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ORIGINAL ARTICLE

Effectiveness of periodontal treatment to improve glycemic control: an umbrella review

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Abstract

Aim The aim of the present umbrella review was to systematically assess existing evidence on the effect of non-surgical periodontal therapy, both per se' and with adjuvants, on glycemic control in patients with type 2 diabetes and periodontitis and to combine quantitative data with a meta-analysis.

Materials and methods A detailed study protocol was registered on PROSPERO (CRD42021222279). Four electronic databases (Medline via Pubmed, EMBASE, Cochrane Database of Systematic Reviews and Scielo) were searched independently and in duplicate to identify potentially eligible systematic reviews up to March 2022. Two pre-calibrated independent reviewers performed study selection, data extraction and quality assessment with two checklists (AMSTAR 2 and PRISMA). Moreover, general characteristics of primary studies included in each systematic review were abstracted, and JADAD scale was used to assess the risk of bias for included randomized controlled trials. Data from the individual studies included in each meta-analysis were analyzed, using both fixed and random effect model. The statistical heterogeneity was calculated using the Q test and the I^2 index. The publication bias was evaluated using a funnel plot and Egger's linear regression method.

Results Sixteen systematic reviews, published between 2010 and 2021, were included for qualitative synthesis. From these systematic reviews, a total of 27 studies were included in the meta-analysis: all of them were randomized clinical trials, except 1 controlled clinical study. A statistically significant mean difference of − 0.49% and of − 0.38% HbA1c reductions was seen respectively at 3- and 6-month post-treatment, favoring the treatment group (non-surgical periodontal therapy alone) compared to the control group (no treatment). The effect of periodontal treatment with the adjunctive use of antibiotics or laser on the glycemic control was not statistically significant compared to non-surgical periodontal therapy alone.

Conclusions The findings of the present study, within its limitations, indicated that non-surgical treatment of periodontitis is an efficacious therapy for improving the glycemic control in type 2 diabetes mellitus patients, both at 3- and 6-month follow-up.

Keywords Periodontitis · Type 2 diabetes · Glycemic control · Non-surgical periodontal therapy · Umbrella review

Introduction

Over the years, there has been an increasing interest in the hypothesis that poor oral health may influence the overall health [1–6]. In this regard, the association between diabetes mellitus (DM) and periodontitis was evaluated since the early 1990s in Pima Indians, whom present the world's highest reported incidence and prevalence of type 2 DM [7–10].

Diabetes is associated with an increased risk of periodontitis onset and progression of 86% [11]. Furthermore, DM patients exhibit a periodontitis of greater severity compared with non-diabetic individuals [12, 13]. On the other hand, the systemic inflammation triggered by periodontitis can

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influence the regulation of the serum glucose level, contributing to the persistence of hyperglycemia [14]. According to current evidences, the periodontitis inflammatory burden constitutes the strongest predictor of poor glycemic control, and it is associated with an increased risk of developing diabetes [13, 15].

Several randomized clinical trials (RCT) have pointed out that non-surgical periodontal treatment (NSPT) not only improves periodontal parameters, but also may positively influence the glycemic control in diabetic patients [16]. According to Sabharwal et al. [17], short-term glycated hemoglobin (HbA1c) reductions obtained consequent to NSPT are comparable to the addition of a second drug into the pharmacological regimen of DM patients. However, this finding was not confirmed by other studies, in which metabolic improvement following scaling and root planing was not detected [18–20].

Over the years, several systematic reviews with meta-analysis unveiled the effect of periodontal non-surgical treatment (NSPT) on glycemic control in DM patients; notwithstanding the results obtained show a high degree of heterogeneity.

Although some other umbrella reviews (UR) on the same topic have been published, nevertheless all of them were limited to qualitative evaluation of the data [16, 21–23].

Therefore, the aim of the present UR is to systematically assess the latest systematic reviews published, in order to clarify existing contradictory findings, through the following focused questions:

- What is the effect of NSPT per se' on glycemic control in patients with type 2 DM, in terms of HbA1c changes?
- What is the effect of NSPT with adjunctive therapies (e.g., local/systemic antibiotics, laser therapy) on glycemic control in patients with type 2 DM, in terms of HbA1c changes?

Moreover, to overcome limits presented in previous UR published in the literature, a meta-analysis is conducted with the purpose of combining quantitative data and understanding the strength of the effectiveness of NSPT on glycemic control in diabetic patients with periodontitis.

Materials and methods

Protocol registration and reporting format

The present UR was registered in the PROSPERO (International Prospective Register of Systematic Reviews) with Identification Number CRD42021222279 and reported in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analysis Extension (PRISMA) guidelines [24], and Joanna Briggs Institute methodology for umbrella reviews [25].

Population, intervention, comparison, outcome, study design (PICOS) question

This following PICOS framework was used to guide the inclusion of studies [26]:

- *Population (P)* Patients with type 2 DM diagnosed with periodontitis, regardless of the classification.
- *Intervention (I)* NSPT with or without adjunctive use of antibiotics or laser therapy.
- *Comparison (C)* NSPT alone, no periodontal treatment (e.g., delayed treatment, supragingival prophylaxis, oral hygiene instructions).
- *Outcome (O)* Changes in HbA1c
- *Study design (S)* Systematic reviews (SRs)

Eligibility criteria

The systematic reviews were eligible for inclusion if they met the following criteria:

1. Systematic reviews that included both RCT and CCT
2. Articles that compared NSPT alone versus no treatment (e.g., delayed treatment, supragingival prophylaxis, oral hygiene instructions) or NSPT with adjunctive therapies (e.g., local/systemic antibiotics, laser therapy) with a control group which included no treatment or NSPT alone
3. Changes in HbA1c, at least 3 months after interventions, as primary outcome
4. Articles written in English.

