EVALUATING THE EFFICACY OF CURCUMIN ORAL GEL AND TOPICAL AMLEXANON IN MANAGING THE RECURRENT APHTHOUS STOMATITIS

Dr. Sanjeet Singh Parihar[1], Dr. Sweta Gupta[2], Dr. Shashank Agarwal[3], Dr. Gaurav Goyal[4], Dr. Surabhi Balakrishnan[5*]

Abstract

Background: RAS (recurrent aphthous stomatitis is a painful condition affecting the oral cavity and presents as shallow oral ulcers surrounded by the erythematous halo with a high recurrence rate and posing difficulties in speech and mastication.

Aim: The present study aimed to assess the efficacy of 2% curcumin oral paste to 5% topical Amlexanox in management of the recurrent aphthous stomatitis concerning the recurrence rates, pain scores, erythema, and ulcer size.

Methods: 96 subjects were assessed and divided into two groups where Group I subject were managed with 2% curcumin oral gel and 48 subjects for Group II with 5% Amlexanox oral paste. Subjects were assessed at 1, 4, and 7 days for pain score, erythema level, and ulcer size. The ulcer recurrence was evaluated at 30, 60, 90, and 180 days and results were formulated.

Results: The study results showed a significant reduction in pain scores and erythema with curcumin use in Group I with respective p-values of 0.01 and 0.03. The ulcer size was reduced in both groups with a non-significant difference. A higher recurrence rate was seen for Group II subjects using Amlexanox compared to Group I where curcumin was used.

Conclusion: The present study concludes that curcumin is a safe and potent substitute for managing recurrent aphthous stomatitis concerning the reduction of recurrence rates, pain, and erythema. However, further studies are needed to assess the efficacy of curcumin in different types of recurrent aphthous stomatitis.

Keywords: Amlexanox, aphthous stomatitis, Curcumin, recurrent aphthous ulcer

[1]MBBS, MS, Senior Consultant ENT, Government Hospital Gandhi Nagar, Jammu, J&K
[2]BDS, MDS, Assistant professor, Departmental of Orthodontics, Patna Dental College and Hospital, Patna, Bihar
[3]Associate Professor, Department of Conservative Dentistry and Endodontics, School of Dental Sciences, Sharda University, Greater Noida, Uttar Pradesh
[4]BDS, MDS, Senior Lecturer, Department of Oral pathology, Himachal Institute of Dental Sciences, Paonta Sahib, Himachal Pradesh
[5*]BDS, MDS, Lecturer, Department of Oral Medicine and Radiology, Index Institute of Dental Sciences, Indore, Madhya Pradesh

***Corresponding Author:** Surabhi Balakrishnan
*****BDS, MDS, Lecturer, Department of Oral Medicine and Radiology, Index Institute of Dental Sciences, Indore, Madhya Pradesh
Email id: dr.surabhinambiar1@gmail.com

DOI:-10.48047/ecb/2023.12.si5a.0383

INTRODUCTION

RAS (recurrent aphthous stomatitis) is a condition affecting the oral mucosa and has a multifactorial etiology.Recurrent aphthous ulcers are also known as canker sores and present as round, small, multiple, ovoid ulcers that are recurrent having a yellow or grey floor and circumscribed margins surrounded by a typical erythematous halo. Aphthous ulcers have a high prevalence globally affecting nearly 20% of the World's population.[1]

Aphthous ulcers are associated with intense discomfort and pain and make the subject refrain from normal oral activities such as swallowing and chewing. As aphthous ulcers have multifactorial etiology, various factors have been attributed to their etiology including the alterations in oral microbial flora, hormonal changes including menstruation and ovulation in females, allergy to particular products from oral care or toothpaste such as sodium lauryl sulfate, psychological stress, and/or local trauma.[2] Also, various systemic conditions have been linked to recurrent aphthous ulcers as deficiencies related to thiamine, zinc, vitamin D, vitamin B 12, vitamin B6, folate, iron, hematinic deficiencies, celiac disease, enteropathy, and/or malabsorption.[3]

Various therapeutic approaches have been adopted for aphthous ulcers including laser therapy, immune- modulatory drugs, nutritional supplements, corticosteroids, antibiotics, topical anesthetics, and/or combination therapy for reduction of the recurrence and efficacy in pain management. C16H14N204 (Amlexanox) is a topical anti-allergic and anti-inflammatory agent that is clinically approved by the US FDA (Food and Drug Administration) for managing recurrent aphthous stomatitis. It acts by inhibiting the release and formation of leukotrienes and histamine from the mononuclear cells, neutrophils, and mast cells.[4]

Another potent herbal counterpart is Curcuma longa which has been assessed for its anti-oxidant and anti- inflammatory effects in various oral diseases where it has been used as an alternative to corticosteroids.[5] The present study aimed to comparatively assess the efficacy of 2% curcumin oral paste to 5% topical Amlexanoxin management of the recurrent aphthous stomatitis concerning the recurrence rates, pain scores, erythema, and ulcer size.

