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Supportive periodontal therapy of furcation sites: non-surgical instrumentation with or without topical doxycycline

Bettina Dannewitz[1,2], Katherine Lippert[2], Niklaus P. Lang[3,4], Maurizio S. Tonetti[3] and Peter Eickholz[2]

[1]Section of Periodontology, Department of Conservative Dentistry, Clinic for Oral, Dental and Maxillofacial Diseases, University Hospital Heidelberg, Heidelberg, Germany; [2]Department of Periodontology, Center for Dental, Oral, and Maxillofacial Medicine (Carolinum), Hospital of the Johann Wolfgang Goethe University Frankfurt/Main, Frankfurt/Main, Germany; [3]European Research Group on Periodontology (ERGO Perio), Genova, Italy; [4]Prince Philip Hospital, University of Hong-Kong, Hong-Kong

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Abstract

Objectives: Evaluation of the clinical effect of topical subgingival application of doxycycline gel adjunctively to scaling and root planing (SRP) at furcation sites during supportive periodontal therapy (SPT).

Material and Methods: In 39 SPT patients exhibiting at least four pockets $\geqslant$5 mm with bleeding on probing, SRP was rendered in all pockets $\geqslant$4 mm. Additionally, 14% doxycycline gel was applied subgingivally in 20 patients after random assignment (SRP&DOXY). Clinical parameters were assessed at baseline, 3, 6, and 12 months after therapy. Additional benefit of topical doxycycline was evaluated as a short-term (3 months) improvement of furcation involvement and influence on the frequency of re-instrumentation up to 12 months.

Results: A total of 323 furcation sites (class 0: 160; class I: 101; class II: 18; and class III: 44) were treated (SRP: 165, SRP&DOXY: 158). SRP&DOXY resulted in better improvement of furcation involvement than SRP alone 3 months after treatment ($p = 0.041$). However, SRP&DOXY failed to show a significant difference between both groups in the number of re-instrumentations.

Conclusion: Single subgingival application of doxycycline in addition to SRP had a short-term effect on furcation involvement. However, it failed to reduce the frequency of re-instrumentation up to 12 months at furcation sites.

Key words: randomised controlled clinical trial; furcation involvement; supportive periodontal treatment; topical subgingival doxycycline

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Furcation-involved molars respond less favourably to periodontal therapy than molars without furcation involvement or single-rooted teeth and are at a greater risk for further attachment loss (Nordland et al. 1987, Loos et al. 1989, Wang et al. 1994) compared with other teeth. This problem was also described by Kalkwarf et al. (1988), who reported the success of different surgical and non-surgical treatment modalities on 158 molars. During the 2-year observation period, the horizontal defect in the furcation area increased independently of the therapy performed.

Numerous factors contribute to a more severe disease progression in furcation-involved molars, recurrent periodontal infection, and as a result an inferior long-term prognosis of these teeth (McGuire & Nunn 1996, Dannewitz et al. 2006, Pretzl et al. 2008). These factors include morphological features such as enamel projections and accessory pulpal canals into the furcation (Pontoriero et al. 1989), anatomy that impedes accessibility for individual oral hygiene in the molar region (Lang et al. 1973), and professional root debridement (Fleischer et al. 1989).

Hirschfeld & Wasserman (1978) examined retrospectively the periodontal conditions of 600 patients who had been previously treated for 15–55 years. Over the 22-year average period of maintenance, 7.1% of all teeth were lost due to periodontal causes. The tooth loss rate of those teeth with furcation involvement was much higher (31%). Similar results were reported by McFall (1982), who observed an overall tooth

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loss of 10% of all teeth and 57% of teeth with probable furcation involvement over a maintenance period of 19 years.

Topical subgingival application of antibiotics may improve the results of non-surgical periodontal treatment (Hanes & Purvis 2003). This has been observed after use of a 14% doxycycline gel in untreated active periodontal therapy (APT) (Eickholz et al. 2002) and SPT patients (Lang et al. 2005). Further, for SPT patients, subgingival application of this doxycycline gel showed clinical results at least as good as scaling and root planing (SRP) (Eickholz et al. 2005).

Thus, topical subgingival use of antimicrobial substances could serve as an effective adjunct to re-instrumentation of furcation sites during SPT. To date, only a few studies have addressed the issue of topical antibiotics in furcations of SPT patients: tetracycline fibres as an adjunct to SRP for treatment of class II furcation defects resulted in better reduction of bleeding on probing (BOP) and probing pocket depth (PPD) 3 months after therapy. However, this effect did not last up to 6 months and change of horizontal attachment loss (PAL-H) or degree of furcation involvement was not assessed (Tonetti et al. 1998). Subgingival application of a doxycycline gel compared with SRP at furcation sites with PPD $\geqslant$ 6 mm resulted in equivalent PPD reduction and vertical attachment (PAL-V) gain as non-surgical instrumentation 9 months after therapy. However, the study failed to assess baseline and 9-month PAL-H gain or class of furcation involvement (Garrett et al. 1999).