Search strategy

A detailed systematic search was conducted in the following targeted electronic databases: Medline via Pubmed, EMBASE, Cochrane Database of Systematic Reviews and Scielo, in order to include high impact journals as well as gray literature.

The following MeSH terms/free terms and their combination were used:

- ("Non-surgical periodontal therapy" OR "nonsurgical periodontal treatment" OR "periodontal therapy" OR "periodontal treatment" OR "scaling and root planning" OR SRP OR "periodontal disease management" OR "photodynamic therapy" OR "systemic antibiotics" OR "systemic doxycycline") AND (diabetes OR "diabetes mellitus" OR "type 1 diabetes" OR "type 2 diabetes" OR "type 2 diabetes mellitus" OR "diabetic patients") AND

("glycosylated hemoglobin" OR "glycated hemoglobin" OR HbA1c OR "fasting glucose" OR "glucose levels" OR glycaemia OR hyperglycemia OR "glycemic control" OR "glycemic control" OR "metabolic control")
- Diabet* AND periodont* AND (systematic review or meta-analysis)

Furthermore, the reference lists of articles retrieved from the databases were reviewed.

No restrictions were assigned regarding the date of publication and journal. Next, the search results were downloaded to a bibliographic database to facilitate duplicate removal and cross-reference checks. The search was conducted on January 2022, and it was re-run prior to final analysis (March, 2022).

Study selection

Two pre-calibrated reviewers (GLDD and MM) screened and evaluated all the titles and abstracts, after duplicates removal, independently and in duplicate.

Afterward, the full text of all publications appearing to meet the inclusion criteria and ones with not sufficient information in the title and/or abstract to make a decision, were obtained. When necessary, authors of the studies were contacted by e-mail for full-text request.

At the next screening phase, the full-text publications were also evaluated in duplicate and independently by the same examiners. Any disagreement on the eligibility of studies was resolved through discussion between both reviewers until consensus was reached or through arbitration by a third reviewer (MdS).

All potentially relevant studies that did not meet the eligibility criteria were excluded, and the reasons for exclusion were recorded and available at Supplementary Table 1.

Data extraction

Data extraction was performed by two calibrated reviewers (GLDD, MM), independently and in duplicate. All relevant data from the selected studies were recorded in a predetermined data extraction form specifically designed for this review.

For each systematic review, aside from the primary outcomes of HbA1c changes (at every follow-up time point), the following details were extracted:

- Authors, title, year of publication;
- Database sources searched and last searching day;
- Number and design of individual studies included;
- Types of diabetes;
- Number of patients (test/control);
- Interventions and control;
- Follow-up period (months);
- Instrument of quality assessment;
- Assessment of risk of bias (RoB) in included studies;
- Assessment of RoB across studies (publication bias);
- Method of statistical analysis;
- Number of studies/comparisons in the meta-analysis.

Subsequently, a list of cited studies across the included systematic reviews was obtained, duplicates were removed, and full-texts were also evaluated in duplicate and independently by the same examiners.

For each study, the following data were recorded:

- Author, title, year of publication;
- study design (i.e., case–control or randomized control study);
- Number of cases and controls;
- Intervention and control;
- Follow-up duration;
- Mean and standard deviation of HbA1c at baseline and at follow-up for each treatment group.

Articles were excluded if they met the following criteria: (1) lack of Hba1c data at baseline and/or follow-up time; (2) use of adjunctive therapies other than antibiotics and laser; (3) inclusion of DM type 1 patients or non-diabetic patients; (4) comparison of two groups other than NSPT alone versus no treatment or NSPT with local/systemic antibiotics or laser therapy versus NSPT alone; (5) full-text not available in English.

Quality assessment

The quality assessment of the included systematic reviews was assessed by two independent reviewers (GLDD and MM) using two analysis tools: AMSTAR 2 (Assessment of Multiple Systematic Reviews) [27] and the check-list PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) [24].

The first checklist included 16 items with three possible response option (yes, no, partial yes). A rating of the overall quality of the systematic reviews (critically low, low, medium, or high quality) was performed using the critical domains recommended by Shea et al. [27] (https://amstar.ca/Amstar_Checklist.php).

Moreover, the relationship between the numbers of items fulfilled by each SR according to the appraisal tool was investigated. An AMSTAR 2 percentage score was calculated according to Fleming et al. [28]. For each of the 16 items, a score of 0 (answer "no"), 1 (answer "yes") or 0.5 (answer "partial yes") was given, summed up and converted to a percentage (%) scale. In the case of SR in which no meta-analysis was undertaken, this percentage score

includes three non-applicable items. The denominators in such cases were therefore reduced accordingly to calculate a score based on the remaining applicable items only.

The second checklist is composed by 27 items, with two possible response options (yes or no). The total score for PRISMA was calculated by summing each score. To classify the quality of the included reviews, the following three categories were used: score < 19.0 (low quality), 19.0–22.5 (moderate quality) and > 22.5 (high quality) [29].

The data collected using the two quality assessment tools were analyzed using descriptive statistics. The mean and standard deviation of the two checklists were calculated.

