**A Comparative Study between topically applied Aloe Vera Gel and injectable Dexamethasone in Patients with Ulcerative Oral Lesions**

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خلاصه:نبات الصبار(الألوفيرا)أستخدم منذ قرون في الأستشفاء طبيعيا,كونه يحتوي على هلام له خواص علاجيه وتجميليه عديده.من الممكن أستخدامه في علاج التقرحات الفمويه الحاده والمزمنه،امراض اللثه وما حول الأسنان ومثبت للأطقم.

**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 oral lesions were enrolled in this study (6 males and 12 females). 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 comparision to dexamethasone injection on long term use.**

**CONCLUSION: Aloe vera gel can be effective as adjuvant in treatment of different oral ulcerative lesions.it proved to reduce pain score, size of ulcer and healing time.**

**KEYWORDS: Dexamethasone, Aloe Vera gel, oral ulcerative lesions**

**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 ifcomes in leaves that contain a gel rich in polysaccharides which give it a lot of benefits.

Biological activities include anti-aging,antifungal activity, anti-inflammatory, anticancer and immune-modulator.**[1]**

The majority of experience in the treatment of aphthus ulcers or lichen planus based on steroids, which are very helpful in reducing pain and considered the first-line treatment. But they cause secondary candidiasis, and sometimes bad taste, nausea, dry mouth, sore throat or swollen mouth. Other complications might include weight gain, osteoporosis and diabetes mellitus.accordingly, theuse of natural products in the prevention and treatment of oral conditions has increased recently and could be of benefit to low socioeconomic levelpeopleor to avoid the unfavourable side effects of using chemically prepared medicines.[2]

**USES OF ALOE VERA IN DENTISTRY**

1. Acute mouth lesions such as herpetic viral lesions, aphthous ulcers & cracks occurring at the corners of our lips.Studies showed that acemannan hydro gel accelerates the healing of aphthous ulcers and reduces the pain associated with them. **[3]**
2. Oral lesions of a patient with systemic involvement of lichen planescleared 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]**
3. Aloe Vera gel reportedly has been used to treat gingivitis and gingival abcess and has beenshownto reduce the depth ofperiodontal pockets. **[5,6]**

**4)** Acemannan promotes dentin formation by stimulating primaryhuman dental pulp cell proliferation, differentiation, extracellular matrix formation, and mineralization. Acemannan also has pulpal biocompatibility and promotes soft tissue organization. **[7]**

**5) Bacteria and viruses**

Results showed 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 is veridical to Herpes simplex virus type 1 and type 2, Varicella zoster virus, pseudo rabies virus and influenza virus.[**9]**

**6. Extracted socket**

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**]

**7. 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]**

**8.**Chronic oral diseases such as Lichen Planus and Benign Pemphigus, gingival problems associated with AIDS and Leukemia.Migratory glossititis, geographic tongue, halitosis and Burning Mouth Syndrome.

**9.**Aspirin burns and dental implants.**[12]**

**MATERIALS AND METHODS**:

1. **Materials:**

**1.1 The sample:**

The study was performed in teaching hospital of Dentistry College, department of oral medicine.18 patients with ulcerative oral lesions were enrolled in the study. The Age range is between 20-50 years.

The oral lesion will be diagnosed by history, clinical presentation and confirmed by biopsy.

**1.2 Criteria of exclusion:**

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

**1.3 Instruments used:**

- Disposable gloves and cotton.

-plane disposable sterilized mouth mirror

-metal vernia to measure size of lesion

-disposable syringes (3ml)

-digital camera

**1.4Materials used:**

-Aloe Vera gel

-Dexamethasone injection(1ml)

- Liquid xylocaine

**2. Methods:**

**2.1 Method of aloe Vera gel preparation:**

A fresh leaf of Aloe Vera plant washed by cold water and the skin is removed with 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 a 500mg vitamin C (powder or crushed tablets) and 400mg of vitamin E to act as natural preservatives. Using a blender the contents are mixed for (5-10 mins) into homogenous consistency and preserved in the refrigerator.

**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 0.5-1ml of dexamethasone and 1ml of xylocaine is slowly inserted in the site of the lesion.

The lesion size is measured before and after the injection a picture is 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
  1. **method of aloe Vera gel application:**

The prepared gel is applied thoroughly over the lesion site using a disposable syringe without the needle. The gel is 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.

