Non-Surgical Therapy for Peri-Implant Diseases: a Systematic Review

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ABSTRACT

Objectives: The purpose of this paper was to systematically evaluate the effectiveness of non-surgical therapy for the treatment of peri-implant diseases including both, mucositis and peri-implantitis lesions.

Material and Methods: An electronic search in two different databases was performed including MEDLINE (PubMed) and EMBASE from 2011 to 2016. Human studies reporting non-surgical treatment of peri-implant mucositis and peri-implantitis with more than 10 implants and at least 6 months follow up published in English language were evaluated. A systematic review was performed to evaluate the effectiveness of the different methods of decontamination employed in the included investigations. Risk of bias assessment was elaborated for included investigations.

Results: Twenty-five articles were identified of which 14 were further evaluated and included in the analysis. Due to significant heterogeneity in between included studies, a meta-analysis could not be performed. Instead, a systematic descriptive review was performed. Included investigations reported the used of different methods for implant decontamination, including self-performed cleaning techniques, and professionally delivered treatment such as laser, photodynamic therapy, supra-/sub-mucosal mechanical debridement, and air-abrasive devices. Follow-up periods ranged from 6 to 60 months.

Conclusions: Non-surgical treatment for peri-implant mucositis seems to be effective while modest and not-predictable outcomes are expected for peri-implantitis lesions. Limitations include different peri-implant diseases definitions, treatment approaches, as well as different implant designs/surfaces and defect characteristics.

Keywords: antibiotic prophylaxis; dental scaling; local anti-infective agents; peri-implantitis.

Accepted for publication: 7 September 2016

To cite this article:

Suárez-López del Amo F, Yu SH, Wang HL.

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J Oral Maxillofac Res 2016;7(3):e13

URL: http://www.ejomr.org/JOMR/archives/2016/3/e13/v7n3e13.pdf

doi: 10.5037/jomr.2016.7313

INTRODUCTION

During the last decades the definition of periimplantitis has suffered several modifications with the development in the understanding of dental implantology and its biological implications. Recently, as described by the American Academy of Periodontology [1] mucositis is defined as an inflammatory process around a dental implant without loss of supporting bone beyond biological bone remodelling. On the other hand, periimplantitis is characterized by both, inflammation of the surrounding peri-implant tissues and loss of supporting bone beyond initial biological bone remodelling. Nonetheless recent investigations have recognized at least 7 definitions of peri-implantitis based on the extension and severity of the bone loss [2]. These interpretations of the peri-implant disease certainly reflect the multifactorial nature of the entity, displaying a multitude of clinical presentations. Hence, it is reasonable to assume that further definitions will appear in upcoming years as we continue performing research in the field. Nonetheless, the complex mechanisms that influence initial bone remodelling, among other variables, will certainly ensure this to be a challenging duty.

With regard to the treatment of the peri-implant diseases, a variety of different approaches have been proposed including but not limited to: non-surgical therapy; surgical management by means of access flap debridement, lasers disinfection, implantoplasty, resective procedures, as well as regenerative approaches [3]. While most of the available evidence agrees on the effectiveness of non-surgical therapy for mucositis lesions [4], conflicting results are found when trying to identify the most effective protocol for peri-implantitis [3,5]. In this sense, a recent systematic review evaluating the effectiveness of periimplantitis treatment has shown that reconstructive procedures do not result in more optimal outcomes when compared to non-reconstructive procedures [5]. This result is in concordance with the majority of the literature available with regard to peri-implantitis treatment which presents with great variability in terms of treatment outcomes. These inconsistencies can be attributed to a variety of different factors, including but not limited to: different aetiologies and contributing factors affecting dental implants, morphology of the defects, case description/selection, implant positioning, and the influence of different implant surfaces.

Non-surgical therapy for peri-implant diseases has traditionally been considered effective for mucositis.

However, results for peri-implantitis lesions were found not to be effective [4]. Surprisingly, newer studies have challenged again this hypothesis achieving exceptional results after non-surgical decontamination of peri-implantitis lesions [6].

Due to the increasing prevalence of both peri-implant mucositis and peri-implantitis, there is an urgent need to understand its aetiology and the multiples variables affecting it development and progression leading to the generation of more predictable treatment approached. Hence, the aim of the present review was to systematically evaluate the effectiveness of current (last 5 years) methodologies for the non-surgical treatment of peri-implant diseases.

MATERIAL AND METHODS Protocol and registration

The methods as well as inclusion/exclusion criteria employed for the present review were determined in advance. This protocol was registered in an international prospective register of systematic reviews 'PROSPERO' with the following registration number: CRD42016037631. The current systematic review was performed by two independent reviewers following the PRISMA guidelines for identification, screening, eligibility, and inclusion [7].

Focus question

The following focus question was developed according to the population, intervention, comparison, and outcome (PICO) study design: 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.

Information sources

The search strategy consisted in the examination of several databases as well as manual screening. The electronic search was performed in several databases, including MEDLINE (PubMed), and EMBASE databases for articles from 2011 up to April 2016 with limitation to English language. Additionally, a manual search of periodontics/implantology-related journals, including "Clinical Oral Implant Research", "Journal of Clinical Periodontology", "Journal of Periodontology", "Clinical Implant Dentistry and Related Research",

and "The International Journal of Periodontics & Restorative Dentistry", from 2011 up to April 2016 was also performed to ensure a thorough screening process. Furthermore, references of all articles reviewed in full text were further screened.

