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Original Research Article

To Evaluate Efficiency of Curcumin and Honey in Patients with Recurrent Aphthous Stomatitis: A Randomized Clinical Controlled Trial

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ABSTRACT

Introduction: Recurrent aphthous stomatitis (RAS) is one of the most common painful oral mucosal conditions seen among patients. Natural products have been used for several years in traditional medicine. Nowadays there are some natural remedies that are being explored for the treatment of aphthae. Herbal medicine will relieve pain, reduce inflammation and prevent infection in aphthous ulcers. Therefore, the present study was conducted to evaluate the efficiency of herbal remedies in the treatment of recurrent aphthous stomatitis.

Materials & Methods: The study population consisting of 105 patients having recurrent minor aphthous ulcer were selected from the outpatients of Department of Oral Medicine and Radiology, SDKS Dental College and Hospital. Patients were divided randomly into three groups ie Curcumin, Honey, Orabase group, each group consisting of 35 patients. Patients were evaluated on size, VAS score, erythema and exudate & were recalled on 3rd and 7th day of the treatment.

Results: The present study showed that all the three groups i.e Curcumin, Honey and Orabase were effective in improving the size, VAS score as well as the erythema and exudation levels. On comparison between the groups, Curcumin group showed statistically significant result as compared to Honey and Orabase group in improving the size, VAS score as well as the erythema and exudation levels. Therefore, Curcumin was the most effective in all the three groups.

Conclusion: Both Curcumin and Honey can be used as an alternative treatment modality in the management of RAS with Curcumin being slightly more effective than Honey.

Keywords: Curcumin, Honey, Aphthous ulcer, RAS.

INTRODUCTION

Recurrent aphthous stomatitis (RAS) is one of the most common painful oral mucosal conditions seen among patients. The term “aphthous” is derived from a Greek word “aphtha” which means ulceration. [1] RAS has been reported as affecting 20% of the general population. [2] The clinical manifestations is characterized by recurrent, painful ulcers that are small, round to ovoid, affecting non-keratinized oral mucosa such as buccal mucosa, lateral and ventral aspects of the tongue, floor of the mouth and soft palatal and oropharyngeal mucosa with a crater form based covered by a grey white pseudo membrane and surrounded by a distinct erythematous halo. Clinically RAS has been classified under three groups major, minor

and herpetiform types depending upon the size of ulcers.

The incidence in both sexes is almost equally affected with a slightly higher incidence in females. The cause of RAS is still unknown, although there are many promoting and exacerbating factors such as positive family history, nutritional deficiency (iron, vitamin B12, folate), food hypersensitivity, immune disturbance, hormonal imbalance, smoking cessation and psychological stress and, trauma. [3] Several microorganisms have also been implicated in the pathogenesis of RAS which includes Streptococci, Varicella zoster, Cytomegalo-virus. [1]

The best treatment for aphthous ulcer includes management of ulcers for the longest period with minimal side effects. The forms of therapy range from topical application to systemic administration of drugs, and even the newer technologies of ultrasound have been tried. The first line treatment options comprise of antiseptics and anti-inflammatory drugs/analgesics. 2% Lidocaine, antiseptics such as chlorhexidine gluconate 0.2%, topical antibiotics such as tetracyclines and their derivatives (doxycycline and minocycline), in gel or rinse form have also been found to lessen the pain and outbreaks of RAS. The most widely used drug in treatment of recurrent aphthous stomatitis is the topical corticosteroid. Triamcinolone acetonide 0.1%, clobetasol propionate 0.05%, fluocinonide 0.05% are most commonly used topical agents. [4]

Natural products have been used for several years in traditional medicine. Nowadays there are some natural remedies that are being explored for the treatment of aphthae. Herbal medicine will relieve pain, reduce inflammation and prevent infection in aphthous ulcers.

Honey has been described in ancient and modern medicine as being effective in the healing of various infected wounds; there have been few reports of its use in the healing of burns, ulcers and open wounds. Honey is known for its antifungal, anti-inflammatory and antibacterial properties. Also, honey is hygroscopic, which means that it has an ability to draw moisture out of the environment and dehydrate bacteria, and its high sugar content and low-level pH can also prevent the microbes from growth.

