

## Editorial

Dear Colleagues,

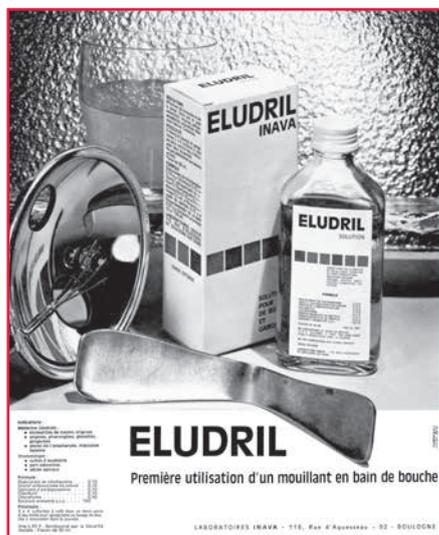
Since 1966, **Chlorhexidine (CHX)** has been part of Pierre Fabre Laboratories' oral health product range. The first product containing this active ingredient was marketed in 1968 (ELUDRIL® mouthwash). Since making its way into our research and development programmes, this antiseptic has been formulated in solutions, sprays, toothpastes, gels, etc.... up to the recent launch of ELUDRIL PERIO® in 2013 (mouthwash, 0.20% chlorhexidine).

This diversity in presentation makes it possible to meet the diverse range of expectations and needs of the profession. Through reference publications, this EluMed supplement reinforces the medical interest of this active ingredient and the suitability of its use in odonto-stomatology.

Collegially yours,

**Dr. Jean-Philippe GATIGNOL**  
Dentist, Medical Department

Pierre Fabre  
ORAL CARE



**ELUDRIL**  
1968

## Chlorhexidine

Oral health care professionals know very well that surgery is often their best option! Nevertheless, it has certain limitations and can be helped, through the use of the Pharmacopoeia in general and antiseptics in particular, by an effective complementary procedure to this "technical" approach.

Technical procedures in dentistry, often surgical, are particularly invasive. Transient bacteremia associated with therapeutic procedures (scaling/root planing, dental extractions, any oral surgical procedure, etc.), can be found in the septic environment represented by the oral cavity.

Furthermore, the wide range of periodontal conditions requires the use of antibacterial treatments, especially antiseptics, in order to neutralize the bacterial component (dental biofilm).

Antisepsis is therefore very important. The top antiseptic used in dentistry since the 1970s is Chlorhexidine (C<sub>22</sub> Cl<sub>2</sub> N<sub>10</sub> H<sub>30</sub>). Chlorhexidine (CHX) belongs to the family of chlorinated biguanides. Its antibacterial action is bacteriostatic or bactericidal, depending on the concentration. It is used in the form of salts (Chlorhexidine digluconate and diacetate) for better solubility. Beyond its broad spectrum antiseptic activity, the characteristics that mean CHX is still essential today, are its capacity to bind to the different oral structures (teeth, mucosa). The optimal dose of CHX generally administered is 20 mg twice per day, giving a better ratio between efficacy, local side effects and acceptability to patients. Finally, note that the Haute Autorité de Santé (French National Health Authority), following its 2010 Transparency Committee, only validates Chlorhexidine as a reference molecule for local adjunct treatment for oral cavity infections, and post-operative care in stomatology.

For nearly 50 years, Chlorhexidine has been the gold standard as an anti-plaque agent (bacterial biofilm), but also as a pre-, per- and post-operative antiseptic in oral surgery. Control of the microbial factor in surgery (avulsion, periodontal and implant surgery, etc.), will be one of the pivotal factors for good healing in oral, periodontal and implant surgery.

Despite an abundance of available data, some questions remain about the efficacy of this antiseptic. At what concentration, what posology, pre- and/or post-operation, is it most effective? Do interactions with other substances interfere in a negative way?

Updated data, combined with an established level of scientific proof, help provide new answers.

