

The Efficacy of *Aloe vera* Gel in Treatment of Oral Lichen Planus

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Keywords:

Aloe vera, erythema, oral lichen planus, placebo

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Received November 16, 2017;

Accepted March 08, 2018

doi: 10.15713/ins.idmjar.85

Abstract

Background: *Aloe vera* (AV) gels with different concentrations are available in the market. In this study, we evaluate the efficacy of AV gel with two different concentrations in the treatment of oral lichen planus (OLP) compared with placebo.

Materials and Methods: A total of 21 females suffering from the clinical signs and symptoms of OLP were grouped into Group (I) patients receiving AV gel divided into two subgroups, subgroup (A) received AV 70% concentration (7 patients) and subgroup (B) received AV 90% concentration (7 patients) and Group (II) control group received placebo (7 patients).

Results: There was no statistically significant difference between ulcer sizes at all points of follow-up in Egyptian and Australian AV compared to placebo. The degree of change was higher in Egyptian than Australian AV regarding size, erythema, reticulation, and total area of lesion. However, there was no statistically significant difference between two types of treatment as regards all measured parameters ($P > 0.05$).

Conclusions: AV gel whether Egyptian or Australian is statistically significantly more effective than placebo in inducing marked improvement clinically of OLP. Therefore, AV gel can be considered a safe alternative treatment for patients with OLP.

Clinical Significance: AV gel can be considered a safe alternative treatment for patients with OLP.

Introduction

Oral lichen planus (OLP) is a chronic inflammatory disease characterized by abnormally keratinized oral mucosa and band-like T-cell infiltration in the upper lamina propria. Consequently, it is referred to as a potentially malignant disorder by the World Health Organization working group. Clinically, OLP is classified into seven forms: Atrophic, bullous, erosive, popular, pigmented, plaque-like, or reticular. The patients with reticular lesions, the most common form, generally have no clinical symptoms, while atrophic, bullous, and erosive lesions cause pain, ranging from mild to severe. Notably, erosive OLP shows a significantly higher rate of malignant transformation than non-erosive OLP.^[1]

The lichen planus antigen is unknown, although it may be a self-peptide (or altered self-peptide). The expression or unmasking of the lichen planus antigen may be induced by drugs (lichenoid drug reaction), contact allergens in dental restorative materials or toothpastes (contact hypersensitivity reaction),

mechanical trauma (Koebner phenomenon), viral infection, or other unidentified agents.^[2]

There is no fully resolutive and effective treatment the management strategy focusing on the use of drugs that counter tissue inflammation and the underlying immunological mechanisms. Some topical corticosteroid therapies may predispose the patient to oral candidiasis. However, this condition is rarely if ever symptomatic, and it generally does not complicate healing of the erosions related to OLP. Topical antimycotics (e.g., nystatin and amphotericin) may be prescribed when an infection is present.^[3]

Erosive OLP that is recalcitrant to topical corticosteroids may respond to topical tacrolimus.^[4] Other potential therapies for recalcitrant OLP include hydroxychloroquine, dapsone, systemic corticosteroids, and topical and systemic retinoids.^[5] The main inconvenience of these treatments is represented by the side effects including insomnia, nervousness, fluid retention, electrolyte imbalance, hyperglycemia, osteoporosis, nephrotoxicity, gingival hyperplasia, nausea, and headache.^[6]

Due to these side effects, the possibility of prolonged treatment with steroids, and the fact that the disease process could still last for years, an alternative therapy is desirable.^[7] Moreover, topical corticosteroids are the mainstay of medical treatment of OLP, although rarely, corticosteroids may be administered intralesionally or systemically. Topical treatment is a good choice because of its less harmful side effects.^[6]

Studies have demonstrated that AV has an important therapeutic uses in the management of oral lesions such as oral submucous fibrosis, radiation-induced mucositis, burning mouth syndrome, xerostomia, and recurrent aphthous ulcers.^[8,9]

The aim of the study is to evaluate the efficacy of AV gel in the treatment of OLP compared with placebo.

Materials and Methods

A total of 21 females from those attending to the Department of Oral Medicine and Periodontology, Faculty of Dentistry, Mansoura University, were included in the study. The patients were suffering from the clinical signs and symptoms of OLP. The first (patients) group received AV gel divided into two subgroups: (A) 7 patients received AV 70% and (B) 7 patients received AV 90%. The second (control) group included seven patients receiving placebo [Table 1].