The aim of the present study was to evaluate the clinical effect of topical subgingival application of a 14% doxycycline gel adjunctive to SRP at furcation sites during supportive periodontal therapy (SPT).

Material and Methods

Patients

Thirty-nine patients under SPT at the Section of Periodontology of the Department of Conservative Dentistry, Clinic for Oral, Dental and Maxillofacial Diseases at the University Hospital of Heidelberg were invited to participate in this randomized single-blinded controlled clinical trial. A flow chart of the study is provided in Fig. 1.

Self-reported smoking history was taken. A patient was classified as an active smoker if he or she smoked more than 10 cigarettes per day regularly. Former smokers were subjects who had previously been smokers but had stopped their habit before the beginning of periodontal therapy. For active and former smokers, the packyears were calculated to assess their lifetime smoking exposure.

Participants had to fulfil the following inclusion criteria:

- Male and female patients of Caucasian origin and at least 18 years of age.
- Recurrent moderate to severe periodontitis (no surgical treatment during the last 24 months) periodically treated for maintenance of periodontal health achieved by the initial periodontal therapy during a minimum period of 2 years.
- Effective individual oral hygiene [plaque control record (PCR) $<25\%$] (O'Leary et al. 1972).
- Each patient had to exhibit at least four teeth with residual PPDs of $\geqslant 5$ mm and a positive BOP. The test teeth ideally should be located in different quadrants.
- At least one furcation site requiring retreatment during SPT.
- Written consent after comprehensive information regarding the risks and benefits as well as the procedures of the clinical trial.
- Females of non-child-bearing age or taking contraceptives were also included.

The following criteria prevented a patient from inclusion:

- Known allergy or other severe adverse reactions to tetracycline in general and especially doxycycline or polyethylene glycol-lactid/glycolid copolymer gel.
- Participation in another clinical trial within the last 4 weeks before baseline examination.
- Failure to provide written informed consent.
- Patients who were expected to show a lack of compliance (mean BOP $>25\%$, PCR $>25\%$).
- Clinically relevant psychological disorders.
- Known alcohol abuse.

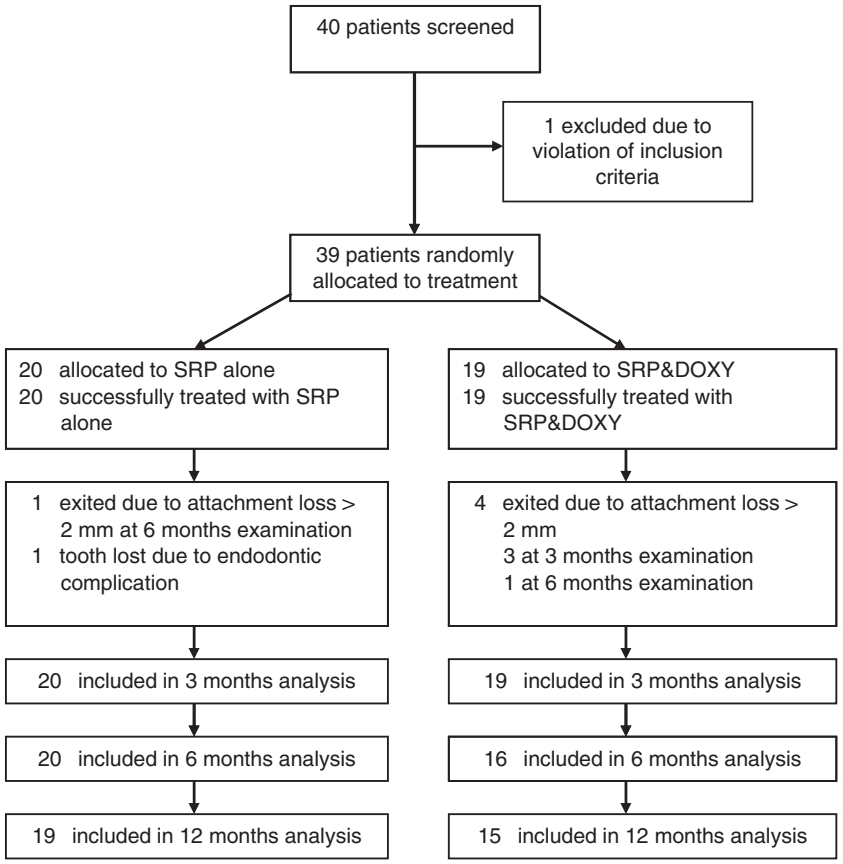

Fig. 1. Study flow chart.

- Chronic diseases of the liver (self-reported).
- Diseases of the kidney (self-reported).
- Known severe chronic or malignant diseases.
- Hematologic disorders (self-reported).
- Disorders of the haematopoietic systems of unknown origin (self-reported).
- Known HIV infection.
- Anticoagulative therapy, gastrointestinal diseases, lactation period (self-reported).
- Local and/or systemic antibiotic therapy within the last 6 months before the baseline examination of the study.

