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This is a pre print version of the following article:

Original Citation:

Availability:

This version is available <http://hdl.handle.net/2318/1639770> since 2017-07-06T11:48:08Z

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Letter to the Editor

FAVOURABLY EFFECTIVE FORMULATION OF SODIUM IODIDE AND SALICYLIC ACID PLUS PROFESSIONAL HYGIENE IN PATIENTS AFFECTED BY DESQUAMATIVE GINGIVITIS.

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Short title: oral hygiene in patients with DG.

Summary

The aim of this prospective pilot study was to evaluate the efficiency of an oral hygiene protocol, in combination with a solution of sodium iodide associated to salicylic acid (SISA), in patients affected by desquamative gingivitis (DG). Patients not totally responding to conventional topical therapies, were selected. They received oral hygiene instruction with non-surgical periodontal therapy in a 21-day cohort study (during 3 weekly appointments). The SISA was used at the end of each session, with an impregnated gauze (with 5 ml of the solution) applied for 15 minutes for the upper jaw, and for other 15 minutes with a novel gauze for the lower. Evaluated clinical outcome variables included the full mouth plaque (FMPS) and bleeding (FMBS) scores, probing depth, patient related outcome and clinical gingival signs. A total of 20 patients were recruited. Two months after concluding the planned protocol, a statistical significant reduction was observed for FMPS ($P=.032$), FMBS ($P=.038$), reported pain ($P=.000$) and gingival clinical improvement ($P=.005$).

Topical application of SISA and professional oral hygiene procedures are connected with worthy improvement of gums status, and decrease of related pain, in subjects affected by severe DG.

Key words: desquamative gingivitis; oral hygiene; non-surgical periodontal treatment; sodium iodide associated to salicylic acid.

Introduction

Desquamative gingivitis (DG) neither is a specific disorder nor recognizes a single aetiopathogenesis; it simply represents the gingival manifestation associated with some heterogeneous mucocutaneous disorders (*e.g.* oral lichen planus, mucous membrane pemphigoid, pemphigus vulgaris and few others); epithelial desquamation, erythema and erosive and/or vesiculo-bullous lesions usually characterize it (1-5). DG has no association with loss of attachment and alveolar bone destruction; nonetheless, it can significantly compromise the patient's approach to proper oral hygiene and this could denote a possible risk factor for long-standing periodontal health (6-9). There have been limited studies regarding therapy for DG (6). We recently demonstrated that detailed oral hygiene procedures and proper non-surgical periodontal therapy could be associated with improvement of clinical and patient-related outcomes in distinctive cases (10-12).

The "Fertomcidina-U"[®] is a novel formulation, realized as a salsobromiodic solution containing salicylic acid and magnesium bisphosphate, having a strong bactericide and fungicide action, applicable on human skin and mucosae for tissues reparation and re-epithelization (13,14). Because of its action, which is related to the sodium-iodide that in the presence of oxygen acts as iodophor, developing small amounts of iodine, this medication should be contraindicated in patients with thyroid disorders.

The aim of this study was to evaluate the clinical efficiency of an oral hygiene protocol, in combination with a solution of sodium iodide associated to salicylic acid, in patients affected by DG not completely responding to conventional topical therapies.

Materials and Methods

Subjects with histologically proven DG [oral lichen planus (OLP), plasma cell gingivitis (PCG), mucous membrane pemphigoid (MMP) and pemphigus vulgaris (PV)] were selected among individuals regularly followed at the Oral Medicine Unit of the CIR – Dental School of the University of Turin, Italy, between January 2012 and September 2015.

Patients were treated topically (and also systemically in cases with a diagnosis of PV) in the preceding 12 months.

Exclusion criteria included: (i) history of periodontal therapy (surgical and non-surgical) in the previous 6 months; (ii) less than 18 teeth, (iii) pregnancy and (iv) diabetes mellitus.

All eligible candidates for this study were informed about the experimental protocol, and signed a consent form. The ethics review board of the CIR - Dental School approved the study (prot. N° II-pato-2011CD).

