Comparison of Aloe Vera Mouthwash With Triamcinolone Acetonide 0.1% on Oral Lichen Planus: A Randomized Double-Blinded Clinical Trial

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Introduction: Corticosteroids are the mainstay for treatment of oral lichen planus (OLP) and have their own side effects. The aim of this study was to compare the therapeutic effects of aloe vera (AV) mouthwash with triamcinolone acetonide 0.1% (TA) on OLP.

Methods: A total of 46 patients with OLP were enrolled in this study. The patients were randomly divided into 2 groups. Each group was treated with received AV mouthwash or TA. The treatment period for both groups was 4 weeks. The baseline data were recorded for each patient. Patients were evaluated on days 8, 16 and after completing the course of treatment (visit 1–3). The last follow-up was 2 months after the start of treatment (visit 4). Visual analogue scale was used for evaluating pain and burning sensation and Thongprasom index for clinical improvement and healing. In addition, lesion sizes were measured and recorded at each visit using a grid.

Results: Baseline characteristics, including pain and burning sensation score, size and clinical characteristics of the lesions according to Thongprasom index, were not different between the 2 treatment groups. Both AV and TA significantly reduced visual analogue scale score, Thongprasom score and size of the lesions after treatment (P < 0.001) and after 2 months of discontinuation of the treatment (P < 0.001). In the AV group, 74% of patients and in the TA group 78% of patients showed some degrees of healing in the last follow-up.

Conclusions: AV mouthwash is an effective substitute for TA in the treatment of OLP.

Key Indexing Terms: Aloe vera; Oral lichen planus; Triamcinolone acetonide. [Am J Med Sci 2011;342(6):447–451.]

Lichen planus is a chronic immune-mediated mucocutaneous disease, which can affect the oral mucosa in 50% of cases. The exact etiology is still unknown, but it is reported that immune system disturbances may play a significant role in its pathogenesis.1,2 In addition, the role of free radicals by producing oxidative stress has been discussed in the etiology of disease.3,4 The common remedies for the disease include systemic corticosteroids, immunosuppressives, retinoids, phototherapy and topical steroids. Corticosteroids are considered as the first-line treatment of oral lichen planus (OLP).2,5 This kind of treatment is symptomatic and will not completely cure the disease. Therefore, shortly after discontinuation of the therapy, there is recurrence of lesions, and the patient should use medicines for a long time.6 In addition, drugs such as cyclosporine and tacrolimus are immunosuppressive and have numerous side effects. The most commonly documented adverse effects of treatment of OLP, including corticosteroid therapy, are local irritation, tingling, burning sensation, steroid-related fungal infection, taste alterations and nausea.7–9

Aloe vera (AV; named Aloe barbadensis in Latin), a plant of dry and warm weather, contains polysaccharides, anthraquinone, lectin, superoxide dismutase (an antioxidant enzyme), glycoprotein, amino acids, vitamin C and E and minerals.10,11 Several studies revealed anti-inflammatory, analgesic, liver protection, antiproliferative, anticarcinogenic and antiaging properties of AV.12–15 It seems that these effects are a result of antioxidant properties, cyclooxygenase-2 suppression and immunomodulatory mechanisms.15,16 Some data suggest that AV can suppress tumor growth and improve the survival of patients. It can also be used in the treatment of asthma, ischemic heart disease, diabetes and skin diseases.16–19

According to the good therapeutic effects of AV on many different diseases and its antioxidant and anticaner effects, in this study, we decided to evaluate the therapeutic effects of AV mouthwash in comparison with triamcinolone acetonide 0.1% (TA) on OLP lesions. Because AV does not possess the immunosuppressive and other side effects of common treatments for OLP, and according to the newly explained etiology considering oxidative stress in OLP pathogenesis,3,18 replacement of AV in the treatment of OLP lesions can be a significant advance in the management of this chronic premalignant disease of oral cavity.

MATERIALS AND METHODS

Patients

This study was a randomized double-blinded clinical trial. Patients with OLP were randomly selected from the department of Oral Medicine, Tehran University of Medical Sciences. Both clinical and histopathologic criteria were used for the diagnosis based on World Health Organization diagnostic criteria (2003).20

Patients with erosive or atrophic OLP confirmed by clinical and histopathologic criteria were included in this study. Patients with any systemic diseases, including: heart disease, renal disease, hypertension, neurologic disorders, etc., were excluded. Patients using any medication for treatment of OLP or any immunosuppressive medication during the 4 weeks preceding the study were excluded. Patients with lichenoid lesions, those whose lesions were in direct contact with amalgam restorations, those who had allergy to other dental materials and those who had dysplastic lesions were also excluded.

