

Non surgical treatment of peri-implant pockets: An exploratory study comparing 0.2% chlorhexidine and 0.8% hyaluronic acid

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ABSTRACT

Background: Peri-implant pathology consists of a chronic infection of the implant supportive tissues; its pathogenesis characterized by either the traditional pathway (from the soft tissues apically to the bone), or retrograde (from the bone to the soft tissues). In non surgical treatment, hyaluronic acid and chlorhexidine appear as eligible substances to apply in non surgical protocols, due to its antimicrobial and healing characteristics. This study aimed to compare the efficacy of a protocol for irrigating peri-implant pockets using a plastic needle with 0.8% HA or 0.2% CHX, through evaluation of clinical parameters included in the implant success criteria. The hypothesis tested was if the treatment success followed the same distribution in the HA and CHX groups. **Methods:** The study enrolled eighteen clients with one implant presenting probing pocket depth up to 6 mm. Bone loss and bleeding on probing were treated through mechanical debridement, and were randomly allocated to either a treatment with 0.8% hyaluronic acid (AH) or with 0.2% chlorhexidine (CHX) gels for irrigation of the peri-implant pocket. The success criteria determined that after the implementation of the protocol, the implants should have a modified bleeding index=0, probing pocket depths ≤ 4 mm, improvement of the attachment level, no suppuration and no clinical mobility. **Results:** The percentage of success for the treatment in both groups was 55 per cent and 89 per cent for the HA and CHX groups respectively. Intragroup analysis when compared to baseline, revealed a statistically significant improvement in both the HA and CHX groups on the clinical indices performed in the final evaluation. No significant differences were found between the two groups in treatment success. **Discussion:** The results obtained in this study favour the adoption of non surgical protocols. The fact that no significant differences were found between both groups supports the research hypothesis in the use of HA in the treatment of pockets up to 5 mm and of CHX for the treatment of pockets up to 6 mm. **Conclusion:** It was possible to conclude within the limitations of this study, that the use of non surgical therapy is effective, making it possible either to treat peri-implant pathologies with a simple protocol, or to prepare the site for surgical therapy in case of an unsuccessful treatment.

RESUMÉ

Contexte : La pathologie péri-implantaire est une infection chronique des tissus qui soutiennent l'implant, dont la pathogénèse se caractérise par le cheminement traditionnel (des tissus mous apicaux vers l'os) ou rétrograde (de l'os vers les tissus mous). Pour le traitement non chirurgical, l'acide hyaluronique et la chlorhexidine semblent être des substances appropriées à appliquer dans les protocoles non chirurgicaux à cause de leurs caractéristiques antimicrobiennes et curatives. Cette étude a donc pour objet de comparer les résultats du traitement non chirurgical des poches péri-implantaires, qui consiste à retirer les débris et à irriguer la poche péri-implantaire avec un gel (d'acide hyaluronique 0,8 % ou de chlorhexidine 0,2 %). **Méthodes :** Dix-huit patients qui ont, à un implant, une poche de 6 mm de profondeur et une perte osseuse et qui saignent au sondage ont été soignés par débridement mécanique et reçu au hasard un traitement de gels à l'acide hyaluronique (AH) 0,8 % ou à la chlorhexidine (CHX) 0,2 % pour irriguer la poche péri-implantaire. Les critères de réussite prévoyaient, après l'application du protocole, un indice de saignement =0 à l'implant, une profondeur de la poche de ≤ 4 mm au sondage, une amélioration du degré de fixation, l'absence de suppuration et de mobilité clinique. **Résultats :** Le pourcentage de réussite du traitement a été de 55 % et 89 % chez les groupes AH et CHX respectivement. L'analyse a révélé une amélioration statistiquement significative chez chacun des deux groupes, AH et CHX, selon les indices cliniques relevés lors de l'évaluation finale comparativement à celle du début. Quant à la réussite du traitement, il n'y avait pas d'écart significatif entre les deux groupes. **Discussion :** Les données favorisent l'adoption des protocoles non chirurgicaux en utilisant le traitement AH des poches ayant une profondeur maximale de 5 mm et le CHX pour les poches allant jusqu'à 6 mm. **Conclusion :** Dans les limites de l'étude, on pouvait conclure que la thérapie non chirurgicale est efficace, car elle permet de traiter les pathologies péri-implantaires avec un protocole simple ou de préparer le site pour la chirurgie si le traitement n'était pas réussi.

