Systematic review

Biomarker Expression 0f Peri-Implantitis Lesions Before and After Treatment: A Systematic Review.

Supplemental Table S2. Details of secondary outcomes of the included studies in the systematic review. *A.a: Aggregatibacter actinomycetemcomitans*, AB: Antibiotic, ALKP: Alkaline Phosphatase, AZM: Azithromycin, BI: Bleeding index, BOP: Bleeding on Probing, CAL: Clinical Attachment Loss, CCL- 5: Chemokine ligand- 5, CHX: Chlorhexidine, CRP: C- Reactive Protein, ELISA: enzyme-linked immunoassay, EMD: Enamel Matrix Derivative, F: Female, *F.n Fusobacterium nucleatum*, GI: Gingival index, GM-CSF: Granulocyte Macrophage Colony-Stimulating Factor, IFN-g: Interferon- gamma, IL-1b: Interleukin-1beta, LILT: Low Intensity Laser Treatment, LDD: Local Drug Delivery, M: Male, MBL: Marginal Bone Loss, MC: Minocycline Hydrochloride, MCP-1 : Monocyte Chemotactic Protein-1, MIP: Macrophage Inflammatory Protein , MMP: Matrix Metallo Proteinase , MPO: Myeloperoxidase, MW: Mouthwash, n: number, NR: Not Reported, NSPT: Non-surgical periodontal treatment, NSSD (No statistically significant differences p>0.05), OC: Osteocalcin, OFD: Open Flap Debridement, OPG: Osteoprotegerin, OPN: Osteopontin, PCR: Polymerase Chain reaction, PDT: Photo Dynamic Therapy, PDGF: Platelet Derived Growth factor, *P.g: Porphyromonas gingivalis*, PI: Plaque Index, PICF: Peri Implant Crevicular Fluid, PIM: peri-Implant Mucositis, PIP :Peri- implantitis, PIH: Peri-implant Health, RANK: Receptor Activator of Nuclear factor Kappa-B, RANKL: Receptor Activator of Nuclear factor Kappa-B Ligand, RBL: Radiographic Bone Loss, rCAL: relative Clinical Attachment Loss, RCT: Randomised Clinical Trial, REC: Recession, SSD (Statistically significantly p<0.05), SUP: Suppuration, *T.d: Treponema denticola, T.f.: Tanerella forsythia*, Ti: titanium, TNF: Tumour Necrosis Factor, PPD: Probing Pocket Depth, TGF: Tissue Growth Factor, VEGF: Vascular Endothelial Growth Factor.

Investigator, year	Study group	Time point	PPD (mm) (Mean ± SD)	CAL (mm) (Mean ± SD)	Recession (mm) (Mean ± SD)	RBL (mm) (Mean ± SD)	BOP (%) (Mean ± SD)	SUP (%) (Mean ± SD)	Plaque index (%) (Mean ± SD)	Microbiome	PICF volume	Others*
Bassetti et al., 2014	LDD (Control)	Baseline	4.39 ± 0.77	2.72 ± 0.72	1.68 ± 1.04	-	4.41 ± 1.47	-	0.21 ± 0.27	Except for *C. rectus* at baseline (P < 0.01), the counts in submucosal biofilm were not SSD between test and control groups at any time point. *P.g* and *T.f* significantly decreased from baseline to 6 months in a-PDT group and to 12 months in LDD group. At baseline, the most frequently identified species	-	- Mean BOP+ ± SD - *: SS change from baseline to 3 months. - †: SS change from baseline to 6 months. - ‡: SS change from baseline to 9 months. - §: SS change from baseline to 12 months. - **: P < 0.01 compared with baseline (Wilcoxon test).
		12 months	3.83 ± 0.85 *†‡§	2.41 ± 0.70	1.41 ± 1.18 *†	-	1.55 ± 1.26 *†§	-	0.00 ± 0.00 *†‡§		-	
	a-PDT(Test)	Baseline	4.19 ± 0.55	2.66 ± 0.73	1.53 ± 0.91	-	4.03 ± 1.66		0.13 ± 0.21		-	