Risk of bias in included studies

The JADAD scale was used to assess the risk of bias for included RCTs [30]. Thus, three items (randomization, double blinding, account for withdrawals and dropouts) were scored as present or not, and one additional point was given for item 1 and 2 if the sequence of randomization and/or the method of double blinding was described, and it was appropriate. Trials were allocated a score between 0 (very poor) and 5 (rigorous).

Data analysis and statistical methodology

Data from the individual studies included in each meta-analysis were analyzed.

To compare the selected studies, a mean treatment effect (T1-baseline) was calculated. Results were combined using standardized mean differences (SMD's) (difference in the mean outcome between groups/SD of outcome among participant) as summary statistics, along with 95% confidence intervals (CI). When the differences between baseline-end were not reported, they were calculated using baseline and final values.

The statistical heterogeneity among studies was calculated using the Q test [31]. As a complement to the latter test, the I^2 index was calculated to know the percentage of variation in the global estimate that was attributable to heterogeneity ($I^2 = 25\%$ low to $I^2 = 75\%$ high).

The specific study estimate was grouped using both fixed and random effect model (Mantel–Haenszel–Peto test and Dersimonian–Laird test, respectively). If heterogeneity resulted significant, then the random effect model results was presented.

In addition, in case of heterogeneity in the primary outcome, the 95% prediction intervals for the summary random effect sizes were reported, to allow more informative inferences and providing the possible range in which the effect sizes of future studies were expected to fall [32].

Forest plots showing the point estimate and confidence intervals for each study were created. Statistical significance was defined as a two-tailed $p < 0.05$.

The publication bias was evaluated using a funnel plot and Egger's linear regression method.

All analyses were performed using the meta-statistical packages in Rstudio (ver. 3.5.2, www.r-project.org) and Stata 15c (command "*mar*").

Results

Study selection

The initial search retrieved 1800 references: 601 titles from PubMed, 302 titles from the Cochrane Library Database, 5 from Scielo and 892 from Embase. Twenty-nine additional studies were found in the gray literature and in the references of the included studies.

The two examiners (GLDD and MM) were calibrated with the first 20 full-text, consecutive publications and displayed high levels of agreement (Cohen's $K = 0.9306$).

After duplicates removal, the titles and abstracts of the 1062 identified records were screened. Any paper considered as potentially relevant was included in the next phase.

One hundred and twelve articles were selected for full-text assessment, out of which 94 were excluded because they did not meet the umbrella review's eligibility criteria, previously defined in the registered study protocol. In total, 16 systematic reviews were included for qualitative synthesis.

The PRISMA flow diagram describing the complete process of studies' identification and selection and the reason for the exclusion of identified full-text articles is presented in Fig. 1.

Systematic review characteristics

The 16 articles, published between 2010 and 2021, described 30 unique meta-analyses:

- A random effects model was used in thirteen articles [33–45];
- A fixed effects model was utilized in one paper [46];
- No meta-analysis was performed in two articles [47, 48].

The main characteristics of the 16 systematic reviews included are shown in Supplementary Tables 2 and 3.

There was significant heterogeneity and lack of standardization in the choice of instruments used to assess methodological quality. The Cochrane Risk Bias Tool was the most commonly used instrument (11 SRs) [35–44, 46], followed by Jadad scale (3 SRs) [45, 47, 48], CONSORT Statement (1 SR) [34] and the Standard Assessment form