Key words: dental implant; irrigation; infection control, dental; chlorhexidine; hyaluronic acid

INTRODUCTION

Peri-implant pathology consists of an inflammatory process affecting the soft and hard tissues surrounding the implant, resulting in rapid loss of supporting bone associated with bleeding and suppuration.¹ Its pathogenesis is characterized by either the traditional pathway (from the soft tissues apically to the bone), or retrograde (from the bone to the soft tissues).²

The treatment of this pathology can be performed through two different interventions: surgical or non surgical approaches. The success of treating peri-implant pathologies through a non surgical approach by means of mechanical debridement has been demonstrated in several studies.³⁻⁵

The needle for irrigation represents an important issue for both the client's comfort and the efficacy in admin-

istering chemical agents when performing non surgical interventions using chemical agents (i.e. pocket irrigation), since it has the potential of provoking mechanical trauma to the client.⁶ Trauma could be discomfort, pain and less compliance, thus affecting the efficacy of treatment. Another important issue lies in the chemical agent used for irrigating the pocket. In this field, chlorhexidine (CHX) represents an efficient antiseptic used in the oral

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Figure 1. Devices for introduction of the CHX gel (upper) and HA gel (lower).

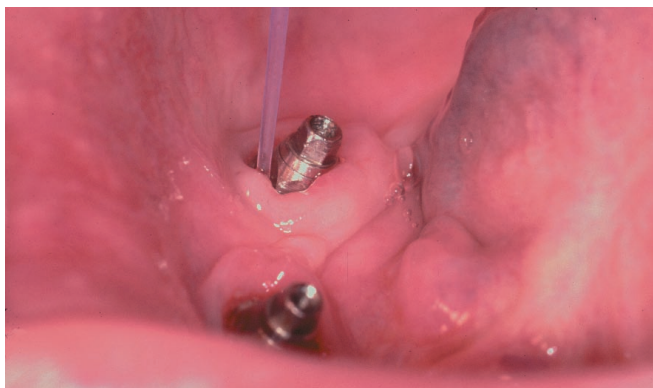


Figure 2. Irrigation of the peri-implant pocket using the device composed by the plastic syringe with the gel inside and a plastic tip.

cavity,^{7,8} since it can inhibit the formation of dental plaque biofilm through several mechanisms, namely, immediate bactericidal effect, prolonged bacteriostatic effect by surface bound CHX, blockage of the acidic groups from the salivary glycoproteins that form the pellicle, binding to the bacterial surface in sublethal amounts so that initial adhesion to the surfaces is inhibited and disturbance of the plaque formation by precipitation of agglutination factors in saliva, and displacement of calcium from the plaques' matrix.⁹

The use of CHX gel in irrigating peri-implant pockets as an adjunctive to mechanical debridement therapy in the treatment of peri-implant pathology is documented with a treatment success of 89 per cent at client level and 85 per cent at implant level.¹⁰ Characteristics of CHX and the results obtained make it the gold standard antiseptic for adjunctive treatment in non surgical therapy.

Hyaluronic acid (HA) is described as a natural organic substance, with physiological therapy activity, it is the main component of the extracellular matrix of many tissues such as skin, synovial joints and periodontal tissues.¹¹

The HA multifunctional role in the healing process of chronic lesions, including those that are observed in periodontal disease,¹² attests to its potential importance in the non surgical treatment. The administration of high molecular weight HA proved to be effective in inducing tissue repair and healing in clients with inflammatory gingivitis and surgical wounds.^{11,13-15} According to the manufacturer, HA can be used professionally at a higher

concentration of 0.8% for the treatment of pockets with probing depths up to 5 mm.¹⁶ However, no studies were found using 0.8% HA in non surgical treatment that could support this hypothesis.

The aim of this study was to compare the efficacy of a protocol for irrigating peri-implant pockets using a plastic needle with 0.8% HA or 0.2% CHX, through the evaluation of clinical parameters included in the implant success criteria. The hypothesis tested was if the treatment success followed the same distribution in the HA and CHX groups.

