Treatment of oral lesions due to removable prostheses

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Abstract

Objectives: The study aimed at assessing the efficacy of a new mouthwash in treating oral lesions due to removable prostheses. **Methods and Materials:** The present prospective randomized clinical trial was performed on 44 patients. The experimentation lasted for 4 weeks and 4 operators participated. The effects of the mouthwash were evaluated subjectively and objectively, with questionnaires, Visual Analogic Scales and clinical examinations. The results were statistically analyzed. The following variables were recorded: presence of mucosal lesions due to unfit removable prostheses and lasting of pain after rinsing. **Results:** Forty-four patients completed the study. The statistical analysis evidenced significant differences between the test and the control group both for the outcome ($p<0.05$) and for the necessary time to achieve pain reduction after rinsing ($p<0.05$). **Discussion:** The recovery of oral lesions was due to the mechanical removal of prosthetic incongruities. The hexetidine- and cholorobutanol-based mouthwash caused prompt and lasting analgesia. **Conclusions:** The tested mouthwash favored the prompt absorption and the lasting efficacy of its chemical components. The hexetidine proved to be effective in reducing the tissue inflammation whereas the chlorobutanol quickly decreased pain.

Clinical Significance: The combined use of hexetidine and chlorobutanol in a mouthwash proved to be effective in reducing pain, improving the patients' quality of life, particularly during a removable prosthodontic treatment.

Key words: Removable prosthesis, oral lesion, mouthwash, hexetidine, chlorobutanol, antiseptic, analgesic, anesthetic, prospective randomized, clinical study.

Introduction

Nowadays, a close correlation between quality/maintenance of oral prostheses and clinical periodontal outcomes in the long term is well known and widely defined in the scientific literature.[1] Several studies evaluated harmful reactions of periodontal tissues in the presence of removable partial or complete prostheses. Clinical, radiographic and histologic techniques were used to analyze such adverse reactions. Particularly, inflammatory and hyperplasic reactions, increased pocket probing depth, tooth mobility and, in most severe cases, marginal bone resorption were evidenced.[1-4]

The main etiological factors of the harmful periodontal reactions in the presence of removable prostheses are: accumulation of mucobacterial plaque and poor oral hygiene, covering of soft tissues due to prosthetic components and functional loads transmitted to the supporting tissues, which participate in mucosal tissues compression.[1-4]

As to plaque accumulation and hygienic maintenance, the presence of a removable prosthesis in the oral cavity influences both quantitatively and qualitatively the microbial ecosystem onto both residual teeth and mucosal tissues.[5, 6] Particularly, the proliferation of Spirochaetes and

