies, according to the Cochrane Handbook for Systematic Reviews of Interventions. Figure 3 shows the risk of bias for each study. Of the 17 included studies, 12 exhibited a moderate risk of bias, with 1 or more domains having an unclear risk of bias, and the remaining 5 studies were considered to have a high risk of bias because of reporting bias (specifically, the absence of SD values for the VAS or PI). Because the number of the included studies was small, a funnel plot could not be made to measure publication bias.

Meta-analysis

After extracting and pooling the statistical data, a meta-analysis was conducted to assess the efficacy of GPAP compared to hand instrumentation and ultrasonic scaling. Since the data were continuous, a random-effects model was adopted. Considering the limited data and discrepancies among studies, it was not appropriate to perform a meta-analysis of outcome measures such as GE scores and bacteria counts.

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Table 1. Characteristics of the included studies (n=17)

Study	Study design, country	Participant age (yr), smoking	Intervention	Other systemic diseases	Baseline measures	Outcome variables	Follow-up	Adverse events
Simon et al. [32]	RCT, split-mouth design, India	20, age range: 20–40, no smokers	Group 1: no treatment; Group 2: ultrasonic scaling; Group 3: SBAP; Group 4: subgingival GPAP	No	PD≥5 mm	PI, GI	3 wk	No
Yuan et al. [9]	RCT, split-mouth design, China	27, age range: 35–62, not excluded	Group 1: subgingival GPAP; Group 2: ultrasonic scaling	No	PD≥4 mm	PI, PD, AL, BOP, patient discomfort/pain	3 mon	Seven test patients had eight adverse events
Zhao et al. [33]	RCT, split-mouth design, China	23, age range: 28–72, no smokers	Group 1: supragingival GPAP; Group 2: ultrasonic scaling	No	PD<5 mm	PD, PI, BI, Rec, SI, patient discomfort/pain	12 wk	No
Li et al. [36]	RCT, split-mouth design, China	40, age range: 26–49, not excluded	Group 1: subgingival GPAP; Group 2: hand instrumentation	No	3 mm≤PD≤6 mm	PD, BOP, IL1/6/8/10, MMP8/TIMP1	7 days and 30 days	Not mentioned
Sun et al. [8]	RCT, split-mouth design, China	26, age range: 15–55, not excluded	Group 1: subgingival GPAP; Group 2: ultrasonic scaling	No	PD≥4 mm	PD, AL, BI, patient discomfort/pain	1 mon	Not mentioned
Xia et al. [35]	RCT, China	40, age range: 32–65, no smokers	Group 1: subgingival GPAP; Group 2: ultrasonic scaling	No	PD>4 mm	PI, PD, AL, BI	3 mon	Not mentioned
Lu et al. [28]	RCT, split-mouth design, China	22, age range: 28–72, no smokers	Group 1: supragingival GPAP; Group 2: ultrasonic scaling	No	PD≤5 mm	PI, PD, BI, BOP, microbiological assessments	12 wk	No
Petersilka et al. [31]	RCT, split-mouth design, USA	27, age range: 18–65, not excluded	Group 1: subgingival GPAP; Group 2: hand instrumentation; Group 3: no treatment	No	3 mm≤PD≤5 mm	PD, bacteria counts, patient discomfort/pain	3 mon	No
Petersilka et al. [30]	RCT, split-mouth design, USA	10, age range: 31–70, not excluded	Group 1: subgingival GPAP; Group 2: SBAP; Group 3: hand instrumentation	No	PD≥5 mm	PD, BOP, PI, Histological assessment	14 days	No
Moene et al. [29]	RCT, parallel design, Switzerland	50, age range: 18–70, not excluded	Group 1: subgingival GPAP; Group 2: hand instrumentation	No	PD≥5 mm	PI, PD, BOP, Rec, patient discomfort/pain	7 days	No
Wennström et al. [21]	RCT, split-mouth design, Sweden	20, age range: 40–71, no smokers	Group 1: subgingival GPAP; Group 2: ultrasonic scaling	No	5 mm≤PD≤8 mm	PD, CAL, BOP, patient discomfort/pain	14 and 60 days	No
Flemmig et al. [20]	RCT, parallel design, USA	30, age range: ≥21, less than 5 cigarettes per day	Group 1: subgingival GPAP; Group 2: hand instrumentation	No	4 mm≤PD≤9 mm	Total subgingival viable bacterial counts, PD, BOP, Rec, PI	10 and 90 days	Seven test patients had eight adverse events
Arora et al. [26]	RCT, split-mouth design, India	10, age range: 18–60, not excluded	Group 1: subgingival GPAP; Group 2: hand instrumentation	No	3 mm≤PD≤5 mm	PI, GI, PD	1 wk	No
Luo et al. [37]	RCT, split-mouth design, China	21, age range: 26–58, no smokers	Group 1: subgingival GPAP; Group 2: ultrasonic scaling	No	PD>4 mm	PD, AL, BI, PL	1, 3 mon	Not mentioned
Hu et al. [5]	RCT, split-mouth design, China	30, age range: 24–62, no smokers	Group 1: subgingival GPAP; Group 2: hand instrumentation	No	3 mm≤PD≤6 mm	PI, PD, BOP	7 days and 30 days	No
Kargas et al. [27]	RCT, split-mouth design, Greece	25, age range: 42.96–62.04, no smokers	Group 1: hand instrumentation; Group 2: subgingival GPAP; Group 3: ultrasonic	No	PD>4 mm	PD, PI, GI, Rec, CAL	1, 3 and 6 mon	No
Liu et al. [34]	RCT, split-mouth design, China	41, age range: 24–56, not excluded	Group 1: subgingival GPAP; Group 2: ultrasonic scaling	No	4 mm≤PD≤5 mm	PD, GI, BI, PI, patient discomfort/pain	1 wk,1 mon	Not mentioned

USA: United States of America, RCT: randomized clinical controlled trials, SBAP: sodium bicarbonate air-polishing, GPAP: glycine powder air-polishing, PD: probing depth, PI: plaque index, GI: gingival index, AL: attachment loss, BOP: bleeding on probing, BI: bleeding index, Rec: gingival recession, SI: staining index, CAL: clinical attachment level, IL: interleukin, MMP: matrix metalloproteinases, TIMP: tissue inhibitors of metalloproteinase.