Not more than 50% of the patients should be active smokers. The study had been approved by the Institutional Review Board for Human Studies of the Medical Faculty of the University of Heidelberg (Approval number L-063/2003).

Examinations

Full-mouth plaque scores (FMPS) were recorded as the percentage of total surfaces (six aspects per tooth) that revealed the presence of plaque (O'Leary et al. 1972). BOP was assessed dichotomously at a force of 0.3 N with a manual pressure-sensitive probe (Kerr-HAWE Click Probe®). Full-mouth bleeding scores (FMBS) were calculated as the percentage of total surfaces (six aspects per tooth).

PPD and marginal recession (REC) were recorded to the nearest millimetre by a single investigator (P. E.) at six sites per tooth (mesiobuccal, midbuccal, distobuccal, disto-oral, midoral, and mesio-oral). All measurements were taken with the pressure-sensitive manual periodontal probe at 0.3 N with a PCP-UNC 15 probe head (Hu-Friedy, Chicago, IL, USA). The horizontal attachment loss (PAL-H) within a furcation was assessed at all furcation sites of maxillary first pre-molars (mesial, distal), maxillary molars (buccal, disto-oral, and mesio-oral), and mandibular molars (buccal, lingual) using a curved, scaled Nabers probe [Q-2N (SS+SSC) Nabers colour coded, Hu-Friedy] and the defect was characterized according to the following classification (Hamp et al. 1975, Eickholz & Staehle 1994):

Degree 0: The furcation is not probable.
Degree I: Horizontal loss of periodontal tissue support up to 3 mm.
Degree II: Horizontal loss of support exceeding 3 mm, but not encompassing the total width of the furcation area.
Degree III: Horizontal ''through-and-through'' destruction of the periodontal tissue in the furcation.

Clinical examinations were performed before subgingival instrumentation (baseline), 3, 6, and 12 months after baseline.

Randomization and therapy assignment

The reported sample is a subsample of a larger multicentre study (Lang et al. 2005). Exclusively, the Heidelberg centre had included examination of furcation involvements. According to a table of random digits, each patient was assigned to one of two treatment modes:

- Either test [SRP&DOXY: subgingival instrumentation (SRP) of all sites $\geqslant$4 mm *with* additional subgingival application of a 14% doxycycline gel: doxycycline-hyclat in a polyethylene glycol–lactid/glycolid copolymer gel (Ivoclar Vivadent AG, Schaan, Liechtenstein)] or
- Control (SRP: subgingival instrumentation of all sites $\geqslant$4 mm *alone*).

Randomization was provided by a central study registrar essentially as described (Cortellini et al. 2001). Treatment allocation was concealed to the therapist using an opaque envelope that was to be opened only upon completion of the mechanical instrumentation portion of the treatment. Allocation was concealed to the independent examiner by preventing access to the relevant portions of the clinical record and data collection forms.

SPT

After completion of APT (anti-infective and surgical periodontal treatment), patients had been enrolled in SPT and were scheduled on 3–6-month intervals. Before recruitment into this study, all patients had experienced at least 2 years of SPT.

At all sites exhibiting PPD $\geqslant$4 mm, SRP was performed using a sonic scaler (Sonicflex, KaVo, Biberach, Germany) with Sonicflex paro tips 60–62 (KaVo). After mechanical instrumentation was accomplished, the encoded envelope was opened. If the respective patient was assigned to control, no further therapy was provided. If the patient was assigned to test, 14% doxycycline gel was applied subgingivally (Eickholz et al. 2002). All patients were treated by the same (B. D.) experienced periodontal specialist.

At each re-examination (3, 6, and 12 months after baseline) all sites exhibiting PPD $\geqslant$4 were debrided subgingivally by B. D. using a sonic scaler (Sonicflex) (re-instrumentation).

Termination criteria

A participant was removed from the study if, despite SPT, progression of periodontal destruction was observed. Progression of periodontal destruction was defined as attachment loss $>$2 mm or an increase of PPD $>$2 mm. Patients were removed from the study if they reported or exhibited adverse events.

Data analysis

All data were entered in duplicate with a time interval of 4 weeks (K. L.) and proofed for entry errors. PAL-V was calculated by addition of PPD and recession.

The patient was looked upon as a statistical unit. The main outcome variable was the short-term (3 months after therapy) change of furcation involvement. The secondary outcome variable was the number of re-instrumentations at the 3-, 6-, and 12-month re-examinations (SPT appointments). All other variables (PPD, PAL-V, PAL-H, and FMBS) were control parameters. Only PPD and PAL-V measurements at furcation sites that were scheduled for subgingival debridement at baseline were entered into the analysis. The means and standard deviations of all control parameters were calculated for SRP and SRP&DOXY at each examination. For PAL-H, means and standard deviations were calculated for the whole sample and separately for baseline furcation degrees 0 and I. Accounting for the small number of degree II furcation lesions in the test group separate analysis for degree II lesions was not performed. Comparisons were made using paired *t*-tests.

