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Systematic review on the effect of rinsing with povidone-iodine during nonsurgical periodontal therapy

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Background and Objective: The existing literature is inconsistent regarding whether there is any additional effect of povidone-iodine (PVP-iodine) as an adjunctive to scaling and root planing, and, if there is an effect, what its size is. Therefore, the aim of this study was to assess the additional effect of PVP-iodine as an adjunct to scaling and root planing compared with water, saline or no rinse in the treatment of chronic periodontitis.

Material and methods: An electronic literature search of the databases PubMed, EMBASE and the Cochrane Central Library, and a handsearch, were performed (up to November 2008). Two reviewers independently identified and selected screened abstracts for possible inclusion, and assessed randomized, controlled clinical trials comparing the additional benefit of PVP-iodine with water, saline rinsing or no rinsing in the nonsurgical periodontal therapy of patients with chronic periodontitis. A fixed-effects meta-analysis was conducted in the absence of statistically significant heterogeneity.

Results: A small, but statistically significant additional beneficial effect of the adjunctive use of PVP-iodine with enhanced probing pocket depth reductions of 0.28 mm (95% confidence interval: 0.08 to 0.48, $p = 0.007$) was found. There was no significant heterogeneity between studies ($I^2 = 0\%$). However, most of the studies included in the meta-analysis were of low quality, and the treatment modalities showed various differences such as the use of PVP-iodine at different concentrations and application modalities. Nevertheless, single-rooted teeth, in particular, showed an additional benefit after scaling and root planing with PVP-iodine, particularly when the treatment was repeated during the healing stage.

Conclusion: The adjunctive use of PVP-iodine during scaling and root planing may increase the clinical pocket depth reduction, although the clinical significance is small to moderate.

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Periodontitis is a common inflammatory disease of the supporting periodontal hard and soft tissues (1–3). It results in a progressive destruction of the periodontal fiber apparatus and alveolar bone with subsequent apical migration of the junctional epithelium (4). The accumulation of bacterial plaque is considered to be the

primarily etiologic factor (5,6). Consequently, the aim of the therapeutic approach is to eliminate biofilm and hard deposits on the root surface. Mechanical plaque removal, using curettes and ultrasonic devices, has become a well-documented and effective treatment modality (7,8). In addition, various attempts to eliminate pathogenic bacteria by additively administered chemical means have been explored: systemically administered antibiotics showed significant benefits in combination with scaling and root planing (9–13) but bear the risk of undesirable side-effects and the development of bacterial resistance (14). Topical application of antiseptics in periodontal pockets as an adjunctive to mechanical debridement has been suggested (15,16) and tested in various clinical trials (17,18), but there is still a lack of clear evidence for its additional benefit (19–21).

Among these pharmaceuticals, povidone-iodine (PVP-iodine) is an antiseptic with a broad antibacterial spectrum that covers gram positive and gram negative bacteria, mycobacteria (22), Staphylococcus spp. and *Candida albicans* (23), and periodontal pathogens (24,25). Several studies showed additional short-term improvements when PVP-iodine was used during subgingival debridement (26–28). Other studies failed to show any additional benefits of a PVP-iodine pocket rinsing step (29–32). This systematic review aimed to assess the potential additional effect of PVP-iodine as an adjunct to scaling and root planing when compared with water, saline or no rinse in the treatment of chronic periodontitis.

Material and methods

Search strategy

In order to conduct a systematic review of the data published on the subject of interest, a literature search of the US National Library of Medicine (Pubmed), the Excerpta Medical Database (Embase) and the Cochrane Central Library was performed. Articles from inception of these databases, up to and including November 2008, were considered. The following search terms were used:

(PVP-iodine) OR (iodine) OR (PVP) OR (povidone);
and
(periodontitis) or (periodontal),
including the according MeSH terms, respectively.

A manual search included the reference list of the reviews and studies concerning the topic as well as the index of context of the Journal of Clinical Periodontology, Journal of Periodontal Research and Journal of Periodontology.

Study selection

In a first step, the two reviewers (PS, PRS) independently screened titles and abstracts of the electronic search and assessed them for possible inclusion in the review. We ordered all potentially eligible studies and assessed their full texts. We did not apply any language restrictions. Any disagreement concerning inclusion was resolved by discussion.

Eligibility criteria for studies

We included randomized, controlled clinical trials comparing the additional benefit of PVP-iodine with water or saline rinsing, or with no rinsing, in nonsurgical periodontal therapy of patients with chronic periodontitis. Only studies reporting on the therapy of chronic periodontitis in otherwise healthy adults were included. Consequently, studies with treatment of aggressive periodontitis, and treatment of nonadults and patients with systemic diseases or manifestations affecting the prognosis and therapy of periodontitis (e.g. diabetic, pregnant or HIV-positive patients), were excluded.

With regard to the instrumentation, the use of either hand curettes or ultrasonic devices was included. Only sole nonsurgical techniques were considered.

Our primary outcome was the periodontal probing depth after 3 mo and at the final follow-up. Secondary outcomes included indices for clinical attachment loss, oral hygiene and gingival bleeding.

Data extraction and quality assessment

The reviewers (PS, PRS) independently extracted the following data: bibliographic details; patient characteristics; description of the interventions; and types of outcomes. Whenever possible, we extracted mean baseline and follow-up values (including standard deviations) for each treatment group as well as differences between groups and corresponding measures for precision [standard errors, 95% confidence intervals (CI)]. The reviewers independently assessed the quality of the included trials by evaluating whether the method of randomization was valid, whether there was concealment of random allocation and whether patients and examiners were masked. Again, any discrepancies for data extraction and quality assessment were resolved by consensus.