Search

Both PubMed and EMBASE databases were screened through advances searchers. For the PubMed library, combinations of controlled terms (MeSH and EMTREE) and keywords were used whenever possible. Into the addition, other terms not indexed as MeSH and filters were applied. As such, the key terms used were: ((((((((("non-surgical")) OR "dental prophylaxis" [MeSH Terms]) OR "dental scaling" [MeSH Terms]) OR "scaling, subgingival" [MeSH Terms]) OR "dental polishing" [MeSH Terms]) OR "diode lasers" [MeSH Terms]) OR "yag laser, erbium" [MeSH Terms]) OR "antibiotic prophylaxis" [MeSH Terms]) OR "agents, local anti infective" [MeSH Terms]) AND "periimplantitis" [MeSH Terms]) OR "peri-implant mucositis") OR "peri-implant maintenance") OR "implant infection") OR "peri-implant infection" AND ("last 5 years" [PDat] AND "Humans" [Mesh]). On the other hand, for EMBASE for following terms were employed: "non-surgical" OR "scaling" OR "laser/exp" OR "laser" OR "subgingival curettage/exp" OR "subgingival curettage" AND ("periimplantitis/exp" OR "'periimplantitis") OR "peri-implant mucositis".

Selection of studies

Titles and abstracts derived from the search were independently screened by two reviewers (FSLA and SHY) based on the inclusion criteria. Both reviewers compared decisions and their eligibility for this review was confirmed after discussion. Full articles were obtained for all the investigations deemed eligible for inclusion in this paper and further evaluated by both reviewers. If needed, a third party was consulted when consensus could not be reached.

Types of publications

The present review included only human studies published in the English language. Letters, editorials, reviews and meta-analysis, PhD thesis, as well as abstracts were not evaluated.

Types of studies

The present investigation included cases series,

prospective, as well randomized controlled trials (RCTs) published between 2011 and April of 2016 that reported on non-surgical treatment for perimplant mucositis and peri-implantitis. Case report, retrospective, as well as studies with less than 10 implants or less than 6 months follow up were excluded.

Types of participants/population

Individuals included in the studies should have had at least one osseointegrated screw-type dental implant that presented with signs of peri-implant mucositis or peri-implantitis and received non-surgical treatment. Nonetheless, included investigations presented with different definitions for the diseases evaluated.

Inclusion and exclusion criteria

Articles were included in this systematic review if they met the following inclusion criteria:

- Investigated non-surgical treatment outcomes for peri-implant mucositis and peri-implantitis in patients with at least one osseointegrated solid screw-type implant;
- All human prospective studies, as well as clinical trials, cohort studies, case-control, and case series studies:
- At least 10 implants;
- At least 6 months follow-up;
- Clinical and/or radiographic changes reported.
 Treatment outcomes reporting changes in PPDs and/or BOP and/or RB changes.

On the contrary, the following articles were excluded:

- Care reports, retrospective investigations, *in vitro* and animal studies;
- Less than 10 implants;
- Less than 6 months of follow-up;
- Surgical treatment for peri-implantitis;
- Human trials with missing information or unclear data.

Sequential search strategy

Initial literature search was conducted in several databases including MEDLINE (PubMed) and EMBASE from 2011 to 2016. All articles titles were screened in order to eliminate non-qualifying studies. Next, screening of abstract was performed followed by elimination of non-qualifying investigations. Finally, full text evaluation of each article was performed in order to confirm the eligibility based on the inclusion and exclusion criteria.

References of full text evaluated investigations were also performed. In addition, a manual search in periodontics/implantology-related journals, including "Clinical Oral Implant Research", "Journal of Dental Research", "Journal of Clinical Periodontology", "Journal of Periodontology", "Clinical Implant Dentistry and Related Research", and "The International Journal of Periodontics & Restorative Dentistry", from 2011 up to 2016, was also performed to ensure a thorough screening process.

Data extraction

Data were extracted from the included studies independently by two reviewers (FSLA and ESHY). If any disagreement occurred, a third reviewer was consulted (HLW).

Assessment of methodological quality

The quality of all selected RCTs was assessed using The Cochrane Collaboration's tool for assessing risk of bias in randomised trials [8]. Parameters evaluated included:

- Random sequence generation;
- Allocation concealment;
- Blinding of participants and personnel;
- Blinding of outcome assessment;
- Incomplete outcome data;
- Selective reporting;
- · Other bias.

The potential risk of bias was categorized as "low", "unclear" or "high" depending on the quality and detailed explanation of provided information about all abovementioned parameters. All assessments were completed by a single examiner (SHY). The Newcastle-Ottawa Scale (NOS) was used to evaluate the methodological quality of nonrandomized included studies [9]. The topics evaluated were selection of study groups, comparability of patients, and outcome. Each included study received a maximum of 10.

Data analyses

Significant heterogeneity between publications in terms of diseases definitions, study designs, patient and defect related characteristics, as well as measured outcomes, among others, prevented the quantitative synthesis of the included studies and consequently a meta-analysis could not be completed. Instead, a qualitative descriptive analysis of the reported outcomes was performed and systematically reviewed in forms of tables.

RESULTS Study selection

Initial screening of electronic databases yielded a total of 2837 articles. Additionally, 21 more articles were found through manual screening. After removal of duplicated studies, a total of 2625 titles and abstract were evaluated. Overall, a total of 26 potentially relevant articles were selected after an evaluation of their titles and abstracts. Full text of these articles was obtained and thoroughly evaluated. Of these, 14 studies fulfilled the inclusion criteria and were subsequently included in the systematic review (Figure 1 and Tables 1 - 2).

Excluded studies

The reasons for exclusion are summarized in Table 3. Four articles presented with short follow up with less than 6 months [10-13], two articles were retrospective in design [6,14], one investigation was a review study [15], three articles employed the same study population than other included investigations in the present analysis [16-18], and 1 investigation presented with unclear and incomplete data [19].

