

The Effect of a New Topical Agent on Recurrent Aphthous Stomatitis

SUMMARY

Background: Recurrent aphthous stomatitis (RAS) is a common condition, which is characterized by multiple recurrent small, round or ovoid, ulcers with circumscribed margins, erythematous haloes, and yellow or grey floors typically presenting in childhood or adolescence. The treatment of RAS is principally directed towards reducing pain and duration of each episode of ulceration. The aim of this study was to determine the efficacy of a new agent Stomatovis®, which is a unique combination of ingredients of moloha, xylitol, aloe vera, vitamin A, vitamin E, and d-panthenol.

Methods: 42 patients with minor RAS were included in the study (13 male, 29 female, mean age: 37.07 years, range 18-62 years). The diagnosis of RAS was based on accepted clinical criteria. The patients with RAS were randomly separated in 2 groups: group 1 with 21 patients treated by Stomatovis® oral pomade (Moloha, xylitol, aloe vera, vitamin A, vitamin E, d-panthenol 5ml - Genesis İlaç Sağlık Ürünleri, Istanbul) and the group 2 with 21 patients treated by Kenacort-A orabase® oral pomade (triamcinolone acetonide 5g - Bristol-Myers Squibb Inc, Istanbul). Both remedies were used 3 times a day during 2 months. RAS status was estimated by the Ulcer Severe Score (USS), concerning symptoms, such as ulcer number, ulcer duration, the disease-free period measured. USS values of 2 groups were compared using independent-sample t test and the non-parametric Mann-Whitney U test.

Results: Before the treatment, USS values were 11 and 13 for the group 1 and 2, respectively, and 7 (for both groups) after the treatment. There was no significant difference between 2 groups with respect to USS values ($p>0.05$) at the entry and at the end of the study. There was a statistically significant difference decrease between the USS values before and after the treatment ($p<0.001$). No side effects were observed in none of the patients.

Conclusions: Similar effects have observed between 2 groups. Stomatovis® seems to be an effective and safe agent which can be used in symptomatic treatment of patients with RAS. It effectively reduces pain symptoms of RAS.

Keywords: Recurrent Aphthous Stomatitis, treatment; Pain

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ORIGINAL PAPER (OP)

Balk J Stom, 2013; 17:44-47

Introduction

Recurrent aphthous stomatitis (RAS) is a common condition, which is characterized by multiple recurrent small, round or ovoid, ulcers with circumscribed margins, erythematous haloes, and yellow or grey floors

typically presenting in childhood or adolescence⁹. RAS is seen worldwide and the prevalence is about 20% of the population⁴. RAS can be clinically characterized into 3 forms, such as minor, major and herpetiform^{9,13}. Minor aphthous ulceration form is the most common form⁹.

The aetiology of RAS remains unknown. Suggested aetiological factors include a family history of RAS, idiopathic haematinic deficiency, food sensitivities, immune defects, menstrual cycle variations. Also, some patients suffer from an increase in RAS episodes caused by cessation of tobacco, due to trauma of oral mucosa or psychological stress^{6,11}.

RAS is a type of lesion of the oral mucosa consisting of sudden acute, painful loss of normal mucosal tissue, being recurrent and fulsome. No efficient treatment has been introduced and medication is usually challenging^{4,10}. Reducing pain and healing time for RAS restores the ability to eat, swallow and talk, improving the quality of life of those who suffers from this condition^{4,8}. The treatment goals are a decrease in symptoms, reduction in ulcer number and size, and an increase in the disease-free period^{8,10}.

Topical steroids have been shown to decrease severity and duration of ulcers, implicating deregulation of the immune system as the causative process^{2,7}. However, there is no proper medication that has been proven to be effective in all RAS patients, and most common treatment choice remains symptomatic.

Stomatovis® is an oral pomade agent and consist of 6 ingredients including: moloha, xylitol, aloe vera, vitamin A, vitamin E, and d-panthenol (Genesis İlac Saglik Urunleri, Istanbul). The topical use of d-panthenol, the stable alcoholic analogue of pantothenic acid, is based on good skin penetration and high local concentrations of d-panthenol when administered in an adequate vehicle, such as water-in-oil emulsion. Topical d-panthenol acts like a moisturizer, improving stratum corneum hydration, reducing trans-epidermal water loss and maintaining skin softness and elasticity. Activation of fibroblast proliferation, which is of relevance in wound healing, has been observed both *in vitro* and *in vivo* with d-panthenol. Accelerated re-epithelization in wound healing, monitored by means of the trans-epidermal water loss as an indicator of the intact epidermal barrier function, has also been seen. Also, d-panthenol has been shown to have an anti-inflammatory effect on experimental ultraviolet-induced erythema³.

