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RESEARCH ARTICLE
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EVALUATING THE EFFICACY OF ALOE VERA GEL VERSUS 5% AMLEXANOX ORAL PASTE IN TREATING MINOR RECURRENT APHTHOUS ULCERS: A RANDOMIZED CLINICAL STUDY

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ABSTRACT
Recurrent aphthous stomatitis/ulceration (RAS) remains one of the most common inflammatory ulcerative conditions affecting the oral mucosa, yet its etiology is still not fully understood. Various systemic and local factors have been proposed as potential contributors to RAS, but due to its complex origins, no definitive treatment exists. Current therapeutic approaches primarily aim to improve the quality of life by alleviating symptoms, speeding up healing, and preventing the recurrence of ulcers. Based on this framework, a study was designed to evaluate and compare the efficacy of Amlexanox oral paste and Aloe vera gel in managing mild RAS. The study enrolled 50 patients with mild recurrent aphthous ulcers, randomly divided into two groups: Group A (Aloe vera gel, 25 patients) and Group B (Amlexanox oral paste, 25 patients). Baseline measurements of erythema, pain, and ulcer size were recorded on the first visit, with follow-up assessments conducted on days three and seven to evaluate changes in ulcer size, pain, and erythema. Additionally, the rate of ulcer recurrence was monitored monthly over six months. The results revealed significant improvements in ulcer size, pain, and erythema in both groups from baseline to day three, baseline to day seven, and from day three to day seven. Both treatment options demonstrated efficacy in reducing ulcer size, pain, and erythema, with Aloe vera gel showing promise due to its unique properties in managing various oral conditions. The study concluded that both Aloe vera and Amlexanox were effective in treating recurrent aphthous stomatitis (RAS), significantly reducing ulcer size, pain, and erythema.

KEY WORDS: Aloe Vera, Amlexanox, Oral Ulcer, Recurrent Apthous Stomatitis

INTRODUCTION

"Recurrent aphthous ulcer (RAU), commonly known as canker sores, is a condition characterized by recurring, painful ulcers confined to the oral mucosa in individuals who exhibit no other signs of systemic disease. It is one of the most prevalent and painful oral mucosal inflammatory conditions, often causing significant discomfort during eating, swallowing, and speaking. The term 'aphthos' is derived from the Greek word 'aphtha,' meaning ulceration[1].

RAU is among the least understood oral diseases, presenting a challenge both to those affected and to clinicians[2,3]. The pathophysiology of aphthous ulcers remains poorly understood, and the incidence in the general population ranges from 5% to 50%. Approximately 80% of patients develop RAU before the age of 30, with the onset typically beginning around age 5 and peaking between ages 10 and 19. Potential triggers for RAU include genetic predisposition, viral and bacterial infections, food allergies, deficiencies in vitamins and microelements, systemic diseases, increased oxidative stress, hormonal changes, menstrual cycles, mechanical injuries, and psychological stress. Recently, immunological factors have gained attention as significant contributors to RAU.

Clinically, RAU can be classified into three main types: minor aphthae, major aphthae, and recurrent herpetiform ulcers. Various treatment options are available, including systemic therapies, topical agents, physical therapies, and laser therapy[4,5]. Immunomodulatory agents such as Thalidomide, Pentoxifylline, Colchicine, and Etanercept have been used to manage RAU over extended periods. However, topical agents are often the first choice for managing RAU due to their cost-effectiveness, safety, and accessibility.

Amlexanox ($C_{16}H_{14}N_2O_4$) is one of the most extensively studied topical treatments for RAU[5]. It possesses anti-inflammatory and anti-allergic properties, inhibiting the formation and release of histamine and leukotrienes from mast cells, neutrophils, and mononuclear cells.

In recent years, natural herbal medicines have also gained popularity as alternative therapies for RAU, with Aloe Vera (Aloe Barbadensis Miller) being a notable example[6]. A member of the Liliaceous family, Aloe Vera has been revered for centuries, even called the 'Plant of Immortality' by the ancient Egyptians for its ability to survive and thrive without soil. The transparent gel derived from Aloe Vera leaves contains over 75 active constituents, including vitamins, enzymes, minerals, sugars, lignin, saponins, salicylic acid, and amino acids. These components contribute to Aloe Vera's immunomodulatory, anti-inflammatory, wound-healing, antioxidant, anti-diabetic, and anti-neoplastic properties, making it a valuable treatment option for RAU." These characteristics prompt the researchers to employ it in the treatment of mild RAS. Due to the ongoing research into the efficacy and recurrence rate of aloe vera, there are limited studies available in the literature regarding its novelty[7]. Thus, the goal of the current study is to evaluate and compare how well Aloe Vera gel and 5% Amlexanox oral paste work to treat mild RAS.

