Photodiagnosis and Photodynamic Therapy 17 (2017) 103–110

Contents lists available at ScienceDirect

Photodiagnosis and Photodynamic Therapy

journal homepage: www.elsevier.com/locate/pdpdt

Efficacy of antimicrobial photodynamic therapy in the disinfection of acrylic denture surfaces: A systematic review

Sergio Varela Kellesarian[a,*], Tariq Abduljabbar[b], Fahim Vohra[b], Hans Malmstrom[a], Michael Yunker[a], Tammy Varela Kellesarian[c], Georgios E. Romanos[d,e], Fawad Javed[a]

[a] Department of General Dentistry, Eastman Institute for Oral Health, University of Rochester, NY, USA
[b] Department of Prosthetic Dentistry, College of Dentistry, King Saud University, Riyadh, Saudi Arabia
[c] College of Health Sciences, Barry University, Miami Shores, FL, USA
[d] Department of Oral Surgery and Implant Dentistry, Dental School, Johann Wolfgang Goethe, University of Frankfurt, Frankfurt, Germany
[e] Department of Periodontology, School of Dental Medicine, Stony Brook University, Stony Brook, NY, USA

ARTICLE INFO

Article history:
Received 1 November 2016
Received in revised form
25 November 2016
Accepted 2 December 2016
Available online 5 December 2016

Keywords:
Photochemotherapy
Dentures
Acrylic resins
Disinfection

ABSTRACT

Background: The aim of the present systematic review was to assess the efficacy of antimicrobial photodynamic therapy (aPDT) in the disinfection of acrylic denture surfaces.
Methods: IN order to address the focused question: "Is aPDT more effective in decontaminating denture surfaces compared with traditional denture-disinfection techniques?" an electronic search without time or language restrictions was conducted up to November 2016 in indexed databases using different key words. The exclusion criteria included qualitative and/or quantitative reviews, case reports, case series, commentaries, letters to the editor, interviews, and updates.
Results: A total of 14 studies were included and processed for data extraction, out of which 1 study was a randomized clinical trial and 13 studies were performed *in vitro*. Results from 12 experimental studies reported that aPDT was effective in reducing bacteria and/or yeast cultured in single or multispecies biofilm growth on acrylic resin specimens. One experimental study reported selective microorganism reduction on acrylic resin after aPDT. One clinical randomized control trial reported that aPDT presented similar microorganism reduction compared with oral antifungal medication for the disinfection of denture surfaces.
Conclusion: The role of aPDT in the disinfection of acrylic resin surfaces is unclear. From a clinical perspective further randomized control trials are needed to assess the efficacy of aPDT in the disinfection of acrylic resin surfaces.

Contents

* Corresponding author at: Department of General Dentistry, Eastman Institute for Oral Health, 625 Elmwood Avenue, University of Rochester, Rochester, NY 14620, USA.
E-mail address: sergio_kellesarian@urmc.rochester.edu (S. Varela Kellesarian).

http://dx.doi.org/10.1016/j.pdpdt.2016.12.001
1572-1000/

1. Introduction

Dentures are commonly used for the oral rehabilitation of partially and completely edentulous individuals. Polymethyl methacrylate (PMMA), commonly known as acrylic resin, has been used traditionally as base material for the fabrication of removable dentures [1]. However, bacteria and yeast (commonly found in the oral biofilm) can colonize the denture surfaces, which if left untreated may cause oral mucosal inflammation [2,3]. This is commonly observed in patients with ill-fitting dentures and poor oral hygiene status [4–6]. Moreover, it has been reported that dentures can serve as a reservoir for pathogenic microbes, such as *Haemophilus influenzae B,* and *Pseudomonas aeruginosa*, which might increase the risk of developing aspiration pneumonia [7].

A variety of methods have been proposed for the disinfection of denture surfaces. These include the use of disinfectants solutions (sodium hypochlorite, alkaline glutaraldehyde, povidine-iodine), antiseptic mouthwashes (chlorhexidine) and microwave disinfection; however, such techniques may result in complications such as, denture bleaching or staining, soft tissues irritation and jeopardize the mechanical properties of the denture (flexural strength, linear stability and elastic modulus) [1,3,4,8–10]. Antimicrobial photodynamic therapy (aPDT) is a modern disinfection protocol that has been used to disinfect dental implants and teeth surfaces [11–14]. aPDT involves interactions between a light source (630–880 wavelength) and a photosensitizer such as methylene blue and toluidine blue, the resulting reaction produces reactive oxygen species that have a bactericidal effect [15]. To our knowledge from indexed literature a limited number of studies [16–29] have assessed the efficacy of aPDT in disinfecting denture surfaces. Zoccolillo et al. [29] reported that aPDT was more effective in reducing *Streptococcus mutans* biofilm grown on acrylic specimens compared with chemical disinfectants (dimethyl sulfoxide). Similarly, Pereira et al. [22] showed that aPDT using erythrosine is effective in reducing the counts of *Candida* species cultures and biofilm from denture surfaces. Similar results were reported by Vilela et al. [27] and Vlahova et al. [28] However, conflicting results has also been reported. In the study by De Freitas-Pontes et al. [16] aPDT was ineffective in reducing the count of microbes from denture surfaces compared with chemical disinfection (ethylene oxide gas).

With this background, the aim of the present systematic review was to assess the efficacy of aPDT in the disinfection of acrylic denture surfaces.

2. Material and methods

2.1. Focused question

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were used to conduct this systematic review [30]. The addressed focused question was "Is aPDT more effective in decontaminating denture surfaces compared with traditional denture-disinfection techniques?"

2.2. Eligibility criteria

Eligibility criteria comprised of the following: (a) original studies; (b) laboratory (*in vitro)* and experimental (animal models) studies; (c) clinical studies; (d) presence of control group; (d) intervention: evaluating efficacy of aPDT in the disinfection of denture surfaces and/or biofilm growth on acrylic resin specimens. The exclusion criteria included qualitative and/or quantitative reviews, case reports, case series, commentaries, letters to the editor, interviews, and updates.