MATERIALS AND METHODS

This prospective clinical study was performed in a private clinic, Malo Clinic, in Lisbon, Portugal. The study comprised eighteen treated clients (mean age 57 years, ranging 45-77 years), 10 males and 8 females, and with 18 implants supporting 18 prostheses. The first client was treated in January 2007, and the last in July 2007. All clients were rehabilitated through an immediate function protocol (implant + abutment + crown/bridge in the same surgical step)^{17,18} with the implants osseointegrated and in function for at least one year.

The clients were included in the study provided that they had at least one implant respecting the following inclusion criteria:

- peri-implant pockets of ≥ 5 mm;
- bleeding on probing;
- absence of implant clinical mobility;
- bone loss between the coronal and the medium $\frac{1}{3}$ of the implant;
- and signed written informed consent to participate in the study.

The clients were randomly allocated to one of the treatment groups (HA or CHX) using a random number sequence generator computed at www.random.org

A homogeneity analysis was performed to the two samples: gender was equally distributed between the two groups (4 females and 5 males in each group); mean age (SD) of 56.2 (1.7) and 58.7 (3.1) for AH and CHX groups, respectively, with no significant difference between both groups ($p=0.494$; t-test).

The rights of the participants were safeguarded, following the indications present in the Declaration of Helsinki. The protocol included the right of cease or refuse to participate in the study, confidentiality, information about the outcome of the study, access to data, justice and beneficence. These rights were explained to participants at the time they were asked for written informed consent to participate in this study.

The evaluation parameters included:

- Marginal bone loss readings from periapical radiographs (taken at the baseline diagnostic appointment), with the bone level registered according to implant thirds: the implants' coronal third, medium third or apical third.
- Modified bleeding index (mBI),¹⁹ assessed by inserting a periodontal probe 1 mm into the sulcus, circumferentially around the implant/abutment, and registered in an ordinal scale with values between 0 and 3 (0=no bleeding visible, 1=isolated bleeding spot visible,

2=the blood forms a confluent red line on the margin, and 3=heavy or profuse bleeding).

- Clinical mobility (Mob),²⁰ evaluated using manual movement to assess individual implant mobility and registered as present or absent.
- Suppuration (Sup),²⁰ evaluated by applying finger pressure to the peri-implant complex and registered as present or absent.
- Probing pocket depth (PPD) assessed to the nearest mm.²¹
- Distance between implant shoulder and mucosal margin (DIM) assessed to the nearest mm (in the presence of a sub gingival implant shoulder, the measurement was recorded as a negative value).²¹
- and Attachment level (AL) computed for each site by adding PPD and DIM.²¹

Before enrolling the clients in this study, a thorough evaluation of the prosthesis was performed to check the client's occlusion and any problems with the design of the prosthesis that could influence the client's oral hygiene.

The predetermined criteria for success in this study included:

- mBI=0;
- PPD \leq 4 mm;
- improvement of the attachment level;
- absence of suppuration, and
- absence of mobility.

All the diagnostic indices were registered as baseline values before implementing the protocol. After registering baseline indices, dental plaque biofilm and calculus were removed in the infected sites, and followed by irrigation with the gel. Irrigation followed the same procedures according to a previously described protocol.¹⁰

The materials used to irrigate the peri-implant pockets were a plastic disposable syringe (BD Plastipak® 15 ml, Becton and Dickinson Company, Lisbon, Portugal), a plastic needle of 0.4 mm of diameter (Capillary tip®, 27 gauge, Ultradent Products Inc, South Jordan, UT, USA) attached to the syringe, and CHX 0.2% gel (Lacer Chlorhexidine Bioadhesive Gel®, Lacer, Barcelona, Spain) or a HA 0.8% gel (Gengigel®, Ricerfarma, Milano, Italy) depending on the group to which the client was allocated. The protocol included the following parameters:

- The area was isolated and dried before the technique was applied.
- The gel was placed into the syringe, and compacted into its lower portion without attaching the needle so that the air could be released from the syringe's interior.
- After this procedure, the needle was attached to the syringe (Figure 1).
- For irrigation, the peri-implant pocket was first gently air dried.
- The needle was positioned inside the full length of the pocket.
- The syringe was pressed so that the gel could be released, filling the peri-implant pocket (Figure 2). Slight coronal-apical-coronal movements were performed so to better administrate the gel in the peri-implant pocket.
- After seeing the gel pouring out of the pocket, the

