UNIVERSIDAD PERUANA CAYETANO HEREDIA | Facultad de ESTOMATOLOGÍA

TREATMENT OF PERI-IMPLANT MUCOSITIS: AN OVERVIEW OF SYSTEMATICS REVIEWS

TRATAMIENTO DE LA MUCOSITIS PERIIMPLANTARIA: UN RESUMEN DE REVISIONES SISTEMÁTICAS

TESIS PARA OPTAR POR EL TÍTULO DE SEGUNDA ESPECIALIDAD PROFESIONAL EN PERIODONCIA E IMPLANTOLOGÍA

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DEDICATORIA

Este trabajo está dedicado a nuestras familias por el apoyo incondicional, y a nuestrosmaestros por sus enseñanzas.

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DECLARACIÓN DE CONFLICTO DE INTERESES

Los autores declaran no tener conflicto de intereses

RESULTADO DEL INFORME DE SIMILITUD

TREATMENT OF PERI-IMPLANT MUCOSITIS: AN OVERVIEW OF SYSTEMATICS REVIEWS

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ABSTRACT

Objective: To synthesize the evidence on the treatment of peri-implant mucositis and to evaluate the quality of the existing systematic reviews. **Materials and methods:** Only systematic reviews with or without meta-analysis investigating any outcome of the treatment of peri-implant mucositis in humans were included. Electronic searches were performed in three databases, until January 2021. The quality assessment was conducted independently and in duplicate based on the Multiple Systematic Review Assessment Tool (AMSTAR 2) guidance. **Results:** 17 studies were included for qualitative analysis, all used a randomized clinical trial design, 9 of the systematic reviews chose this study design only. The selected systematic reviews evaluated the following treatments for peri-implant mucositis: Mechanical debridement alone (MDA), Mechanical debridement (MD) + probiotics, MD + antiseptic therapy, MD + photodynamic therapy and laser therapy, MD + air polishing, MD + growth factors. The adjuvants did not outperform mechanical debridement. None of the included systematic reviews met all of the AMSTAR 2 criteria. **Conclusions:** The adequate implementation of non-surgical therapy through mechanical debridement, in order to remove the etiological factor that is the biofilm, followed by compliance with oral hygiene instructions by the patient, accompanied by periodic maintenance according to individual risk, it will allow the resolution of peri-implant mucositis without the need for adjuvants, all of this observed and supervised by the professional.

Keywords: Mucositis, dental implants, systematic review.

RESUMEN

Objetivo: Sintetizar la evidencia existente sobre el tratamiento de la mucositis periimplantaria y evaluar la calidad de las revisiones sistemáticas existentes. **Materiales y métodos:** Sólo se incluyeron revisiones sistemáticas con o sin metanálisis que investigaran cualquier resultado del tratamiento de la mucositis periimplantaria en humanos. Se realizaron búsquedas electrónicas en tres bases de datos, hasta enero del 2021. La evaluación de la calidad fue realizada de forma independiente y por duplicado con base en la guía de la herramienta Assessment of Multiple Systematic Reviews (AMSTAR 2). **Resultados:** Se incluyeron 17 estudios para el análisis cualitativo, todos utilizaron un diseño de ensayo clínico aleatorizado, nueve de las revisiones sistemáticas eligieron este diseño de estudio únicamente. Las revisiones sistemáticas seleccionadas evaluaron los siguientes tratamientos para la mucositis periimplantaria: Desbridamiento mecánicos solo (DMS), Desbridamiento mecánico (DM) + probióticos, DM + terapia antiséptica, DM + terapia fotodinámica y terapia con láser, DM + pulido al aire, DM + factores de crecimiento. Los coadyuvantes no superaron en eficacia al desbridamiento mecánico. Ninguna de las revisiones sistemáticas incluidas cumplió con todos los criterios de AMSTAR 2. **Conclusiones*:*** La adecuada implementación de la terapia no quirúrgica mediante el desbridamiento mecánico, para eliminar el factor etiológico que es la placa bacteriana, seguido del cumplimiento de las instrucciones de higiene oral por parte del paciente, acompañado de mantenimientos periódicos según el riesgo individual, permitirá la resolución de la mucositis periimplantaria sin necesidad de coadyuvantes, todo esto observado y supervisado por el operador.

Palabras clave: *mucositis, implantes dentales, revisión sistemática*

I. PREAMBLE:

In the last decades partially and totally edentulous patients have been treated successfully with osseointegrated dental implants[1], which have high survival rates (≥10 years) when supporting different types of dental prostheses[2,3]. As a result of a large part of the population has been rehabilitated with this prosthesis system, therefore prevention, diagnosis and treatment of peri-implant diseases are of great importance to maintain the quality of life of patients through healthy oral conditions[1,4] In a recent systematic review the prevalence of peri-implant mucositis has been reported, and it ranged from 19% to 65%[3]. In consequence, early diagnosis of peri-implant diseases, are extremely important, since for a peri-implantitis to appear, the implant will always have a history of peri-implant mucositis, which if not treated on time, will result in the loss of the implant[4] .

Peri-implant mucositis has been defined as the presence of bleeding and / or suppuration with or without greater depth of probing compared to previous examinations. Furthermore, the absence of bone loss complements the definition of peri-implant mucositis [2, 5]. The main characteristic of peri-implant mucositis is bleeding on soft probing and can be accompanied by swelling, erythema and even suppuration[6].

The presence and accumulation of dental biofilm is of vital importance in the etiology of the inflammatory reaction of peri-implant mucositis, the relationship between this disease and bacterial accumulation has been investigated in the past, and it has been shown that the persistence of this biofilm in a period of approximately 3 weeks will cause inflammation of the peri-implant tissues[6-8]. In relation to the accumulation of biofilm, a current systematic review concluded that

mechanical debridement therapy could be considered the standard treatment of peri-implant mucositis, in relation to the evidence low of adjuvant agents[8].

Actually, different alternatives have been proposed additional to mechanical debridement for the treatment of peri-implant mucositis, which have shown beneficial results, such as such as the use of chlorhexidine, glycine powder, laser, among others[7-9].

The information is extensive and is presented in various systematic reviews with different focus questions and diverse results, however, an overview compiling all evidence from the existing systematic reviews on this topic have not been performed so far.