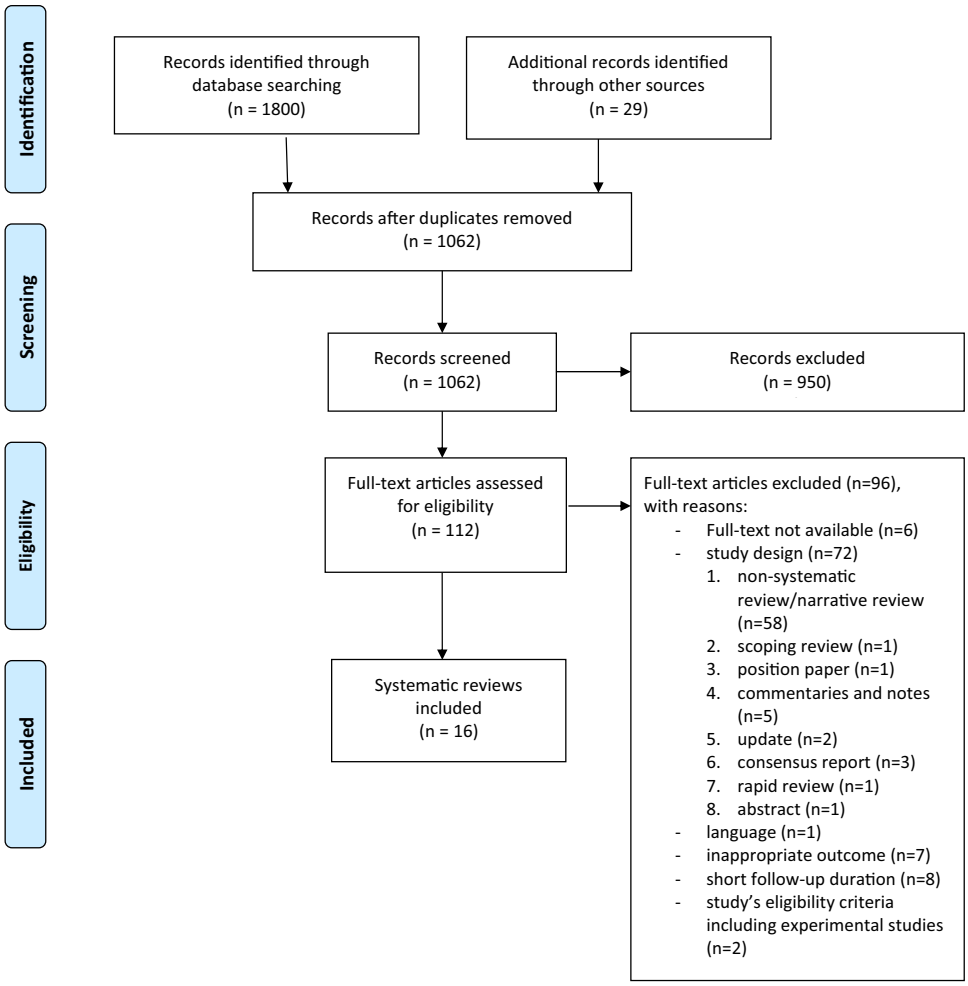

Fig. 1 PRISMA flow diagram of the screening process performed for the selection of SRs

developed by the Dutch Cochrane Centre and the Dutch Institute for Healthcare Improvement CBO (1 SR) [33].

Publication bias was assessed in nine out of 16 SRs [34–36, 39–43, 45].

Effect of non-surgical periodontal treatment per se'

The effect of non-surgical periodontal treatment on glycemic control was evaluated in 12 meta-analyses [33–43, 45]. Out of these, only three meta-analyses were performed on HbA1c results at 3–4 months [37, 40, 42] and one on results at 6 months [37]. Two meta-analyses reported a statistically significant reduction in HbA1c at 3–4 months for the NSPT group of − 0.38% (95% CI [− 0.53, − 0.23], $p < 0.00001$) [37] and − 0.27% (95% CI [− 0.46, − 0.07]; $p = 0.007$) [40], while Cao et al. [42] reported a non-significant reduction of 0.45% (95% CI [0.00, 0.89]). Regarding data at 6-month post-treatment, Corbella et al. [37] review showed a non-significant HbA1c reduction of − 0.31 (95% CI [− 0.74, 0.11], $p = 0.15$).

Effect of non-surgical periodontal treatment with the adjunctive use of antibiotics

Data from three meta-analyses are available comparing the effect of NSPT plus antibiotics comparing to NSPT alone in reducing HbA1c after a period of 3–4 months [37, 42, 46]. The most notable issue about these studies is the diversity of the antibiotics used, and the way they are administered (systemic or topical) (Supplementary Table 2). In all three reviews, the results were non-significant 0.21% (95% CI [− 0.03, 0.45]) [42], − 0.238% (95% CI [− 0.616, 0.140], $p = 0.217$) [46] and 0.13% (95% CI [− 0.10, 0.35]; $p = 0.28$) [37]. Only the Corbella et al. (2013) review [37] reported data at 6-month post-treatment, which came from Rodrigues et al. [49] and O'Connell et al. [50] trials, showing a non-statistically significant HbA1c reduction of − 0.27% (95% CI [− 40.11, 39.56], $p = 0.99$).

Effect of non-surgical periodontal treatment with the adjunctive use of laser

The effect of NSPT plus laser therapy to NSPT alone in reducing HbA1c was evaluated in two meta-analyses: both studies reported a significant reduction of 0.19% after a period of 3 months (95% CI [0.10, 0.28], $p < 0.0001$) and 95% CI [0.08, 0.3]) [42, 44] and a significant reduction of 0.22% (95% CI [0.03, 0.41], $p = 0.03$) at 6-month follow-up [44].

No meta-analyses are available on the effect at 6 months. Only one study reported data on the effect at 6 months [51].

Quality assessment of SRs

The quality assessment scores using AMSTAR-2 and PRISMA checklist are displayed in Supplementary Table 4 and 5.

None of the reviews that were included in this study satisfied all of the AMSTAR criteria (Supplementary Table 6). The scores varied between 5.5 points and 13 points, with an average of 10.2 ± 1.9 points. None of the reviews scored on question 10 ("Did the review authors report on the sources of funding for the studies included in the review?").

In rating overall confidence in the results of the SR according to Shea et al. [43], none of the reviews were rated "high," one was "moderate," one was "low" [34] and 14 were "critically low" (33, 35–42, 44–48].

The mean AMSTAR 2 percentage score was 59.6% (SD 11.3%) in a wide range from 42 to 81%. The corresponding AMSTAR 2 percentage scores for the 164 "critically low" reviews ranged from 42 to 69%, whereas the "low" review had 72% and the "moderate" review had 81%.

Regarding the PRISMA checklist, the scores varied between 14 and 26 points, with an average of 21.6 ± 3.2 points. All of the reviews scored 1 (yes) for questions 1, 2, 3, 9, 10, 17, 24, 25 and 26. (Supplementary Table 7).

The overall score was "high" in eight studies [35, 37, 40–45], "moderate" in six reviews [33, 34, 36, 38, 39, 46] and "low" in two papers [47, 48].

Studies included in the meta-analysis

The number of individual studies included in the systematic reviews ranged from 4 to 23, with an average of 10.4 ± 5.5 articles. The majority of SRs included < 10 articles ($n = 10$), four SRs included a number between 10 and 15 articles, and the other two SRs included > 20 articles (Supplementary Table 2). In total, 73 studies were identified from the 16 SRs.