BOP

As shown in Figure 4, GPAP had a lower BOP (difference of means, −8.02%; 95% CI, −12.10% to −3.95%; P<0.00001) than the use of hand instruments. Both hand instrumentation and GPAP significantly reduced BOP at the sites treated, but GPAP may be preferable.

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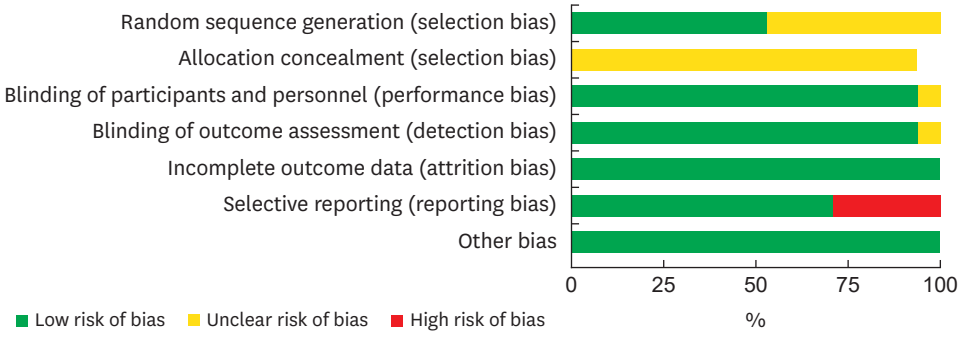

Figure 2. Risk of bias graph. The review authors' judgements about each item assessing risk of bias are presented as percentages across all included studies. Green, yellow, and red refer to low risk of bias, unclear risk of bias, and high risk of bias, respectively.

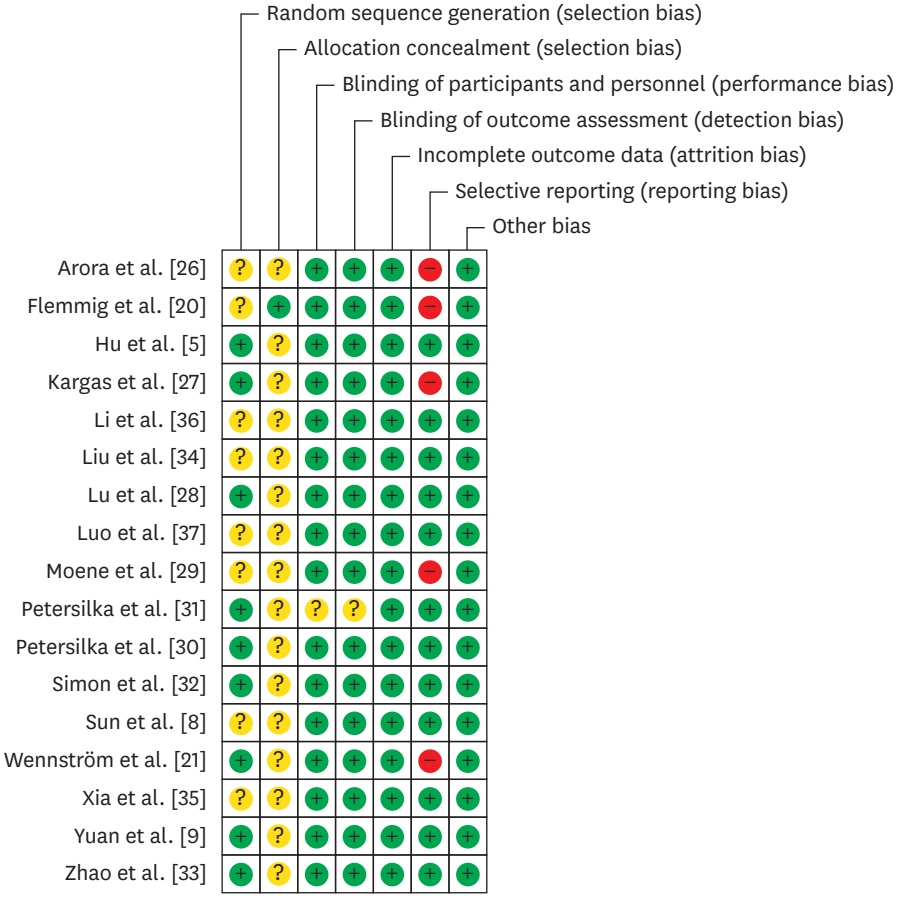

Figure 3. Risk of bias summary. The review authors' judgements about each item assessing risk of bias are presented for each included study. Green, yellow, and red refer to low risk of bias, unclear risk of bias, and high risk of bias, respectively.

