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a cross-over, randomized,
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 **WILEY-BLACKWELL**

Chlorhexidine with an anti discoloration system after periodontal flap surgery: a cross-over, randomized, triple-blind clinical trial

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Abstract

The use of chlorhexidine (CHX) has been recommended for a number of clinical applications including plaque control in the post-operative period. However, the use of CHX is burdened by some side effects that could affect the compliance of the patient. The aim of this clinical trial was to evaluate the side effects, the staining in particular, the patient acceptance, and the efficacy of a 0.2% CHX mouthwash containing an anti discoloration system (ADS) compared with a 0.2% CHX alone, after periodontal flap surgery.

Material and Methods: This single-centre, cross-over, triple-blind randomized clinical trial was carried out on 48 consecutive patients. After periodontal flap surgery, the patients were prescribed to rinse two times per day for 1 min for 1 week with 10 ml of test or control CHX, contained in anonymous bottles coded K or M and assigned randomly. No brushing and interdental cleaning of the surgical area was allowed. At week 1, after suture removal, patients received full-mouth prophylaxis and were given a second anonymous bottle, reversing the products, with the same instructions as at baseline. Patients resumed tooth-brushing but not interdental cleaning. At the end of week 2, prophylaxis was repeated, mouth rinsing was discontinued and patients resumed normal oral hygiene. At weeks 1 and 2, the following variables were recorded: presence of pigmentation, gingival parameters at the surgically treated sites (gingival inflammation, tissue inflammation around the sutures, gingival swelling and presence of granulation tissue), patient perception and acceptance of the 2 mouthwashes.

Results: Forty-seven patients completed the study. The difference between treatments related to gingival variables was not statistically significant. The test CHX caused consistently less pigmentations than the control CHX in all the evaluated areas of the dental surfaces (odds ratio (OR) = 0.083 $p < 0.0001$ in the incisal area, OR = 0.036 $p < 0.0001$ in the approximal area and OR = 0.065 $p < 0.0001$ in the gingival area). The CHX ADS was found to be more tolerated by patients than the control mouthwash and to cause less food alteration, less alterations to the perception of salt and to be less irritant for the oral tissues.

Conclusions: (1) CHX ADS caused less pigmentation, was burdened by less side effects and was more agreeable than the control CHX; (2) CHX ADS was as effective as CHX without ADS in reducing gingival signs of inflammation in the post-surgical early healing phase; (3) the use of CHX ADS could be of value in treatment protocols in which the patient compliance with a CHX mouthwash prescription is relevant.

Key words: chlorhexidine; mouthrinses; periodontal surgery; post-surgical protocols; staining

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Conflict of interest and source of funding statement

The authors declare that they have no conflict of interest.

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The use of chlorhexidine (CHX) as an agent able to inhibit plaque formation and gingivitis development is well documented over a period of more than 30 years (Loe & Schiott 1970, Addy 2003). CHX digluconate is a broad-spectrum antiseptic, with a pronounced effect on both Gram-negative and Gram-positive bacteria. It has been shown to have both bacteriostatic and bactericidal activity, at a low and a high concentration, respectively (Hugo & Longworth 1964, 1965, 1966). Its antiseptic activity derives from its capacity to link to anionic groups (phosphate, sulphate and carboxylic group) present on the bacterial surface, causing an increase in cellular permeability and so an alteration in osmotic equilibrium (Davies 1973). The CHX molecule is also able to link to the oral mucosa, enamel surface, salivary pellicle and salivary proteins. It is then slowly released into the oral cavity, maintaining effective concentrations on microorganisms in the following 24 h, showing therefore a high *substantivity* (Jones 1997).

The use of CHX has been recommended for a number of clinical applications including post-operative periods to prevent plaque formation and early bacterial re-colonization of the treated area when mechanical cleaning may be impaired (Addy 1986, 2003, Lang & Brex 1986, Newman et al. 1989, Sanz et al. 1989, Quirynen et al. 1995, 2002, Addy & Renton-Harper 1996, Favari et al. 2006).

However, the use of CHX is burdened by some side effects, mainly related to stains, alterations in taste and erythematous – desquamative lesions of oral mucosa. Among them, the most frequent is represented by brown pigmentations that appear on the dental surfaces, prosthetic and composite restorations and tongue after its prolonged use (Addy et al. 1985, Eriksen et al. 1985, Leard & Addy 1997). Because the effective-

ness of the CHX is strongly correlated to the compliance of the patient, different systems have been introduced in order to reduce the brown pigmentations and other side effects caused by the use of this type of mouthwash, adding to CHX different products such as peroxiborate, polyvinyl pyrrolidone or sodium metabisulphite and ascorbic acid (Gründemann et al. 2000, Claydon et al. 2001, Bernardi et al. 2004, Addy et al. 2005, Arweiler et al. 2006).