Two *Aloe vera* (AV) types were used: AV manufactured locally by Faculty of Pharmaceutical Sciences of Mansoura University. It is consisted of 70% AV mucilage, sorbitol, potassium sorbate, sodium metabisulfite, and hydroxyethyl cellulose. AV was expiated from Australia with concentration 90% AV mucilage, sorbitol, potassium sorbate, sodium metabisulfite, and hydroxyethyl cellulose. The placebo gel expiated from Australia with concentration 90% AV mucilage, sorbitol, potassium sorbate, sodium metabisulfite, and hydroxyethyl cellulose.

Each patient was instructed to apply the AV twice daily by finger/cotton tip application on dry lesion after meals without eating for at least ½ h to obtain better absorption.

Lesions were measured with a flexible, transparent grid divided into calibrated squares of 1 mm², and a thin indelible, ink marker. The grid was placed over the lesion, and area of ulceration, erythema, and reticulation were traced with the ink marker. Quantitative measurements of the lesion were calculated from the grid by collecting the number of squares by 1 mm².^[10]

The pain was scored by visual analog scale. Patients were asked to score their intensity of pain at each visit as follow: 0 = no pain, 1 = mild pain, 2 = moderate pain, and 3 = severe pain.

Test of significance was done: $P > 0.05$ = non-significant, $P < 0.05^*$ = significant, and $P < 0.01^{**}$ = highly significant.

Results

There was no statistically significant difference between ulcer sizes at all points of follow-up in Egyptian and Australian AV compared to placebo [Figure 1 and Table 2]. Erythema score among study groups at different times the erythema score decreased in both types of AV. There was no statistically

significant difference between erythema at 2 and 4 weeks of follow-up in Egyptian (Group I/A) and Australian AV (Group I/B) compared to placebo. However, statistically significant difference was found between Australian AV and placebo treatment at final visit ($P < 0.05$) [Figure 2 and Table 3]. The mean reticulations decreased in both Egyptian and Australian groups at 2, 4, 6, and 8 weeks with a statistically significant difference were found between for Egyptian and Australian AV compared to placebo treatment at 4 and 6 weeks visits ($P < 0.05$) [Table 4]. The mean total area of lesion decreased in both Egyptian and Australian groups at 2, 4, 6, and 8 weeks with a statistically significant difference was found between for Egyptian AV compared to placebo treatment at 6 and 8 weeks visits ($P < 0.05$) [Table 5]. Pain score evaluation decreased in both Egyptian at the 6th week and Australian groups at 4, 6, and 8 weeks with a statistically significant difference ($P < 0.05$) [Table 6]. The degree of change was higher in Egyptian than Australian AV regarding size, erythema, reticulation, and total area of lesion. However, there was no statistically significant difference between two types of treatment as regards all measured parameters ($P > 0.05$) [Figure 3 and Table 7].

Table 1: Mean age of studied groups

Intervention	Egyptian AV (70%)	Australian AV (90%)	Placebo (n=5)	P
Age mean±SD	53.8±4.4	50.1±3.8	57.6±13.3	0.2

There was no statistically significant difference between study groups as regards age. SD: Standard deviation, AV: *Aloe vera*



Figure 1: Case 1 (a) shows erosive type of lichen planus on the left buccal mucosa of 55-year-old women with 2 years duration before treatment. (b) After treatment with Egyptian *Aloe vera*



Figure 2: Case 2 (a) reticular type of lichen planus on the right buccal mucosa before treatment. (b) After treatment with Egyptian *Aloe vera*

Table 2: Size of ulceration among study groups at different times

Timing of follow-up	Median (range)			Significance		
	Egyptian AV	Australian AV	Placebo	P		
	(Group I/a)	(Group I/b)	(Group II)	P_3	P_2	P_1
	(n=7)	(n=7)	(n=5)			
Baseline	70 (45–200)	60 (39–90)	50 (30–78)	0.2	0.1	0.2
2 weeks (2 nd visit)	69 (40–200)	55 (36–76)	50 (30–80)	0.5	0.2	0.4
P_4 value	0.2	0.08	1			
1 month (3 rd visit)	60 (25–110)	35 (23–65)	50 (30–78)	0.4	0.8	0.5
P_4 value	0.04	0.01	0.3			
2 months (4 th visit)	45 (15–69)	35 (10–45)	50 (33–80)	0.1	0.4	0.2
P_4 value	0.01	0.01	0.1			
5 th (visit)	35 (0–70)	35 (0–50)	50 (35–80)	0.04*	0.1	0.1
P_4 value	0.02*	0.01*	0.1			

P_1 : Compression between three groups, P_2 : Compression between Egyptian AV and control group, P_3 : Compression between Australian AV and control group, P_4 : Compression between baseline with each follow-up visit. AV: *Aloe vera*