2.3. Literature search protocol

The international database of Prospectively Registered Systematic Reviews in Health and Social Care (PROSPERO) and the Cochrane Register of Systematic Reviews were searched (SVK) in October 2016, and presented no existing or current review protocols assessing the efficacy of aPDT in the disinfection of denture surfaces and/or biofilm growth on acrylic resin specimens. In order to identify studies relevant to the focused question, two authors (SVK and TVK) conducted a structured and logical electronic search without time or language limitations up to November 1st 2016 in PubMed (National Library of Medicine), Google-Scholar, Scopus, EMBASE, MEDLINE (OVID) and Web of Knowledge databases. The following Medical Subject Headings (MeSH) were used: (1) photochemotherapy, (2) dentures, (3) acrylic resins, and (4) denture stomatitis. Other related non-MeSH terms were used in the search strategy to detect additional articles. These included: (5) photodynamic therapy and (6) acrylic. These keywords were used in the following combinations: (a) 1 or 5; and 2; (b) 1 or 5; and 3; (c) 1 or 5; and 4; (d) 1 or 5; and 6.

To minimize the potential for reviewer bias, titles and abstracts of studies identified using the above-described protocol were independently screened by 2 reviewers (SVK, and TVK) and checked for agreement. Full-texts of studies judged by title and abstract to be relevant were read and independently evaluated for the stated eligibility criteria. Reference lists of original studies were hand searched to identify any articles that could have been missed during the initial search. Hand searching of the following journals was performed: Journal of Prosthetic Dentistry, Clinical Oral Investigation, Journal of Prosthodontics, Lasers in Medical Science, Journal of Photochemistry and Photobiology, and Photodiagnosis and Photodynamic Therapy. Any disagreements in the study selection were resolved via discussion and consensus. Cohen's kappa value [31] was used to determine the inter-reviewer reliability between the 2

reviewers. The kappa coefficient for inter-reviewer agreement was 0.84.

2.4. Quality assessment

In an attempt to increase the strength of the present systematic review a quality assessment of studies included was performed. The 15 studies included underwent a quality assessment with the Critical Appraisal Skills Program (CASP) guidelines [32]. The CASP tool uses a systematic approach based on 12 specific criteria: 1) Study issue is clearly focused (aPDT efficacy in acrylic resin surfaces disinfection); 2) Cohort is recruited in an acceptable way; 3) Exposure is accurately measured; 4) Outcome is accurately measured. 5) Confounding factors are addressed; 6) Follow-up is long and complete; 7) Results are clear; 8) Results are precise; 9) Results are credible; 10) Results can be applied to the local population; 11) Results fit with available evidence; and 12) There are important clinical implications. Each criterion was given a response of either "Yes", "No", or "cannot tell". Each study could have a maximum score of 12.

3. Results

3.1. Study selection

Two hundred fifteen potential articles were initially identified, out of which 214 were identified thru electronic database searching and 1 study with hand searching. After title and abstract screening 197 publications, which did not fulfill the eligibility criteria were excluded. In the second step, 4 more articles were excluded because did not answer the focused question, aPDT was applied only in the palatal mucosa or reported a case-series. A total of 14 studies [16–29] were included in the present systematic review and processed for data extraction (Fig. 1), out of which, 1 study [20] was a randomized clinical trial and 13 studies [16–19,21–29] were performed *in vitro*.

3.2. Experimental studies

3.2.1. General characteristics of the studies included

Nine studies [16–19,21,26–29] assessed the efficacy of aPDT on single-species biofilm growth on acrylic resin. In 4 studies [17,21,27,29] the potential of aPDT was assessed on biofilm-associated cultures of *S. mutans* on denture acrylic surfaces. Reduction of biofilm formed on acrylic specimens by *S. aureus* or *P. aeruginosa* after aPDT irradiation was assessed in 4 studies [16,18,27,28] and 3 studies [16,18,28], respectively. Mima et al. [19] fabricated and inoculated 34 dentures with strains of *C. albicans*, *C. glabrata*, *C. tropicalis*, *C. dubliniensis* and *C. krusei*, to evaluate the effectiveness of aPDT for the inactivation of different species of *Candida* on maxillary complete dentures. Four studies [16,26,28,33] assessed *C. albicans* viability on acrylic resin samples after aPDT irradiation. Two studies [16,27] assessed the efficacy of aPDT on the viability of single biofilms formed by *E. coli* in acrylic discs. Mantareva et al. [18] and Pereira et al. [21] studied the specific effects of aPDT on the viability of *E. faecalis* and *S. sanguinis* on acrylic specimens, respectively.

Two studies [24,25] evaluated the effectiveness of aPDT application against a multispecies biofilm formed by *C. albicans*, *C. glabrata*, and *S. mutans* on acrylic resin specimens. Pereira et al. [22] assessed the potential of aPDT on planktonic culture, biofilms and virulence factors of *Candida* strains *(C. albicans, C. glabrata, C. tropicalis, C. dubliniensis*) isolated from individuals wearing removable maxillary prostheses with DS. One study [23] reported the specific effects of aPDT on the viability of single, dual and three species biofilms formed by *C. albicans*, *S. aureus*, and/or *S. mutans*.

3.2.2. Laser parameters

In 10 studies [16,18,19,21,22,24–26,28,29] diode lasers with wavelengths ranging between 435 nm and 667 nm were used. Three studies [17,23,27] used InGaAlP laser with a 660 nm wavelength. In eleven studies [17,19,21–29] duration of laser application per acrylic specimen ranged between 90 s and 26 min. De Freitas-Pontes et al. [16] and Mantareva et al. [18] did not report the acrylic surfaces irradiation time. In 12 studies [16–19,21–24,26–29] a single aPDT session was applied at baseline. Quishida et al. [25] applied a single aPDT session or 3 consecutive aPDT applications with intervals of 20 min (Table 2).