The percentages of change of furcation involvement from baseline (degrees

increase or decrease) were calculated for each examination time point for the whole sample and for each baseline furcation degree separately.

Different patients contributed different numbers of defects to this study. To identify the factors influencing the therapeutic benefits, the primary and secondary endpoints were analysed by application of a multilevel regression model (Goldstein 1995, Goldstein et al. 2002). For this analysis the basic level ''site'' was nested in the upper level ''patient'' and patient effects on the outcome were assumed to be random. The following influencing factors were entered in the analysis to explain the dependent variable change of furcation involvement after 3 months: therapy (SRP or SRP&DOXY), and baseline furcation degree. Therapy was defined by indicator variables.

All patients who had been recruited and were treated according to the study protocol were considered as an intent-to-treat (ITT) population. All patients who completed at least one of the three re-examinations (3, 6, or 12 months) were defined as the safety population.

Results

Forty patients were screened and 39 were entered into the study during the time from July 2003 to May 2004. One screened patient did not have a single furcation site exhibiting PPD $\geqslant 4$ plus BOP at baseline (Fig. 1). Table 1 presents the baseline patient characteristics. Test (SRP&DOXY) and control (SRP) did not demonstrate any statistically significant differences regarding sex, smoking, age, baseline FMPS, and FMBS (Table 1).

A total of 323 furcation sites (class 0: 160; class I: 101; class II: 18; and class III: 44) were treated (SRP: 165, SRP&DOXY: 158) and re-examined 3 months after therapy. In the SRP group, more degree II furcations were treated than in the SRP&DOXY group and degree III furcations vice versa (Table 2). A total of 42 furcation site third molars were treated (35 without furcation involvement, seven with degree I lesions, and none with degree II or III lesions). Five patients were excluded 3 (SRP&DOXY: 3) and 6 months (SRP: 1; SRP&DOXY 1) after baseline due to attachment loss >2 mm. They received rescue therapy according to clinical standards. Attachment losses >2 mm occurred at a total of 14 sites at 13 teeth: eight sites at eight single-rooted teeth, and six sites at five multi-rooted teeth, of which only one site was a furcation site (Table 3). One patient in the SRP group lost a molar between the 3- and 6-month examination due to an endodontic reason.

The control variables PPD and PAL-V at the furcation sites at baseline, 3, 6, and 12 months are given in Tables 4 and 5. Analysis failed to identify statistically significant differences between the SRP and the SRP&DOXY group at any examination. Table 6 presents PAL-H at the furcation sites at baseline, 3, 6, and 12 months and change to baseline for the whole sample as well as for baseline furcation degree 0 and I separately. At baseline and after 3 months, the SRP&DOXY group exhibited a statistically significantly lower PAL-H than the SRP group. In degree I furcation, there is a tendency for more PAL-H gain after 3 months in the SRP&DOXY group ($p = 0.043$).

Most furcations did not exhibit any change of furcation involvement from baseline to 3, 6, and 12 months (SRP: 64.3–66.7%; SRP&DOXY: 71.3–81%) (Tables 7a–c). Three months after baseline both treatments resulted in similar rates of improvement, i.e. reduction of furcation involvement (SRP: 20.6%; SRP&DOXY: 19.6%). However, SRP alone exhibited a higher rate of deterioration, i.e. increase of furcation involvement, (12.7%) than SRP&DOXY (7.0%) (Tables 7a–c). The maximum change was observed in degree I furcations, with an 68.3% (SRP&DOXY) and a 41.7% (SRP) decrease from degree I to 0 at 3 months (Table 7a). Multilevel analysis accounting for therapy mode and degree of furcation involvement showed that SRP&DOXY resulted in better improvement of furcation involvement than SRP alone 3 months after treatment ($p = 0.041$) (Table 8). Six and 12 months after topical subgingival application of the 14% doxycycline gel in the test group, the percentage of sites with decreasing degree of furcation involvement for SRP alone (6 months: 18.3%; 12 months: 16%) was higher than for SRP&DOXY (6 months: 6.9%; 12 months: 11.1%). However, the percentage of sites with increasing degree of furcation involvement for SRP alone (6 months: 15.2%; 12 months: 19.7%) was also higher than for SRP&DOXY (6 months: 12.1%; 12 months: 17.6%) (Tables 7a–c). Thus, on average, there was no statistically significant difference between both treatments 6 and 12 months after baseline (multilevel analyses; data not shown).

More than half of all furcation sites that met the criteria for instrumentation at baseline (all sites $\geqslant 4$ mm) had to be re-instrumented 3, 6, and 12 months later again (Table 9). Additional topical subgingival application of the 14%

Table 1. Patient characteristics

Parameter	SRP ($n = 20$)	SRP&DOXY ($n = 19$)	p
Sex (female)	14	9	0.151
Active smokers	5	5	0.925
Age	50.3 ± 8.2	52.6 ± 9.7	0.492
FMPS	15.7 ± 9.1	15.4 ± 7.2	0.916
FMBS	24.0 ± 9.9	21.2 ± 7.2	0.309

FMPS, full-mouth plaque scores; FMBS, full-mouth bleeding scores; SRP, scaling and root planing.

