



Efficacy of mechanical debridement with and without adjunct antimicrobial photodynamic therapy in the treatment of peri-implantitis among moderate cigarette-smokers and waterpipe-users

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ARTICLE INFO

Keywords:

Antimicrobial photodynamic therapy
Alveolar bone loss
Inflammation
Dental implant
Peri-implantitis

ABSTRACT

Objective: The aim was to assess the efficacy of mechanical debridement (MD) with and without adjunct antimicrobial photodynamic therapy (aPDT) in the treatment of peri-implantitis among cigarette-smokers and waterpipe-users.

Materials and methods: Patients diagnosed with peri-implantitis were included. Demographic data was collected using a questionnaire. Individuals in the test- and control-groups underwent MD with adjunct aPDT and MD alone, respectively. Peri-implant clinical (plaque-index [PI], bleeding on probing [BOP] and probing depth [PD]) and radiographic (crestal bone loss [CBL]) inflammatory parameters were measured at baseline and at 6- and 12-months follow-up. Sample-size estimation was performed, and statistical analysis was done. P-values < 0.05 were considered statistically significant.

Results: Ninety-eight male patients with peri-implantitis (34 cigarette-smokers, 32 waterpipe-users and 32 never-smokers) were included. At baseline, there was no difference in the peri-implant PI, PD and CBL in all groups; and BOP levels were significantly high among never-smokers (n = 16) (P < 0.01) than cigarette-smokers (n = 17) and waterpipe-users (n = 16). There was no difference in PI, BOP, PD and CBL among cigarette-smokers (n = 17) and waterpipe-users (n = 16) that underwent MD alone at 3- and 6-months' follow-up compared with baseline. Compared with baseline, PI (P < 0.05) and PD (P < 0.05) were significantly lower among cigarette-smokers (n = 17) and waterpipe-users (n = 16) that underwent MD + aPDT at 3-months' follow-up. At 6-months' follow-up, PI, BOP and PD were significantly lower in never-smokers (n = 16) than their respective baseline and 3-months' follow up outcomes.

Conclusion: MD with adjunct aPDT is effective for the treatment of peri-implantitis. Routine oral hygiene maintenance plays a role in the overall success of MD with or without aPDT in patients with peri-implantitis.

1. Introduction

Habitual tobacco-smoking is a risk-factor for peri-implant diseases, namely peri-implant mucositis and periimplantitis [1]. Studies have shown that the rate of failure of osseointegration is higher in smokers compared with non-smokers [2]. Cavalcati et al. showed that after 5 years of loading, the rate of implant failure is nearly doubled in cigarette-smokers compared with individuals not using tobacco products

(never-smokers) [3]. Besides cigarettes, another form of tobacco smoking which originated from Middle-Eastern countries (such as Qatar, Egypt, Saudi Arabia and Kuwait) and has gained popularity in the United States is waterpipe (synonym narghile, hookah and shisha) smoking [4,5]. Waterpipe-users often perceive that this form of tobacco smoking is less hazardous to health as the tobacco filters through water, which absorbs toxins present in tobacco-smoke [6–8]; however, waterpipe use is associated with nearly a 4-fold greater CO exposure and

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<https://doi.org/10.1016/j.pdpdt.2019.09.003>

Received 6 July 2019; Received in revised form 6 September 2019; Accepted 12 September 2019

Available online 13 September 2019

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56-fold greater inhaled smoke volume than cigarette smoking [9]. Studies [6–8] have shown that peri-implant soft tissue inflammatory parameters (plaque index [PI] and probing depth [PD]) and crestal bone loss (CBL) are worse in waterpipe-users and cigarette-smokers than never-smokers. Moreover, habitual waterpipe usage has been associated with an increased accumulation of pathogenic microbes, such as *Acinetobacter*, *Moraxella* and *Candida* species, in the subgingival oral biofilm, which are risk factors of periodontal and peri-implant diseases [10–15]. In a recent study, Alqahtani et al. [7] showed that habitual waterpipe-usage enhances the expression of cotinine (a metabolite of nicotine) in the peri-implant sulcular fluid. This study [7] also showed that cotinine levels are comparable among cigarette-smokers and waterpipe-users.

