Research Article **AJODRR (2020) 3:30**

American Journal of Dermatological Research and Reviews

(ISSN:2638-1893)

Treatment of Recurrent Aphthous Stomatitis by Crude Topical Sesame Seed Oil in Comparison with Crude Topical Pumpkin Seed Oil

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ABSTRACT

Background: Recurrent aphthous stomatitis (RAS) is the most common disease of the oral mucosa in the general population. Multifactorial etiopathogenesis has been suggested to explain the cause of RAS but the exact etiology and pathogenesis still unknown. Its therapy whether topical or systemic can induce clearance but the relapse rate is high. **Objective:** To evaluate the efficacy and prophylactic effects of topical Sesame seed oil in comparison with Pumpkin seed oil in the management of recurrent aphthous stomatitis. **Patients and Methods:** This is a single, blinded, clinical, therapeutic, comparative study where 35 patients with early onset RAS were examined in Center of Dermatology -Baghdad Teaching Hospital, Medical City ,Baghdad, Iraq from April 2018-October 2019. All socio-demographic data related to the disease was obtained from each patient, in addition to clinical examination was performed for each patient. Patients were divided into 2 groups: Group A (15 patients) used crude Sesame seed oil twice daily. Group B (20 patients) was instructed to use Pumpkin seed oil 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). A long term assessment was done for each patient to assess the prophylactic effect of drug by using OCMI before, after 1, 2 and 3 months of therapy. They were seen regularly to record any local or systemic side effects. **Results:** The patients enrolled in this study were 19 (54.3%) males and 16(45.7%) females, male to female ratio was 1.1: 1. Their ages ranged from 12-60 (35.33 ± 12.06) years. The mean of OCMI in Group A started to decline directly after 4 days of therapy and went to its lower level after 8 days of therapy, and it was statistically significant (P value <0.05). The change in the mean of OCMI of Group B after 8 days of therapy was also statistically significant (P value <0.05). The difference in the response rates after 8 days between Group A and B was statistically significant (P value <0.05). Both groups showed statistically significant prophylactic effect after 1, 2 and 3 months from starting therapy, but sesame seed oil was statistically more significant than pumpkin oil effect during 2nd & 3rd months of therapy. No significant side effects were noticed in both groups as both oils are edible foods. **Conclusion**: Sesame and pumpkin seed oil have an effective therapeutic and prophylactic action against RAS. No local or systemic side effects were observed during the course of therapy.

Keywords: Sesame seed oil, Pumpkin seed oil, recurrent aphthous stomatitis.

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How to cite this article:

Adil A. Noaimi, Douaa S. Ahmed. Treatment of Recurrent Aphthous Stomatitis by Crude Topical Sesame Seed Oil in Comparison with Crude Topical Pumpkin Seed Oil. American Journal of Dermatological Research and Reviews, 2020, 3:30

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Website: https://escipub.com/

Introduction

Recurrent aphthous stomatitis (RAS) is one of the most common painful oral mucosal disease that probably afflicts at least 20% of population, present first in childhood or adolescence [1]. Multifactorial etiopathogenesis has been suggested to explain the cause of RAS but the exact etiology and pathogenesis still not well elucidated [2].Despite numerous clinical trials, no medication gives completely reliable cure [3].Still some patients might get remission either as a result of therapy or spontaneously[4]. A large number of therapies both topical and systemic have been used in treatment of RAS, including topical , intralesional and oral steroid[3] ,tetracycline,[5]topical honey,[6]lactic acid 5% mouthwash,[7,8] BCG vaccine,[9]nigella sativa oil,[10] oral dapsone and oral zinc sulfate, [11] oral colchicine, [12]oral isotretinoin,[13]oral thalidomide,[14] oral clofazmine[15] and others. But unfortunately none of them was uniformly had 100% curable and prophylactic effects in treatment of RAS. For that reason, the physicians still searching for a new remedy to manage this disease.

