

Lactic Acid 5% Mouthwash is an Effective Therapeutic and Prophylactic Agent in Treatment of Recurrent Aphthous Ulcer (Single blind placebo controlled therapeutic study)

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ABSTRACT:

BACKGROUND:

Recurrent aphthous ulcer (RAU) is a common oral disease. It is treated by a variety of agents. Lactic acid has been used in the treatment of many skin diseases.

OBJECTIVE:

To assess the therapeutic, prophylactic effectiveness and safety of 5% lactic acid mouthwash in management of patients with RAU.

PATIENTS AND METHODS:

This single blind placebo controlled therapeutic study where 40 patients with early onset RAU were recruited in Department of Dermatology -Baghdad Teaching Hospital from April 2005-April 2006. Patients ages ranged 20-60 (29.6 ±9.6) years and were divided randomly into 2 groups (20 patients for each one): Group A used 5% lactic acid mouthwash, 5 ml twice daily. Group B was instructed to use distilled water as placebo in a similar way to Group A. Short term assessment of each patient of both groups was done to evaluate the therapeutic effect of drug by using oral clinical manifestation index (OCMI), mean size of largest diameter of ulcers. A long term assessment was done for each patient to evaluate the prophylactic effect of drug by using OCMI before, after 1, 2 & 3 months of therapy.

RESULTS:

The mean of OCMI in group A started to decline directly after 4 days of therapy and to its lower level after 8 days, and it was statistically significant (P value <0.05). The change in mean of OCMI of group B after 4 and 8 days of therapy was also statistically significant (P value <0.05). The response rate after 4 days of therapy in Group A was 33.3% and in Group B was 6.44%, while the response rate after 8 days of therapy in Group A was 69.16% and in Group B was 44.98%. The difference in response rates after 4 and 8 days between groups A and B was statistically significant (P value <0.05). The mean size of ulcers in Group A started to decline directly after 4 days of therapy and to its lower level after 8 days of therapy. It was statistically significant (P value <0.05). The change in mean size of ulcers of group B after 4 and 8 days of therapy was also statistically significant (P value <0.05). The response rate after 4 days of therapy in group A was 44.92% and in Group B was 15.08%, while the response rate after 8 days of therapy in group A was 85.68% and in group B was 55.36%. The difference in response rates after 4 & 8 days between Groups A and B was statistically significant (P value <0.05). The therapeutic action of lactic acid mouth wash was statistically significant more effective than placebo. Lactic acid mouth wash showed statistically significant prophylactic effect in comparison to placebo after 1, 2 & 3 months from starting therapy using oral clinical manifestation index, (P value <0.05).

CONCLUSION:

Lactic acid 5% mouthwash is a new, safe effective therapeutic and prophylactic remedy in management of RAU.

KEYWORDS: lactic acid, RAU, mouthwash.

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INTRODUCTION:

Recurrent aphthous ulcer (RAU) is the most common oral mucosal disease in adolescent and adult as it afflicts at least 20% of the population⁽¹⁾. RAU characteristically begins in childhood or early adulthood in more than 50% of the patients, the onset of the disease occurred between age 10-30

years, Also it rarely occurred for the first time after the age of 50^(2,3).

RAU is characterized by recurring episodes of ulcers, each lasting from 1-4 weeks before healing, Aphthies typically are multiple round or ovoid ulcer with circumscribed margin, erythematous halo and a yellow or grey floor⁽¹⁾.

Multifactorial etiopathogenesis have been suggested to explain the cause of lesions of RAU, including genetic predisposition, trauma, infectious agents and immunological dysfunction, but the exact etiology and pathogenesis are not well known⁽¹⁾.

It is likely that immune-mediated destruction of the epithelium is the final common pathway in RAU pathogenesis⁽⁴⁾, accordingly there is no uniform effective therapy for this disease.

A large number of therapies both topical and systemic have been used in treatment of RAU, including chlorohexidine⁽⁵⁾, tetracycline⁽¹⁾, honey⁽⁶⁾, benodryl and Maalox, sucrolofate⁽²⁾, topical, intralesional and oral steroids⁽²⁾, dapsone⁽²⁾, colchicine⁽⁴⁾, pentoxifylline⁽⁷⁾, thalidomide⁽⁴⁾, low intensity ultrasound⁽⁸⁾ and BCG⁽⁹⁾. These therapies act through different mechanisms with variable success rates and most of them were associated with a variety of side effects.