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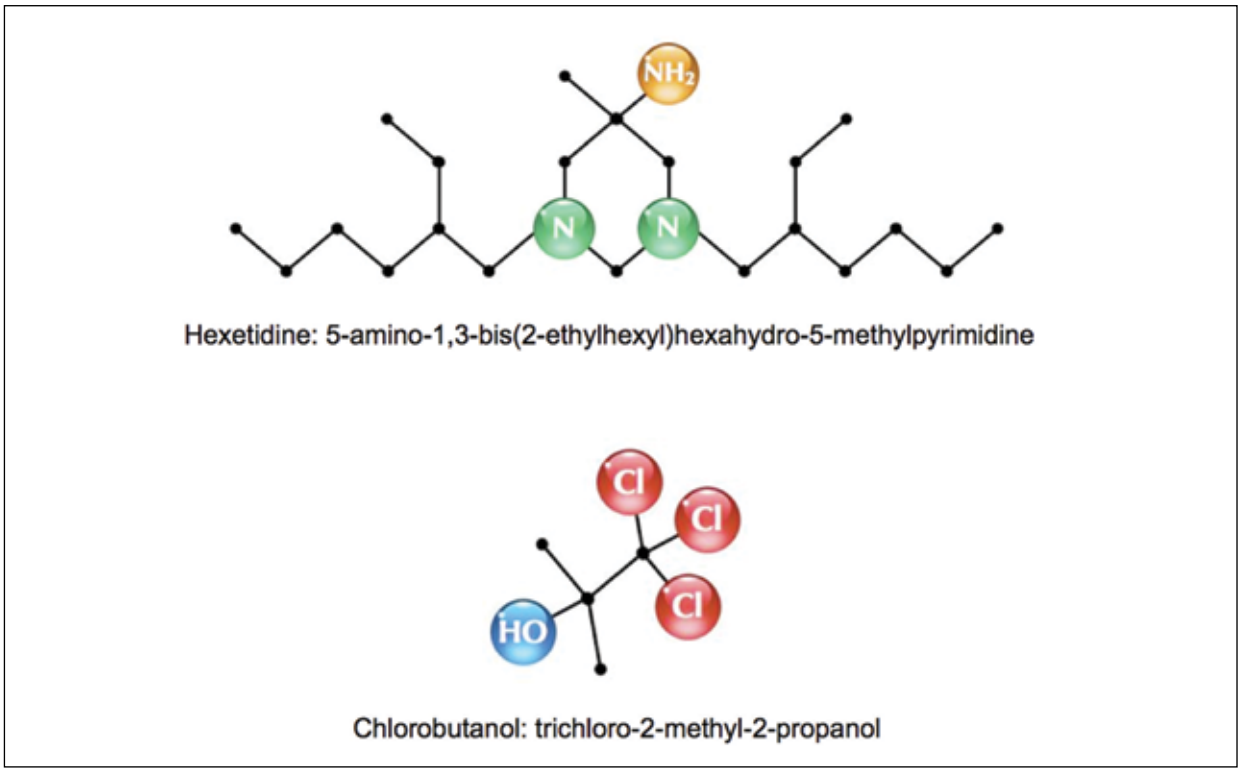

Figure 1.

Fusobacteria was showed to be favoured by the presence of partial removable prostheses.[6]

Particular care should be devoted to the hygienic maintenance of the impression surface of any kind of removable prostheses, since it is almost in continuous contact with mucosal tissues.[7] The control of mucobacterial plaque as well as the periodic professional check of removable dentures should be sufficient to guarantee the long term success of such prostheses.[8-10]

Similarly to subjects with natural teeth, mucobacterial plaque formation and growing in patients wearing removable prostheses could be efficiently controlled by means of mechanical hygienic procedures of both oral tissues and dentures together with the use of mouthwashes.[11-15]

Several chemical substances were described to be used in the formulation of such compounds, like antiseptics for local use, analgesics for aphthae, aphthous stomatitis, prosthesis-induced ulcers and lesions, traumas and biting injuries, thermic and chemical irritations and mouthwashes for the treatment of halitosis.[11-15]

Hexetidine (5-amino-1,3-bis(2-ethylhexyl)hexahydro-5-methylpyrimidine; Figure 1) belongs to the pharmacological category of antiseptics for local use.[16] It is a cationic antiseptic with a wide spectrum bacteriostatic activity at concentrations ranging between 5-10 mg/l and 100-150 mg/l against Gram-positive and Gram-negative microorganisms respectively as well as against fungi (e.g. Candida Albicans); at higher concentrations, it shows bactericidal activity. At a therapeutic concentration of 0.1%, hexetidine kills in less than 1 minute microorganisms just like Staphylococcus Aureus and Klebsiella Pneumoniae. Pharmacological studies proved that the main mechanism of action is due to the interference with metabolic processes necessary to the growth of such bacteria. Possible resistance phenomena to hexetidine were demonstrated to be transient.[16, 17]