Study characteristics

The characteristics of the 14 included articles are summarized in Tables 1 and 2. The publications include several study types: 9 randomized controlled trials (RCTs) with parallel designs [20-28], 1 single-armed cohort study [29], 4 non-controlled prospective studies and case series [30-33]. The follow-up periods of the studies ranged from 6 to 60 months. There were several different definitions regarding peri-implant mucositis and peri-implantitis, being the definitions for peri-implantitis more variable than those of mucositis. In the Deppe et al. [32] study, they classified peri-implantitis into moderate and severe groups based on the severity of the bone loss.

Most articles reported the subject numbers as well as the implants evaluated in the studies, however 3 articles failed to report the numbers of the implants that were evaluated in the studies [23,24,27] while 1 article only presented the mean number of implants for each patient [28].

Regarding the description of the diseased sites, most studies provided information on PPD and BOP of the affected implants, however, 2 articles did not present PPD for the implants affected by mucositis [30,33]. Eleven articles reported RB loss [20-28,32,33]. Some articles reported on

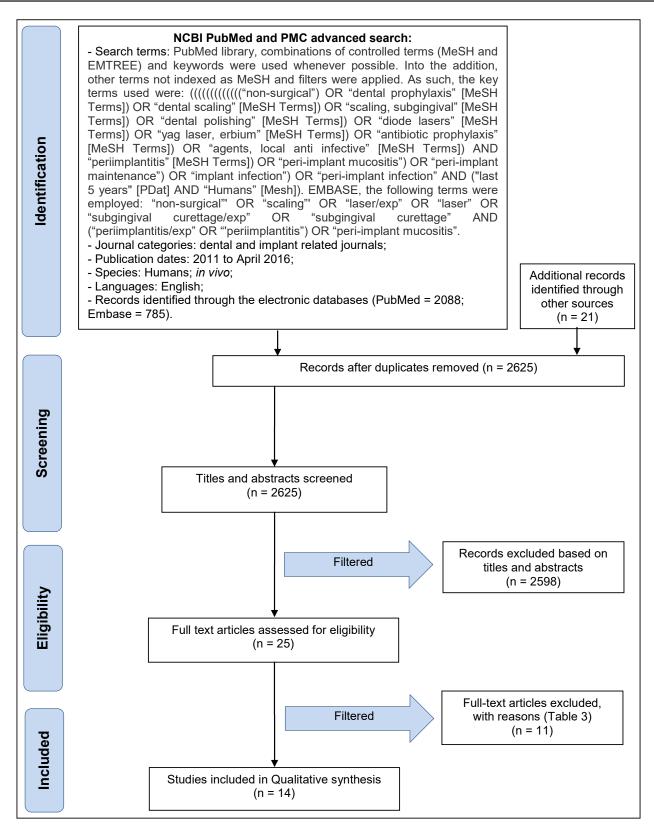


Figure 1. PRISMA flowchart of the screening process in the different databases.

the implant characteristics including the systems and the surface materials, implant functioning time and the prosthetic design [20-24,27-29,31,33]. One study particularly excluded implants with titanium plasma sprayed or hydroxyapatite coated implants [25]. Five articles performed microbial test [20,21,23,26,28].

Some articles reported the locations (i.e. maxilla or mandible; anterior or posterior) of the implants evaluated in the studies, however, none of the articles presented the bucco-lingual position of the implants and no articles reported the possible aetiology and/or contributory factors of peri-implant mucositis or peri-implantitis.