Lactic acid is a fermentation product of lactose (milk sugar); it is present in milk, leban, yogurt and cottage cheese⁽¹⁰⁾.

Lactic acid has been used in treatment of many skin diseases, including warts, xerosis, ichthyosis, seborrheic keratosis and actinic keratosis, where it works mainly as exfoliates and reduces the thickness of stratum corneum⁽¹¹⁾. Also it may stimulate the production of collagen and elastin, therefore it is used in chemical peeling for treatment of wrinkling, and roughness and mottled pigmentation of photo-damaged skin⁽¹¹⁾.

Lactic acid has antioxidant action and this might help in re-pigmentation of patch of vitiligo⁽¹²⁾. Topically applied lactic acid increases spontaneous secretion of vascular endothelial growth factor (VEGF) by human reconstructed epidermis⁽¹³⁾, VEGF is a multifunctional angiogenic cytokine involved in angiogenesis and wound healing, and found that its level is low in early active stage of RAS when compared with its level in late remission stage⁽¹⁴⁾.

It is also reported that lactic acid can be used as a safe and effective antibacterial agent for local application⁽¹⁵⁾.

Recently lactic acid was used as therapeutic agent for controlling RAU in the form of 5% mouthwash⁽¹⁶⁾.

So, the present work was arranged to evaluate the therapeutic and prophylactic action in management of RAU.

PATIENTS AND METHODS:

This is a single blind placebo controlled study to evaluate the therapeutic and prophylactic efficacy of 5% lactic acid mouth wash in patients with RAU in comparison to placebo.

Patients with RAU included in this study were those who attended Baghdad Teaching Hospital - Department of Dermatology between April 2005 and April 2006.

Patients with RAUs included in this study were those in whom the ulcerations were had early onset (less than 3 days duration) and little or no benefit had been obtained from other conventional therapy in the previous attacks. Patients were requested to avoid the use of any remedy throughout the trial.

The diagnosis of RAU was based on history and clinical examination. Detailed history regarding age, sex, occupation, history of disease, the recurrence rate, their general health and previous medical history and history of the same condition or other illness in the family. Also, they were asked about any aggravating factors including food, stress, trauma and smoking or associated symptoms. All patients were fully examined regarding shape, size and number of the lesions.

Investigations were done for all patients regarding pathergy test, complete blood picture, ESR and HLA typing for HLA-B5, 51 and HLA-B27 to exclude patients with Behcet's disease and other internal causes of oral ulcerations. All patients were seen by ophthalmologists to exclude findings suggestive for Behcet's disease.

Forty patients with early onset oral ulcerations were included in this study. The patients were divided into two groups:-

Group A on 5% lactic acid (obtained from Hopkins & Williams LTD Company) mouth wash, group B on distilled water mouth wash as control group.

Patients in **Group A** (lactic acid), and **B** (distilled water) were instructed to use medication as 5 ml mouth wash two times daily for 3 months.

An oral clinical manifestations index (OCMI)^(9, 17) table (1), for each patient in both groups was calculated before therapy and during the course of treatment.

Short term assessment (The therapeutic effect of drugs):

An assessment was performed for each patient on day 4 and 8 from starting therapy using OCMI with exclusion of the score of frequency of attacks since

we are trying to evaluate the therapeutic efficacy of the therapies used in the trial in short time. Also on each visit, the size of each oral ulcer depending on the largest diameter was recorded before starting therapy and on day 4 and 8 after starting therapy, then mean size of ulcers was calculated for each patient on each visit.

Long term assessment (The prophylactic effect of drugs):

The OCMI score was recalculated for each patient monthly for 3 months after starting the therapy to evaluate the prophylactic efficacy of each therapy used in the study.

The data were analyzed, and the paired t-test was

used to compare the means of OCMI before, after 4 days and after 8 days of therapy of both groups.

The response rate was estimated by calculating the percentage of change in the means of OCMI after 4 and 8 days of treatment from the baseline of mean of OCMI before treatment.

Also paired t- test was used to compare the response rates after 4 and 8 days of therapy between the two groups included in this study.

P-value of less than 0.05 was considered to be statistically significant.

ANOVA test was used to compare the mean of OCMI, the mean size of ulcer and symptoms after treatment between these two groups.