## Contents

- p2** **The efficacy of 0.12% Chlorhexidine mouthrinse compared with 0.20% on plaque accumulation and periodontal parameters: a systematic review.**  
C.E. BERCHIER, D.E. SLOT, G.A. VAN DER WEIJDEN
- p4** **Effect of a Chlorhexidine mouthrinse on plaque, gingival inflammation and staining in gingivitis patients: a systematic review.**  
D.A.C. VAN STRYDONCK, D.E. SLOT, U. VAN DER VELDEN, F. VAN DER WEIJDEN
- p6** **Chlorhexidine mouthwash and sodium lauryl sulphate dentifrice: do they mix effectively or interfere?**  
T.A. ELKERBOUT, D.E. SLOT, E.W.P. BAKKER, G.A. VAN DER WEIJDEN
- p8** **Extract of: Local interventions for the management of alveolar osteitis (dry socket)**  
DALY, M.O. SHARIF, T. NEWTON, K. JONES, H.V. WORTHINGTON.

# The efficacy of 0.12% Chlorhexidine mouthrinse compared with 0.20% on plaque accumulation and periodontal parameters: a systematic review

## BACKGROUND:

Chlorhexidine (CHX) digluconate, a cationic bisbiguanide, is the gold standard anti-plaque agent. Its activity is **dose-dependent**.

## OBJECTIVE OF THE STUDY:

To assess, by comparing them, the effects of 0.12% and 0.20% Chlorhexidine mouthrinses on dental plaque and the periodontal parameters in adult patients.

# 1

## METHODOLOGY

### Two publications were used as sources for this study:

- The National Library of Medicine, Washington, DC (MEDLINE-PubMed).
- Cochrane Central Register of Controlled Trials (CENTRAL).

### Principal eligibility criteria for the studies chosen:

- Randomized controlled clinical trials (RCT) or controlled clinical trials (CCT).

### 409 preselected titles and summaries:

8 eligible studies (see list opposite, adapted according to Berchier et al. 2010)

NUMBER	AUTHOR YEAR	TITLE	DESIGN, BLINDING, EVALUATION PERIOD, WASHOUT PERIOD	RISK OF BIAS ACCORDING TO THE AUTHORS
I	Harper et al. (1995)	An approach to efficacy screening of mouthrinses: studies on a group of French products (II). Inhibition of salivary bacteria and plaque in vivo	Crossover RCT Double-blind 4 days (2.5 days)	Low
II	Keijser et al. (2003)	Comparison of 2 commercially available Chlorhexidine mouthrinses	Parallel RCT Single-blind 3 days	Moderate
III	Neto et al. (2008)	Comparative analysis of the effect of two Chlorhexidine mouthrinses on plaque accumulation and gingival bleeding	Crossover RCT Double-blind 14 days (7 days)	Low
IV	Pizzo et al. (2006)	The effects of antimicrobial sprays and mouthrinses on supragingival plaque regrowth: a comparative study	Crossover RCT Single-blind 4 days (10 days)	Low
V	Quirynen et al. (2001)	Effect of different Chlorhexidine formulations in mouthrinses on de novo plaque formation	Crossover RCT Double-blind 11 days (3 weeks)	Low
VI	Segreto et al. (1986)	A comparison of mouthrinses containing two concentrations of Chlorhexidine	Parallel RCT Double-blind 3 months	Low
VII	Smith et al. (1995)	Comparative staining in vitro and plaque inhibitory properties in vivo of 0.12% and 0.2% Chlorhexidine mouthrinses	Crossover RCT Double-blind 4 days (10 days)	Low
VIII	Van Strydonck et al. (2005)	Plaque inhibition of two commercially available Chlorhexidine mouthrinses	Parallel RCT Single-blind 3 days	Moderate