Hexetidine is used as a mouthwash against local infections as well as for oral hygiene maintenance, particularly in the pre- and post-operative treatment of dental and oral surgery. It is indicated for symptomatic treatment of throat irritations, ulcers and recurring aphthae, inflammations of tonsils, pharynx, larynx and gingivae, ulcerative stomatitis and oral candidiasis; the use of hexetidine was proved to be effective in the treatment of halitosis as well. It also acts as a local anesthetic and has an efficacy against mucobacterial plaque accumulation.[16, 17]

As regards its pharmacodynamic properties, studies using radioactively marked hexetidine proved that the substantivity on both oral mucosae and mucobacterial

Table 1 – Pain relief perception (I = immediate, D = delayed, N = none) after rinsing. Weekly scores were obtained considering the prevalence of patients' responses recorded in case report forms.

TEST GROUP					CONTROL GROUP				
Patient	Week 1	Week 2	Week 3	Week 4	Patient	Week 1	Week 2	Week 3	Week 4
1	I	I	I	I	23	N	D	D	D
2	I	I	I	I	24	D	D	D	D
3	I	I	I	I	25	I	I	I	I
4	D	I	I	I	26	N	N	D	D
5	I	I	I	I	27	D	D	N	D
6	I	I	I	I	28	D	D	D	D
7	I	I	I	I	29	I	I	I	I
8	I	I	I	I	30	I	I	I	I
9	I	I	D	I	31	D	D	D	D
10	I	I	I	I	32	D	D	D	D
11	I	I	I	I	33	N	D	D	D
12	I	I	I	I	34	N	N	D	N
13	I	D	I	I	35	D	D	D	D
14	I	I	I	I	36	I	I	I	I
15	I	I	I	I	37	N	D	D	D
16	I	I	I	I	38	D	D	I	D
17	I	I	I	I	39	D	D	D	D
18	D	I	I	I	40	I	I	I	I
19	I	I	I	I	41	N	N	D	N
20	I	I	I	I	42	N	D	N	N
21	I	I	I	I	43	D	D	D	D
22	I	I	I	I	44	N	D	D	D

plaque ranges between 8 and 10 hours after a single rinse; in a few cases, such effect lasted for 65 hours. [16, 17]

Chlorobutanol (trichloro-2-methyl-2-propanol; Figure 1) belongs to the pharmacological category of general anesthetics.[18] It looks like an uncolored or whitish crystalline compound with camphoraceous smell and taste. It is widely used in various pharmacologic preparations as a conservant; particularly, it is an active component in some oral sedatives, local anesthetics, ophthalmological and otorhinolaryngologic drops and mouthwashes. It is effective against bacteria and fungi.[18, 19]

Chlorobutanol exists both in hydrous ($C_4H_7Cl_3O \cdot 1/2\ H_2O$) and anhydrous ($C_4H_7Cl_3O$) forms. It is usually used at 0.5% concentration, since it is stable in preparations containing various compounds; moreover, it is stable at room temperature and atmospheric pressure. Chlorobutanol is lightly soluble in water, alcohol and glycerol whereas it is highly soluble in chloroform and ether. [20, 21]

The aim of the present prospective, randomized, triple-blind controlled clinical trial was to evaluate the efficacy of an innovative mouthwash (emulsion) in the treatment of lesions of oral mucosae due to removable prostheses. The tested preparation contained two active molecules: a topical antiseptic (0.1% hexetidine) and a local anesthetic (0.5% chlorobutanol).

Materials and methods

The present study is a single-centre, prospective, randomized, triple-blind controlled clinical trial on 44 consecutive patients, comparing a mouthwash containing

Table 2 – Weekly evolution of mucosal lesions (W = worsening, S = stable, B = bettering, H = healing).