Curcumin is one of the most active constituent and principal curcuminoid found in turmeric. Demethoxycurcumin and bisdemethoxycurcumin are other curcuminoids found in turmeric. Curcumin is known for its antioxidant, antiseptic, antibacterial, anti-inflammatory, immuno-modulatory, and analgesic properties. The anti-inflammatory properties of curcumin may be attributed to its ability to inhibit both biosynthesis of inflammatory prostaglandins which further blocks cyclooxygenase and lipoxygenase activity, thereby inhibiting prostaglandin leukotriene release and neutrophil function during inflammatory states. [5]

In view of the multiple and varied agents that have been used to treat RAU, it would seem appropriate to use the least toxic and most safe agent that can accomplish symptomatic relief. Therefore, the present study was conducted to evaluate the efficiency of herbal remedies i.e. curcumin and honey in the treatment of recurrent aphthous stomatitis.

MATERIALS & METHOD

The present study was conducted in the Department of Oral Medicine and Radiology, Swargiya Dadasaheb Kalmegh Smruti Dental College and Hospital after taking approval from the Institutional Ethics Committee. An informed written consent was obtained from all the patients along with the explanation of the procedure to be performed. Only those patients who were willing to participate in the study were considered.

Men and women aged between 18-65 years presenting with 1-5 aphthous ulcers of less than 48 hours duration were included in the study. While patients who are recently undergoing any therapy for aphthous ulcers, pregnant and lactating women, individuals

with any known systemic disorders and clinical conditions including serious liver, kidney and heart dysfunction were excluded from the study.

The study population consisting of 105 patients were divided randomly into three groups ie Curcumin, Honey, Orabase group, each group consisting of 35 patients.

METHODOLOGY

A detailed case history of all the individuals was taken and recorded on the first visit before drug application. A thorough clinical examination was performed with the diagnosis of aphthous stomatitis. The following parameters were noted

• **For Pain Score measurement: -** Intensity of pain was recorded using a Numerical Rating, Visual Analogue Scale.

• **For Ulcer Size measurement: -** The size of ulcer will be measured using sterile calibrated Williams periodontal probe in millimeters and longest diameter was used as measurement at each follow-up.

• **For Erythema and Exudate level measurement: -** Degree of erythema and exudate was evaluated on a four-point scale ranging from 0 to 3 based upon the methods of Bhat S Sujatha D (2013) [8] derived from scale given by Greer et al(1993). [9] The subjective assessment was carried out by three different observers including the principal investigator and two subject experts to eliminate the observer bias in erythema and exudation scores. The subject experts were same throughout the study.

Method of application:

All the patients were asked to apply the given medication 3 times daily topically directly to the ulcerated area for 7 days. On day 1, application of medication to the ulcer was carried out in the clinic. Patients were asked to apply the medication after meals and not to consume food or water for half an hour after the application of the honey.

All the patients were evaluated with above mentioned parameters on 1st, 3rd and 7th day.

STATISTICAL ANALYSIS:

Data was entered in Microsoft Excel and analyzed using Stata version 14. Continuous variable, age was expressed as mean (standard deviation). The distribution of categorical variables like age categories, gender was expressed as proportions. The change in size, erythema and exudation within the groups before and after the treatment was assessed using a paired t test. Between the groups, the comparison of size, VAS score, erythema and exudation were assessed using an independent t test.

RESULTS

The present study was carried out in the department of Oral Medicine and Radiology. A group of 105 patients having minor aphthous ulcers between the age group of 18-65 years were selected which were divided randomly into three groups i.e Curcumin, Honey, Orabase group, each group consisting of 35 patients.

Out of 105 patients, 25(71%) patients of Curcumin group, 24(69%) patients of Honey group and 24(68.6) patients of Orabase group were in the age group of 18-45 years. The distribution of subject according to age is given in Table 1.The present study consisted more numbers of females as compared to males. Distribution of subjects according to gender is given in Table 2

Comparison of size of ulcer (Table 3)

- On comparison between change in size of aphthous ulcer at different time point between Curcumin and Orabase it was found that curcumin showed significant reduction in size of ulcer as compared to Orabase on 3rdday ($p=0.001$) and 7th day ($p=<0.001$).
- On comparison between change in size of aphthous ulcer at different time point between Honey and Orabase it was found that Honey showed significant reduction in size of ulcer as compared to Orabase on 7th day ($p < 0.045$).
- On comparison between change in size of aphthous ulcer at different time point

between Curcumin and Honey it was found that Curcumin showed significant reduction in size of ulcer as compared to honey on 3rd day (p = 0.003)and 7th day(p <0.001).