One of the main components of a SR is the evaluation of its methodological quality. There are several ways of evaluating quality using validated tools, among which is the AMSTAR (a measurement tool to evaluate multiple systematic reviews)[10], which was introduced in 2007 and proved to be reliable and valid, one of its characteristics was evaluating systematic reviews of randomized clinical trials only, however, it received criticism due to some shortcomings related to its domains of evaluation[11].

In 2017, seeking to correct the deficiencies of AMSTAR, an improved version (AMSTAR 2)[12] was developed, which simplify the answers, align the research question with the PICO components, justify why the inclusion of different study designs both randomized and non-randomized, justify the exclusion of studies, determine if a sufficiently detailed assessment of the risk of bias was carried out for included studies and whether risk of bias was considered during statistical combining and interpretation of results. Furthermore, it also differs from AMSTAR

in that it allows a more detailed evaluation and includes non-randomized studies, since the latter are increasingly included in systematic reviews[12]. The AMSTAR 2 tool considered the need to increase the domains to their original ones, seeking to be more thorough in the analysis of systematic reviews. The AMSTAR 2 tool does not provide an overall score for systematic reviews, but it allows, through 7 critical domains, to frame the quality of the studies in 4 levels of confidence: high, moderate, low and critically low[12].

In 2016, the Risk of Bias in Systematic Reviews (ROBIS) tool was published, to provide a complete assessment of the level of bias within the systematic review[13]. This tool is composed of three phases, the first is optional to assess the applicability of the review; the second phase consists of 20 items within four main domains and serves to identify concerns about the conduct of the review; the third phase consists of three questions to generally assess the bias rating[13].

Studies have been carried out comparing AMSTAR 2 and ROBIS[14], which in their results obtained a considerable overlap in the domains of both tools and indicated that ROBIS does not assess whether there is a detailed list of included and excluded studies or whether conflicts of interest were declared both of the primary studies as well as in reviews, this point is essential in terms of methodological quality and could also be potential risks of bias. Regarding applicability, the 3 evaluators found AMSTAR 2 easier and faster to use compared to ROBIS, this may be due to the fact that no systematic or methodological experience is required to complete this tool, which is why AMSTAR is the ideal tool for authors who are starting in the field of research related to systematic reviews[15], they concluded that the choice to use one or the other depends on the purpose of the researchers, that is, to evaluate

the general methodological quality, which is achieved with the AMSTAR 2, or to evaluate the risk of bias only, which is obtained with ROBIS, without neglecting the factor of experience with the instrument or time limitations.

Therefore, the aim of our study is to synthesize the evidence on the treatment of peri-implant mucositis and to evaluate the quality of the existing systematic reviews.

II. OBJECTIVES

General Objective:

To synthesize evidence on the treatment of peri-implant mucositis and to evaluate the quality of the existing systematic reviews.

Specific objectives:

To identify and select information about the treatment of peri-implant mucositis.

To assess the effectiveness of different treatments of peri-implant mucositis.

III. MATERIALS AND METHODS

The design of the present study was an overview of systematic reviews.

Eligibility criteria

Inclusion Criteria:

- Systematic reviews with or without meta-analysis that evaluated any peri-implant mucositis treatment outcome.
- Studies on humans.

Exclusion Criteria:

- Systematic reviews in which outcomes were not directly related to peri-implant mucositis.
- Literature review, consensus reports, interventional studies, observational studies, laboratory research, abstracts, case-reports, protocols, personal opinions, letters, and posters.

Development of a protocol and registration:

This systematic review was registered in the PROSPERO database (International prospective register under number CRD42021210588 and was written in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement[16].

Focused question:

What is the available evidence and the quality of the existing systematic reviews on the treatment of peri-implant mucositis?

Search strategy

The search strategy incorporated both electronic and manual searches. Electronic searches were performed in three databases: The National Library of

Medicine (MEDLINE via PubMed), the Cochrane Database of Systematic Reviews (CDSR), and Web of Science. The search strategy included terms related to the intervention and used the following combinations of key words: (((((peri-implant mucositis) OR (periimplant mucositis)) OR (peri-implant disease)) OR (mucositis [MeSH Terms])) AND (((((((((debridement [MeSH Terms]) OR (antibiotic)) OR (glycine)) OR (probiotics [MeSH Terms])) OR (laser)) OR (Photodynamic therapy)) OR (chlorhexidine)) OR (Periochip)) OR (Air flow))) AND ((((systematic review) OR (review)) OR (meta-analysis)) OR (metaanalysis)). The results were limited to human studies. Also, an electronic screening of grey literature through Literature Report[17] and OpenGrey databases[18] as well as the consulting of references list of included studies were conducted to detect potential eligible titles. The following journals were also screened up to January 2021: Clinical Oral Implants Research, Clinical Implant Dentistry and Related Research, European Journal of Oral Implantology, Implant Dentistry, International Journal of Oral and Maxillofacial Implants, International Journal of Periodontics and Restorative Dentistry, Journal of Clinical Periodontology, Journal of Dental Research, Journal of Oral and Maxillofacial Surgery, Journal of Periodontology. A manual search was also made in the bibliographies of the articles included. Only articles in English were included.

Screening methods and data extraction

It was conducted independently and in triplicate by three reviewers (A.L.P, P.S.V.G and C.R.Z). According to selection criteria, titles and abstracts of search

results were screened using an online software (Rayyan, Qatar Computing Research Institute). Potential articles, or those with insufficient data to make a clear decision, were analyzed in full text for the eligibility criteria. Disagreements are resolved by discussion and consultation with a fourth author (M.A.A). The reasons for exclusion at this or at subsequent stages were recorded. The level of agreement between reviewers against titles eligibility was done using kappa scores (Cohen's κ coefficient) and interpreted according to Landis and Koch scale[19].

The following information are extracted in predefined Excel´s spreadsheets by three authors (A.L.P, P.S.V.G and C.R.Z) and considering: Author, year, objectives/research questions, number of included primary studies, type of studies, intervention/comparison groups, main conclusion and founding sources. The data extraction was ascertained for adequacy by a fourth author (M.A.A), disagreements were solved by consensus.