Of these, a total of 27 studies were included in the meta-analysis: All of them were randomized clinical trials, except one controlled clinical study [52].

A full list of the included and excluded studies, with the reasons for exclusion, is presented respectively in Supplementary Tables 8 and 9.

Risk of bias in included studies

Three studies out of 27 RCTs scored 5 [53–55], 11 studies scored 4 [19, 51, 56–64], five studies scored 3 [20, 50, 65–67], seven studies scored 2 [52, 68–73], and only one scored 1 [49]. (Supplementary Table 10).

Risk of bias across included studies (publication bias)

Eggers' test indicated the absence of significant publication bias among studies (no funnel plot asymmetry). (Supplementary Table 11).

Summary of evidence

Effect of non-surgical periodontal treatment per se' on glycemic control

Eighteen studies cited in these above-mentioned SRs were included in the present meta-analysis on the effect of NSPT at 3–4 months. Sixteen studies were parallel arm two-group studies, while two studies included three treatment groups. In the three groups studies, both treatment groups received scaling and root planning only [58, 65]. The mean treatment effect of the interventions in the individual studies is shown in Fig. 2. A statistically significant mean difference of −0.49% (95% CI [−0.63, −0.35], $p < 0.001$) HbA1c reduction was seen, favoring the treatment group (NSPT alone).

Regarding the effect at 6-month post-treatment, six studies identified from these SRs were included, showing a statistically significant mean difference of −0.38% (95% CI [−0.61, −0.16], $p = 0.0009$) HbA1c reduction, favoring the treatment group. (Fig. 3).

Heterogeneity among studies expressed as I^2 varied from 46 to 52%, depending on the outcome measure follow-up (6 months and 3 months, respectively).

Effect of periodontal treatment with the adjunctive use of antibiotics on the glycemic control

Nine studies identified from these SRs were included in the present meta-analysis on the effect of NSPT plus antibiotics comparing to NSPT alone at 3-month of follow-up. A non-statistically significant mean difference of −0.13% (95% CI [−0.32, −0.06], $p = 0.186$) HbA1c reduction was observed between the groups. (Fig. 4).

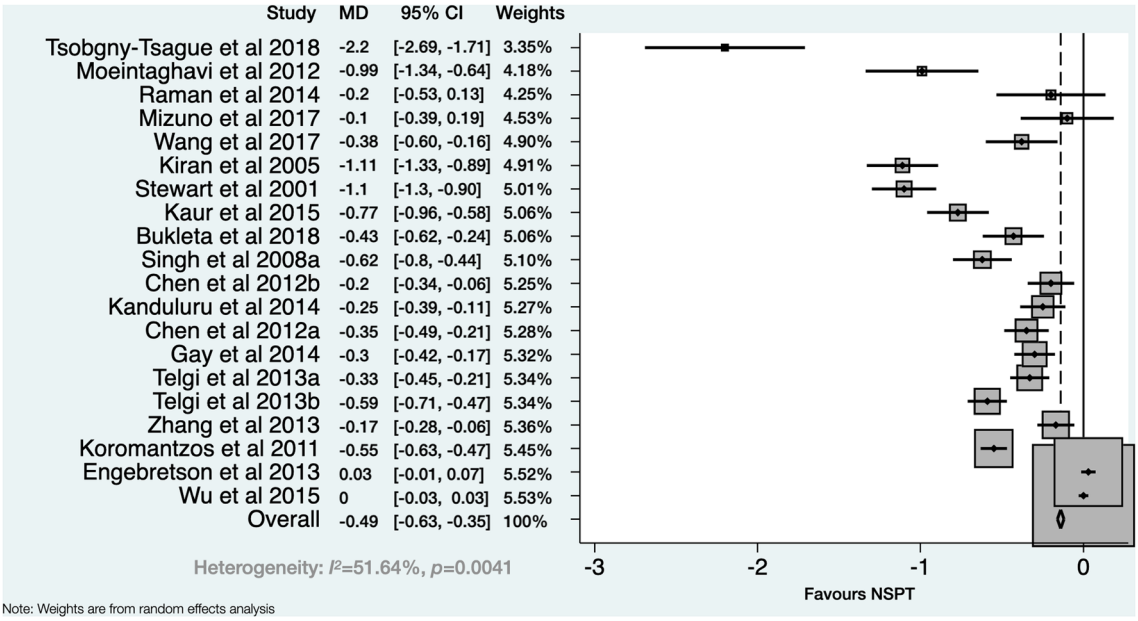

Fig. 2 Mean differences between non-surgical periodontal treatment (NSPT) and no treatment for HbA1c changes at 3–4 months