Comparison of VAS score (Table 4)

- On comparison between change in VAS score of aphthous ulcer at different time point between Curcumin and Orabase it was found that curcumin showed significant reduction in VAS score of aphthous ulcer as compared to Orabase on 3rdday (p = <0.001) and 7th day (p=<0.001).
- On comparison between change in size of aphthous ulcer at different time point between Honey and Orabase it was found that Honey showed significant reduction in size of ulcer as compared to Orabase on 7th day (p < 0.045).
- On comparison between change in size of aphthous ulcer at different time point between Curcumin and Honey it was found that Curcumin showed significant reduction in size of ulcer as compared to honey on 3rd day (p = 0.003) and 7th day (p <0.001).

Comparison of Erythema (Table 5)

- On comparison between change in erythema of aphthous ulcer at different time point between Curcumin and Orabase it was found that curcumin showed significant reduction in erythema of aphthous ulcer as compared to Orabase on 3rdday (p = < 0.002) and 7th day (p= <0.001).
- On comparison between change in erythema of aphthous ulcer at different time point between Honey and Orabase it was found that Honey showed significant reduction in erythema as compared to Orabase on 3rdday (p = < 0.03) and 7th day (p < 0.005).
- On comparison between change in exudate at different time point between Curcumin and Honey it was found that Curcumin showed significant reduction in erythema of ulcer as compared to honey on 7th day (p <0.001).

Table 1: Age wise distribution of subjects in Curcumin, Honey and Orabase groups.

Group	Age in years			Chi-square Value	P value
	18-45	45 -60	>60		
Curcumin	25 (71.4)	9 (25.7)	1 (2.9)	1.2	0.874*
Honey	24 (68.6)	11 (31.4)	0		
Orabase	24 (68.6)	10 (28.6)	1 (2.9)		
Total (N =105)	73 (69.5)	30 (28.6)	2 (1.9)		
* Non-Significant, tested using Chi-square test					

Table 2: Distribution of subjects based on gender in Curcumin, Honey and Orabase groups.

Group	Female N (%)	Male N (%)	Chi-square Value	P value
Curcumin	23 (65.7)	12 (34.3)	0.5602	0.756*
Honey	20 (57.14)	15 (42.9)		
Orabase	21 (60.00)	14 (40.0)		
Total (N=105)	64 (60.9)	41 (39.1)		
* Non-Significant, tested using Chi-square test				

Table 3: Comparison of change in size of aphthous ulcer at different time pointin Curcumin, Honey and Orabase groups.

Changes in size of ulcer at different time point	Mean ± SD (in mm)		
	Curcumin (N=35)	Honey (N = 35)	Orabase (N=35)
Size at day 1	5.8 ± 1.7	6.3 ± 1.6	6.02 ± 1.5
Size at day 3	4.3 ± 1.5	5.4 ± 1.5	5.54 ± 1.6
Size at day 7	1.4 ± 1.4	2.7 ± 1.4	3.4 ± 1.5

Table 4: Comparison of VAS score of aphthous ulcer at different time point in Curcumin, Honey and Orabase groups.

Changes in VAS score of aphthous ulcer at different time point	Mean ± SD(in mm)		
	Curcumin (N=35)	Honey (N = 35)	Orabase (N=35)
VAS Score at day 1	6.2 ± 1.5	6.3 ± 1.3	6.2 ± 1.6
VAS Score at day 3	4.4 ± 1.4	5.4 ± 1.6	5.5 ± 1.3
VAS Score at day 7	0.8 ± 1.2	3.2 ± 1.9	3.6 ± 1.7

Table 5: Comparison of erythema of aphthous ulcer at different time point in Curcumin, Honey and Orabase groups.

Changes in erythema of aphthous ulcer at different time point	Mean ± SD (in mm)		
	Curcumin (N=35)	Honey (N = 35)	Orabase (N=35)
Erythema at day 1	2.6 ± 0.5	2.5 ± 0.6	2.5 ± 0.6
Erythema at day 3	2.1 ± 0.5	2.5 ± 0.6	2.5 ± 0.6
Erythema at day 7	0.7 ± 0.6	1.7 ± 0.7	1.7 ± 0.7

Table 6:Comparison of exudateof aphthous ulcer at different time point in Curcumin, Honey and Orabase groups.