Quality assessment

The quality assessment was carried out independently and in duplicate by two authors (P.S.V.G and C.R.Z) based on guidance from the Assessment of Multiple Systematic Reviews (AMSTAR 2) tool[12], used to evaluate the methodological quality of the included studies. Both authors underwent a calibration process for the use of the AMSTAR 2 tool, and the level of agreement between reviewers for quality assessment calibration was done using kappa scores (Cohen's κ coefficient) and interpreted according to Landis and Koch scale[19].

The AMSTAR 2 guidelines feature 16 items that were responded on the website (https://amstar.ca/Amstar_Checklist.php) using ‘yes’, ‘partial yes’, ‘no’ or in some cases ‘not applicable’. A final categorization of the systematic reviews was generated to classify them as of high, moderate, low or critically low quality. Finally, the results were ascertained for adequacy by a third author (M.A.A) and disagreements were solved by consensus.

IV. RESULTS

The initial search identified a total of 359 records in both electronic and manual searches. After removal of duplicates and the title and abstract screening, a total of 51 articles remained for full-text assessment (Fig.1). Seventeen studies were finally included for qualitative analysis[20-36]. The reviewers showed an almost perfect level of agreement, both in the calibration for the quality assessment, and also in the eligibility of the included titles (k = 0.91). The most common study design in the search was literature reviews, so they were excluded. The excluded papers and the reasons for exclusion are listed in Table 1.

Study characteristics

The number of the included studies ranged from 3 to 13 articles and all of them used a randomized clinical trial design, thirteen SRs chose this study design only. Within the included reviews, 8 were self-financed, 7 were financed by private institutions, and 2 SRs did not report their funding sources. The main characteristics of the included studies are summarized in Table 2.

Qualitative analysis

The included SRs evaluated the following treatments for peri-implant mucositis: Mechanical debridement alone (MDA) [20-36], Mechanical debridement (MD) + probiotics[21,22,34], MD + antiseptic therapy [20,24,26,28-30,36], MD + photodynamic therapy[25], MD +laser therapy[23,25,31-33], MD + glycine air polishing [27], MD + growth factors[35].

In this overview mechanical debridement alone was the treatment of the control and intervention groups in all SRs included, so this is the standard treatment for peri-implant mucositis. 5 out of 17 studies evaluated chlorhexidine as an adjunct to

mechanical debridement[20,28-30,36], and it was the treatment most found in the included SRs, that concluded that MD with the additional use of chlorhexidine did not improve clinical results compared to MDA. The treatments that include antiseptic therapy[20,24,26,28-30,36] (glycine, systemic antibiotics, triclosan paste) and MD, mentioned that they did not give superior results to mechanical debridement alone, however they influence in the commitment to oral hygiene by the patient.

The SRs that include mechanical debridement together with probiotics[21,22,34] concluded that the use of probiotics such as lactobacillus, added to non-surgical therapy, has limited benefits in the treatment of peri-implant mucositis.

The addition of photodynamic and laser therapy[23,25,29,31-33] to mechanical debridement, found that photodynamic therapy its complementary efficacy to mechanical debridement remains debatable, but 1 study[32] conclude that the use of diode laser, as a coadyuvant in the conventional treatment of peri-implant mucositis, is effectiveness in reducing the clinical signs of inflammation. The SR on mechanical debridement + glycine air polishing[27], resolved that glycine air polishing is as effective as non-surgical mechanical debridement for the treatment of peri-implant mucositis. The most innovative recent treatment we found in the search of this overview, was a systematic review that talk about of the addition of growth factors[30], and it concluded that these growth factors might be associated with better outcomes in terms of pocket depth (PD) and bleeding on probing (BOP). (Table 2)

As mentioned, mechanical debridement is the conventional and selection treatment for peri-implant mucositis, and no adjuvant mentioned above showed superiority in clinical efficacy compared to this treatment.

Quality assessment

None of the SRs included satisfied all the AMSTAR 2 criteria (Table 3). Items 1, 5, 7, 15 and 16 were rated with the highest positive score for all included reviews. Explaining the selection of the study designs for inclusion (item 3) and reporting on the sources of funding for the studies included (item 10) were the items with highest negative score. While almost all the systematic reviews used a satisfactorytechnique to assess the risk of bias of the RCTs (item 9a), when evaluating the non-randomized intervention studies, only two systematic reviews made a correctassessment of the risk of bias for this type of study (item 9b). Only six SRs reportedhaving a priori design.

V. DISCUSSION

The aim of this overview was to synthetize the available evidence and the quality of systematic reviews reporting specific treatments for peri-implant mucositis in humans. In the manuscripts included in this overview, the treatment of first choice has been mechanical debridement as the most reported, and in the search for better clinical results, adjuvants have been implemented such as: chlorhexidine, glycine in air powder, laser, photodynamic therapy, probiotics, local antibiotics, triclosan, growth factors, among others (Table 2). Of all the adjuvants implemented, none of them demonstrated superiority compared to mechanical debridement alone. In assessing the quality of the systematic reviews included in this overview, it demonstrated moderate to low quality according to AMSTAR 2 tool, it is hoped that the application and validation of this tool may encourage future systematic reviews that to use it within their methodology.

The use of chlorhexidine (CHX) either in gel or irrigant as a complement in the treatment of peri-implant mucositis has been evaluated over time, however, it has not been possible to show that it presents significant improvements compared to mechanical debridement alone[36]. The SRs included in this overview found no clinical improvements when using CHX as an adjunct to mechanical debridement. The reduced effectiveness of CHX as a complementary therapy can be explained by behaving differently in terms of its substantivity between tooth and implant surfaces[30]. CHX has been shown to have superior bond to the tooth, but its adhesion to the implant surface will depend on its roughness and the concentration of CHX[32]. There is evidence that CHX can alter the biocompatibility of the implant surface and, therefore, it should not be recommended for disinfection of the implant

surface[37]. There is still a lack of evidence to support the use of chemical agents such as CHX for improvement of clinical parameters[20].

Air polishing devices are safe and efficient in removing bacterial biofilm from tooth surfaces[38]. Glycine powder has been used in the treatment of peri-implant mucositis and has been shown to be less abrasive to the implant surface than sodium bicarbonate and its use has been reported to cause no adverse effects[27]. Air polishing with glycine powder has been successful in moderate and deep periodontal pockets[38]. A clinical trial included in Riben-Grundstrom SR, concluded that air polishing with glycine powder was effective in reducing inflammation, but there were difficulties in achieving complete resolution of the disease in the peri-implant tissues[39].

