



Interleukin 10 supplement to reduce episodes of recurrent aphthous stomatitis

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Specialty type: Medical laboratory technology

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's classification

Scientific Quality: Grade C

Novelty: Grade B

Creativity or Innovation: Grade B

Scientific Significance: Grade B

P-Reviewer: Tovani-Palone MR

Received: July 15, 2024

Revised: January 3, 2025

Accepted: February 8, 2025

Published online: September 20, 2025

Processing time: 233 Days and 17.5 Hours



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Abstract

Recurrent aphthous stomatitis (RAS) is a very frequent condition in developed countries whose basic symptom is a lesion referred to as an aphthous ulcer. High levels of interleukin (IL)-1 and IL-6 and low salivary levels of IL-10 are the basis of RAS pathogenesis. Sublingual supplements based on IL-10 can be very useful in reducing the phenomenon of aphthous recurrence in patients with RAS. An observational clinical experience with a group of 5 patients with RAS receiving a commercially available IL-10-based supplement was reported by the authors. The findings revealed a subsequent reduction in the incidence of mouth ulcers.

Key Words: Recurrent aphthous stomatitis; Interleukin 10; Low-dose medicine; Aphthosis; Interleukin

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Core Tip: Aphthous lesions and recurrent aphthous stomatitis are among the most common oral diseases and are often very painful. In some patients, the frequency of new onset is greater than once a month. The pathogenetic mechanism involves high levels of interleukin (IL)-1 and IL-6 and low levels of IL-10. Although several aids that are able to reduce healing times and pain have been proposed in the scientific literature, there is still no treatment that drastically reduces the frequency of lesion onset. Supplements based on IL-10, administered at low doses for prolonged periods, referred to as low-dose medicine, could be effective in reducing relapses.

Citation: Casu C, Inchingolo AM, Orrù G. Interleukin 10 supplement to reduce episodes of recurrent aphthous stomatitis. *World J Methodol* 2025; 15(3): 99176

URL: <https://www.wjgnet.com/2222-0682/full/v15/i3/99176.htm>

DOI: <https://dx.doi.org/10.5662/wjm.v15.i3.99176>

INTRODUCTION

Recurrent aphthous stomatitis (RAS) is a very frequent condition in developed countries whose basic symptom is an aphthous ulcer, a lesion generally round or oval with an erythematous halo[1]. Depending on the size of the aphthosis, three different clinical variants can be determined: aphthosis minor, with lesions smaller than 1 cm in maximum diameter (> 80% of cases); aphthosis major, with lesions greater than 1 cm (15% of cases); and aphthosis herpetiformis, with a multitude of very small lesions of 2-3 mm. Minor aphthosis is characterized by the presence of multiple lesions that heal within 7-14 days without scars, whereas in major aphthosis, patients may have single lesions that generally heal within 30-40 days and can leave scars[1-3]. There must be at least 3-4 episodes of aphthosis per year to be able to define it as RAS, and this is an extremely disabling condition in some cases. The pain and burning sensation associated with the onset of canker sores can lead to difficulty in eating food, resulting in malnutrition[1,2].

A percentage of cases can be associated with systemic diseases (celiac disease, Chron's disease) or syndromic conditions (Behcet syndrome, mouth and genital ulcers with inflamed cartilage syndrome, and periodic fever adenitis pharyngitis aphthosis syndrome)[3]. The pathogenetic process that leads to the development of canker sores is vasculitis, an autoimmune inflammation in which interleukin (IL)-1 and IL-6 participate and where low levels of IL-10 are found. The latter is a fundamental cytokine for stopping the inflammatory process, and several studies have shown that patients with RAS have low salivary levels of IL-10, a molecule that could reduce the vasculitis phenomena underlying canker sores[4].

Various treatments for canker sores, such as cortisone and topical immunosuppressants[5], gels based on aloe vera and hyaluronic acid[1,2], low-level laser therapy[6], and photodynamic therapy[7], are well documented in the literature; however, currently, there is no treatment that is capable of reducing severe relapses from aphthosis. There is a supplement based on IL-10 on the market (GUNA® IL-10, Milan, Italy), whose concentration of IL-10 is on the order of picograms and which can be purchased without any requirement for a medical prescription. The aim of this work was to report the findings of some patients with particularly RAS and to provide scientific evidence on the potential efficacy of IL-10-based supplements in patients with aphthous lesions.

OBSERVATION REPORT

A number of patients characterized by a history of recurrent relapsing aphthous stomatitis showing new episodes on a monthly basis gained access to the Department of Surgical Science in San Giovanni Hospital, University of Cagliari, for a routine dental visit. All patients were adults (3 women and 2 men) aged between 36 years and 75 years; none of these patients had syndromic symptoms associated with RAS, and the IL-10 supplement was recommended.