AIM & OBJECTIVES

1. To assess Aloe Vera gel's effectiveness in treating mild RAS.
2. To assess the effectiveness of Amlexanox paste at 5% in the management of mild RAS.
3. To compare the effectiveness of 5% Amlexanox oral paste versus Aloe Vera gel in the management of mild RAS.

MATERIAL AND METHODS

40 patients with small recurrent aphthous ulcers who visit the department of Oral Medicine and Radiology department in Shree Bankey Bihari Dental College & Research Centre, Ghaziabad are part of a randomized clinical trial.

Inclusion criteria- Patients with ages ranging from eighteen to fifty, Presenting for less than 48 hours with one or more mild RAS, Ulcers should be located in areas including the floor of the tongue, buccal mucosa, and labial mucosa that are easily accessible for assessment and treatment.

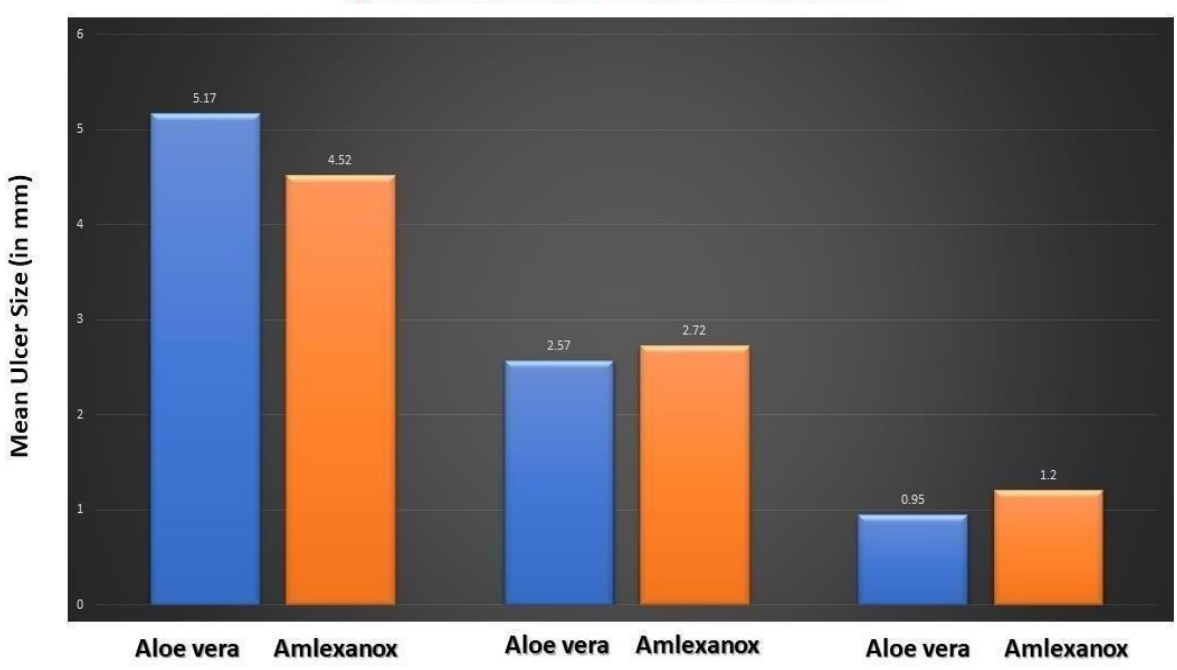
Exclusion criteria - Lactation & pregnancy, Past history of Amlexanox & Aloe Vera allergies , Individuals on systemic antibiotics, immune modulating medications, or NSAIDs, Individuals using any other oral topical drug, those who suffer from bleeding issues, Individuals using corticosteroids.

Patient selection- The study included patients with mild RAS who came to the outpatient department of Shree Bankey Bihari Dental College & Research Centre, Ghaziabad. The particular inclusion and exclusion criteria were followed in the selection of the patients. Patients were informed about the entire study procedure beforehand, and their informed consent was acquired. The institutional ethical board granted the ethical clearance.