Table 1A. Characteristics of the included articles

				Tr	eatment provided					Diagnosis			Treatn	nent outco	omes				
Study	Year of publication	Type of study	Groups	Self- Professionally- performed delivered			N patients	N implants	Follow- up (months)	Mucositis/ peri- implantitis	PDs reduction Mean (SD), mm	Radiographic MBL changes Mean (SD), mm	BOP changes Mean (SD), mm		PI or MPI (SD) changes	CAL Mean (SD), mm	Recession Mean (SD), mm	Microbiological results	Conclusions
			Control	ОНІ	MD	MD		24			4.38 (0.42) to 4.17 (0.41)	2.35 (0.56) to 2.63 (0.53)	100 to 100%	NA	91.7 to 41.7%	NA	NA		
Arisan et al. [20]	2015	RCT	Test	ОНІ	MD + diode lass (energy density time: 1 rr power density: 40 energy: 1. spot diameter	y: 3 J/cm ² ; nin; 00 mW/cm ² ; .5 J;	5	24	6	Peri-implantitis	4.71 (0.67) to 4.54 (0.74)	2.13 (0.47) to 2.79 (0.48)	100 to 95.8%	NA	91.7 to 54.2%	NA	NA	No changes in microbiota after 1 month	Laser does not provide any additional benefit when compared to SRP alone.
Bassetti	2014	RCT	Control	Instructions in the use of	MD + Airpolishing + 3% hydrogen peroxide irrigation + Arestin		20	20	12		4.39 (0.77) to 3.83 (0.85)	NA	Sites: 4.41 (1.47) to 1.55 (1.26) (65% reduction)	NA	0.21 (0.27) to 0 (0)	2.72 (0.72) to 2.41 (0.7)	1.68 (1.04) to 1.41 (1.18)	P. gingivalis, T. forsythia, T. denticola, C. rectus, F. nucleatum and E. corrodens demonstrated statistically significant decrease from baseline.	Similar results clinically and microbiologically for both.
et al. [21]	2014	RCI	Test	superfloss	MD + Airpolish (660 nm, power den + 3% hydrogen irrigatio	nsity 100 mW) peroxide	20	20	12	Peri-implantitis	4.19 (0.55) to 4.08 (0.81)	NA	Sites: 4.03 (1.66) to 1.74 (1.37) (57% reduction)	NA	0.13 (0.21) to 0.01 (0.04)	2.66 (0.73) to 2.58 (0.94)	1.53 (0.91) to 1.5 (0.86)	No statistically significant difference with the exception for <i>F. nucleatum</i> .	Complete disease resolution not routinely achieved.
Esposito	posito	RCT	Control	In surgery group: CHX mouthwash 0.12% for 1 min twice a day for 2	Bone loss between 3 - 5 mm: implant surface DE bone loss > 5 mm: surgery, full-	No adjunct treatment	40	100	100	Peri-implantitis	6.45 (2.15) to 5.5 (1.94)	4.9 (2.07) to 5.03 (2.51)	Bleeding scores: 2.68 (1.25) to 1.28 (1.11)	NA	Mean plaque scores: 2.15 (1.64) to 0.93 (0.94)	NA	NA	NA	Adjunctive use of LAD therapy with mechanical debridement did not improve any clinical
et al. [22]		All gourps: gentle wiping with a soft DE, LAD	40	101		Peri-impiantitis	6.23 (1.62) to 5.14 (1.83)	4.5 (1.75) to 4.5 (1.67)	Bleeding scores: 2.95 (1.32) to 1.35 (1.32)	NA	Mean plaque scores: 2.18 (1.53) to 0.89 (0.94)	NA	NA	NA	outcomes when compared to mechanical cleaning alone up to 1 year after treatment.				
Hallstrom	Hallstrom	D.C.T.	Control T	ОНІ	MD with titanium curettes + polishing		21	NA			4.6 (0.9) to 4.1 (1.2)	NA	Full mouth BOP %: 24.2 (16.7) to 18.4 (17.4)	NA	Mean PI at implant %: 22 (29.2) to 17.9 (28.4)	NA	NA	No significant differences in bacterial count. Statistical analysis by intent to treat failed to	No short-term differences between groups. The clinical improvements observed at 6 months may be attributed to
et al. [23]	2012	RCT		OHI	MD with titaniu + polishing - (Azithromycin® 5 and 250 mg days	+ ABX 600 mg day 1	22	NA	- 6	Mucositis	4.4 (1) to 3.5 (1.1)	NA	Full mouth BOP %: 28.2 (20.6) to 10.1 (6.9)	NA	Mean PI at implant %: 33.7 (35.5) to 6.8 (13.8)	NA	NA	identify within group differences comparing baseline data with all other time points.	improvements in oral hygiene.

ABX = antibiotics treatment; BOP = bleeding on probing; CAL = clinical attachment level; CHX = chlorhexidine digluconate; DE = debridement; LAD = light-activated disinfection; LD = local delivery; MBL = marginal bone level; MD = mechanical debridement; MPI = modified plaque index; NA = not available; OHI = oral hygiene instructions; PD = probing depth; PDT = photodynamic therapy; PI = plaque index; PR = prospective study; RB = radiographic bone; RCT = randomized controlled trials; SD = standard deviation.