Lasers in the treatment of peri-implant mucositis have been defended based on their ability to debride soft tissues, bacterial inactivation as in photodynamic therapy and removal of dental stones[40]. Chala et al., in a recent systematic review showed no additional benefit with lasers after 6 months[31]. More randomized controlled trials are required to generate conclusive evidence for the use of laser in peri-implant mucositis[30].

In the treatment of peri-implant mucositis, a type of non-invasive phototherapy has also been implemented to eliminate bacterial colonies from the implant surface and has been called photodynamic therapy[41]. The mechanism of action of photodynamic therapy is through the use of a reduced wavelength laser in combination with photosensitizers, and it is carried out by generating reactive oxygen that causes cytotoxicity and consequently death of bacteria in the peri-implant groove[40]. Albaker et al., determined their results inconclusive due to methodological

heterogeneity of the studies included in that SR[25]. Another systematic review[42] that was not included in the present overview because it took both animal and human studies for its analysis, did not find that the use of photodynamic therapy in combination with mechanical debridement improves clinical outcomes than debridement alone and concluded that its efficacy is debatable, therefore, more studies are needed that can show that its use brings improvements to the treatment of peri-implant mucositis.

Probiotics have been introduced as adjuvants in peri-implant health acting as mediators in the reduction of gingival inflammation[22]. These mediators are live bacteria that are distributed in the host to benefit health, among them are lactobacillus brevis and lactobacillus reuteri that have been studied in peri-implant disease[43,44]. Despite its use as an adjunct in the treatment of peri-implant mucositis, it was reported to have no additional clinical or microbiological benefit1[6, 34]. The probable reason for its no benefit could be explained by insufficient mechanical debridement added to the complex structure of the implants and the morphology of peri-implant defects[45]. And also, it could hide the action of probiotics because it has been reported that probiotics, they have limited action against intact biology[46].

The application of local antimicrobials as an adjunct to mechanical debridement did not result in any additional benefit in the treatment of peri-implant mucositis[47]. In fact, it only provides minimal clinical improvements in pocket depth and bleeding on probing reduction[48]. The combination with other complementary antiseptic therapies is always present when placing local antibiotics and even in those cases the benefits are limited and it does not exceed the mechanical debridment administered by the professional[23,24].

Triclosan, is a biphenolic and non-cationic active agent, incorporated in toothpastes, for control gingivitis around natural teeth[49]. has also been studied around dental implants, showing that its use reduces clinical signs of inflammation in previously established mucositis and also favored peri-implant maintenance by reducing dental plaque and bleeding[50]. Despite these clinical improvements, only one systematic review included in this overview concluded that the use of 0.3% triclosan toothpaste was effective as an adjunct to mechanical debridement[28], so more studies are needed to reinforce its efficacy in the treatment of peri-implant mucositis.

Growth factors have emerged as an innovative therapy in the treatment of peri-implant mucositis[35]. Growth factors have long been used in regenerative dentistry, and these include enamel-derived matrix (EMD) and platelet derivatives[51]. The purpose of growth factors is to stimulate adjacent cells promoting proliferation and differentiation, resulting in regeneration[52]. Amelogenins, which are a group of proteins that compose EMD and perhaps the most important, have shown important clinical results in the treatment of periodontal and peri-implant diseases[53]. Despite the efficacy of EMD in the treatment of periodontal diseases, studies related to its use in peri-implant diseases are limited[54]. Khouly et al., suggested that the addition of EMD could improve the outcome of the treatment of peri-implant mucositis in terms of PD and BOP at 3 months of follow-up, however, the treatment had a limited effect[35].

Actually, there is no evidence from a summary of systematic reviews on the treatment of peri-implant mucositis, which analyzes the quality of the scientific evidence and also that could indicate a unified result on the treatments that are implemented as adjuvants in the non-surgical setting of peri-implant mucositis

therapy. This overview identified that the standard treatment for peri-implant mucositis is MD and that the other adjuvants were not shown to be superior (Table 2). These findings are similar to the recent meta-analysis by Barrotchi et al[8].

The second aim of this overview of systematic reviews was to assess the quality of systematic reviews reporting specific treatments for peri-implant mucositis, in humans. In relation to this, the quality of most of the systematic reviews included in this summary was moderate to low (Table 3). Among the parameters of the AMSTAR 2 that did not meet the items were: the decision to include study designs, duplicate data extraction, funding sources for the included studies, consideration of the risk of bias of the studies, and interpretation or discussion of individual studies from each review[12]. Unlike those that obtained the best scores, which were: the inclusion of PICO components, the use of a satisfactory technique to assess the risk of bias, and information on sources of financing and conflicts of interest[12]. In this context, the studies that didn't comply with the items mentioned above, obtained this rating due to this limitation[12].

Nine studies were rated low confidence level[20,21,23,24,26,29,33,34,36], of these, 8 failed in the domain of interpretation and discussion of risk of bias and 1 in the appropriate statistical combination methods. Four studies obtained moderate confidence level[22,30,32,35], all of these failed in the domain of types of included study designs, three in the domain of funding sources of included studies, two in duplicate data extraction and one in the selection of studies in duplicate. Four studies were rated critically low[25,27,28,31], three studies failed in the domains of excluded studies and interpretation and discussion of bias, one failed in the search strategy and another in the analysis of publication bias. We must emphasize that the AMSTAR2 tool

allows the exhaustive evaluation of the risk of bias included through domain 9, which indicates the great importance of this tool, because it motivates the search for biases, also using the tools recommended by the Cochrane collaboration for both RCTs as for CCTs, so although the vast majority of the primary studies were RCTs, a small but important number of studies were CCTs, which does not cause any concern since the aforementioned domain of AMSTAR2 allowed to investigate and determine individual risks of potential bias present regardless of the primary study design included in the assessed systematic reviews. Taking these data, we must emphasize that the high standards established by AMSTAR2 make future reviews to raise their methodological quality, not only based on the use of the PRISMA statement, but also guided by quality assessment tools such as the one used in the present overview. The AMSTAR2 tool has been published for some years, but even so there are low-quality systematic reviews, which leads us to the need to recommend to scientific journals that for admission and publication, tools of methodological quality should be used so that they are potentiated for future research. Now it is also true that, although many reviews may be classified as low quality, this does not necessarily mean that the included studies are also of low quality and at that point it is essential to evaluate the methodological rigor of assessing the risks of bias, for which the AMSTAR2 assesses this very important point in its critical domain of evaluation of risk of bias for both RCTs and EINAS. Having specified all of the above, it is expected that awareness of the use of this methodological quality tool will comprehensively raise the preparation and writing of future systematic reviews so that the risks of bias decrease.