Table 2. Distribution of furcation involvement at baseline according to jaw (maxilla/mandible) and number of pre-molar furcation sites

Degree of furcation involvement	SRP (20 patients; 165 furcations)	SRP&DOXY (19 patients; 158 furcations)	p
0	77 (46.6%)	83 (52.5%)	0.374
Maxilla (pre-molar)	70 (24)	72 (13)	
Mandible	7	11	
I	60 (36.4%)	41 (26.0%)	0.093
Maxilla (pre-molar)	46 (5)	37 (7)	
Mandible	14	4	
II	14 (8.5%)	4 (2.5%)	0.027
Maxilla (pre-molar)	10 (0)	4 (0)	
Mandible	4	0	
III	14 (8.5%)	30 (19.0%)	0.009
Maxilla (pre-molar)	8 (0)	23 (5)	
Mandible	6	7	

doxycycline gel once at baseline (SRP&DOXY) resulted in better improvement of furcation involvement than SRP alone 3 months after baseline. However, SRP&DOXY failed to result in a significant reduction of the number of re-instrumentations compared with SRP alone during the 12 months of SPT (Table 10).

Discussion

Numerous studies have demonstrated that furcation-involved molars respond less favourably to periodontal therapy than molars without furcation involvement or single-rooted teeth, and are at a greater risk of further loss of attachment than other teeth (Nordland et al. 1987, Kalkwarf et al. 1988, Loos et al. 1989, Wang et al. 1994). More severe disease progression in furcation-involved molars results in an inferior long-term prognosis of these teeth (McGuire & Nunn 1996, Dannewitz et al. 2006, Pretzl et al. 2008). These observations may be explained by an anatomy that impedes accessibility for individual oral hygiene in the molar region (Lang et al. 1973), and professional root debridement (Fleischer et al. 1989). Topical subgingival use of antimicrobial substances could serve as an effective adjunct to re-instrumentation of furcation sites during SPT.

To date, only a few studies have addressed the issue of topical antibiotics in furcations: tetracycline fibres as an adjunct to SRP for treatment of class II furcation defects resulted in better reduction of BOP and PPD 3 months after therapy. However, this effect did not last up to 6 months and change of horizontal attachment loss (PAL-H) or degree of furcation involvement was not assessed (Tonetti et al. 1998). Subgingival application of a doxycycline gel compared with SRP at furcation sites with PPD $\geqslant$6 mm resulted in equivalent PPD reduction and vertical attachment (PAL-V) gain as non-surgical instrumentation 9 months after therapy

Table 3. Termination of study due to attachment loss >2 mm

Patient	Group	Teeth with attachment loss >2 mm	Re-examination after
04	SRP&DOXY	43	3 months
07	SRP	11	6 months
10	SRP&DOXY	35	3 months
20	SRP&DOXY	14 mb, 24 mb, 27 db, 26 do, 43, 35	6 months
22	SRP&DOXY	11, 36 mb/db, 35, 43	3 months

mb, mesiobuccal; db, distobuccal; do, disto-oral.

Table 4. Probing pocket depth (mm)

	Patients	Furcations	SRP	SRP&DOXY	*p*
Baseline	20/19	165/158	4.89 ± 1.01	4.96 ± 1.29	0.182
3 months	20/19	165/158	4.14 ± 1.12	4.03 ± 1.37	0.381
6 months	20/16	164/116	3.99 ± 1.04	3.85 ± 1.12	0.396
12 months	19/15	157/108	4.19 ± 1.18	4.08 ± 1.25	0.410

SRP, scaling and root planing.

Table 5. Vertical probing attachment level (mm)

	Patients	Furcations	SRP	SRP&DOXY	*p*
Baseline	20/19	165/158	5.56 ± 2.20	5.96 ± 2.41	0.368
3 months	20/19	165/158	4.88 ± 2.30	4.88 ± 2.44	0.520
6 months	20/16	164/116	4.71 ± 2.16	4.56 ± 2.30	0.685
12 months	19/15	157/108	4.67 ± 2.12	4.69 ± 2.20	0.506

SRP, scaling and root planing.