CONTROL GROUP					TEST GROUP				
Patient	Week 1	Week 2	Week 3	Week 4	Patient	Week 1	Week 2	Week 3	Week 4
1	H	H	H	H	23	S	H	H	H
2	H	H	H	H	24	B	H	H	H
3	S	H	H	H	25	B	W	H	H
4	H	H	H	H	26	H	H	H	H
5	H	H	H	H	27	B	H	H	H
6	H	H	H	H	28	B	S	H	H
7	H	H	H	H	29	S	H	H	H
8	B	H	H	H	30	B	H	H	H
9	B	H	H	H	31	S	B	H	H
10	H	H	H	H	32	H	H	H	H
11	H	H	H	H	33	W	B	H	H
12	S	H	H	H	34	H	H	H	H
13	H	H	H	H	35	S	H	H	H
14	H	H	H	H	36	S	H	H	H
15	B	H	H	H	37	B	H	H	H
16	H	H	H	H	38	H	H	H	H
17	H	H	H	H	39	S	S	H	H
18	H	H	H	H	40	S	H	H	H
19	H	H	H	H	41	S	H	H	H
20	H	H	H	H	42	B	S	H	H
21	H	H	H	H	43	B	H	H	H
22	H	H	H	H	44	S	H	H	H

0.1% hexetidine and 0.5% chlorobutanol with a 0.20% chlorhexidine mouthwash. The study was conducted in the Department of Prosthodontics of the University "Federico II" of Naples (Italy) in a 4-week period between February and March 2010.

The present study was designed according to the CONSORT clinical trial guideline.[22]

Study population

The study population was selected among the patients of the Department of Prosthodontics of the University "Federico II" of Naples (Italy). Patients wearing removable partial or complete dentures, in general good health, presenting lesions of oral mucosae due to prostheses were considered to be eligible for this study.

In order to participate in the study, patients had to satisfy the following inclusion criteria: [23, 24]

- Use of removable partial or complete dentures;
- Presence of lesions of oral mucosae due to dentures;
- Absence of any concomitant local or systemic pathology;
- Absence of pregnancy or breastfeeding;
- Negative allergic anamnesis;
- Negative anamnesis for recurrent aphthous stomatitis;
- No taking medicines with potential pharmacologic interactions with molecules to be tested;
- No taking antibiotics and/or painkillers for at least 6 months before entering the experimentation;
- Good oral hygiene with a full-mouth plaque score ≤25%;
- Non smoking or light smoking (≤10 cigarettes/day) status.

Missing one or more of the above described conditions automatically excluded a subject from the study. [23, 24]

Fifty-one patients were assessed for eligibility and 7 were

Table 3 – Results of Student's T-test for prognosis (presence of lesions vs healing) between the test group (Y) and the control group (X).

PAIRED SAMPLES STATISTICS					
		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	*Y*	,4667	22	,51640	,13333
	X	,8667	22	,35187	,09085

PAIRED SAMPLES CORRELATIONS				
		N	Correlation	Sig.
Pair 1	*Y&X*	22	,367	,179

PAIRED SAMPLES TEST									
		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	*Y-X*	-,40000	,50709	,13093	-,68082	-,11918	-3,055	14	,009

excluded: 5 did not meet inclusion criteria (2 were affected by diabetes and 3 took antibiotics and/or painkillers in the 6 months preceding the experimentation) and 2 refused to participate.

Forty-four patients of both genders (19 males and 25 females), whose age ranged between 37 and 79, were selected for the study. Twenty-two patients were allocated to intervention (test group) and 22 were allocated to control (control group).

The patients selected for the experimentation entered the study freely after undergoing exhaustive oral explanations and signing a written consent form according to the Declaration of Helsinki. [23]

Experimental design

The present clinical trial had a whole observational period of 4 weeks. The study was designed, performed, checked and reported according to the Guidelines for Good Clinical Practice. [25] The experimental protocol was reviewed and approved by the Ethical Committee of the University "Federico II" of Naples.

The study was performed in the Department of Prosthodontics of the University "Federico II" of Naples (Italy) by a team of 4 operators: 1 recruiter (study supervisor), 2 clinicians (1 dentist and 1 dental hygienist) and 1 statistician. The study supervisor was the unique recruiter of study population.