Data analysis

We expressed treatment effects as mean differences (in mm) in periodontal probing depth and corresponding 95% CI. We pooled data across studies in the absence of significant heterogeneity ($p > 0.1$ for χ^2) using fixed-effects (inverse variance method) and random-effects (DerSimonian–Laird method) models. As the results from fixed-effects models and random-effects models were identical, we only reported the results from the fixed-effects models. Heterogeneity was assessed using the chi-squared statistic, and the proportion of variation as a result of to heterogeneity was expressed as I^2. In the absence of a clear definition of what constitutes a clinically relevant effect, we considered a Cohen's effect size $\left(\mathrm{d} = \frac{\text{mean value}}{\text{standard deviation}}\right)$ (33) of 0.2 to represent a small effect and of 0.5 to represent a moderate effect. We conducted all analyses using STATA for Windows, version 10.0 (Stata Corp., College Station, TX, USA).

Results

Search and screening

From the 186 titles initially obtained from the literature search, 32 full texts

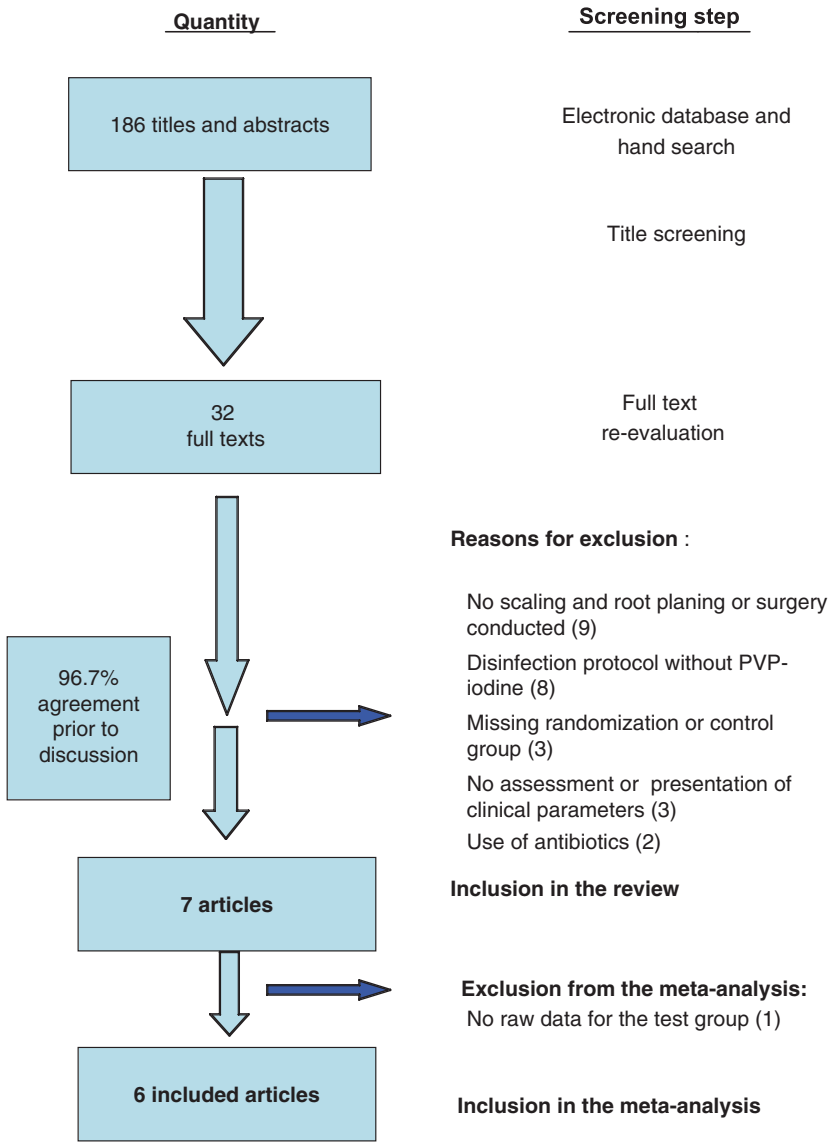

Fig. 1. Screening method. PVP-iodine, povidone-iodine.

were assessed separately and independently by both reviewers for possible inclusion in the review (Fig. 1). Twenty-five articles were excluded for the following reasons (Table 1): no scaling and root planing conducted or additional surgery (nine studies); disinfection protocol without PVP-iodine (eight studies); no assessment or presentation of clinical parameters (three studies); missing control group or randomization (three studies); or additional use of antibiotics (two studies). Reviewers agreed in 96.7% (30/31 studies) about inclusion and exclusion, and resolved disagreement for one paper by discussion.

From the remaining seven original articles (26–30,32), the data for the assessment parameters and any available information on randomization method, concealment and blinding were extracted. These studies included data from 424 patients (Table 2).

Description of studies

Five of the seven studies included in the review were designed as parallel studies (26,27,29,30,32) and two were designed as split-mouth studies (28,31).

As a result of different inclusion criteria, the teeth investigated varied, across studies, in the number of roots, pocket locations (such as possible assessment of furcation sites) and pocket depths (Table 3). Baseline values for probing depths varied from 3.9 ± 0.9 mm (15) to ≥ 6 mm (28,31).