		12 months	4.08 ± 0.81 (N = 19) *†‡	2.58 ± 0.94 (N = 19)	1.5 ± 0.86 (N = 19) *†‡	-	1.74 ± 1.37 *†‡§	-	0.01 ± 0.04 (N = 19) *†‡§	in the submucosal biofilm were *C. gingivalis, F. nucleatum, P. micra and T. forsythia.*	-	
Bhavsar et al., 2019	PIH (Control)	Baseline	2.56 ± 0.60	-	-	-	20.8 (5/24)	0	-	-	-	
		Post-surgery	-	-	-	-	-	-				
	AF+Anti-infective therapy	Baseline	4.85 ± 1.38	-	-	-	91.7 * (22/24)	16.7 (4/24)	-	-	-	-
		Post-surgery	4.11 ± 1.27 *	-	-	-	61.9 (13/21) †	0†				*: Statistically significant difference between groups are represented as (*P*-value ≤ 0.05). † SSD before and after Tx in test group
De Mendonga et al., 2009	AF+ abrasive air powder + resin curette	Baseline	6.7 ± 1.2	-	-	-	100	30.0± 26.9	-	-	-	-
		12 months post-surgery	4.3 ± 1.0*	2.0 ± 0.64	-	-	26.6 ± 16.1*	0 *	-	-	-	*: SSD from baseline to final assessment. NSSD for - CAL red (mm), PPD reduction at 3 and 12 months.

Duarte et al., 2009	PIH	Baseline	2.0 ± 0.4	-	-	-	4.0 ± 8.7		11.8 ± 10.3	-	-	Data reported for clinical parameters mean of full mouth data for PIH group.
		3 months after TX	-				-	-	-			Data reported for PIM and PIP are reported in site level
	PIM	Baseline	5.4 ± 1.4	-	-	-	93.3 ± 14.1		85.0 ± 24.18	-	-	
		3 months post TX	3.9 ± 0.8 *				25.0 ± 41.0		28.3 ± 41.6 *†			*: SSD before and after Tx.
	PIP	Baseline	7.5 ± 2.2	-	-	-	100		90 ± 30.8	-	-	
		3 months post TX	4.4 ± 1.1 *				52.5± 41.3 *		50 ± 39.4* †			†: SSD before and after treatment
Esberg et al., 2019			No raw data for secondary outcome reported in the study. Cluster 2 of the proteome was associated with implant loss and BOP. Cluster 3 was associated with implant survival and EMD treatment.									
Gershenfeld et al., 2018	AZM+ NSPT	Baseline	Baseline data were counted as zero. 0	-	Baseline data were counted as zero. 0	4.98 ± 1.24	Baseline data were counted as zero. 0	Baseline data were counted as zero. 0	Baseline data were counted as zero. 0	Orange complex had highest frequency at all times. Red complex bacteria had lowest frequency. NSSD in bacterial at baseline between 2 groups.		No raw data reported, estimation based on the presented graphs.
		6 months	Mean change: 0	-	-1	4.77 ± 1.21	-55	-20	-0.15			
	Placebo +NSPT	Baseline	Baseline data were counted as zero 0	-	Baseline data were counted as zero.	6.21 ± 1.57	Baseline data were counted as zero.	Baseline data were counted as zero.	Baseline data were counted as zero.		-	-

Study	Group	Time										
						0		0	0	0		
		6 months	Mean change: -1	-	0.4	6.22 ± 1.39	-20	-18	-0.4			-	
Granfeldt et al., 2010						No data for secondary outcome reported in the study.							
Hallstrom et al., 2016	Probiotic supplement	Baseline	4.3	-	-	-	54	13	26	NSSD over time between groups.	-	- *: SSD compared to baseline
		26 weeks	3.7	-	-	-	14*	2	12	The most prevalent strains were *F.n., P. micra, P. i and P. nigrescens*	-	
	Placebo supplement	Baseline	4	-	-	-	58	5	32		-	
		26 weeks	3.5	-	-	-	17*	2	15		-	
Kalos et al., 2015	AZM	Baseline	-	-	-	-	-	-	-	NSSD in treatment groups among the effect of treatment in aerobic and anaerobic bacterial count.	-	
		6 months										
	Placebo	Baseline	-	-	-	-	-	-	-			
		6 months										
Komatsu et al., 2018	Laser group	Baseline	6.6 ± 1.4	6.9 ± 1.5	-	-	94.4	-	-	NSSD in both G+ and G- in laser group at any time point.	-	- *: SSD from baseline to 1 months(P=0.002).
		3 months	6 ± 1.4 *†	6.4 ± 1.9	-	-	66.7	-	-			- †: SSD from baseline to 3 months (P=0.007).
		Baseline	6.1 ± 1.2	6.3 ± 1.7	-	-	84.2	-	-			

