

Analyzing Efficacy of AMLEXANOX in Treatment of Recurrent Oral Aphthosis

Sanjeev Laller¹, Mamta Malik^{2,*}, Ravinder S Saini³, Divya Vardaini⁴, Meenakshi Sharma⁵, Anjali Ahlawat⁶

^{1,2}Reader, ^{5,6}Tutor, Dept. of Oral Medicine & Radiology, PDM Dental College & Research Institute, Haryana, ³Prosthodontics, Dept. of Dental Technology, COAMS, KKU, Saudi Arabia, ⁴PG Student, Dept. of Pharmacology, Santosh Medical College, Uttar Pradesh

***Corresponding Author:**

Email: mamta_laller@yahoo.com

Abstract

Background: Recurrent aphthous stomatitis (RAS) is a multifactorial disorder which is common in 20% of society characterized by recurrent oral ulcer in person who does not have other sign of sickness. The aim this study was to evaluate and compare efficacy of anti-inflammatory agent amlexanox and topical anesthetic agent in reducing ulcer size and pain.

Materials and Methods: The effectiveness of healing ulcer measured using two parameters, which are the ulcer size and pain score. Thirty patients (n = 30) with minor recurrent aphthous stomatitis were selected for the study, with no known medical illness. Subjects were divided into two groups. Study group (Group-A) received Amlexanox (5%) and the other control group (Group-B) received topical anesthetic agent. The subjects were required to apply the medication 4 times per day. Ulcer size and pain were been measured on treatment days 1 and 4. Data were analyzed using t test for independent sample.

Results: Significant reduction in ulcer size and pain was noticed in study group (Group-A) as compared to control group (Group-B).

Conclusion: Amlexanox can reduce the ulcer size and pain associated with the aphthous ulcers with no side effects of the drug.

Keywords: Recurrent aphthous stomatitis (RAS), Oral Aphthosis, Amlexanox, Visual Analogue Scale (VAS).

Introduction

The first clinical description of RAS was given by Mikulicz and Kummel in 1888. It is defined as a disorder with recurrent oral ulceration in an individual who does not have any other sign of illness. It affects almost 20% of the society. The etiology is multifactorial but local trauma, stress, immunodeficiency, zinc deficiency and hormonal changes, with suspected bacteria and viruses may play a pivotal role in pathogenesis of RAS. Oral aphthosis is described by recurrent, painful ulcers that are small, round to ovoid and affects non keratinized oral mucosa, commonly buccal and labial mucosa, tongue, floor of mouth and soft palate. The clinical presentation of ulcer is central grey white pseudomembrane surrounded by red halo. Aphthous ulcers can be classified into minor, major and herpetic form.^{1,2,3}

As the etiology is not well known, no curative definitive therapy is available presently. The mainstay of treatment is to relieve symptoms and accelerate healing. Most systemic agents are highly effective but have side effects that limit their general use. Thus topical agents remain the first choice for treatment of recurrent oral aphthosis.⁴

Amlexanox is a topical anti-inflammatory, anti-allergic drug used as 5% topical oral paste, chemically proven and approved by US FDA for treatment of aphthous ulcers. Anti-inflammatory and anti-allergic action of this drug is because it potentially inhibits the formation and release of histamine and leukotrienes from mast cells.⁵

The present study was conducted with the aim to evaluate the efficacy of amlexanox in resolving pain

and decreasing ulcer size, as compared to topical anesthetic agent as placebo.

Materials and Methods

A total of 50 patients with minor aphthous ulcer were enrolled for study from outpatient department of oral medicine and radiology. Study sample comprises of College students of BDS and MDS with age ranging from 18-28 years were included so that the follow up will be easy. Patients were selected by utilizing the following inclusion criteria: (1) Patients giving history of recurrence ulcers in the oral cavity with at least 2 episodes per year and with no signs of any systemic disease (2) Patients above 12 years with apparently normal immune system. Exclusion criteria comprised of: (1) Patient with any systemic disease causing oral ulcerations like- gastrointestinal disorders (ulcerative colitis, Cohn's disease), Bechets disease, Reiter syndrome, hematological diseases, nutritional deficiencies and allergic conditions (2) Patients who are receiving or have received chemotherapeutic drugs, Immune-modulators or systemic corticosteroids in the recent 1 year (3) Patient having other mucosal lesions, with recurrent minor aphthous ulcers (4) Pregnant and lactating mothers.