The patient populations varied by means of explicit exclusion of smokers in four studies (27,29–31), and the exclusive treatment of single-rooted (15) or nonmolar teeth only (31). The majority of the publications reported oral hygiene instructions, (15,29–32)), and three included supragingival scaling and removal of plaque-retentive factors (30–32). The concentration of PVP-iodine used for treatment ranged from 0.1 to 10%. The individual studies reported on different recall intervals and study periods. The shortest re-evaluation periods ranged from 1 mo to 5 wk, but most studies contained data covering several time-periods of re-investigation. In addition to the comparison of the final results at the end of the investigation periods, an analysis after a collective observation period was made: three studies reported evaluable values for probing depth at 3 mo after intervention (Fig. 2) (26,27,32).

One study (26) included nearly one-half of the overall patient population (see Table 2).

Quality assessment

Six of seven studies (27–32) were reported to be randomized trials (Table 4). For one trial (26), uncertainty remained but the authors of that study confirmed randomization when we contacted them. Twenty-nine per cent of the studies described their methods of randomization (29,30), 43% described the concealment of random allocation (28,29,31) and 57% gave information about the methodology of 'blinding' or 'masking' of the examiner (27,29,31,32) (Table 2).

Effects of additional rinsing with PVP-iodine on periodontal probing depth

We could not include one of the seven trials in the meta-analyses because the

Table 1. Excluded studies

Christersson LA, Rosling BG, Dunford RG, Wikesjö UM, Zambon JJ, Genco RJ. Monitoring of subgingival *Bacteroides gingivalis* and *Actinobacillus actinomycetemcomitans* in the management of advanced periodontitis. Adv Dent Res 1988;2:382–8	No randomization, no comparable control group
Campbell D. Enhanced maintenance using ultrasonics and full-mouth decontamination with polyvinyl pyrrolidone plus iodine. (Abstract Academy Report 1999 Annual Meeting)	No control group
Cigana F, Kerebel B, David J, Doumenjou F, Da Costa Noble R. [A clinical and histological study of the efficacy of betadine on gingival inflammation.] J Biol Buccale 1991;19:173–84	No scaling and root planing or surgery conducted
Collins JG, Offenbacher S, Arnold RR. Effects of a combination therapy to eliminate *Porphyromonas gingivalis* in refractory periodontitis. J Periodontol 1993;64:998–1007	Use of antibiotics
David AT, Kurien S, Udupa N, Verma BR. Formulation and evaluation of controlled release dental implants of povidone iodine for periodontitis. Indian J Dent Res 1994;5(3):101–4.Links	No scaling and root planing or surgery conducted
Kövesi G. [The use of Betadine antiseptic in the treatment of oral surgical, parodontological and oral mucosal diseases.] Fogorv Sz 1999;92(8):243–50	No scaling and root planing or surgery conducted
Forabosco A, Galetti R, Spinato S, Colao P, Casolari C. A comparative study of a surgical method and scaling and root planing using the Odontoson. J Clin Periodontol 1996;23:611–4	No scaling and root planing or surgery conducted
Grossi SG, Skrepcinski FB, DeCaro T, Robertson DC, Ho AW, Dunford RG, Genco RJ. Treatment of periodontal disease in diabetics reduces glycated hemoglobin. J Periodontol 1997;68:713–9	Use of antibiotics
Hagiwara S, Ogura N, Kuchira M, Seki T, Ishikawa I. [Effect of subgingival plaque control by a direct irrigation technic. I. The clinical and microbiological changes after the irrigation with distilled water or 1/30 diluted iodine complex solution] J Clin Okubyo Gakkai Zasshi 1988;55:492–501	No scaling and root planing or surgery conducted
Slots J, Rosling BG. Suppression of the periodontopathic microflora in localized juvenile periodontitis by systemic tetracycline. Periodontology 1983;10:465–86	Disinfection protocol without PVP-iodine
Heller P. [Treatment of inflammatory periodontal disease with Dontisolon (tested by smears and staining with Schiller's iodine solution).] DDZ 1965;19:317–26	Disinfection protocol without PVP-iodine
Kligerman BA, Bissada NF. Clinical study of iodine as a chemotherapeutic agent for the control of dental plaque and gingivitis in man. J Periodontol 1975;46:478–87	No scaling and root planing or surgery conducted
Leonhardt A, Bergström C, Krok L, Cardaropoli G. Microbiological effect of the use of an ultrasonic device and iodine irrigation in patients with severe chronic periodontal disease: a randomized controlled clinical study. Acta Odontol Scand 2007;65:52–9	Disinfection protocol without PVP-iodine
Betadine mouthwash and gargle (Announcement). South African Medical Journal 1974;48:1089	No scaling and root planing or surgery conducted
Ribeiro EDP, Bittencourt S, Sallum EA, Nociti Jr FH, Sallum AW, Casati MZ. Povidone-iodine associated with non-surgical therapy in bifurcation lesions (Abstract). Brazilian Journal of Oral Sciences 2005;14, 4	No assessment or presentation of clinical parameters
Rosling BG, Slots J, Christersson LA, Genco RJ. Topical chemical antimicrobial therapy in the management of the subgingival microflora and periodontal disease. J Periodont Res 1982;17:541–3	Disinfection protocol without PVP-iodine
Rosling BG, Slots J, Webber RL, Christersson LA, Genco RJ. Microbiological and clinical effects of topical subgingival antimicrobial treatment on human periodontal disease. J Clin Periodontol 1983;10:487–514	Disinfection protocol without PVP-iodine
Salle C, Mautone JF, Pita J. Iodine System in the treatment of the Marginal Periodontitis. Journal of Dental Research 1983;62, 516	No assessment or presentation of clinical parameters
Trachtenberg B. [Treating chronic inflammations of the periodontium by iodine ionization]. Czas Stomatol. 1966;19:621-6	Disinfection protocol without PVP-iodine