Patient discomfort/pain

In 9 studies [8,9,20,21,26,29,31,33,34], the subjects were asked to use a VAS to rate the discomfort that they felt following their treatment. Due to incomplete data from 5 studies [20,21,26,29,31], VAS results (Figure 5) were analysed based on the other 4 studies [8,9,33,34], which revealed that the subjects perceived the treatment with GPAP to be significantly more comfortable (difference of means, –1.48; 95% CI, –1.90 to –1.06; P<0.00001) than treatment with ultrasonic instruments. Substantial heterogeneity was observed (I^2=83%).

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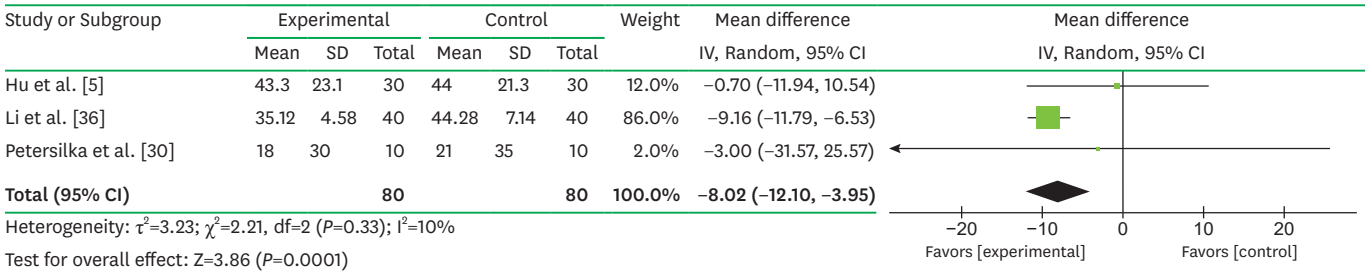

Figure 4. Forest plot of BOP, comparing GPAP (experimental group) with hand instrumentation (control group).
BOP: bleeding on probing, GPAP: glycine powder air-polishing, SD: standard deviation, CI: confidence interval, IV: inverse variance.

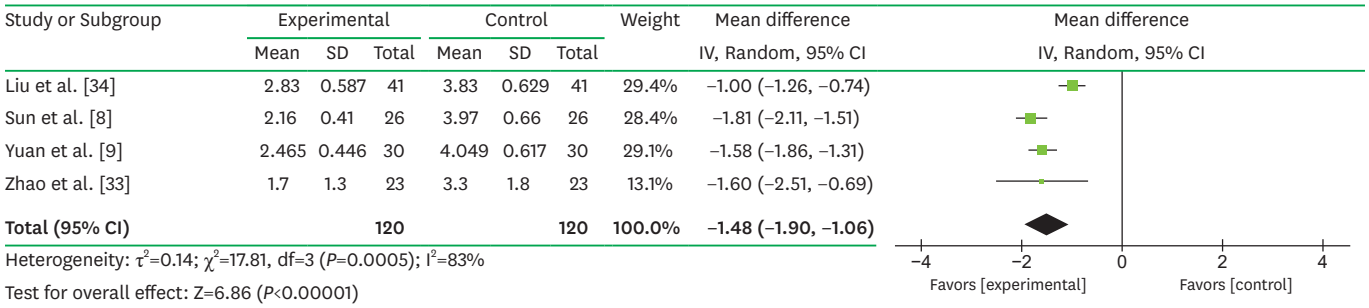

Figure 5. Forest plot of the VAS of patient discomfort/pain, comparing GPAP (experimental group) with ultrasonic scaling (control group).
VAS: visual analogue scale, GPAP: glycine powder air-polishing, SD: standard deviation, CI: confidence interval, IV: inverse variance.

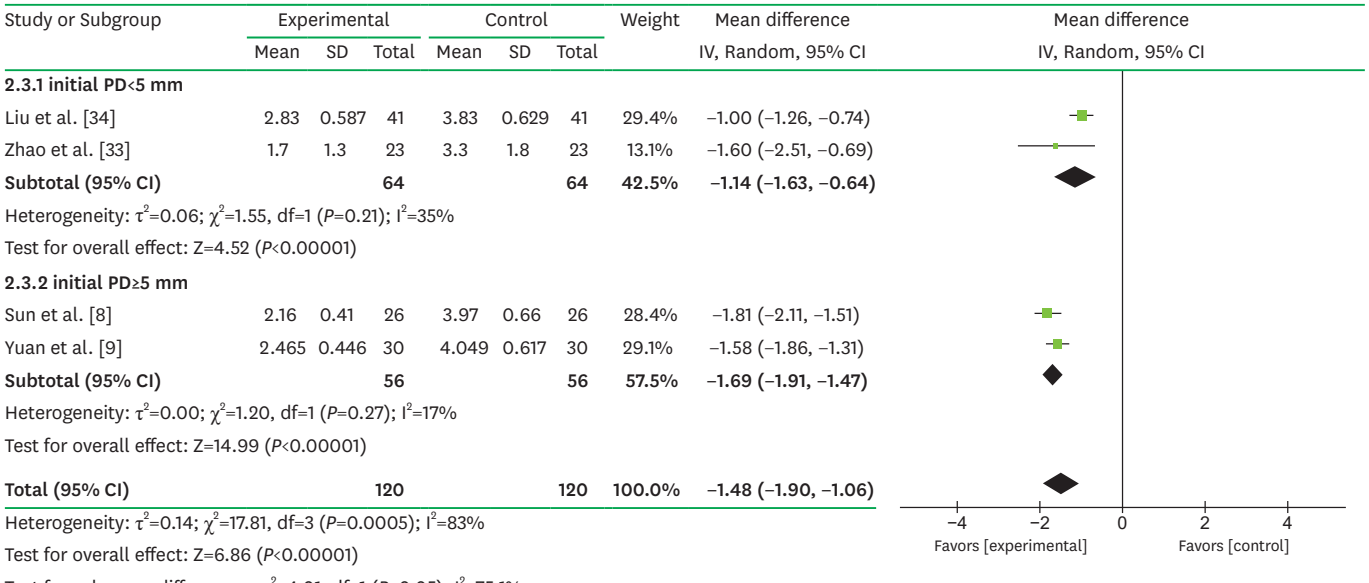

Figure 6. Forest plot of the subgroup meta-analysis evaluating the difference in the VAS of patient discomfort/pain among selected studies for different initial PD values, comparing GPAP (experimental group) with ultrasonic scaling (control group).
VAS: visual analogue scale, PD: probing depth, GPAP: glycine powder air-polishing, SD: standard deviation, CI: confidence interval, IV: inverse variance.