After fulfilling inclusion and exclusion criteria 41 patients were selected for study. After approval from ethical committee aim of study was explained to them and an informed consent was obtained. All patients were requested to go for routine hematological investigation to rule out any hematological abnormalities. Then all study subjects underwent a clinical examination to assess the ulcer size with

calibrated periodontal probe and pain using VAS (Visual analogue scale) from 1 to 10 (10 being most severe). Patients were divided into two groups. Study group (Group-A) comprises of 21 patients selected randomly to receive 5% amlexanox (Lexanox) oral paste at first visit, with instructions to apply locally 4 times per day for one week. Control group (Group-B) comprises of rest 20 patients who received topical anesthetic agent (Lignocaine gel) as placebo.

The patients were then recalled on 4th day following the onset of treatment. Only 30 patients 15 from group-A and 15 from group-B reported to the department, rest 11 patients were lost for the follow up. The effectiveness of both the treatment modalities was assessed on basis of reduction in ulcer size and pain at different time period on day 1 and day 4th.

Statistical package for social science was used for data entry and data analysis. Descriptive statistic of study subjects such as mean and standard deviation (SD) was calculated. The collected data was analyzed for significant differences between the groups using independent t-test. $P < 0.05$ was considered statistically significant.

Results

A total of 50 patients with minor aphthous ulcer were enrolled for the study, out of which only 30 served as study samples which were randomly divided into group-A and group-B. 13 were males and 17 were females with age ranging from 18-28 years (mean 24 years). The comparison of ulcer size and maximum pain were made between first day values (baseline value) and fourth day.

Study group showed significant results [Table 1 and 2] between 1st day and 4th day with respect to ulcer size (mean±SD 4.18±0.78 and 1.73±0.90 respectively) and maximum pain (6.66±1.25 and 2.00±1.11 respectively). Similarly comparing the control group also yielded significant difference [Table 1 and 2] in ulcer size (mean±SD 3.72±2.15 and 2.51±1.74 respectively) and pain (6.33±1.23 and 4.06±1.53 respectively) between both time periods. On comparing the pain of ulcer between two groups, significant difference was observed between both time periods as shown in Table 3 and 4, indicating significant reduction in pain of ulcers in study group as compared to control group. Whereas the reduction in ulcer size was more in study group than control [Table 3 and 4], was not significant but found considerable reduction in ulcer size.

Table 1: Pain score of all subjects using Amlexanox and Topical anesthetic agent

| Groups | Day-1 | Day-4 | T value | P value |
|-----------|-----------|-----------|---------|---------|
| Amlexanox | 6.66±1.25 | 2.00±1.11 | 37.401 | 0.001 |
| Placebo | 6.33±1.23 | 4.06±1.53 | 12.475 | 0.001 |

Table 2: Ulcer size of all subjects using Amlexanox and Topical anesthetic agent

| Groups | Day-1 | Day-4 | T value | P value |
|-----------|-----------|-----------|---------|---------|
| Amlexanox | 4.18±0.78 | 1.73±0.90 | 9.958 | 0.001 |
| Placebo | 3.72±2.15 | 2.51±1.74 | 8.522 | 0.001 |

Table 3: Comparison of Pain score differences between Amlexanox and Topical anesthetic agent

| Groups | Amlexanox | Placebo | T value | P value |
|--------|-----------|-----------|---------|---------|
| Day-1 | 6.66±1.25 | 6.33±1.23 | 0.777 | 0.444 |
| Day-4 | 2.00±1.11 | 4.06±1.53 | 4.041 | 0.001 |

Table 4: Comparison of Ulcer size differences between Amlexanox and Topical anesthetic agent

| Groups | Amlexanox | Placebo | T value | P value |
|--------|-----------|-----------|---------|---------|
| Day-1 | 4.18±0.78 | 3.72±2.15 | 0.627 | 0.535 |
| Day-4 | 1.73±0.90 | 2.51±1.74 | 0.541 | 0.135 |