Recently, an Iraqi study showed that Pumpkin seed oil has an effective therapeutic and prophylactic effect in management of RAS, Pumpkin seed oil are good source of vitamins, minerals and antioxidants, it has both anti-inflammatory and antioxidant effects. [16]This study encouraged us to conduct the present work using topical Sesame seed oil in comparison with Pumpkin seed oil.

So, the aim of the present work is to evaluate the efficacy and prophylactic effects of topical Sesame seed oil in comparison with Pumpkin seed oil in the management of RAS.

Patients and Methods

This is a single, blinded, therapeutic, comparative work to evaluate the effectiveness of topical Sesame seed oil in treatment and prophylaxis of RAS in comparison with Pumpkin seed oil. Patients with RAS enrolled in this study were those who attended Baghdad Teaching Hospital - Centre of Dermatology, Medical City in the period between February 2018 and October 2019.

Formal consent was taken from each patient and/or their parents before starting the trial after a full explanation for the nature of the disease, causes, prognosis, the drug, the method of treatment, duration of follow up and the possible side effects. The ethical approval was granted from the Scientific Committee of the Scientific Council of Dermatology, Iraqi Board for Medical Specializations.

The demographic information like age, gender, occupation, marital status, age of the disease at presentation, associated symptoms, onset, family history of the same disease, past medical, surgical and drug history were recorded. The clinical examination was done in each patient regarding sites involved, morphology, and any associated features.

Inclusion criteria: Patients with RAS in the present work were those with early onset ulceration (less than 3 days duration) and had little or no benefit obtained from other conventional therapy in previous attacks and stopped their treatment at least two months before. Patients were requested to not use any oral or topical medicaments throughout the trial. The diagnosis of RAS was based on history and clinical examination. History was obtained regarding: age, gender, occupation, past medical history, drug history, smoking and alcohol intake, the recurrence rate and history of the same condition or other illness in the family. Also, they were asked about any aggravating factors including food, stress and trauma or associated symptoms. All patients were fully examined regarding shape, size and number of the lesions. Investigations were done for all patients including: pathergy test, complete blood picture, ESR and HLA-B51 to exclude patients with Behcet's disease and other internal causes of oral ulcerations. All patients were seen by ophthalmologists, Neurologist and Rheumatologist to exclude findings suggestive for Behcet's disease.

Thirty five patients with early onset oral ulcerations were involved in this work. The patients

were divided into two groups depending to the type of therapy:-

Group A: on topical Sesame seed oil & **Group B:** on topical Pumpkin seed oil.

Drug preparation: Both oils were ready made in Iraq-Mosul Factory, EMAD trade mark, kept in a clean and tight dark container till usage. Patients instructed to use both seeds oils topically using cotton piece and applied to the entire oral mucosa two times daily for 3 months.

All patients instructed not take any other drug for their apthous ulcer during the course of the study, and to return if they developed drug side effects. An oral clinical manifestations index (OCMI) [16]. Table (1), for each patient was calculated before and during the therapy to assess the response to treatment.

Follow up:

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. Also, the size of each oral ulcer 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. The size of ulcer was estimated depending on the largest diameter of the ulcer.

Long term assessment: The OCMI score was recalculated monthly for 3 months after starting the therapy to evaluate the prophylactic efficacy of both therapies and to record any local or systemic side effects.

Statistical analysis: 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.

The data analysis was done using Statistical Package for Social Sciences (SPSS) version 24.

Results

Thirty-five patients were enrolled in this study; 19 males (54.3%) and 16 females (45.7%), their ages ranged between 12-60 years with a mean ± SD of 35.33 ± 12.06 years. All investigations for all patients were negative.

The therapeutic effect of drugs:

►The effect on OCMI scores:

1- Group A Sesame seed oil): In this group (15 patients), 9 males and 6 females; their ages ranged between 12-60 years with a mean ± SD of 37.75 ± 11.97 years. The OCMI before therapy ranged from 7–16 with a mean ± SD of 12.7+3.6, the mean started to decline significantly to a lower level within 4 days of treatment to be 3.9±2.45. While after 8 days of treatment a significant lower level of data was recorded, the mean was: 0.8±1.2 with a P<0.001 which was statistically highly significant (Table-2).