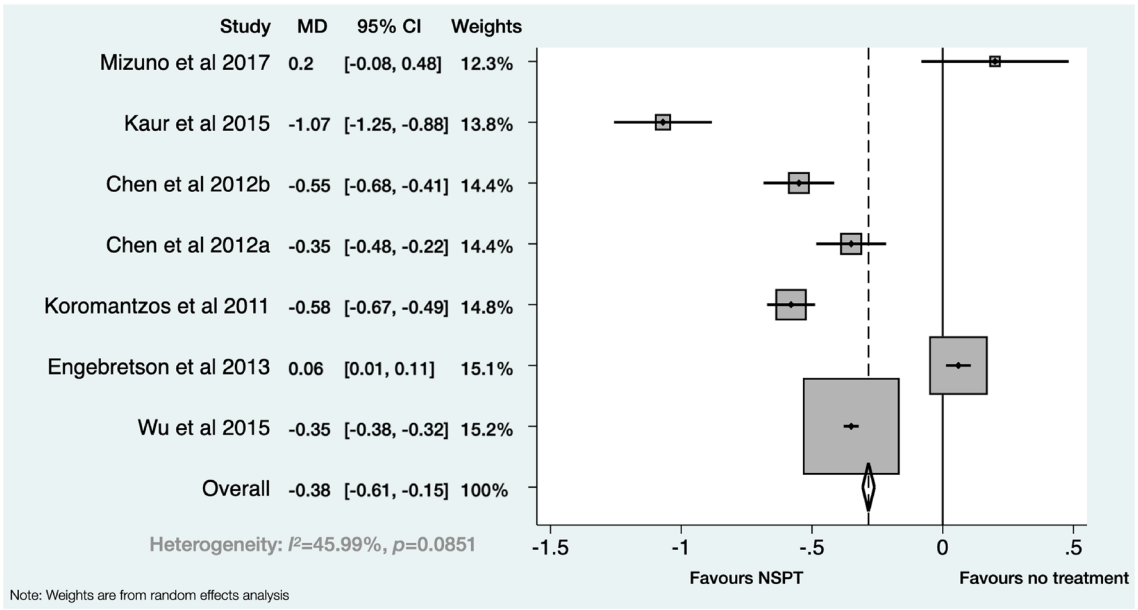

Fig. 3 Mean differences between non-surgical periodontal treatment (NSPT) and no treatment for HbA1c changes at 6 months

Regarding the effect at 6 months, our analysis was conducted on two studies [55, 59] other than those included by Corbella et al. [37] and reported a non-statistically significant mean difference of 0.11% (95% CI [− 0.31, 0.53], $p = 0.602$) HbA1c reduction between the groups. (Fig. 5).

Heterogeneity among studies expressed as I^2 varied from 0 to 57%, depending on the outcome measure follow-up.

Effect of periodontal treatment with the adjunctive use of laser on the glycemic control

Two studies cited in these SRs [51, 64] were included in the present meta-analyses, which showed a non-statistically significant mean difference of − 0.28% (95% CI − 0.73, 0.17; $p = 0.227$) HbA1c reduction between the groups (Fig. 6). Heterogeneity among studies expressed as I^2 was 0%.

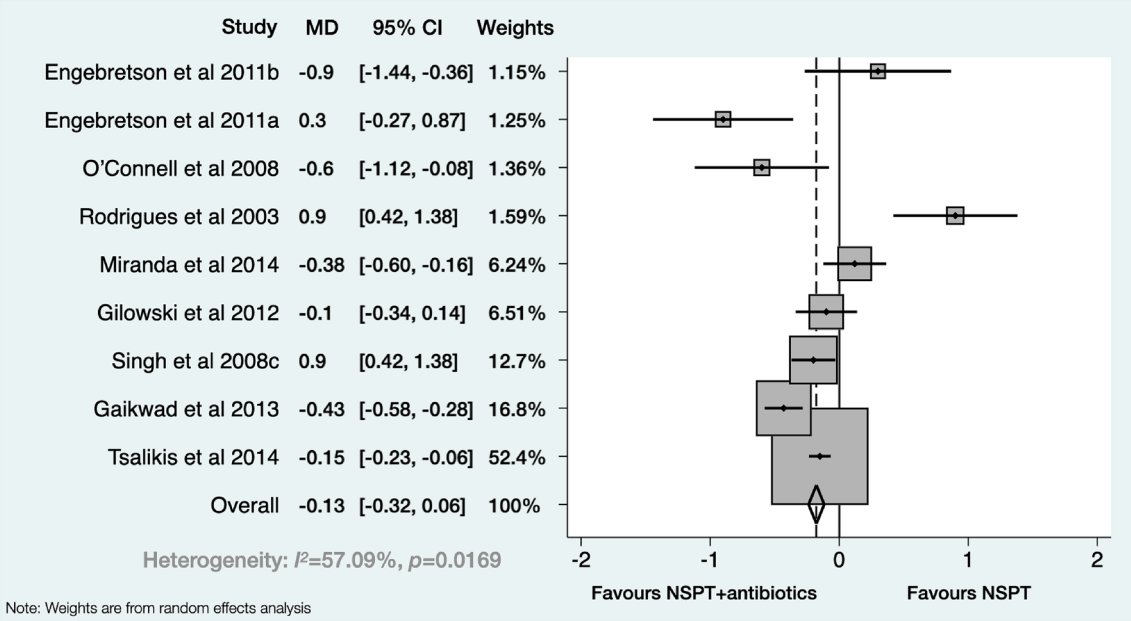

Fig. 4 Mean differences between non-surgical periodontal treatment with antibiotics (NSPT + antibiotics) and NSPT for HbA1c changes at 3–4 months