Changes in exudation of Aphthous ulcer at different time point	Mean ± SD(in mm)		
	Curcumin (N=35)	Honey (N=35)	Orabase (N=35)
Exudation at day 1	2.8 ± 0.4	2.9 ± 0.2	2.9 ± 0.2
Exudation at day 3	2.4 ± 0.7	2.7 ± 0.5	2.9 ± 0.3
Exudation at day 7	0.7 ± 0.9	1.5 ± 0.9	2.2 ± 0.9

Comparison of Exudate (Table 6)

- On comparison between change in exudate of aphthous ulcer at different time point between Curcumin and

Orabase it was found that curcumin showed significant reduction in exudate of aphthous ulcer as compared to Orabase on 3rd day (p = < 0.002) and 7th day (p= <0.001).

- On comparison between change in exudate of aphthous ulcer at different time point between Honey and Orabase it was found that Honey showed significant reduction in exudate as compared to Orabase on 3rd day (p = < 0.049) and 7th day (p = 0.008).
- On comparison between change in exudate at different time point between Curcumin and Honey it was found that Curcumin showed significant reduction in exudate as compared to honey on 3rd day (p= 0.02)and 7th day (p = <0.001).

Table 7: Comparison of clinical parameters before and after treatment in CurcuminGroup.

Clinical Findings	Time period	N	Mean ± SD	Std. Error Mean	t-value	p-value
Size	Before Treatment	35	5.8 ± 1.7	0.29	27.6	<0.001*
	After Treatment	35	1.4 ± 1.4	0.24		
VAS	Before Treatment	35	6.2 ± 1.5	0.25	17.7	<0.001*
	After Treatment	35	0.8 ± 0.2	0.21		
Erythema	Before Treatment	35	2.6 ± 0.5	0.08	14.3	<0.001*
	After Treatment	35	0.7 ± 0.6	0.1		
Exudate	Before Treatment	35	2.6 ± 0.5	0.8	13.6	<0.001*
	After Treatment	35	0.7 ± 0.9	0.16		
* Highly Significant, tested using paired t test.						

Table 8: Comparison of clinical parameters before and after treatment in Honey Group

Clinical Findings	Time period	N	Mean ± SD	Std. Error Mean	t-value	p-value
Size (in mm)	Before Treatment	35	6.3 ± 1.6	0.27	18	<0.001*
	After Treatment	35	2.7 ± 1.4	0.2		
VAS	Before Treatment	35	6.3 ± 1.3	0.2	11.9	<0.001*
	After Treatment	35	3.2 ± 1.9	0.3		
Erythema	Before Treatment	35	2.6 ± 0.5	0.08	9.8	<0.001*
	After Treatment	35	1.2 ± 0.6	0.1		
Exudate	Before Treatment	35	2.9 ± 0.2	0.04	9.4	<0.001*
	After Treatment	35	1.5 ± 0.9	0.16		
*Highly Significant, tested using paired t test.						

Table 9: Comparison of clinical parameters before and after treatment in Orabase Group

Clinical Findings	Time period	N	Mean ± SD	Std. Error Mean	t-value	p-value
Size (in mm)	Before Treatment	35	6.02 ± 1.5	0.26	14.2	<0.001*
	After Treatment	35	3.4 ± 1.5	0.26		
VAS	Before Treatment	35	6.2 ± 1.6	0.27	9.6	<0.001*
	After Treatment	35	3.6 ± 1.7	0.28		
Erythema	Before Treatment	35	2.5 ± 0.6	0.1	7.3	<0.001*
	After Treatment	35	1.7 ± 0.7	0.1		
Exudate	Before Treatment	35	2.9 ± 0.03	0.04	5	<0.001*
	After Treatment	35	2.2 ± 0.9	0.17		
*Highly Significant , tested using paired t test.						

DISCUSSION

In the present study a total of 105 patients were selected from the outpatients of department of oral medicine and radiology and were divided into three groups i.e. Curcumin group (Group I), Honey group (Group II) and the control group Orabase (Group III) containing 35 patients in each group.

In this study most of the patients, 25(71%) patients of Curcumin group, 24(69%) patients of Honey group and 24(68.6) patients of Orabase group were in the age group of 18-45 years. The present study showed more number of females as compared to males.