The aim of this cross-over, triple-blind, randomized clinical trial was to evaluate the side effects like staining, in particular, the patient acceptance and the efficacy of a 0.2% CHX mouthwash containing an anti discoloration system (ADS) as compared with a mouthwash containing 0.2% CHX alone, after periodontal flap surgery.

Material and Methods

This study is a single-centre, cross-over, triple-blind randomized clinical trial on 48 consecutive patients scheduled for periodontal flap surgery, comparing a 0.2% CHX mouthwash containing an ADS with a mouthwash containing only 0.2% CHX. The study was conducted in a private practice setting (P. C.) in a 4-month period between September and December 2006.

Study population and experimental design

Patients with advanced periodontal disease, in general good health, presenting with at least one sextant scheduled for periodontal flap surgery, were considered to be eligible for this study. Patients were included after completion of cause-related therapy consisting of scaling and root planing, motivation and oral hygiene instructions. All subjects gave informed written consent.

The inclusion criteria were as follows:

1. *Absence of relevant medical conditions.* Patients with uncontrolled or poorly controlled diabetes, unstable or life-threatening conditions or requiring antibiotic prophylaxis were excluded.
2. *Smoking status.* Non smokers and light smokers were included (<20 cigarettes/day).
3. *Good oral hygiene.* Full-mouth plaque score $\leq 25\%$.
4. *Low levels of residual infection.* Full-mouth bleeding score $\leq 25\%$.

5. *Need for periodontal surgery.* Presence of at least one sextant with at least two teeth scheduled for periodontal flap surgery.

Experimental design

At baseline, patients were surgically treated with periodontal flap surgery by one surgeon (P. C.). Bone surgery was performed according to clinical indications. Interrupted passing or external mattress silk sutures (4-0) were applied to close the flaps at the end of surgery. Immediately before surgery, full-mouth prophylaxis was performed with a low-speed rubber cup. All patients received an anonymous bottle containing a mouthwash along with a 10 ml calibrated glass. The bottles were coded with either a K or an M. Patients were prescribed to rinse two times per day with 10 ml of the mouthwash for 1 min, for the whole week and the amount of product per bottle was calibrated to satisfy this prescription. The bottle contained either the test or the control CHX, according to random assignment. The test mouthwash contained 0.2% alcohol-free CHX and ADS; this formulation was obtained by adding sodium metabisulphite and ascorbic acid (Curasept™; Curaden Healthcare srl, Saronno, Italy). The control mouthwash contained 0.2% alcohol-free CHX with no additional products. Brushing and interdental cleaning of the surgical area were interrupted in the post-surgical week. At week 1, patients were examined and sutures were removed. Full-mouth prophylaxis was performed with a low-speed rubber cup. A second anonymous bottle of mouthwash, containing the other tested product (K to patients that had previously received M and vice versa), was given to the patient with the same instructions as at baseline. Patients resumed tooth-brushing but not interdental cleaning. At the end of week 2, patients were re-examined, prophylaxis was repeated and mouth rinsing was discontinued. At this time, patients resumed mechanical full oral hygiene. At week 1 and 2 examination visits, patients were asked to report on their compliance with the rinsing prescription and to bring back the bottles to directly check for compliance.

Clinical measures

At weeks 1 and 2, the following variables were recorded (A.L.):

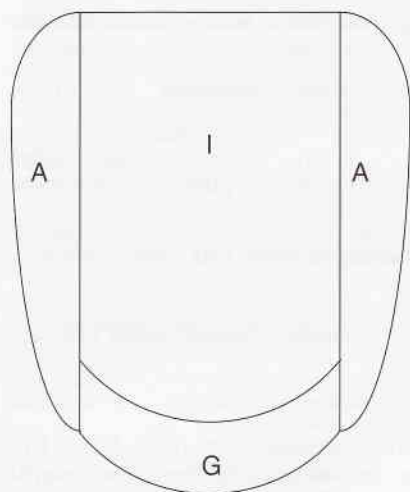


Fig. 1. Tooth surfaces where staining was assessed according to the intensity stain index of Lobene (1968), modified by Gründemann et al. (2000). A, approximal; I, incisal; G, gingival.