2- Group B Pumpkin seed oil): In this group (20 patients), 8 males and 12 females; their ages ranged between 14-58 years with a mean ± SD of 38.55 ± 10.71, the OCMI before therapy ranged between 7 and 16 with a mean ± SD 13.4±3.1, the mean started to decline significantly to a lower level within 4 days of treatment to be 4.2±2.3. While after 8 days of treatment a significant lower level of data was recorded, the mean was 1.3±1.6 with a P < 0.05 which was statistically significant (Table-2).

The difference in response rate between both groups was statistically not significant (p =0.678) at 4 days of treatment, while statistically significant (p=0.049) at 8 days of treatment (Table-3).

►The effect on mean size of ulcers:

1. Group A Sesame seed oil): The mean size of oral aphthous ulcers in this group before therapy ranged between5-10 mm with a mean ±SD of 8.33±1.91, the mean started to decline

significantly to a lower level within 4 days of therapy to be 3.06±3.11 and continued to decline till the 8th day of the course of therapy to be 0.36±0.66 with a P<0.05 (Table-4).

2- Group B Pumpkin seed oil): The mean size of oral aphthous ulcers in this group before therapy ranged between 5-10 mm with a mean ±SD of 8.05±1.93, the mean started to decline significantly to a lower level within days of therapy to be 4.5±3.18 and continued to decline till the 8th day of the course of therapy to be 0.8+0.95 with a P < 0.05 (Table-4).

The difference in response rate between both groups in size of ulcer at day 4 (p=0.048) and day 8 (p=0.028) was statistically significant (Table-5).

Table 1): Oral clinical manifestation index.

Type	Type Scoring
Minor ulcer	1
Herpetiform ulcer	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	
Uncomfortable	1
Painful , but not interfere with eating or Swallowing	2
Interfere with solid feeding	3
Interfere with liquid feeding	4

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 (P=0.002 P<0.05) (Table-7).

But, using the independent t test, sesame seed oil showed statistically significant prophylactic effect in comparison to pumpkin seed oil after 2 & 3 months from starting therapy (Table-8).

No local or systemic side effects were reported during the treatment and follow-up period.

Table-2: The effect of Sesame oil and Pumpkin oil on OCMI of the ulcers.

		Sesame oil			Pumpkin oil	
	Range	**Mean**	**SD**	**Range**	**Mean**	**SD**
At day 0	7 – 16	12.7667	3.62637	7 - 16	13.4500	3.10305
At day 4	0 – 6	3.9667	2.45628	0 - 6	4.2500	2.33678
At day 8	0 – 4	.8000	1.29721	0 - 4	1.3000	1.62546
P value	**P=0.000P<0.001 HS**			**P=0.002 P<0.05 Significant**		

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

Sesame oil vs Pumpkin oil	**P-value**	**Sig**
Difference in score 0 & 4	0.383	NS*
Difference in score 0 & 8	0.678	NS*
Difference in score 4 & 8	0.049	S

*P>0.05 Non significant

Table-4: The effect of Sesame oil and Pumpkin oil on size of ulcers.

	Sesame oil			**Pumpkin oil**		
Mean size of Ulcer	**Range**	**Mean**	**SD**	**Range**	**Mean**	**SD**
At day 0	5 - 10 mm	8.3333	1.91785	5 - 10 mm	8.0500	1.93241
At day 4	0 - 8 mm	3.0667	3.11762	0 -8 mm	4.3000	3.18053
At day 8	0 – 2mm	0.3667	0.66868	0 – 2mm	0.8000	0.95145
P value	P=0.001 P<0.05 Significant			P=0.008 P<0.05 Significant		

Table-5: The significance of response rates size of ulcers between both groups.