Traditionally, mechanical debridement (MD) of implant surfaces and peri-implant tissues is performed for the treatment of peri-implant diseases [16,17]; however, adjunct therapies such as antimicrobial photodynamic therapy (aPDT) have been shown to enhance the overall healing following MD [18–20]. The aPDT involves interactions between a visible laser-light source and a photosensitizer (such as methylene blue and toluidine blue) in the presence of oxygen. This results in the generation of free oxygen radicals that damage target bacterial cells and accelerate the healing process [21]. The aPDT has also been reported to destroy bacteria associated with the peri-implant disease such as *Prevotella intermedia* (*P. intermedia*), *Aggregatibacter actinomycetemcomitans* (*A. actinomycetemcomitans*) and *Porphyromonas gingivalis* (*P. gingivalis*) [22]. It is well-known that habitual use of tobacco-products retards wound healing and compromises the reduction in probing depths following MD [23]; and increases the likelihood of infection at the surgical site [24]. In an in-vitro experiment, Lallier et al. assessed the influence of tobacco-smoke extracts (TSE) on cell survival of gingival fibroblasts [25]. The results showed that TSE jeopardize the function of oral fibroblasts, which in turn damages periodontal tissues [25]. To the authors' knowledge, there are no studies in indexed literature that have compared the efficacy of MD with and/or without adjunct aPDT for the treatment of peri-implantitis among cigarette-smokers and waterpipe-users. It is therefore hypothesized that the outcomes of MD with or without adjunct aPDT are compromised in cigarette-smokers and waterpipe users compared with never-smokers with peri-implantitis.

With this background, the aim was to assess the efficacy of MD with and without adjunct aPDT in the treatment of peri-implantitis among moderate cigarette-smokers, waterpipe-users and never-smokers.

2. Materials and methods

2.1. Ethical guidelines

Guidelines recognized by Helsinki-Declaration for experimentation involving humans were followed. The study was reviewed and approved by the Research Ethics Committee of the Dental Health Department at the King Saud University, Riyadh, Saudi Arabia (OR/018/0244C). Participants were recruited from the Outpatient Department of the Dental Health Department at the King Saud University, Riyadh, Saudi Arabia. The study was performed between March 2018 and February 2019. Volunteering individuals were given an information sheet printed in simple English and Arabic which explained the objectives and methodology used. A consent form (written in simple English and Arabic) was provided to all volunteering individuals and requested to sign and return it in case they agreed to participate in the present study. It was mandatory for all volunteers to have read and signed the written informed consent form before being included in the present study. Participants were given the liberty to withdraw their participation at any stage of the investigation without consequences.

2.2. Inclusion and exclusion criteria

The following inclusion criteria were imposed: (a) adult individuals (age ≥ 18 years) having undergone dental implant therapy; (b) moderate cigarette-smokers: patients that were smoking at least 11 cigarette daily [26]; (c) waterpipe-users: individuals that used waterpipe at least once daily for the past 60-months [27]; (d) never-smokers: individuals that reported to have never used tobacco in any form [28] and (e) patients diagnosed with peri-implantitis (peri-implant PD of ≥ 4 mm, and CBL (mesial and/or distal) of ≥ 3 mm [29,30]. The exclusion comprised of the following: (a) refusal to read and/or sign the informed consent form; (b) dual-smoking (smoking cigarettes and using other tobacco products, including smokeless tobacco); (c) pregnancy and/or lactation; (d) edentulism; (e) patients with self-reported systemic diseases such as diabetes mellitus, prediabetes, cardiovascular diseases, renal diseases, hepatic disorders and HIV/acquired immune deficiency syndrome.

2.3. Study groups

Self-reported age- and gender-matched cigarette-smokers, waterpipe-users and never-smokers (as defined above) were included in the present study. Therapeutically, individuals in each group were randomly and equally divided into two subgroups as follows: (a) patients that underwent MD alone; and (b) patients that underwent MD with adjunct aPDT. Randomization was done by tossing a coin.

2.4. Questionnaire

Data regarding age, gender, family history of smoking, duration of cigarette-smoking and waterpipe usage, number of cigarettes smoked daily and number of times waterpipe was used per day, family history of smoking, duration of implants in function, number of implants per person and location of implants in the jaws was recorded using a questionnaire. The questionnaire was administered to all participants by a trained and calibrated investigator (*Kappa* 0.92).

