

Effects of two different post-surgical protocols including either 0.05 % chlorhexidine herbal extract or 0.1 % chlorhexidine on post-surgical plaque control, early wound healing and patient acceptance following standard periodontal surgery and implant placement

Oliver Laugisch¹ · Christoph A. Ramseier¹ · Giovanni E. Salvi¹ · Tobias T. Hägi¹ · Walter Bürgin² · Sigrun Eick¹ · Anton Sculean¹

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Abstract

Objectives The aim of this study was to compare early wound healing, tooth staining and patient acceptance with two different post-surgical maintenance protocols.

Materials and methods Forty patients scheduled for flap surgery to treat periodontal pockets or accommodate dental implants were randomly assigned to receive the following two different post-surgical maintenance protocols: (a) 2 weeks rinsing with a 0.05 % chlorhexidine digluconate (CHX)/herbal extract combination (test) or (b) a 0.1 % CHX solution (control). Early wound healing was evaluated clinically and immunologically. Tooth staining and patient acceptance were assessed by means of visual analogue scale (VAS).

Results Both groups presented with comparable wound healing profiles. No statistically significant differences were observed between the two protocols regarding early wound healing and plaque index ($p > 0.05$). However, in the control group, statistically significantly more patients felt discomfort due to tooth staining ($p = 0.0467$). Compared with patients from the test group, patients in the control group reported statistically significant more irritation of taste at week 1 ($p = 0.0359$) and at week 2 ($p = 0.0042$).

Conclusions The present findings indicate that the two CHX protocols resulted in comparable healing and inhibition of plaque formation. Tooth staining and subjective discomfort related to irritation of taste were more frequent in the control group.

Clinical relevance A post-operative protocol including 0.05 % CHX/herbal extract may have the potential to improve patient compliance during post-operative maintenance.

Keywords Chlorhexidine digluconate · Herbal extract · Periodontal wound healing · Tooth staining · Patient compliance · Taste irritation

Introduction

Following various surgical approaches intended to treat periodontal pockets or accommodate dental implants, prevention of bacterial contamination of the operated area is essential to prevent wound infection and create a favourable environment for the healing process [1–6]. It has been shown that the early stages of post-surgical wound healing are dominated by inflammation which, in turn, enhances biofilm formation [7, 8]. If plaque formation is hindered, periodontal and peri-implant wounds heal faster and show less complications while periodontal surgery at plaque-infected sites leads to lack of clinical improvements or even worsening [1–6, 9].

It has been extensively documented that mechanical plaque control represents the gold standard to prevent periodontal and peri-implant breakdown and to re-establish and maintain periodontal and peri-implant health [1–6, 10–13]. However, only a few studies have evaluated the effect of mechanical cleaning

Oliver Laugisch and Christoph A. Ramseier contributed equally to the manuscript

✉ Anton Sculean
anton.sculean@zmk.unibe.ch

¹ Department of Periodontology, School of Dental Medicine, University of Bern, Freiburgstrasse 7, 3010 Bern, Switzerland

² School of Dental Medicine, University of Bern, Bern, Switzerland

during wound healing following periodontal or implant placement surgery [1–5, 14].

Despite the convincing evidence supporting the positive effects of patient-performed mechanical plaque control during post-surgical maintenance on the clinical outcomes, many patients report discomfort and sensitivity in the operated areas. For this reason, various maintenance protocols including chlorhexidine digluconate (CHX)-based chemical plaque control have been introduced [15–18]. CHX is nowadays accepted as gold standard due to its antibacterial properties [15–21]. Its use following nonsurgical and surgical periodontal therapy is to enhance wound healing and reduces post-operative complications [15–21]. In an animal study, post-operative maintenance using 0.2 % CHX was compared with physiologic saline. Histologic data revealed only a slight inflammatory infiltrate in the CHX group while in the saline group a pronounced inflammatory response was observed [21]. Another study on post-surgical healing investigated the effect of CHX embedded in a periodontal dressing. When the CHX-embedded dressing was compared to control teeth, surgical sites presented with less bleeding on probing and a lower amount of gingival exudate in the observation period of 5 weeks [15].