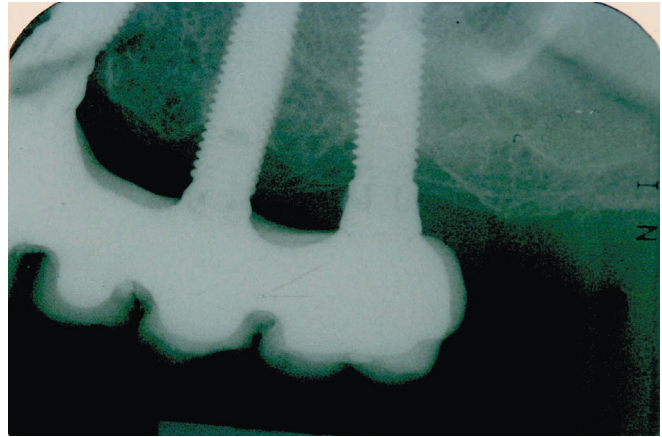


Figure 3. Clinical situation. Periapical x-ray at baseline evaluation. Note the vertical 2-wall bone defect in implants #25 and #26.

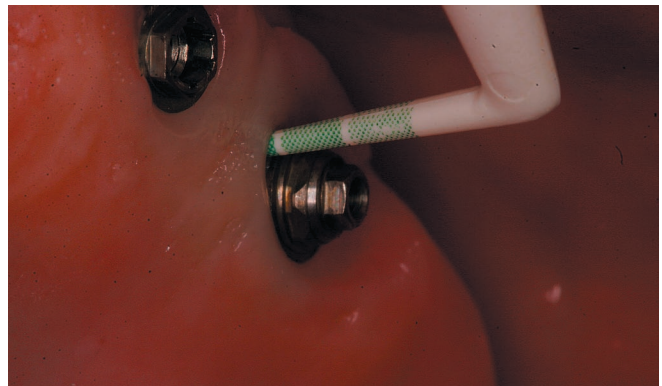


Figure 4. Clinical situation. Baseline evaluation of implants #25 and #26. Note the diagnosis of a peri-implant pocket of 5 mm on the mesial aspect of implant #26.

pressure in the syringe was stopped, and the needle was removed from the peri-implant pocket.

This procedure was repeated in all peri-implant pockets. After the irrigation, the client was instructed not to eat, drink or rinse for at least half an hour so that the gel could remain in the pocket for the longest period possible. A clinical situation is illustrated in figures 3–5.

For self care, the client received dental hygiene instructions to brush with a 0.2% CHX gel or a 0.2% HA gel (according to the group distribution) and a soft toothbrush. One month later all indices were re-evaluated, to assess if the implants met the success criteria.

Descriptive statistics were used to perform univariate analysis of the clinical indices (mPII, mBI, PPD, DIM, AL). Inferential statistical analysis was used to determine the equality of mean ranks in the clinical indices in intragroup (post treatment evaluation vs. baseline) and intergroup evaluation, and for the comparison of success between both groups ($\alpha=.05$).

RESULTS

At baseline, the overall mPII ranged from 0 to 3 (mean of 1.5); mBI 1–3 (mean of 2.1); PPD 5–7 mm (mean of 5.6 mm); DIM -4 to 0 mm (mean of -2.4 mm); AL 1–5 mm (mean of 3.2 mm). Four of the 18 implants presented bone loss localized in the medium third of the implant, whereas 14 implants presented bone loss in the coronal third of

