

A Comparative Study between Topically Applied Aloe Vera Gel and Injectable Dexamethasone in Patients with Ulcerative Oral Lesions

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Abstract: Background: Aloe Vera has been used as a natural medicine for centuries; it contains a gel that has multiple therapeutic and cosmetic applications. It can be used in acute and chronic ulcerative oral lesions, gingivitis and periodontal pockets and as denture adhesive. Aims of Study: the present study was designed to evaluate the effect of topical application of aloe Vera gel on various ulcerative oral lesions and to compare the use of aloe Vera gel with dexamethasone injection for the treatment of the ulcerative oral lesions. Materials and Methods: Eighteen patients complaining of various oral lesions were enrolled in this study. They were divided into 2 groups, one treated with dexamethasone intra-lesional injection, the other with topical Aloe Vera gel. Results: Aloe Vera gel showed highly significant difference regarding healing time, pain score and size of ulcerative area in comparison to dexamethasone injection on long term use. Conclusion: Aloe Vera gel can be used as adjuvant in treating different oral ulcerative lesions. It can be useful in reducing pain score, size of ulcer and healing time.

Keywords: Dexamethasone, Aloe Vera gel, oral ulcer, recurrent lesions, topical

1. Introduction

Aloe Vera has been used for thousands of years as a traditional medicine to induce wound healing. It is a natural remedy that made a revolution in cosmetic industry. Usually the plant's leaves contain gel rich in polysaccharides which carries a lot of benefits due to the gel's biological activities that include anti-aging, antifungal, anti-inflammatory, anticancer and immune-modulating activity.^[1]

Regarding ulcerative diseases, the majority of experience in the treatment of aphthous ulcers or lichen planus were based on steroids, which are very helpful in reducing pain and considered the first-line treatment. Unfortunately, they can cause various secondary effects and side effects, for example, candidiasis, sometimes bad taste, nausea, dry mouth, sore throat and/or swollen mouth. Other complications might include weight gain, osteoporosis and diabetes mellitus. Accordingly, the use of natural products in the prevention and treatment of oral conditions has increased recently and could be of benefit to low socioeconomic level people or to avoid the unfavourable side effects of using chemically prepared medicines^[2].

2. Uses of Aloe Vera in Dentistry

It has been shown that Acemannan which considered the active ingredient of the hydro gel accelerates the healing of aphthous ulcers and reduces the pain associated with them^[3].

A long list of uses can be reviewed, for instance, herpetic viral lesions, aphthous ulcers & cracks occurring at the corners of our lips. Studies showed that oral lesions of a patient with systemic involvement of lichen planus cleared up within 4 weeks after aloe Vera gel therapy. Also, Aloe Vera mouthwash is an effective alternative for Triamcinolone in the treatment of oral lichen planus^[4].

Aloe Vera gel reportedly has been used to treat gingivitis and gingival abscess and has been shown to reduce the depth of periodontal pockets. It's reported to be useful in treating Benign Pemphigus, Migratory glossitis, geographic tongue, halitosis and Burning Mouth Syndrome^[5,6].

Acemannan promotes dentin formation by stimulating primary human dental pulp cell proliferation, differentiation, extracellular matrix formation, and mineralization. Acemannan also has pulpal biocompatibility and promotes soft tissue organization^[7]. Researcher also claimed that Aloe Vera tooth gel and the toothpastes were equally effective against *C. albicans*, *Streptococcus mutans*, *Lactobacillus acidophilus*, *Enterococcus faecalis*, *Prevotella intermedia*, and *Peptostreptococcus anaerobius*. Aloe Vera tooth gel demonstrated enhanced antibacterial effect against *S. mitis*^[8]. Aloe Vera has found to be veridical to Herpes simplex virus type 1 and type 2, Varicella zoster virus, pseudo rabies virus and influenza virus.^[9]

The results of a scientific research done on extracted sockets showed that Salicept Patch (a freeze-dried pledget that contains Acemannan Hydro gel) significantly reduces the incidence of Alveolar Ostitis compared with clindamycin-soaked Gel foam^[10]. It can be used as a Denture adhesive because of the sticky and viscous nature of Acemannan. It was formulated into a denture adhesive and evaluated for adhesive strength in both wet and dry medium. It can be used by denture patients with sore ridges and ill-fitting dentures^[11]. It can be beneficial in Aspirin burns and dental implants^[12].