Table 1: Oral Clinical Manifestation index

Type	Scoring
Minor ulcer	1
Herpetiform	2
Major ulcer	3
Number of ulcers/ attack	
1-3	1
4-6	2
7-9	3
9-12	4
More than 12.	5
Duration of the attack	
1-4 days.	1
5-8 days.	2
9-12 days.	3
More than 12 days.	4
Frequency (attack/date)	
0-2 weeks.	5
3-4 weeks.	4
5-6 weeks.	3
7-8 weeks.	2
More than 8 weeks.	1
Associated symptoms (pain score)	
Uncomfortable.	1
Painful, but not interfere with eating or swallowing.	2
Interfere with solid feeding.	3
Interfere with liquid eating.	4

RESULTS:

Forty patients were included in this study; 19 males (47.5%) and 21 females (52.5%), female to male ratio was 1.1: 1. Their ages ranged between 20-60 years with a mean ± SD of 29.6 ± 9.6 years.

All investigations were negative.

The therapeutic effect of drugs:

► **The effect of drugs on OCMI scores:**

1- Group A (5% lactic acid mouth wash):

In this group (20 patients), 12 males and 8 females;

their ages ranged between 20-60 years with a mean ± SD of 40.3 ± 12.65 years , the OCMI before therapy ranged between 12 and 21 with a mean ± SD 17.5±2.91, the mean started to decline significantly to a lower level within 4 days of treatment to be 11.8±4.14. While after 8 days of treatment a significant lower level of data was recorded, the mean was 5.55±5.72. P< 0.05, which was statistically significant(Table-2).

The response rate was estimated by calculating the percentage of change in the mean of OCMI after 4 and 8 days of treatment from the baseline of mean before treatment, it was 33.30±25.02 after 4 days of treatment and 69.16 ± 32.12 after 8 days of treatment.

2- Group B (Distilled water mouth wash):

In this group (20 patients), 7 males and 13 females; their ages ranged between 20-58 years with a mean ± SD of 38.55 ± 10.71 , the OCMI before therapy ranged between 10 and 21 with a mean ± SD 14.6±3.23, the mean started to decline significantly to a lower level within 4 days of treatment to be 13.5±2.42. While after 8 days of treatment a significant lower level of data was recorded, the mean was 8.30±5.83.(P< 0.05, which was statistically significant (Table- 2)).

The response rate was 6.44±7.81after 4days of treatment and 44.98±38.05 after 8 days of treatment.

The difference in response rate between both groups was statistically significant (Table 3).

► **The effect of drugs on mean size of ulcers:**

1. Group A (5% lactic acid mouth wash):

The mean size of oral aphthous ulcers in this group before therapy ranged between 4-10mm with a mean ±SD of 6.63±1.72, the mean started to decline significantly to a lower level within 4 days of therapy to be 3.70±1.82 and continued to decline till the 8th day of the course of therapy to be 1.05±1.47.(P < 0.05 (Table-4)).

The response rate was 44.92±21.56 after 4days of treatment and 85.68±19.48 after 8 days of treatment.

2- Group B (distilled water mouth wash):

The mean size of oral aphthous ulcers in this group before therapy ranged between 3-10 mm with a mean ±SD of 5.67±2.23, the mean started to decline significantly to a lower level within days of therapy to be 4.82±1.98 and continued to decline till the 8th day of the course of therapy to be 3.00±2.40.(P < 0.05 (Table- 4)).

The response rate was 15.08±13.12 after 4 days of treatment and 55.36±31.48 after 8 days of treatment.

The difference in response rate between both groups was statistically significant (Table -5).

Table 2: The effect of lactic acid and placebo on OCMI of ulcers.

OCMI score	Lactic acid MW	Placebo
	Mean ±SD Min-Max	Mean ±SD Min-Max
At day 0	17.5±2.91 12.0-21.0	14.6±3.23 10.0-21.0
At day 4	11.8±4.14 0-15.0	13.5±2.42 10.0-18.0
At day 8	5.55±5.72 0-12.0	8.30±5.83 0-16.0
P value	0.000001	0.000007

Table 3: The significance of response rates on OCMI between both groups

	Lactic acid x Placebo
Difference in size 0 & 4	0.0001*
Difference in size 0 & 8	0.001*
Difference in size 4 & 8	0.012*

*Significant difference between groups using independent t test (P<0.05)

Table 4: The effect of lactic acid and placebo on the mean size of largest diameter of ulcers.