3.2.3. Photosensitizer parameters

Methylene blue, toluidine blue and malachite green with concentrations ranging between 37.5 μM and 3000 μM were applied as photosensitizer in 5 studies [16,18,23,26,27], 2 studies [17,27] and 1 study [27], respectively. One study [25] used a derivative of chlorine (Photodithazine®) with concentrations ranging between 175 mg/ml and 200 mg/ml. Vlahova et al. [28] studied the efficacy of water-soluble phthalocyanine complexes (gallium, zinc and silicon) as photosensitizers for the disinfection of acrylic surfaces. Mantareva et al. [18] investigated the efficacy of visible light-absorbing cationic water-soluble gallium phthalocyanines peripherally substituted with four or eight methylpyridyloxi groups, zinc phthalocyanine and methylene blue with concentrations ranging between 3 μM and 6 μM. One study [24] evaluated the potential of curcumin-mediated aPDT on multiple species biofilm on acrylic samples. Two studies [21,22] applied erythrosine with concentrations ranging between 5 μM and 400 μM as photosensitizer. Porphyrin derivatives and protoporphyrin IX were used in 2 studies [19,29] and 1 study [26], respectively. Pereira et al. [21] evaluated the effects of aPDT using Rose Bengal (5 μM). In 12 studies [17–19,21–29] the photosensitization period prior laser application ranged between 5 min and 90 min. In one study [16] the pre-irradiation photosensitization time was not reported (Table 3).

3.2.4. Main outcomes

In 9 studies [17–19,21,23,26–29], aPDT was effective reducing single-species biofilm growth on acrylic surfaces. Four studies [22–25] reported that aPDT resulted in microorganism colony-forming units (CFU) reduction on multispecies biofilm. One study [16] reported that aPDT was effective in reducing *E.coli* count, but ineffective reducing other species such as *C. albicans* and *S. mutans*. Quisihida et al. [25] reported that 3 consecutive applications of aPDT were more effective reducing cell viability and total biomass compared with a single aPDT application.

3.2.5. Quality assessment

Quality score of the experimental studies [16–19,21–29] ranged from 8 to 9. Quality assessment identified that in general, exposure and outcome were adequately performed in these studies [16–19,21–29]. The most common limitation was the short term and incomplete follow-up of the experimental groups. Furthermore, as all studies [16–19,21–29] were performed *in vitro*, the application of these results to human population is still limited. Thus, on average, the quality of included experimental studies [16–19,21–29] on the efficacy of aPDT on the disinfection of acrylic resin surfaces was good, limitations of short term follow up and lack of clinical studies limit the application of these study outcomes in clinical practice. Quality assessment of the individual papers is summarized in Table 4.

Table 1
General characteristics of included studies.

Experimental studies

Authors et al. (Region of study and year)	Microbes investigated	Intervention	Study groups	Outcome
De Freitas-Pontes et al. [16] (Brazil, 2014)	*S. mutans, S. aureus, E. coli, P. aeruginosa, C. albicans* strains	Single-species biofilm growth on acrylic resin specimens	Group 1: Control Group 2: PS + PDT 10 J/cm^2 Group 3: PS + PDT 30 J/cm^2 Group 4: PS Group 5: PDT 10 J/cm^2 Group 6: PDT 30 J/cm^2 Group 7: Ethylene oxide gas	aPDT reduced *E. coli* counts only
De Sousa Farias et al. [17] (Brazil, 2016)	*S. mutans* strains	Single-species biofilm growth on acrylic resin specimens	Group 1: 0.9% NaCl Group 2: 0.12% CHX Group 3: PS + PDT 320 J/cm^2 Group 4: PS + PDT 640 J/cm^2	aPDT and CHX presented similar levels of denture disinfection
Mantareva et al. [18] (Bulgaria, 2011)	MRSA, *E. faecalis, C. albicans* and *P. aeruginosa* strains	Single-species biofilm growth on acrylic resin specimens	Group 1: Control Group 2: PS only Group 3: PDT Group 4: PS + PDT	aPDT was effective in reducing microbial counts in acrylic surfaces
Mima et al. [19] (Brazil, 2011)	*C. albicans, C. glabrata, C. tropicalis, C. dubliniensis* and *C. krusei* strains	Single-species biofilm growth on dentures	Group 1: Control Group 2: PDT only Group 3: PS only Group 4: PS + PDT	aPDT was effective in reducing microbial counts in acrylic surfaces
Pereira et al. [23] (Brazil, 2011)	*C. albicans, S. aureus,* and *S. mutans* strains and suspension	Single-species and multispecies biofilm growth on acrylic resin specimens	Group 1: Control Group 2: PS only Group 3: PS + PDT Group 4: PDT only	aPDT was effective in reducing microbial counts in acrylic surfaces
Pereira et al. [21] (Brazil, 2013)	*S. mutans* and *S. sanguinis* strains	Single-species biofilm growth on acrylic resin specimens	Group 1: Control Group 2: PDT only Group 3: PS + PDT	aPDT was effective in reducing microbial counts in acrylic surfaces
Pereira et al. [22] (Brazil, 2015)	Cultures of *C. albicans, C. glabrata, C. tropicalis and C. dubliniensis* from patients with denture stomatitis	Single-species and multispecies biofilm growth on acrylic resin specimens	Group 1: Control Group 2: PS only Group 3: PS + PDT Group 4: PDT only	aPDT was effective in reducing microbial counts in acrylic surfaces
Quishida et al. [25] (Brazil, 2015)	*C. albicans, C. glabatra, and S. mutans* suspension	Multispecies biofilm growth on acrylic resin specimens	Group 1: Control Group 2: PS only Group 3: PS + PDT Group 4: PDT only	aPDT was effective in reducing microbial counts in acrylic surfaces
Quishida et al. [24] (Brazil, 2016)	*C. albicans, C. glabrata, CS. mutans* suspension	Multispecies biofilm growth on acrylic resin specimens	Group 1: Control Group 2: PS only Group 3: PDT only Group 4: PS 80 μM + PDT Group 5: PS 100 μM + PDT Group 6: PS 120 μM + PDT	aPDT was effective in reducing microbial counts in acrylic surfaces
Sousa et al. [26] (Brazil, 2016)	*C. albicans* strains	Single-species biofilm growth on acrylic resin specimens	Group 1: Control Group 2: PS only Group 3: PS + 120 s PDT Group 4: PS + 240 s PDT Group 5: PS + 480 s PDT Group 6: PS + 600 s PDT	Compared with PPIX, aPDT was more effective in reducing the microbial counts when MB was used as PS.
Vilela et al. [27] (Brazil, 2012)	*S. aureus* and *E. coli* strains	Single-species biofilm growth on acrylic resin specimens	Group 1: PS only Group 2: PDT only Group 3: PS + PDT	Compared with MB and TB, aPDT was more effective in reducing the microbial counts when MG was used as PS.
Vlahova et al. [28] (Bulgaria, 2012)	MRSA, *C. albicans* and *P. aeruginosa* strains	Single species biofilm growth on acrylic resin specimens	Group 1: Control Group 2: 0.5% NaOCl solution Group 3: $NaHCO_3$ tablets Group 4: PS ZnPc1 + PDT Group 5: PS SiPc1 + PDT Group 6: PS GaPc1 + PDT	aPDT was effective in reducing microbial counts in acrylic surfaces
Zoccolillo et al. [29] (USA, 2016)	*S. mutans* strains	Single species biofilm growth on acrylic resin specimens	Group 1: Control Group 2: PS only Group 3: Dimethyl Sulfoxide Group 4: PS +PDT 15 J/cm^2 Group 5: PS +PDT 30 J/cm^2 Group 6: PS +PDT 45 J/cm^2	aPDT was effective in reducing microbial counts in acrylic surfaces