In the subgroup analysis based on the initial PD (Figure 6), less heterogeneity was shown in the subgroup of patients with an initial PD<5 mm (χ^2=1.55; df=1; P=0.21; I^2=35%) as well as in the subgroup of patients with an initial PD≥5 mm (χ^2=1.20; df=1; P=0.27; I^2=17%).

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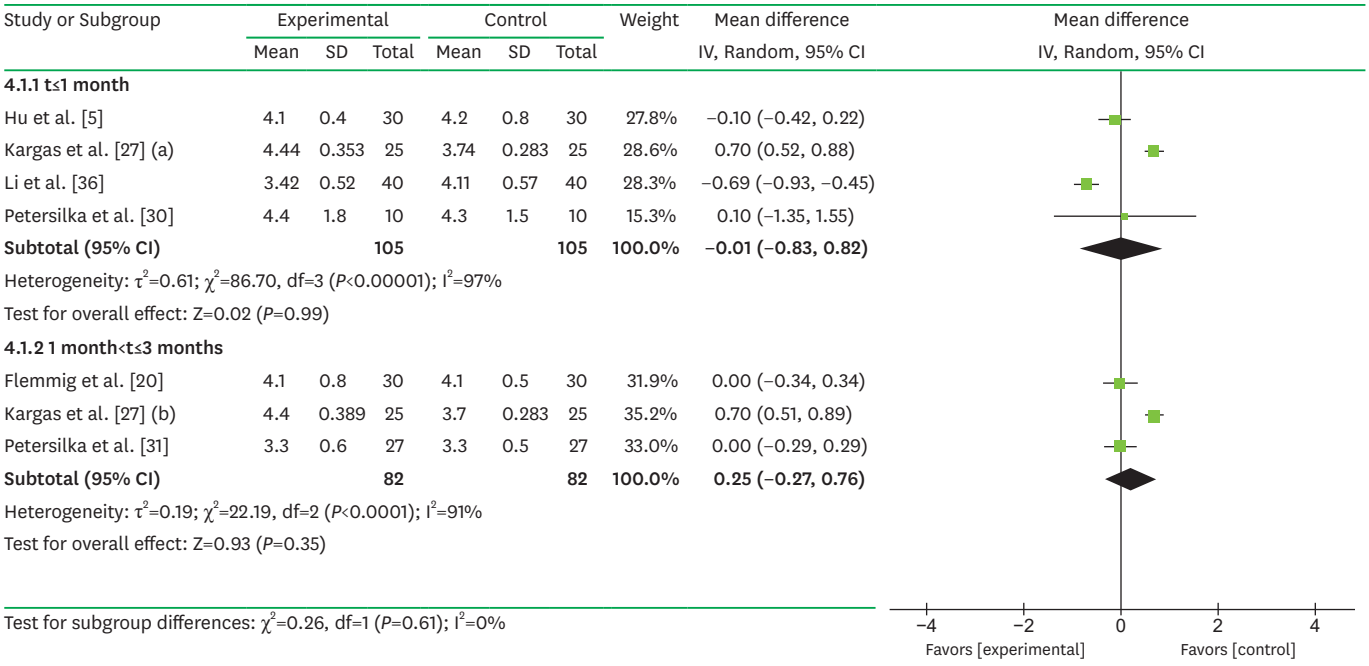

Figure 7. Forest plot of PD, comparing GPAP (experimental group) with hand instrumentation (control group).
PD: probing depth, GPAP: glycine powder air-polishing, SD: standard deviation, CI: confidence interval, IV: inverse variance.

PD

1) GPAP versus hand instrumentation

According to the results, the difference of means for PD in the GPAP group was 0.01 mm (95% CI, −0.83 to 0.82 mm; $P>0.05$; $I^2=97\%$) lower than that in the control group with an evaluation time point of no more than 1 month, and was 0.25 mm (95% CI, −0.27 to 0.76 mm; $P>0.05$; $I^2=91\%$) higher than that in the hand instrumentation group at evaluation time points of 1–3 months (Figure 7). Substantial heterogeneity existed ($I^2=97\%$; $I^2=91\%$). In a subgroup analysis based on different smoking status, a low degree of heterogeneity was found (Figures 8 and 9).

2) GPAP versus ultrasonic scaling

Comparing GPAP and ultrasonic scaling, the results showed that when the follow-up period was no more than 1 month, the PD in the GPAP group was lower (Figure 10) than that in the ultrasonic scaling group. When the follow-up period was between 1 month and 3 months, the difference of means of PD was higher (Figure 10) in the GPAP group than in the ultrasonic group.

Rec

1) GPAP versus hand instrumentation

The results showed that the difference of means of Rec was slightly higher (difference of means, 0.04 mm; 95% CI, −0.40 to 0.49 mm; $P>0.05$) in the GPAP group than in the control group (Figure 11), although there was no significant difference between the 2 groups.