Between September 2009 and June 2010, a total of 57 randomly selected subjects were evaluated for inclusion to the study. On the basis of the criteria, 46 subjects were enrolled in this study. This study was approved by the ethics committee of the Oral Medicine Department (AM, MS-J, JM-B), School of Dental Medicine, Tehran University of Medical Sciences; Craniomaxillofacial Research Center (RA-R), Shariati Hospital, Tehran University of Medical Sciences; Dental Research Center (FM-H), Shariati Hospital, Tehran University of Medical Sciences; and School of Medicine (OK), Tehran University of Medical Sciences, Tehran, Iran. Submitted January 6, 2011, accepted in revised form February 23, 2011. Correspondence: Fatemeh Momen-Heravi, DDS, Craniomaxillofacial Research Center, Shariati Hospital, Tehran University of Medical Sciences, Enghelab Avenue, Tehran, Iran (E-mail: f_m_heravi@yahoo.com).
Tehran University of Medical Sciences. The whole process was explained for patients to decide whether they are willing to take part in the study, and informed consent was obtained. All steps of the study were planned and conformed to the principles outlined in the Declaration of Helsinki and ethical codes provided by ethics committee of Tehran University of Medical Sciences.

**Study Design and Intervention**

After determining eligibility and obtaining consent, to guarantee blinding, a random number was generated for each participant using the SPSS software (version 16.0; SPSS, Chicago, IL), and patients were referred to the pharmacist to pick up their assigned medication according to their number. The patients were randomly divided to an AV mouthwash group (n = 23) and a TA group (n = 23). Both medications had identical sealed package. The patients in the AV group were asked to rinse the mouth with 2 tablespoons of AV mouthwash (Barij Essence Company, Tehran, Iran) for 2 minutes, 4 times a day and expectorate.

The patients in the TA group were instructed to apply a thin layer of triamcinolone acetonide 0.1% paste (Adcortyl, Bristol-Myers Squibb, Anagni, Italy) on the oral lesions, 4 times daily. The patients were asked not to eat, drink or smoke for 20 minutes after each application and continue treatment for 1 month. The patients were asked to report immediately if there was any side effect at any time of the study until 6 months after treatment. Patients were also assessed for any possible side effects by researchers at each appointment. All of the patients were truly monitored and were compliant to the drugs.

**History of any systemic diseases, demographic information and clinical data related to lesions were recorded for each patient in a separate questionnaire.**

The baseline data were recorded for each patient. The treatment period for both groups was 4 weeks. Patients were evaluated on days 8, 16 and after completing the course of treatment (visit 1–3). The last follow-up was 2 months after the start of treatment (visit 4). All the measurements and evaluations were performed by 1 clinician who was blind to the type of treatment.

**Measurements**

Size of the lesions were measured and recorded for each patient using a grid. Intensity of pain was also recorded for each patient using visual analogue scale. For this purpose, a 10-cm ruler was used, and each patient correlated his/her degree of pain to a number on this scale. Zero score was considered for a patient without any pain, whereas a score of 10 was given to the highest level of perceived pain. Clinical characteristics of the lesions were scored using Thongprasom criteria. According to Thongprasom et al., clinical presentation of OLP can be scored from 0 to 5 according to the following findings: 0, no lesion; 1, mild white lesions without erythematous areas; 2, white striae with atrophic lesions <1 cm; 3, white striae with atrophic lesions >1 cm; 4, white lesions with ulcerative areas <1 cm; and 5, white lesions with ulcerative areas >1 cm.

**Statistical Analysis**

Data were analyzed using SPSS software (version 16.0; SPSS). The required sample size for this study using \( \alpha = 0.05 \) and power = 0.80 was calculated to be 23 patients in each group. The null hypothesis was assumed that the level of healing of OLP would be similar between the AV and TA groups. Quantitative variables are expressed as mean ± standard error of mean. To evaluate the efficacy of each individual treatment on OLP, before-and-after analysis was performed using paired sample t test for comparison of variables with normal distribution or nonparametric Wilcoxon’s rank test for variables deviated from normal distribution. The baseline characteristics and the changes occurred in the characteristics of the 2 groups after treatment were compared using \( \chi^2 \) analysis for categorical variables, Student’s sample \( t \) test for normally distributed continuous variables and Mann-Whitney U test for continuous variables, which were deviated from normal distribution. A \( P \) value <0.05 was considered statistically significant.