Table 1B. Characteristics of the included articles

				Treatment provided					Diagnosis	Treatment outcomes									
Study	Year of publication	Type of study	Groups	Self- performed	Professionally- delivered	N patients	N implants	Follow- up (months)	Mucositis/ peri- implantitis	PDs reduction Mean (SD), mm Radiographic MBL changes Mean (SD), mm		BOP changes Mean (SD), mm	Exudate changes	PI or MPI (SD) changes	CAL Mean (SD), mm	Recession Mean (SD) mm	Microbiological results	Conclusions	
			AAD	OHI on 2 to 4 appointments	Submucosal AAD employed with amino acid glycine powder (Air- Flow® Perio Powder, EMS)	12	18		Peri- implantitis	3.7 (1) to 3.2 (1.1)	NA	99 (4.1) to 57.8 (30.7)%	NA	1.2 (1.1) to 1.8 (1.1)	5.2 (1.9) to 4.6 (1.8)	1.5 (1.4) to 1.4 (1.3)	NA	Both treatments resulted in comparable but limited CAL gains	
John et al. [24]	2015	RCT	MD (carbon curettes + local antiseptic therapy)	OHI on 2 to 4 appointments	MD was performed using carbon curets followed by pocket irrigation with a 0.1 % CHX solution and submucosal application of 1 % CHX gel	13	18	12		3.9 (1.1) to 3.5 (1.2)	NA	94.7 (13.7) to 78.1 (30)%	NA	1.2 (1) to 0.9 (0.7)	5 (1.5) to 4.5 (1.3)	1 (1.1) to 0.9 (1.1)	NA	at 12 months. AAD was associated with significantly higher BOP decrease than MDA.	
Machtei et	2012	Double-	Control	OHI patients were given sodium fluoride toothpaste	Surface MD+ biodegradable crosslinked gelatin matrix chip (placebo)	30	37		Peri-	7.21 to 5.48	NA	100 to 42.5%	NA	NA	7.63 (0.3) to 5.94 (0.3)	NA	NA	Substantial reduction in PD, gain in	
al. [25]	2012	blind RCT	Test	OHI patients were given sodium fluoride toothpaste	Surface MD+ matrix containing 2.5 mg CHX chips	30	40	6	implantitis	7.60 to 5.47	NA	100 to 59%	NA	NA	7.88 (0.2) to 5.7 (0.3)	NA	NA	CAL and reduction in BOP in sites with peri-implantitis.	
Persson et	2011	D.C.T.	Er:YAG laser	OHI and patients received a sonic toothbrush	(Er:YAG) laser: 100 mJ/ pulse and 10 Hz (12.7 J/ cm²)	21	55		Peri-	PD reductions: 0.9 (0.8)	Statistical analyses failed to demonstrate differences in bone-level changes between baseline and 6 months	Statistical analyses also failed to demonstrate differences in the BOP at 6 weeks after treatment	NA	NA	NA	NA	Both treatments failed to reduce bacterial counts at 6 months. <i>Porphyromona</i> .	reduced in the air-abrasive group,	
al. [26]	2011	RCT	AAD subgingival polishing	OHI patients received a sonic toothbrush	AAD subgingival polishing for 15 sec in each position	21	45	6	implantitis	PD reductions: 0.8 (0.5)	Statistical analyses failed to demonstrate differences in bone-level changes between baseline and 6 months	Statistical analyses also failed to demonstrate differences in the BOP at 6 weeks after treatment	NA	NA	NA	NA	gingivalis counts were higher in cases with progressive peri- implantitis	month data demonstrated that both methods failed to reduce bacterial counts. Clinical improvements were limited.	
Riben-			Glycine powder air- polishing group	ОНІ	Glycine powder air- polishing was performed at baseline, 3 and 6 months. Supragingival DE was provided at month 9 and 12.	18	NA			NA	NA	43.9 (7.3) to 12.1 (3.8)	No differences were found	Implant 25.5 (6.8) to 5.6 (3.8)	NA	No differences were found	NA	Non-surgical treatment with a glycine powder air-polishing or ultrasonic device is effective in reducing inflammation and number of peri-implant pockets subject to patient compliance	
Grundstrom et al. [27]	2015	RCT	Ultrasonic group	ОНІ	Cleaning with ultrasonic was performed at baseline, 3 and 7 months. Supragingival MD was provided at month 9 and 12.	18	NA	12	Mucositis	NA	NA	53.7 (7.9) to 18.6 (6.4)	No differences were found	Implant 24.1 (6.6) to 7.4 (6.4)	NA	No differences were found	NA		
Swierkot et al. [28]	2013	RCT	Sonic toothbrush group	Brush 2 min twice daily with toothpaste, brush their teeth with sonic tooth brush according to the manufacturer's instructions	1	35	35 Mean count: 4.19		No peri- implantitis, 22% mucositis	3.4 (0.88) to 3.4 (0.8)	NA	0.22 (0.3) to 0.27 (0.26)	NA	to	4.64 (1.63) to 5.1 (1.78)	to	After 12 months, both groups exhibited a small increase in total bacterial load at implants and teeth <i>P gingivalis</i> , <i>P micra</i> and <i>D. pneumosintes</i> were		
[=0]			Manual toothbrush group		NA	36	Mean count: 4.32		No peri- implantitis, 19% mucositis	3.13 (0.75) to 3.13 (0.78)	NA	0.19 (0.28) to 0.28 (0.38)	NA	to	4.41 (1.65) to 4.43 (1.28)	to	consistently detected at nearly every examination time for implant and teeth groups.	a period of 12 months at implants	

AAD = air-abrasive device; BOP = bleeding on probing; CAL = clinical attachment level; CHX = chlorhexidine digluconate; DE = debridement; LD = local delivery; MBL = marginal bone level; MD = mechanical debridement; MPI = modified plaque index; NA = not available; OHI = oral hygiene instructions; PD = probing depth; PI = plaque index; RB = radiographic bone; RCT = randomized controlled trials; SD = standard deviation.