2) GPAP versus ultrasonic scaling

The GPAP group had 0.05 mm (95% CI, −0.15 to 0.25 mm; $P>0.05$) more Rec than the ultrasonic scaling group (Figure 12).

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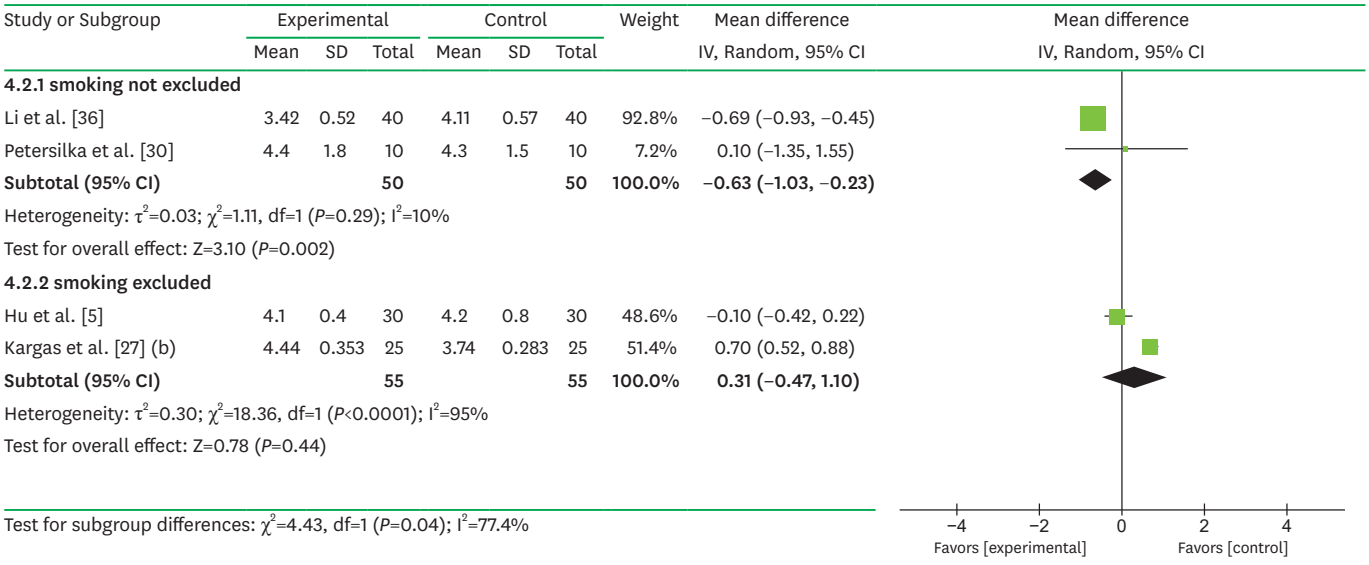

Figure 8. Forest plot of the subgroup meta-analysis evaluating the difference in PD (t≤1 month) among selected studies for different smoking statuses, comparing GPAP (experimental group) with hand instrumentation (control group).
PD: probing depth, GPAP: glycine powder air-polishing, SD: standard deviation, CI: confidence interval, IV: inverse variance.

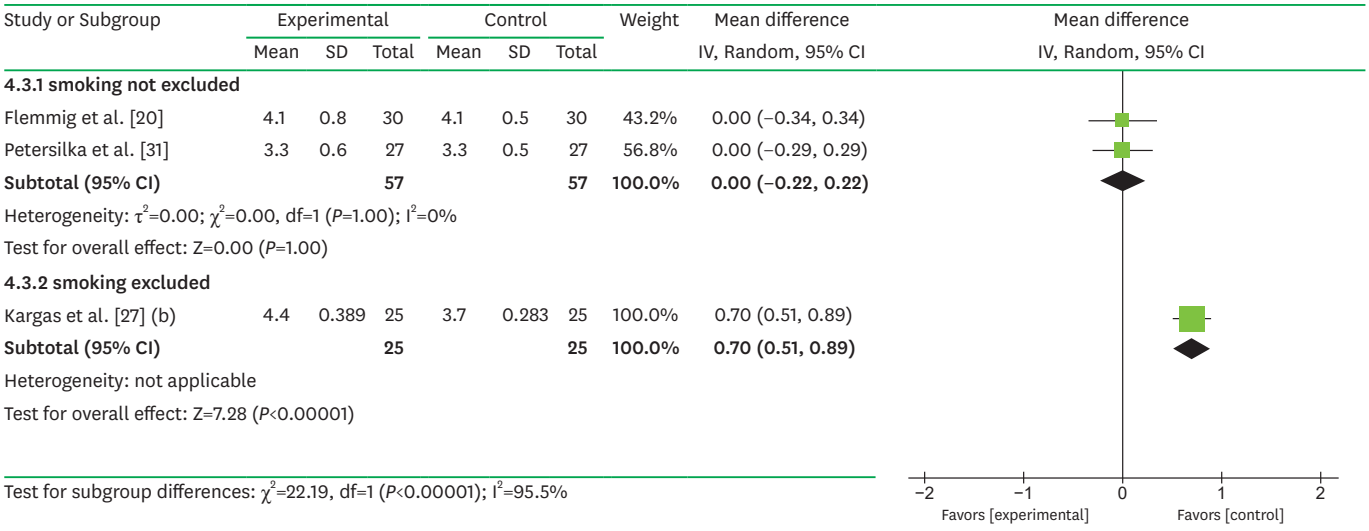

Figure 9. Forest plot of the subgroup meta-analysis evaluating the difference in PD (1 month<t≤3 months) among selected studies for different smoking statuses, comparing GPAP (experimental group) with hand instrumentation (control group).
PD: probing depth, GPAP: glycine powder air-polishing, SD: standard deviation, CI: confidence interval, IV: inverse variance.