Sesame oil vs Pumpkin oil		**P-value**	**Sig**
Difference in score 0 & 4	At day 0	0.998	NS
Difference in score 0 & 8	At day 4	0.048	S
Difference in score 4 & 8	At day 8	0.028	S

*P<0.05 Significant

Table-6: The prophylactic effect of Sesame oil and Pumpkin oil on OCMI score during course of therapy.

	Sesame oil			Pumpkin oil		
OCMI score	**Range**	**Mean**	**SD**	**Range**	**Mean**	**SD**
At day 0	7 - 16	12.7667	3.62637	7 - 16	13.4500	3.10305
At month 1	0 - 10	2.9667	3.16754	0 - 10	2.7500	3.85084
At month 2	0 - 8	2.6333	2.65854	0 - 13	6.3500	5.44131
At month 3	0 - 8	3.4333	2.64814	0 - 13	9.8000	5.09489
P value	P=0.000 P<0.001 HS			P=0.006 P<0.05 Significant		

Table-7: The significance of prophylactic effect on OCMI scores between Sesame oil & Pumpkin oil.

OCMI score	P-value	Sig
At day 0	0.383	NS
At month 1	0.163	NS
At month 2	0.001	S
At month 3	0.000	HS

Discussion

Despite numerous clinical trials, no medication gives completely reliable cure [4]. A large number of therapies both topical and systemic have been used in treatment of RAS, including topical, intralesional and oral steroid[3] ,tetracycline,[5] topical honey,[6] lactic acid 5% mouthwash,[7,8] BCG vaccine,[9]nigella sativa oil,[10] oral dapsone and oral zinc sulfate, [11] oral colchicine, [12]oral isotretinoin,[13]oral thalidomide,[14] oral clofazmine[15] and others.

A recent Iraqi study had shown that Pumpkin seed oil has an effective therapeutic and prophylactic effect in management of RAS because pumpkin seed oil are considered as good source of vitamins, minerals and anti-oxidants. [16]

Sesame oil contains Sesamin 0.4-1.1%, sesamolin 0.3-0.6% and traces of sesamol contribute to the unique properties of sesame oil. [17] Sesame contains ample amounts of oleic, linoleic, palmitic and stearic acid which together comprise 96% of the total fatty acids. [18]

Sesame oil and its lignan sesamol have been proved to be potent anti-inflammatory agents. They have an excellent protective effect against endotoxin-associated inflammatory damage because they inhibit the release of inflammatory mediators. Sesamol also inhibits endotoxins from binding to its receptor; this reduces inflammatory transcription factor NF-κB activation. [19]

Sesame oil has a high content of unsaturated fatty acids (palmitic, stearic, oleic and linoleic acids), well as well presence of lignans (sesamin, asarinin, sesamolin, and sesamol) and gamma-tocopherol. These compounds may be responsible for the pharmacological activities, since several studies have indicated that fatty acids reduce the levels of prostaglandins and leukotrienes. [20]

Vitamin E, a fat soluble antioxidant, protects the body from harmful oxidizing compounds. Sesame seed oil contains gamma tocopherols along with sesaminol and sesamin which possess Vitamin E like activity. [21]

The results of the present work showed that both therapies are effective as therapeutic and prophylactic agents in controlling RAS.

The effect of both therapies on OCMI was statistically significant after 4 days of therapy and remained statistically significant throughout the course of therapy.

Sesame seed oil was statistically significantly better than Pumpkin seed oil at 2 and 3 months of prophylaxis.

Local or systemic side effects were not noticed because both agents are edible oils.

The mechanism of action of sesame seed oil in treatment of RAS cannot be clearly explained, but probable mechanisms of action may be through its anti-inflammatory,[18,19] and antioxidant actions[20,21] .

So in conclusion sesame seed oil is a safe and effective therapeutic and prophylactic agent in management of RAS.

Disclosure: This study was an independent study and not funded by any of the drug companies.

Acknowledgements: We would like to express our special thanks and gratitude to Professor Khalifa E. Sharquie as the original idea of this work was inspired by him.

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