Table 6. Horizontal probing attachment level (mm)

	Patients	Furcations	SRP	SRP&DOXY	*p*
All furcation sites					
Baseline	20/19	151/128	1.24 ± 1.57	0.79 ± 1.32	0.012
3 months	20/19	148/127	0.98 ± 1.49	0.46 ± 1.04	0.001
Difference to baseline			0.18 ± 1.42	0.32 ± 1.26	0.380
6 months	20/16	146/96	1.08 ± 1.51	0.76 ± 1.29	0.080
Difference to baseline			0.06 ± 1.27	−0.17 ± 0.86	0.102
12 months	19/15	137/90	1.12 ± 1.43	0.79 ± 1.30	0.077
Difference to baseline			−0.08 ± 1.33	−0.12 ± 1.04	0.806
Baseline furcation degree 0					
Baseline		77/83	0.00	0.00	
3 months and difference to baseline			0.40 ± 1.02	0.20 ± 0.65	0.136
6 months and difference to baseline		77/68	0.37 ± 0.87	0.27 ± 0.75	0.438
12 months and difference to baseline		73/62	0.56 ± 1.18	0.44 ± 0.90	0.491
Baseline furcation degree I					
Baseline		60/41	2.06 ± 0.92	1.96 ± 0.91	0.611
3 months		60/41	1.48 ± 1.60	0.82 ± 1.25	0.028
Difference to baseline			0.58 ± 1.41	1.15 ± 1.31	0.043
6 months		58/26	1.72 ± 1.68	1.73 ± 1.31	0.967
Difference to baseline			0.31 ± 1.38	0.08 ± 1.12	0.450
12 months		54/25	1.62 ± 1.30	1.22 ± 1.26	0.203
Difference to baseline			0.35 ± 1.06	0.58 ± 0.99	0.271

SRP, scaling and root planing.

Table 7a. Change of furcation involvement from baseline to 3 months

	SRP	SRP&DOXY	Total
All furcation sites			
Change of furcation involvement (degrees)	20 patients; 165 furcations	19 patients; 158 furcations	
Increase			
III	0	1 (0.7%)	1
II	1 (0.6%)	0	1
I	20 (12.1%)	10 (6.3%)	30
No change	110 (66.7%)	116 (73.4%)	226
Decrease			
I	31 (18.8%)	28 (17.7%)	59
II	3 (1.8%)	3 (1.9%)	6
Baseline furcation degree 0			
	77 furcations	83 furcations	160
Increase			
III	0	1 (1.2%)	1
II	1 (1.2%)	0	1
I	11 (14.3%)	9 (10.8%)	20
No change	65 (84.5%)	73 (88.0%)	138
Baseline furcation degree I			
	60 furcations	41 furcations	101
Increase			
II	0	0	0
I	6 (10.0%)	0	6
No change	29 (48.3%)	13 (31.7%)	42
Decrease			
I	25 (41.7%)	28 (68.3%)	53
Baseline furcation degree II			
	14 furcations	4 furcations	18
Increase			
I	3 (21.4%)	1 (25%)	4
No change	2 (14.3%)	1 (25%)	3
Decrease			
I	6 (42.9%)	0	6
II	3 (21.4%)	2 (50%)	5
Baseline furcation degree III			
	14 furcations	30 furcations	44
No change	14 (100%)	29 (96.6%)	43
Decrease			
I	0	0	0
II	0	1 (3.3%)	1
III	0	0	0

(Garrett et al. 1999). A clinical placebo-controlled randomized double-blind multi-centre study comparing SRP alone, SRP with additional subgingival application of minocycline microspheres, and SRP with subgingival application of the vehicle reported a statistically significant better PPD reduction 1, 3, 6, and 9 months after treatment in molar teeth for the minocycline group (Williams et al. 2001). However, both studies failed to assess baseline and post-treatment PAL-H or class of furcation involvement. Thus, to date, there do not exist any published data on the effect of topically subgingival antibiotics on furcation involvement.

A clinical placebo-controlled randomized double-blind multi-centre study had compared SRP alone, SRP with an adjunctive subgingival 14% biodegradable doxycycline gel (test), and SRP with an adjunctive vehicle gel (placebo) for APT in anteriors and pre-molars of patients with untreated or recurrent periodontitis. Six months after treatment test therapy resulted in a statistically significantly better PPD reduction and PAL-V gain than SRP alone or SRP plus vehicle (Eickholz et al. 2002). Another randomized single-blind study compared SRP alone with exclusively topically subgingival application of the 14% doxycycline gel for treatment of persisting and recurring pockets in single-rooted teeth during SPT. The 14% doxycycline gel resulted in at least as good a PPD reduction and PAL-V gain as SRP (Eickholz et al. 2005). Thus, the efficacy of the 14% doxycycline gel for topical subgingival application has been demonstrated. However, conclusions regarding the effect of the 14% doxycycline gel in furcation-involved teeth cannot be drawn from these trials because pre-molars with furcation involvement and molars were excluded.

Which parameter is most appropriate to assess treatment success at furcation sites? The main problem of furcation involvement is periodontal destruction between the roots of multi-rooted teeth, i.e. horizontal attachment loss. Measurement of horizontal probing attachment levels (PAL-H) provides the most precise measurement. However, PAL-H cannot be measured at degree III furcation sites (Eickholz & Staehle 1994). Thus, using PAL-H as an outcome variable, degree III furcations are not covered. Additionally, different degrees of furcation involvement are related to different levels of prognosis (McGuire & Nunn 1996, Dannewitz et al. 2006). Using furcation degrees as the main outcome, variable degree III lesions are covered and a relation to prognosis may be deduced.