1. *Tooth pigmentation at the patient level.* Stain was recorded at the buccal surfaces of the four upper incisors and at the surgically treated teeth. Pigmentation of the dental surface was evaluated using a modification of the stain index (Lobene 1968). The tooth surface was divided into three areas (Fig. 1): incisal (I), approximal (A) and gingival (G), and pigmentation was separately evaluated in the three areas. When at least one area of the considered teeth in a patient was found to be pigmented, that area was considered to be positive at the patient level.
2. *Gingival variables at the surgically treated sites.* The same scale (0 = absent, 1 = present) was used to record gingival inflammation, tissue inflammation detected around the sutures, gingival swelling and presence of granulation tissue at the experimental sites.
3. *Patient perception and acceptance of the two mouthwashes.* Patient perception and acceptance was evaluated with a questionnaire administered at suture removal (week 1) and at the week-2 examination visit. Responses were quantified with a visual – analogic scale (VAS) of 10 cm as described previously (Cortellini et al. 2001, Tonetti et al. 2004).

The questionnaire included the following variables:

- Taste of the product (0 = bad taste ÷ 10 = good taste).

- Alterations in food taste (0 = no alteration ÷ 10 = relevant alteration).
- Alterations in perception of salt (0 = no alteration ÷ 10 = relevant alteration).
- Irritation of mucosa (0 = no irritation ÷ 10 = relevant irritation).
- Different side effects (0 = no side effect ÷ 10 = relevant side effect).

Randomization and allocation concealment

Random assignment was performed by tossing a coin (R. Z.) and assigning the code K or M to a table of consecutive numbers (1–48). The randomization list was concealed from the surgeon and the measurer. Patients were sequentially entered into the study and each of them received a numbered sealed opaque envelope containing the product assignment. The sealed and numbered envelope was opened at the end of surgery. The measurer did not receive any information about allocation. The patients were unaware of the type of mouthwash used. All the active participants in the study, the surgeon (P. C.), the measurer (A. L.) and the statistician (M. N.) remained blinded until the statistical analysis was performed (triple-blind study). The code (K and M) was broken at the time of paper writing.

Sample size calculation

The study was designed to have 80% power to detect an odds ratio (OR) = 0.25 for pigmentation of the test CHX versus control CHX. The α level was set at 0.05. The proportion of pigmentation in the control group was set at 0.6 and the correlation coefficient for staining between paired data was set at 0.1 (Dupont & Plummer 1990). The required number of patients was 39. The final number was set to 48 considering a potential 20% patient dropout from the study.

Data analysis

Quantitative data are presented as means and standard deviations (SD) and qualitative data are presented as frequency and percentage. Statistical software packages used to analyse the data were MLwiN 1.00 1998 © Multilevel Models Project Institute of Education and JMP[®] 7.0 2007 SAS Institute Inc.

The primary outcome variable was patient pigmentation. Differences in the pigmentation area were tested between the two different treatments within the same patient and between weeks 1 and 2 with multilevel logistic models with estimation procedure “restricted iterative generalized least square” and “predictive quasi likelihood” at two levels: patient and period (Goldstein 1995). The interaction between week and treatment was also considered, exploring in particular a potential difference in the effect of the two tested products in week 1 or in week 2. When the interaction was insignificant, it was deleted from the model.

The null hypothesis of no differences between the two products in terms of *gingival conditions* was tested at week 1 with the Fisher exact test. Because at week 2 the positive events were exceptional occurrences, the week 2 statistical analysis was not performed.

The variables related to patient acceptance (taste, food taste, salt perception, mucosal irritation, other side effects) have been studied with linear models with a patient block approach (same patient receiving the test and control treatments) with weeks 1 and 2 and test/control treatment as explicative variables. The interaction between week and treatment was also considered but if it was insignificant it was deleted from the model.