In a randomized controlled clinical trial, rinsing with 0.2 % CHX twice daily for 6 months yielded similar outcomes after 6, 12 and 24 months than those obtained with a professional tooth-cleaning programme performed every 2 weeks during the same period [16]. A further controlled clinical study reporting on post-surgical treatment recommended in addition to daily rinsing with CHX, mechanical cleansing with ultra-soft toothbrush and local application of CHX [18].

The use of CHX as a mouth rinse has two major side effects that may affect patient compliance. These include a temporary loss or impairment of taste [22] and staining on the entire dentition including prosthetic appliances or the back of the tongue [23, 24]. Different systems have been introduced to reduce tooth staining and other side effects by adding different products such as peroxiborate, polyvinyl pyrrolidone or sodium metabisulphite and ascorbic acid [25–28]. Recently, a novel 0.05 % chlorhexidine/herbal extract has been compared with a 0.1 % chlorhexidine mouth rinse as an adjunct to periodontal surgery [29]. The data suggest that this novel mouthwash may yield less tooth staining compared to the use of standard 0.1 % or 0.12 % CHX solution. The rinse is based on a 0.05 % CHX digluconate solution and plant extracts (peppermint oil 0.1 g, tincture myrrhæ 1.9 mg, salvia aetheroleum 0.5 mg, sodium fluoride 0.11 g, xylitol 3 g, H₂O 77.8 g, glycerine 3.0 g and alcohol 15 % vol). This mouth rinse was approved by Swissmedic (Bern, Switzerland) 2005 and is empirically employed by many clinicians. However, at present, there are virtually no data evaluating the effects of this novel 0.05 % chlorhexidine/herbal extract on early wound healing, patient acceptance, discomfort and side effects (e.g. tooth staining) following periodontal or implant surgery.

Therefore, the purpose of this study was to compare the above-mentioned parameters during post-surgical maintenance using either the novel 0.05 % CHX/herbal extract mouthwash or 0.1 % standard CHX.

Materials and methods

Patients

This study was approved by the Swiss Agency for Therapeutic Products (Swissmedic) and the Ethics Committee of the Canton of Bern, Switzerland (KEK 151/10 UB 12-147). GCP guidelines were strictly followed.

Upon written informed consent, the patients were evaluated at the Department of Periodontology, University of Bern, Switzerland. All patients 21 years or older were diagnosed with chronic periodontitis and treated with initial periodontal therapy 3 months prior to enrolment. The patients did not take any relevant medications e.g. oral corticosteroids and/or cytostatics >20 mg/day, did not suffer from diabetes mellitus or anaemia (Hb < 6 mmol/l), were non-smokers or light smokers (< 5 cigarettes per day) and presented with both good oral hygiene with full-mouth plaque scores (FMPS) [30] <25 % and low levels of residual infection with full-mouth bleeding scores (FMBS) [31] of <25 %. In addition, all patients had to present with an indication for periodontal or standard implant placement surgery (i.e. without additional bone augmentation) in at least one sextant. Indication for periodontal surgery was given when sites exhibiting residual probing depths (PD) of ≥6 mm were still present at 3 months re-evaluation following nonsurgical therapy. At least 2 mm of keratinized soft tissue (i.e. gingiva or mucosa) had to be present at each surgical site.

Patients were excluded from the study when (1) their medical condition may have had a potential influence on healing conditions, (2) they were treated with systemic antibiotics 6 months prior to enrolment, (3) they were smokers with five or more cigarettes per day or (4) a non-compliance with therapy or study protocol was expected, (5) females are pregnant or breastfeeding, (6) there is a need of reconstructive periodontal surgery involving regenerative materials or implant surgery with bone augmentation and (7) they have undergone periodontal surgery or implant placement in anterior areas (i.e. from 13 to 23 and 33 to 43).