At the first visit, each patient underwent an accurate clinical examination and professional oral hygiene. Moreover, a clinical evaluation checklist was created in a case report form for each patient; such checklist was updated during all the follow-up visits. The case report form was used to record the following information:

- date of the visit;
- operator's initials;
- patient's identification numerical code;
- patient's age and gender;
- anamnestic data;
- diagnosis;
- taking of medicines;
- incoming allergies;
- use of tobacco (yes, no, occasional=up to 10 cigarettes per day);
- alcohol drinking (yes, no, occasional=up to the equivalent of 1 glass of wine per day);
- type of prosthesis (resin removable partial denture, metal-resin removable partial denture, removable complete denture, overdenture);

Table 4 – Results of Student's T-test for lasting of painful symptomatology (presence vs absence of pain after rinsing) between the test group (Y) and the control group (X).

PAIRED SAMPLES STATISTICS					
		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	*Y*	,2000	22	,41404	,10690
	X	,8667	22	,35187	,09085

PAIRED SAMPLES CORRELATIONS				
		N	Correlation	Sig.
Pair 1	*Y&X*	22	,196	,484

PAIRED SAMPLES TEST									
		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	*Y-X*	-,66667	,48795	,12599	-,93688	-,39645	-5,292	14	,000

- intraoral position of prosthesis.

Once the mucosal lesions were identified, clinicians verified the presence of compression areas due to removable prostheses and removed excessive pressure using the conventional prosthodontic procedures of base relining, finishing and polishing.

The experimental mouthwash (Buccagel®, Curaden Healthcare, Saronno, Italy) was made up of the following formulation: purified water, dicaprylyl-ether, coco-caprylate caprate, xylitol, glyceryl-stearate, ceteareth-20, ceteareth-12, cetyl-palmitate, cetearyl-alcohol, chlorobutanol, aroma, hexetidine, methylparaben, propylparaben, sodium saccharin, citric acid and colorant C.I. 16255.

Conversely, a conventional commercial mouthwash (Curasept® ADS 0.20%, Curaden Healthcare, Saronno, Italy) containing the following compounds was used in the control group: water, xylitol, propylenglycol, Peg-40 of hydrogenated ricin oil, ascorbic acid, chlorhexidine digluconate, aroma, poloxamer 407, sodium metabisulfite, sodium citrate and colorant C.I. 42090.

Only the study supervisor was aware of the chemical composition of the mouthwashes. All of the patients received an anonymous bottle containing either the control or the test mouthwash along with a 15 ml calibrated glass. [15] Bottles were identical in shape and opaque, in order not to influence either patients and clinicians with different colors or viscosity of mouthwashes.[23, 25] Bottles were coded with either A or B and randomly distributed to patients.

Patients were instructed and motivated by a dental hygienist in performing correct home procedures of oral hygiene and particular care was dedicated to the correct use of mouthwashes. They were prescribed to rinse 3 times per day (after breakfast, lunch and dinner) for 1 minute with 15 ml of mouthwash after performing the conventional hygienic procedures of both oral tissues and prostheses;[23, 25] the amount of product per bottle was calibrated to satisfy this prescription. Furthermore, patients were instructed neither to brush mucosal lesions nor to drink or rinse with water for at least 30 minutes after using mouthwashes, in order to increase the substantivity of active molecules.[23, 25]

During all experimentation, patients were forbidden

from using other mouthwashes, undergoing dental treatments and taking medicines potentially interacting with molecules to be tested. Such limitations were particularly related to direct or indirect use of painkillers and local anesthetics, which could influence the real effects of the active molecules to be studied on patients' pain perception.[23, 25]

Clinical measures

The presence of mucosal lesions due to unfit removable prostheses and pain relief effects of the tested mouthwashes were evaluated both subjectively and objectively by means of VASs with soft data collection and clinical examinations respectively.[23, 25]

At each weekly follow-up visit, the parameters reported in the above mentioned case report form were updated and clinicians recorded the development of lesions on the basis of objective clinical signs, reporting worsening, stability, bettering or healing of lesions. The following parameters were also recorded:

- edema (no, light, moderate, severe);
- erythema (no, light, moderate, severe);
- bleeding (yes, no);
- pain (no, light, moderate, severe).