Antioxidant vitamins and trace elements counteract potential damage caused by reactive oxygen species to cellular tissues and modulate immune cell function through regulation of redox-sensitive transcription factors, and affect production of cytokines and prostaglandins. Adequate intake of vitamins B(6), folates, B(12), C, E, and of selenium, zinc, copper, and iron, supports a Th1 cytokine-mediated immune response with sufficient production of pro-inflammatory cytokines, which maintains an effective immune response. Vitamins A and D play important roles in both cell-mediated and humoral antibody response and support a Th2-mediated anti-inflammatory cytokine profile¹⁴. Vitamin A deficiency impairs both innate immunity (mucosal epithelial

regeneration) and adaptive immune response to infection, resulting in an impaired ability to counteract extracellular pathogens. Overall, inadequate intake and status of these vitamins and minerals may lead to suppressed immunity, which predisposes to infections and aggravates malnutrition¹⁴.

The aim of this study was to determine the efficacy of a new topical agent Stomatovis® and to compare the outcomes with Kencaort-A orabase®, as a topical corticosteroid.

Materials and Methods

Patient Selection

The sample consisted of 42 patients (13 male, 29 female, mean age: 37.07 years, range 18-62 years) suffering from minor RAS. Study subjects were chosen from patients presenting for treatment at the Istanbul University, Faculty of Dentistry, Oral Surgery Department. The diagnosis of RAS based on the accepted clinical criteria. Patients were at least 18 years old at the time of enrolment, and did not have RAS associated with other conditions such as anaemia, vitamin deficiencies, inflammatory bowel disease, celiac disease, Behcet's disease, Reiter's disease or HIV-associated immunosuppression. Exclusion criteria also included a history of allergy to ingredients of the products used in the study.

Study Design

The patients with RAS were randomly separated in 2 groups: group 1, with 21 patients, was treated by Stomatovis® oral pomade (Moloha, xylitol, aloe vera, vitamin A, vitamin E, d-panthenol 5ml - Genesis İlac Saglik Urunleri, Istanbul) and the group 2, with 21 patients, was treated by Kenacort-A orabase® oral pomade (triamcinolone acetonide 5g - Bristol-Myers Squibb Inc, Istanbul). Both remedies were used 3 times a day, during 2 months. Patients were asked not to use any other product for prevention or treatment of RAS while participating in the study.

RAS status was estimated by the Ulcer Severe Score (USS). The rating was assigned as follows: **number** - 0 = no ulcer, 1 = minor ulcer, 2 = major ulcer; **duration** - 0=zero day, 1= less than 7 days, 2=7 days, 3= more than 7 days; **ulcer-free period**: 0 = more than 30 days, 1 = 15-29 days, 2 = 1-14 days, 3 = no ulcer-free period; **site** - 0= no ulcer, 1= 1 site of oral mucosa, 2 = 2 sites of oral mucosa, 3 = more than 2 sites of oral mucosa; **pain** - 0 = no pain, 1 = mild pain, 2 = moderate pain, 3 = severe pain. USS scores differed between 0-14 to identify the severity of lesions for each patient with RAS - 14 was the highest severity score, 0 was the minimum severity score. According to the Helsinki

declaration, a witness assisted the patients before signing the informed consent form.

Statistical Methods

USS values of 2 groups were compared using independent-sample t-test and the non-parametric Mann-Whitney U test.

Results

Of the 42 patients enrolled in the study, all patients completed at least 2 month of follow-up. Overall, the compliance rate in this study was 100%. Before the treatment, USS values were 11 and 13 for the group 1 and 2, respectively, and 7 (for both groups) after the treatment. There was no significant difference between 2 groups with respect to USS values ($p>0.05$) at the entry and at the end of the study. There was a statistically significant decrease between the USS values before and after the treatment ($p<0.001$) (Table1). No side effects were observed in none of the patients.

Table 1. USS (Ulcer Severity Score) values of study groups

	Before the treatment	After the treatment	P value
Group 1*	11	7	$P<0.001$
Group 2**	13	7	$P<0.001$

*Stomatovis®

**Kenacorte-A Orabase®

Discussion

RAS has been described as presenting in 3 different forms including minor, major, and herpetiform³. Minor form of RAS accounts for 80-85% of all RAS cases and can involve any non-keratinized part of the oral cavity mucosa¹. The characteristic lesions are smaller than 10 millimetres and heal within 7-14 days without scarring. Major form of RAS, comprising 10-15% of RAS cases, are larger, of longer healing time. They are more severe than minor form and tend to leave scars after healing. The herpetiform ulcers represent only 5-10% of RAS cases and consist of multiple 1-3 millimetres resembling herpes simplex, but involving non-keratinized mucosa^{4,10}. In our study, all of the subjects were diagnosed with minor form of RAS.