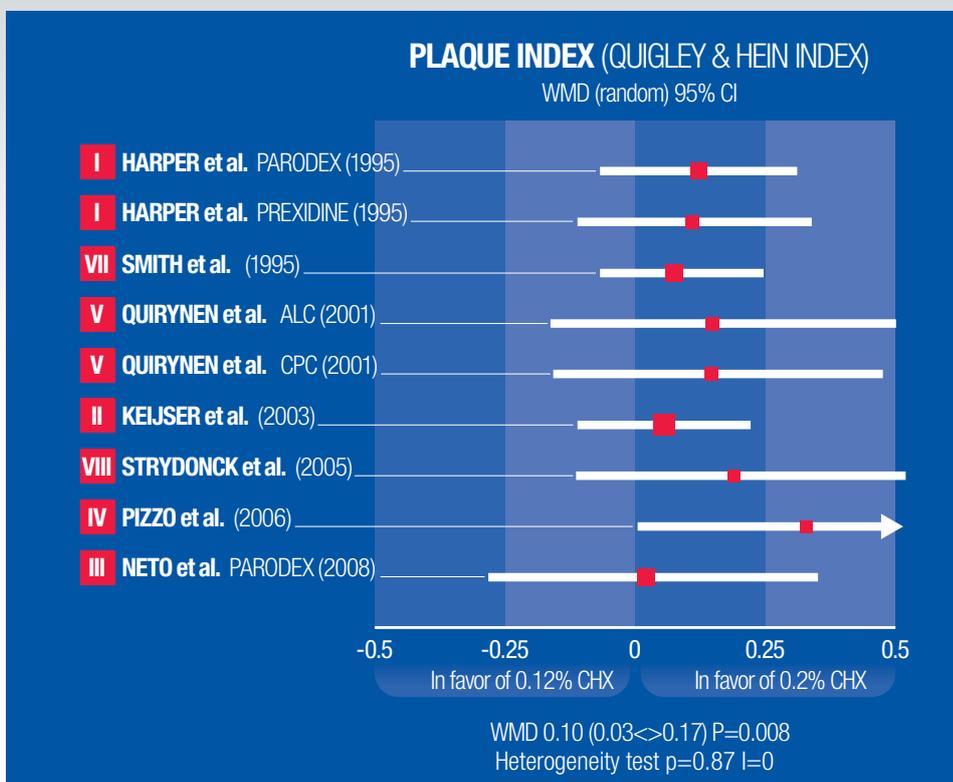
- For all the studies except two (IV and VI), the volume used was 15 ml for the 0.12% CHX mouthrinse and 10 ml for the 0.20% CHX mouthrinse.
- The mouthrinses were used twice a day for 30 or 60 seconds depending on the protocol.
- Clinical parameters studied:  
**Plaque score:** Quigley & Hein plaque index; Quigley & Hein plaque index modified by Turesky et al. (1970); Quigley & Hein plaque index (1962) modified by Turesky et al. (1970) then by Lobene et al. (1982) and Silness & Loë plaque index (Silness & Loë 1964).  
**Bleeding:** 3 studies assessed gingival bleeding (III, V, VI).  
**Gingivitis:** only one study assessed gingivitis according to the papillary marginal gingival index (VI).  
 No study was found comparing the two dosages of CHX and assessing pocket depth by probing and/or the level of periodontal attachment.

Summary\* written by Dr. J.P. GATIGNOL.

\*For educational purposes, the style is adapted to the review's editorial policy, with strict adherence to content.

## 2 PRINCIPAL RESULTS

- None of the eight studies showed a statistical difference in terms of plaque scores for either dosage.
- The studies assessing bleeding did not show a statistical difference between the groups using either concentration: 0.12% and 0.20% CHX (III, V and VI).
- A meta-analysis of the plaque scores was carried out and the weighted mean differences (WMD) were calculated.
  - 182 and 183 subjects in each group.
  - The plaque index scores (Quigley & Hein 1962) **showed a significant difference in terms of effect on plaque between the 0.12% and 0.20% CHX.** (Fig. 1 adapted according to Berchier et al. 2010).
  - The WMD is 0.10 in favor of the 0.20% CHX mouthrinse with a confidence interval of 95% (CI: [0.03–0.17]).
  - The overall assessment showed a **statistically significant value (p = 0.008) in favor of the 0.20% concentration**
  - The “clinical difference” in the plaque scores did not translate into a difference in gingival inflammation.