2.5. Implant-related parameters

Patients' dental records were evaluated to determine the (a) diameter and length of the implants; (b) surface characteristics (moderately-rough or smooth); and (c) implant geometry (platform-switched or non-platform switched).

2.6. Clinical and radiographic evaluation (primary outcome measures)

One trained and calibrated investigator (*Kappa*: 0.90) blinded to the study groups measured and recorded the bleeding on probing (BOP), PI, PD and CBL (mesial and distal) around all implants as described elsewhere [31–33]. The CBL was measured on digital bitewing radiographs, which were standardized using long cone paralleling technique [34,35]. The CBL was presented in millimeters (mm) as an average of bone loss on the mesial and distal surfaces of implants. All clinical and radiographic parameters were measured at baseline and at 3- and 6-months' follow-up.

2.7. Mechanical debridement

In all participants, supra- and subgingival plaque and calculus deposits from all teeth surfaces were removed by a trained and calibrated investigator (*Kappa* 0.88) who was blinded to individuals in the respective study groups. The MD was performed using an ultrasonic scaler (Dentsply Sirona, Surrey KT13 0NY, UK); and peri-implant supra- and sub-gingival debridement was done using plastic hand curettes (Implant Prophy® Plastic Dental-Instrument-System-Kit, Tess Corporation, WI, U.S.A.). This procedure was done at baseline after assessment of clinical

and radiographic parameters. Oral hygiene instructions regarding toothbrushing and flossing were also given to all individuals.

2.8. Photodynamic therapy

In all patients, aPDT was done after MD by one trained and calibrated investigator (Kappa 0.90) who was blinded to individuals in the respective study groups. The protocol for aPDT is described elsewhere [36]. In brief, using a blunt needle, 0.005% of Methylene blue was applied into the deepest buccal peri-implant pocket and left in place for 10 s. The dye was then irradiated with a continuous wave diode laser (660 nm) at a power output of 150 mW for 60 s per site. The flexible fiber tip was placed in the periodontal pocket on the buccal surface and moved in mesio-buccal, mid-buccal and disto-buccal directions. The fiber diameter, energy fluence of the laser used, and total energy were 600 μm , 0.0125 J/cm² per site and 3 joules, respectively. In the present study, aPDT was done once, at baseline, by a trained investigator (Kappa 0.92).

2.9. Statistics and power analysis

Statistical analysis was carried out using a software program (IBM SPSS®, Ver. 20, Chicago, IL, U.S.A.). Comparisons of peri-implant BOP, PI, PD, and CBL in all groups was performed using the Wilcoxon rank-sum test. For multiple comparisons, the Bonferroni *Post-hoc* adjustment test was performed. The study sample-size were determined using a computer-based software (nQuery Advisor-6, Statistical-Solutions, Saugas; M.A., U.S.A). With the inclusion of at least 32 individuals/group, the study power was estimated to be 95% with a two-sided significance level of 0.05. P values under 0.05 were considered statistically significant.

3. Results

3.1. General characteristics

In total, 98 male individuals (34 cigarette-smokers, 32 waterpipe-users and 32 never-smokers) with peri-implantitis were included. The mean age of cigarette-smokers, waterpipe-smokers and never-smokers was 52.3 \pm 2.2, 55.6 \pm 1.6 and 54.2 \pm 2.2 years, respectively. Cigarette-smokers and waterpipe-users were using their respective tobacco-products for 23.6 \pm 4.6 and 20.5 \pm 5.2 years, respectively. Cigarette-smokers smoked one cigarette in 9.3 \pm 0.4 min; and each session of waterpipe usage lasted for 20.4 \pm 5.6 min. A family history of tobacco-smoking was more often reported by cigarette-smokers (64.7%) and waterpipe-users (62.5%) compared with never-smokers (21.8%) (Table 1). Among the groups, each patient had one dental implant placed in either jaws in the premolar or molar region. The implants were in function since 5.6 \pm 0.2, 4.8 \pm 0.5 and 5.1 \pm 0.8 years, among cigarette-smokers, waterpipe-users and never-smokers, respectively. All implants were platform-switched with moderately rough surfaces. The length and diameter of the implants placed in the patients' groups ranged between 11 to 14 mm and 4.1 and 4.8 mm, respectively.