Results

One patient from the group that used the test CHX in the first week did not complete the study, because he missed the first-week examination visit for personal reasons. A total of 47 patients (32 females), mean age 44.3 ± 12.9 years (minimum: 21; maximum: 78 years), completed the study. In week 1, a group of 23 patients used the CHX test and a group of 24 used the CHX control. At week 2, according to protocol, the groups crossed the mouthwash. Fifteen patients (seven in the group using the test CHX in the first week) were smokers. All patients were treated with flap surgery for pocket elimination/reduction, according to clinical indications and were re-evaluated at days 7 and 14 after surgery. No patients reported any complication or unexpected complaint. All patients reportedly used the mouthwashes according to prescriptions and this was confirmed by the control on

Table 1. Descriptive statistics at week 1 examination visit

	Test n = 23	Control n = 24
Pigmentation zone I	2 (9%)	17 (71%)
Pigmentation zone A	9 (39%)	20 (83%)
Pigmentation zone G	2 (9%)	14 (58%)
Gingival inflammation	8 (35%)	5 (21%)
Oedema	8 (35%)	10 (42%)
Inflammation around sutures	11 (48%)	15 (62%)
Granulation tissue	1 (4%)	1 (4%)
Mouthwash taste	7.86 (1.41)	5.20 (2.06)
Food taste	0.54 (1.02)	2.21 (1.85)
Salt perception	0.63 (1.07)	2.47 (2.05)
Mucosal irritation	0.14 (0.51)	0.76 (1.03)
Other side effects	0.0 (0.0)	0.0 (0.0)

The table reports the number and the percent of positive observations. The variables "pigmentation" and the ones related to the gingival condition are expressed in binomial values with 0 representing the negative event (absence of pigmentation or inflammation) and 1 representing the positive event (or presence of). Pigmentation (see Fig. 1): incisal (I), approximal (A) and gingival (G).

Table 2. Descriptive statistics at week 2 examination visit

	Test n = 24	Control n = 23
Pigmentation zone I	6 (25%)	12 (52%)
Pigmentation zone A	15 (62%)	22 (96%)
Pigmentation zone G	5 (21%)	12 (52%)
Gingival inflammation	0 (0%)	0 (0%)
Oedema	0 (0%)	1 (4%)
Inflammation around sutures	—	—
Granulation tissue	0 (0%)	1 (4%)
Mouthwash taste	7.72 (1.25)	4.88 (1.76)
Food taste	0.63 (0.76)	2.60 (1.33)
Salt perception	0.77 (1.02)	2.80 (1.44)
Mucosal irritation	0.10 (0.29)	0.66 (1.02)
Other side effects	0.0 (0.0)	0.0 (0.0)

The table reports the number and the percent of positive observations (for explanations on the construction of the table see Table 1).

the recollected bottles at week 1 and 2 examination visits.

Tables 1 and 2 show the clinical outcomes following the use of the test and the control product at weeks 1 and 2, respectively.

Differences in pigmentation were calculated between treatments within the same patient with logistic multilevel models (Tables 3–5). The interaction term was deleted from the three models when insignificant. The test ADS CHX

Table 3. Multilevel logistic model considering the relationships between mouth rinse and presence of pigmentation in the incisal zone

Variable	Coefficient	SE	p-value	Odds ratio	95% CI; OR
Intercept	0.582	0.427			
Mouth rinse (ADS CHX)	-2.493	0.537	<0.0001	0.083	0.029; 0.237
Week (1)	0.032	0.517	0.9506	1.033	0.375; 2.844
Variance	0.940	0.804			

CI, confidence interval; OR, odds ratio; ADS, anti discoloration system; CHX, chlorhexidine.

Table 4. Multilevel logistic model considering the relationships between mouth rinse and presence of pigmentation in the approximal zone

Variable	Coefficient	SE	p-value	Odds ratio	95% CI; OR
Intercept	4.186	1.034			
Mouth rinse (ADS CHX)	-3.338	0.855	<0.0001	0.036	0.007; 0.190
Week (1)	-1.599	0.790	0.0430	0.202	0.043; 0.951
Variance	4.142	1.934			

CI, confidence interval; OR, odds ratio; ADS, anti discoloration system; CHX, chlorhexidine.

Table 5. Multilevel logistic model considering the relationships between mouth rinse and presence of pigmentation in the gingival zone

Variable	Coefficient	SE	p-value	Odds ratio	95% CI; OR
Intercept	0.450	0.503			
Mouth rinse (ADS CHX)	-2.732	0.626	<0.0001	0.065	0.019; 0.222
Week (1)	-0.266	0.593	0.6537	0.766	0.240; 2.450
Variance	2.478	1.225			

CI, confidence interval; OR, odds ratio; ADS, anti discoloration system; CHX, chlorhexidine.

