An evaluation of a chemical cautery agent and an anti-inflammatory ointment for the treatment of recurrent aphthous stomatitis: A pilot study

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Objective: *Recurrent aphthous stomatitis is a very common condition, currently treated with anti-inflammatory agents, which palliate the symptoms. The purpose of this clinical trial was to compare a medication commonly used to treat recurrent aphthous stomatitis, Kenalog-in-Orabase, and a newer agent, Debacterol.*
Method and materials: *Sixty patients diagnosed with recurrent aphthous stomatitis were enrolled in the study. Twenty patients were assigned to each of the two treatment groups, and 20 age- and sex-matched patients were assigned to the control group, which received no treatment. After the diagnosis was made, clinical examinations and ulcer measurements were performed, and a subjective evaluation of symptoms (100-mm visual analog scale) was completed by each subject. The subjects did not use any other medications. Both agents were applied topically (the frequency varied depending on the group of subjects) at specified intervals. Ulcer measurements and subjective evaluations were made at days 0, 3, 6, and 10 for all subjects.*
Results: *In both treatment groups, by day 10, 100% of the ulcers had clinically healed and were no longer causing pain. Patients in the Debacterol group reported a significantly greater decrease in pain at 3 days (> 70%) than did subjects in the other groups (< 20%), although the size of the ulcer did not differ significantly in any of the groups. After day 6, 80% of the ulcers in the Debacterol group had clinically disappeared and no longer caused symptoms, as compared to about 30% in the other groups.*
Conclusion: *Patients subjectively reported significantly greater relief from symptoms with Debacterol than with Kenalog-in-Orabase or no treatment. The relief of symptoms associated with recurrent aphthous stomatitis may or may not correspond to clinical improvement, and these two topical medications may affect signs and symptoms of the lesions differently.* (Quintessence Int 1998;29:769–773)

Key words: aphthous ulcer, chemical cautery, corticosteroid, lesion, recurrent aphthous stomatitis

Clinical relevance

This article will help the dental clinician to recognize and treat recurrent aphthous stomatitis, which is a very common and painful problem for which many dental patients seek relief.

Recurrent aphthous stomatitis (RAS) is the most common recurrent oral mucosal ulcerative condition in the world.[1–3] This condition is characterized by painful, pesky, aggravating, oral ulcers, also known as *canker sores*. Epidemiologic studies have indicated that as much as 25% of the general population suffers periodically from this troublesome problem.[1,3]

Recurrent aphthous stomatitis is characterized by single or multiple, sometimes coalescing, and always painful ulcerations of the oral mucosa. Typically the ulcers are small (2 to 4 mm in diameter, termed *minor aphthae*) and shallow, have a gray-yellow psuedomembrane, and are surrounded by an erythematous halo. These ulcers appear on the fluctuant, nonkeratinized (or less keratinized) oral mucosal tissues and usually regress spontaneously within 14 days.

However, major aphthae, which may approach 8 to 10 mm in diameter, may occur and are much more painful.[4,5] These major aphthae also require a much longer healing period. The presence of multiple major aphthae can be nearly debilitating for affected individuals. In certain patients, the ulcers are large and very painful, tend to heal very slowly, and are present almost continuously. This situation, of course, results in significant discomfort, especially during eating, chewing, and speaking.[5–7]

A third form of RAS is the herpetiform type, in which the lesions are usually multiple, may be coalescing, and resemble herpes simplex viral lesions.[5–7]

The etiology of RAS is unknown. The lesions

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(T-cell lymphocyte) response. Associations with systemic disease such as diabetes mellitus, inflammatory bowel disease or other gastrointestinal disturbances, anemia, and immunosuppression have been reported. Precipitating factors include stress, trauma, allergies, hormonal alterations, nutritional inadequacies, and infectious agents (eg, human immunodeficiency virus).[4-6]

The treatment for RAS historically has been palliative and relatively unsuccessful, usually only partially relieving the symptoms.[5-13] Other than topical anesthetics, such as benzocaine, anti-inflammatory ointments, applied to the oral mucosa much the same as on skin, are used to palliate the pain and reduce symptoms. Probably the most widely recommended agents have been preparations of hydrocortisone and triamcinolone acenotinide 0.1% (Kenalog, Apothecon), which are applied topically.[9,13,14]

The purpose of this clinical trial was to compare a medication commonly used for RAS treatment, Kenalog-in-Orabase and Debacterol (Northern Research Laboratories). Debacterol is a commercially available chemical cautery agent, consisting of 50% sulfuric acid and 28% sulfonated phenolics in aqueous solution. The rationale for use of this agent is that it cauterizes the epithelial tissue affected by the immune response.