Table 1
General characteristics of the study participants.

Parameters	Cigarette-smokers	Waterpipe-smokers	Never-smokers
Participants (n)	34	32	32
Gender (male)	34	32	32
Age in years (mean \pm SD)	52.3 \pm 2.2 years	55.6 \pm 1.6 years	54.2 \pm 2.2
Duration of habit in years (mean \pm SD)	23.6 \pm 4.6 years	20.5 \pm 5.2 years	NA
Daily frequency of smoking	14.5 \pm 3.6 cigarettes/day	6.6 \pm 1.7 times/day	NA
Duration of each session of smoking in minutes (mean \pm SD)	9.3 \pm 0.4 min	20.4 \pm 5.6 min	NA
Family history of tobacco-smoking (n) (%)	22 (64.7%)	20 (62.5%)	7 (21.8%)

3.2. Baseline

Peri-implant PI, PD and CBL were comparable among all individuals that underwent MD alone or with adjunct aPDT. Scores for BOP were significantly high among never-smokers ($P < 0.01$) compared with cigarette-smokers and waterpipe-users (Table 2). The deepest periodontal pockets were located on the buccal surfaces in all individuals.

3.3. Mechanical debridement alone

There was no statistically significant difference in PI, BOP, PD and CBL among cigarette-smokers and waterpipe-users at 3- and 6-months' follow-up compared with baseline. Among never-smokers, PI ($P < 0.05$), BOP ($P < 0.05$) and PD ($P < 0.05$) were significantly high at baseline compared with 3- and 6-months' follow-up. There was no significant difference in peri-implant CBL among all groups at all time intervals (Table 2).

3.4. Mechanical debridement with adjunct photodynamic therapy

Compared with baseline, PI ($P < 0.05$) and PD ($P < 0.05$) were significantly lower among cigarette-smokers and waterpipe-users at 3-months' follow-up. There was no significant difference in BOP and CBL among cigarette-smokers and waterpipe-users at all time intervals. At 6-months follow-up, all peri-implant parameters were comparable with their respective baseline values among cigarette-smokers and waterpipe-users (Table 2).

3.5. Comparison of clinical and radiographic parameters in all groups at 3- and 6-months' follow-up

At 3- and 6-months' follow-up, there was no statistically significant difference in PI, BOP, PD and CBL among cigarette-smokers and waterpipe-users that underwent MD with or without adjunct aPDT. Among never-smokers that underwent MD with or without aPDT, there was no significant difference in clinical and radiographic parameters at 3- and 6-months' follow-up (Table 2).

4. Discussion

The present results showed that scores of PI ($P < 0.05$) and PD ($P < 0.05$) were significantly lower among cigarette-smokers and waterpipe-users that underwent MD + aPDT at 3-months' follow-up compared with tobacco-product users that underwent MD alone; however, among never-smokers the beneficial effects of MD with adjunct aPDT were evident up to 6-months' follow-up. These results applaud the outcomes of previous clinical studies [20,37], which reported that MD with adjunct aPDT is beneficial for the treatment of periodontal and peri-implant diseases. One explanation for this is associated with the mechanism of action of aPDT in which, visible light a suitable wavelength activates a photosensitizer in the presence of oxygen to generate singlet-oxygen and other highly reactive free-radicals, which are toxic to pathogenic microbes and their products [22,38]. In a recent experimental study, Sayar et al. [39] assessed the effectiveness of aPDT

Table 2
Peri-implant parameters at baseline and at 3- and 6-months' follow-up.