Table 3: Erythema score among study groups at different times (mean±SD)

Timing of follow-up	Egyptian AV	Australian AV	Placebo	P		
	n=7	n=7	n=5	P_3	P_2	P_1
Baseline	129.3±58.7	94.14±33.11	102.2±32.4	0.9	0.6	0.3
2 weeks (2 nd visit)	122.14±59.3	83.7±28.5	101.8±33.03	0.7	0.8	0.2
P_4 value	0.2	0.02*	0.3			
4 weeks (3 rd visit)	97.14±52.7	65.0±17.5	102.2±32.4	0.1	0.9	0.1
P_4 value	0.02*	0.01*	---			
6 weeks (4 th visit)	69.14±28.07	49.3±17.6	102.0±32.9	0.05	0.2	0.01
P_4 value	0.02*	0.01*	0.7			
8 weeks (5 th visit)	60.0±37.7	34.3±17.0	103.2±31.9	0.01*	0.15	0.01
P_4 value	0.03*	0.004*	0.3			

P_1 : Compression between three groups, P_2 : Compression between Egyptian AV and control group, P_3 : Compression between Australian AV and control group, P_4 : Compression between baseline with each follow-up visit. SD: Standard deviation. AV: *Aloe vera*



Figure 3: Case 3 (a) shows erosive type of lichen planus on the left buccal mucosa of 49 years women with 1 year duration before treatment. (b) After treatment with Australian *Aloe vera*

Discussion

In this study, women only were chosen to get rid of inherent variation in the immune responses in females versus males, which might account for the higher prevalence of autoimmune diseases among females. It has recently been shown that females have a stronger TH1 immune response mediated by interferon gamma. Several animal studies have shown that female mice have greater antibody production capacity, increased cell-mediated responses, and increased production of interferon gamma, interleukin (IL)-1, and IL-6 compared to males. Human vaccination studies have confirmed similar patterns.^[11]

Table 4: Reticulation among study groups at different times (mean±SD)

Timing of follow-up	Egyptian AV	Australian AV	Placebo	P		
	n=7	n=7	(Group II) n=5	P ₃	P ₂	P ₁
Baseline	144.3±60.2	128.6±34.3	183.2±50.4	0.07	0.1	0.1
2 weeks (2 nd visit)	143.7±64.7	115.0±30.9	184.±49.2	0.03	0.1	0.09
P ₄ value	0.8	0.006*	0.7			
4 weeks (3 rd visit)	111.4±60.6	87.7±28.4	183.2±50.4	0.004	0.02	0.01
P ₄ value	0.01	<0.001*	--			
6 weeks (4 th visit)	87.14±50.3	70.14±34.6	185.2±48.9	<0.001	0.002	0.001
P ₄ value	0.02	<0.001*	0.3			
8 weeks (5 th visit)	15	50	176	0.005	0.01	0.01
Range	0–200	0–150	130–260			
P ₄ value	0.03	0.01	0.1			

P₁: Compression between three groups, P₂: Compression between Egyptian AV and control group, P₃: Compression between Australian AV and control group, P₄: Compression between baseline with each follow-up visit. SD: Standard deviation, AV: *Aloe vera*

Table 5: Total area of lesion in mm at different times (mean±SD)

Timing of follow-up	Egyptian AV	Australian AV	Placebo	P		
	n=7	n=7	(Group II) n=5	(Kruskal Wallis test)		
				P ₃	P ₂	P ₁
Baseline	345.7±87.6	286.14±55.5	336.0±78.4	0.2	0.8	0.3
2 weeks (2 nd visit)	352.14±111.6	256.8±45.8	336±82.2	0.1	0.7	0.1
P ₄ value	0.7	0.004*	1			
4 weeks (3 rd visit)	267.14±96.04	194.14±45.0	338±82.3	0.006	0.1	0.01
P ₄ value	0.01*	<0.001*	0.3			
6 weeks (4 th visit)	209.7±111.8	150.8±56.3	338.8±79.6	0.002	0.02	0.007
P ₄ value	0.02*	<0.001*	0.3			
8 weeks (5 th visit)	120	125	346.4±82.5	0.003	0.03	0.01
Range	10–380	0–270	350 270–470			
P ₄ value	0.01*	0.01*	0.1			

P₁: Compression between three groups, P₂: Compression between Egyptian AV and control group, P₃: Compression between Australian AV and control group, P₄: Compression between baseline with each follow-up visit. SD: Standard deviation, AV: *Aloe vera*

As regarded to size of ulceration, reticulation, and erythema of both types of AV, they were decrease significantly after 6 and 8 weeks. However, the size of ulceration, reticulation, and erythema of placebo was same.^[7,12] The authors confirmed that the AV is more efficient than placebo in ulceration, reticulation, and erythema reduction. Choonhakarn *et al.*^[7] stated that the difference is statistically significant, while Salazar-Sanchez *et al.*^[12] stated that it is insignificant. Another study done by Mansourian *et al.*^[13] and Reddy *et al.*^[14] demonstrated that AV and triamcinolone acetonide (TA) had comparable effect in the ulceration, reticulation, and erythema reduction with no statistically significant difference and both medications

lead to significant reduction in ulceration, reticulation, and erythema.