**Fig. 1 - Meta-analysis** comparing the plaque index between 0.12 and 0.20% Chlorhexidine



Photograph of stained dental plaque. Coll. L. Sanguinol

### Focus on:

- As a complement to tooth brushing and appropriate treatment, a CHX-based mouthrinse is the preferred solution for reducing plaque and gingivitis.
- The studies show a **slight but significant difference between the 0.12% and 0.20% concentrations**.
- A dosage of **0.20% CHX** has a statistically significant **advantage on the reduction of plaque** (p=0.008).
- The available information does not show **any difference on gingivitis**.

# Effect of a Chlorhexidine mouthrinse on plaque, gingival inflammation and staining in gingivitis patients: a systematic review

D.A.C. VAN STRYDONCK,  
D.E. SLOT,  
U. VAN DER VELDEN,  
F. VAN DER WEIJDEN  
J Clin Periodontol 2012; 39: 1042–1055.

Summary\* written by DR. J.P. GATIGNOL.  
\*For educational purposes, the style is adapted to the review's editorial policy, with strict adherence to content.

## BACKGROUND:

In the absence of tooth brushing, a mouthrinse of 60 seconds twice a day with 10 ml of 0.20% CHX solution (dose of 20 mg) is likely to:

- inhibit the reformation of plaque by around 60%,
- reduce the severity of gingivitis by 50-80%.

## OBJECTIVE OF THE STUDY:

To assess the effectiveness of Chlorhexidine (CHX)-based mouthrinses on plaque, gingival inflammation and dyschromia in patients suffering from gingivitis.

## Focus on:

- **In patients suffering from gingivitis,** CHX mouthrinses, combined with oral and dental hygiene measures, result in:
  - Significant reductions in plaque scores and gingivitis scores, in comparison with placebo or control mouthrinses,
  - A significant increase in reversible dyschromia scores.
- All the studies included assessed the use of CHX in addition to mechanical oral hygiene measures.
- This systematic review highlights **the anti-plaque and anti-gingivitis effectiveness of a CHX mouthrinse** used in addition to regular oral hygiene measures in patients suffering from gingivitis.
- The use of a CHX mouthrinse in addition to oral hygiene measures reduces plaque by around 33% and gingivitis by 26% in comparison with control groups.

## 1 METHODOLOGY

### Publications used as sources for this study:

- Medline, EMBASE and Cochrane Central Register of Controlled Trials up to April 2011.

### Principal eligibility criteria for the studies chosen:

- Randomized controlled clinical trials lasting 4 weeks or more, comparing CHX to placebo/control mouthrinses or oral hygiene measures (OH).

### 30 publications were selected;

A meta-analysis (MA) was carried out.

## 2 PRINCIPAL RESULTS

A significant difference was seen in favor of the CHX group compared to the control group:

- A 33% reduction in plaque (Quigley & Hein 1962).
- A 26% reduction in gingivitis (Löe & Silness 1963).

The CHX mouthrinse groups showed significantly more dyschromia than the control groups.

**According to the American Dental Association (ADA)** in the "Acceptance Guidelines for Chemotherapeutic Products for Control of Gingivitis (2008)", it can be concluded that CHX-based mouthrinses effectively reduce plaque and gingivitis, although they do not eliminate them completely.



**Fig. 4** - Photograph of plaque-induced gingivitis  
Coll. L. Sanguinol

# Chlorhexidine mouthwash and sodium lauryl sulphate dentifrice: do they mix effectively or interfere?

T.A. ELKERBOUT,  
D.E. SLOT, E.W.P.  
BAKKER, G.A.  
VAN DER WEIJDEN,  
Int J Dent Hygiene 2016 Feb;14(1):42-52.

Summary\* written by Dr. J.P. GATIGNOL.  
\*For educational purposes, the style is adapted to the review's editorial policy, with strict adherence to content.