	Mechanical debridement			Mechanical debridement + Photodynamic therapy		
	Cigarette-smokers	Waterpipe-smokers	Never-smokers	Cigarette-smokers	Waterpipe-smokers	Never-smokers
Participants (n)	17	16	16	17	16	16
Baseline						
PI (%)	54.6 ± 12.2 %	52.3 ± 10.4 %	39.6 ± 6.7 % [†]	54.6 ± 12.2 % [‡]	52.3 ± 10.4 % [§]	39.6 ± 6.7 %
BOP (%)	12.7 ± 2.6 % [*]	14.1 ± 1.8 % [*]	44.1 ± 6.3 % [†]	12.7 ± 2.6 %	14.1 ± 1.8 %	44.1 ± 6.3 %
PD (in mm)	5.2 ± 0.4 mm	4.8 ± 0.2 mm	4.5 ± 0.2 mm [†]	5.2 ± 0.4 mm [‡]	4.8 ± 0.2 mm [§]	4.5 ± 0.2 mm
CBL (in mm)	5.2 ± 0.3 mm	4.6 ± 0.3 mm	4.3 ± 0.2 mm	5.2 ± 0.3 mm	4.6 ± 0.3 mm	4.3 ± 0.2 mm
3-months' follow-up						
PI (%)	42.5 ± 7.9 %	42.1 ± 6.4 %	26.5 ± 5.7 %	31.3 ± 5.5 %	30.5 ± 4.2 %	12.4 ± 2.8 %
BOP (%)	11.2 ± 1.7 %	12.5 ± 1.6 %	20.9 ± 4.3 %	8.1 ± 1.2 %	9.3 ± 0.8 %	6.1 ± 1.2 %
PD (in mm)	4.6 ± 0.7 mm	4.1 ± 0.5 mm	3.9 ± 0.4 mm	2.5 ± 0.2 mm	2.6 ± 0.3 mm	2.2 ± 0.4 mm
CBL (in mm)	5 ± 0.2 mm	4.6 ± 0.2 mm	4.3 ± 0.3 mm	5 ± 0.1 mm	4.6 ± 0.2 mm	3.7 ± 0.3 mm
6-months' follow-up						
PI (%)	43.7 ± 8.2 %	40.6 ± 9.3 %	23.4 ± 3.5 %	46.5 ± 7.3 %	44.2 ± 4.8 %	14.1 ± 3.1 %
BOP (%)	13.5 ± 5.6 %	12.7 ± 5.5 %	20.8 ± 4.1 %	12.6 ± 3.8 %	13.3 ± 6.1 %	8.2 ± 1.5 %
PD (in mm)	4.4 ± 0.3 mm	4 ± 0.6 mm	2.6 ± 0.4 mm	4.6 ± 0.2 mm	4.2 ± 0.3 mm	2.4 ± 0.5 mm
CBL (in mm)	5.1 ± 0.3 mm	4.7 ± 0.8 mm	4.1 ± 0.2 mm	5 ± 0.2 mm	4.6 ± 0.2 mm	3.3 ± 0.4 mm

* Compared with never-smokers at baseline ($P < 0.01$).

[†] Compared with never-smokers at 3- ($P < 0.05$) and 6-months' ($P < 0.05$) follow-up.

[‡] Compared with cigarette-smokers at 3-months' follow-up ($P < 0.05$).

[§] Compared with waterpipe-smokers at 3-months' follow-up ($P < 0.05$).

^{||} Compared with never-smokers at 3- ($P < 0.05$) and 6-months' ($P < 0.05$) follow-up.

towards reduction in the counts of *A. actinomycetemcomitans* biofilm formed on Laser-Lok titanium discs. In this study, the discs were inoculated with *A. actinomycetemcomitans* to form biofilm and were randomly treated with either aPDT or chlorhexidine. Number of colony-forming-units formed on the surface of all titanium discs were counted and the outcomes were statistically assessed. The results of this experiment showed a statistically significant reduction in the colony-forming-units on the titanium discs treated with aPDT as compared to those in the control group (chlorhexidine group) [39]. It is worth mentioning that pathogenic microbes including *A. actinomycetemcomitans* are commonly present in higher counts in the oral biofilm of patients with than without peri-implant diseases [40]; therefore, it is hypothesized that MD with adjunct aPDT markedly reduced the counts of pathogenic microbes in the supra- and subgingival oral biofilms of all patients with peri-implant diseases than MD alone. This is an explanation for the significant reduction in PI and PD among all patient groups at least up to 3-months of follow-up. However, at 6-months follow-up, the present study showed that periodontal parameters were comparable with the respective baseline levels among cigarette-smokers and waterpipe users. Various explanations may be posed in this regard, Firstly, although tobacco-smokers included in the present study were advised to quit (or at least significantly reduce smoking) and were offered assistance in this regard as well; it is speculated that cigarette-smokers and waterpipe users continued to smoke tobacco after MD with or without aPDT. Eggert et al. [41] reported that tobacco-smoking offers a favorable environment for pathogenic microbes including *P. gingivalis*, *P. intermedia*, and *A. actinomycetemcomitans* and facilitates their growth and proliferation. It has been reported that tobacco smoking compromises the outcomes of surgical and non-surgical therapeutic interventions [23,42]. This is one explanation for the relapse of peri-implant soft inflammatory conditions in cigarette-smokers and waterpipe users compared with never-smokers that demonstrated significantly improved periodontal health status up to 6-months of follow-up. The authors emphasize that all possible attempts should be made through community-based awareness programs to educate the public about the detrimental effects of smoking on overall health and the significance of routine oral hygiene maintenance towards a healthy oral and systemic health. Routine anti-tobacco awareness campaigns and didactic programs related to quitting tobacco product use may be beneficial.