Table 1C. Characteristics of the included articles

				Treatmen				Diagnosis	Treatment outcomes										
Study	Year of publication	Type of study	Groups	Self- performed	Professionally- delivered	N patients		Follow-up (months)	Mucositis/ peri- implantitis	PDs reduction Mean (SD), mm	Radiographic MBL changes Mean (SD), mm	BOP changes Mean (SD), mm	Exudate changes	\ /	CAL Mean (SD), mm	Recession Mean (SD), mm	Microbiological results	Conclusions	
Gomes et al. [29]	2015	Single-arm cohort	Test	Multi-tufted TB, dental floss and/or interdental TB. Non-therapeutic fluoride toothpaste	Weekly supragingival/ supramucosal MD for 1 month, then every 3 months	14	59	13	Mucositis	3.62 (0.31) to 2.55 (0.16)	NA	Sites: 54.05 (5.88) to 4.96 (1.78)%	NA	18.98 (5.89) to 2.7 (1.47)% /390 days	NA	NA	NA	The supragingival-supramucosal biofilm control benefited both teeth and implants	
Corbella	2011	Non-controlled	Mucositis	CHX 0.2% mouthwash twice a day for 10 days, interdental brushes	Powered and manual devices MD	61	244	60	Mucositis	2.2 (0.87)	to NA I 2.46 (0.5)	Sites: Index 0: 88.2 to 100% Index 1: 1.4 to 0%;	NA	Sites/6 and 58 months Index 0: 58.3% to 88.5%; Index 1: 2.8 to 7.3%; Index 2: 9.7 to 1%; Index 3: 29.2 to 3.2%	, NA	NA	NA	Systematic hygienic protocol is effective in keeping low the incidence of peri-implant mucositis as well as in	
et al. [30]	2011	prospective study	Peri- implantitis	CHX 0.2% mouthwash, interdental brushes	Powered and manual devices + LD of CHX 1% + Sx MD		2		Peri-implantiti	2.46 (0.5)		Index 2: 10.4 to 0%; Index 3: 0 to 0%.						controlling plaque accumulation and clinical attachment loss.	
Costa et	2012	Prospective	Control	No	No	41	41 183 60	60	Mucositis	16.7% sites with PD ≥ 5 mm	41.5% implants show BL	Sites: 50.2 to 62.6%	NA	1.6 (0.6) to 1.9 (0.5)	% sites > 3 mm CAL 14.9 (16.7) to 22.7 (23.2)	NA	NA	The absence of preventive maintenance in individuals with pre-existing peri-implant mucositis was associated with a high incidence of peri-implantitis.	
al. [31]	2012	study	Test	ОНІ	At least 5 SC, coronal prophylaxis	39	157	00		5.9% sites with PD≥5 mm	17.9% implants show BL	Sites: 41.7 to 33.3%	NA	1.4 (0.6) to 1.4 (0.7)	% sites > 3 mm CAL 15.9 (19) to 20.1 (23)	NA	NA		
Deppe et	2012	Prospective	Moderate bone loss	OHI, plaque control	Calculus removal	16	10			3.3 (0.8) to 2.9 (0.5)	3.9 (0.8) to 3.6 (0.8) mm	Sulcus bleeding index: 1.8 (1.3) to 1.1 (0.9)	NA	NA	3.8 (1.3) to 3.6 (0.7)	0.5 (0.5) to 0.7 (0.4)	NA	Non-surgical PDT could stop bone resorption in moderate peri-implant defects but not in severe defects. marginal tissue recession was not significantly different in both groups.	
al. [32]	2013	study	Severe bone lost	with use of CHX solution (0.3%)	+ antimicrobial PDT	16	8	6	Peri-implantitis	5.8 (0.8) to 6.5 (0.9)	6.8 (0.8) to 8.7 (0.7)	Sulcus bleeding index: 1.5 (1.2) to 1.3 (1.1)	NA	NA	6.7 (0.9) to 8.1 (0.9)	0.9 (1.2) to 1.6 (1.2)	NA		
			MD + local antiseptic (MD + CHX)	ОНІ	Supragingival calculus removal and supramucosal/gingival professional implant/ tooth cleaning + MD + CHX	17	24		Mucositis	3.4 (0.5) to 3.3 (0.5)	NA	46.3 (23.5) to 8.3 (10.4)%	NA	0.7 (0.6) to 0.4 (0.5)	NA	NA	NA	Non-surgical treatment of either peri- implant mucositis using MD + CHX or peri-implantitis using laser therapy	
Schwarz et al. [33]	2015	Prospective case series	Er:YAG laser therapy	ОНІ	Supragingival calculus removal and supramucosal/ gingival professional implant/ tooth cleaning + laser tx	17	21	6	Peri-implantitis	5.5 (0.5) to 4.5 (0.7)	NA	45 (18.5) to 14.2 (11.6)%	NA	0.6 (0.3) to 0.1 (0.1)	NA	NA	NA	at zirconia implants was associated with significant short-term clinical improvements. A complete disease resolution, however, was not achieved in the majority of the patients.	

ABX = antibiotics treatment; BOP = bleeding on probing; CAL = clinical attachment level; CHX = chlorhexidine digluconate; LD = local delivery; MBL = marginal bone level; MD = mechanical debridement; MPI = modified plaque index; NA = not available; PD = probing depth; PDT = photodynamic therapy; PI = plaque index; RB = radiographic bone; SD = standard deviation; Sx = surgery; TB = tooth brush.

Table 2. Characteristics of the included articles: description of affected sites, implant characteristics, prosthetic factors)