3. Materials and Methods

3.1 Materials

3.1.1 The sample

The study was performed in teaching hospital of Baghdad Dentistry College, department of oral medicine. 18 patients (10 females & 8 males) with ulcerative oral lesions (RAS, lichen planus and pemphigus vulgaris) were enrolled in the study. The Age range was between 40-45 years. The oral lesions diagnosed by history, clinical presentation and confirmed by biopsy.

3.1.2 Criteria of exclusion

Medically compromised patients, smokers, Alcohol consumers, pregnant women and patients taking medications during sample collection were excluded.

3.1.3 Instruments used

- Disposable gloves and cotton.
- Plane disposable sterilized mouth mirror
- Metal vernier to measure size of lesion
- Disposable syringes (3ml)
- Digital camera

3.1.4 Materials used

- Aloe Vera gel
- Dexamethasone injection (1ml)
- Liquid xylocaine

3.2 Methods

3.2.1 Method of aloe Vera gel preparation:

The method of gel extraction was self- created to be simple and keeps as much as organic constituents as possible without artificial additives. A fresh leaf of Aloe Vera plant washed by cold water and the skin is removed with a sharp knife. A clear gel will be exposed and can be scooped off with a spoon.

The gel will be collected in a clean glass jar and for every 1/4 cup of the gel we added a 500mg vitamin C (powder or crushed tablets) and 400mg of vitamin E to act as natural preservatives. By using a blender, the contents are mixed for (5-10 min) into homogenous consistency and preserved in the refrigerator.

3.2.2 Method of dexamethasone administration to the patient

By using gloved hands, reflection of the patient's lips and cheeks is done and a disposable 3ml syringe loaded with dexamethasone (4mg/ml to inject 0.1 cc/1 cm lesion) and 1ml of xylocaine is slowly inserted to the submucosal layer of the lesion.^[13]

The lesion size is measured before and after the injection and a photo was taken before and after to evaluate the

difference. The lesion will be examined for the following criteria:

- Healing time(days, weeks)
- The patient's pain score (visual analogue scale)
- The lesion diameter and its surroundings

3.3 Method of Aloe Vera gel application:

The prepared gel was applied thoroughly (2-3ml) over the lesion site using a disposable syringe without the needle^[14]. A sterile container of 50ml filled with the gel was given to the patient to apply at home 3times daily, to be followed after 3to 7 days later. The patient will be instructed not to eat or drink for a half an hour after application.

3.4 Statistical Analysis

The following statistical data analysis approaches were used in order to analyze and assess the results of the study under application of statistical package (SPSS) version (10.0):

3.4.1 Descriptive data analysis

- 1) Summary statistics, such that: mean of score (MS), standard deviation (SD), standard error (SE), 95% confidence interval for population mean value, and the two extreme values (minimum and maximum).
- 2) Frequency and percent.
- 3) Graphical presentation by: Bar Chart, and Simple High – Low – Close of Summaries Separate Plot.

3.4.2 Inferential data analysis:

These were used to accept or reject the statistical hypotheses, which included:

- 1) Test of Between-Subjects Effects for repeated of several periods of time.
- 2) Least significant difference (LSD) test for multiple comparisons.
- 3) Matched paired of two related sample t-test.
- 4) Two independent samples t-test.

For the abbreviations of the comparison significant (C.S.), used the followings:

NS: Non significant at P>0.05

S: Significant at P<0.05HS: Highly significant at P<0.01

4. Results

This part presents the findings of data analysis systematically in tables and these correspond with the objectives of this study, and as follows:

4.1 Distribution of Studied (GIV):

Table (1-1) shows distribution of studied "General Information" variables (GIV) included duration of healing at the studied two techniques with comparisons significant.