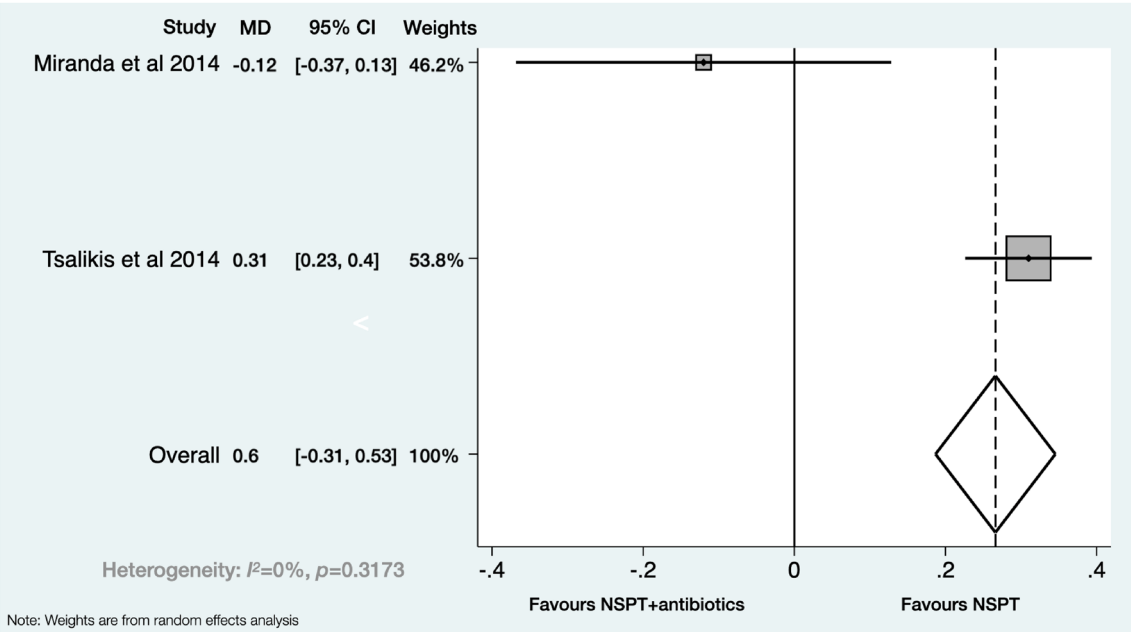

Fig. 5 Mean differences between non-surgical periodontal treatment with antibiotics (NSPT + antibiotics) and NSPT for HbA1c changes at 6 months

Discussion

This umbrella review was carried out to evaluate the existing evidence on the effect of non-surgical periodontal therapy, both per se' and with adjuvants, on glycemic control in patients with type 2 diabetes and to combine quantitative data with a meta-analysis.

The presented systematic research identified and included 16 SRs, 14 of which performed one or more meta-analyses.

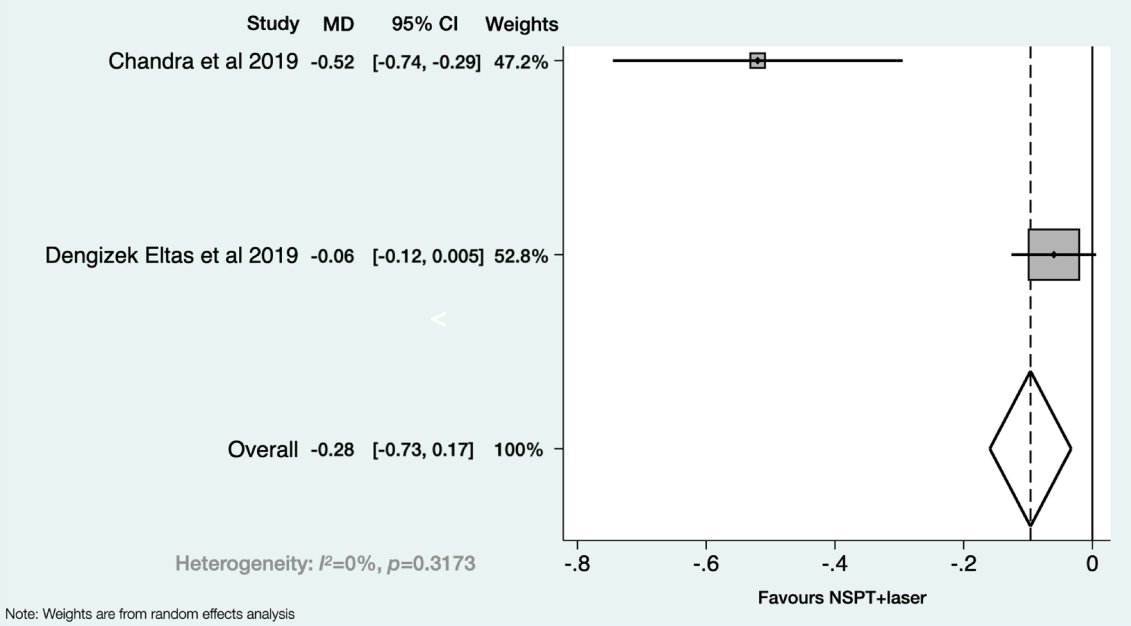

Fig. 6 Mean differences between non-surgical periodontal treatment with laser therapy (NSPT + laser) and NSPT for HbA1c changes at 3–4 months

The quality of each systematic review was assessed with two quality tools. The AMSTAR 2 tool results showed that the majority of SRs (14 out of 16) had "critically low" quality. The most common factors that affected quality were the absence of "a priori" design, of the search of potential impact of risk of bias and of publication bias and discussion of their impact on the results. In addition, each SRs was appraised using also PRISMA checklist and, according to the proposed scale by Tian et al. [29], only two SRs has been classed as "low" quality, while the remaining either as "moderate" ($n = 6$) or "high" ($n = 8$). Although the two checklists included the same items, it is interesting to notice the contradictory results derived from them. For this reason, the quality tools should help the reader to assess which critical components a systematic review did not include, rather than the total score or percentage, in order to appropriately interpret the results and its implications.

