

**Supplemental Table S1. Search strategy**

Source	Keywords	No. of articles	Date
Pubmed	Search: (((periodontitis) AND (diabetes mellitus)) AND (systemic antibiotics)) AND (amoxicillin) AND (metronidazole) AND (nonsurgical therapy) Filters: Randomized Controlled Trial, from 2000/1/1 - 2022/1/31 (("periodontal"[All Fields] OR "periodontally"[All Fields] OR "periodontically"[All Fields] OR "periodontics"[MeSH Terms] OR "periodontics"[All Fields] OR "periodontic"[All Fields] OR "periodontitis"[MeSH Terms] OR "periodontitis"[All Fields] OR "periodontitides"[All Fields]) AND ("diabetes mellitus"[MeSH Terms] OR ("diabetes"[All Fields] AND "mellitus"[All Fields]) OR "diabetes mellitus"[All Fields]) AND (("systemic"[All Fields] OR "systemically"[All Fields] OR "systemics"[All Fields]) AND ("anti bacterial agents"[Pharmacological Action] OR "anti bacterial agents"[MeSH Terms] OR ("anti bacterial"[All Fields] AND "agents"[All Fields]) OR "anti bacterial agents"[All Fields] OR "antibiotic"[All Fields] OR "antibiotics"[All Fields] OR "antibiotic s"[All Fields] OR "antibiotical"[All Fields])) AND ("amoxicillin"[MeSH Terms] OR "amoxicillin"[All Fields] OR "amoxicilline"[All Fields] OR "amoxicillins"[All Fields]) AND ("metronidazole"[MeSH Terms] OR "metronidazole"[All Fields] OR "metronidazol"[All Fields] OR "metronidazoles"[All Fields]) AND ("non-surgical"[All Fields] AND ("therapeutics"[MeSH Terms] OR "therapeutics"[All Fields] OR "therapies"[All Fields] OR "therapy"[MeSH Subheading] OR "therapy"[All Fields] OR "therapy s"[All Fields] OR "therapys"[All Fields]))) AND ((randomizedcontrolledtrial[Filter]) AND (2000/1/1:2022/1/31[pdat]))	20	31.01.2022
WOS	(((TS=(periodontitis)) AND TS=(diabetes mellitus )) AND TS=(systemic antibiotics)) AND TS=(amoxicillin)) AND TS=( metronidazole )) AND TS=(nonsurgical therapy) and Clinical Trial (Document Types) and English (Languages)	24	31.01.2022
Scopus	( ALL ( periodontitis ) AND ALL (diabetes AND mellitus ) AND ALL ( systemic AND antibiotics ) AND ALL ( amoxicillin AND with AND metronidazole ) AND ALL ( non-surgical AND therapy ) AND ALL ( randomized AND clinical AND trial ) ) AND PUBYEAR > 1999 AND PUBYEAR < 2023 AND ( LIMIT-TO ( DOCTYPE , "ar" ) ) AND ( LIMIT-TO ( LANGUAGE , "English" ) ) AND ( LIMIT-TO ( SRCTYPE , "j" ) )	567	31.01.2022

**Supplemental Table S2.** Comparison of diagnostic criteria of periodontitis, details of type 2 diabetes mellitus, funding, and additional parameters.

Author	Year	Age	Diagnosis of Periodontitis	Duration of DM	Mean HbA1c	Microbiological Parameters	Cytokine Levels	Follow-Up	Adverse Effects	Funding
El-Makaky	2019	Test group: 52.95±6.523 Control group: 52.23 ± 7.028	Chronic periodontitis diagnosed as presence of ≥4 teeth with CAL ≥ 3 mm and PPD ≥ 4 mm in more than 30% of sites	Uncontrolled type 2 diabetes (HbA1c from 7% to 9%) diagnosed for more than 5 years	Test group-baseline: 8.12±0.74 and at 3 months: 7.27±0.5; Control group-baseline: 8.21±0.71 and at 3 months: 8.21±0.71			3 months	No adverse events reported	Funded by authors
Miranda et al	2014	Test group: 54.0 ± 8.2 and Control group: 53.7 ± 8.0	Generalized chronic periodontitis - more than 30% of the sites with PD and CAL ≥ 4 mm and ≥ 6 teeth with at least one site with PD and CAL ≥ 5 mm and bleeding on probing (BoP) at baseline	Type 2 DM for ≥ 5 years, treated with diet and insulin or oral hypoglycemic agents, mean duration of DM- Test group: 8.0 ± 3.2 and Control group: 7.4 ± 3.6	Test group-baseline: 8.53 ± 1.56 and at 3 months: 8.60 ± 2.01; Control group-baseline: 8.99 ± 1.63 and at 3 months: 8.94 ± 1.71	The antibiotic-treated group also presented reduced levels and greater decreases of the three red complex species, Eubacterium nodatum and Prevotella intermedia, compared to the control group at 1 year		12 months with follow-up at 3 months and 6 months	Diarrhea (Test group: n=7; Control group n=3) Headache (Test group: n=4; Control group n=1) Metallic taste (Test group: n=4; Control group n=2) Nausea/Vomiting (Test group: n=5; Control group n=2)	São Paulo State Research Foundation (São Paulo, São Paulo, Brazil, # 2011/14872-4; 2013/01072-5)
Gómez-Sandoval JR et al	2020	AMX+MET group: 52.5 ± 8.0 and Clindamycin group: 52.0 ± 10.6	Moderate localized chronic periodontitis	Type 2 diabetes with a HbA1C < 8% and a fasting plasmagluco (FPG) < 180 mg/dL diagnosed less than 10 years back	AMX+MET group: 7.1 ± 0.4; Clindamycin group: 7.3 ± 0.4			24 months	No adverse events reported	No specific grant from any funding agency in the public, commercial or not-for-profit sectors
Mendonça et al	2012	53.2 ± 9.1 years	Generalized chronic periodontitis with at least two non-contiguous RP per half contralateral quadrant at 12 months after pre-study periodontal therapy	7.1 ± 0.9 years	11.3 ± 2.3%		Levels of all cytokines - IL-4, IFN-γ, IL-17 and IL-23 were increased after SD compared with NSD	6 months with 3 month follow-up	diarrhoea, vomiting, headache, metallic taste or irritability	São Paulo State Research Foundation (São Paulo, São Paulo, Brazil, #2008/09687-0; #2008/04280-0) and Maranhão State Research Foundation (São Luís, Maranhão, Brazil)