Table 1. (Continued)

Ueda M, Teranishi Y, Yamamoto M, Ohno S, Kobayashi R, Ogata C, Ushijima S, Nakagaki N, Kawasaki H, Kawashima E, *et al.* [A study of ultrasonic scaling in combination with povidone-iodine solution]. Nippon Shishubyo Gakkai Kaishi 1990;32:309–19	No randomization
Wang D, Koshy G, Nagasawa T, Kawashima Y, Kiji M, Nitta H, Oda S, Ishikawa I. Antibody response after single-visit full-mouth ultrasonic debridement versus quadrant-wise therapy. J Clin Periodontol 2006;33:632–8. Epub 2006 Jul 20	No assessment or presentation of clinical parameters
Witzenberger T, O'Leary TJ, Gillette WB. Effect of a local germicide on the occurrence of bacteremia during subgingival scaling. J Periodontol 1982;53:172–9	No assessment or presentation of clinical parameters
Wolff LF, Bakdash MB, Pilhlstrom BL, Bandt CL, Aeppli DM. The effect of professional and home subgingival irrigation with antimicrobial agents on gingivitis and early periodontitis J Dent Hyg 1989;63:222–5, 241	No scaling and root planing or surgery conducted
Xiang X. Zhu L. Li C. Clinical effects of subgingival irrigation combined with four different drugs in patients with advanced periodontitis. Medical Journal of Wuhan University 2005; 26:509–511	Disinfection protocol without PVP-iodine
Haffajee AD, Patel M, Socransky SS. Microbiological changes associated with four different periodontal therapies for the treatment of chronic periodontitis. Oral Microbiol Immunol 2008;23:148–57.	Disinfection protocol without PVP-iodine

PVP-iodine, povidone-iodine.

Table 2. Data sources for weighting of the studies

Author, year of publication	Study design	Patients (total)	Patients (total after drop-out)	Patients per group		Sites per patient	Sites total	Sites per test group
				Test	Control			
Rosling 2001	P	223	190	67	123	≥ 2	≥ 380 (≥ 2 × 190)	≥ 134
Hoang 2003	Sm	16	16	16	16	≥ 16 (×2)	≥ 32	≥ 16
Koshy 2005	P	36	36	12	12	≥ 2	≥ 48	≥ 24
Del Peloso Ribeiro 2006	P	48	44	23	21	≥ 1	57	26
Leonhardt 2006	Sm	20	20	20	20	≥ 1 × 4	≥ 40	≥ 20
Forabosco 2006	P	60	60	20	20	≥ 7	≥ 280	≥ 140
Zanatta 2006	P	45	40	15	12	≥ 8	≥ 512	≥ 270

P, parallel design; Sm, split-mouth design.

data were not fully reported (31). In all studies, the mean baseline values for the periodontal probing depth of control and test sites were similar. They ranged between 3.9 ± 0.9 mm and 5.96 ± 1.16 mm. After 3 mo the periodontal probing depth values ranged from 2.7 to 4.0 mm for the test sites and from 2.9 to 4.5 mm for the control sites (Fig. 2, Table 6).

The meta-analyses performed at the end of the studies' follow-up periods showed a statistically significant additional effect of PVP-iodine, with regard to periodontal probing depth change, of 0.28 mm (95% CI: 0.08–0.48) ($p = 0.007$, Fig. 3). Effect-size indices ranged from 0.2 to 0.48.

For the 3 mo follow-up, the additional effect for PVP-iodine in the meta-analysis for three evaluable studies was 0.23 mm (95% CI: −0.03 to 0.48) (Fig. 2).

Table 2 shows the data according to the number of patients. An analysis based on the number of pockets was statistically not possible because we could not account for the within-person variability when more than one pocket was treated.

Effects of iodine on secondary outcomes

Table 7 shows how attachment levels changed from baseline to the 3-mo follow-up and to the final follow-up. At the end of the studies, the differences between test and control groups in attachment level changes ranged from −0.13 mm (altogether two studies favoring the control group) to 0.95 mm (with four studies favoring the test group). Values for the plaque index and bleeding on probing are given in Tables 8 and 9. The mean values of the plaque index varied at baseline from 3.9 to 61% and were reduced equally for test and control sites. Bleeding on probing scores of initially 27–80% dropped without remarkable differences for both groups.