Study	Group	Time								Notes		Comments
	Minocycline Group	3 months	5.7 ± 2.0	6.2 ± 2.0	-	-	63.2	-	-	SSD decrease of all bacterial groups at 3 months after treatment.		
Malik et al., 2015	PIH	Baseline	2	-	-	-	mBI 0.1	-	mPI 0.8	-	-	- No raw data reported, estimation carried out based on reported bar charts.
		3 months	-	-	-	-	-	-	-	-	-	-
	PIP+NSPT	Baseline	5.1	-	-	-	mBI 2.3	-	mPI 2.5	-	-	-
		3 months	4.8	-	-	-	mBI 0.7	-	mPI 0.7	-	-	-
Peres Pimentel et al., 2019	Triclosan/fluoride toothpaste	Baseline	3.1 ± 1.0	rCAL 9.0 ± 1.5	-	-	0.0 ± 0.0	-	6.9 ± 10.4c	-	-	[a]: Significant intra-group differences by the ANOVA/Tukey when compared to baseline ($p < 0.05$). - [b]: Significant inter-group differences by the ANOVA/ Tukey ($p < 0.05$). - [c]: Significant intra-group differences by the ANOVA/Tukey when compared to baseline and 3 days ($p < 0.05$). - [d]: Significant intra-group differences by the ANOVA/Tukey when compared to baseline, 3 and 7 days ($p < 0.05$).
		3 weeks	2.7 ± 0.7	rCAL 8.6 ± 1.3	-	-	0.0 ± 0.0	-	74.0 ± 19.1d	-	-	
	Fluoride toothpaste	Baseline	3.6 ± 0.5	rCAL 9.2 ± 1.1	-	-	0.0 ± 0.0	-	9.8 ± 13.2	-	-	
		3 weeks	3.7 ± 0.9	rCAL 9.2 ± 1.1	-	-	6.9 ± 16.8	-	75.5 ± 17.7	-	-	
Renvert et al., 2017	Overall	Baseline	6.4	-	-	Bone level:	100	41.5	-	-	-	-

Study	Group	Time										Notes
						5.6						
		6 months	5.5	-	-	Bone level: 5.8	63	12.2	-	-	-	-
Ribeiro et al., 2018	Triclosan-fluoride toothpaste	Baseline	3.1 ± 0.8	8.9 ± 1.1	-	-	0.0 ± 0.0	-	9.1 ± 14.3	-	-	Different capital letters represent significant intergroup differences by ANOVA/Tukey ($P < 0.05$). Different non-capital letters represent significant intragroup differences by ANOVA/Tukey ($P < 0.05$).
		3 weeks	3.6 ± 0.9	9.2 ± 1.1	-	-	8.4 ± 10.1	-	56.9 ± 19.0	-	-	
	Fluoride toothpaste	Baseline	3.1 ± 1.2	8.3 ± 1.2	-	-	0.0 ± 0.0	-	12.8 ± 12.7	-	-	
		3 weeks	3.4 ± 0.9	8.9 ± 1.0	-	-	13.6 ± 17.2	-	61.1 ± 23.7	-	-	
Thierbach et al., 2016	Healthy/Gingivitis	Baseline	Total PD (Mean (SD)) 2.9 (0.4)	-	-	-	15.8 (12.3)	-	-	-	-	-
		6 months	-	-	-	-	-	-	-	-	-	-
	Periodontitis	Baseline	3.5 (0.8)	-	-	-	28.3 (14.8)	-	-	-	-	
		6 months	-	-	-	-	-	-	-	-	-	-

Wohlfahrt et al., 2014	PIP TX with porous Ti	No clinical data per group is reported in study. Overall no differences in clinical parameter between test and control group were found.									
	PIP Tx without porous Ti										
Hentenaar et al., 2021	PIH		1.9 (±0.6)	-	-	0.56 (±0.5)	3.4	0	NR	NR	0.14	SSD between PIH and PIP at baseline in terms of PPD and MBL, no SSD at baseline and after 3 months in PIP group
	PIP	Baseline	5.0 (±1.1)	-	-	4.17 (±1.75)	58.4	19.2	17.3		0.42	
		3 months	4.7 (±1.3)	-	-	4.24 (±1.84)	47.5	20.8	6.6		0.39	