A prospective case series protocol was designed. Patients received a complete periodontal examination at baseline visit, including full mouth plaque scores (FMPS), full mouth bleeding upon probing scores (FMBS) and probing pocket depth (PPD). Activity scores [modified from Escudier and co-workers (15)], including extent and severity of the gingival lesion (site score), were documented as previously reported (10). Score ranged from 1 to 12, with higher results indicating a worse clinical aspect. Patient related outcomes included pain perception assessed at each visit by Visual Analogue Scale (VAS). The VAS consisted of a 10 cm-horizontal line marked with 0 (=no pain) to 10 (=most severe pain experienced). Total resolution of all clinical symptoms was defined as the absence of any discomfort, corresponding to a zero VAS score. Partial response, worsening, or persistence of the patient's condition meant a decrease, increase, or no change at all in the patient's score respectively.

An experienced dental hygienist provided thorough supra- and sub-gingival scaling within 3 weeks (once weekly). During each visit, subjects were instructed about proper oral hygiene maintenance at home; such instructions were reinforced at each visit and were personalised when necessary. The “Fertomcidina-U”[®] (Theriaca S.r.l., Rome, Italy) was used at the end of each of the 3 sessions performed: a gauze impregnated with 5 ml of the solution was applied for 15 minutes for the upper jaw and for other 15 minutes for the lower using another new gauze impregnated. Patients were advised not to swallow the medication, and to avoid eating and drinking for at least 3 hours after the treatment.

The technical procedures provided in the protocol are fully detailed in Table I.

Comparative statistics were performed between T0 and T5. Paired samples test was used to test the difference in FMBS, FMPS and PPD. Wilcoxon’s signed rank was used to calculate the significance of the patient related outcomes (VAS) and in clinical outcome (activity score). P-values $\leq .05$ were considered to be statistically significant. SPSS (SPSS for windows, version 11, SPSS inc, Chicago, IL, USA) statistical software was utilized.

Authors participation

PG. Arduino and R. Broccoletti led the clinical team. All authors followed the patients or visited them over the entire period. P. Carcieri performed the oral hygiene protocol and made the periodontal measurements. R. Broccoletti performed the statistical analysis. PG. Arduino, D. Conrotto, A. Gambino and M. Cabras reviewed the literature, wrote sections, revised the full text and approved the submitted version.

Results

Twenty patients were included: 9 had OLP, 6 had PV, 4 had GPC and 1 had MMP.

The mean age at baseline was 56.95 (\pm 16.75) years. Three were male (15%).

Table II reports the comparison of selected data during the protocol period. A reduction in FMBS ($P=.032$) and FMPS ($P=.038$) were observed. Moreover, a statistical significant reduction in symptoms reported was observed with a reduction in VAS scores ($P=.000$). Also interestingly, the clinical gingival involvement improved after the proposed therapy ($P=.005$).

All subjects were initially advised of the possible unpleasant taste of the medication, and 60% of them still reported this problem at the end of the follow-up period, but none of them were not able to complete the treatment. No patient complained of other adverse effects.

Discussion

This is the first prospective case series of DG patients treated with a solution of sodium iodide associated to salicylic acid in combination with non-surgical periodontal therapy. This initial pilot analysis suggested that the proposed protocol could be a possible mean for reducing clinical gingival inflammation and improve patient related outcomes in patients with different forms of DG.

It has been reported that several systemic diseases, affecting the gingiva, could have an inflammatory profile composed of two main reasons: one may be a non-specific inflammatory response to plaque (thus a plaque-induced inflammation); another response may be due to a specific disease or agent, today not well understood (5,6).

No concluding standard of care has been set for DG and there is no prospective literature on long-term management of these subjects (4). The present report was developed by taking motivation from conclusions achieved by earlier works reporting that patients affected by different DG conditions, and treated with non-surgical

periodontal therapy, are connected with improvement of gingival status and decrease in gingival-related pain (10-12). However, plaque removal alone cannot induce severe DG regression. That's why we decided to add "Fertomcidina-U"[®] topically to accelerate the healing process. In fact, it has been reported that the salicylic acid acts by environment acidification, with different anti-inflammatory assets, sometimes comparable to corticosteroids (16). The keratoplastic properties are showed by studies reporting both an increased thickness of epithelial tissues and mitotic index of the basal layer (17,18). This is the rationale to use this compound in treating epithelial inflammatory diseases. Moreover, this medication could be used to treat dissimilar kind of oral pathogens, not only the typical periodontal ones but also others quite different, normally resident in the oral cavity as well as introduced in other ways (19, 20).