STATISTICAL ANALYSIS

A paired t-test was used to assess, within each group, the mean decrease in lesion diameter and rise in inflammation diameter at various follow-up intervals relative to baseline was compared using Mann-Whitney U test and Wilcoxon post Hoc analysis . The mean differences shown with their 95% confidence interval and p-value. P values less than 0.05 are deemed statistically significant. The statistical analysis was conducted using IBM SPSS statistical software, version 21.

RESULTS

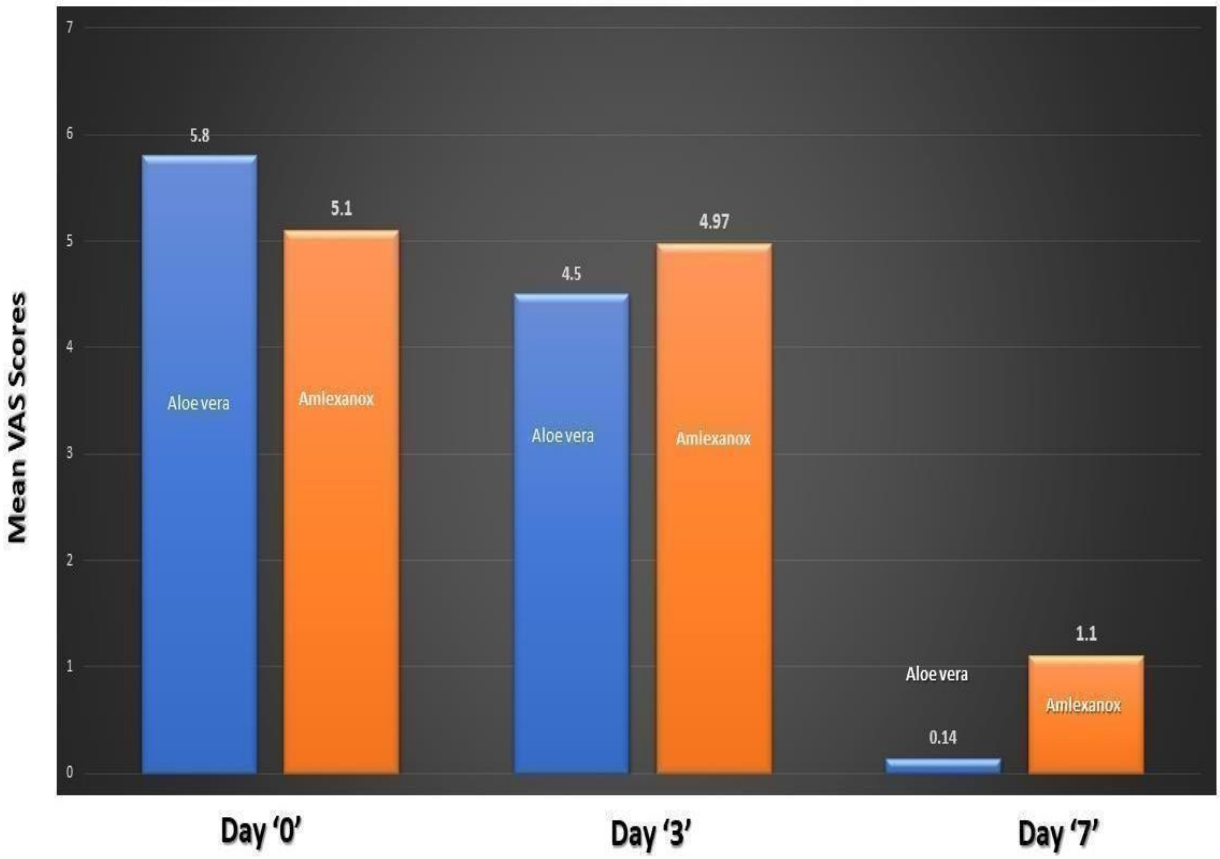


Graph-1 : Comparison of mean ulceration size at different time interval.