Furthermore, patients were required to quantify the entity of the perceived subjective symptomatology by means of a Visual Analogic Scale (VAS) of 10 cm ranging from 0 to 10 (0 = no pain ÷ 10 = extreme pain). [15, 25]

Each patient was provided with a personal datebook to record pain reduction after every rinse (immediate, delayed, none), the possible complete healing and the compliance to the experimental protocol.

Moreover, patients' perception and acceptance of the mouthwashes were evaluated with a questionnaire administered at each weekly follow-up visit and responses were recorded with VASs.[15] The questionnaire included the following parameters:[15]

- Taste of the mouthwash (0 = bad taste ÷ 10 = good taste);
- Irritation of oral mucosae (0 = no irritation ÷ 10 = severe irritation);
- Alterations in food taste (0 = no alteration ÷ 10 = relevant alteration);
- Different side effects (0 = no side effects ÷ 10 = relevant side effects).

Randomization and allocation concealment

Randomization was performed by the scientific supervisor by tossing a coin and assigning the code A or B to a table of consecutive numbers from 1 to 44. In order to keep patients' privacy safe as well as to limit experimental bias, a confidential list in which each patient was unambiguously identified by means of a numerical code was printed and kept by the study supervisor; neither the clinicians nor the statistician knew the sensitive data of any patient. Similarly, only the study supervisor was informed about the randomization list. Patients were sequentially entered into the experimentation. Each patient received a numbered sealed opaque envelope containing the mouthwash assignment; such envelope was opened at the end of the first visit.

Either the clinicians and the statistician and the patients remain blinded about which mouthwash was randomly assigned for the entire study. In order to guarantee the objectivity of the experimentation as well as to limit interpretational bias, the code was broken by the study supervisor in the presence of a representative of the manufacturer after the statistical analyses were carried out.

Sample size calculation

The study was designed to have 80% power. The level of significance was set at $p<0.05$. The required number of patients was 36; the final number was set to 44 considering a potential 20% patient dropout from the study.

Data analyses

The statistical analyses were performed by a statistician blind to the clinical procedures of the experimentation. Recorded data were statistically analyzed with a dedicated software (SPSS 16 for MAC OS X, SPSS Inc., Chicago, IL, USA) using the Student's T-test.

The primary outcome variable was prognosis (e.g. presence of mucosal lesions due to unfit removable prostheses) while the secondary outcome variable was lasting of painful symptomatology after rinsing. Differences in both variables were tested between the two different treatments.

Two different null hypotheses were tested:

- no association between the use of control or test mouthwash and the prognosis of mucosal lesions due to unfit removable prostheses;
- no association between the use of control or test mouthwash and the lasting of painful symptomatology.

The parameters related to patients' acceptance were studied only as soft data recording patients' responses.

Results

None of the patients was lost at follow-up or discontinued intervention. A total of 44 patients (19 males and 25 females), mean age 58.1 ± 13.1 years (minimum 37, maximum 79 years) completed the study; all of them were analyzed. Nine patients (6 in the test group and 3 in the control group) were light smokers.

All patients were treated for mucosal lesions due to unfit removable prostheses according to conventional clinical procedures and were recalled at follow-up each week for 4 weeks. No complications or complaints were recorded. All patients showed perfect compliance to prescriptions.

All of them had achieved the complete healing, although at different times. None of them lamented neither xerostomy nor altered or bad taste due to the use of mouthwashes. In both experimental groups undesired secondary effects were not evidenced.