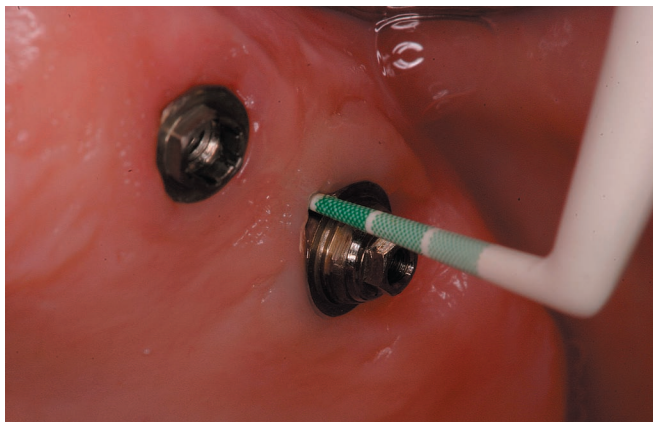


Figure 5. Clinical situation. Post treatment evaluation of implant #26 after one month. Note the reduction of the pocket to 3 mm.

the implant. The baseline clinical indices distributed by group are presented in Table 1. Post treatment diagnosis revealed significant changes in the clinical parameters which are presented in Table 2. Overall, the mPIL ranged from 0 to 2 (mean of 0.6); mBI 0–3 (mean of 0.8); PPD 3–7 mm (mean of 4.3 mm); DIM -4 to 1 mm (mean of -2.1 mm); AL 0–4 mm (mean of 2.2). No suppuration or clinical mobility was recorded for any implant in the post treatment evaluation. Significant differences were found in the intragroup evaluation (baseline vs. post treatment) for mPIL, PPD and AL in the HA group; and for PPD and AL in the CHX group. Applying the criteria of success, the therapy was considered successful in 5 of 9 clients of the HA group. In the CHX group, the therapy was considered

a success in 8 of 9 clients, with no significant difference between the two groups ($p=0.294$; Chi-square test). For the five implants that did not meet the success criteria, surgical treatment was performed and the clients were withdrawn from the study.

After one year, the clinical parameters were again documented. During the follow-up period between post treatment and 1-year evaluations, one client died due to causes unrelated to the treatment (HA group), and five clients failed to comply with the control appointment (3 in the HA group; 2 in the CHX group).

Overall, the mPIL ranged from 0 to 2 (mean of 1.0); mBI 0–1 (mean of 0.3); PPD 2–4 mm (mean of 3.3 mm); DIM -2 to 2 mm (mean of -0.7 mm); AL 0–5 mm (mean of 2.6).

DISCUSSION

The different etiopathogenesis of peri-implant pathology makes it challenging to treat. However, by applying a non surgical therapy, it is possible to treat the pathology successfully, or at least to initiate the hygienic phase of the treatment prior to surgery (in case the non surgical therapy fails). In this protocol, the infection control takes part as the most important variable. By performing an optimal diagnosis first,²² following the removal of the aetiological factor (removal of deposits and decontamination of the pocket), and guaranteeing a good client self care, it is possible to achieve good outcomes in the treatment of these pathologies. It was the objective of this study to compare the efficacy of two non surgical protocols for the treatment of peri-implant pathology.

The mPIL results allow to conclude that the client's self

Table 1: Pre treatment evaluation in HA and CHX groups

N	Implant position	mPIL	mBI	PPD	DIM	AL	Bone loss (implant thirds)
HA group							
1	44	0	3	5	-3	2	Medium third
2	22	2	3	6	-4	2	Medium third
3	13	1	2	5	-2	3	Coronal third
4	36	2	2	6	-3	4	Coronal third
5	46	2	3	5	-3	2	Coronal third
6	46	2	1	6	-3	3	Coronal third
7	22	2	1	6	-3	3	Coronal third
8	16	0	3	6	-2	4	Coronal third
9	42	0	2	5	0	5	Coronal third
Mean	-----	1.2	2.2	5.6	-2.6	3.1	-----
CHX group							
1	42	3	2	7	-3	4	Coronal third
2	16	0	0	6	-3	3	Coronal third
3	15	2	2	6	-2	4	Coronal third
4	21	2	2	6	-3	3	Medium third
5	45	1	1	5	-2	3	Medium third
6	42	1	2	6	-2	4	Coronal third
7	42	3	3	5	-1	4	Coronal third
8	36	1	2	5	-1	4	Coronal third
9	42	3	3	5	-4	1	Coronal third
Mean	-----	1.8	1.9	5.7	-2.3	3.3	-----