			D	escription	of affected sites			1	mplant characteris	stics		Prost	hetic factors			
Study	Groups	PDs, mm	RB loss (SD), mm	ВОР	Exudate	CAL (SD), mm	Recession (SD), mm	Systems	Time in function	Surface	Screwed/ cemented	Internal/ external	Splinted/ non splinted	Restoration type	Additional info	
Arisan et al. [20]	Control	4 to 6	< 3 mm MBL	Yes	Yes And/or suppuration Yes And/or suppuration		NA	Multiple	19.4 months	Rough (acid etching and sand blasting)	Cemented	NA	NA	Fixed metal-ceramic	Supportunisting removed for measurements	
Affsan et al. [20]	Test	4 to 6	< 3 mm MBL	Yes			NA	Withtiple	19.4 months	Rough (acid etching and sand blasting)	Cemented	NA	NA	prostheses	Suprastructures removed for measurements	
Bassetti et al. [21]	Control: LDD Test: PDT	4 to 6	0.5 to 2 0.5 to 2	Yes	NA	2.72 (0.72) 2.66 (0.73)		- Straumann tissue level	7.2 (2.6 - 15) years 7.3 (4 - 14.8) years	⊢ SLA ∣	Screwed	NA	NA	NA	NA	
Esposito et al. [22]	Control	6.45	Mean 4.73 (2.11)	Yes	Pus exudation and/or soft tissue swelling	NA	NA	NA	6.13 years	- NA	NA	NA	NA	NA	In some of the Sx treated cases, unsupported threads were removed and polished based on	
	Test	Deepest pocket only: 6.23	Mean 4.4 (1.58)		and/or soft tissue redness				5.65 years						the clinician's decision	
Hallstrom et al.	Control	- ≥4	< 2mm bone loss	Yes	And/or	NA	NA	Multiple	10.9 years	- NA	Cemented: 52.6%; Screwed: 47.4%	- NA	NA	NA	NA	
[23]	Test		2 Zililii Oolic 1033	103	suppuration	IVA	NA	Манирге	10 years	IVA	Cemented: 59.1%; Screwed: 40.9%	IVA	IVA	IVA	IVA	
	AAD				Yes	5.2 (1.9)	1.5 (1.4)	-					Single tooth	NA		
John et al. [24]	MD (carbon curettes + local antiseptic therapy)	≥ 4	Loss of supporting bone ≤ 30%	Yes		5 (1.5)	1 (1.1)	Multiple	NA	Machined surface, microrough surface	Screwed	NA	and bridgework restorations		Without overhangings or margins	
Machtei et al. [25]	Control Test	6 to 10	≥ 2	Yes	NA	7.63 (0.3) 7.88 (0.2)	NA	NA	NA	Exclude Titanium Plasma- sprayed or hydroxylapatite coated implants	NA	NA	NA	NA	NA	
	Er:YAG laser	≥ 5				7.00 (0.2)				Machined surfaces					Superstructures were removed to enhance	
Persson et al. [26]	AAD subgingival polishing	≥ 6	≥ 2	Yes	And/or suppuration	NA	NA	NA	NA	and medium-rough surfaces	NA	NA	NA	NA	assessments of PD and BOP and to improve the ability to collect bacterial samples.	
Riben-Grundstrom et al. [27]	Glycine powder air-polishing Ultrasonic debridement	≥ 4	≤2	Yes	And/or suppuration	NA	NA	Multiple	NA	NA	NA	NA	NA	NA	NA	
Swierkot et al. [28]	Sonic toothbrush group Manual toothbrush	≥5	<1	Yes/ no	NA	4.64	1.24	Nobel Replace Straight Groovy	At least 12 months	Rough	Screwed	NA	NA	Single implant or fixed prosthesis	NA	
	group	≥ 0				4.41	1.28		At least 13 months							
Gomes et al. [29]	Test Mucositis	2.23 (0.09) NA	NA	Yes	NA	NA	NA	Nobel Biocare NA	5.7 (2.5) years	NA	NA	NA	NA	NA	NA NA	
Corbella et al. [30]	Peri-implantitis	>4	NA	Bleeding index ≥ 2	NA	NA	NA	IVA	NA	NA	NA	NA	NA	Immediately loaded full- arch rehabilitation	NA	
Costa et al. [31]	Control Test	> 5	No	Yes	Yes	NA	NA	Multiple	80.5 months 77.4 months	NA	NA	NA	NA	Single crowns and/ or fixed partial prosthetic	NA	
Deppe et al. [32]	Moderate bone loss	< 5	3.9 (0.8)	Yes	NA	3.8 (1.3)	0.5 (0.5)	- NA	NA	NA	NA	NA	NA	NA	All restorations were left in situ	
	Severe bone lost	5 to 8	6.8 (0.8)	ics	IVA	6.7 (0.9)	0.9 (1.2)	IVA	IVA		INA	IVA	IVA	IVA	All restorations were left in situ	
Schwarz et al. [33]	MD + local antiseptic (MD + CHX)	NA	No	- Yes	No	- NA	NA	Zirconia implants (ZV4, Zircon Vision	NA	Modified (roughness: Ra = approx. 7 μm/ Rz = approx. 41 μm)	Screwed	NA	NA	NA	NA	
	Er:YAG laser therapy	≥ 6	Changes in RB level		And/or suppuration		NA	GmbH, Wolfratshausen, Germany)		Modified (roughness: Ra = approx. 7 μm/ Rz = approx. 42 μm)					INA	

AAD = air-abrasive device; BOP = bleeding on probing; CAL = clinical attachment level; CHX = chlorhexidine digluconate; LD = local delivery; MBL = marginal bone level; MD = mechanical debridement; NA = not available; PD = probing depth; PDT = photodynamic therapy; RB = radiographic bone; SD = standard deviation; SLA = sandblasted and acid-etched implant.

Year of Study Reasons for exclusion publication Mettraux et al. [6] 2015 Retrospective study Heitz-Mayfield et al. [10] 2011 Short follow-up Ji et al. [11] 2014 Short follow-up McKenna et al. [12] Short follow-up 2013 2013 Short follow-up Mussano et al. [13] Lerario et al. [14] 2016 Retrospective study Parma-Benfenati et al. [15] 2013 Review Renvert et al. [16] 2011 Same sample as Persson et al. [26] Sahm et al. [17] 2011 Same sample as John et al. [24] Schär et al. [18] 2013 Same sample as Bassetti et al. [21] Unclear and incomplete data Sreenivasan et al. [19] 2011

Table 3. Excluded articles with reasons for exclusion

Treatment interventions of individual studies

Most of the studies included oral hygiene instructions of using interdental brushes or other required techniques indicated in the protocol before initiating different treatment modalities [20,21,23-27,31-33]. One study reported self-performed cleaning techniques including certain toothpaste and toothbrush [28]. One article presented the model of systemic administration of antimicrobial agent [23] while Bassetti et al. [21] in 2014 reported the effect of locally delivered antibiotics adjunct to scaling and root planning (SRP) and air-polishing; and another article evaluated the effect of chlorhexidine chip (Perio® chip) in treating peri-implantitis [25]. Of importance to mention is that Bassetti and colleagues [21] repeated the treatment in BOP positive sites after 3, 6, 9, and 12 months. Other professional-performed interventions that were presented in the articles include laser, photodynamic therapy, supra-/submucosal mechanical debridement, and air-abrasive devices. Four articles reported the use of lasers in conjunction to SRP [20,22,26,33]. Lasers employed were diode laser [20], Er:YAG laser [26,33] and lightactivated disinfection treatment (FotoSan). Three other articles reported on photodynamic therapy [21,22,32].