MATERIALS AND METHODS

The present clinical study aimed to comparatively assess the efficacy of 2% curcumin oral paste to 5% topical Amlexanox in management of the recurrent aphthous stomatitis concerning the recurrence rates, pain scores, erythema, and ulcer size. The study subjects were from the Department of Oral Medicine and Radiology of the Institute. A well-explained verbal and written informed consent was taken from all the study participants for study participation.

The study assessed 96 subjects from both genders that were randomly and equally divided into two groups where Group I subject were managed with 2% curcumin oral gel and 48 subjects for Group II with 5% Amlexanox oral paste. The inclusion criteria for the study were subjects of age 18-30 years, having 1-3 minorrecurrent aphthous ulcers of <48 hours duration, history of minor RAS for a minimum of two episodes every year with <10mm ulcers that heal without scarring within 4-14 days and gave consent for study participation. The exclusion criteria were subjects with allergies to food or medicine, subjects on immune suppressants, systemic steroids, or NSAIDs, subjects that underwent any dental procedure or dental extraction within the last 2 weeks, subjects under active orthodontic therapy, alcoholics, smokers, lactating females, pregnant females, and subjects with any underlying systemic disease or conditions.

After final inclusion, detailed history was recorded followed by a comprehensive oral examination of all the subjects. The clinical parameters assessed at baseline were exudation, erythema, pain, number, size, and site of the ulcers. This was followed by an evaluation and diagnosis of the ulcer. The instructions concerning the use of the study drugs were communicated to the study subjects in both written and verbal form. Both 2% curcumin oral gel and 5% oral Amlexanox oral paste were placed in identical packaging and were given to the study subjects that were completely unaware of the drug that they were using.

The subjects were asked to clean wipe the ulcer-affected area with a sterile cotton piece. Group I subjects were asked to apply a very little gel to make a thin smear over the ulcer region, whereas, Group II subjects were asked to take a paste of approximately 0.5cm which was applied over the affected area. The subjects from both groups were asked to apply the given gel four times daily in the morning after brushing, after lunch, after dinner, and before going to the bed. The maximum diameter of the ulcers was assessed using William's calibrated periodontal probe on days 1, 4, and 7.

VAS (Visual Analog scale) was used for assessment of the pain from no pain to excruciating pain. The subjects were asked to identify and mark the point that best describes the pain condition. The

erythema for the ulcers was assessed using a modified Greer scale[6] on a scale having 4 points where 0, 1, 2, and 3 scores described no erythema, light red/pink color, red but not dark in color, and very red, dark color respectively. All the subjects were assessed on days 1, 4, and 7 for all the parameters. The recurrence was assessed on 30, 60, 90, and 180 days. A complete oral assessment was done at all the recalls and subjects were also asked about any encountered adverse event.

The gathered data were statistically assessed using SPSS software version 21.0 and independent t-tests in both groups. The chi-square test was used for the intergroup comparison. The statistical significance was taken at a p-value of <0.05.

RESULTS

The present clinical study aimed to comparatively assess the efficacy of 2% curcumin oral paste to 5% topical Amlexanox in management of the recurrent aphthous stomatitis concerning the recurrence rates, pain scores, erythema, and ulcer size. The study assessed 96 subjects from both genders that were randomly and equally divided into two groups where Group I subject were managed with 2% curcumin oral gel and 48 subjects for Group II with 5% Amlexanox oral paste. The study had 96 subjects from both genders with a mean age of 32.4±2.6 years and an age range of 18-57 years. There were 37.5% (n=36) male and 62.5% (n=60) female subjects in the study.

In comparing the ulcer size in two groups of study subjects, the results are summarized in Table 1. On day 1, the mean ulcer size was 3.86±1.23 mm and 3.4±1.7 mm for Groups I and II respectively. The difference was statistically non-significant with p=0.44. On day 3, the mean ulcer size was 2.73±1.96 mm for Group I and 2.65±1.47 mm for Group II which showed a statistically non-significant with p=0.92. The mean ulcer sizewas 1.25±1.47 and 1.2±0.83 mm for Group I and II respectively. This difference was statistically non-significant with p=0.06.

On intergroup comparison of the pain scores in the two groups of study subjects, it was seen that on day 1, themean pain scores for group I and group II were 3.23±1.24 and 3.14±1.45 respectively showing a non- significant difference with p=0.52. A similar non-significant difference was seen in pain scores on day 3 where mean scores were 1.94±1.81 and 2.31±1.58 respectively with p=0.57. However, on day 7, significantlyhigher pain scores were seen for Group II Amlexanox with 0.56±0.77 compared to 0.06±0.26 which was seenfor Group I curcumin with p=0.01 as shown in Table 2.