Mean size of ulcers	Lactic acid MW	Placebo
	Mean \pm SD Min-Max	Mean \pm SD Min-Max
At day 0	6.63 \pm 1.72 4.0-10.0	5.67 \pm 2.23 3.0-10.0
At day 4	3.70 \pm 1.82 1.50-8.0	4.82 \pm 1.98 2.0-8.0
At day 8	1.05 \pm 1.47 0-4.0	3.00 \pm 2.40 0-7.0
P value	0.0000001	0.0003

Table 5: The significance of response rates on the mean of largest diameter of ulcers between both groups.

	Lactic acid x Placebo
Difference in score 0 & 4	0.0001*
Difference in score 0 & 8	0.036*
Difference in score 4 & 8	0.331

*Significant difference between groups using independent t test (P<0.05)

The prophylactic effect of drugs:

Both groups showed statistically significant effect on the OCMI of ulcers after 1, 2 and 3 months from starting therapy (Table -6).

Using the independent t test, lactic acid mouth wash showed statistically significant prophylactic effect in comparison to placebo after 1,2& 3 months from startingtherapy;(Table-7).

Table 6: The prophylactic effect of lactic acid and placebo on OCMI score.

OCMI score	Lactic acid MW	Placebo
	Mean \pm SD Min-Max	Mean \pm SD Min-Max
At day 0	17.50 \pm 2.91 12.0-21.0	14.60 \pm 3.23 10.0-21.0
At month 1	6.40 \pm 6.13 0-16.0	13.50 \pm 2.95 10.0-18.0
At month 2	4.90 \pm 5.66 0-14.0	10.90 \pm 6.30 0-20.0
At month 3	4.10 \pm 4.72 0-11.0	8.35 \pm 6.46 0-16.0
P value	0.000001	0.00039

Table 7: The significance of prophylactic effect on OCMI score between both groups.

OCMI Score	Lactic acid x Placebo
At day 0	0.005*
At month 1	0.0001*
At month 2	0.003*
At month 3	0.023*

*Significant difference between groups using independent t test (P<0.05)

DISCUSSION:

Recurrent aphthous ulcer is a major oral health problem where its etiopathogenesis is not well established. Although, the immune mediated destruction of the epithelium is the final common pathway in RAU pathogenesis, there are diversity types of therapies both topical and systemic, have been used in treatment of RAU, including chlorohexidine⁽⁵⁾, honey⁽⁶⁾, topical, intralesional and oral steroids⁽²⁾, dapsone⁽²⁾, colchicine⁽⁴⁾, and BCG⁽⁹⁾.

Lactic acid has been used in treatment of many skin problems with antioxidant effect⁽¹²⁾ and topically applied lactic acid increases spontaneous secretion of vascular endothelial growth factor (VEGF) by human reconstructed epidermis⁽¹³⁾, VEGF is a multifunctional angiogenic cytokine involved in angiogenesis and wound healing⁽¹⁴⁾. Also, it may stimulate the production of collagen and elastin⁽¹¹⁾. Lactic acid has been used as mouth wash in RAU as an effective therapeutic agent for RAU⁽¹⁶⁾ while the present work showed that lactic acid mouth

wash had both therapeutic and prophylactic role in management of RAU. As it is a natural product of lactose (milk sugar) fermentation⁽¹⁰⁾, it is safe, non toxic and with no side effects. Although the placebo gave obvious therapeutic effect which was showing the natural course of the disease but statistically was much less than lactic acid therapy. Although RUA might resolve spontaneously during short term but in the long term, it is chronic process. In the present work, follow up for 3 months showed that there was a change in the course of RUA where there was much decrease in the symptoms, frequency and the size of ulcers.

The mechanism of action might be related to its ability to increase spontaneous secretion of VEGF⁽¹³⁾, as immuno-modulator by inverting the decreasing CD4/CD8 ratio in aphthous ulcers and its antibacterial action against *Streptococcus sanguis* which is considered as possible pathogenic agent that might be associated with RAU. Also lactic acid might act as a local analgesic agent

allying the pain of RAU by cauterization of cutaneous nerve endings.

CONCLUSION:

5% lactic acid mouth wash is a safe, effective new therapeutic and prophylactic agent used in management of RAU.

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