Table (1-1): Distribution of studied sample according to duration of healing of the studied two techniques with comparisons significant

GIV	Technique	Dexamethasone Injection		Technique	Aloe Vera Gel		C.S. (*) [P-value]
		No.	%		No.	%	
Duration (week)	4 w.	7	70	3.0 w.	5	62.5	t = 4.429 P=0.000 (HS)
	6 w.	3	30	3.5 w.	3	37.5	
	Total	10	100	Total	8	100	
	Mean ± SD	4.600 ± 0.966		Mean ± SD	3.188 ± 0.259		

Statistical Hypotheses based on t-test and Binomial tests.

The results indicated highly significant difference accounted at P<0.01 between duration of healing times (per weeks) in light of testing equality of mean values, which shows that "Aloe Vera Gel" technique reported short time of healing compared with "Dexamethasone Injection" technique.

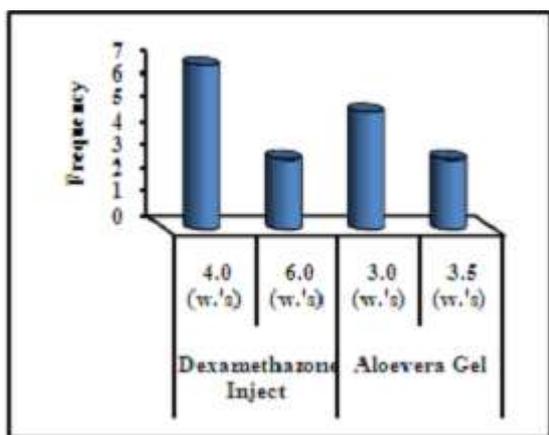


Figure (1-1): Graphical illustration distribution of different classes of studied.

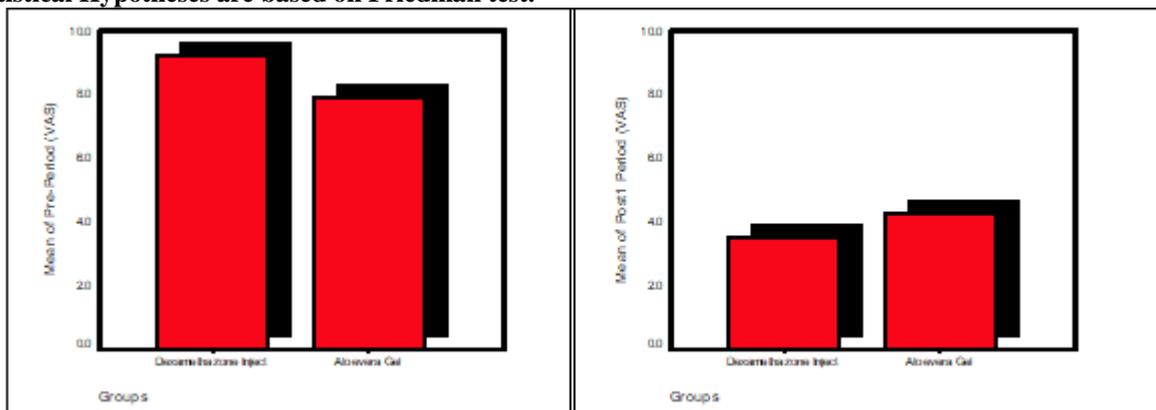
4.2 VAS concerning studied techniques along different periods of times:

Table (2-1) shows summary statistics (mean of score (MS), standard deviation (SD), and relative sufficiency's (RS %) concerning studied techniques along different periods of times. Results shows that in light of each technique highly significant difference of decays responding are accounted at P<0.01, while statistical test are reported no significant different at P>0.05 for each contrast of studied periods of different techniques.

Table (2-1): Summary statistics of VAS (visual analogue scale) concerning studied techniques along different periods of times with comparisons significant

Technique	Periods	No.	MS	SD	RS%	C.S. (*) [P-value]	
						F	t
Dexamethasone Inject	Pre	10	9.20	0.63	92	F=994.09 P=0.000 HS	Pre – Period t=1.979 P=0.082 (NS)
	Post1	10	3.50	0.97	35		Post1 – Period t=1.085 P=0.294 (NS)
	Post2	10	0.80	0.92	8		
Aloe Vera Gel	Pre	8	7.25	1.83	72.5	F=72.1 P=0.000 HS	Pre – Period t=1.085 P=0.294 (NS)
	Post1	8	4.25	1.91	42.5		Post2 – Period t=0.675 P=0.509 (NS)
	Post2	8	1.13	1.13	11.3		

The Statistical Hypotheses are based on Friedman test.