Method and materials

For this study, a subject population of 60 individuals was enrolled. There were 20 patients (16 female and four male) in each of three groups (Debacterol [D] treatment; Kenalog-in-Orabase [KO] treatment; and control [C], which was no treatment). The mean age was 37.3 years.

A definitive diagnosis of RAS was made by a single experienced, calibrated clinician based on the classic clinical presentation of RAS (ie, a relatively shallow, pseudomembranous, gray-yellow ulcer with a surrounding erythematous halo, found on the less keratinized or nonkeratinized mucous membranes of the oral cavity). For the patient to be enrolled in the study, the RAS ulcer had to be less than 48 hours old (that is, from the time the subject had first noticed it).

The subjects were generally healthy adult volunteers with no major medical diagnoses and who had not been medicated with antibiotics, anti-inflammatory agents, or analgesics within 2 weeks of the study. Smokers were excluded from participation.

Clinical assessments of all subjects were made at days 0, 3, 6, and 10. The maximum diameter of the ulcer and the erythematous halo was measured with a periodontal probe (Fig 1). These measurements were made by the same experienced, calibrated clinician at days 0, 3, 6, and 10, or until the ulcer had clinically healed.

Also made at days 0, 3, 6, and 10. The subject's perception of pain from the ulcer was recorded on a 100-mm visual analog scale (VAS) in which 0 represented no pain and 100 represented the worst pain imaginable.

The test agents were applied topically to the lesions at specified intervals. After the surface of the lesion was dried thoroughly, Debacterol was applied to the ulcerated mucosa, a single time, directly over the margins (including the halo) of the ulcer for a period of exactly 10 seconds (Figs 2 and 3). The area was then thoroughly flushed with water and dried thoroughly with a cotton-tipped applicator. Kenalog-in-Orabase was applied liberally over the ulcer three times every day by the subject. Subjects were instructed in the proper use of KO.

The control subjects were evaluated precisely in the same manner but received no treatment.

The subjects did not use any other medications during the study period.

Results

Figures 4 to 8 indicate the degree of healing and reepithelialization of representative aphthae after treatment with Debacterol.

The size of the ulcers had not changed significantly in any of the groups by day 3 (Table 1 and Fig 9). However, a significant decrease in the VAS (Table 2 and Fig 10) in the D group at day 3 indicated a significant improvement in pain (> 70%) compared to the KO group (< 20%) and the C group (> 30%).

By day 6, 70% of the ulcers had clinically disappeared, and there was resolution of symptoms in 100% of the subjects in the D group. Only 30% of the lesions had disappeared in the KO and C groups. In a few individuals in the KO group, there was a significantly greater decrease in the clinical measurement (ulcer size) over the D and C groups, but the VAS revealed no significant change in the perception of pain among these patients.

By day 10, 100% of the ulcers had clinically healed and were causing no pain in both treatment groups (D and KO). At day 10, 10% of the control group still had clinical ulcers present, with an average VAS of 18 mm.

Discussion

Treatment for recurrent aphthous stomatitis has traditionally been palliative and/or has involved anti-inflammatory agents. Topical steroids and chemical cautery agents have been used previously to treat oral mucosal disorders, such as RAS, with limited success. At the present time, the treatments available have been largely unsuccessful.

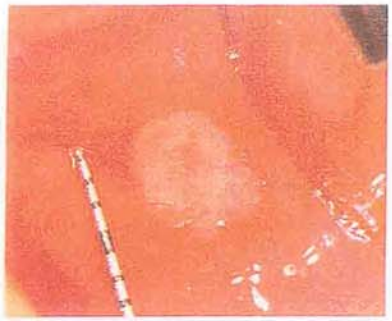

Fig 1 Aphthous ulcer prior to treatment with Debacterol. A periodontal probe is used to measure ulcer size by *(1)* maximal diameter, including the erythematous halo zone and *(2)* perpendicular to maximal diameter.