At baseline, the mean ulcer size for patients in group A was 5.17±2.94, whereas group B had 4.52±2.80. On day three and day seven, patients were recalled and it was observed that Group A had an average ulcer size of 2.57 ± 1.26 on day 3, while Group B had an average ulcer size of 2.72 ± 1.46. Group A and Group B had mean ulcer sizes of 0.95 ± 083 and 1.20 ± 0.84, respectively, on day seven. The results indicated a substantial decrease in ulcer size in both Group A and Group B on day 3 (2.57 ± 1.26 and 2.72 ± 1.46, respectively) and day 7 (0.95 ± 083 and 1.20 ± 0.84), relative to their respective baseline values of 5.17 ± 2.94 and 4.52 ± 2.80) Statistically on third day comparison between Group A and Group B (Graph-1) was identified as non-significant(P=0.68). whereas on the

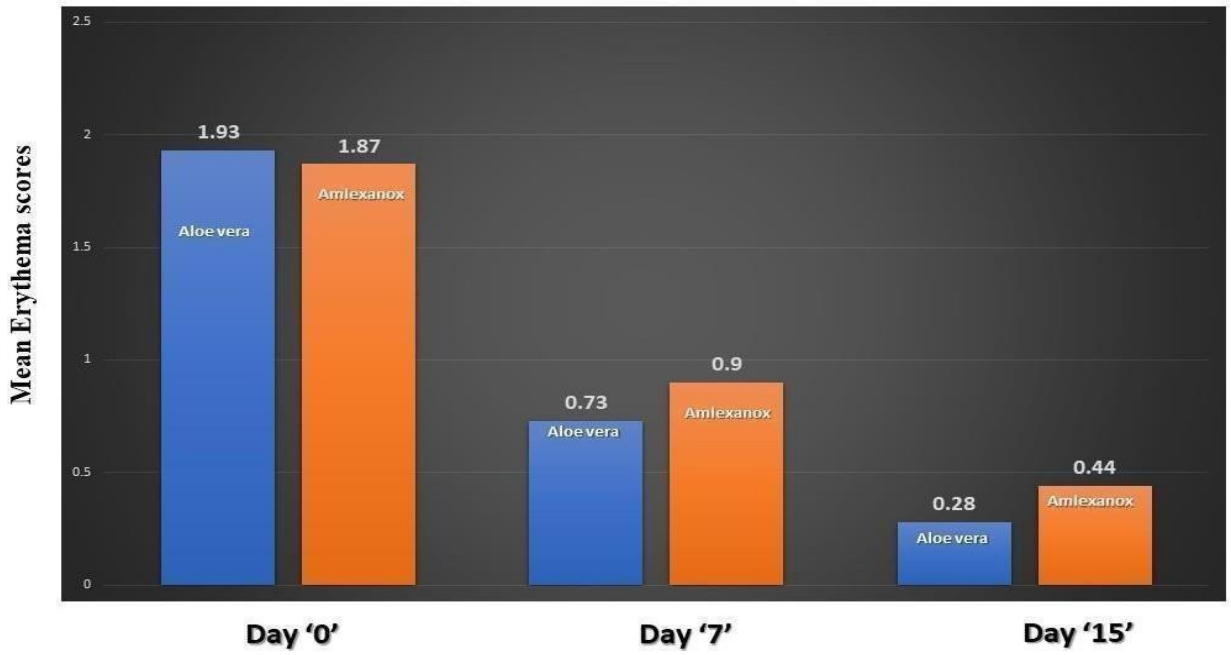
seventh day, a distinction between Group A and Group B was identified as highly statistically significant (P=0.001).
At baseline, the average pain score for Group A patients was 5.80 ± 1.87, whereas Group B patients had a mean pain score of 5.10 ± 11.05. On day three, Group A and Group B recorded mean pain scores of 4.50 ± 1.31 and 4.97 ± 1.44, respectively.

Group A and Group B recorded pain scores of 0.14±0.74 and 1.10±0.54, respectively, on day seven. The data indicate a significant decrease in pain levels in both Group A and Group B from their respective baselines (5.80 ± 1.87 and 5.10 ± 1.05) on day three (4.50 ± 1.31 and 4.97 ± 1.44) and day seven (0.14 ± 0.74 and 1.10 ± 0.54)Statistically on third day comparison between Group A and Group B (graph-2) was identified as non- significant(P=0.44). whereas on the seventh day, a distinction between Group A and Group B was identified as highly statistically significant (P=0.001).



Graph-2 : Comparison of mean VAS score at different time interval.