## BACKGROUND:

- The foaming agent most commonly used in toothpaste is the anionic surfactant sodium lauryl sulphate (SLS). It helps to solubilize the flavoring agents and active ingredients.
- *In vitro*, SLS and CHX can have antagonistic effects. *In vivo*, rinsing with an aqueous solution of SLS before a CHX-based mouthrinse significantly reduces the anti-plaque action of the CHX.
- A **previous systematic review concluded that the interval between brushing teeth and using a CHX-based mouthrinse should be at least 30 minutes.**
- On a daily basis, if a CHX mouthrinse is advised, it is generally recommended to use an SLS-free toothpaste or to wait at least 30 minutes after brushing before rinsing.
- However, **two recent *in vivo* studies showed no significant difference** in the accumulation of dental plaque when the CHX mouthrinse was used after brushing with a **toothpaste containing SLS.**

These contradictory results justified exhaustive research and a systematic analysis of the publications currently available.

## OBJECTIVE OF THE STUDY:

To systematically analyze the various publications examining the effects of a CHX mouthrinse combined with toothpaste containing SLS on the parameters for dental plaque and gingivitis.

## 1 METHODOLOGY

- Conducted in accordance with the **Transparent Reporting of Systematic Reviews and Meta-analyses guidelines.**
- Main inclusion criteria for the studies chosen:
  - Randomized controlled clinical trials (RCT) or controlled clinical trials (CCT).
  - Procedure: CHX mouthrinse combined with a toothpaste containing SLS, or a rinse with a mixture of water/toothpaste containing SLS (or slurry).
  - Comparison: CHX mouthrinse alone or combined with an SLS-free toothpaste or with a mixture of water and SLS-free toothpaste.
  - Assessment parameters for the results: plaque, bleeding and gingivitis scores.
- 3 studies conducted with 0.20% CHX, 1 study conducted with 0.12% CHX.
  - The 4 clinical trials show a certain heterogeneity in terms of study design (crossover study, split-mouth, and parallel study) and rinsing and toothpaste routine.
  - The potential risk of bias was thus estimated as being low for the 4 studies.

## 2 PRINCIPAL RESULTS

- No significant difference was observed in comparing brushing teeth with a toothpaste containing SLS combined with a CHX mouthrinse, with a mouthrinse alone or combined with an SLS-free toothpaste.

→ A further sub-analysis showed no significant sub-group differences ( $P=0.85$ ) between the combined use of a CHX mouthrinse and a toothpaste containing SLS, and that of a mouthrinse alone or combined with an SLS-free toothpaste.

- For the studies involving brushing, no significant difference between the sub-groups was observed ( $P=0.73$ ) in terms of sequence of use.

- The strength of recommendations should be considered "moderate" regarding the use of a toothpaste containing SLS combined with a CHX mouthrinse.

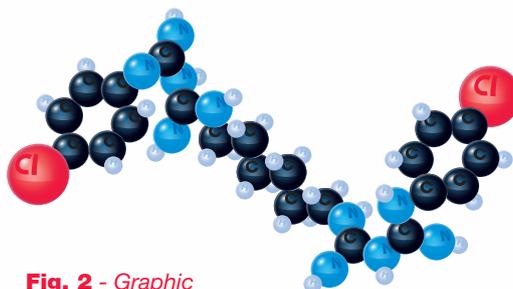


Fig. 2 - Graphic representation of a Chlorhexidine molecule  $C_{22}H_{30}Cl_2N_{10}$



Fig. 3 - Graphic representation of a Sodium-Lauryl-Sulphate molecule  $NaC_{12}H_{25}SO$

## Focus on:

The majority of the studies included in this publication conclude that:

When a CHX mouthrinse is recommended, it can be used:

- **In combination with a toothpaste containing SLS without it interfering with the anti-plaque action of the CHX.**
- **No matter what the sequence of use.**
- **The combination of toothpaste and CHX mouthrinse is not contraindicated.**
- **This recommendation is classified as moderate.**

# Extract of: Local interventions for the management of alveolar osteitis (dry socket)

B. DALY, M.O. SHARIF,  
T. NEWTON, K. JONES,  
H.V. WORTHINGTON,

Cochrane Database Syst Rev. 2012; 12: CD006968.  
T DODSON, Department of oral and  
maxillofacial surgery, Center for Applied Clinical Investiga-  
tion, Massachusetts General Hospital, Boston, USA  
Evidence-Based Dentistry (2013) 14, 13-14.