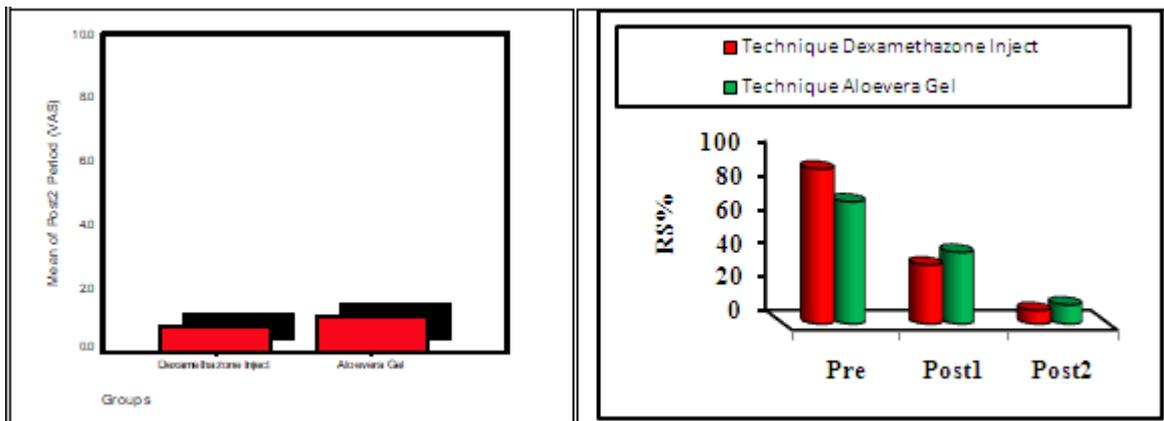


Figure (3-1): Bar charts of VAS Relative Sufficiency's Mean of Score for studied Techniques of different periods of times

Finally, simple high – low – close of summaries plot are used through applying VAS score to create a chart summary that separates high and low (and optional close) variables within categories of another variable (two different techniques), which indicates that treatment with "Aloe Vera Gel" recorded partial improvement along periods pre to post-1 in contrast of "Dexamethasone Injection" technique, while the result shows reversed behavior, since "Dexamethasone Injection" recorded partial improvement along periods post-1 to post-2 in contrast of "Aloe Vera Gel" technique.

Size of the most Ulcerative Area:

Table (3-1) represents summary statistics of studied size of the most ulcerative area concerning (Dexamethasone Injection and Aloe Vera Gel) techniques used, such as mean of score, standard deviation, standard error, 95% confidence interval for population mean value, and two extreme values (minimum and maximum) readings.

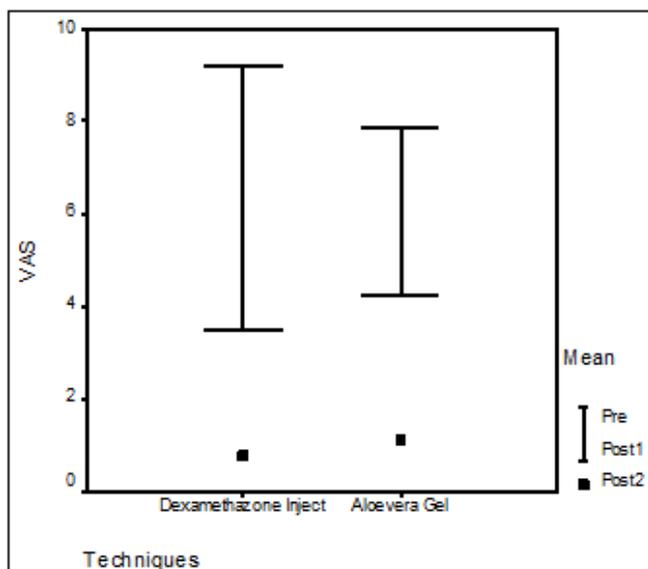


Figure (4-1): illustrated graphically simple high – low – close of summaries separate plot