Regarding the risk of bias, fifteen systematic reviews used the Cochrane risk of bias

assessment tool for RCTs, one[28] used the tool of the Center for Evidence-based Medicine at the University of Oxford and the Jadad scale, and another review[31] used the GRADE scale to assess the risk of bias to evaluate the included primary studies. Of the 15 systematic SRs included in this overview that used the Cochrane risk of bias assessment tool for RCTs, 4 SRs had high risk of bias, 5 SRs had low risk of bias, and 6 SRs had unclear risk of bias. The key domains that were at low risk of bias were: Sequence randomization, selective reporting, incomplete outcome data. Key domains that were at high risk of bias were: Blinding of participants and staff, blinding of outcome assessment. Regarding the studies that did not use the Cochrane assessment tool, Ata-Ali et al., included only RCTs, of which 4 were of high quality and 3 of low quality, while Chala et al., included high quality studies with a score of 4 to 5 according to the GRADE scale. In relation to this, we can mention that most of the systematic reviews included used appropriate risk of bias assessment tools recommended by the Cochrane collaboration, which shows the high degree of concern for investigating possible biases and minimizing systematic mistakes, this also allows us to analyze that despite the fact that the asses of the methodological quality of the included systematic reviews is not the one desired by the researchers, the primary studies do have a high degree of validity and a moderate to low risk of bias, due to which the results and conclusions of these studies are reliable in such a way that they can and should be taken into account to be applied in the clinical practice, in order of improving the health of patients when seeking to treat peri-implant mucositis.

As this is the first overview of systematic reviews on the treatment of peri-implant mucositis that also evaluates quality, it is not possible to argue with a similar review,

however, if it is possible to discuss the implementation of AMSTAR2 with other reviews. In this sense, it was possible to observe that the implementation of AMSTAR2 reveals the deficit of methodological quality of many reviews and that also the discussion of the impact of quality in the overviews is not carried out properly as it should, so that the reader can interpret it correctly[55], Taylor et al., found that, of 52 included studies, 92.3% of the systematic reviews and meta-analyzes had a low or critically low confidence level, and called for the implementation of AMSTAR2 to improve the quality standards of systematic reviews and also from the included primary studies. An overview that evaluated bruxism and chronic pain, included 9 studies and all of them were RCTs, however, they obtained a varied level of confidence that ranged from critically low to high, but only 2 of the 9 studies were of high quality[56]. Another study that evaluated the quality of studies of the impact of implant rehabilitation in patients with bisphosphonate therapy, found that, of the 7 systematic reviews included, none obtained the highest score in the evaluation of quality and the mean between the domains positive out of between 5 and 14 of the 16[57]. All this indicates the need to apply the evaluation of the methodological quality through the use of the AMSTAR2 tool.

Finally, based on the results, we must indicate that the adequate implementation of non-surgical therapy through mechanical debridement, in order to remove the etiological factor that is the biofilm, followed by compliance with oral hygiene instructions by the patient, accompanied by periodic maintenance according to individual risk, it will allow the resolution of peri-implant mucositis without the need for adjuvants, all of this observed and supervised by the professional.

Within the limitations of the present study, it is possible to list: 1) Studies only in English, which could have led to the non-detection of some manuscripts in other languages, which could have increased the number of elements included and the enrichment of the study; 2) Definitions of peri-implant mucositis would be very heterogeneous; the ideal would have been to have homogeneous definitions for all the interventions included in the reviews; 3) Lack of use of high methodological standards in the preparation of the systematic reviews included.

VI. CONCLUSIONS

Regarding the treatments of peri-implant mucositis, it can be concluded that the adjuvants of the non-surgical therapy showed limited benefit.

Peri-implant mucositis can be successfully treated by non-surgical mechanical debridement, in addition to proper oral hygiene instruction by the professional, and its compliance by the patient.

Regarding the evaluation of the quality of the systematic reviews included in this study, it was determined that the quality was moderate to low, and it is expected that the application of the AMSTAR 2 tool will improve the preparation and updating of future SRs.

It should be noted that, to the knowledge of the authors, this is the first review of the treatment of peri-implant mucositis, which assesses the quality of the available evidence.

VII. REFERENCES

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VIII. Tables, grafics and figures