The improvement of ulceration, reticulation, and erythema can be explained by that AV can inhibit the inflammatory process by its interfering actions on the arachidonic acid pathway through cyclooxygenase. Moreover, the healing powers of AV through high-molecular-weight polypeptide constituent from the gel demonstrated a healing effect on excisional wounds in rats.^[15] Yagi *et al.*^[16] reported that AV gel contains a glycoprotein with cell proliferating-promoting activity, while Davis *et al.*^[17] noted that AV increasing blood supply, which increased oxygenation as result.^[18] As regarded to erythema score among study groups at different times, decreased in both types of AV. However, final follow-up

Table 6: Pain evaluation among study groups at different times

Timing of follow-up	Mean±SD			P		
	Egyptian AV (Group I/a)	Australian AV (Group I/b)	Placebo (Group II)	P ₃	P ₂	P ₁
	n=7	n=7	n=5			
Baseline	3	3	3	0.5	0.7	0.4
	0.3-3	3-Feb	3-Feb			
2 weeks (2 nd visit)	3	3	3	0.7	0.5	0.4
	3-Feb	3-Feb	3-Feb			
P	0.1	0.3	1			
4 weeks (3 rd visit)	3	2	3	0.4	0.8	0.6
	3-Jan	3-Feb	3-Feb			
P	0.4	0.04*	1			
6 weeks (4 th visit)	2	2	3	0.03	0.07	0.05
	0-3	2-Jan	3-Feb			
P	0.3	0.02*	1			
8 weeks (5 th visit)	2	1	3	0.01	0.2	0.05
	0-3	0-2	3-Feb			
(Range)						
P	0.2	0.02*	1			

SD: Standard deviation, AV: *Aloe vera***Table 7:** Average degree of change after treatment in Australian and Egyptian AV

Intervention change type	Egyptian AV n=7	Australian AV n=7	P
Size of ulceration in mm (Median)	70	60	0.6
Erythema (Mean)	128.7	93.7	0.09
Reticulation (Mean)	143.9	128.2	0.5
Total area of lesion (Mean)	345.2	285.8	0.2
Pain severity (Median)	1	0	0.5

AV: *Aloe vera*

visit, erythema was less in Australian AV (34.3 ± 17.0) compared to Egyptian one (60.0 ± 37.7). This decrease in erythema score may be explained by increase in concentration of the Australian group (90%) compared to the Egyptian group (70%).

Both types of AV show decrease in pain perception as compared to placebo. This result was in agreement with both Choonhakarn *et al.*^[7] and Salazar-Sanchez *et al.*^[12] studies who confirmed that the AV is more efficient than placebo in pain reduction. Choonhakarn *et al.*^[7] stated that the difference is statistically significant, while Salazar-Sanchez *et al.*^[12] stated that it is insignificant. Mansourian *et al.*^[13] and Reddy *et al.*^[14] demonstrated that AV and TA had comparable effect in the pain reduction with no statistically significant difference and both medications lead to significant reduction in pain.

The decreased pain perception with AV can be explained by decrease in the size of ulceration showed in both AV groups. Moreover, AV shows to breakdown bradykinin an inflammatory

substance that induced the pain.^[15] Regards to the pain there was decrease significantly in Australian AV after 4 weeks, while in Egyptian AV pain was decreased after 6 weeks. That is explained by that the pain is respond well to high concentration of AV.

Patients receiving AV gel reported burning and mild itching at the lesion within the 1st week, but symptoms spontaneously disappeared when patients continued to use the gel. No significant complaint was reported in placebo group.

Conclusion

AV gel whether Egyptian or Australian is statistically significantly more effective than placebo in inducing marked improvement clinically of OLP. Therefore, AV gel can be considered a safe alternative treatment for patients with OLP.

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How to cite this article: Ahmed SS, Gadalla LM, Elmeadawy SH, Badria F. The efficacy of *Aloe vera* gel in treatment of oral lichen planus. Int Dent Med J Adv Res 2018;4:1-6.

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