Summary\* written by Dr. J.P. **GATIGNOL**.  
\*For educational purposes, the style is adapted  
to the review's editorial policy,  
with strict adherence to content.

## OBJECTIVE OF THE STUDY:

To present and discuss the results published in the Cochrane review entitled: *Local interventions for the management of alveolar osteitis (AO)*.

## 1 METHODOLOGY

■ A systematic review supported and published by the Cochrane group represents the gold standard in substantiating clinical decision-making.

■ Only randomized controlled trials (RCT) were considered.

■ 21 trials were included; 2,570 participants

- 18 trials (2,376 participants) involved prevention.
- 3 trials (194 participants) involved treatment.

## 2 PRINCIPAL RESULTS

■ A moderate level of evidence (4 trials, 750 participants) suggested that:

- Chlorhexidine-based mouthrinses (concentrations of 0.12% to 0.20%) before and after extraction(s) **prevent around 42% of cases of alveolar osteitis** with an RR of 0.58 ( $P < 0.001$ ).

- The number of patients receiving Chlorhexidine-based treatment (0.12% and 0.20%) to prevent the occurrence of alveolar osteitis was 232, 47 and 8 for prevalences of 1%, 5% and 30% respectively.

■ Moderate evidence (2 trials, 133 participants) suggested that applying a Chlorhexidine gel (0.20%) after extraction prevented around 58% of cases of alveolar osteitis.

■ There is insufficient evidence to determine the effect of other intra-alveolar preventive interventions (each assessed by a single study) or that of interventions to treat alveolar osteitis.

■ Adverse effects:

- This review found evidence attributing the occurrence of mild adverse effects

to the use of 0.12%, 0.20% and 2% Chlorhexidine-based mouthrinses.

- No adverse effects associated with the use of 0.20% Chlorhexidine gel directly in the alveolus were reported.

- In view of the 2 cases recently reported in the UK of severe adverse effects associated with the irrigation of dry sockets with a Chlorhexidine-based mouthrinse, we recommend that health professionals able to prescribe such products be aware of possible adverse effects, whether minor or severe.

■ The reported frequencies of AO (alveolar osteitis) range from 0 to 37.5%. This broad spectrum may be due to differences in practical definitions according to the studies.

■ In this report, the diagnosis criteria for AO have not been listed.

■ Each of the studies included agreed prospectively on the diagnosis criteria.

■ The results of this study suggest that the use of a Chlorhexidine-based mouthrinse or the intra-alveolar application has a minimal to moderate effect on the incidence of AO.

■ Despite the warnings from the authors, which seem exaggerated to us, the risk of adverse effects following short-term exposure to Chlorhexidine remains minimal.

■ The authors have reviewed the use of Chlorhexidine to prevent AO but have not put forward an opinion regarding other local treatments to prevent (10 other intra-alveolar interventions) or treat (5 AO interventions).

- The data being "insufficient" to determine their effects.

- In view of the data provided, numerous studies have been unable to show a difference between the various local treatments for preventing AO.

- In 2 out of 3 studies, the intra-alveolar application of antibiotics (metronidazole or clindamycin) was statistically effective in reducing the frequency of AO, and the direction of the effects of treatment was in favor of the groups on antibiotics, thus suggesting a promising area for research.

- The authors of the review cited 5 studies that used a topical anesthetic.

- Given the results of this review, **the authors modified the peri-operative treatment to include pre- and post-operative rinses with Chlorhexidine.**

## Focus on:

- There is evidence of efficacy associated with the use of a Chlorhexidine mouthrinse (0.12% to 0.20%) (or the application of a 0.20% gel) **in the prevention of alveolar osteitis following a dental extraction.**

- Given the results of the Cochrane review, the authors modified the peri-operative treatment **to include pre- and post-operative rinses with Chlorhexidine.**

# Chlorhexidine in practice and in pictures



## ■ Use of Chlorhexidine in oral surgery

Healing very satisfactory at 8 days after surgery. Suture of the flap with vestibular incision in the context of germectomy of tooth 48.