Table 1: Excluded articles with reasons

Authors (Year)	Title	Reason for exclusion
Lang NP. et al. (1997)	Clinical trials on therapies for peri-implant infections.	Literature review
Heitz-Mayfield LA. et al. (2004)	Antimicrobial treatment of peri-implant diseases.	Literature review
Heitz-Mayfield LA. et al. (2008)	Diagnosis and management of peri-implant diseases.	Literature review
López-Cerero L. et al. (2008)	Dental implant-related infections.	Literature review
Sánchez-Espinel JA. et al. (2009)	[Bone-integration and bone-biomimicry of dental implants: role of peri-implant infections].	Literature review
Bumgardner JD. et al. (2011)	Emerging antibacterial biomaterial strategies for the prevention of peri-implant inflammatory diseases.	Literature review
Romanos GE. et al. (2012)	Therapy of peri-implant diseases. Where is the evidence?	Literature review
Esposito M. et al. (2012)	Interventions for replacing missing teeth: management of soft tissues for dental implants	Soft tissue augmentation
Murray CM. et al. (2013)	Peri-implant disease: current understanding and future direction.	Literature review
Figuero E. et al. (2014)	Management of peri-implant mucositis and peri-implantitis.	Literature review
Hsu YT. et al. (2014)	Biological implant complications and their management.	Literature review
Pedrazzi V. et al. (2014)	Antimicrobial mouthrinse use as an adjunct method in peri-implant biofilm control	Literature review
Valderrama P. et al. (2014)	Detoxification of Implant Surfaces Affected by Peri-Implant Disease: An Overview of Non-surgical Methods.	Literature review
Vohra F. et al. (2014)	Efficacy of mechanical debridement with adjunct antimicrobial photodynamic therapy for the management of peri-implant diseases: a systematic review	Periimplantitis
Romanos GE. et al. (2015)	Peri-implant diseases: a review of treatment interventions.	Literature review
Renvert S. et al. (2015)	Clinical approaches to treat peri-implant mucositis and peri-implantitis	Literature review
Al Habashneh R. et al. (2015)	Photodynamic therapy in periodontal and peri-implant diseases	Literature review
Sculean A. et al. (2015)	Is Photodynamic Therapy an Effective Treatment for Periodontal and Peri-Implant Infections?	Literature review
Faggion CM. et al. (2015)	Laser therapy as an adjunct treatment for peri-implant mucositis and peri-implantitis provides no extra benefit for most clinical outcomes	Literature review
Khammissa RAG. et al. (2015)	Peri-implant mucositis and peri-implantitis: clinical and histopathological characteristics and treatment.	Literature review
Renvert S. et al. (2015)	Treatment modalities for peri-implant mucositis and peri-implantitis	Literature review
Neuschl M. et al. (2015)	Therapeutic options in the treatment of peri-implant diseases	Literature review
Wang YL. et al. (2016)	Health, Maintenance, and Recovery of Soft Tissues around Implants	Literature review
Alshehri FA. et al. (2016)	The role of lasers in the treatment of peri-implant diseases: A review	Literature review
Pokrowiecki R. et al. (2017)	Oral microbiome and peri-implant diseases: where are we now?	Literature review
Sinjab K. et al. (2018)	Decision Making for Management of Periimplant Diseases.	Literature review
Sivaramakrishnan G. et al. (2018)	Photodynamic therapy for the treatment of peri-implant diseases: A network meta-analysis of randomized controlled trials	Periimplantitis
Lin GH. et al. (2018)	Laser therapy for treatment of peri-implant mucositis and peri-implantitis: An American Academy of Periodontology best evidence review.	Periimplantitis
Lang NP. et al. (2019)	Nonsurgical therapy for teeth and implants-When and why?	Literature review
Novaes Junior AB. et al. (2019)	New strategies and developments for peri-implant disease.	Literature review
Checchi V. et al. (2019)	Role of Dental Implant Homecare in Mucositis and Peri-implantitis Prevention: A Literature Overview	Literature review
Kelekis-Cholakis A. et al. (2019)	Maintenance of Implant Patients: A Narrative Review	Literature review
Lin CY. et al. (2019)	The effect of supportive care in preventing peri-implant diseases and implant loss: A systematic review and meta-analysis	Maintenance and incidence
Farsai PS. et al. (2020)	Supportive therapy (spt) can potentially improve implant survival rate (sr), peri-implantitis, and peri-implant mucositis	Literature review

Table 2: Characteristics of the included systematic reviews

Table 2. Characteristics of the included systematic reviews

Author (Year)	Objectives or research question	Intervention (Exposure)	Comparisson	No. of Studies Included	Type of Studies Included	Main conclusion	Funding source
Barootchi S. *et al.* (2020)	In patients with peri-implant mucositis, what is the effect of non-surgical therapy alone, compared with adjuvants such as chlorhexidine, polishing with glycine, probiotics and photodynamic therapy, for the treatment of peri-implant mucositis?	MDA	MD + chlorhexidine	13	RCT	Conventional nonsurgical MDA may be considered the standard treatment for peri-implant mucositis as there is still a lack of evidence supporting the use of additional chemical/mechanical agents for clinical and/or microbiological improvement	University of Michigan Periodontal Graduate Student Research Fund.
Gao JX. *et al.* (2020)	Does Lactobacillus provide an additional effect to the nonsurgical treatment of patients with periimplant diseases, including peri-implant mucositis and peri-implantitis?	MD + probiotic	MDA	3	RCT	Lactobacillus in conjunction with nonsurgical treatment have limited benefits to the management of peri-implant mucositis and compared with placebo.	National Natural Science Foundation of China and the Fundamental Research Funds for the Central Universities.
Albaker AM. *et al.* (2019)	To evaluate the effect of probiotics compared with conventional intervention/placebo in patients with peri-implant diseases on peri-implant inflammatory parameters.	MD + probiotics	MDA	5	RCT	The efficacy of probiotics in the treatment of peri-implant diseases remains debatable.	Self-supported.
Albaker AM. *et al.* (2018)	Is photodynamic therapy and laser therapy effective in the management of peri-implant mucositis?	MD + photodinamic and laser therapy	MDA	5	RCT, CS	Inconclusive findings were found to show the effect of photodynamic therapy or laser therapy.	Deanship of Scientific Research at King Saud University.
Suárez-López Del Amo F. *et al.* (2016)	In patient suffering from peri-implant mucositis or peri-implantitis, what is the effectiveness of non-surgical therapy by means of different techniques and/or approaches for clinical and radiographically resolution of disease, including bleeding on probing (BOP), probing pocket depth (PPD), and radiographic bone (RB) level changes?	MD + antiseptic/antibiotic theraphy	MDA	4	RCT, Cohort, Prospective	Professional-performed MD is effective in reducing inflammation and pocket depths.	University of Michigan Periodontal Graduate Student Research Fund.
Ata-Ali J. *et al.* (2015)	To determine the most effective treatment for periimplant mucositis in patients with dental implants compared with a control group.	MDA	MD + chlorhexidine	7	RCT	Chlorhexidine, azithromycin through the systemic route, and glycine powder air polishhing are not effective for the treatment of periimplant mucositis over the long term. The only effective treatment identified was the use of toothpaste with 0.3% triclosan.	Not reported.
Schwarz F. *et al.* (2015)	In patients with peri-implant mucositis and peri-implantitis, what is the efficacy of non-surgical (that is, referring to peri-implant mucositis and peri-implantitis) and surgical (that is, referring to peri-implantitis) treatments with alternative or adjuvant measures about the changing signs? of inflammation compared to conventional surgical and non-surgical treatments alone?	MD + antiseptic/antibiotic theraphy	MDA	8	RCT, CCT	Oral hygiene instructions + MDA was found to be effective for the management of peri-implant mucositis.	Geistlich Biomaterials, Osteology Foundation and EMS.
Schwarz F. *et al.* (2015)	In patients with peri-implant mucositis, what is the efficacy of professionally administered plaque removal with adjunctive measures on changing signs of inflammation compared with professionally administered plaque remova alone?	MD + antiseptic/antibiotic theraphy	MDA	7	RCT	Adjunctive antiseptic, antibiotic or mechanical therapy may not improve the efficacy of professionally administered plaque removal.	Self-supported.
Schwarz F. *et al.* (2015)	In patients suffering from peri-implant diseases, what is the efficacy of air polishing on changing signs of inflammation compared with control treatments?	MD + Glycine powder	MDA	3	RCT, CCT	Glycine powder air polishing is as effective as the control treatments at mucositis sites.	Self-supported.