Table 3. Description of studies

Author, year of publication	Population	Treatment prior to intervention	Intervention test/control	Intervention	Control	Parameter assessment	Investigation period	Maintenance
Rosling, 2001	*n* = 223 (9/31 excluded = losers, advanced periodontitis, healthy, minimum 8 nonmolar teeth, ppd ≥ 6 mm at ≥ 2 teeth/each quadrant, rx bone loss ≥ 40%	Case presentation, oral hygiene instruction, 'hopeless' teeth removed	US-Sc (Odontoson), (local anesthesia) 4–6 60-min visits within 1 wk	PVP-iodine 0.1%	Tap water	Periodontal probing depth (6 sites/tooth, PCP15, AL, plaque index, BoP, gingival index, radiological bone height	12 mo	Supportive periodontal treatment every 3–4 mo, including ScPr at periodontal probing depth ≥ 5 mm with/without iodine
			Parallel design			After 3, 6, 12 mo, annually		
Hoang, 2003	*n* = 16 (3 diabetes II, 1 psychiatric, 1 down), [26,73a] ≥ 1 pocket ≥ 6 mm/each quadrant, 1 pocket per test/control site 7/9 m/f	Mb testing, oral hygiene instruction	ScRp with hand curettes (local anesthesia) ≥ 2 h	PVP-iodine 10%, repeated irrigations for 5 min	Sterile saline	Periodontal probing depth (6 sites/tooth, manual), plaque index, BoP, microbial testing	5 wk	Microbial testing, ScRp except test/control teeth (5 wk)
			Split-mouth design			5 wk		
Koshy, 2005	*n* = 36, [34-66a], ≥ 2 pockets ≥ 5 mm, nonsmokers, moderate-to-advanced chronic periodontitis, 13/23 m/f	1–2× tooth-brushing visits including id	Single-visit US-Sc, supragingival and subgingival (PiezonMaster 400 EMS/Perio slim tip) (local anesthesia)	PVP-iodine 1%	Distilled water	Periodontal probing depth (6 sites/tooth, PCP15), AL, plaque index, BoP, mobility	6 mo	Test-group: 0.05% CHX mouthwash 2×/daily, tongue-brushing, oral hygiene remotivation + professional tooth cleaning 1×/montly without US
			Parallel design			at 1 mo, 3 mo, 6 mo		
Del Peloso Ribeiro, 2006	*n* = 48 (4 fall-outs)) healthy nonsmokers Chronic periodontitis with Class II + III Furcation, BoP+, ≥ 1 tooth with PD ≥ 5 mm, 20/24 m/f	Oral hygiene motivation, information about etiology, removal of plaque-retentive factors	Subgingival instrumentation with ultrasonic device (local anesthesia)	PVP-iodine 10%	Distilled water	Periodontal probing depth (1 site/tooth, PCP15, stents)	6 mo	Professional supragingival plaque control, oral hygiene instruction every 15 d (first month) then once/month. At 3 mo: subgingival ScRp

Table 3. (Continued)

Author, year of publication	Population	Treatment prior to intervention	Intervention test/control	Intervention	Control	Parameter assessment	Investigation period	Maintenance
Leonhardt, 2006	*n* = 20 [39–68a], advanced periodontitis, at least 1 single-rooted with at least 1 PD ≥ 6 mm, BoP+, nonsmokers 8/12 m/f	Information about periodontal condition, supragingival scaling, hygiene instruction for 1 mo brushing/id, when PI ≤ 15% treatment start	Parallel design US-Sc Odontogain (local anesthesia) 4 min/tooth by a dental hygienist	PVP-iodine 0.5% for 5 min/tooth	Sterile saline-solution for 5 min/tooth	At 1 mo, 3 mo, 6 mo Periodontal probing depth (6 sites/tooth, PCP15), plaque index, BoP	6 mo	–
			Split-mouth design			At 6 mo		
Forabosco, 2006	*n* = 60 with adult periodontitis, [35-65a], nonsmokers (for at least 5 years), PD ≥ 5 mm at monoradicular teeth, BoP+, at 7 teeth or more, 25/35 m/f	–	ScRp	Odontoson + PVP-iodine 10%	Odonto-son + NaCl (20)	Periodontal probing depth (manual), AL, BoP, mobility	4 mo	Group-specific ScRp with/without PVP-iodine after 1 mo
Zanatta, 2006	*n* = 45 (5 drop-out: 3 losers ≥ 2 mm), advanced chronic periodontitis, ≥ 8 teeth with periodontal probing depth ≥ 5 mm, BoP+ 27 mo, 18 wk	Removal of supragingival plaque-retention factors, filling of cavities	Parallel design Ultrasonic debridement: 45 min full-mouth	PVP-iodine 0.5%	0.9% NaCl	At 1 mo , 3 mo, 4 mo Periodontal probing depth (6 sites/tooth, PCP15) CAL, plaque index, BoP, recession	3 mo	Oral antiseptics interdicted, clinical parameters 2 wk following initial treatment, at 1 mo, 3 mo
			Parallel design			At 3 mo		

AL, attachment level; BoP, bleeding on probing; CAL, clinical attachment loss; id, interdental; m/f, ratio males/females; PVP-iodine, povidone-iodine; ScRp, scaling and root planing; US, ultrasonic device; PPD, periodontal probing depth; rx, radiological; PCP15, manual probe type; [n, ma], patient age from n to m; Mb, microbiological testing; CHX, chlorhexidine; PI, plaque index; US-Sc, ultrasound scaler.