Clinical studies

Authors et al. (Region of study and year)	Subjects	Intervention	Study groups	Outcome
Mima et al. [20] (Brazil, 2012)	40 patients	Treatment of denture stomatitis	Group 1: PS + PDT Group 2: Nystatin suspension rinses.	Antimicrobial effects of aPDT and nystatine gel were comparable

PS: photosensitizer PDT: photodynamic therapy *S. mutans: Streptococcus mutans MRSA:Methicillin-resistant S. aureus*.
E. coli: Escherichia coli P. aeruginosa: Pseudomonas aeruginosa C. albicans: Candida albicans C. krusei: Candida krusei.
C. glabrata: Candida glabrata C. tropicalis: Candida tropicalis C. dubliniensis: Candida dubliniensis J: joules.
CFU: colony forming-unit ER: erythrosine PDZ: photodithazine PPIX: protoporphyrin IX MB: methylene blue.
NaOCl: sodium hypochlorite $NaHCO_3$: sodium bicarbonate GaPc1: gallium phthalocyanine *E. faecalis: Enterococcus faecalis.*
ZnPc1: zinc phthalocyanine SiPc1: silicon phthalocyanine TB: toluidine blue MG: malachite green.
S. sanguinis: *Streptococcus sanguinis* RB: Rose Bengal NaCl: sodium chloride CHX: chlorhexidine digluconate.

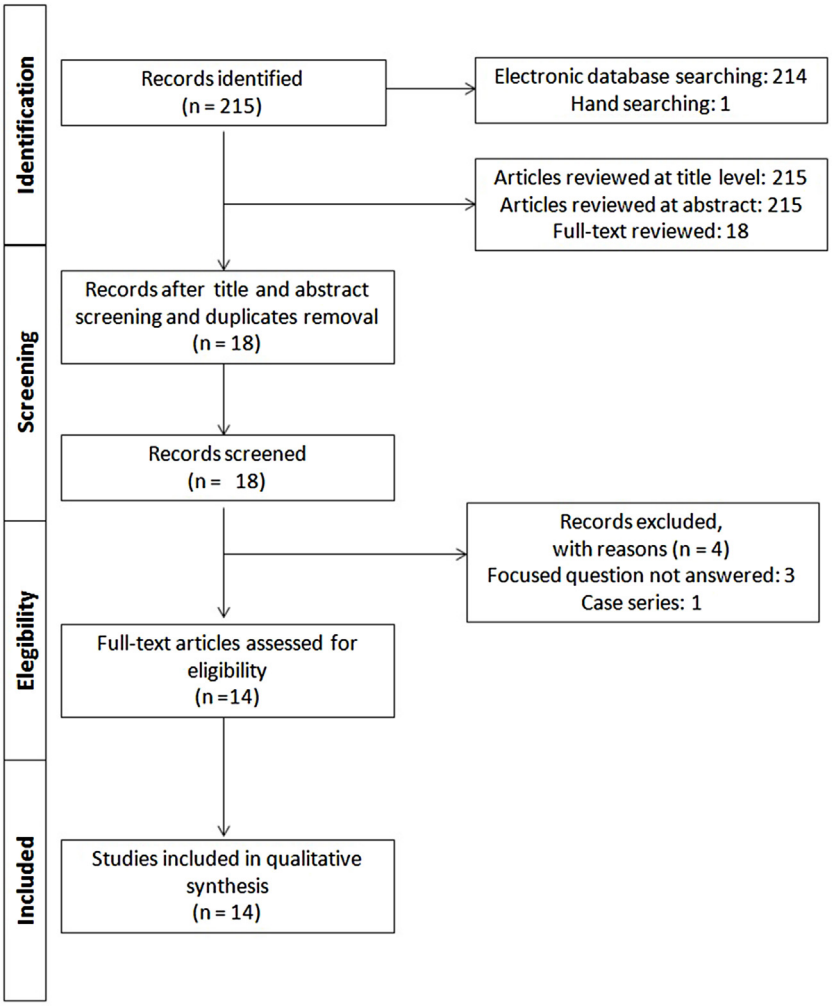

Fig. 1. Article selection flow chart for the systematic review according to PRISMA guidelines.