Whereas, mean erythema score of 1.93 ± 0.56 was recorded for Group A at the beginning of the study, while the mean value for Group B was 1.87 ± 0.41. During the third day, the average erythema scores for Group A was 0.73±0.66 and for Group B, it was 0.90±0.71. Group A had a mean erythema score of 0.28 ± 0.38 on day 7, while Group B had a mean score of 0.44 ± 0.48 after the same number of days. Based on the baseline values of 1.93 ± 0.56 and 1.87 ± 0.41, the results indicate a moderate decrease in erythema in both Group A and Group B on day 3 (0.73 ± 0.66 and 0.90 ± 0.71) respectively, as well as on day 7 (0.28 ± 0.38 and 0.44 ± 0.48) respectively. On day third comparing the erythema in Group A and Group B there was no statistically significant(P=0.33). When comparing Group A and Group B (Graph-3) in terms of erythema decrease on the third and seventh day, there was no statistically significant difference found between the two groups.



Graph-3: Comparison of mean erythema scores at different time interval.

DISCUSSION

The primary goals of treating recurrent aphthous stomatitis (RAS) are to restore normal oral function, reduce the size and duration of ulcers, and alleviate pain. Secondary objectives include maintaining remission and minimizing the frequency and severity of recurrences[8]. Among the most studied topical treatments for RAS is Amlexanox (C16H14N2O4), known for its anti-inflammatory and anti-allergic properties, which inhibit the production and release of histamine and leukotrienes from mast cells, neutrophils, and mononuclear cells[9]. Aloe vera, another therapeutic agent for mild RAS, contains a clear gel rich in naturally occurring compounds with immunomodulatory, anti-inflammatory, wound-healing, antioxidant, anti-diabetic, and anti-neoplastic properties[10].

In a study comparing these two treatments, significant improvements in ***Ulcer Size*** were observed in both the Amlexanox and Aloe vera groups between baseline and day three, baseline and day seven, and day three and day seven. This aligns with research by Babaee et al (2012)[10], which found Aloe vera gel effective in reducing ulcer size. By day seven, a substantial difference was noted in ulcer size reduction between the Amlexanox and Aloe vera groups ($P = 0.001$). Aloe vera's effectiveness is attributed to its bioactive compounds, such as gibberellin, a growth hormone, and glucomannan, a polysaccharide, which interact with fibroblast growth factor receptors to enhance collagen synthesis[11,12].

Pain reduction, as measured by Visual Analog Scale (VAS) scores, also showed significant improvement in both groups from baseline to day three, baseline to day seven, and day three to day seven. Notably, Aloe vera gel demonstrated a greater impact on pain reduction by day seven compared to Amlexanox ($P = 0.001$). This supports the findings of Babaee et al. (2012)[10], which highlighted Aloe vera's efficacy in relieving ulcer pain. The pain-relieving properties of Aloe vera are linked to its ability to reduce prostaglandin E2 production from arachidonic acid and inhibit the cyclooxygenase pathway. Additionally, a new anti-inflammatory compound, C-glucosyl chromone, has been isolated from Aloe vera gel, further contributing to pain relief[13].

Although both Amlexanox and Aloe vera showed noticeable improvements in erythema associated with RAS between baseline and subsequent assessments (day three, day seven), there were no statistically significant differences between the groups in erythema reduction at any of the follow-up visits ($P = 0.59$, $P = 0.30$, and $P = 0.14$, respectively). This suggests that Amlexanox is equally effective as Aloe vera in reducing erythema, consistent with the findings of Katti et al (2011)[14].

CONCLUSION

Recurrent aphthous stomatitis is a common and painful inflammatory condition of the oral mucosa, often making it challenging to eat, swallow, and speak. This disorder can significantly impact quality of life and general well-being. Due to its unclear etiology and various treatment options, it has attracted considerable clinical and academic interest. This comparative study demonstrates that both Aloe Vera gel and 5% Amlexanox oral paste are effective in treating mild RAS, leading to a reduction in ulcer size, discomfort, and erythema within seven days, as well as a decrease in recurrence**.**

FUTURE RECOMMENDATIONS

To better understand the role of Aloe Vera gel in managing and preventing the recurrence of RAS, future research should involve larger sample sizes and longer-term randomized controlled trials. Further studies are essential to fully elucidate the multiple mechanisms of action, safety, and efficacy of Aloe Vera gel, aiming to optimize its therapeutic benefits. Additionally, exploring the potential use of systemic Aloe Vera in RAS treatment is warranted, particularly given the systemic concerns associated with immunomodulators.

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