Clinical procedures

In all patients, nonsurgical periodontal therapy was completed at least 3 months prior to enrolment. Following periodontal re-evaluation, patients were either scheduled for an open-flap procedure for periodontal surgery without regenerative procedures or dental implant placement without soft and hard tissue augmentation.

During periodontal surgery, root surfaces were debrided with either hand or ultrasonic instruments. All surgical wounds were rinsed with sterile 0.9 % w/v sodium chloride solutions, and surgical flaps were repositioned using interrupted single sutures.

Experimental design

Following the surgical intervention, patients were randomly assigned to either test or control group using a computer-generated randomization table. Patients from both groups were instructed to strictly follow post-surgical maintenance protocols according to their group assignment.

Post-operative maintenance

Patients in the control group were instructed to rinse with 15 ml CHX 0.1 % mouth rinse (Chlorhexamed®, GlaxoSmithKline, Brentford, UK) for 60 s twice per day. Following this procedure, further rinsing with water, eating, or drinking were not allowed for the subsequent hour. Patients had to brush all other teeth (i.e. not included in the surgical area) three times daily with Elmex® toothpaste (GABA®, Lörrach, Germany) known to be sodium lauryl sulphate-free. From days 3 to 14, patients had to brush their teeth three times daily to ensure the best possible plaque control and healing conditions. The surgical area had to be wiped with slight vertical strokes using an ultra-soft toothbrush loaded with Elmex® toothpaste (GABA®, Lörrach, Germany).

Patients in the test group were instructed to rinse with 15 ml Parodontosan® CHX 0.05 %/herbal extract mouth rinse (Tentan AG, Itingen, Switzerland) for 60 s twice per day. Further rinsing with water, eating or drinking were not allowed for the subsequent hour. Patients were further instructed to brush the teeth outside the surgical site three times daily with Parodontosan® toothpaste (Tentan AG, Itingen, Switzerland) known to be CHX- and sodium lauryl sulphate-free, but contained allantoin, myrrh, sage, silica and sodium monofluorophosphate. From day 3 to day 14, patients had to brush their teeth three times daily. The surgical area had to be wiped with slight vertical strokes using an ultra-soft toothbrush loaded with Parodontosan® toothpaste (Tentan AG, Itingen, Switzerland).

At both examinations 1 week and 2 weeks following baseline, a professional debridement with rubber cups was performed on all teeth and interdental cleaning using super floss. Sutures were removed after 7 days.

Clinical assessment

The following clinical parameters were recorded at baseline, at 1 week and at 2 weeks after surgery by the same calibrated examiner (O. L.) who was not involved in providing treatment

and who was masked with respect to test and control groups. The measurements were taken using a standardized manual periodontal probe with a tip diameter of 0.5 mm (UNC 15, Hu-Friedy, Chicago, IL, USA).

FMPS was recorded as the percentage of dental surfaces covered with plaque detected by the use of a periodontal probe. FMBS was assessed following probing pocket depth measurements based on the presence or absence of bleeding up to 30 s. Post-operative healing was assessed by the early wound healing index (EHI) [32] differentiating between the following 5 degrees:

1. Complete flap closure–no fibrin line in interproximal area
2. Complete flap closure–fibrin line in interproximal area
3. Complete flap closure–fibrin clot in the interproximal area
4. Incomplete flap closure–partial necrosis of interproximal tissue
5. Incomplete flap closure–complete necrosis of the interproximal tissue

Tooth staining was assessed on all oral and vestibular aspects by means of a modification of the discoloration index (DI) and is reported in percentage [33].

Intra-examiner reproducibility

One single examiner performed measurements of clinical parameters (O. L.). Calibrations for the validation of intra-examiner reproducibility were performed with one subject not included in the study. During post-operative maintenance using 0.1 % chlorhexidine, all clinical measurements were used for the calibration of the examiner on two separate occasions during the same day, however, at least 4 h apart. Intra-class correlation analysis was used to calculate intra-examiner agreement for repeated measurements. The calibration was accepted if both measurements were similar in more than 90 % (intra-class correlation coefficient >0.900).