Curcumin group (Table 7)

The results of the present study showed that there is significant improvement in size of ulcer in Curcumin group with mean of 5.8±1.7 before treatment to 1.4±1.4 after treatment. This was in accordance with study conducted by Manifer S et al (2012), [5] Deshmukh RA (2014) [7]

There was a mean reduction in VAS score in curcumin group from 6.2±1.5 before treatment to 0.8±0.2 after treatment which was in accordance with study conducted by Nurdiana, Krishnasamy S (2016); [10] while study conducted by Singh H et al (2018) [11] showed less improvement in reduction of VAS score in comparison with the present study.

Similarly, significant results were found in improvement of erythema level with a mean of 2.6±0.5 before treatment to 0.7±0.6 after treatment and improvement in the exudation levels with a mean of 2.6± 0.5 before treatment to 0.7 ±0.9 on seven days of treatment. There are no studies reported in the literature about the change in the erythema and exudation level on treatment with curcumin on aphthous ulcer.

Honey group (Table 8)

The results of our study showed that there is significant improvement in size of ulcer in Honey group with mean of 6.3±1.6 before treatment to 2.7 ±1.4 after 7 days of treatment. Similarly, in the study conducted by Mohammed SS, Al-Douri AS (2008), [6] El-Haddad SA, Asiri FYL and Hussain Al-QH.(2014) [12]

Also, Honey showed significant improvement in reducing the VAS score of ulcers with a mean of 6.3±1.3 before treatment to 3.2±1.9 after treatment in the present study. This was found in co-relation with the study conducted by Halim DS et al(2013) [13] and Gichki AS et.al(2012) [14] in reducing the pain as compared to present study.

The present study also showed significant improvement in the erythema with a mean of 2.6±0.5 before treatment to 1.2± 0.6 after treatment and improvement in the exudation levels with a mean of 2.9± 0.2 before treatment to 1.5 ±0.9 after treatment respectively. In a study conducted by Gupta S, Lohe VK , Bhowate R (2018), [15] El-Haddad SA, Asiri FYL and Hussain Al-QH.(2014) [12]

Orabase group (Table 9)

Orabase which was used as an control group in the present study also showed significant improvement in reducing the size of ulcer from 6.02±1.5 before treatment to 3.4 ±1.5 after treatment, reduction in VAS score was observed from 6.2±1.6 before treatment to 3.6±1.7 after treatment. This was found in accordance with study conducted by El-Haddad SA, Asiri FYL and Hussain Al-QH.(2014). [12]

Orabase group also showed significant improvement in the erythema with a mean of 2.5±0.6 before treatment to 1.7± 0.7 after treatment and improvement in the exudation levels with a mean of 2.9± 0.03 before treatment to 2.2 ±0.9 after treatment respectively. El-Haddad SA, Asiri FYL and Hussain Al-QH.(2014) [12] also showed similar improvements.

COMPARISION BETWEEN THE GROUPS

Comparison of size, VAS score, erythema and exudation between the groups were assessed using an independent t test. On comparison between the Curcumin and Orabase groups, Curcumin group showed significant improvement in size, VAS score, erythema and exudation levels in comparison with the Orabase group. Similar results were obtained by Maha T Al–Saffar(2006), [16] Manifer S et al (2012) [5]

On comparison between the Honey and Orabase groups, Honey showed significant improvement in size, erythema and exudation levels in comparison with the Orabase group (Table 8a,8c, 8d). However, there was similar reduction in VAS score in both groups and there was no statistical significance. (Table 8b). This was in contrast with the previous studies conducted by Mohammed SS, Al-Douri AS (2008), [6] Gichki AS et.al(2012), [14] Deshmukh RA (2014) [7]

On comparison between the Curcumin and Honey groups, Curcumin group showed significant improvement in size, VAS score, erythema and exudation levels in comparison with the Honey group. Review of literature reveals no studies on

comparative evaluation of the effect of Curcumin and Honey on aphthous ulcers.

CONCLUSION

It can be concluded that both Curcumin and Honey can be used as an alternative treatment modality in the management of RAS with Curcumin being slightly more effective than Honey. These herbal remedies can be recommended for use in place of conventional treatment modality in the management of recurrent aphthous stomatitis as these herbal remedies are cost-effective, easily available and without any possible adverse effects.

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