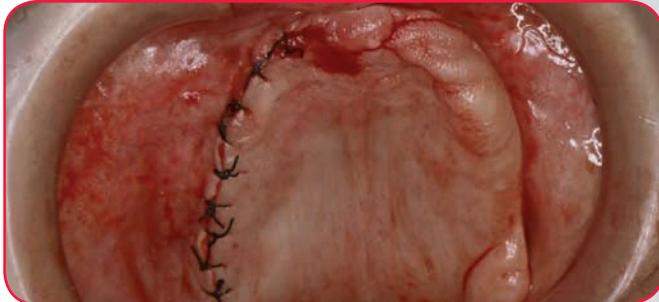
*Coll. D. Gauzeran*



## ■ Use of Chlorhexidine in oral surgery

End of the procedure (removal of multiple odontoids in an 8-year-old child): suture of the L-flap by separate stitches.

*Coll. D. Gauzeran*



## ■ Use of Chlorhexidine in plastic surgery

End of the first plastic surgery intervention (hypertrophic mobile ridge): suture by separate stitches.

*Coll. D. Gauzeran*



## ■ Use of Chlorhexidine in implantology

End of placement of 3 implants: suture of the flap by separate stitches with offset vestibular incision.

*Coll. D. Gauzeran*



## ■ Use of Chlorhexidine in the context of periodontitis.

Photograph of chronic periodontitis.

*Coll. L. Sanguinol*

# Opinion

## CHLORHEXIDINE – A COMPANION-IN-ARMS

I experienced the use of chlorhexidine digluconate very early in my professional career due to the influence of the Norwegian Professors who visited our Lisbon Dental School in the late 70s. However, Oral rinses with chlorhexidine did not exist in Portugal at that time. We could only find "Hibitane" produced at that time by ICI, a chlorhexidine product for hospital use, applied as a disinfectant. It came in a 20% concentration. I found a local pharmacy which diluted it into small 100ml bottles, diluted down to 0.2% and which patients could buy from them on a regular basis. At that time, we used it in cases of ANUG, which were more prevalent than nowadays and as a post-op rinse. This latter use came as a revolution for periodontal surgery therapy since, until then, the use of a periodontal dressing was mandatory. From then on, the dressing almost disappeared from use since chlorhexidine was very efficient in controlling the microbiota of the surgical wound.

The use and the indications of chlorhexidine expanded over the years and was introduced by many different pharmaceutical companies in their armamentaria. It became one of the most important chemical tools for the clinician as well as for the patient's home use in certain indications.

The amount of research which started accumulating in the late 70s and 80s has clearly demonstrated that chlorhexidine digluconate was extremely effective in reducing dramatically certain pathogens to levels which were conducive to health. Another property which made chlorhexidine digluconate different from other efficient antimicrobials was its substantivity. The fact that its antimicrobial power is retained in the oral cavity following rinsing makes it extremely appealing from a pharmacological as well as from a clinical point of view. This retained chlorhexidine will be then slowly released into the oral fluids.

Many indications have been advocated for the chlorhexidine digluconate rinse. Even though it is my antimicrobial rinse of choice, I reserve it for certain and very specific situations. I do not use this chemical at these high concentrations as a long-term rinse, unless the Patient is handicapped or cannot perform a proper daily mechanical plaque control due to any other reason. Nowadays, it would be very difficult to function on a daily basis without the use of chlorhexidine digluconate as an antimicrobial agent.

Following many research papers showing the highly efficient decrease in microbiological volume in the oral cavity after a single rinse of one minute with chlorhexidine, I administer a rinse to all my patients before any kind of dental procedure, even the very simple ones.

My second major use will definitely be the post-op care. Rinsing at least twice a day for one or two minutes with a the higher concentration of chlorhexidine digluconate gives the surgical wound a chance to heal without the presence of a pathological bacterial load. In this area, the chlorhexidine gels also introduced a new avenue in order to deliver the active compound in the most specific area, reducing the side effects to the rest of the oral cavity, such as staining.

ICI: Imperial Chemical Industries  
ANUG: Acute Necrotizing Ulcerative Gingivitis



**GIL ALCOFORADO**

DMD, PH.D.

FICD: Fellow of International College of Dentists  
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