Determination of inflammatory mediators

Samples were taken at the margin of the periodontal wound following surgical intervention. The area was first isolated with cotton rolls and a saliva ejector and air-dried. Gingival crevicular fluid (GCF) around teeth or peri-implant sulcus fluid (PISF) around dental implants, respectively, were collected by means of sterile paper strips (Periopaper, Oraflow Inc., Smithtown, NY, USA). The paper strips were placed and left in place for 30 s. Subsequently, the paper strips were transferred to tubes placed in dry ice. The samples were eluted at 4 °C overnight into 750 µl phosphate-buffered saline containing proteinase inhibitors (Sigma-Aldrich, St. Louis, MO, USA). Subsequently, the eluates were centrifuged with 3000 g

for 10 min. The supernatants of the eluates were stored at -80°C until further analysis.

From the eluates, the levels of interleukin (IL)-1 β , matrix-metalloproteinase (MMP)-13 and MMP-8 were determined using commercially available enzyme-linked immunosorbent assay (ELISA) kits (R&D Systems Europe Ltd., Abingdon, UK) according to the manufacturer's instruction. The detection levels of the kits were 1 pg/site for IL-1 β , 2.5 pg/site for MMP-13 and 25 pg/site MMP-8.

Human neutrophil granulocyte elastase (NE) activity was measured with a microplate assay using the chromogenic substrate *N*-methoxysuccinyl-Ala-Ala-pro-Val-pNa. Myeloperoxidase (MPO) activity was assayed using *O*-dianisidine. The detection levels were 0.25 mU/site for MPO and 10 mU for NE activities. By discarding the sediments, only the molecules that were not inside or attached to host cells, e.g. neutrophils, were determined with this procedure.

Evaluation of patient acceptance

Questionnaires using visual analogue scale (VAS) have been used to assess subjective patient acceptance. Post-operative pain, malaise, irritation of taste and dentine hypersensitivity have been assessed using a scale of 10 cm. Additionally, patients have been asked to mark subjectively how much teeth have been stained using VAS with 0 cm representing none and 10 cm all teeth, respectively.

Table 1 Demographics in test group (CHX 0.05 %/herbal extracts) and control group (CHX 0.1 %) at baseline presented either as mean, min-max, standard deviation (SD) or as the total number (*n*) and percentage (%) including *p* values

| Variable | Category | CHX 0.05 % /herbal extract | CHX 0.1 % | <i>p</i> values |
|----------|----------------------------------|----------------------------|-----------------------|-----------------|
| | | Mean, range, SD | Mean, range, SD | |
| General | Age (years) | 58.7, 35–83, 12.7 | 59.2, 35–82, 13 | ns |
| | Weight (kg) | 75.4, 56–100, 12.4 | 67.4, 50–90, 13.3 | ns |
| | Height (m) | 1.70, 1.53–1.86, 0.09 | 1.67, 1.54–1.88, 0.09 | ns |
| | | <i>n</i> (%) | <i>n</i> (%) | |
| Gender | Male (%) | 7 (35) | 8 (40) | ns |
| | Female (%) | 13 (65) | 12 (60) | ns |
| Smoking | Smokers <5 cigarettes (%) | 3 (15) | 4 (20) | ns |
| | Former smokers (%) | 5 (25) | 6 (30) | ns |
| | Non-smokers (%) | 12 (60) | 10 (50) | ns |
| | Allergies (%) | 2 (10) | 0 (0) | ns |
| | Hypertension (%) | 2 (10) | 2 (10) | ns |
| | | | <i>n</i> (%) | <i>n</i> (%) |
| Surgery | Periodontal surgery | 11 (55) | 14 (70) | ns |
| | Implant surgery | 9 (45) | 6 (30) | ns |
| | | Mean, range, SD | Mean, range, SD | |
| | Number of teeth | 1.75, 1–4, 0.8 | 1.75, 1–4, 0.91 | ns |
| | Keratinized Mucosa | 3.45, 3–5, 0.69 | 3.6, 3–6, 0.8 | ns |
| | Patient sensation difficulty VAS | 2.6 0.1–6.5, 1.8 | 2.9 0.2–6.9, 1.5 | ns |
| | Pain during surgery VAS | 0.7, 0–3.4, 1 | 0.7, 0–4.1, 1.1 | ns |

ns no statistical significance ($p > 0.05$)