**1.4 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):**

1. **Descriptive data analysis:**
2. **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).**
3. **Frequency and percent.**
4. **Graphical presentation by: Bar Chart, and Simple High – Low – Close of Summaries Separate Plot.**
5. **Inferential data analysis:**

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

1. **Test of Between-Subjects Effectsfor 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**

**RESULTS**

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

1. **Distribution of Studied (GIV):**

**Table (1-1) shows distribution of studied "General Information" variables (GIV), such as gender and duration of healing at the studied two techniques with comparisons significant.**

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

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **GIV** | **Technique** | **Dexamethazone**  **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** | |
| **Gender** | **Male** | **3** | **30** | **P=0.344**  **(NS)** | **3** | **37.5** | **P=0.727**  **(NS)** |
| **Female** | **7** | **70** | **5** | **62.5** |

**Statistical Hypothesesbased on t-test and Binomial tests.**

**The results indicated that there were no significant differences at P>0.05 among studied (GIV) concerning gender, and this is reliable for this study indeed, since any deviation possibly will accounted could be interpreted to actual differences concerning treatment's techniques, while 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 " Dexamethazone Injection" technique.**

|  |  |
| --- | --- |
|  |  |

**Figure (1-1) illustrated graphically distribution of different classes of studied (GIV).**

1. **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]** | |
| **Dexamethazone**  **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 – Period**  **t=1.085**  **P=0.294 (NS)**  **Post2 – Period**  **t=0.675**  **P=0.509 (NS)** |
| **Post1** | **10** | **3.50** | **0.97** | **35** |
| **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** |
| **Post1** | **8** | **4.25** | **1.91** | **42.5** |
| **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 "Dexamethazone Injection" technique, while the result shows reversed behavior, since "Dexamethazone Injection" recorded partial improvement along periods post-1 to post-2 in contrast of "Aloe Vera Gel" technique.**



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

1. **Size of the most Ulcerative Area:**

**Table (3-1) represents summary statistics of studied size of the most ulcerative area concerning (Dexamethazone Injectionand 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.**

**Table (3-1): Summary Statistics of the studied readings of (Dexamethazone 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.** |
| **Dexamethazone**  **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 improvementaccounted 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 "Dexamethazone 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 "Dexamethazone Injection" technique.**



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

**Table (4-1) represents summary statistics of differences in light of before and after treatment by (Dexamethazone 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.**

**Table (4-1): Statistics of treated by (Dexamethazone 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** |
| **Dexamethazone Injection** | **Before** | **2.650** | **17.667** | **9** | **0.000**  **HS** | **t=6.865**  **P=0.000**  **HS** |
| **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**.

**Results shows that subject's treated by (Dexamethazone 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 (Dexamethazone 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 "Dexamethazone 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 ulcer area, while relative subjects of "Dexamethazone Injection" technique needs what the other technique content.**



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

**DISCUSSION**

The natural phytochemicals isolated from medicinal plantsused in traditional medicine have been considered usefulalternatives to synthetic drugs. Many medicinal plantsand their products are widely used for prevention andtreatment of oral infections and among them AloeVera is of particular interest and has been used therapeuticallyfor a long time.[13]

In 2012, Keenan A. used dexamethasone ointment on oral aphthus ulcers to observe that it helped in reducing pain, ulcer size and shortened healing time.[14]

Aloe Vera oral gel is not only effective in decreasing the recurrent apthous stomatitis patient’s pain score and wound size but also decreases the apthous wound healing period. Acute mouth lesions are improved by directapplication in gel form on herpetic viral lesions or aphthous ulcers. It has been reported that acemannan hydrogel accelerates the healing of aphthous ulcers and reduces the pain associated with them.

Acemannan, which is one of the polysaccharide components in Aloe Vera, has been used for the treatment of oral apthous ulceration in patients who wish to avoid the use of steroid medication.

United states Food and Drug Administration have also found a derivative of Aloe Vera an effective treatment alternative in treating oral ulcers.[15]

It was explained by increased blood supply and oxigination, which stimulates fibroblast activity and collagen proliferation.in addition to Aloe vitamins content and folic acid.[16]

Aloe Vera has proved to have 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.[17]

The decrease in general pain may be attributed to theanalgesic effect of aloe Vera, as it contains anthraquinnons, these are chemical compounds used to arrest pain and heal wounds.Whereas, the evident decrease in ulceration or mucositislevels could be attributed to its antibacterial constitute called propolis, giving a cell-stimulationeffect.[18]

Aloe Vera has also been used to treat lichen planus. The topical application of AV, three times a day improves the pain, the severity of the 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.

Steroids have remained the mainstay treatment modality in case of lichen planus; however, longterm steroids therapy is associated with multiple systemic complications which provide Aloe Verawith an added advantage due its lesser side effects. Also, when compared with triamcinolone better results were obtained with topical Aloe vera.[19,20]

**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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