RCT, randomized controlled trial ; CCT, clinical controlled trial; CS, case series; MD, mechanical debridment; MDA, mechanical debridment alone.

Table 2: Characteristics of the included systematic reviews (continued)

Grusovin MG. *et al.* (2010)	To assess the effects of different interventions for maintaining and recovering soft tissue health around osseointegrated dental implants.	MDA	MD + chlorhexidine	8	RCT	There was not any reliable evidence for which are the most effective therapy for recovering soft tissue health.	University of Manchester, UK.
Liu S. *et al.* (2020)	Does local application of CHX improve outcomes in patients undergoing non-surgic¬al treatment of peri-implant mucositis or peri-implantitis?	MDA	MD + chlorhexidine	4	RCT	Adjunctive therapy with chlorhexidine may not improve outcomes with non-surgical management of periimplant mucositis.	Not reported.
Chala M. *et al.* (2020)	To compare the effectiveness of the adjunctive use of lasers for the treatment of peri-implant mucositis or peri-implantitis compared to the conventional treatment	MDA	MD + laser therapy	2	RCT	The adjunctive use of lasers in the treatment of peri-implant inflammation does not offer any additional benefit compared to conventional treatment after six months.	Self-supported.
Sanchez-Martos R. *et al.* (2020)	Is the diode laser therapy effective reducing the signs of inflammation as an adjunctive element in the non-surgical treatment of peri-implant mucositis?.	MDA	MD + laser therapy	8	RCT	The use of diode laser, as a coadyuvant in the non-surgical conventional treatment of peri-implant mucositis, is effectiveness in reducing the clinical signs of inflammation.	Self-supported.
Saneja R. *et al.* (2020)	What is the role of laser as a primary or as an adjunctive treatment modality in comparison with the one treated with only conventional surgical or nonsurgical treatment protocols in reducing PD and increasing clinical attachment level in patients having peri-implant diseases?	MDA	MD + laser therapy	2	RCT	Laser treatment did not show any specific advantage as a treatment approach over conventional methods.	Self-supported.
Pires Silva A. *et al.* (2020)	What is the clinical effect of the use of probiotics as an adjuvant therapy on the non-surgical treatment of peri-implant diseases, when compared to mechanical therapy and the use of other chemical agents, for the reduction of bleeding at probing and depth of probing?	MDA	MD + probiotics	4	RCT	There is currently insufficient evidence to demonstrate the benefits of the use of probiotics as an adjunctive therapy in patients with peri-implant diseases	Self-supported.
Khouly I. *et al.* (2020)	Is there any difference for the use of growth factors for surgical or non-surgical treatment of peri-implant diseases, in terms of changes on bleeding on probing, pocket depth and bone level, evaluated before and after treatment, versus comparative growth factor treatment or no growth factors, in human subjects?	MDA	MD + growth factors	2	RCT	The addition of growth factors for the treatment of peri-implant mucositis might be associated with better outcomes.	Self-supported.
Zhao P. *et al.* (2020)	In patients with peri-implant mucositis, what is the the efficacy of clorhexidine as an adjunctive therapy to mechanical debridement, versus mechanical debridement alone?	MDA	MD + chlorhexidine	5	RCT	MD with additional use of chlorhexidine did not enhance the clinical results when compared to MDA.	National Natural Science Foundation of China, The International Cooperation Project of Chengdu Municipal Science and Technology Bureau and the International Scientific Cooperation and Exchanges Project of Sichuan Province.