Statistical analysis

Since no previous data were available, the study was planned as a pilot, randomized, controlled clinical study. Thus, no sample size calculation was made. The primary endpoint of the study was the early wound healing index at week 1 [32]. The secondary endpoints were early wound healing index at week 2, differences in patient acceptance, side effects (e.g. subjective tooth staining), the clinically assessed tooth staining index [33], patient comfort during the test treatment, plaque index and inflammatory markers.

Following descriptive statistics for both groups, analytical statistics was performed. First, both groups were tested for a normal distribution and subsequently compared by Students *t* test, Wilcoxon-matched pairs signed rank test or Chi-square test and Fischer's exact test. The significance level was set at $p = 0.05$.

Results

Patients

A total of 40 patients were recruited for this study and comprised 20 males and 20 females with a mean age of 58.9 years. Overall, 7 patients were registered as light smokers (<5 cigarettes per day), 11 as former smokers and 22 as non-smokers. The mean percentage of FMBS and FMPS at the time of

Table 2 Full-mouth bleeding scores (FMBS) (%) and full-mouth plaque scores (FMPS) (%) in test group (CHX 0.05 %/herbal extract) and control group (CHX 0.1 %) at baseline before inclusion of patients

| Baseline | Group | Number | Median (%)/min-max, SD | <i>p</i> value |
|----------|---------|--------|------------------------|----------------|
| FMBS (%) | Test | 20 | 10/1–22, 6 | ns |
| | Control | 20 | 12/1–25, 7 | ns |
| FMPS (%) | Test | 20 | 12/5–20, 5 | ns |
| | Control | 20 | 12/3–20, 5 | ns |

ns no statistical significance (*p* > 0.05)

inclusion was 11 and 13 %, respectively. Patient demographics (Table 1) as well as bleeding on probing and plaque indices (Table 2) at baseline did not reveal any statistically significant difference between the two groups.

Characteristics of surgical sites

In 63 % of all interventions, an open-flap debridement without regenerative approach was performed. In only 37 % of the patients’ dental implants were placed. In 62.5 % of all sites, the width of keratinized soft tissue was 3 mm while 22.5 % showed 4 mm, and 15 % presented with a width of 5 mm. A comparison of these characteristics of the surgical sites between both groups (Table 1) did not reveal any statistical significance between both groups.

Evaluation of plaque control and tooth staining

Both groups demonstrated comparable plaque indices. Changes between week 1 and week 2 were not statistically significant between the two groups. Differences of the tooth staining index did not reach statistical significance between the groups

Table 3 Follow-up of clinical parameters as well as answers in questionnaires (VAS) in test group (CHX 0.05 %/herbal extract) and control group (CHX 0.1 %) at weeks 1 and 2 baseline either presented