Concerning the erythema scores in two study groups, on day 1, mean erythema scores in Groups I and II were1.56±0.76 and 1.73±1.14 respectively. On day 3, the mean erythema scores for Groups I and II were 1.21±1.34 and 1.40±1.74 respectively. On day 7, the mean erythema scores were 0.56±0.75 and 0.25±0.53 respectively as depicted in Table 3.

For the recurrence rates in Group I and II study subjects, on day 3, a very low recurrence was seen in 4.16% (n=2) and 8.33% (n=4) subjects respectively. On day 60, the recurrence was seen in 29.1% (n=14) subjects of Group I and 45.83% (n=22) subjects from Group II. On day 90, 37.5% (n=18) of subjects from Group I and 66.6% (n=32) of subjects from Group II showed the recurrence of aphthous ulcers. On day 180, the recurrence was seen in 50% (n=24) subjects from Group I and in 91.66% (n=44) subjects from Group II as shown in Table 4.

Day	Groups	Number (n)	Mean ± S. D	p-value
1	**I**	48	3.86±1.23	0.44
	II	48	3.4±1.7	
3	**I**	48	2.73±1.96	0.92
	II	48	2.65±1.47	
7	**I**	48	1.25±1.47	0.06
	II	48	1.2±0.83	

Table 1: Intergroup comparison of the ulcer size in the two groups of study subjects

Day	Groups	Number (n)	Mean ± S. D	p-value
1	**I**	48	3.23±1.24	0.52
	II	48	3.14±1.45	
3	**I**	48	1.94±1.81	0.57
	II	48	2.31±1.58	
7	**I**	48	0.06±0.26	**0.01**
	II	48	0.56±0.77	

Table 2: Intergroup comparison of the pain scores in the two groups of study subjects

Day	Groups	Number (n)	Erythema score
1	**I**	48	1.56±0.76
	II	48	1.73±1.14
3	**I**	48	1.21±1.34
	II	48	1.40±1.74
7	**I**	48	0.56±0.75
	II	48	0.25±0.53

Table 3: Intergroup comparison of the erythema scores in the two groups of study subjects

Day	Groups	Number (n)	Recurrence rate n (%)
3	**I**	48	4.16 (2)
	II	48	8.33 (4)
60	**I**	48	29.1 (14)
	II	48	45.83 (22)
90	**I**	48	37.5 (18)
	II	48	66.6 (32)
180	**I**	48	50 (24)
	II	48	91.66 (44)

Table 4: Intergroup comparison of the recurrence rates in the two groups of study subjects

DISCUSSION

The present study assessed 96 subjects from both genders that were randomly and equally divided into two groups where Group I subject were managed with 2% curcumin oral gel and 48 subjects for Group II with 5% Amlexanox oral paste. The study had 96 subjects from both genders with a mean age of 32.4±2.6 years and an age range of 18-57 years. There were 37.5% (n=36) male and 62.5% (n=60) female subjects in the study. These data were compared to the studies of Scully C et al[7] in 2003 and Grimaux X et al[8] in 2018 where authors assessed subjects with demographic data comparable to the present study. The study results showed that on comparing the ulcer size in two groups of study subjects, on day 1, the mean ulcer size was 3.86±1.23 mm and 3.4±1.7 mm for Groups I and II respectively. The difference was statistically non-significant with p=0.44. On day 3, the mean ulcer size was 2.73±1.96 mm for Group I and 2.65±1.47 mm for Group II which showed a statistically non-significant with p=0.92. The mean ulcer sizewas 1.25±1.47 and 1.2±0.83 mm for Group I and II respectively. This difference was statistically non-significant with p=0.06. These results were consistent with the studies of Nolan A et al[9] in 2006 and Byahatti SM[10] in 2013 where authors reported similar sizes of aphthous ulcers on topical oral gel use.

For the intergroup comparison of the pain scores in the two groups of study subjects, it was seen that on day1, the mean pain scores for group I and group II were 3.23±1.24 and 3.14±1.45 respectively showing a non- significant difference with p=0.52. A similar non-significant difference was seen in pain scores on day 3 where mean scores were 1.94±1.81 and 2.31±1.58 respectively with p=0.57. However, on day 7, significantly higher pain scores were seen for Group II Amlexanox with 0.56±0.77 compared to 0.06±0.26 which was seenfor Group I curcumin with p=0.01. These findings were in agreement with the findings of Raman P et al[11] in 2020 and Bell J[12] in 2005 where authors suggested similar pain relief by using curcumin and Amlexanox for recurrent aphthous stomatitis

On assessing the erythema scores in two study groups, on day 1, mean erythema scores in Groups I and II were 1.56±0.76 and 1.73±1.14 respectively. On day 3, the mean erythema scores for Groups I and II were 1.21±1.34 and 1.40±1.74 respectively. On day 7, the mean erythema scores were 0.56±0.75 and 0.25±0.53 respectively. These results were in line with the results of Martins C et al[13] in 2009 and Mirzaci H et al[14] in 2017 where authors suggested similar changes in erythema scores over time after treatment of recurrent aphthous ulcers.