Table 2
Laser parameters.

Authors et al.	Source	Wavelength (nm)	Power output (mW)	Power density (mW/cm^2)	Energy fluence (J/cm^2)	Duration of laser application (minutes)	Number of applications (Time interval)
Experimental							
De Freitas-Pontes et al. [16]	LED	530–652	150	NA	10 and 30	NA	1
De Sousa Farias et al. [17]	InGaAlP laser	660	100	NA	320 or 640	90 and 180 s	1
Mantareva et al. [18]	LED	635	NA	60	50	NA	1
Mima et al. [19]	LED	440–460	NA	24	37.5	26	1
Pereira et al. [23]	InGaAlP laser	660	100	NA	350	98 s	1
Pereira et al. [21]	LED	455 ± 20	200	526	95	3	1
Pereira et al. [22]	LED	532 ± 10	90	237	42.63	3	1
Quishida et al. [25]	LED	660	NA	71.7	37.5	9	1 or 3 (20 min)
Quishida et al. [24]	LED	440–460	NA	22	37.5	20	1
Sousa et al. [26]	LED	MB: 660 PPIX: 630	MB: 808 PPIX: 777	MB: 285 PPIX: 275	MB: 34–171 PPIX: 33–165	2, 4, 8 and 10	1
Vilela et al. [27]	InGaAlP laser	660	100	105	20	188 s	1
Vlahova et al. [28]	LED	635	NA	NA	NA	10	1
Zoccolillo et al. [29]	LED	664 ± 3	1700	150	15, 30 and 45	100, 200 and 300 s	1
Clinical							
Mima et al. [20]	LED	440–460	260	Denture: 24 Palate: 102	Denture: 37.5 Palate: 122	Denture: 26 Palate: 20	6 (Three times a week)

GaAlAs: gallium-aluminum-arsenide InGaAlP: indium-gallium-aluminum-phosphide LED: light-emitting diode.
PPIX: protoporphyrin IX MB: methylene blue nm: nanometer mW: milliwatts J: joules.

Table 3
Characteristics of photosensitizers used.

Authors et al.	Treatment of	Types of PS	Concentration of PS	PS drug delivery	Pre-irradiation time (in min)
Experimental					
De Freitas-Pontes et al. [16]	Experimental single-species biofilm	MB	500 mg/L	Topical	NA
De Sousa Farias et al. [17]	Experimental single-species biofilm	TB	100 mg/L	Topical (immersion)	5
Mantareva et al. [18] (Bulgaria, 2011)	Experimental single-species biofilm	TMPO GaPc1, OMPO GaPc1, ZnPc1 and MB	TMPO GaPc1: 3–6 μM OMPO GaPc1: 3–6 μM ZnPc1: 6 μM MB: 6 μM	Topical (immersion)	Bacteria: 15 Fungus: 90
Mima et al. [19]	Experimental single-species biofilm	Porphyrin derivative	5 mL	Denture surfaces were sprayed	30
Pereira et al. [23]	Experimental single and multispecies biofilm	MB	100 mg/L	Topical (immersion)	5
Pereira et al. [21]	Experimental single-species biofilm	ER and RB	5 μM	Topical (immersion)	5
Pereira et al. [22]	Experimental single and multispecies biofilm	ER	Candida strains: 200 μM Biofilm: 400 μM	Topical (immersion + shaker)	5
Quishida et al. [25]	Experimental multispecies biofilm	PDZ	175 and 200 mg/L	Topical (immersion)	20
Quishida et al. [24]	Experimental multispecies biofilm	Curcumin	2 mL	Topical (immersion)	20
Sousa et al. [26]	Experimental single-species biofilm	MB and PPIX	MB: 50 μM PPIX: 10 μM	Topical (immersion)	10
Vilela et al. [27]	Experimental single-species biofilm	MB, TB and MG	37.5, 75, 150, 300, 600, 1800 and 3000 μM	Topical (immersion + shaker)	5
Vlahova et al. [28]	Experimental single-species biofilm	GaPc1, ZnPc1 and SoPc1	NA	Topical (immersion)	10
Zoccolillo et al. [29]	Experimental single-species biofilm	Porphyrin derivative (purpurine)	2500 mg/L	Topical (immersion)	30
Clinical					
Mima et al. [20]	Denture stomatitis	Porphyrin derivative	500 mg/L	Denture surface and palate were sprayed	Palate:30 Denture: 30

MB: methylene blue PPIX: protoporphyrin IX PDZ: photodithazine ER:erythrosine GaPc1: gallium.
ZnPc1: zinc SiPc1: silicon phthalocyanine TB: toluidine blue MG: malachite green RB: Rose Bengal.

Table 4
CASP quality assessment of the reviewed papers.

Authors	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11	Item 12	Total quality score (0–12)
Experimental													
De Freitas-Pontes et al. [16]	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	No	Yes	8
De Sousa Farias et al. [17]	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	9
Mantareva et al. [18]	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	9
Mima et al. [19]	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	9
Pereira et al. [23]	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	9
Pereira et al. [21]	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	9
Pereira et al. [22]	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	9
Quishida et al. [25]	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	9
Quishida et al. [24]	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	9
Sousa et al. [26]	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	9
Vilela et al. [27]	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	9
Vlahova et al. [28]	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	9
Zoccolillo et al. [29]	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	9
Clinical													
Mima et al. [20]	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	11

Item 1: study issue is clearly focused; *item 2*: cohort is recruited in an acceptable way; *item 3*: exposure is accurately measured; *item 4*: outcome is accurately measured; *item 5*: confounding factors are addressed; *item 6:* follow-up is long and complete; *item 7:* results are clear; *item 8:* results are precise; *item 9:* results are credible; *item 10:* results can be applied to the local population; *item 11:* results fit with available evidence; *item 12:* there are important clinical implication.