The test mouthwash proved to be faster and more effective than the control mouthwash in reducing pain (Table 1). All of the patients in the test group referred an immediate pain relief perception after rinsing; on the contrary, only 5 patients of the control group referred the same sensation.

As to the healing achievement, disappearance of mucosal lesions was observed in 4 patients after 1 week, in 12 patients after 2 weeks and in the remaining 6 patients after 3 weeks of treatment in the control group, whereas it was observed in 17 patients after 1 week and in the remaining 5 patients after 2 weeks of treatment in the test group (Table 2).

The statistical analysis showed statistically significant differences between the experimental groups both for the prognosis ($p<0.05$, Table 3) and for the necessary time to achieve pain reduction after rinsing ($p<0.05$, Table 4). Consequently, both the tested null hypotheses were rejected.

Discussion

The present prospective, randomized, triple-blind study proved that the combined use of hexetidine and chlorobutanol is effective in reducing pain and enhancing healing of mucosal lesions due to unfit removable prostheses when used for at least 1 week. Patients' compliance with prescriptions is paramount to make the treatment effective. When necessary, patients have to be instructed to modify their habits to maintain a good oral hygiene.

As widely demonstrated in the literature, remission of painful symptoms caused by mucosal lesions due to dentures as well as complete healing of soft tissues are enhanced by mechanical removal of causal factors, such as prosthetic pressure spots causing excessive compression. Nevertheless, the chemical treatment of such lesions by using mouthwashes could represent a valid approach to improve hygienic maintenance of oral cavity, enhancing detersion of lesions and reducing the risk of bacterial superinfection.[1-3, 5, 6, 8-15]

It was proven that the prolonged use of chlorhexidine may cause a yellowish-brownish pigmentation not only of teeth and tongue but also of acrylic resin prostheses. [26] Although such pigmentation is reversible on oral tissues, mouthwashes chlorhexidine-free or containing anti-discoloration substances are highly appreciated by patients.

It was also demonstrated that mouthwashes containing ethanol concentrations >10% may cause painful symptoms.[27] Consequently, elimination or reduction of ethanol to concentrations <10% could be a useful characteristic for therapeutic preparations to be used locally in oral cavity. Furthermore, it is worth remembering that prolonged use of alcohol may alter intracellular metabolism making cells more susceptible to carcinogens. Similarly, oral mucosae may absorb certain compounds transferring them to blood circulation. [27, 28]

The test mouthwash is a homogeneous emulsion made up of two functional compounds dispersed in two different phases (e.g. oil in water without alcohol): hexetidine in both hydrous and oily phases with an antiseptic and antiinflammatory function and chlorobutanol in oily phase with an anesthetic function (Figure 2). Such formulation enhances a rapid absorption and a prolonged effectiveness of its components. The presence of lipophilic complexes with high substantivity on gingivae and dentin allows the formation of a lipidic film that prolongs the efficacy of active molecules. The lipophilic film protects oral mucosae mechanically making cellular renewal faster (Figure 3).

According to the results of previous studies, in the present investigation chlorobutanol reduced pain quickly[20], while hexetidine decreased inflammation and bacterial presence.[17]

The test mouthwash showed a wide and complete therapeutic effectiveness in the presence of both single or multiple lesions, irrespectively to their dimensions.

The control mouthwash reduced the inflammation of soft tissues creating a lipidic film on oral mucosae. This also

contributed to improve the general hygienic conditions of oral cavity but, differently from the test group, the control mouthwash did not produce analgesia, neither prolonged nor transient, after rinsing.

Conclusions

Within the limitations of the present study, the following conclusions can be drawn:

- although the mechanical removal of prosthetic incongruities is paramount, the use of mouthwashes proved to be useful to achieve healing of mucosal lesions;
- the use of the tested active molecules was effective in reducing painful symptoms, making the patients' quality of life better and promoting their compliance to a correct maintenance of oral hygiene.

Conflict of interest

The authors declare that they have no conflict of interest.

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