PI

The difference of means of PI (Figure 13) was almost the same in the experimental group as in the control group (difference of means, 0.00; 95% CI, −0.12 to 0.11; $P>0.05$), with no significant difference observed in this study.

CAL

The difference of means of CAL in the patients receiving GPAP was 0.3 mm (95% CI, −0.15 to 0.75 mm; $P>0.05$) higher than that of patients in the hand instrumentation group (Figure 14).

Because of the small number of trials included in the meta-analysis, publication bias could not be assessed.

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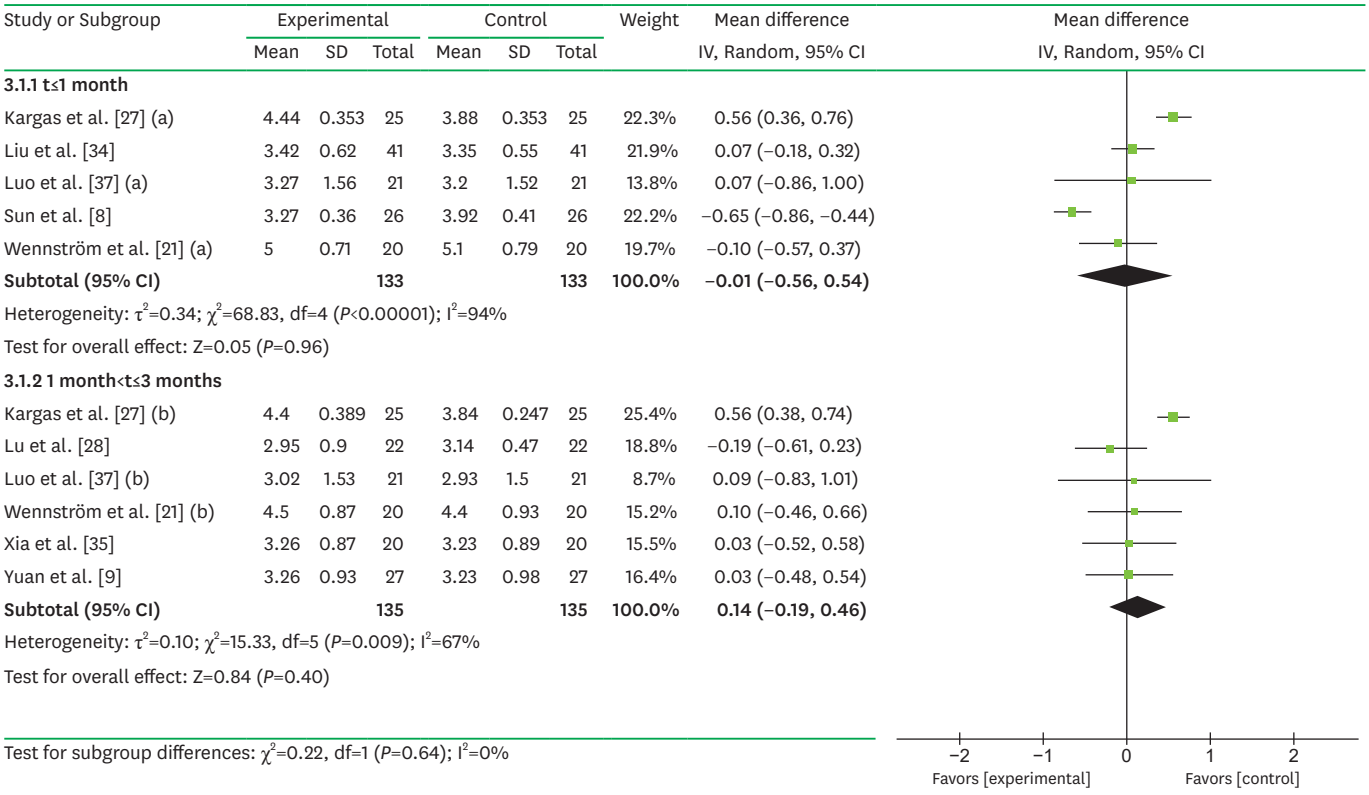

Figure 10. Forest plot of PD, comparing GPAP (experimental group) with ultrasonic scaling (control group).
PD: probing depth, GPAP: glycine powder air-polishing, SD: standard deviation, CI: confidence interval, IV: inverse variance.

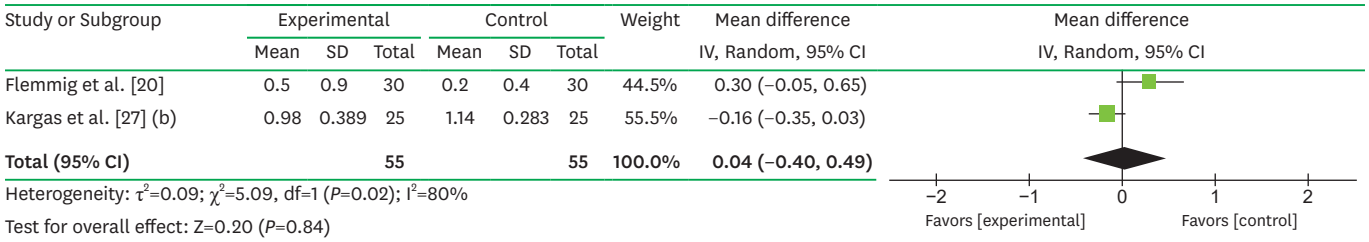

Figure 11. Forest plot of Rec, comparing GPAP (experimental group) with hand instrumentation (control group).
Rec: gingival recession, GPAP: glycine powder air-polishing, SD: standard deviation, CI: confidence interval, IV: inverse variance.