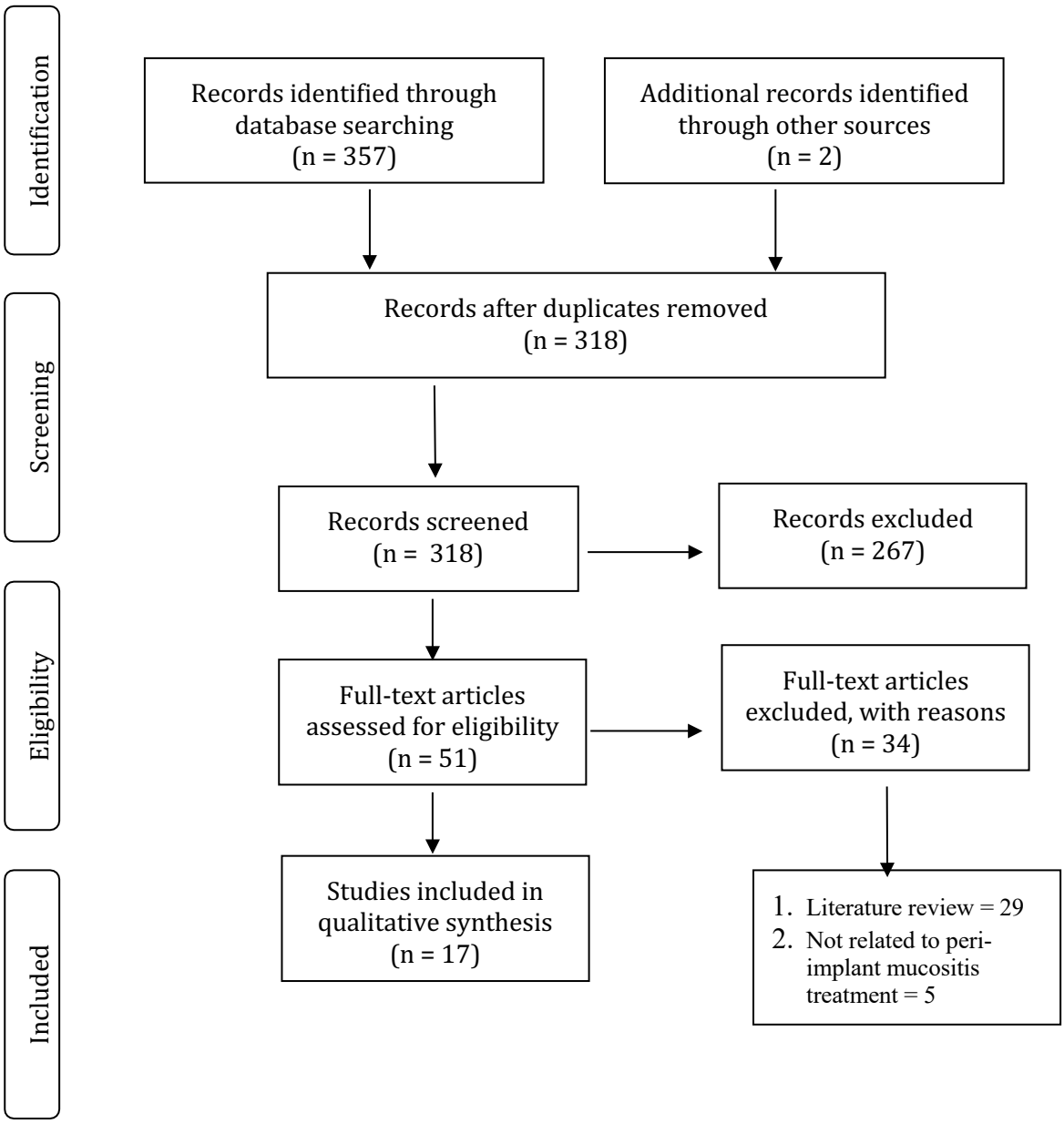
RCT, randomized controlled trial ; CCT, clinical controlled trial; CS, case series; MD, mechanical debridment; MDA, mechanical debridment alone.

Table 3: AMSTAR 2 Quality Assesment

N	Author (Year)	AMSTAR 2 Items																Score	Overall
		1	2	3	4	5	6	7	8	9a	9b	10	11	12	13	14	15	16	
1	Barootchi S. *et al.* (2020)	Y	Y	Y	P/Y	Y	Y	Y	P/Y	Y	N/A	N	Y	N	N	Y	Y	Y	11	Low
2	Gao JX. *et al.* (2020)	Y	Y	N	P/Y	Y	Y	Y	P/Y	Y	N/A	N	N	Y	Y	Y	Y	Y	11	Low
3	Albaker AM. *et al.* (2019)	Y	P/Y	N	P/Y	Y	N	N	P/Y	Y	N	N	N/A	N/A	N	Y	N/A	Y	5	Critically low
4	Albaker AM. *et al.* (2019)	Y	Y	N	P/Y	N	N	Y	Y	Y	N/A	Y	Y	Y	Y	Y	Y	Y	12	Moderate
5	Suárez-López Del Amo F. *et al.* (2016)	Y	Y	N	P/Y	Y	Y	Y	P/Y	Y	P/Y	N	N/A	N/A	N	N	N/A	Y	7	Low
6	Ata-Ali J. *et al.* (2015)	N	P/Y	N	N	Y	N	N	P/Y	Y	N/A	N	N/A	N/A	Y	Y	N/A	Y	5	Critically low
7	Schwarz F. *et al.* (2015)	Y	P/Y	N	P/Y	Y	Y	Y	P/Y	Y	N	N	Y	N	N	N	N	Y	7	Critically low
8	Schwarz F. *et al.* (2015)	Y	P/Y	N	P/Y	Y	N	Y	P/Y	Y	N	N	Y	Y	N	Y	Y	Y	9	Low
9	Schwarz F. *et al.* (2015)	Y	P/Y	N	P/Y	Y	N	Y	P/Y	Y	N/A	N	Y	Y	N	Y	Y	Y	9	Low
10	Grusovin MG. *et al.* (2010)	Y	Y	Y	P/Y	Y	Y	Y	P/Y	Y	Y	N	N/A	N/A	N	N	N/A	Y	9	Low
11	Liu S. *et al.* (2020)	Y	Y	N	P/Y	Y	Y	Y	P/Y	Y	N/A	N	Y	Y	Y	Y	Y	Y	12	Moderate
12	Chala M. *et al.* (2020)	Y	Y	N	P/Y	N	N	N	P/Y	P/Y	N/A	N	N/A	N/A	N	Y	N/A	Y	4	Critically low
13	Sanchez-Martos R. *et al.* (2020)	Y	Y	N	P/Y	Y	N	Y	P/Y	Y	N/A	N	Y	Y	Y	Y	Y	Y	11	Moderate
14	Seneja R. *et al.* (2020)	Y	Y	Y	P/Y	Y	Y	Y	P/Y	Y	N/A	N	Y	Y	N	Y	Y	Y	12	Low
15	Pires Silva A. *et al.* (2020)	Y	Y	N	P/Y	Y	Y	Y	P/Y	Y	N/A	N	N/A	N/A	N	Y	N/A	Y	8	Low
16	Khouly I. *et al.* (2020)	Y	Y	N	P/Y	Y	Y	Y	P/Y	Y	N/A	N	Y	Y	Y	Y	Y	Y	12	Moderate
17	Zhao P. *et al.* (2020)	Y	P/Y	N	P/Y	Y	Y	Y	P/Y	Y	N/A	N	Y	Y	N	Y	Y	Y	10	Low

* Y, yes; N, no; P/Y, partial yes; N/A, not applicable.

Figure # 1.


Identification
Screening
Eligibility
Included
Records identified through database searching (n = 357)
Additional records identified through other sources (n = 2)
Records after duplicates removed (n = 318)
Records screened (n = 318)
Records excluded (n = 267)
Full-text articles assessed for eligibility (n = 51)
Full-text articles excluded, with reasons (n = 34)
Studies included in qualitative synthesis (n = 17)
1. Literature review = 29
2. Not related to peri-implant mucositis treatment = 5