**RESULTS**

Baseline characteristics of the study participants are presented in Table 1. The patients were between 33 and 75 years old. There were no significant differences between groups with respect to age, sex, duration of lesions and type or site of OLP. The most prevalent site for OLP lesions was buccal mucosa followed by tongue and gingival area. All patients in both groups had involvement of buccal area. Baseline pain and burning sensation score was not different between the 2 treatment groups. Furthermore, there was no significant difference between the 2 groups in baseline size and clinical characteristics of the lesions according to Thongprasom score (Table 1).

Both AV and TA 0.1% significantly reduced pain and burning sensation score, Thongprasom score and size of the lesions after treatment (\( P < 0.001 \)) and after 2 months of discontinuation of the treatment (\( P < 0.001 \); Figure 1). In the AV group, 74% of patients and in the TA group 78% of patients showed some degrees of healing in the last follow-up step. Characteristics of the study participants during treatment and follow-up visits are presented in Table 2. The changes occurred in size of lesions and Thongprasom score, and pain and burning sensation score were not statistically different between the 2 groups in any of the 4 evaluations.

### Table 1. Baseline characteristics of the study participants

| Variable                        | Aloe vera (n = 23) | Triamcinolone acetonide 0.1% (n = 23) |
|---------------------------------|-------------------|---------------------------------------|
| Sex (males, %)                  | 8 (34.8)          | 9 (39.1)                              |
| Age (yr)                        | 47.2 ± 2.0        | 50.7 ± 2.1                            |
| Site of OLP (n, %)              |                   |                                       |
| Buccal                          | 23 (100)          | 23 (100)                              |
| Tongue                          | 5 (21.7)          | 6 (26.1)                              |
| Gingiva                         | 6 (26.1)          | 5 (21.7)                              |
| Palate                          | 2 (8.7)           | 3 (13.0)                              |
| Ridge                           | 3 (13.0)          | 2 (8.7)                               |
| Duration of lesions (mo)        | 25.9 ± 2.8        | 24.9 ± 2.7                            |
| Type of OLP (n, %)              |                   |                                       |
| Reticular                       | 9 (39.1)          | 8 (34.8)                              |
| Atrophic                        | 3 (13.0)          | 2 (8.7)                               |
| Erosive                         | 11 (47.7)         | 12 (52.2)                             |
| Pain and burning sensation score (cm) | 4.12 ± 0.36      | 3.99 ± 0.40                           |
| Thongprasom score               | 3.15 ± 0.28       | 3.08 ± 0.27                           |
| Size of lesion (mm)             | 23.09 ± 2.63      | 21.04 ± 2.15                          |

Variables are expressed as mean ± standard error of mean, unless otherwise is stated.

OLP, oral lichen planus.
DISCUSSION

The main aim of the current therapies for OLP is to reduce pain and eliminate the lesions. Although it is accepted that there is no definitive cure for OLP, the basic treatment in mild to moderate cases is corticosteroid therapy. Treatment is primarily aimed at reducing the severity and duration of lesions.2–6 Because there is no definite cure for the disease, the therapy that has its efficacy at the least side effects is most favorable. The results of this study, for the first time, showed that AV can be an effective treatment of OLP lesions. Both AV and TA significantly reduced pain and burning sensation score and the size of lesions after treatment and after 2 months of discontinuation of the treatment. In addition, both AV and TA treatment groups showed the same degree of healing after discontinuation of the treatment.

Recent researches have shown that an increase in intracellular adhesion molecules and secreting cytokines, such as interleukin (IL)-10, tumor necrosis factor alpha, IL2 and IL4, by activated lymphocytes and keratinocytes can contribute to the pathogenesis of OLP.3,23 In addition, an imbalance between the level of free radicals and reactive oxygen species probably has a significant influence on initiation and progression of oral inflammatory lesions. It has been shown that oxidative stress is far greater in patients with OLP than in healthy subjects.3,24–26 AV exhibits some anti-inflammatory effects by inhibiting cyclooxygenase and reducing leukocyte adhesion molecules and tumor necrosis factor alpha level.27 Stimulatory effects of AV can increase antibody production and accelerate wound healing by increasing growth factors. Furthermore, it has antioxidant properties and eliminates production of free radicals.11–13,28 Therefore, our results, which show the good efficacy of AV in the treatment of OLP, are of considerable pathophysiologic relevance.