According to the parent company's directions, the authors recommended taking 20 drops under the tongue 2 times per day for 3 months. As part of routine dental care, the mucous membranes were also examined, and the patients were interviewed to determine whether any other mouth ulcers had appeared. In all 5 patients, a remarkable reduction in the number of canker sores affecting the mouth was observed after 3 months and after 6 months (3 months after the supplement). The reduction in the number of canker sores in the various subjects occurred after the first month following the administration of the IL-10 supplement. Additional patient details follow. Two patients reduced the number of canker sores from 3 (present at the first visit) to 1 at a 3 months follow-up appointment. One patient's canker sores were reduced from 3 to 0 in the second month of follow-up, and the reduction was maintained at 3 months. One patient with 2 canker sores presented at T0 with 0 canker sores. One patient had 2 canker sores at time T0 and presented 1 canker sore at 2 months; and again, 2 canker sores at a 3 months follow-up appointment. The average number of canker sores present in the 5 patients was 2.6, whereas the average posttreatment (T3) was 0.8 canker sores. Despite one patient being refractory, with an initial reduction and the presence of 2 new lesions at the final visit, the other 4 had a reduction in the number of canker sores.

At 6 months, only 2 out of 5 patients reported the onset of a new minor aphthous ulcer during the previous 3 months but did not report aphthae at the time of the follow-up visit. It would have been very interesting to carry out salivary measurements of IL-1, IL-6, and IL-10 in these patients before and after consuming this supplement. The treatment proposed for patients with aphthosis is shown in [Figure 1](#).

CONCLUSION

Since this type of supplement available on the market contains a concentration of IL-10 on the order of picograms, this treatment falls within the concept of low-dose medicine, which is the administration of very low concentrations of a certain active ingredient (supplement in this case), and repeated consistently for long periods of time. Low dose medicine

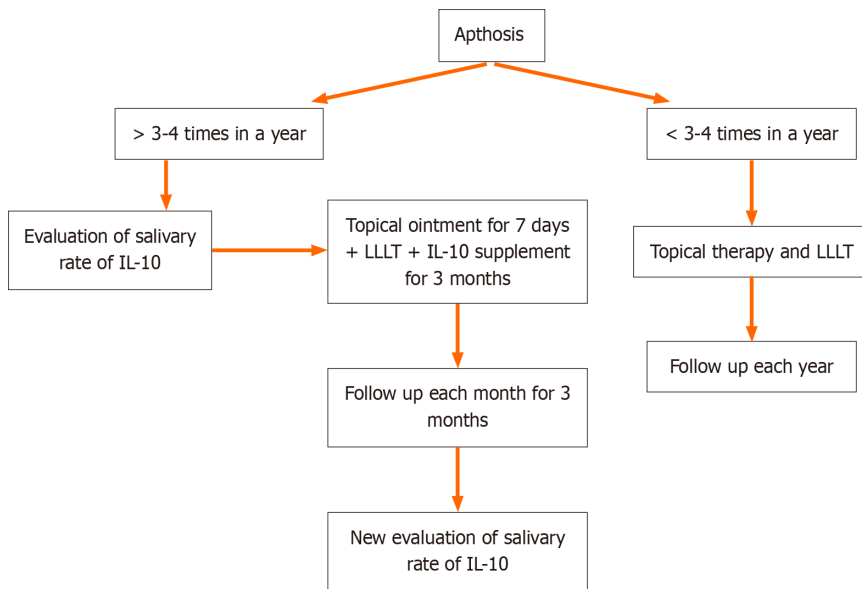


Figure 1 Flow chart of type of treatment proposed in patients with aphthosis. Interleukin 10 and low level laser therapy are proposed as new methods to reduce recurrent aphthous stomatitis. IL: Interleukin; LLLT: Low level laser therapy.

is able to create a new balance, and its effect is much longer lasting over time than that which would be achieved with an attack pharmacological therapy administered for much shorter periods of time (for example, cortisone and systemic immunosuppressants). This concept is highlighted very well in a randomized clinical trial[8], in which the same type of supplement recommended by the authors and purchased directly by the patient, administered following the same directions described by the authors, was used to determine a significant regression of lesions and flare-ups in patients with psoriasis vulgaris, another autoimmune phenomenon. The same commercial product, which is considered safe and without any side effects observed in the cited clinical trial, has also been administered for the management of chronic inflammatory diseases by other authors[9]. Other IL-2 supplements, which are always low-dose medicines, have recently been successfully tested in a clinical trial on bullous pemphigoid, an autoimmune disease that affects the oral cavity[10].

Based on this simple empirical observation of patients and analysis of the pathogenetic mechanisms underlying the phenomenon of canker sore formation, the use of IL-10-based supplements could be a new path to reduce the incidence of recurrences in patients with RAS, an already widespread phenomenon that is often somewhat underestimated, as it is not associated with malignant transformation but is capable of profoundly altering the quality of life of affected patients.

Limits

We observed a very small number of patients who spontaneously appeared to the Department of Surgical Sciences for dental care; it would be necessary to observe the effect of the suggested supplement on a much larger number of patients, with much longer observation times, to confirm these initial findings. In this work, we report our experience with patients who suffered from RAS and who appeared at the hospital outpatient clinic for routine dental care. The recommended product can be purchased without a prescription; therefore, it is not necessary to obtain approval from the Ethics Committee. The principles set out in the Declaration of Helsinki were respected.

FOOTNOTES

Author contributions: Casu C and Orrù G observed the patients, collected data, made maps, and consulted the literature, they contributed equally to this article, they are the co-corresponding authors of this manuscript; Casu C and Inchingolo AM wrote the manuscript; Inchingolo AM and Orrù G revised the manuscript and the literature citations; and all authors have read and approved the final manuscript.

Conflict-of-interest statement: All the authors report no relevant conflicts of interest for this article.

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S-Editor: Bai Y

L-Editor: A

P-Editor: Guo X

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