The aetiology of RAS is still unknown; thus, there is no safe and conclusive treatment that can decrease the frequency of ulceration episodes in a patient. There is no gold standard on how to evaluate relief for this

condition in the literature; therefore, in this study, we aimed to evaluate the success which included decrease in symptoms, reduction in pain, ulcer number, duration, size, and an increase in the disease-free period. The most significant outcome of this study was to compare USS values before and after treatment. The data showed that there was a significant reduce between USS values registered before and after treatment in both group ($p<0.001$). Data revealed that USS values of the group 1 (Stomatovis®) were 11 before the treatment and that were reduced to 7 after treatment; on the other hand, in group 2, USS values were reduced from 13 to 7. These data indicate that both products can be used for improving discomfort associated with RAS. The other significant outcome of this study was that no significant differences were found between 2 groups with respect to USS values ($p>0.05$). It seems that both products have a positive effect on symptomatic treatment of RAS, without any significant differences.

Many topical treatments (corticosteroids, benzydamine, chlorhexidine, amlexanox, triclosan, tetracyclines, low intensity ultrasound, dentifrices, barrier techniques, laser and etc.) have been used to improve discomfort associated with RAS¹². Topical medications appear to be the first choice for symptomatic treatment of RAS. The topical agents have limitations respect to drug application and retention on the oral mucosa⁵. Although none of our patients complained about the taste, local tolerability, or way of application of the product, we think these features probably impact our study.

The dosage of Stomatovis® was 3 times a day in this study, in accordance to manufacturer advice. Further studies can challenge with a different types of regime to figure the best adequate.

In our study no side effects were observed in none of the patients. The present data indicate that Stomatovis® safely and conveniently reduces the pain of RAS.

One of the limitations of this study was a short follow-up time (2 months) to detect stronger statistical analysis to evaluate the ulcer free-period.

We hope that a larger scale study will allow for stronger statistical trends to be identified. While a larger sample size is necessary, on the basis of our data showed in this study, Stomatovis® seems to be an effective and safe agent, which can be used for symptomatic treatment in patients with RAS.

References

1. Akintoye SO, Greenberg MS. Recurrent aphthous stomatitis. *Dent Clin North Am*, 2005; 49(1):31-47.
2. Barrons RW. Treatment strategies for recurrent oral aphthous ulcers. *Am J Health Syst Pharm*, 2001; 58(1):41-50.

3. Ebner F, Heller A, Rippke F, Tausch I. Topical use of dexpanthenol in skin disorders. *Am J Clin Dermatol*, 2002; 3(6):427-433.
4. Femiano F, Lanza A, Buonaiuto C, Gombos F, Nunziata M, Piccolo S, Cirillo N. Guidelines for diagnosis and management of aphthous stomatitis. *Pediatr Infect Dis J*, 2007; 26:728-732.
5. Kaiser AB, Kernodle DS. Synergism between poly-(1-6)-beta-D-glucopyranosyl-(1-3)-beta-D-glucopyranose glucan and cefazolin in prophylaxis of staphylococcal wound infection in a guinea pig model. *Antimicrob Agents Chemother*, 1998; 42(9):2449-2451.
6. McCullough MJ, Abdel-Hafeth S, Scully C. Recurrent aphthous stomatitis revisited; clinical features, associations, and new association with infant feeding practices? *J Oral Pathol Med*, 2007; 36:615-620.
7. Natah SS, Konttinen YT, Enattah NS, Ashammakhi N, Sharkey KA, Hayrinen-Immonen R. Recurrent aphthous ulcers today: a review of the growing knowledge. *Int J Oral Maxillofac Surg*, 2004; 33:221-234.
8. Porter S, Scully C. Aphthous ulcers (recurrent). *Clin Evid*, 2005; 13:1687-1694.
9. Preeti L, Magesh KT, Rajkumar K, Karthik R. Recurrent aphthous stomatitis. *J Oral Maxillofac Pathol*, 2011; 15:252-256.
10. Scully C, Gorsky M, Lozada-Nur F. The diagnosis and management of recurrent aphthous stomatitis: a consensus approach. *J Am Dent Assoc*, 2003; 134:200-207.
11. Scully C. Aphthous ulceration. *N Engl J Med*, 2006; 355:165-172.
12. Scully C, Porter S. Oral mucosal disease: Recurrent aphthous stomatitis. *Br J Oral Maxillofac Surg*, 2008; 46:198-206.
13. Stanley HR. Aphthous lesions. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*, 1972; 30:407-416.
14. Wintergerst ES, Maggini S, Hornig DH. Contribution of selected vitamins and trace elements to immune function. *Ann Nutr Metab*, 2007; 51(4):301-323.

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