3.3. Clinical studies

3.3.1. General characteristics

Mima et al. [20] conducted a parallel, 2 groups, randomized control trial comparing the effectiveness of aPDT with oral antifungal medication in the treatment of DS. Forty patients (age range: 41–80 years) with clinical evidence of DS were recruited. The con-

trol group was treated with nystatin oral suspension rinses (100000 IU), 4 times daily for 15 days (Table 1) [20].

3.3.2. Laser parameters

Two LED lasers with a wavelength range between 440 nm and 460 nm were used. The dentures were irradiated for 26 min with one laser and the palate for 20 min with the other laser. aPDT was performed 3 times a week for 15 days (6 sessions) [20].

3.3.3. Photosensitizer parameters

Mima et al. [20] sprayed a haematoporphyrin derivative (500 mg/L) in the inner and outer surfaces of acrylic dentures and left them in dark for 30 min. Additionally, the palate was sprayed with photosensitizer solution prior irradiation (30 min).

3.3.4. Main outcomes

Both groups (nystatin and aPDT) presented similar clinical success rates (53% vs 45%, respectively) reducing *Candida* spp. after 30 days [20].

3.3.5. Quality assessment

Quality score of the study [20] was 11. Quality assessment identified that in general, recruitment of the patients, exposure and outcome were adequately performed. The results could be considered to be applicable to the local population. The major shortcoming in the study [20] was the short follow-up.

4. Discussion

In the present study, only a qualitative analysis was performed since the significant heterogeneity among the studies did not allow pooling of the results and quantitative analysis. Results from nearly 92% of the experimental studies [17–19,21–29] reported that aPDT was effective in reducing bacteria and/or yeast cultured in single or multispecies biofilm growth on acrylic resin specimens compared with controls. It is therefore tempting to speculate that aPDT is an effective treatment strategy for disinfection of dentures surfaces. However, it is noteworthy that there was a discrepancy on the definition of control groups amongst the experimental studies [16–19,21–29]. In nearly 31% of the experimental studies [16,17,28,29], the efficacy of aPDT was compared with traditional chemical disinfectants such as chlorhexidine and ethylene oxide gas. The only clinical study [20] which fulfilled our eligibility criteria compared the efficacy of aPDT with nystatine gel for disinfection of denture surfaces. The result showed comparable outcomes on terms of microbial reduction in both groups; whereas, in the remaining experimental studies [18,19,21–27] (approximately 69%) a control group comprised of treatment with photosensitizer alone or no treatment. It is therefore hypothesized that if a traditional disinfecting agent was used as a control in these studies, comparable outcomes could have been obtained with reference to reduction in microbial counts on denture surfaces treated with or without aPDT. Traditionally, aPDT is used as an adjunct therapy to conventional therapeutic protocols, for example in the treatment of periodontal and peri-implant diseases aPDT is used as an adjunct to mechanical debridement to reduce oral inflammation [11–14]. In an attempt to elucidate the efficacy of aPDT in disinfecting denture surfaces well-designed studies with precisely defined groups are needed. An example of such study design might be based in the following groups: group 1- disinfection of denture surface with chemical disinfectant alone; group 2–disinfection of denture surface using chemical disinfectant with adjunct aPDT; group 3-disinfection of denture surface with aPDT alone, and group 4–no treatment.

It seems exigent to choose an optimal and effective photosensitizer which could offer the most predictable outcome in terms of disinfection of dentures acrylic surfaces. For instance, Pereira et al. [23] reported that aPDT with methylene blue (100 mg/L) was effective reducing the total biomass and CFU of single-species and multispecies biofilm growth of *C. albicans, S. aureus*, and *S. mutans*; whereas, Quishida et al. [25] used up to 200 mg/L of photodithazine to inhibit the total biomass of *Candida spp*. and *S. mutans*. Furthermore, the pre-irradiation time also varied significantly among the experimental studies [16–19,21–29]. For example, Pereira et al. [21–23] and Vilela et al. [27] applied photosensitizer for 5 min prior irradiation; whereas, Mima et al. [19] and Zoccolillo et al. [29] used 30 min. This reflects that there is a lack of consensus regarding the ideal photosensitizer and the exposure time prior irradiation among the experimental studies. Therefore, seems challenging to implement a specific protocol in terms of photosensitizer, concentration and pre-irradiation time to disinfect acrylic resin denture surfaces in a clinical setting. Moreover, the duration of irradiation time varied significantly among included studies [16–19,21–29]. For example, Vlahova et al. [28] used a InGaAlP laser for 10 min; whereas, Pereira et al. [21] used a diode laser for 3 min. In most of the experimental studies [17–19,21–24,26–29] aPDT was done once. This may pose another challenge for clinicians for determining the precise frequencies of aPDT required before attaining denture disinfection. Therefore, additional well-designed clinical studies are needed in this regard.

From a clinical perspective confounding parameters such as low salivary flow rate, smoking, poorly controlled diabetes mellitus, medication, immunosuppression and nutritional factors, might play an important role in microorganisms adherence [5,34–36]. Moreover, denture-related factors such as deficient oral/denture hygiene, increased age of denture, denture trauma, continuous denture wearing, denture relines and denture surface porosity, may also influence the microorganism colonization [37–39]. Since approximately 93% of the studies [16–19,21–29] including in this systematic review were performed *in vitro*, it remains to be determined whether or not aPDT in a clinical scenario would result in acrylic resin surfaces disinfection among patients with a poor plaque control, systemically compromised and habitual tobacco product users. Therefore, additional clinical studies assessing these parameters are needed.