Table 2: Post treatment evaluation in HA and CHX groups

N	Implant position	mPlI	mBI	PPD	DIM	AL	Bone loss	Treatment success/failure
HA group								
1	44	0	0	4	-2	2	Medium	Success
2	22	1	2	6	-4	2	Medium	Failure
3	13	0	0	3	-2	1	Coronal	Success
4	36	1	1	4	-2	2	Coronal	Success
5	46	1	1	4	-3	1	Coronal	Success
6	46	1	3	7	-3	4	Coronal	Failure
7	22	1	1	5	-3	2	Coronal	Failure
8	16	0	1	5	-2	3	Coronal	Failure
9	42	0	0	2	1	3	Coronal	Success
Mean	-----	0.6 ^a	1.0	4.4 ^b	-2.2	2.2 ^c	-----	-----
CHX group								
1	42	2	2	7	-3	4	Coronal	Failure
2	16	0	0	4	-3	1	Coronal	Success
3	15	0	0	4	-2	2	Coronal	Success
4	21	0	1	4	-2	2	Medium	Success
5	45	0	2	4	-2	2	Medium	Success
6	42	1	1	4	-1	3	Coronal	Success
7	42	1	0	4	-1	3	Coronal	Success
8	36	0	0	3	-1	2	Coronal	Success
9	42	1	0	3	-3	0	Coronal	Success
Mean	-----	0.6	0.7	4.1 ^d	-2.0	2.1 ^e	-----	-----

^a Significantly different when compared to baseline ($p=0.007$; Chi-square test); ^b significantly different when compared to baseline ($p=0.031$; Chi-square test); ^c significantly different when compared to baseline ($p=0.046$; Wilcoxon test); ^d significantly different when compared to baseline ($p=0.008$; Wilcoxon test); ^e significantly different when compared to baseline ($p=0.009$; Wilcoxon test)

care plays a major role in the success of the treatment: it allowed for removal of the aetiological cause of the disease, and this way establishing good conditions for the healing of the soft tissue.²³⁻²⁵ The decrease in the mPlI index between baseline and post treatment diagnosis (significantly different for the HA group) was due to better self care performed by the clients.

In this study, the significant reduction of PPD and AL in both groups is indicative of disease control. Taking into consideration that DIM did not differ significantly between baseline and post treatment, the changes in AL can be interpreted as a reduction of the peri-implant pocket and gingival inflammation.

The non surgical protocols rendered 56 per cent and 89 per cent success in the HA and CHX groups, respectively. However, the difference in the treatment success distribution between both groups was not significant, supporting the research hypothesis. The results obtained with this approach are comparable to other studies, where the combined use of CHX with mechanical treatment produced good results in the treatment of peri-implant infections.^{3-5,26-28} Specifically, it is possible to reproduce the results from the CHX group with a previous study following the same protocol.¹⁰

It is possible to increase its efficacy in the treatment of peri-implant pathologies with the long-acting antimicrobial properties and substantivity of CHX,²⁹⁻³¹ and by keeping the chemical inside the pocket for a long period, in a way similar to periodontal treatment.³²⁻³⁸

Taking into consideration the results achieved with HA (with a successful outcome for pockets equal to 5 mm, but only one successful treatment in pockets of 6 mm), the authors suggest that this treatment should be administered only in cases of mucositis and peri-implant pathologies with probing depths up to 5 mm, following the specifications for 0.8% HA use provided by the manufacturer.¹⁶

The overall clinical parameter results at 1-year follow-up tended to further improve (compared to post treatment) or stabilize below those of the baseline (Table 3), a result that finds parallel in similar studies.¹⁰

Despite the efforts for controlling the threats to internal validity, some threats existed, namely, the small sample size, the number of withdrawn clients and the involvement of only one clinic. The small sample size may have a possible influence on two levels: the statistics, in relation to the outcome (success/failure) and consequently the testing of the hypothesis; and on the representativeness of the population (limited to the middle aged population and a predominance of males) making it mandatory to extrapolate the results from this study to the general population with caution. The large number of withdrawn clients at the 1-year follow-up (a total of six clients) is the main limitation, as it may also influence the statistics in relation to monitoring of clinical parameters in the long term. However it is important to point out the difference between the efficacy of the non surgical treatment, suitable to be evaluated in the short term as successful or unsuccessful, and the maintenance of that efficacy, suitable to be evalu-

Table 3: Mean values of clinical parameters measured

	Baseline	Post treatment	1-year follow-up
mPLI (0-3)	1.5	0.6	1.0
mBI (0-3)	2.1	0.8	0.3
PPD (mm)	5.6	4.3	3.3
DIM (mm)	-2.4	-2.1	-0.7
AL (mm)	3.2	2.2	2.6

ated in the long term.