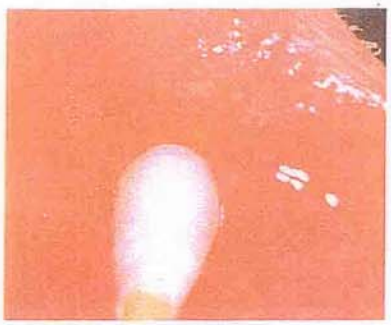

Fig 2 Aphthous ulcer being dried with a cotton-tipped applicator.

Fig 3 Aphthous ulcer being treated with Debacterol, applied for 10 seconds. After application, the area is thoroughly rinsed with water and dried.

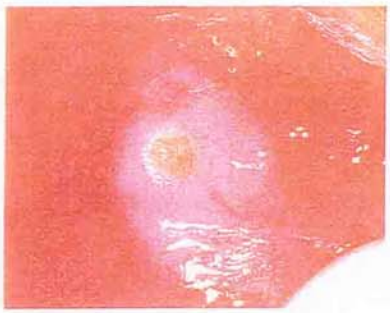

Fig 4 Aphthous ulcer immediately after treatment with Debacterol. Note the zone of epithelial cauterization.

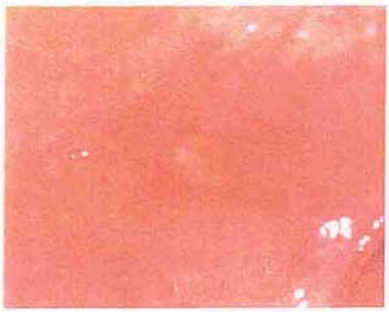

Fig 5 Aphthous ulcer treated with Debacterol: Day 1. Healing is evidenced by initial reepithelialization.

Fig 6 Aphthous ulcer treated with Debacterol: Day 2. Healing is evidenced by progressing reepithelialization.

Fig 7 Aphthous ulcer treated with Debacterol: Day 3. Healing is evidenced by progressing reepithelialization.

TABLE 1 Changes in ulcer size in subject groups (maximum diameter break in mm × 10)

Day	Ulcer size–D	Ulcer size–KO	Ulcer size–C	Significance
1	56.9 ± 16.1	42.8 ± 18.4	59.1 ± 15.6	NS
3	46.5 ± 7.8	33.9 ± 14.3	49.9 ± 18.8	NS
6	7.8 ± 4.7	24.8 ± 8.2	28.4 ± 14.3	$P < 0.001$*
10	Healed	Healed	7.6 ± 3.3	$P < 0.001$**

D = Debacterol; KO = Kenalog-in-Orabase; C = control (no treatment).
*Significance, by Student's *t* test, of Debacterol *over* Kenalog-in-Orabase and no treatment.
**Significance, by Student's *t* test, of Debacterol *and* Kenalog-in-Orabase over no treatment.

TABLE 2 Changes in pain symptoms in subject groups, using the 100-mm visual analog scale (VAS)

Day	VAS–D	VAS–KO	VAS–C	Significance
1	56.4 ± 18.1	52.2 ± 18.4	58.9 ± 18.6	NS
3	11.4 ± 7.8	37.9 ± 14.3	39.7 ± 15.8	$P < 0.001$*
6	No pain	20.6 ± 8.2	22.4 ± 12.3	$P < 0.001$*
10	No pain	No pain	2.6 ± 1.3	$P < 0.001$**

D = Debacterol; KO = Kenalog-in-Orabase; C = control (no treatment).
*Significance, by Student's *t* test, of Debacterol *over* Kenalog-in-Orabase and no treatment.
**Significance, b… no treatment.