The efficacy of TA in the treatment of OLP is reported in previous studies.29 In a study conducted by Thongprasom et al,30 the effect of 0.1% solution of fluocinolone acetonide was evaluated on OLP lesions. Approximately 73% of patients using this topical treatment showed complete improvement after treatment. In another study by Thongprasom et al,31 the effect of topical cyclosporine was compared with TA 0.1% in OLP lesions. The study was conducted on 13 patients, and the results showed that 50% of patients treated with TA had complete improvement and 50% showed partial healing. In patients receiving cyclosporine, 33.5% showed partial improvement and 66.75% did not show any response to the treatment. González-García et al32 evaluated the effects of TA 0.3% and 0.5% on OLP erosive lesions. Of the total of 35 patients enrolled in their study and similarly in both groups, 80% had complete improvement at the end of sixth month.

**FIGURE 1.** Treatment with both aloe vera and triamcinolone acetonide 0.1% significantly (P < 0.001) reduced pain and burning sensation score (A) and Thongprasom score (B) after the treatment period (third visit) and after 2 months of discontinuation of the treatment (fourth visit). Handles represent standard error of mean.

**TABLE 2.** Characteristics of the study participant during treatment and follow-up visits

|                      | Aloe Vera (n = 23) | Triamcinolone Acetonide 0.1% (n = 23) |
|----------------------|--------------------|----------------------------------------|
| Size of lesion (mm)  |                    |                                        |
| Baseline             | 23.09 ± 2.63       | 21.04 ± 2.15                           |
| 1st visit (day 8)    | 20.28 ± 2.01       | 18.80 ± 1.83                           |
| 2nd visit (day 16)   | 10.39 ± 1.20       | 8.60 ± 0.84                            |
| 3rd visit (after 2 mo)| 7.26 ± 0.77       | 5.27 ± 0.59                            |
| 4th visit (after 4 mo)| 5.39 ± 0.48      | 3.87 ± 0.36                            |
| Thongprasom score    |                    |                                        |
| Baseline             | 3.15 ± 0.28        | 3.08 ± 0.27                            |
| 1st visit (day 8)    | 2.96 ± 0.25        | 2.80 ± 0.22                            |
| 2nd visit (day 16)   | 2.30 ± 0.22        | 2.43 ± 0.20                            |
| 3rd visit (after 2 mo)| 1.39 ± 0.16       | 1.10 ± 0.10                            |
| 4th visit (after 4 mo)| 0.91 ± 0.10       | 0.83 ± 0.09                            |
| Pain and burning sensation score (cm) | | |
| Baseline             | 4.12 ± 0.36        | 3.99 ± 0.40                            |
| 1st visit (day 8)    | 3.04 ± 0.29        | 2.20 ± 0.34                            |
| 2nd visit (day 16)   | 1.42 ± 0.20        | 1.60 ± 0.17                            |
| 3rd visit (after 2 mo)| 0.83 ± 0.11       | 0.87 ± 0.10                            |
| 4th visit (after 4 mo)| 0.81 ± 0.08       | 0.75 ± 0.08                            |

The changes occurred in each of the characteristics from baseline to either the 1st, 2nd, 3rd, or 4th visits were not significantly different between aloe vera or triamcinolone acetonide 0.1% groups.
whereas 17% showed partial improvement. In our study, 78% of patients treated with TA showed clinical improvement, which is more or less similar to the results reported in other studies.

In a study conducted by Salazar-Sánchez et al, AV solution consisting of 70% aloe juice was used. Of 32 cases in the AV group, complete pain remission was achieved in 31.2% of the cases after 6 weeks and in 61% after 12 weeks. In the placebo group, these percentages were 17.2% and 41.6%, respectively. The results of their study revealed that the topical application of AV, 3 times a day, improves the pain, the oral lesions and the oral quality of life of the patients with OLP. In our study, AV solution consisting of 94.5% of AV juice was used proposed by Su et al. The better efficacy achieved in our study compared with that in the above-mentioned study may be due to the difference in concentration.

Nowadays, oromucosal drug delivery methods are at the forefront of treatment of oral diseases. In addition, some regions in the oral cavity, including buccal, sublingual, palatal and gingival sites, could effectively absorb drugs. It seems reasonable to assume that gel form of a same medication should be used instead of synthetic drugs. Further studies in managing OLP, particularly in patients who prefer to use herbal medicine instead of synthetic drugs. Further studies in other populations and with more duration of follow-up are necessary to confirm our results.

In conclusion, our study demonstrated that AV has similar therapeutic effects with TA in the treatment of OLP lesions. AV has both antioxidant and anti-inflammatory effects, which may significantly contribute to its clinical effects. Considering the chronicity of the disease, and the need for the long-term treatment modalities, AV can be proposed as a good treatment for OLP. Our results provide practical hints for better management of OLP, particularly in patients who prefer to use herbal medicine instead of synthetic drugs. Further studies in other populations and with more duration of follow-up are necessary to confirm our results.

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