Moreover, the included SRs appear to follow very similar methodologies regarding study design and research question, nevertheless they differ for the reported estimates. The performed quality appraisal allowed us to identify potential methodological differences among SRs in order to explain the variability in results. The different number of the included studies in each meta-analysis is the first aspect that has emerged, although they adopted the same eligibility criteria. Secondly, not all studies reported the information of individual trials. Furthermore, when data from the included RCTs were reported, discrepancy among these ones has been observed in the various meta-analysis.

To overcome this potential bias, reviewers retrieved the full text of the articles included in the SRs and carried out a data extraction in order to perform a "de novo" meta-analysis. The 63% ($n = 46$) of the aforementioned articles were not considered eligible for further analysis due to certain types of selective reporting in RCTs, presence of inclusion criteria not fulfilled and full-text not available in English language.

The meta-analysis performed showed a statistically significant benefit in favor of the non-surgical periodontal treatment alone, with a difference of −0.49% and −0.38% in HbA1c changes compared to no treatment, at 3- and 6-month follow-up, respectively. These data are in line with those published in previous systematic reviews in which the HbA1c reductions range from 0.27 to 0.48% at 3–4 months [37, 40]. More recently, a SR reported no statistically significant results for non-surgical periodontal therapy [42]. This difference seems to be justified because of a low number of articles included in the Cao meta-analysis ($n = 3$), compared to those considered by our calculations ($n = 16$), although the same selection criteria were adopted.

The adjunctive use of both systemic and local antibiotics did not improve the HbA1c level as compared to NSPT alone. This is in line with the previous evidence available [37, 42, 46]. The scientific rationale to justify an antimicrobial therapy in conjunction with periodontal treatment is due to the possible augmented efficacy of mechanical therapy to eliminate bacteria, as demonstrated in severe cases of periodontitis [5]. However, the current evidence showed that the clinical performance of the non-surgical

periodontal treatment per se' can be considered effective for the resolution of periodontitis in diabetic patients, and thus for the HbA1c reduction, irrespective of the adjunctive use of systemic antibiotics. Hence, considering also the global concerns about the development of antibiotic resistance, it is appropriate to adopt a conservative approach in the administration of antibiotics for these specific patients. This is in line with what is currently recommended to systematically healthy patients with chronic periodontitis: the decision of antibiotic adjunct to NSPT should depend on the individual periodontal destruction severity and be restricted to the most severe cases [5].

As regards to the efficacy of adjunctive laser application, the results of the present meta-analysis included two RCTs [51, 64] and revealed a non-statistically significantly improved outcome compared to NSPT alone. Keeping in mind that the adjunctive application of lasers to subgingival instrumentation is still debatable [5], the presence of unclear risk of bias, difference in terms of laser type, wavelength and settings employed and the exiguous number of available RCT's extend this uncertainty also to the diabetic patients with periodontitis.

In recent years, several umbrella reviews have investigated the effects of periodontal treatment on glycemic control in patients affected by diabetes and periodontitis [16, 21–23]. Those studies provide a narrative or qualitative synthesis of the findings from each systematic review and the summary estimates from the original pairwise meta-analysis.

To the best of author's knowledge, this is the first analysis aimed to assess the efficacy of non-surgical periodontal treatment in type 2 diabetes patients through the conduction of an umbrella review with a meta-analysis.

One of the advantages of this research protocol is to provide a synthesis of the results and conclusions at the systematic review level, overcoming the bias due to the inclusion of the same primary studies in two or more reviews. The "new" meta-analysis allowed to assess what the overall true effect should have been if all relevant studies were collected and synthesized appropriately.

Nonetheless, several limitations of the present meta-analysis should be recognized. Not all the studies on this topic were identified, since we planned to synthesize results of only empirical studies included in systematic reviews.

Another major issue is the heterogeneity of results. Differences in criteria adopted for the definition of periodontitis, as well as differences across therapeutic regimen of the patients, could explain the observed heterogeneity. Moreover, as the literature on the topic is limited, it appears difficult to perform separate analyses for the sub-groups of treatments (e.g., systemic versus local antibiotics); nonetheless, this would yield more information on the factors underlying this heterogeneity.

Furthermore, the methodological quality of a subset of the studies included in the meta-analysis is far from ideal; unfortunately, the limited amount of available evidence does not allow the meta-analysis to be restricted to research with a higher-quality threshold.

Conclusions

In conclusion and within the limitations of the present study, a comprehensive search and analysis of the available literature based on systematic reviews demonstrated that non-surgical treatment of periodontitis is efficacious to improve the glycemic control in type 2 DM patients, both at 3- and 6-month follow-up.

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Author contributions Study conception was done by GLDD; Study design was done by MdS; Data acquisition was done by GLDD, MM and ND; Data analysis was done by ND and AA; Data interpretation was done by GLDD, MM and ND; Manuscript revision was done by MdS; Final approval was done by MdS.

Declarations

Conflict of interest The authors have no conflicts of interest to declare that are relevant to the content of this article.

Ethical approval This study is a systematic review and meta-analysis of randomized controlled trials, data are collected from related articles, and all of them are referenced in the manuscript. This research does not directly include any human participants or animals.

Informed consent For this type of study, written informed consent is not required.

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