Larger randomized controlled trials are needed to further study the efficacy of local antimicrobials on bacteria present in the peri-implant pocket when managing peri-implant pathology.

CONCLUSION

Within the limitations of this study, the authors conclude that the use of non surgical therapy for the treatment of peri-implant pathology is possible, and with good outcomes in the short term follow-up. There was no significant difference in the treatment success between HA and CHX groups. However, the use of HA did not produce successful results in the treatment of pockets with more than 5 mm, while the treatment with CHX produced reliable results in the short term follow-up in pockets of 5 mm and 6 mm.

REFERENCES

- Romeo E, Ghisolfi M, Carmagnola D. Peri-implant diseases. A systematic review of the literature. *Minerva Stomatol.* 2004;53:215–30.
- Meffert R. Research in implantology at Louisiana State University School of Dentistry. *Int J Oral Implantol.* 1990;6:15–21.
- Porras R, Anderson GB, Caffesse R, Narendran S, Trejo PM. Clinical response to 2 different therapeutic regimens to treat periimplant mucositis. *J Periodontol.* 2002;73:1118–25.
- Schwarz F, Sculean A, Rothamel D, Schwenzer K, Georg T, Becker J. Clinical evaluation of an Er:YAG laser for non-surgical treatment of peri-implantitis: a pilot study. *Clin Oral Implants Res.* 2005;16:44–52.
- Karring ES, Stavropoulos A, Ellegaard B, Karring T. Treatment of peri-implantitis by the vector system. *Clin Oral Implants Res.* 2005;16:288–93.
- Kalaitzakis CJ, Tynelius-Bratthall G, Attstrom R. Clinical and microbiological effects of subgingival application of a chlorhexidine gel in chronic periodontitis. A pilot study. *Swed Dent J.* 1993;17:129–37.
- Kamagate A, Kone D, Coulibaly NT, Brou E, Sixou M. In vitro study of chlorhexidine resistance in subgingival bacteria. *Odontostomatol Trop.* 2002;25:5–10.
- Eren K, Ozmeric o N, Sardas S. Monitoring of buccal epithelial cells by alkaline comet assay (single cell gel electrophoresis technique) in cytogenetic evaluation of chlorhexidine. *Clin Oral Investig.* 2002;6:150–54.
- Quirynen M, Avontroodt P, Peeters W, Pauwels M, Coucke W, Van Steenberghe D. Effect of different chlorhexidine formulations in mouthrinses on de novo plaque formation. *J Clin Periodontol.* 2001;28:1127–36.
- De Araújo Nobre M, Capelas C, Alves A, Almeida T, Carvalho R, Antunes E, Oliveira D, Cardador A, Malo P. Non-surgical treatment of peri-implant pathology. *Int J Dent Hyg.* 2006;4:84–90.
- Rabasseda X. The role of hyaluronic acid in the management of periodontal disease. *Drugs Today.* 2000;36:1–20.
- Mesa FL, Aneiros J, Cabrera A et al. Antiproliferative effect of topic hyaluronic acid gel. Study in gingival biopsies of patients with periodontal disease. *Histol Histopathol.* 2002;17:747–53.
- Vangelisti R, Pagnacco O, Erra C. Hyaluronic acid in the topical treatment of gingival inflammations: preliminary clinical trial. (Translation) *Attualità Terapeutica Int.* 1997;3:1–7.
- Jentsch H, Pomowski R, Kundt G, Gocke R. Treatment of gingivitis with hyaluronan. *J Clin Periodontol.* 2003;30:159–64.
- Pagnacco O, Vangelisti R, Erra C, Poma A. Double-blind clinical trial vs. Placebo of a new sodium-hyaluronate-based gingival gel. (Translation) *Attualità Terapeutica Int.* 1997;4:1–12.
- Ricerfarma [cited 2008 July 25]. Available from: <http://www.ricerfarma.com/ProductProfessionalSyringes.htm>