5. Conclusion

The role of aPDT in the disinfection of acrylic resin surfaces is unclear. From a clinical perspective further randomized control trials are needed to assess the efficacy of aPDT in the disinfection of acrylic resin surfaces.

Conflict of interest

None declared.

Acknowledgment

The authors extend their sincere appreciations to Deanship of Scientific Research at King Saud University for its funding of this prolific research group (PRG-1437-38).

References

[1] A.R. Moussa, W.M. Dehis, A.N. Elboraey, H.S. ElGabry, A comparative clinical study of the effect of denture cleansing on the surface roughness and hardness of two denture base materials, Open Access Maced. J. Med. Sci. 4 (2016) 476–481.

[2] A. Nawasrah, A. AlNimr, A.A. Ali, Antifungal effect of henna against candida albicans adhered to acrylic resin as a possible method for prevention of denture stomatitis, Int. J. Environ. Res. Public Health (2016) 13.

[3] I.A. Orsi, A.G. Junior, C.A. Villabona, F.H. Fernandes, I.Y. Ito, Evaluation of the efficacy of chemical disinfectants for disinfection of heat-polymerised acrylic resin, Gerodontology 28 (2011) 253–257.
[4] G. Aoun, M. Saadeh, A. Berberi, Effectiveness of hexetidine 0.1% compared to chlorhexidine digluconate 0.12% in eliminating *Candida albicans* colonizing dentures: a randomized clinical In vivo study, J. Int. Oral Health 7 (2015) 5–8.
[5] C.M. Bianchi, H.A. Bianchi, T. Tadano, C.R. Paula, H.D. Hoffmann-Santos, D.P. Leite Jr., et al., Factors related to oral candidiasis in elderly users and non-users of removable dental prostheses, Rev. Inst. Med. Trop. Sao Paulo 58 (2016) 17.
[6] I.P. Thilakumara, J.A. Jayatilake, R.W. Pallegama, A.N. Ellepola, Denture-induced stomatitis and associated factors in a group of patients attending a university dental hospital in Sri Lanka, J. Investig. Clin. Dent. (2016).
[7] L.E. O'Donnell, K. Smith, C. Williams, C.J. Nile, D.F. Lappin, D. Bradshaw, et al., Dentures are a reservoir for respiratory pathogens, J. Prosthodont. 25 (2016) 99–104.
[8] S.A. Bamigboye, O.O. Dosumu, D.M. Ajayi, Microwave disinfection of maxillary and mandibular denture bases contaminated with *Candida albican*, Afr. J. Med. Med. Sci. 44 (2015) 221–228.
[9] H. Matsuo, H. Suenaga, M. Takahashi, O. Suzuki, K. Sasaki, N. Takahashi, Deterioration of polymethyl methacrylate dentures in the oral cavity, Dent. Mater. J. 34 (2015) 234–239.
[10] N. Polychronakis, S. Yannikakis, A. Zissis, The effect of repeated microwaving disinfection on the dimensional stability of acrylic dentures, Acta Stomatol. Croat. 48 (2014) 279–284.
[11] M.D. Al Amri, S.V. Kellesarian, A. Ahmed, A.A. Al-Kheraif, G.E. Romanos, F. Javed, Efficacy of periimplant mechanical debridement with and without adjunct antimicrobial photodynamic therapy in patients with type 2 diabetes mellitus, Photodiagn. Photodyn. Ther. (2016).
[12] A. Ghanem, S. Pasumarthy, V. Ranna, S.V. Kellesarian, T. Abduljabbar, F. Vohra, et al., Is mechanical curettage with adjunct photodynamic therapy more effective in the treatment of peri-implantitis than mechanical curettage alone? Photodiagn. Photodyn. Ther. (2016).
[13] F. Javed, T. Abduljabbar, G. Carranza, E. Gholamiazizi, D.K. Mazgaj, S.V. Kellesarian, et al., Efficacy of periimplant mechanical debridement with and without adjunct antimicrobial photodynamic therapy in the treatment of periimplant diseases among cigarette smokers and non-smokers, Photodiagn. Photodyn. Ther. (2016).
[14] S.V. Kellesarian, V.R. Malignaggi, T. Abduljabbar, F. Vohra, H. Malmstrom, G.E. Romanos, et al., Efficacy of scaling and root planing with and without adjunct antimicrobial photodynamic therapy on the expression of cytokines in the gingival crevicular fluid of patients with periodontitis: a systematic review, Photodiagn. Photodyn. Ther. (2016).
[15] M.R. Hamblin, Antimicrobial photodynamic inactivation: a bright new technique to kill resistant microbes, Curr. Opin. Microbiol. 33 (2016) 67–73.
[16] K.M. de Freitas-Pontes, C.E. Gomes, B.M. de Carvalho, S. Saboia Rde, B.A. Garcia, Photosensitization of in vitro biofilms formed on denture base resin, J. Prosthet. Dent. 112 (2014) 632–637.
[17] S.S. de Sousa Farias, M.A. Nemezio, S.A. Corona, C.P. Aires, M.C. Borsatto, Effects of low-level laser therapy combined with toluidine blue on polysaccharides and biofilm of *Streptococcus mutans*, Lasers Med. Sci. 31 (2016) 1011–1016.
[18] V. Mantareva, V. Kussovski, I. Angelov, D. Wohrle, R. Dimitrov, E. Popova, et al., Non-aggregated Ga(III)-phthalocyanines in the photodynamic inactivation of planktonic and biofilm cultures of pathogenic microorganisms, Photochem. Photobiol. Sci. 10 (2011) 91–102.