Treatment outcomes

PPD was reported as direct or the percentage change except one article [27]. Majority of studies demonstrated that the change of PPD are within 1 mm. Bleeding index or the percentage of BOP also decreases after different treatment modalities in most of the studies. Regarding the laser studies, 3 studies showed that there were no additional positive effect beyond the traditional mechanical debridement and

had limited influence in treating peri-implantitis [20,22,26] while other one article presented significant clinical improvement [21]. Regarding self-performed hygiene techniques, most of the studies demonstrated that with the application of hygiene protocol, it is effective to improve clinical parameters and also keeping the low incidence of developing peri-implant mucositis [28]. For professional-performed mechanical debridement, studies in general demonstrated effectiveness in reducing inflammation and PPD [24,27,30-32].

Assessment of methodological quality

The results of risk of bias assessment for included RCTs were summarized in Table 4. In addition, 6 studies were non-RCT and qualitative assessments were analysed with NOS. The mean NOS score for the evaluated studies was 6 ± 1 .

DISCUSSION

Dental implants have become the gold standard when aiming at reconstruction of the missing dentition. Decades of investigation have proven dental implants to be reliable alternative providing function and aesthetics with long-term success. However, with the increasing number of fixtures being installed yearly, there has also been a significant increase in the number of patients suffering from peri-implant diseases. According to a recent systematic review peri-implant mucositis and peri-implantitis have a prevalence ranging from 19 to 65% and from 1 to 47%, respectively. On the other hand, mean prevalence for peri-implant mucosistis and peri-implantitis are 43% and 22%, respectively [34]. Consequently, treatment of peri-implant diseases

Table 4. Risk of bias assessment of the included studies

Study	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias
Arisan et al. [20]	+	-	-	?	+	+	?
Bassetti et al. [21]	+	-	-	+	+	+	?
Esposito et al. [22]	+	-	-	+	+	+	+
Hallström et al. [23]	+	+	-	-	+	+	+
John et al. [24]	+	-	-	+	+	-	?
Machtei et al. [25]	+	+	+	+	+	+	?
Persson et al. [26]	+	-	-	?	+	+	?
Riben-Grundstrom et al. [27]	+	+	-	+	+	-	?
Swierkot et al. [28]	+	-	-	+	+	+	+

^{+ =} low risk; ? = unclear risk; - = high risk.

has become one of the main focus of the investigations in periodontology. During the last decades, this inflammatory condition has witnessed a tremendous advance in terms of understanding of its aetiology as well as the surgical management. As an example, studies focusing on the different aspects of this disease have been multiplied by more than 100 times during the last two decades.

While initially thought as a periodontitis like lesion surrounding a dental implant, peri-implantitis has recently been related to multiple other variables. In fact, there are a great variety of factors that have been related with marginal bone loss (MBL) and/or periimplantitis that often differ with the ones associated with periodontitis. To name a few: surgical trauma, infection, plaque and poor oral hygiene, alcohol and tobacco consumption, as well as biological bone remodelling [35-38]. Moreover, the possible existence of an imbalance between the implant fixture and the surrounding bone has recently been proposed as a possible etiological factor. Although solely based on narrative reviews [39], the hypothesis of a foreign body reaction as another causative agent for MBL has also been proposed $[\underline{40}]$. In addition, the influence of the different implant surfaces and the presence of titanium particles embedded into the surrounding periimplant tissues have been recently investigated.

Regardless of the aetiology of the peri-implant diseases, multiple investigations are being conducted trying to elucidate the most effective treatment approach. However, while the determination of the most effective treatment seems a challenging duty and over the years conflicting results have been shown, the importance of prevention for prompt intervention seems to be in agreement by researchers. Today, the prevention as well as early detection of peri-implant mucositis remains as key components in successful

dental implantology. These statements are supported by the effectiveness in treatment of mucositis while treatment of peri-implantitis remains unpredictable. Consequently, current evidence shows that peri-implant mucositis can be successfully treated by non-surgical therapy. Locally delivered antibiotics, lasers, mechanical sub- and supra- gingival SRP, as well as air-polishing, among others can be used for the non-surgical treatment of peri-implant mucositis. In addition, repeated treatment of diseased sites seems to be effective.

Substantial improvements are to be made in research regarding treatment of peri-implantitis and peri-implant mucositis. It is of paramount importance the identification of both local and systemic factors affecting the incidence and severity of such conditions for the proper management. Now a day, most of the investigations have failed to provide proper documentation with regard to implant system and position, which have been demonstrated to be significant contributing factors influencing the clinical outcome of different treatment modalities. Moreover, depending on the presence and severity of these local and systemic factors, in many instances, the treatment of choice should be explanation of the fixture.

Limitations

Within the limitation of the present investigations, the major drawback is the multitude of different definitions regarding peri-implant mucositis and peri-implantitis that were employed in the included investigations. Also, multiple different treatment approaches, different implant designs as well as surface characteristics, and wide variation in terms of follow-up periods may have played a role in the treatment outcomes.

CONCLUSIONS

Multitude of different treatment approaches is available for the non-surgical treatment of perimplant diseases. While significant variations exist in term of treatment outcomes, the non-surgical treatment seems to effective for peri-implant mucositis. Self-performed hygiene techniques are effective improving clinical parameters and maintaining a low incidence of developing perimplant mucositis. Professional-performed mechanical

debridement is effective in reducing inflammation and pocket depths.

ACKNOWLEDGMENTS AND DISCLOSURE STATEMENTS

The authors do not have any financial interests, either directly or indirectly, in the products or information listed in the paper. This paper was partially supported by the University of Michigan Periodontal Graduate Student Research Fund.

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To cite this article:

Suárez-López del Amo F, Yu SH, Wang HL.

Non-Surgical Therapy for Peri-Implant Diseases: a Systematic Review

J Oral Maxillofac Res 2016;7(3):e13

URL: http://www.ejomr.org/JOMR/archives/2016/3/e13/v7n3e13.pdf

doi: 10.5037/jomr.2016.7313

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