- Malo P, Rangert B, Dvarsater L. Immediate function of Branemark implants in the esthetic zone: a retrospective clinical study with 6 months to 4 years of follow-up. *Clin Implant Dent Relat Res.* 2000;2:138–46.
- Malo P, Rangert B, Nobre M. 'All-on-Four' immediate-function concept with Branemark system implants for completely edentulous mandibles: a retrospective clinical study. *Clin Implant Dent Relat Res.* 2003;5(Suppl.1):2–9.
- Mombelli A, van Oosten MA, Schurch E Jr., Land NP. The microbiota associated with successful or failing osseointegrated titanium implants. *Oral Microbiol Immunol.* 1987;2:145–51.
- Malo P, Nobre Mde A, Petersson U, Wigren S. A pilot study of complete edentulous rehabilitation with immediate function using a new implant design: case series. *Clin Implant Dent Relat Res.* 2006;8:223–32.
- Buser D, Weber HP, Lang NP. Tissue integration of non-submerged implants. 1-year results of a prospective study with 100 ITI hollow-cylinder and hollow-screw implants. *Clin Oral Impl Res.* 1990;1:33–40.
- Lang NP, Tonetti MS. Periodontal risk assessment (PRA) for patients in supportive periodontal therapy (SPT). *Oral Health Prev Dent.* 2003;1:7–16.
- Jovanovic S. Peri-implant tissue response to pathological insults. *Adv Dent Res.* 1999;13:82–86.
- Clarizio LF. Peri-implant infections. Abstract. *Atlas Oral Maxillofac Surg Clin North Am.* 2000;8:35–44.
- Quirynen M, DeSoete M, VanStreenberghe D. Infectious risks for oral implants: a review of the literature. *Clin Oral Implant Res.* 2002;13:1–19.
- Meffert RM. Maintenance and treatment of the ailing and failing implant. *J Indiana Dent Assoc.* 1994;73:22–24.
- Jolkovsky DL, Waki MY, Newman MG et al. Clinical and microbiological effects of subgingival and gingival marginal irrigation with chlorhexidine gluconate. *J Periodontol.* 1990;61:663–69.
- Mombelli A, Lang NP. Antimicrobial treatment of peri-implant infections. *Clin Oral Impl Res.* 1992;3:162–68.
- Hennessey TD. Antibacterial properties of hibitane. *J Periodont Res.* 1977;4:36–48.
- Salas Campos L, Gomez FO, Villar MH, Martin RB. Antiseptic agents: chlorhexidine. *Rev Enferm.* 2000;23:637–40.
- Moshrefi A. Chlorhexidine. *J West Soc Periodontol Periodont Abstr.* 2002;50:5–9.
- Newman MG, Sanz M, Nachnani S, Saltini C, Anderson L. Effect of 0.12% chlorhexidine on bacterial recolonization following periodontal surgery. *J Periodontol.* 1989;60:577–81.
- Hanes PJ, Purvis JP. Local anti-infective therapy: pharmacological agents. A systematic review. *Ann Periodontol.* 2003;8:79–98.
- Loesche WJ, Giordano J, Soehren S et al. Nonsurgical treatment of patients with periodontal disease. *Oral Surg Oral Med Oral Pathol.* 1996;81:533–43.
- Salvi GE, Mombelli A, Mayfield L et al. Local antimicrobial therapy after initial periodontal treatment. A randomized clinical trial comparing three biodegradable sustained release polymers. *J Clin Periodontol.* 2000;29:540–50.
- Heasman PA, Heasman F, Stacey F, McCracken GI. Local delivery of chlorhexidine gluconate (periochip) in periodontal maintenance patients. *J Clin Periodontol.* 2001;28:90–95.
- Azmak N, Atilla G, Luoto H, Sorsa T. The effect of subgingival controlled-release delivery of chlorhexidine chip on clinical parameters and matrix metalloproteinase-8 levels in gingival crevicular fluid. *J Periodontol.* 2002;73:608–15.
- Killooy W. The clinical significance of local chemotherapies. *J Clin Periodontol.* 2002;29:22–29.