In the present study, either treatment was provided for 4 mm pockets already. However, an earlier study had shown that the additional effect of the doxycycline gel is more pronounced at deeper pockets (Eickholz et al. 2002). Thus, only patients exhibiting at least four teeth with PPD $\geqslant$5 mm were included in the study to be able to observe clear effects.

In the present study, at most sites, furcation involvement did not change after therapy. Evidently, furcation sites without furcation involvement can only change if deterioration occurs, i.e. increase of furcation involvement. However, at least 75% of degree 0 furcations in both groups did not change up to 12 months after baseline therapy. Vice versa, sites with degree III involvement at baseline may change only if furcation involvement decreases. However, in degree III furcations, only three changes were observed over the whole observation period. Keeping in mind the fact that through-and-through furcations are almost impossible to close at least using non-surgical techniques, these improvements may be interpreted as measurement errors. Both therapy options resulted in similar rates of improvement after 3 months. However, SRP alone exhibited a higher rate of increased

Table 7b. Change of furcation involvement from baseline to 6 months

	SRP	SRP&DOXY	Total
All furcation sites			
Change of furcation involvement (degrees)	20 patients; 164 furcations	16 patients; 116 furcations	
Increase			
III	0	1 (0.9%)	1
II	2 (1.2%)	3 (2.6%)	5
I	23 (14.0%)	10 (8.6%)	33
No change	109 (66.5%)	94 (81.0%)	203
Decrease			
I	29 (17.7%)	8 (6.9%)	37
II	1 (0.6%)	0	1
Baseline furcation degree 0			
	77 furcations	69 furcations	146
Increase			
III	0	1 (1.4%)	1
II	0	0	0
I	14 (18.1%)	9 (13.0%)	23
No change	63 (81.9%)	59 (85.6%)	122
Baseline furcation degree I			
	60 furcations	29 furcations	89
Increase			
II	2 (3.3%)	3 (10.3%)	5
I	6 (14.6%)	0	6
No change	30 (64.3%)	18 (71.3%)	48
Decrease			
I	22 (13.4%)	8 (11.1%)	30
Baseline furcation degree II			
	14 furcations	3 furcations	17
Increase			
I	3 (21.4%)	1 (33.3%)	4
No change	3 (21.4%)	2 (66.7%)	5
Decrease			
I	7 (50.0%)	0	7
II	1 (7.2%)	0	1
Baseline furcation degree III			
	13 furcations	15 furcations	28
No change	13 (100%)	15 (100%)	28
Decrease			
I	0	0	0
II	0	0	0
III	0	0	0

furcation involvement after 3 months than SRP&DOXY. Multilevel analysis accounting for therapy mode and degree of furcation involvement revealed that SRP&DOXY on average resulted in better improvement of furcation involvement than SRP alone 3 months after treatment. Thus, SRP&DOXY was beneficial by providing less progression of furcation involvement. Six and 12 months after baseline treatment, changes of furcation involvement were similar for both treatment groups. This is in agreement with another study reporting better clinical results (PPD, BOP) 3 months after a single topical subgingival application of tetracycline fibres as an adjunct to SRP at class II furcation sites. Six months after therapy, the advantage of the subgingival tetracycline was no longer observed (Tonetti et al. 1998).

The lack of differences in the proportions of sites with change of furcation degree between SRP and SRP&DOXY 6 and 12 months after therapy may also be due to a reduction of test power caused by exiting patients. A calculation of sample size was performed for the original multi-centre trial. To show a difference in PPD reduction between SRP and SRP&DOXY, a minimal required sample size of 119 subjects in each arm had been calculated. The present study represents the analysis of furcation sites that was only performed at the Heidelberg centre. Thus, the test power is too low to show equality.

Besides the treatment mode, multilevel analysis showed the baseline degree of furcation involvement to influence its change. Whereas degree 0 was associated with deterioration (increase of furcation involvement), degrees I and II were associated with improvement. Baseline class 0 furcation involvement is likely to show an increase in a second measurement due to measurement error: an improvement of class 0 cannot be expected.

There is evidence that machine-driven instrumentation is as effective as hand instrumentation for subgingival debridement. However, machine-driven instrumentation saves time and is less exhausting (Tunkel et al. 2002, Hallman & Rees 2003). We intended to provide results relevant to clinical practice where time and practicability are significant factors. Thus, we decided to use exclusively machine-driven instruments, i.e. in this case sonic instruments.