Discussion

The mucosa lining of the oral cavity is susceptible to many inflammatory, atrophic and ulcerative conditions, including aphthous stomatitis, lichen planus, erythema multiforme and Behcet's syndrome. Recurrent aphthous stomatitis (RAS) is one of the most common oral disorder with painful, recurring oral ulcers. The oral symptoms of RAS include pain, weakness and major alterations in oral functions, such as speech, chewing and swallowing. 5% Amlexanox (Lexanox), a topical anti-inflammatory agent has recently been found to have significant role in management of minor aphthous ulcers.⁶

In the present study first day values (baseline value) of all patients were collected i.e. size of ulcers and maximum pain recorded on VAS. Following administration of amlexanox in the study group and topical anesthetic agent in the control group, the patients were recalled on 4th day and the values were collected again for both the groups, and considerable and significant reduction in size and pain of ulcers in study group as compared to control group was found. In the present study size of ulcer reduced significantly in both the groups. Patient on amlexanox reported significant reduced size of ulcers on 4th day on comparison to baseline values though the size reduced was of less significance in control group. On comparison between the groups the size was not significant but considerable and pain was significantly lower in the study group than the control group, showed near approximation with previous studies done by Girish Katti, Jie Liu et al and Greer et al.^{1,7,8}

Signs and symptoms in both the groups had reduced which was noted by reduction in the VAS scores throughout treatment period. This indicates that both drugs could bring about reduction in the pain. However, on comparing between two groups, the patients on amlexanox had a significant lower VAS values than the control group, which showed approximation with previous studies done by Girish Katti, Darshan D and Atul Khandwala et al.^{1,9,10}

Literature reveals that other studies were also conducted which along with the size of ulcer and pain in VAS also included number of ulcers and erythema of ulcers. Significant reduction in all the parameters was noticed with patient on amlexanox when compared to control group at different time intervals.¹

Conclusion

Amlexanox 5% oral paste is an anti-inflammatory and anti-allergic medicine that is easily available and inexpensive, demonstrated significant reduction in the amount of pain and size of ulcer without any side effects. Therefore in clinical practice amlexanox oral paste may be a better choice for RAS treatment.

References

1. Katti G, Darshan D. Amlexanox in the treatment of recurrent minor aphthous ulcers. *International Journal of Dental Clinics* 2011-3(3):23-26.
2. Atai Z, Ansari M, Torabi N. Efficacy of Olive Leaf in the Treatment of Minor Aphthous Ulcers. *American Journal of Infectious Diseases* 2007-3(1):24-26.
3. Ship JA. Recurrent aphthous stomatitis: an update. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology.* 1996;81(2):141-7.
4. Akintoye SO, Greenberg MS. Recurrent aphthous stomatitis. *Dent Clin North Am* 2005,49:31-47.
5. Meng W, Dong Y, Liu J et al. A clinical evaluation of amlexanox oral adhesive pellicles in the treatment of recurrent aphthous stomatitis and comparison with amlexanox oral tablets: a randomized, placebo controlled, blinded, multicenter clinical trial. *BioMed Xentral* 2009, www.trialsjournal.com/content/10/1/30.
6. Hamishehkar H, Nokhodchi A, Ghanbarzadeh S, Kouhsoltani M. Triamcinolone Acetonide Oromucosal Adhesive Paste for Treatment of Aphthous Stomatitis. *Adv Pharm Bull*, 2015,5(2),277-282.
7. Liu J, Zeng X, Chen Q, Cai Y, Chen F, Wang Y, et al. An evaluation on the efficacy and safety of amlexanox oral adhesive tablets in the treatment of recurrent minor aphthous ulceration in a Chinese cohort: a randomized, double-blind, vehicle-controlled, unparallel multicenter clinical trial. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology.* 2006;102(4):475-81.
8. Greer Jr RO, Lindenmuth JE, Juarez T, Khandwala A. A double-blind study of topically applied 5% amlexanox in the treatment of aphthous ulcers. *Journal of oral and maxillofacial surgery.* 1993;51(3):243-8.
9. Khandwala A, Van Inwegen RG, Alfano MC. 5% Amlexanox oral paste, a new treatment for recurrent minor aphthous ulcers: I. Clinical demonstration of acceleration of healing and resolution of pain. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology.* 1997;83(2):222-30.
10. Khandwala A, Van Inwegen RG, Charney MR, Alfano MC. 5% Amlexanox oral paste, a new treatment for recurrent minor aphthous ulcers: II: Pharmacokinetics and demonstration of clinical safety. *Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology.* 1997;83(2):231-8.