| Follow up | Week 1 | | | Week 2 | | |
|--------------------------------|-------------------------------|----------------|----------------|-------------------------------|----------------|----------------|
| | CHX 0.05 %/ herbal extract | CHX 0.1 % | <i>p</i> value | CHX 0.05 %/ herbal extract | CHX 0.1 % | <i>p</i> value |
| Plaque index | 15/1–44, 11 | 15/5–57, 12 | ns | 13/1–45, 10 | 12/2–39, 10 | ns |
| Staining index | 17/0–43, 14 | 22/2–65, 20 | ns | 16/1–38, 10 | 27/2–78, 23 | ns |
| Irritation of taste (VAS) | 2 (10) | 8 (40) | *0.0359 | 1 (5) | 9 (45) | *0.0042 |
| Dentin hypersensitivity (VAS) | 5 (25) | 8 (40) | ns | 6 (30) | 6 (30) | ns |
| Patient sensation staining VAS | 5 (25) | 8 (40) | ns | 4 (20) | 10 (50) | *0.0467 |
| Intensity stain VAS | 0.3/0–3.3, 0.8 | 1.1/0–4.7, 1.5 | ns | 0.6/0–8.4, 1.9 | 1.4/0–7.5, 2.2 | ns |
| Patient claim staining VAS | 3 (15) | 6 (30) | ns | 3 (15) | 7 (35) | ns |
| Intensity claim VAS | 1.2/0–10, 2.9 | 2.1/0–10, 3.6 | ns | 0.6/0–10, 2.2 | 2/0–8.7, 3.3 | ns |

ns no statistical significance (*p* > 0.05)

* statistically significant

at either both visits (*p* = 0.1668) and between week 1 and week 2 (test *p* = 0.5675; control *p* = 0.2458) (Table 3).

Evaluation of patient acceptance

The patients in both groups felt comparable discomfort during the first post-operative week. The sensation of pain during the observation period again did not reveal any differences between test and control. Patients in the control group reported an irritation of taste being higher than in the test group (*p* = 0.0359 at week 1 and *p* = 0.0042 at week 2). In the test group, statistically significantly more patients reported subjective tooth staining and have felt discomfort related to this staining at week 2 (*p* = 0.0467) (Table 3).

Evaluation of wound healing

Post-surgical maintenance protocols resulted in comparable wound healing profiles in both groups without statistically significant differences at weeks 1 and 2 (week 1 *p* = 0.2039 and week 2 *p* = 0.0428). None of the surgical sites was characterized with an early wound healing index of more than 4. In the test group, the mean-distribution of degrees 1, 2 and 3 was 60, 30 and 10 % at week 1 and 80, 15 and 5 % at week 2, respectively. In the control group, the distribution was 40, 40 and 20 % as well as 90, 90 and 5 % respectively. The profile of inflammatory mediators in both groups at week 1 and week 2 is shown in Table 4.

Discussion

In the present randomized controlled clinical trial, a post-surgical protocol including rinsing with a 0.05 % CHX supplement in combination with essential oils resulted in

as mean, min-max, standard deviation (SD) or as total number (*n*) and percentage (%) including *p* values

Table 4 Follow-up of inflammatory mediators in test group (CHX 0.05 %/herbal extract) and control group (CHX 0.1 %) at weeks 1 and 2 baseline presented as mean, min-max, standard deviation (SD) including *p* values

| Follow up | Week 1 | | | Week 2 | | |
|------------------------|-------------------------------|-------------------------|----------------|-----------------------------|-------------------------|----------------|
| | CHX 0.05 %/ herbal extract | CHX 0.1 % | <i>p</i> value | CHX 0.05/ herbal extract | CHX 0.1 % | <i>p</i> value |
| MMP 8 (pg/site) | 812.180–2533.6, 829.12 | 1190.130–2681.8, 820.38 | ns | 601.220–2562.38, 729.78 | 452,360–1364.52, 434.73 | ns |
| MMP 13 (pg/site) | 4.970–16.24, 5.65 | 8.030–19.86, 6.32 | ns | 4.560–18.03, 5.27 | 10.030–34.533, 8.6 | ns |
| IL-1 β (pg/site) | 4.520–26.05, 8.54 | 7.450–57.06, 14.55 | ns | 3.250–43.88, 9.76 | 0.370–4.75, 1.11 | ns |
| MPO (mU/site) | 2.140.12–7.89, 2.09 | 2.880.46–7.57, 2.27 | ns | 2.370.71–11.17, 2.92 | 1.510.06–3.13, 0.96 | ns |
| Elastase (mU/site) | 930–817.5, 197.87 | 208.880–1552.5, 420.54 | ns | 198.380–1267.5, 362.25 | 46.130–120, 41.67 | ns |