More than half of all furcation sites that met the criteria for instrumentation at baseline (all sites $\geqslant 4$ mm) had to be re-instrumented again 3, 6, and 12 months later. Despite resulting in better improvement of furcation involvement than SRP alone 3 months after baseline, additional topical subgingival application of the 14% doxycycline gel once at baseline failed to result in a significant difference between both groups regarding the number of re-instrumentations during the 3-, 6-, and 12-month SPT appointments. If the need for re-instrumentation is not reduced by additional subgingival doxycycline, what benefit does the short-term (after 3 months) improvement of furcation involvement have? The present study investigated the additional effect of a single subgingival application of doxycycline. We can only speculate what effect further subgingival doxycycline applications at 3 and 6 months after baseline may have had. Perhaps doxycycline instead of or additional to SRP at each SPT appointment may have reduced the number of re-instrumentations. However, this issue can only be elucidated in further clinical trials addressing the effect of repeated subgingival doxycycline on furcation involvement and number of re-instrumentations.

Conclusions

Within the limitations of the present study, we may draw the following conclusions: Subgingival doxycycline in addition to SRP has a moderate short-

Table 7c. Change of furcation involvement from baseline to 12 months

	SRP	SRP&DOXY	Total
All furcation sites			
Change of furcation involvement (degrees)	19 patients; 157 furcations	15 patients; 108 furcations	
Increase			
III	2 (1.3%)	1 (0.9%)	3
II	6 (3.8%)	3 (2.8%)	9
I	23 (14.6%)	15 (13.9%)	38
No change	101 (64.3%)	77 (71.3%)	178
Decrease			
I	21 (13.4%)	12 (11.1%)	33
II	3 (1.9%)	0	3
III	1 (0.7%)	0	1
Baseline furcation degree 0			
	75 furcations	63 furcations	138
Increase			
III	2 (2.7%)	1 (1.6%)	3
II	2 (2.7%)	0	2
I	15 (20.0%)	14 (22.2%)	29
No change	56 (74.6%)	48 (76.2%)	104
Baseline furcation degree I			
	58 furcations	28 furcations	86
Increase			
II	4 (6.9%)	3 (10.7%)	7
I	2 (3.4%)	1 (3.6%)	3
No change	35 (60.3%)	13 (46.4%)	48
Decrease			
I	17 (29.4%)	11 (39.3%)	28
Baseline furcation degree II			
	14 furcations	3 furcations	17
Increase			
I	6 (42.8%)	0	6
No change	2 (14.3%)	2 (66.7%)	4
Decrease			
I	4 (28.6%)	1 (33.3%)	5
II	2 (14.3%)	0	2
Baseline furcation degree III			
	10 furcations	14 furcations	24
No change	8 (80.0%)	14 (100%)	22
Decrease			
I	0	0	0
II	1 (10.0%)	0	1
III	1 (10.0%)	0	1

Table 8. Multilevel regression analysis

	Estimate	Standard error	*Z* value	*p*
Intercept	− 0.043	0.094	− 0.458	0.647
SRP&DOXY	0.130	0.063	2.042	0.041
Furcation degree 0	− 0.173	0.094	− 1.834	0.067
Furcation degree I	0.441	0.100	4.405	<0.001
Furcation degree II	0.688	0.153	4.492	<0.001

Dependent variable: change of furcation involvement 3 months after therapy (furcation degree) 39 patients/323 furcation sites.

term effect on furcation involvement. However, when applied only once at baseline, it fails to reduce the frequency of the need for re-instrumentation at furcation sites during SPT for a time period of 12 months.

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Table 9. Number of re-instrumentations

SRP	SRP&DOXY	Total
3 months after baseline		
20 patients; 165 furcations	19 patients; 158 furcations	
108 (65.5%)	95 (60.1%)	203
6 months after baseline		
20 patients; 164 furcations	16 patients; 116 furcations	
103 (62.8%)	70 (60.3%)	173
12 months after baseline		
19 patients; 157 furcations	15 patients; 108 furcations	
108 (68.8%)	65 (60.2%)	173

Table 10. Multilevel regression analysis

	Estimate	Standard error	*Z* value	*p*
Intercept	− 1.855	0.611	− 3.036	0.002
Age	0.016	0.010	1.660	0.097
Baseline probing depth	0.451	0.060	7.496	<0.001
Baseline full-mouth bleeding score	0.026	0.009	2.776	0.005

Dependent variable: number of re-instrumentations from baseline to 12 months 34 patients/265 furcation sites.

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Address:
Peter Eickholz
Department of Periodontology
Center for Dental, Oral, and Maxillofacial Medicine (Carolinum)
Hospital of the Johann Wolfgang Goethe-University Frankfurt am Main
Theodor-Stern-Kai 7
60590 Frankfurt am Main
Germany
E-mail: eickholz@med.uni-frankfurt.de

Clinical Relevance

Scientific rationale for the study: Furcation-involved molars are reported to respond less favourably to periodontal therapy and are at a greater risk of disease progression than molars without furcation involvement or single-rooted teeth. Topical subgingival application of a 14% doxycycline gel during SPT may improve furcation involvement.
Principal findings: SRP plus subgingival 14% doxycycline gel during SPT resulted in better reduction of furcation involvement in molars than SRP alone.
Practical implications: Subgingival 14% doxycycline gel may be an aid to maintain furcation-involved molars during SPT.