Original Article

Evaluation of the Effect of a Clobetasol Propionate and Nystatin Mouthwash on Recurrent Aphthous Stomataitis

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Abstract:

Statement of problem: Recurrent aphthous stomatitis (RAS) is one of the most common diseases affecting human oral mucosa. The etiology of this disease remains unclear; therefore a definitive treatment has not yet been established and corticosteroids might be prescribed to reduce the symptoms associated with RAS.

Purpose: The aim of this study was to determine the effects of a mouthwash containing 0.05% clobetasol and nystatin on aphthous ulcers.

Materials and Methods: Forty patients with RAS, 18 males and 22 females with an age range of 11-50 years, participated in this double-blind placebo-controlled clinical trial. The subjects were randomly divided into two equal groups. Group A received a mouthwash containing 0.05% clobetasol and 100,000 IU/cc nystatin with instructions to rinse with 20 drops for 5 minutes, 3 times daily. Group B (control) received placebo and was asked to follow the same instructions. All symptoms along with possible adverse effects were measured and recorded during the 2-week study period. Statistical analysis was performed using chi-square and independent paired t-tests.

Results: Complete resolution of the lesions and their symptoms was observed in 85% of the participants in group A. Two (10%) patients showed no response to treatment and the symptoms increased in 5% (1 patient). There were no measurable changes in pain or healing time of the ulcers in the control group.

Conclusion: The use of the tested mouthwash was found to be a safe and efficacious treatment for RAS of the oral mucosa.

Key Words: Recurrent aphthous stomatitis (RAS); Nystatin; Clobetasol

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INTRODUCTION

Recurrent aphthous stomatitis (RAS) is one of the most common oral mucosal diseases affectting humans. A variety of causative agents have been suggested as etiologic factors including trauma, psychologic stress, anxiety, food allergy, immunologic abnormalities, etc., but the etiology of this disease remains unclear [1].

RAS demonstrates a tendency to recur which causes intense pain, and interferes with daily activities such as eating, drinking, talking and maintaining normal social activities [2].

Many medications have been used in an attempt to resolve this disease, including local anesthesia, zinc diclofenac, ferrous sulfate and corticosteroid [3-6]. Clobetasol propionate, the most potent topical corticosteroid, can be considered as a safe and efficacious treatment for RAS. However, it may be difficult for patients with severe and extensive ulcerations, to place the adhesive paste on the entire

lesional surface. Clobetasol propionate in aqueous solution along with nystatin in the form of a mouthwash has been reported to be an excellent alternative topical approach in these patients [7]. The mouth wash provides ready access and coverage of the ulcers with excellent control of the contact time between the drug and the lesions.

The purpose of the present study was to evaluate the response of patients with recurrent aphthous stomatitis to treatment with a mouthwash containing clobetasol propionate and nystatin in aqueous solution, and to record any adverse effects related to treatment.

MATERIALS AND METHODS

A double-blind clinical trial was designed at the Oral Medicine department of Shahed Dental School. The inclusion criteria were presence of severe pain, soreness, extensive and/or multiple ulcerations in different areas of the oral mucosa, interference with daily life activities, difficulty in eating, drinking, talking and maintaining normal relationships. Patients with systemic disease whom could not use corticosteroids were excluded from the investigation.

Assessments were made by use of following pain and soreness scale:

Mild: Pain and soreness did not interfere with eating, drinking and talking.

Moderate: Pain and soreness interfered with eating, drinking and talking.

Severe: Pain and soreness caused difficulty in normal eating, drinking and talking.

The study group consisted of 40 patients with recurrent aphthous ulcerations. Diagnosis was based on dental and medical history and clinical examination. The subjects were divided into two groups of 20 patients. Each participant was asked to complete a questionnaire regarding information about the number, width, type (major, minor, herpetiform) and site of the lesions and the severity of their pain.

In group A, all subjects received an aqueous solution containing 0.05% clobetasol propionate and 100000 IU/cc nystatin. They were asked to rinse their mouth with 10 cc of the solution for 5 minutes 3 times a day; after breakfast, lunch and dinner. The patients were instructed not to swallow the solution. Group B participants received mint-flavored normal saline (placebo) with the same instructions as group A. Each of the solutions (clobetasol and placebo) was poured in mono color, opaque glasses and could not be differentiated from each other by their appearance. The mouthwashes were presented to the patients by a student with no previous information on the type of the solutions.

Follow-up visits were scheduled for days 3 and 5 and also the first and second weeks after the beginning of treatment.

All variables including pain, soreness, ulceration and interference with daily activities, as well as the healing process were independently evaluated by the same experienced clinician, for each patient. The results were compared using independent *t*-test for healing time and chi-square test for evaluation of pain and soreness between two groups.

RESULTS

Each group consisted of 45% men and 55 % women, with an age range of 11 to 50 years.

In group A, 40% of the patients had one lesion and 60% had multiple lesions. Forty-five percent of the ulcerations were on the lip mucosa, 15% on the buccal mucosa, 10% on the vestibule, 20% under the tongue around the midline and 10% in other sites. All subjects demonstrated minor aphthous ulcerations.

In group B, 50% had one lesion and 50% had multiple lesions. Forty percent of the lesions were on the lip mucosa, 15% on the buccal mucosa, 15% on the vestibule, 25% under the tongue around the midline and 5% in other sites.

Data on post-treatment evaluation of patients

regarding pain, soreness and duration of healing are shown in Figures 1 and 2.