[19] E.G. Mima, A.C. Pavarina, D.G. Ribeiro, L.N. Dovigo, C.E. Vergani, V.S. Bagnato, Effectiveness of photodynamic therapy for the inactivation of *Candida* spp. on dentures: in vitro study, Photomed. Laser Surg. 29 (2011) 827–833.
[20] E.G. Mima, C.E. Vergani, A.L. Machado, E.M. Massucato, A.L. Colombo, V.S. Bagnato, et al., Comparison of Photodynamic Therapy versus conventional antifungal therapy for the treatment of denture stomatitis: a randomized clinical trial, Clin. Microbiol. Infect. 18 (2012) E380–8.
[21] C.A. Pereira, A.C. Costa, C.M. Carreira, J.C. Junqueira, A.O. Jorge, Photodynamic inactivation of *Streptococcus mutans* and *Streptococcus sanguinis* biofilms in vitro, Lasers Med. Sci. 28 (2013) 859–864.
[22] C.A. Pereira, N. Domingues, M.P. Silva, A.C. Costa, J.C. Junqueira, A.O. Jorge, Photodynamic inactivation of virulence factors of *Candida* strains isolated from patients with denture stomatitis, J. Photochem. Photobiol. B 153 (2015) 82–89.
[23] C.A. Pereira, R.L. Romeiro, A.C. Costa, A.K. Machado, J.C. Junqueira, A.O. Jorge, Susceptibility of *Candida albicans*, *Staphylococcus aureus*, and *Streptococcus mutans* biofilms to photodynamic inactivation: an in vitro study, Lasers Med. Sci. 26 (2011) 341–348.
[24] C.C. Quishida, E.G. De Oliveira Mima, J.H. Jorge, C.E. Vergani, V.S. Bagnato, A.C. Pavarina, Photodynamic inactivation of a multispecies biofilm using curcumin and LED light, Lasers Med. Sci. 31 (2016) 997–1009.
[25] C.C. Quishida, E.G. Mima, L.N. Dovigo, J.H. Jorge, V.S. Bagnato, A.C. Pavarina, Photodynamic inactivation of a multispecies biofilm using Photodithazine((R)) and LED light after one and three successive applications, Lasers Med. Sci. 30 (2015) 2303–2312.
[26] A.S. Sousa, R.A. Prates, M.E. de Santi, R.G. Lopes, S.K. Bussadori, L.R. Ferreira, et al., Photodynamic inactivation of *Candida albicans* biofilm: influence of the radiant energy and photosensitizer charge, Photodiagn. Photodyn. Ther. 14 (2016) 111–114.
[27] S.F. Vilela, J.C. Junqueira, J.O. Barbosa, M. Majewski, E. Munin, A.O. Jorge, Photodynamic inactivation of *Staphylococcus aureus* and *Escherichia coli* biofilms by malachite green and phenothiazine dyes: an in vitro study, Arch. Oral Biol. 57 (2012) 704–710.
[28] A.P. Vlahova, C.K. Kisov, E.V. Popova, I.A. Haydushka, V.N. Mantareva, A new method for photodynamic disinfection of prosthetic constructions and impressions in prosthetic dentistry, Folia Med. 54 (2012) 51–57.
[29] M.L. Zoccolillo, S.C. Rogers, T.S. Mang, Antimicrobial photodynamic therapy of *S. mutans* biofilms attached to relevant dental materials, Lasers Surg. Med. (2016).
[30] D. Moher, A. Liberati, J. Tetzlaff, D.G. Altman, Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement, PLoS Med. 6 (2009) e1000097.
[31] C. Roberts, Modelling patterns of agreement for nominal scales, Stat. Med. 27 (2008) 810–830.
[32] X. Zeng, Y. Zhang, J.S. Kwong, C. Zhang, S. Li, F. Sun, et al., The methodological quality assessment tools for preclinical and clinical studies, systematic review and meta-analysis, and clinical practice guideline: a systematic review, J. Evid.-Based Med. 8 (2015) 2–10.
[33] V. Mantareva, I. Angelov, V. Kussovski, R. Dimitrov, L. Lapok, D. Wohrle, Photodynamic efficacy of water-soluble Si(IV) and Ge(IV) phthalocyanines towards *Candida albicans* planktonic and biofilm cultures, Eur. J. Med. Chem. 46 (2011) 4430–4440.
[34] S. Altarawneh, S. Bencharit, L. Mendoza, A. Curran, D. Barrow, S. Barros, et al., Clinical and histological findings of denture stomatitis as related to intraoral colonization patterns of *Candida albicans*, salivary flow, and dry mouth, J. Prosthodont. 22 (2013) 13–22.
[35] A.R. Jagadeeshwaran, D. Arora, V.R. Kumar, G.R. Kumar, T. Balamurugan, P.S. Prabu, Pharmaco-prosthodontics revisited, J. Pharm. Bioallied Sci. 4 (2012) S338–40.
[36] B. Dorocka-Bobkowska, D. Zozulinska-Ziolkiewicz, B. Wierusz-Wysocka, W. Hedzelek, A. Szumala-Kakol, E. Budtz-Jorgensen, *Candida*-associated denture stomatitis in type 2 diabetes mellitus, Diabetes Res. Clin. Pract. 90 (2010) 81–86.
[37] T. Wu, W. Hu, L. Guo, M. Finnegan, D.J. Bradshaw, P. Webster, et al., Development of a new model system to study microbial colonization on dentures, J. Prosthodont. 22 (2013) 344–350.
[38] D.M. Bohnenkamp, Traumatic stomatitis following an intraoral denture reline: a clinical report, J. Prosthet. Dent. 76 (1996) 113–114.
[39] J.A. Skupien, F. Valentini, N. Boscato, T. Pereira-Cenci, Prevention and treatment of *Candida* colonization on denture liners: a systematic review, J. Prosthet. Dent. 110 (2013) 356–362.