Table 6. Difference between the two treatments in terms of gingival tissue variables, at week 1 (Fisher's exact test)

	Test n = 23	Control n = 24	p-value
Gingival inflammation	8 (35%)	5 (21%)	0.3412
Oedema	8 (35%)	10 (42%)	0.7661
Inflammation around suture	11 (48%)	15 (62%)	0.3852
Granulation tissue	1 (4%)	1 (4%)	1.0000

caused consistently less pigmentations than the control CHX in all the evaluated areas of the dental surface. In the incisal area, the OR for less pigmentation was 0.083 [95% confidence interval (CI) = 0.029–0.237], in the approximal area the OR was 0.036 (95% CI = 0.007–0.190) and in the gingival area the OR was 0.065 (95% CI = 0.019–0.222). In the first week, there was less pigmentation with respect to the second week in the approximal area (OR = 0.202, 95% CI = 0.043–0.951). No significant difference was found between weeks 1 and 2 for pigmentation in the incisal and gingival areas.

The differences between treatments related to gingival inflammation, oedema, inflammation around sutures and

presence of granulation tissue were investigated only at 1 week post-surgery, because positive cases in the second week were a very rare occurrence (Table 2). No significant differences between the two treatments were found for any of these variables at week 1 (Table 6).

The variables related to patient acceptance were studied with linear models with a patient block approach (the same patient receiving the test and the control treatment) with week (1–2) and treatment (test or control) as explicative variables. In terms of patient perception of the mouthwash taste, the test CHX was found to be more tolerated than the control mouthwash ($R^2 = 0.82$, Table 7). The difference between mouthwashes was 2.75 (95%

Table 7. Linear model to investigate the patient acceptance of the product in terms of perceived mouthwash taste, alterations in food taste, alterations in salt perception, and mucosal irritation

	Mouthwash taste perception			Food taste alteration			Salt perception			Mucosal irritation		
	estimate	SE	p-value	estimate	SE	p-value	estimate	SE	p-value	estimate	SE	p-value
Intercept	7.68	0.23	<0.0001	0.71	0.22	0.0020	0.81	0.23	<0.0001	0.09	0.11	0.4405
Blocks		0.92	0.0058		0.85	0.1871		0.92	0.1071		0.45	0.0112
Week (1)	0.23	0.27	0.3970	-0.24	0.25	0.3416	-0.23	0.27	0.3980	0.07	0.13	0.5828
CH (ADS)	2.75	0.27	<0.0001	-1.82	0.25	<0.0001	-1.93	0.27	<0.0001	-0.59	0.13	<0.0001
R ²		0.82			0.72			0.72			0.71	

For the model a patient block approach (the same patient receiving the test and the control treatment) was used with week (1–2) and treatment (test or control) as explicative variables.

CI = 2.21–3.30). No significant differences were found between the first and the second week. In terms of food taste alteration, the test CHX was found to cause less food taste alterations than the control one ($R^2 = 0.72$, Table 7). The difference between mouthwashes was -1.82 (95% CI = -2.32 to -1.31). No significant differences were found between the first and the second week. The test mouthwash was also found to cause less alterations to the perception of salt ($R^2 = 0.72$, Table 7). The difference between the two products was -1.93 (95% CI = -2.47 to -1.39). No significant differences were found between the first and the second week.

The test CHX was found to be less irritant for the oral tissues than the control one ($R^2 = 0.71$, Table 7). The difference between products was -0.59 (95% CI = -0.85 to -0.32). No differences were found between the first and the second week.

Discussion

This randomized, crossover, triple-blind study demonstrates that 0.2% alcohol-free CHX with an ADS system causes less pigmentation than an alcohol-free 0.2% CHX without ADS, when used after periodontal flap surgery for a period of 2 weeks. In addition, the test product consistently caused less side effects in terms of salt perception, bad taste and soft tissue irritation. Overall, it was more agreeable for the patients than CHX alone.

Compliance of patients with prescriptions is a critical issue in periodontology. The post-surgical early healing period is a critical span of time lasting a few weeks during which the patient is required to modify his/her behaviour and to take medications. Well-established post-surgical protocols