Response to treatment during the follow-up period was approximately 6.8 days in the experimental group and 9.5 days in the control group. Rinsing with clobetasol and nystatin solution decreased the duration of the ulcers to 1.8 days (Fig. 1). Pain and soreness were relieved at 3.6 and 7.3 days in the clobetasol and control groups, respectively. A significant difference was observed in the clearing of symptoms between the two groups (Fig. 2).

The response to treatment was excellent in group A. In the first week after treatment, 50% of the ulcerations were completely treated. After two weeks, 85% of the lesions and their pain and soreness disappeared. There was no change in 10% and the symptoms increased in 5% of the cases (1 patient). As a result of incorrect consumption of the mouthwash in this patient, pain and soreness became intensive during the treatment period. Otherwise none of the patients demonstrate any adverse effects.

DISCUSSION

Eighty-five percent of the patients had complete absence of pain and ulcerations at the end of the treatment period. According to the results obtained in the present investigation, clobetasol propionate has been found to be an effective and rapid treatment of RAS.

Previous studies have used clobetasol propionate in an adhesive paste for the treatment of severe erosive disease and reported complete to excellent results in most cases, and failure in 8.3%. They concluded that their treatment was efficacious and safe [9].

The smaller number of failed responses observed in the current study may be attributed to the improved access of the mouthwash to all lesional areas and to the prolonged contact time between the administered mouth rinse and ulcers. Application of adhesive pastes seems more difficult for the patients and various factors like mouth movement can dislodge it. In addition, the clinician cannot be certain if it has been used correctly or the desired contact time has been achieved. Nevertheless, Orabase has been reported to be a good vehicle especially when used with a tray on palatal and gingival lesions [8].

Gonzalez-Moles et al [7,8] studied the effect of topical treatment with clobetasol mouthwash in 30 patients with severe oral erosive lesions. Five of their patients (16.6%) presented with adverse effects to corticosteroids, 4 of which (13.3%) could be exclusively attributed to the use of clobetasol propionate. There were 3 cases of moon face and 2 of hirsutism, all of which presented between weeks 4 and 6 of the treatment [8]. Lozada-Nur et al [9] reported side effects in 20.8% (5 patients) of their series with pseudomem-

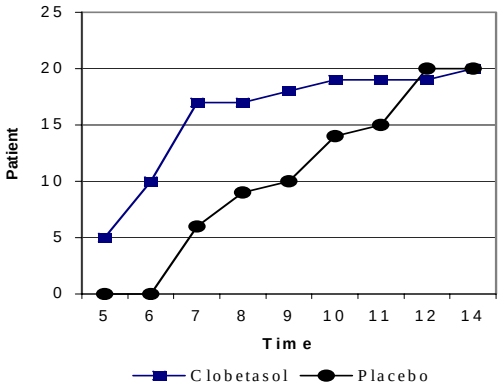

Fig. 1: post-treatment evaluation of patients regarding duration of healing

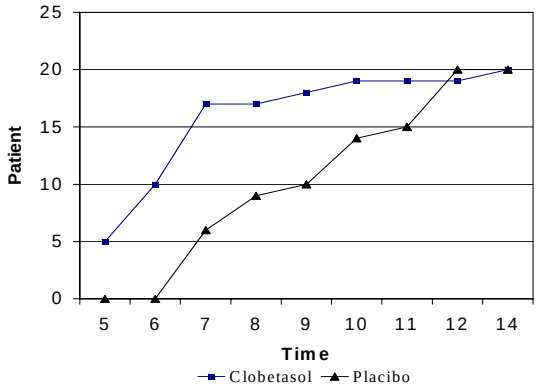

Fig. 2: Improvement of patients with complete response of pain and soreness during study period.

branous or erythematous candidiasis being the most frequent (12.5%; 3 patients). They observed no cases of moon face or other systemic adverse reactions. These authors attributed the low incidence of candidiasis to the low doses of clobetasol (0.025%), the small surface area application, and the wet environment. They concluded that candidiasis could be prevented by anti-fungal treatments and that individuals at risk could be identified by means of pretreatment cultures and counts of colony-forming units [9].

The concentration of clobetasol (0.05%) was higher in the current investigation. In addition, the surface area that comes into contact with aqueous solutions is generally larger than adhesive pastes. Therefore in order to minimize the occurrence of candidiasis, 100000 IU/cc nystatin was added to the experimental mouthwash used in the present study.

The innocuous nature of nystatin, low cost, and the fact that symptoms related to candidiasis (erythema and buccal pain or soreness) may be confused with treatment failure, indicate its use in patients receiving clobetasol mouthwash treatment [8]. None of the patients participating in the present study showed any sign of oral candidiasis during the 2-week period.

The pathogenesis and definitive cause of RAS remains unclear. At best it has been described as a disease process that is triggered by a variety of causative agents, each of which is capable of producing the disease in certain subgroups of patients [3]. Therefore various treatment modalities have been proposed for the different types of this pathosis. Meiller et al [10] studied the effect of Listerine mouthwash (which is similar to Iranian Irsha mouthrinse) on RAS and reported that rinsing with this solution can be of clinical value in reducing the occurrence of aphthous in susceptible patients. They also found it to have a significant additional value in decreasing the duration and severity of this disease. Tohidast-Ekrad and Salehi-Sormaghi [11] tested Persica mouthwash on RAS and described its positive effects in decreasing pain and soreness of the ulcerations.

CONCLUSION

The use of mouthwashes containing 0.05% clobetasol propionate plus 100,000 IU/cc nystatin in aqueous solution is a safe and efficacious treatment for RAS of the oral mucosa.

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