ns no statistical significance ($p > 0.05$)

comparable early wound healing outcomes, biofilm formation rates and better patient acceptance when compared to rinsing with 0.1 % CHX. Although tooth staining occurred in both groups, patient discomfort was higher in the group rinsing with 0.1 % CHX. This was due to the more frequent tooth staining observed following rinsing with 0.1 % CHX. This finding is in agreement with recently published data using the same 0.05 % CHX supplement and has reported statistically significantly less tooth staining when compared with CHX 0.1 % over a period of 4 weeks and 12 weeks, respectively [29]. At 12 weeks, the results also revealed comparable reductions in terms of periodontal pathogens and probing pocket depths to the use of 0.1 % CHX [29]. Moreover, since both protocols yielded comparable outcomes in terms of early wound healing and cytokine profiles, the present findings provide additional support for the clinical efficacy of this CHX formulation. In addition, a greater patient acceptance has been documented in patients rinsing with 0.05 % CHX/herbal extract. Tooth staining has been observed in both groups, although a trend, reaching almost statistical significance, towards less stain has been observed in week 1 and week 2 at lower concentration.

An important aspect of the present study is related to the fact that the two post-surgical maintenance protocols were evaluated for both conventional periodontal and dental implant placement surgeries (i.e. without any regenerative approaches). Implant surgeries have been included to increase the generalizability of the results (i.e. the clinical applicability of the tested protocol for both surgical indications). Since a potential effect of various regenerative materials (i.e. biologic agents, bone grafts, membranes etc.) on the early wound healing cannot be ruled out, patients needing such procedures were excluded from the study.

It is well documented that the early wound healing phase after any type of surgery decisively influences the clinical outcomes. Therefore, in order to ensure the best possible environment for wound healing and to maximize the clinical outcomes, the post-operative maintenance protocol following periodontal or implant surgery is essential. The most common

protocol includes the use of CHX mouthwash in order to chemically control biofilm formation [16–18, 28, 29, 34].

However, in the present study, the post-operative protocol consisted in both groups from twice daily rinses with either 15 ml CHX 0.1 % mouth rinse or 15 ml Parodontosan® CHX 0.05 %/herbal extract mouth rinse for 60 s combined with mechanical cleaning of the surgical area using an ultra-soft toothbrush loaded with either Elmex® or Parodontosan® toothpaste. Additionally, in order to reduce the supragingival bacterial load to a minimum, patients brushed the rest of the dentition from days 3 to 14 three times daily. When interpreting the findings, it is important to be kept in mind that the present study has evaluated a special post-surgical treatment concept consisting of mouth rinses and mechanical cleaning. Therefore, no conclusions can be drawn on the possible results that might have been obtained by using the mouth rinses alone (i.e. without mechanical cleaning). Moreover, this may also serve, at least partly, as explanation for the fact that the present analysis has failed to reveal statistically significant differences between the two protocols, despite the observed trend favouring the Parodontosan® CHX 0.05 %/herbal extract mouth rinse-containing protocol.

On the other hand, when comparing the present results with those from the previously mentioned study, it has to be pointed to the different observation periods (e.g. 2 weeks versus 12 weeks) [29]. Thus, it cannot be excluded that after a period of 12 weeks, statistically significant differences may occur. Overall, the 0.05 % CHX/herbal extract was significantly better tolerated than the control 0.1 % concentration. Using the latter during post-surgical maintenance, patients subjectively reported more tooth staining and less taste irritation.

Since it has been suggested that foaming agents like lauryl sulphate temporarily or concomitantly used in combination with CHX may inhibit its efficacy, in order to prevent bias, the maintenance protocol was accordingly adapted for both groups [35]. Therefore, patients from both groups were instructed to strictly follow post-surgical maintenance protocols according to the group assignment including the use of natrium lauryl sulphate-free toothpaste. Furthermore, the used

toothpaste contained neither CHX nor agents known to remove tooth staining.