DISCUSSION

As a new device for periodontal treatment during SPT, GPAP has the advantage of being less time-consuming and less abrasive than conventional methods, making it a promising potential alternative [31]. However, some discrepancies regarding this issue exist, as some investigators have reported no significant differences between GPAP and conventional methods. This inconsistency has hindered the promotion of GPAP. Therefore, we conducted this meta-analysis to evaluate the effectiveness of GPAP for SPT compared to hand instrumentation and ultrasonic scaling.

The meta-analysis in the current study showed that compared to hand instrumentation, the BOP for the GPAP group was reduced by 8.02% (95% CI, −12.10% to −3.95%; *P*<0.00001). BOP refers to bleeding that is induced by gentle manipulation of the tissue at the depth of

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Study or Subgroup	Experimental			Control			Weight	Mean difference	Mean difference
	Mean	SD	Total	Mean	SD	Total		IV, Random, 95% CI	IV, Random, 95% CI
7.1.1 t≤1 month									
Liu et al. [34]	1.87	0.34	41	1.83	0.38	41	81.1%	0.04 (−0.12, 0.20)	
Luo et al. [37] (a)	1.27	0.55	21	1.19	0.52	21	18.9%	0.08 (−0.24, 0.40)	
Subtotal (95% CI)			**62**			**62**	**100.0%**	**0.05 (−0.09, 0.19)**	
Heterogeneity: τ^2=0.00; χ^2=0.05, df=1 (*P*=0.83); I^2=0%									
Test for overall effect: Z=0.66 (*P*=0.51)									
7.1.2 1 month<t≤3 months									
Luo et al. [37] (b)	1.09	0.53	21	1.13	0.51	21	42.3%	−0.04 (−0.35, 0.27)	
Xia et al. [35]	1.23	0.75	20	1.35	0.28	20	34.0%	−0.12 (−0.47, 0.23)	
Yuan et al. [9]	1.13	0.74	27	1.36	0.83	27	23.8%	−0.23 (−0.65, 0.19)	
Subtotal (95% CI)			**68**			**68**	**100.0%**	**−0.11 (−0.32, 0.09)**	
Heterogeneity: τ^2=0.00; χ^2=0.51, df=2 (*P*=0.78); I^2=0%									
Test for overall effect: Z=1.08 (*P*=0.28)									
Test for subgroup differences: χ^2=1.59, df=1 (*P*=0.21); I^2=37.3%									

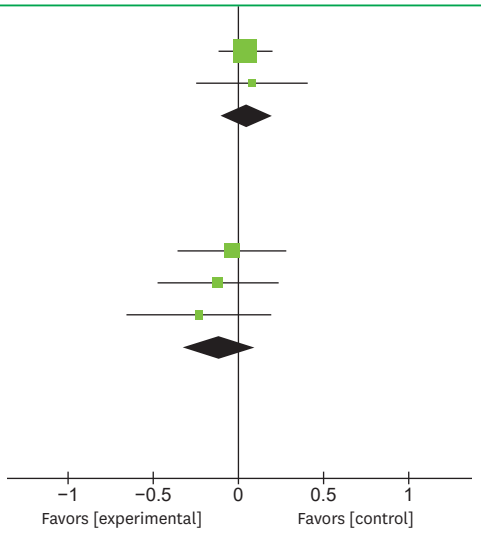

Figure 12. Forest plot of Rec, comparing GPAP (experimental group) with ultrasonic scaling (control group).
Rec: gingival recession, GPAP: glycine powder air-polishing, SD: standard deviation, CI: confidence interval, IV: inverse variance.

Study or Subgroup	Experimental			Control			Weight	Mean difference	Mean difference
	Mean	SD	Total	Mean	SD	Total		IV, Random, 95% CI	IV, Random, 95% CI
Kargas et al. [27]	5.38	0.424	25	4.76	0.389	25	44.6%	0.62 (0.39, 0.85)	
Xia et al. [35]	4.34	1.03	20	4.35	0.92	20	26.4%	−0.01 (−0.62, 0.60)	
Yuan et al. [9]	4.42	1.05	27	4.34	0.99	27	29.0%	0.08 (−0.46, 0.62)	
Total (95% CI)			**72**			**72**	**100.0%**	**0.30 (−0.15, 0.75)**	
Heterogeneity: τ^2=0.11; χ^2=6.07, df=2 (*P*=0.05); I^2=67%									
Test for overall effect: Z=1.29 (*P*=0.20)									

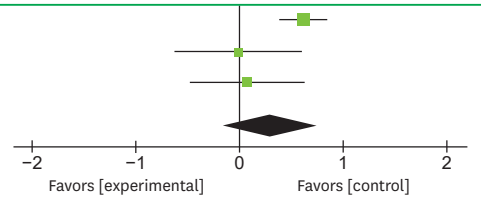

Figure 13. Forest plot of PI, comparing GPAP (experimental group) with ultrasonic scaling (control group).
PI: plaque index, GPAP: glycine powder air-polishing, SD: standard deviation, CI: confidence interval, IV: inverse variance.