include modifications of the mechanical patient oral hygiene that could favour early bacterial re-colonization of the treated area. Control of plaque accumulation and bacterial re-colonization is therefore most of the times implemented, recommending the patient to use CHX mouthrinsings (Addy 1986, 2003, Lang & Brex 1986, Newman et al. 1989, Sanz et al. 1989, Quirynen et al. 1995, 2002, Addy & Renton-Harper 1996, Guarnelli et al. 2004, Faveri et al. 2006). However, it is well documented that CHX can cause a series of side effects that include pigmentation, alteration of food taste and mucosal irritation (Addy et al. 1985, Eriksen et al. 1985, Leard & Addy 1997). The occurrence of one or more of these negative events could influence the compliance of the patient with respect to the regular and proper use of CHX, thereby being potentially detrimental to the wound-healing process. This relevant issue has been approached by attempting to reduce the pigmentations and other side effects caused by CHX adding substances such as peroxiborate, polyvinyl pyrrolidone or sodium metabisulphite and ascorbic acid. One of these preparations (CHX with ADS), has been tested recently in 2 clinical trials and in an in vitro setting. Bernardi et al. (2004) tested the anti-plaque efficacy and the staining capacity of the 0.2% CHX ADS preparation compared with a 0.2% CHX on a sample of 15 patients. The authors reported that there was no statistically significant difference in the ability of the two mouthwashes to prevent bacterial plaque accumulation and gingival inflammation, while the staining associated with the CHX ADS was significantly reduced with respect to regular CHX. The study by Addy et al. (2005) was designed to test in vitro whether CHX ADS rinses do or do not bind dietary

chromogens. The authors concluded that the CHX ADS rinses will have the same anti-plaque and anti-gingivitis efficacy, but also the same potential to cause stain as established CHX rinse products. An in vivo cross-over study on 21 patients (Arweiler et al. 2006) compared conventional 0.2 CHX with CHX ADS and with a placebo. The authors reported a significant anti-plaque effect of the two tested CHX on top of the placebo. Conventional CHX was found to be superior to CHX ADS in inhibiting plaque regrowth and reducing bacterial vitality. In other words, the reported studies support the efficacy of CHX ADS as an anti-plaque and anti-gingivitis agent; however, the in vitro study (Addy et al. 2005) does not confirm the anti-staining properties reported by the clinical one, and the Arweiler study shows a greater anti-plaque activity for conventional CHX in vivo.

The present clinical trial supports the efficacy of the CHX ADS mouth-rinse showing no differences in terms of gingival variables, like inflammation and oedema after periodontal flap surgery in the early 15 days of healing between the test and control products (Table 6). The test product, however, reduced tooth pigmentation consistently at week 1 and 2, confirming the outcomes reported by Bernardi et al. (2004). This is in disagreement with the study in vitro by Addy et al. (2005). A possible explanation for this difference could be the lack of control with respect to dietary chromogen intake in both the clinical studies.

In the present study, the peculiar experimental design (2-week post-surgical protocol) did not allow for a wash-out period between the two tested CHX. It should be taken into account, however, that the CHX formulation was the same in both the tested products and the only difference was the ADS; hence, the

washout is related to ADS and not to CHX. At the end of week 1, when the patients reversed the products, an accurate prophylaxis was performed to eliminate residual pigmentation from all the tooth surfaces as much as possible. However, the lack of a wash-out period should be taken into account for a potential carry-over effect that could explain, at least in part, the greater approximal pigmentation detected in the second week.

Overall, the CHX ADS was significantly better tolerated by the patients than the control CHX (Table 7). Patients consistently reported less food taste alterations, less alterations to the perception of salt and less irritation to the oral tissues during the use of the test CHX ADS when compared with the control one (Table 7).

The following conclusions can be drawn from the present cross-over, randomized, triple-blind clinical trial: (1) 0.2% alcohol-free CHX ADS caused less pigmentation (or staining) than the control, 0.2% alcohol-free CHX; (2) CHX ADS is as effective as CHX without ADS in reducing gingival signs of inflammation in the post-surgical early healing phase; (3) It is more agreeable, more tolerated and less burdened by side effects than CHX without ADS; (4) The use of CHX ADS could be of value in treatment protocols in which the patient compliance with a CHX mouthwash prescription is relevant.

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Clinical Relevance

Scientific rationale for the study. The use of CHX mouth-rinsing after periodontal flap surgery is a well-established protocol to supplement modified and less effective mechanical oral hygiene measures. CHX, however, can cause some side effects that could affect patient compliance.

A CHX ADS has been proposed that could be burdened by less side effects.

Principal findings. Use of CHX ADS compared with CHX without ADS resulted in similar efficacy in terms of reduction of post-surgical gingival inflammation, and caused less side effects in terms of staining, alteration

of food taste and salt perception and was overall preferred by patients to conventional CHX.

Practical implications. The use of CHX ADS could help patients to comply with professional prescriptions in treatment protocols in which the use of CHX mouthwash is relevant.