Non-surgical periodontal therapy is the most common therapeutic procedure for patients with periodontal diseases, eliminating or reducing the microbial counts of subgingival flora following improvements in clinical parameters and oral health of patients (21). And it is now clear that the previous statement is effective also for DG.

Oral hygiene improved in all participants. This is bound to the time devoted to oral hygiene enactment and home directives. Patients were favourably motivated to perform their routinely home maintenance, and their cooperation was above all indispensable.

The positive clinical results obtained with appropriate professional oral hygiene could serve as a basis of recommending this as complementary line therapeutic intervention, especially in patients with pure gingival involvement, in order to decrease gingival inflammation and related pain and help affected patients in maintaining a good oral hygiene. And the simple use of a topically applied solution of sodium iodide

associated to salicylic acid could improve the healing progression, without adverse effects. However, it is chief to remember that the main limitations are the lack of a control group, and that there were no intra-reliability analysis of the examiner and no blinding included in the design. For these motivations, additional randomized trials, with different approaches and larger sample size, are however needed.

Acknowledgements

The authors disclose that they have no conflict of interest related to this study. Authors' own institution funded the study.

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Table I. **Clinical protocol used.**

Time 0 (T0):

- Oral evaluation and comprehensive measurements*

Time 1_Day 7 (T1):

- Scaling and root planning
- “Fertomcidina-U” topical application
- Oral hygiene instruction:
 - a) use a ultra-soft toothbrush¹ for manual brushes, placing the bristles at a 45° angle to the tooth surface at the gum edge and then move the bristles back and forth in short (tooth-wide) strokes or small circular movements

Time 2_Day 14 (T2):

- Scaling and root planing
- “Fertomcidina-U” topical application

Time 3_Day 21 (T3):

- Scaling and root planing
- “Fertomcidina-U” topical application
- Oral hygiene instruction:
 - a) use a super-soft toothbrush² for manual brushes, placing the bristles at a 45° angle to the tooth surface at the gum edge and then move the bristles back and forth in short (tooth-wide) strokes or small circular movements

Time 4_Day 49 (T4_1 month after finishing the proposed protocol):

- Oral hygiene instruction:
 - a) use a soft toothbrush³ for manual brushes, placing the bristles at a 45° angle to the tooth surface at the gum edge and then move the bristles back and forth in short (tooth-wide)
-

strokes or small circular movements

- Oral evaluation; VAS measurement and activity score

Time 5_Day 77 (T5_2 months after finishing the proposed protocol):

- Oral evaluation and comprehensive measurements*

* Comprehensive measurements include:

- VAS (visual analogue scale), a chromatic scale graduated from 0 (no pain) to 10 (unbearable pain), where it defines intensity of pain strong or very strong.
- FMBS (full mouth bleeding score).
- FMPS (full mouth plaque score).
- PPD (probing pocket depth).
- Activity Score: to value the extent and severity of the gingival lesion.

¹Curaprox CS 5460

²Curaprox CS 3960

³Curaprox CS 1560

Table II. The comparison of selected data at time 0 (T0), and at one (T4) or two (T5) months after the proposed protocol.

| | T0 | T4 | T5 | p* |
|--------------------------------------|---------------|-------------|---------------|-----------|
| Full mouth bleeding score (%) | 59.00 ± 16.25 | - | 23.88 ± 11.11 | .032 |
| Full mouth plaque score (%) | 45.02 ± 13.63 | - | 29.20 ± 2.73 | .038 |
| Probing depth (mm) | 2.48 ± 0.51 | - | 2.29 ± 0.67 | .791 |
| Referred symptoms (VAS score) | 5 ± 1.32 | 3.38 ± 1.19 | 2.44 ± 1.42 | .000 |
| Activity score | 6.48 ± 1.20 | 3.08 ± 1.77 | 2.81 ± 1.79 | .005 |

*Comparative statistics were performed between T0 and T5. Paired samples test was used to test the difference in FMBS, FMPS and PPD. Wilcoxon's signed rank was used to calculate the significance of the patient related outcomes and in gingival clinical outcome (activity score).