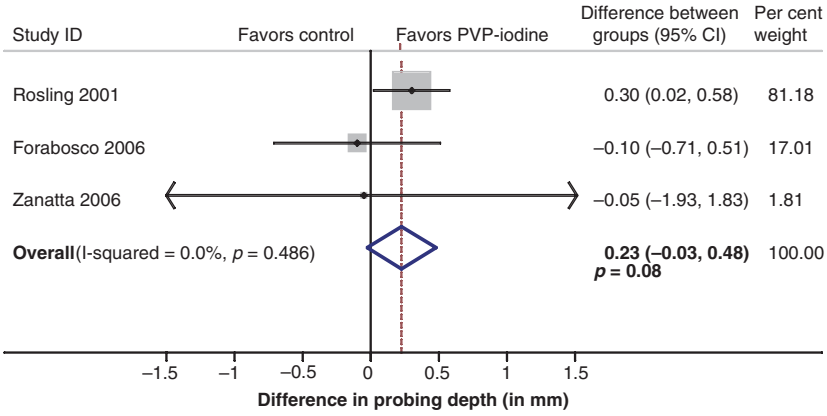

Fig. 2. Studies investigating an additional effect of povidone-iodine (PVP-iodine), 3 mo after intervention.

Table 4. Quality assessment

Author, year of publication	Method of randomization	Concealment	Blinding of the examiner
Rosling, 2001	–[a]	–	–
Hoang, 2003	–	+	–
Koshy, 2005	+ Computer generated, no stratification or balancing of factors	+	+
Del Peloso Ribeiro, 2006	+ Coin toss	–	–
Forabosco, 2006	–	–	+
Zanatta, 2006	–	–	+
Leonhardt, 2006	–	+	+

+, yes; –, claimed without any further information.
[a]confirmed by correspondence with the authors.

Discussion

PVP-iodine has been used in various studies as an antiseptic adjunctive during nonsurgical periodontitis therapy, but inconsistent results have been obtained (26–32,34). Comparing six studies in a meta-analysis, this systematic review showed a small, but statistically significant effect of additional PVP-iodine rinsing during deep scaling and root planing with regard to reduction of periodontal probing depth in patients with chronic periodontitis. In the 3-mo meta-analysis the effect was less pronounced. The results published for clinical attachment gain (Table 7) support the findings for the probing depth (Table 7). Equally distributed values for the oral hygiene indices periodontal index and bleeding on probing showed similar oral hygiene levels in control and treatment groups.

This systematic review was performed strictly according to the guidelines and recommendations of the QUOROM statement for meta-analyses (35).

However, it was not possible to contact the authors of all studies included to obtain more detailed data, which would have been helpful, espe-

Table 5. Development of probing depth: Total investigation period

Author, year of publication	Study period	Prestaging	PVP-iodine rinsing periodontal probing depth (mm)			Control group periodontal probing depth (mm)			d
			Baseline	End of study	Change	Baseline	End of study	Change	
Rosling, 2001	12 mo		3.9 ± 0.9	2.7	1.2	3.7 ± 0.9	2.9	0.8	
Hoang, 2003	5 wk		≥ 6 mm		1.8 ± 1.8	≥ 6 mm		1.6 ± 1.1	
Koshy, 2005	6 mo	Single rooted: mod	5.42 ± 0.1	2.4 ± 0.2	3 ± 0.2	5.43 ± 0.1	2.46 ± 0.5	2.96 ± 0.5	
		Deep	7.92 ± 0.5	3.9 ± 1.4	4.02 ± 1.4	7.74 ± 0.6	3.5 ± 1.4	4.26 ± 1.1	
		Multirooted: mod	5.44 ± 0.2	3.12 ± 0.5	2.34 ± 0.7	5.49 ± 0.2	2.87 ± 0.6	2.62 ± 0.6	
		Deep	8.0 ± 0.6	4.55 ± 1.4	3.44 ± 1.1	8.2 ± 0.5	4.38 ± 0.6	3.81 ± 0.7	
		Tot			1.73 ± 0.6			1.74 ± 0.5	
Del Peloso	6 mo	Mod			1.75 ± 0.91			1.76 ± 1.03	
Ribeiro,		Deep			3.67 ± 1.5			3.35 ± 1.21	
2006		Total	5.96 ± 1.16		2.31	6.61 ± 1.17		2.31	
Leonhardt, 2006	6 mo		100% > 6 mm	84.2% < 6 mm	–	100% > 6 mm	84.2% < 6 mm	–	
Forabosco, 2006	4 mo		5.8	4.0		5.7	4.5		
Zanatta, 2006	3 mo		5.71 ± 0.62	3.18 ± 0.51	2.53 ± 0.50	5.52 ± 0.58	2.95 ± 0.33	2.58 ± 0.60	[0.2;0.48]

Mod, moderate pockets (3–5 mm); PVP-iodine, povidone-iodine; Tot, total collective.

Table 6. Development of probing depth: at 3 mo of observation period

Author, year of publication	Prestaging	PVP-iodine rinsing Periodontal probing depth (mm)			Control group Periodontal probing depth (mm)		
		Baseline	After 3 mo	Change	Baseline	After 3 mo	Change
Rosling, 2001		3.9 ± 0.9	2.8	1.1	3.7 ± 0.9	2.9	0.8
Hoang, 2003				–			–
Koshy, 2005				–			–
Del Peloso	Mod			1.85 ± 0.87			1.70 ± 1.06
Ribeiro, 2006	Deep			3.84 ± 1.33			3.71 ± 0.89
Leonhardt, 2006		100% > 6 mm	68.4% < 6 mm		100% > 6 mm	78.9% < 6 mm	
Forabosco, 2006		5.8	3.4		5.7	4.2	
Zanatta, 2006		5.71 ± 0.62	3.18 ± 0.51	*2.53 ± 0.50*	5.52 ± 0.58	2.95 ± 0.33	2.58 ± 0.60

Mod, moderate pockets (3–5 mm); PVP-iodine, povidone-iodine.
(Hoang 2003 and Koshy 2005; no results after 3 mo reported).