It is well documented that CHX can cause side effects including irritation of taste, pigmentation and mucosal irritation [22, 24, 36, 37]. These effects may influence patient acceptance and compliance with regard to regular and proper use of CHX with potential negative consequences on the wound healing process. An irritation of taste was also reported to be more frequent with higher CHX concentrations, while a better taste of CHX in lower concentrations was described in the literature when comparing 0.1 % CHX and 0.2 % [22, 34, 35]. In contrast, patients reported comparable taste acceptance when 0.3 and 0.2 % CHX mouthwashes were compared [38]. Therefore, manufacturers have addressed these relevant issues in order to reduce tooth staining and other side effects by adding substances such as peroxiborate, polyvinyl pyrrolidone, sodium metabisulphite or ascorbic acid to a CHX solution. Consequently, several studies were performed with an additional anti-discoloration system (ADS) [28, 39]. A recent study has been performed in order to evaluate its effectiveness on tooth staining, plaque accumulation and gingivitis. The authors concluded that ADS in addition to CHX did not prevent plaque or gingivitis development and in fact, it showed no superior effect over placebo on oral hygiene or prevention of gingivitis [39].

A few studies have evaluated the effects of CHX mouthwashes in lower concentrations. Jenkins and co-workers do not report a linear dose dependent effect on plaque growth but rather a highest inhibition between 0.01 % CHX and 0.05 % CHX [40]. No difference with regard to plaque growth has been reported when twice daily rinsing with 0.1 % CHX was compared with 0.06 % CHX over a period of 24 h.

On the other hand, data from long-term studies evaluating the possible effects of low concentrations of CHX are still sparse. Hoffmann and co-workers compared the effect of 0.06 % CHX and 0.1 % CHX solutions over a period of 6 months following nonsurgical periodontal therapy and found superior results for the higher concentration in terms of reduction of inflammation (i.e. reduction in gingival index) [41]. On the other hand, adding 0.05 % cetylpyridinium chloride (CPC), a quaternary ammonium compound with an antiseptic effect, to a 0.05 % CHX non-alcoholic solution, failed to reveal statistically significant differences when compared with 0.2 % CHX-alcoholic formulation [42]. Interestingly, the subjective ratings related to the taste of the product appeared to favour the CHX-CPC formulation but were but less impressive for the staining of teeth and tongue when compared with the 0.2 % CHX-alcohol formulation [42].

Thus, taken together, the available data appear to suggest that low concentrations of CHX may represent an effective antiplaque agent for long-term use with reduced subjective side effects.

When discussing the clinical application of CHX and essential oil mouthwashes (EOMW), it needs to be pointed out that CHX mouthwashes provided significantly better effects regarding plaque reduction than EOMW but did not show any significant difference with respect to reduction of gingival inflammation [43]. On the other hand, in vitro data indicate that the combination of CHX and EOMW may act synergistically against certain bacteria such as *Staphylococcus epidermidis*, thus pointing to the potential for improving antimicrobial activity by means of such combinations [44].

In conclusion, the present findings indicate that the two CHX-based post-surgical maintenance post-surgical maintenance protocols yielded comparable healing and inhibition of plaque formation. Since tooth staining and subjective discomfort related to irritation of taste were more frequent in the control group, it can be suggested that post-operative rinsing with 0.05 % CHX/herbal extract may have the potential to improve patient compliance during post-operative maintenance.

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Compliance with ethical standards This study was approved by the Swiss Agency for Therapeutic Products (Swissmedic) and the Ethical Committee of the Canton of Bern, Switzerland (KEK 151/10 UB 12-147). GCP guidelines were strictly followed.

Conflict of interest All authors declare that they have no conflict of interest related to this study.

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Informed consent The patients screened and included in the study gave written informed consent, approved by the Ethical Committee of the Canton of Bern, Switzerland (KEK 151/10 UB 12-147).

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