Concerning the recurrence rates in Group I and II study subjects, on day 3, a very low recurrence was seen in 4.16% (n=2) and 8.33% (n=4) subjects respectively. On day 60, the recurrence was seen in 29.1% (n=14) subjects of Group I and 45.83% (n=22) subjects from Group II. On day 90, 37.5% (n=18) of subjects from Group I and 66.6% (n=32) of subjects from Group II showed the recurrence of aphthous ulcers. On day 180, the recurrence was seen in 50% (n=24) subjects from Group I and in 91.66% (n=44) subjects from Group II. These results were comparable to the studies of Rodriguez M et al[15] in 2007 and Murray B et al[16]

in 2006 where similar recurrence rates were seen for recurrent aphthous stomatitis in their study subjects.

CONCLUSION

Considering its limitations, the present study concludes that curcumin is a safe and potent substitute for managing recurrent aphthous stomatitis concerning the reduction of recurrence rates, pain, and erythema. However, further studies are needed to assess the efficacy of curcumin in different types of recurrent aphthousstomatitis.

CONFLICT OF INTEREST: None

REFERENCES

1. Patil S, Reddy SN, Maheshwari S, Khandelwal S, Shruthi D, Doni B. Prevalence of recurrent aphthous ulceration in the Indian Population. J Clin Exp Dent 2014;6:e36-40.
2. Akintoye SO, Greenberg MS. Recurrent aphthous stomatitis. Dent Clin North Am. 2005;49:31-47.
3. Bijelic B, Matić IZ, Besu I, Janković L, Juranić Z, Marušić S, et al. Celiac disease-specific and inflammatory bowel disease-related antibodies in patients with recurrent aphthous stomatitis. Immunobiology 2019;224:75-9.
4. Malayil S, Thomas J, Rani Mol P, Vineet DA, Thomas S, Vivek V. Frequency of patients presenting with recurrent aphthous stomatitis: A pilot study. J Dent Med Sci2014;13:63-6
5. Edgar NR, Saleh D, Miller RA. Recurrent aphthous stomatitis: A review. J Clin Aesthet Dermatol 2017;10:26-36
6. Greer RO Jr, Lindenmuth JE, Juarez T, Khandwala A. A double-blind study of topically applied 5% amlexanox in the treatment of aphthous ulcers. J Oral Maxillofac Surg 1993;51:243-8
7. Scully C, Gorsky M, Lozada-Nur F. The diagnosis and management of recurrent aphthous stomatitis: A consensus approach. J Am Dent Assoc 2003;134:200-7.
8. Grimaux X, LeducqS, Goupille P, Aubourg A, Miquelestorena-StandleyE, Samimi M. Aphthous mouth ulcers as an initial manifestation of secukinumab-induced inflammatory bowel disease. Ann Dermatol Venereol 2018;145:676-82.
9. Nolan A, Baillie C, Badminton J, Rudralingham M, Seymour RA. The efficacy of topical hyaluronic acid in the management of recurrent aphthous ulceration. J Oral Pathol Med. 2006;35:461-5.
10. Byahatti SM. Incidence of Recurrent Aphthous ulcers in a group of the student population in Libya: A Questionnaire Study. Arch Cran Oro FacSc 2013;1:26-30.
11. Raman P, Pitty R, Krithika CL, Anand SPN, Subramani GP. Topical curcumin and triamcinolone acetonide in recurrent minor aphthous ulcers: A pilot trial. J Contemp Dent Pract 2020;21:884-90
12. Bell J. Amlexanox for the treatment of recurrent aphthous ulcers. Clin Drug Investig 2005;25:555-66.
13. Martins C, da Silva DL, Neres AT, Magalhães TF, Watanabe GA, Modolo LV, et al. Curcumin is a promising antifungal of clinical interest. J. Antimicrob. Chemother 2009;63:337-9.
14. Mirzaei H, Shakeri A, Rashidi B, Jalili A, Banikazemi Z, Sahebkar A. Phytosomal curcumin: A review of pharmacokinetic, experimental and clinical studies. Biomed Pharmacother 2017;85:102-12.
15. Rodrıguez, M Rubio JA, Sanchez R. Effectiveness of two oral pastes for the treatment of recurrent aphthous stomatitis. Oral Dis 2007;13:490-4.
16. Murray B, Biagioni PA, Lamey PJ. The efficacy of amelxanox Ora Disc™ on the prevention of recurrent minor aphthous ulceration. J Oral Pathol Med 2006;35: 117-22.