Table (3-1): Summary Statistics of the studied readings of (Dexamethasone Injection and Aloe Vera Gel) techniques at different periods of times

Technique	Periods	No.	MS	S.D.	S.E.	95% Confidence Interval for Mean		Min.	Max.
						L.B.	U.B.		
Dexamethasone Injection	(Before)	10	4.00	0.78	0.25	3.44	4.56	3.0	5.0
	(After)	10	1.35	0.58	0.18	0.94	1.76	0.5	2.0
Aloe Vera Gel	(Before)	8	1.388	0.65	0.23	0.847	1.928	0.3	2.0
	(After)	8	0.275	0.23	0.08	0.087	0.463	0.0	0.5

Mean values shows that high gaps of improvement accounted throughout different periods of time. Figures (5-1) represents chart containing two lines. Each line connects a

series of points, one for each category, case or variable on the category axis.

The area between two lines indicates the actual difference between effectiveness of the studied techniques, which shows that rather than "Dexamethasone Injection" technique had high gaps occurred in the light of the other technique, but "Aloe Vera Gel" technique recorded improvement area and had completely degenerated of the size of the most ulcerative area, that decayed within "Dexamethasone Injection" technique.

Table (4-1) represents summary statistics of differences in light of before and after treatment by (Dexamethasone Injection and Aloe Vera Gel) techniques, as well as comparison significant accounted throughout matched paired t-test for each group, and two independent samples t-test for comparison significant between the studied groups in light of differences of responding before and after the application of the two studied treatments.

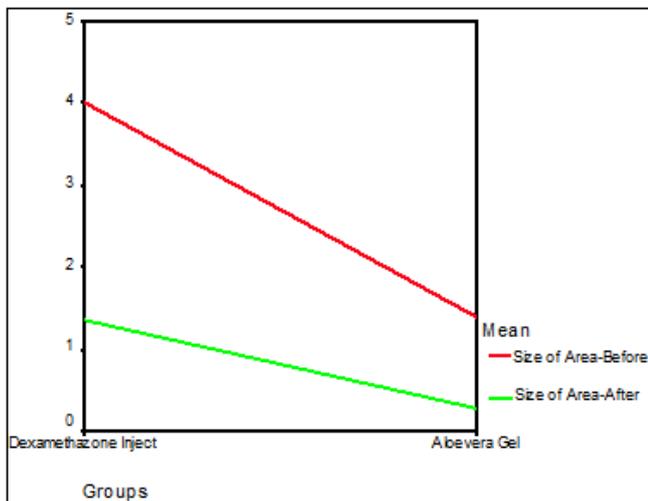


Figure (5-1): Stem-Leaf & Bar chart plots for studied readings of Dexamethasone Injection and Aloe Vera Gel techniques in two different periods

Table (4-1): Statistics of treated by (Dexamethasone Injection and Aloe Vera Gel) techniques with comparisons significant

Technique	Periods	Mean of Diff.	M.P. t-test	d.f.	Sig. ^(*) (2-tailed)	C.S. P-value
Dexamethasone Injection	Before	2.650	17.667	9	0.000	t=6.865
	After					
Aloe Vera Gel	Before	1.112	6.690	7	0.000	HS
	After					

The Statistical Hypotheses Are Based on Matched Paired t-test, and two independent samples t-test.

ulcer area, while relative subjects of "Dexamethasone Injection" technique needs what the other technique content.

Results show that subject's treated by (Dexamethasone Injection) technique, reported highly decreasing level at the post period, and statistically reported high significant difference at $P < 0.01$, which indicated that treatment by (Dexamethasone Injection) technique had a meaningful effectiveness on studied sample. In addition to that, result shows that subject's treated by (Aloe Vera Gel) technique, reported highly decreasing level at the post period, and statistically reported high significant difference at $P < 0.01$, which indicated that treatment by (Aloe Vera Gel) technique had a meaningful effectiveness on studied sample.