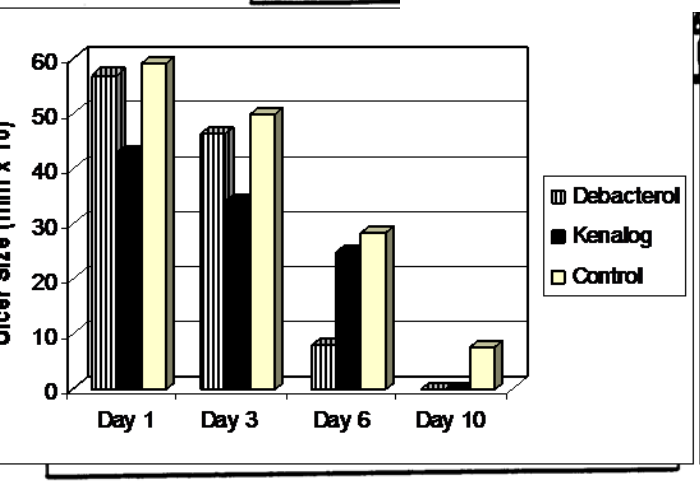

Fig 9 Objective measurement of RAS ulcer size by day following treatment. Scores are reported in mm ×10 (eg, 4.4-mm ulcer = 44). By day 6, the Debacterol group ulcer size had been reduced to approximately one third compared to the Kenalog and control groups. By day 10, the ulcers in both the Debacterol and Kenalog groups had completely healed, unlike those in the control group.

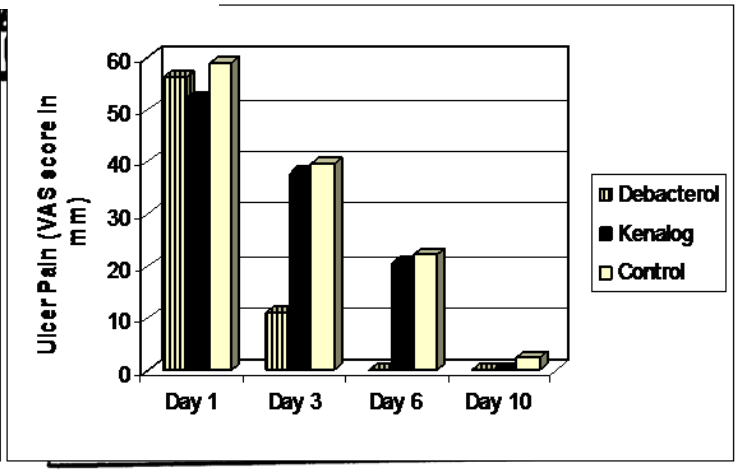

Fig 10 Subjective evaluation of RAS ulcer pain with a visual analog scale score by day following treatment. Scores are reported in mm (maximum = 100 mm). By day 6, the subjects in the Debacterol group had no pain, in contrast to patients in the Kenalog and control groups.

Recently, Binnie et al[15] published the results of three multicentered clinical trials demonstrating the efficacy of Aphthasol (Block Drug) (5% amlexanox) paste. In that particular study, after 3 days of treatment with the 5% Amlexanox, 21% of the RAS lesions had clinically healed and 44% of the subjects had resolution of painful symptoms. In the present pilot study of Debacterol (which had a much smaller number of subjects), after 3 days of treatment, approximately the same number of RAS lesions had completely healed, but the VAS indicated that there was more than 70% resolution of pain. Likewise, after 6 days of treatment, more than 70% of the lesions treated with Debacterol had completely healed, and relief of pain was complete in 100% of the subjects. This can be compared with the results with 5% Amlexanox paste where, after 6 days, approximately the same percentage of RAS lesions had healed, but there was complete resolution of pain in only 68% of the subjects.[15]

The study of 5% Amlexanox was indeed much larger: it reported results of 1,124 subjects, compared with only 60 patients in the present study. The results of the present pilot study must be interpreted in that context. This clinical trial, in a small number of subjects, demonstrated the effectiveness of a chemical cautery agent, Debacterol, in relieving the symptoms of and expediting healing in RAS lesions. Compared with other agents presently available for the treatment of RAS, Debacterol shows promise in expediting the healing of the RAS ulcer.

Conclusion

The results indicated that immediate and significant relief of the pain accompanying RAS was achieved in a large majority of subjects with RAS through the use of Debacterol as compared to Kenalog-in-Orabase or no treatment. The clinical healing of the RAS ulcers was also expedited with the use of Debacterol as compared to Kenalog-in-Orabase or no treatment, although this difference was not quite as dramatic as the symptomatic relief. The results indicated that relief of the symptoms accompanying RAS may or may not correspond to clinical improvement and that these two topical medications may affect signs and symptoms of RAS differently.

Further research is presently being conducted to histologically investigate the epithelial wound-healing process (of rabbit mucosa) after treatment with Debacterol and Kenalog-in-Orabase.

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