Study or Subgroup	Experimental			Control			Weight	Mean difference	Mean difference
	Mean	SD	Total	Mean	SD	Total		IV, Random, 95% CI	IV, Random, 95% CI
Kargas et al. [27] (b)	0.98	0.389	25	0.92	0.389	25	87.8%	0.06 (−0.16, 0.28)	
Zhao et al. [33]	0	1	23	0	1	23	12.2%	0.00 (−0.58, 0.58)	
Total (95% CI)			**48**			**48**	**100.0%**	**0.05 (−0.15, 0.25)**	
Heterogeneity: τ^2=0.00; χ^2=0.04, df=1 (*P*=0.85); I^2=0%									
Test for overall effect: Z=0.51 (*P*=0.61)									

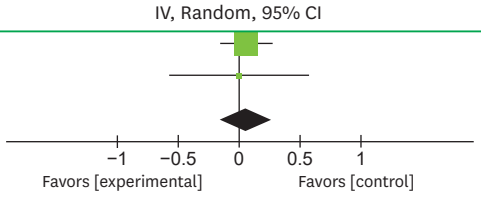

Figure 14. Forest plot of clinical attachment level (CAL), comparing GPAP (experimental group) with ultrasonic scaling (control group).
GPAP: glycine powder air-polishing, SD: standard deviation, CI: confidence interval, IV: inverse variance.

the gingival sulcus or interface between the gingiva and a tooth. BOP is a sign of gingival inflammation and indicates some degree of destruction and erosion of the linking of the gingival sulcus [38] or ulceration of the epithelium. The reduction of BOP in response to GPAP may have resulted from the ability of GPAP to alleviate gingival inflammation effectively. First, bacterial biofilms initiate periodontal inflammation, and GPAP can effectively remove bacterial biofilms. Second, the powder used in GPAP is glycine, which has immunomodulatory, anti-inflammatory, and cytoprotective effects on periodontal tissue [18]. However, no significant differences were found in PD, Rec, PI, or CAL between the

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GPAP and control groups, possibly due to variation in the follow-up period among different studies. Thus, further studies are still needed to prove the efficacy of GPAP.

Patients strongly prefer a higher comfort level during the treatment process. Furthermore, since SPT requires a long treatment cycle, good treatment experiences of patients contribute to their long-term follow-up, which is beneficial to the prognosis of periodontitis. Therefore, in this study, discomfort/pain levels were assessed using a VAS (patients were required to complete a VAS, ranging from extremely comfortable [value of 0] to extremely painful [value of 10]). The results for VAS scores (difference of means, −1.48; 95% CI, −1.90 to −1.06; $P<0.00001$) between the GPAP group and the ultrasonic scaling group confirmed that patients felt less discomfort/pain when using the new devices. This may be due to the minimally abrasive nature of glycine powder, as well as the specially designed delivery tip and handpiece used in GPAP, which may lead to less hard tissue damage and reduced tooth sensitivity.

In this present study, for results that could be quantitatively assessed, such as BOP, patient discomfort/pain (measured by VAS), PD, Rec, PI and CAL, RevMan 5.3 was used to calculate the *P* values, while a qualitative analysis was conducted for GE scoring and subgingival bacteria counts to maximize the reliability of the results.

Over the years, GPAP has also been used in the treatment of peri-implantitis due to the safety of glycine powder. Professional cleaning of implant prostheses was recommended because of the rebound of bacterial levels, and the use of glycine powder abrasion was suggested at each visit rather than plastic curettes [39]. Proper use of air-polishing is important to minimize the risk of air emphysema. It has been estimated that the risk of air emphysema following GPAP is approximately 1 in 666,666 [40].

At the same time, there were some limitations to our current study. First, the investigators of the included studies only evaluated short-term efficacy, which cannot fully prove the difference between GPAP and mechanical instrumentation. Second, according to the Cochrane Handbook for Systematic Reviews of Interventions, 12 of the included studies had a moderate risk of bias, and 5 were considered to have a high risk of bias. Those biases were associated with random sequence generation, allocation concealment, blinding of participants, blinding of outcome assessors, incomplete outcome data, selective reporting, and other biases. However, a certain level of bias existed in most meta-analysis[23]. Third, there was substantial heterogeneity among some studies, possibly because of the differences noted with initial PD and the exclusion of smoking or not. Finally, researchers did not detect the clinical parameters and patient discomfort/pain at the same time point, and high heterogeneity was possible when doing a meta-analysis.

Because of the substantial heterogeneity among some studies, subgroup analyses were conducted. The subgroup meta-analysis suggested that initial PD had some association with the degree of heterogeneity for VAS and PD between GPAP and ultrasonic scaling. Moreover, smoking status showed a significant degree of heterogeneity for PD between the GPAP and hand instrumentation groups. Although the subgroup analysis of PD showed that in non-smokers, hand instrumentation might be more effective than GPAP, the evidence was insufficient to prove the superiority of hand instrumentation over GPAP, since only 1 study was included in this subgroup.

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In the light of the results and limitations mentioned above, some suggestions can be made for further research. First, investigators should devote more attention to the long-term efficacy of GPAP. Moreover, the experimental design of further studies should be more rigorous. For example, investigators should detect the outcome measures at the same time point, and the inclusion criteria should be consistent.

In conclusion, this study demonstrated that GPAP might alleviate gingival inflammation more effectively and be less painful. Since GPAP is more expensive than hand instrumentation and ultrasonic scaling because of the instruments needed and glycine powder used, practitioners should carefully balance the costs that patients can afford and the benefits that patients may obtain when deciding to use GPAP for SPT. With regards to PD, Rec, PI, and CAL, the evidence was insufficient to support a difference between GPAP and mechanical instrumentation during SPT. More studies with a longer evaluation period are urgently needed to further analyse the efficacy of GPAP.

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