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Supplemental information

Cross-kingdom microbial interactions in dental implant-related infections: is Candida albicans a new villain?

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SUPPLEMENTAL MATERIAL

This systematic review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (PMID: 33780438, 25554246). Inclusion criteria included studies that assessed the ability of *Candida* to colonize or form biofilms on the titanium dental implant surface. Studies were excluded when they could not be categorized as clinical or experimental studies. Letters to editors, congress abstracts, literature reviews, case reports, or when they did not assess the presence of the *Candida* or the study data were unavailable, were excluded. Electronic and systematic searches of scientific studies were conducted in April 2021 without restrictions on publication year but a restriction on language (English, Portuguese and Spanish). Medline/PubMed, Embase, Cochrane, Clinical Trials, Web of Science, Scopus, and Open Grey databases were screened. MeSH and free terms were combined in different search strings for each database (Table 1). An additional manual search was conducted on the reference lists of all selected studies and underwent all the selection steps mentioned above. The identified records were exported to the reference manager *MyEndNoteWeb*® and duplicates were removed. The authors (V.A, A.A.S) independently reviewed titles and abstracts to select studies that met the eligibility criteria and read the selected studies' full texts. Disagreements in the first or second phases were resolved by discussion and mutual agreement between the authors (V.A, A.A.S) (Cohen’s kappa= 0.767). In case of persistent disagreement, a researcher with experience on the subject was consulted (J.G.S). The reports included were read in detail, and the information of interest has been extracted (Table 2, 3 and 4).

Table 1 – *Search strategies*

Databases	Medline/Pubmed	Scopus	Web of Science	Clinical Trials	Cochrane Library	Embase	OpenGray
	(((Candida OR C albicans OR albicans OR yeasts OR fungi OR fungus) AND (Biofilms OR Biofilm OR Microbiological) AND (Dental implant OR Dental implants OR Titanium OR Titania) AND (Peri-Implantitis OR Peri implantitis OR Periimplantitis OR Peri-implantititis OR Periimplantitides OR Mucositis OR Mucositides)))	(((Candida OR C albicans OR albicans OR yeasts OR fungi OR fungus) AND (Biofilms OR Biofilm OR Microbiological) AND (Dental implant OR Dental implants OR Titanium OR Titania) AND (Peri-Implantitis OR Peri implantitis OR Periimplantitis OR Peri-implantitides OR Periimplantitides OR Mucositis OR Mucositides)))	(((Candida OR C albicans OR albicans OR yeasts OR fungi OR fungus) AND (Biofilms OR Biofilm OR Microbiological) AND (Dental implant OR Dental implants OR Titanium OR Titania) AND (Peri-Implantitis OR Peri implantitis OR Periimplantitis OR Peri-implantitides OR Periimplantitides OR Mucositis OR Mucositides)))	Peri-implantitis	((Candida) AND (Peri-Implantitis))	(((Candida OR C albicans OR albicans OR yeasts OR fungi OR fungus) AND (Biofilms OR Biofilm OR Microbiological) AND (Dental implant OR Dental implants OR Titanium OR Titania) AND (Peri-Implantitis OR Peri implantitis OR Periimplantitis OR Peri-implantitides OR Periimplantitides OR Mucositis OR Mucositides)))	((Candida) AND (Peri-implantitis))

Filters	Completed studies

Table 2. Summary of *in situ* included studies

Study	Surface	Individuals	Location of the *in situ* device	Duration time	*Candida* species	Other species	Microbiological test	Main results
Do Nascimento et al., 2013	Ti pre-machined, Zirconia, Ti casting	Healthy men aged between 21 and 27 years (mean age: 24 years)	Upper jaw (Two discs were located in the anterior region and two in the posterior region)	24 h	5 species (*C. albicans, C. dubliniensis, C. glabrata, C. krusei* and *C. tropicalis*)	-	DNA checkerboard hybridization and scanning electron microscope	For Ti pre-machined surface, all five *Candida* strains showed similar levels (%) on covered biofilms formed in situ. *C. albicans* shows approximately 2.6x10^5 for cell counts on Ti pre-machined.
Koch et al., 2020	Ti-Zr alloy	Natural dentition but unknown periodontal status	Maxillary splint	24h	*Candida* species	Any oral microorganism isolated on agar plates is used.	MALDI-ToF-MS using a Microflex LT™ and the Biotyper™ Software	*Neisseria, Staphylococcus,* and *Streptococcus* species were most abundant. *C. albicans* were observed on the plates from one individual (from 6).

Table 3. Summary of animal included studies.

Author	Animal	Implants insertion sites	Surface	Infection time	Microbial inoculum	*Candida* specie	Other species	Results
Eke *et al*., 1998	Monkeys	Root and plate-form implants with fixed prosthesis	NR	0, 1, 2, 3, and 6 months	Normal oral flora	*Candida spp.*	*A.actinomycetemcomitans, F. nucleatum, P. intermedia, Porphyromonas sp., Spirochetes, Haemophilus sp., Actinomyces sp., Oral Campylobacter sp., E. corrodens,* Enteric rods,, *Capnocytophaga sp.*	*Candida* spp. were detected only at baseline (0 months) in a frequency of 30%.
Shibli *et al*., 2003	Dogs	Implants inserted in the edentulous mandibles	Commercially pure titanium, titanium plasma-sprayed (TPS), hydroxyapatite (HA), and acid-etched.	0, 20, 40, and 60 days	Individual microbiome (ligatures)	*C. albicans*	*P gingivalis, P intermedia/nigrescens, Fusobacterium spp, Capnocytophaga spp, beta-hemolytic Streptococcus, Campylobacter spp,* and *A. actinomycetemcomitans.*	*Candida* spp was isolated at only 6 dental implants (2 cpTi, 1 TPS, 2HA, and 1 acid-etched) on day 20.
Kucharíková et al., 2015	Mice	Lower back	Vancomycin or caspofungin (CAS) coated titanium discs and control (commercially pure)	Bacterial and fungal biofilms were left to develop for 4 and 2 days, respectively.	For inoculation of the discs with *S. aureus* or *C. albicans*	*C. albicans*	*S. aureus*	89% reduction in biofilm formation of *C. albicans* on CAS-Ti substrates, compared with control substrate.

Note: NR = not reported