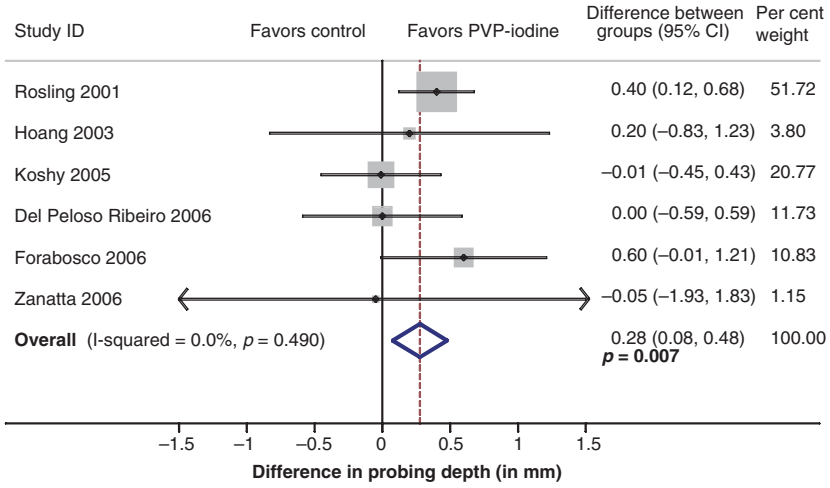

Fig. 3. Studies investigating an additional effect of povidone-iodine (PVP-iodine), at the study end.

Table 7. Development of attachment level

Author, year of publication	Study period	Prestaging	PVP-iodine rinsing Clinical attachment level (mm)			Control group Clinical attachment level (mm)		
			Baseline	Change after 3 mo	Change end of study	Baseline	Change after 3 mo	Change end of study
Rosling, 2001	12 mo	–		0.44	0.4		0.24	0.18
Hoang, 2003	5 wk	–	–	–	–	–	–	–
Koshy, 2005	6 mo	–			1.07 ± 0.4			1.2 ± 0.3
Del Peloso Ribeiro, 2006	6 mo	Mod		1.00 ± 0.87	0.80 ± 0.87		0.94 ± 1.06	0.76 ± 1.03
		Deep		2.17 ± 1.47	2.17 ± 1.37		2.08 ± 1.11	1.93 ± 1.07
		Tot	8.56 ± 1.21			9.03 ± 1.46		
Leonhardt, 2006	6 mo			0.5 ± 1.1	0.7 ± 1.2		0.6 ± 0.3	0.6 ± 0.9
Forabosco, 2006	4 mo		3.1	1.3	1.3	3.4	0.4	0.4
Zanatta, 2006	3 mo		6.12 ± 0.65	1.94 ± 0.70	1.94 ± 0.70	5.94 ± 0.75	1.99 ± 0.92	1.99 ± 0.92

Mod, moderate pockets (3–5 mm); PVP-iodine, povidone-iodine; Tot, total collective.

cially in the case of the Leonhardt study (31), which had to be excluded from the meta-analysis as a result of insufficient data reporting of the probing depth. Also, the studies included in this review were of low to moderate quality, according to the classification of Schulz (Table 2) (36). The latter overview showed that studies which do not report the sensitive details of subverting the purpose of randomization and allocation conceal-

Table 8. Development of the plaque index

Author, year of publication	Study period	Prestaging	PVP-iodine rinsing Plaque index (%)			Control group Plaque index (%)		
			Baseline	3 mo	End of study	Baseline	3 mo	End of study
Rosling, 2001	12 mo		30 ± 33	8 ± 16	8 ± 14	30 ± 29	4 ± 10	6 ± 15
Hoang, 2003	5 wk		–	–	–	–	–	–
Koshy, 2005	6 mo				Δ14.66 ± 12.8			Δ13.54 ± 13.2
Del Peloso Ribeiro, 2006	6 mo		47.11 ± 14.58	32.64 ± 12.24	31.15 ± 15.59	47.35 ± 16.94	34.73 ± 14.94	34.02 ± 13.78
Leonhardt, 2006	6 mo		6.6 ± 14.0	11.8 ± 25.5	9.2 ± 23.9	3.9 ± 9.4	2.6 ± 7.9	2.6 ± 7.9
Forabosco, 2006	4 mo		–	–	–	–	–	–
Zanatta, 2006	3 mo		60 ± 23	18 ± 6	18 ± 6	61 ± 18	22 ± 17	22 ± 17

PVP-iodine, povidone-iodine.

Table 9. Development of bleeding on probing

Author, year of publication	Study period	Prestaging	PVP-iodine rinsing Bleeding on probing (%)			Control group Bleeding on probing (%)		
			Baseline	3 mo	End of study	Baseline	3 mo	End of study
Rosling, 2001	12 mo		69 ± 31	–	22 ± 22	66 ± 34		25 ± 21
Hoang, 2003	5 wk		–	–	–	–	–	–
Koshy, 2005	6 mo		–		56.4 ± 13.5	–	–	61.9 ± 13.1
Del Peloso Ribeiro, 2006	6 mo		27.52 ± 11.69	17.48 ± 8.19	16.48 ± 8.69	34.42 ± 11.63	18.83 ± 9.97	18.40 ± 6.01
Leonhardt, 2006	6 mo		80.3 ± 15.3	36.8 ± 24.1	30.6 ± 26.5	78.9 ± 15.1	34.2 ± 26.5	31.9 ± 28.2
Forabosco, 2006	4 mo		–	–	80%	–	–	50%
Zanatta, 2006	3 mo		43 ± 12	19 ± 18	19 ± 18	46 ± 10	18 ± 7	18 ± 7

PVP-iodine, povidone-iodine.

ment have been associated with larger treatment effects.