Finally, simple high – low – close of summaries separate plot are used through applying VAS score to create a chart summarizing separate high and low (and optional close) variables within categories of another variable (two different techniques), which indicate that treatment with "Aloe Vera Gel" recorded high degree of improvement along periods pre to post in contrast of "Dexamethasone Injection" technique, besides results showed high gaps occurred in the light of the last technique between the studied periods, since "Aloe Vera Gel" technique recorded a complement improvement along degeneration of the size of the most

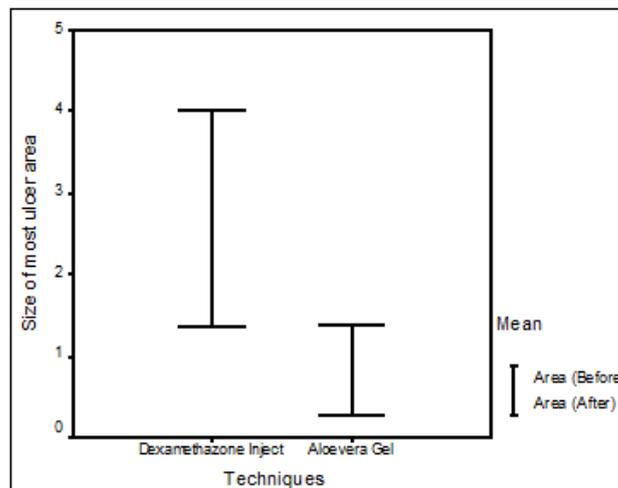


Figure (6-1): illustrated graphically simple high – low – close of summaries separate plot.

DISCUSSION

The natural phytochemicals isolated from medicinal plants used in traditional medicine have been considered useful alternatives to synthetic drugs. Many medicinal plants and

their products are widely used for prevention and treatment of oral infections and among them Aloe Vera which is of particular interest and has been used therapeutically for a long time^[15].

In 2012, Keenan A. used dexamethasone ointment on oral aphthous ulcers to observe that helped in reducing pain, ulcer size and shortened healing time^[16].

Aloe Vera oral gel is not only effective in decreasing the recurrent aphthous stomatitis patient's pain score and wound size but also decreases the aphthous wound healing period. Acute mouth lesions are improved by direct application in gel form on herpetic viral lesions or aphthous ulcers.

Acemannan, which is one of the polysaccharide components in Aloe Vera, has been used for the treatment of oral aphthous ulceration in patients who wish to avoid the use of steroid medication. It has been reported that Acemannan hydrogel accelerates healing of aphthous ulcers and reduces the pain associated with them.

United States Food and Drug Administration have also found a derivative of Aloe Vera an effective treatment alternative in treating oral ulcers^[17]. It was explained by increased blood supply and oxygenation, which stimulates fibroblast activity and collagen proliferation. In addition to Aloe vitamins content and folic acid^[18].

Aloe Vera has proved to have an anti-inflammatory effect. It contains carboxypeptidase which inactivates bradykinin and has anti prostaglandin synthesis properties. AV known to inhibit histamine formation in mast cells. It decreases number and prevent migration of PMNL^[19].

The decrease in general pain may be attributed to the analgesic effect of aloe Vera, as it contains anthraquinones, these are chemical compounds used to arrest pain and heal wounds. Whereas, the evident decrease in ulceration or mucositis levels could be attributed to its antibacterial constitute called propolis, giving a cell-stimulation effect^[20].

Aloe Vera also used to treat lichen planus. The topical application of AV, three times a day improved pain, severity of oral lesions, and the oral quality of life of the patients with OLP.

Many studies performed to determine the efficacy of topical and injectable steroids on oral lesions over years. As steroids remained the mainstay treatment modality in case of lichen planus for long time; however, long term steroids therapy is associated with multiple systemic complications which provide Aloe Vera with an added advantage due its fewer side effects. Also, when compared with triamcinolone, better results were obtained with topical Aloe Vera application^[21,22].

The current study concluded that Aloe vera gel can be a safer, more effective on longer term basis, easier to use and certainly a cheaper alternative to steroid therapy regarding different ulcerative oral lesions.

N.B. 1. This study is considered to be the first in Iraq that intended to use Aloe Vera gel in treating oral diseases.

2. FDA first approved aloe Vera ointment as an over the counter medication for skin burns. Otherwise, it's only approved as natural food flavouring.

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