The present results showed that scores of PI were lower in never-smokers compared with cigarette-smokers and waterpipe users. This suggests that a superior oral hygiene status plays a role in the overall effectiveness of MD with or without adjunct aPDT. The authors applaud the study by Romeo et al. [43], in which the authors emphasized that routine oral hygiene maintenance plays a significant role in the overall success of aPDT when performed as an adjuvant to MD for the treatment of peri-implantitis. The current results showed no significant difference in CBL in all patients that underwent MD with or without adjunct aPDT. This could possibly be associated with the relatively short duration of the present study (6-months' follow-up). It is however pertinent to mention that at 6-months' follow-up, a trend towards new bone formation (NBF) was evident among never-smokers that underwent MD with adjunct aPDT compared with individuals that underwent MD alone. It is therefore hypothesized that routine multiple sessions of MD with adjunct aPDT reduces soft tissue inflammation and enhances NBF among never-smokers with peri-implantitis. Further studies are needed to test this hypothesis.

One limitation of the present study is that cigarette-smokers, waterpipe users and controls with CP were categorized as groups that underwent MD with or without adjunct aPDT. It is known that a split-mouth trial (SMT) design subcategorizes the oral cavity into sextants, quadrants, posterior sextants, contra- or ipsilateral sextants or a combination of these. According to Hujuel and Loesche [44], a SMT increases the proficiency of statistical comparisons and provides a powerful tool for the evaluations related to periodontal therapeutic interventions such as MD with or without adjunct aPDT [44]. Moreover, in our study, aPDT was done once (at baseline) throughout the study period. It remains debatable whether multiple postoperative aPDT sessions are more effective in the reduction of periodontal inflammation than a single session of aPDT [37,45,46]; For instance, studies [37,45] have reported that multiple sessions of aPDT (for instance at 2, 7, 14 and 27 postoperative days) as an adjuvant to MD significantly improves clinical parameters as compared to a single session of aPDT; however, results from a recent randomized clinical trial [46] showed no additional effect (in terms of clinical, immunological, and microbiological benefits) of multiples postoperative episodes of aPDT tobacco-smokers when compared SRP alone in patients with CP. It is speculated that multiple postoperative sessions of aPDT are more effective in the treatment of peri-implantitis in cigarette-smokers and

waterpipe-users than a single session of aPDT following MD. Such a therapeutic protocol may result in a statistically significant decrease in peri-implant PI and PD compared with a single session of MD with adjunct aPDT among tobacco-product users. To the authors' knowledge, there are no set guidelines and/or protocols regarding the frequency of aPDT for the treatment of CP and peri-implant diseases. Furthermore, stringent eligibility criteria (such as exclusion of patients with self-reported hyperglycemic conditions) were adopted in the present study. A state of chronic hyperglycemia has been associated with delayed wound healing and increased CBL around dental implants [47]. This further raises a concern regarding the frequency of MD with adjunct aPDT in hyperglycemic smokers and never-smokers with peri-implant diseases. This warrants further studies.

5. Conclusion

Within the limits of the present study, it is concluded that in the short-term, MD with adjunct aPDT is effective for the treatment of peri-implantitis. Routine oral hygiene maintenance plays a role in the overall success of MD with or without aPDT in patients with peri-implantitis.

Acknowledgements

The authors are grateful to the Deanship of Scientific Research at King Saud University, Riyadh, Saudi Arabia for funding this research through Vice Deanship of Scientific Research Chairs.

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