We observed little heterogeneity ($I^2 = 0$) across studies: the initial probing depths of intervention and control groups were similar, and the pocket depth reduction in the control groups, from 0.8 mm (for pockets of initially 3.9 ± 0.9 mm) (26) to 2.31 mm (from pockets initially 5.96 ± 1.16 mm) (30) were within the accepted range published previously (24,37).

Effect sizes for additional rinsing with PVP-iodine were between 0.2 and 0.48 and, according to Cohen's effect size (33), were small (≥ 0.2) to moderate (≥ 0.5). Indirect comparison of the adjunctive use of PVP-iodine with other additional treatment types indicates that it is likely to have an effect similar to that of systemic administration of the antibiotic spiromycin (additional probing depth reduction of 0.3 mm) (10,38,39) or a full-mouth disinfection regimen in single-rooted teeth (additional probing depth reduction of 0.3 mm) (40,41).

However, the results of the individual studies were inconsistent. Two different reasons for this must be taken into consideration. First, the two studies supporting an overall favorable effect of PVP-iodine use (26,27) investigated single-rooted teeth, whereas two of the studies with a less favorable outcome (30,32) explicitly referred to multirooted teeth. Notably, one of the latter studies found a statistically significant additional benefit for PVP-iodine in a subgroup with "deep" sites (periodontal pocket depth > 5 mm) for all re-evaluation time-points (30). Another study that investigated the effect of PVP-iodine during scaling and root planing on single-rooted teeth was excluded from the review as a result of missing randomization, but also confirmed an additional benefit for this antiseptic (34). The conclusion of this comparison is that the treatment of single-rooted teeth with PVP-iodine might result in a more pronounced additional probing depth reduction than the overall results. Second, the two studies that showed an additional benefit for PVP-iodine use (26,27) had another relevant fact in common: both studies reported a second scaling and root planing of the test and control teeth, with or without the use of PVP-iodine, 1 mo (27) or 3–4 mo after the first intervention (26). Likewise, a second scaling was performed after 3 mo by Del Peloso Ribeiro *et al*. (30), and favorable results were obtained for PVP-iodine use in deep pockets. Therefore, a second scaling and root planing carried out at least 1 mo after the first instrumentation seems to result in a significant additional pocket depth reduction potential if PVP-iodine is used, compared with a water or a saline rinse. This finding corresponds well with investigations demonstrating recolonization of the periodontal pocket between 4 wk (42) and 9 wk (43) after scaling and root planing, which is successively followed by a redeepening of the periodontal pockets.

Interestingly, no correlation was found between the concentration of PVP-iodine used in the studies and

additional benefit in terms of periodontal probing depth reduction. Furthermore, no correlation was found between the contact time and reduction in periodontal probing depth. This finding contrasts with the assumption of a previous review on the effect of PVP-iodine, where the concentration and contact time were suspected to be crucial parameters for success with the iodine rinse (44). The lack of correlation between the concentration of PVP-iodine and the extent of periodontal probing depth reduction is consistent with findings stating that the maximum bactericidal effect occurs at a low concentration of PVP-iodine, of 0.1% (44) because of the higher rate of release of the iodine in the PVP complex (45). After placing PVP-iodine in the periodontal pockets, preparations that are more highly concentrated become diluted by the gingival crevicular fluid and blood, until a low concentration of 0.1% is presumably reached.

The exclusion of smokers in some studies did not result in different outcomes in pocket depth reductions. Even in studies excluding smokers (27,29,30) the results were discordant about an additional benefit of PVP-iodine use.

In the publications examined for this review we could not find any reports on adverse effects following PVP-iodine use. Although dermatological studies indicate skin irritations after long-term use of PVP-iodine (46), adverse effects for this antiseptic are considered to be rare and mild (47). Furthermore, there is no known bacterial resistance to PVP-iodine (23,48,49). The chairside application of PVP-iodine does not cause permanent staining of the dental soft and hard tissues. Unpleasant staining of clothing and of the dental unit may be removed by the application of an aqueous solution of sodium thiosulphate.

Nevertheless, the topical application of PVP-iodine during nonsurgical scaling and root planing seems a promising way in which to improve clinical outcomes. However, further clinical studies with PVP-iodine are needed to investigate and to improve its beneficial effect in the therapy of periodontitis. This review indicated, first, that the assumption that concentration is a key parameter for povidone's effectiveness could not be verified. Second, investigations with a very similar study design are discordant on whether there really is an additional effect when PVP-iodine is used and, if there is, about its extent. Third, the results of this review are limited to the data of not more than six randomized controlled clinical trials. Therefore, we need further clinical studies that investigate treatment variations (such as repeated applications) to render the additional benefit of the inexpensive and nonhazardous broad-spectrum antiseptic PVP-iodine as reliable. Furthermore, the effect of repeated rinsing or the application of PVP-iodine in a pharmaceutical form with a higher substantivity should be investigated.

Conclusion

The adjunctive use of PVP-iodine during scaling and root planing significantly increased clinical pocket depth reduction; however, the clinical significance of this was small.

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