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EFFICACY OF ALPHA LIPOIC ACID AS AN ADJUNCT TO INTRALESIONAL INJECTION TRIAMCINOLONE ACETONIDE AND INJECTION HYALURONIDASE IN THE MANAGEMENT OF ORAL SUBMUCOUS FIBROSIS

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ABSTRACT

Background: *Oral Submucous Fibrosis (OSMF) is a chronic and potentially malignant disorder of the oral cavity. Despite numerous therapeutic approaches, treatment outcomes remain inconsistent. Alpha Lipoic Acid (ALA), with its potent antioxidant and anti-inflammatory properties, may enhance the effects of conventional therapy. This study evaluated the efficacy of ALA as an adjunct in OSMF management.*

Materials and Methodology: *A randomized controlled clinical trial was conducted over 1.5 years on 100 clinically diagnosed OSMF patients. Participants were randomly divided into two groups. Group I (ALA group) and Group II (non-ALA group) on the same schedule. Clinical symptoms were assessed using a Visual Analogue Scale (VAS), and inter-incisal distance was measured before and after treatment. Statistical analysis was performed using SPSS.*

Results: *Males constituted 83% of participants. The most common habit observed was tobacco chewing (95%), followed by betel nut chewing (73%). Majority of cases had normal haemoglobin levels, while 15% showed decreased haemoglobin (Hb) levels. The ALA group showed significantly greater improvement in burning sensation, dryness, trismus, and fibrosis. Mean mouth opening improved from 1.56 cm to 3.24 cm in the ALA group and 1.77 cm to 2.52 cm in the non-ALA group. Seventy-two percent of ALA-treated patients regressed to Grade 1 disease compared to 14% in the control group.*

Conclusion: *ALA significantly enhances symptom relief, mouth opening, and disease regression, establishing it as a safe and effective adjunct in OSMF treatment.*

INTRODUCTION:

OSMF is a chronic, insidious, and potentially malignant disorder primarily associated with areca nut consumption [1]. It predominantly affects individuals aged 20–35 years and has a high prevalence in India and Southeast Asia [2]. The increasing popularity of commercially processed areca nut products such as gutkha, particularly among the youth, has contributed to the rising incidence of OSMF [3].

Clinically, it presents with progressive mucosal fibrosis leading to trismus, burning sensation, and impaired oral function [4]. Despite various treatment options, management remains difficult due to its multifactorial etiology and irreversible fibrosis [4].

Intralesional triamcinolone acetonide and hyaluronidase are established treatment modalities. The corticosteroid reduces inflammation and fibroblast activity, while hyaluronidase enhances tissue permeability and flexibility by degrading hyaluronic acid [5, 6].

Alpha-lipoic acid (ALA), a potent antioxidant, reduces oxidative stress and supports mitochondrial function. Its adjunctive use has been associated with improved mouth opening and reduced burning sensation, suggesting a synergistic effect with intralesional therapy [7]. Owing to the persistent clinical challenges in achieving optimal outcomes with conventional therapy alone, the present study aims to evaluate the efficacy of ALA as an adjunct to triamcinolone acetonide and hyaluronidase in the management of OSMF.

MATERIALS AND METHODOLOGY

This randomized controlled trial conducted over a period of 1.5 years at a tertiary care center. A total of 100 eligible participants were enrolled in the study. Prior to commencement of the study, the ethical approval was obtained and written informed consent was secured from all participants.

Both male and female patients aged 18–60 years who provided consent for enrollment and follow-up, including those previously treated without improvement, were included in the study. Immunocompromised patients, individuals with other mucosal disorders, those with known allergies to hyaluronidase, triamcinolone acetonide, or alpha-lipoic acid, and pregnant or lactating females were excluded.

Diagnosis was established based on a detailed history and clinical assessment. Each patient was interviewed with particular reference to the type and duration of oral abusive habits. Symptoms and signs were recorded using a 0–4 point VAS. Mouth opening was measured, and patients were randomly assigned to two groups:

Group I – ALA Group: Patients received dietary modification and oral alpha-lipoic acid twice daily for 4 weeks, in addition to intralesional injections of triamcinolone acetonide and hyaluronidase (1500 IU) administered weekly via multiple punctures for 4 weeks.

Group II – Non-ALA Group: Patients received intralesional injections of triamcinolone acetonide and hyaluronidase (1500 IU) weekly via multiple punctures for 4 weeks.

Signs and symptoms were compared before and after treatment. All patients were followed up for 3 months after completion of therapy in both groups.

Statistical Analysis: The collected data were entered into a Microsoft Excel sheet and analyzed using SPSS version 26. Quantitative data with a normal distribution were expressed as mean ± standard deviation or median and range, as appropriate. Qualitative categorical data were expressed as ratios. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Table No.1: Demographic and Habitual Profile of Study Participants

Variable	Category	No. of Cases (%)
Age (years)	Up to 20	3(3.00%)
	21–30	15(15.00%)
	31–40	39(39.00%)
	41–50	27(27.00%)
	51–60	16(16.00%
Gender	Male	83(83.00%)
	Female	17(17.00%)
Habit	Tobacco	95(95.00%)
	Betelnut	73(73.00%)
	Pan Masala	13(13.00%)
	Alcohol	32(32.00%)
	Smoking	36(36.00%)

Table 1 shows the demographic and habitual profile of the study participants. The majority of patients belonged to the age group of 31–40 years (39%), followed by 41–50 years (27%) and 21–30 years (15%). Only 3% of participants were below 20 years of age. In the present study, males constituted 83% of the cases, while females accounted for 17%. With regard to habitual factors, the most common habit observed was tobacco chewing (95%), followed by betel nut chewing (73%). Smoking (36%), alcohol consumption (32%), and pan masala use (13%) were also noted among the participants.

Table No.2: Distribution of Haemoglobin Levels among Study Participants

Haemoglobin (Hb) Levels	No. of Cases	Percentage (%)
Decreased	15	15.00%
Normal	85	85.00%
Total	100	100.00%

Table 2 presents the distribution of haemoglobin levels among the study participants. It was observed that 85% of participants had normal Hb levels, while 15% showed decreased haemoglobin levels. This finding suggests that a proportion of patients with oral submucous fibrosis had mild anaemia, which may have been associated with nutritional deficiency or chronic tobacco use.

Table No.3: Baseline Symptom Scores of Study Participants in ALA and Non-ALA Groups

Symptom	ALA Group	Non-ALA Group	Overall Mean
Burning	4.34	4.2	4.27
Dryness	4.02	3.98	4
Trismus	3.8	3.14	3.47
Blanching	4.06	4.38	4.22
Fibrous Bands	4.5	4.44	4.47
Tongue Movement Restriction	3.04	2.92	2.98
Stomatitis	3.94	4.08	4.01
Soft Palate	4.46	4.24	4.35
Inter-incisal Distance (cm)	1.564	1.776	1.67

Table 3 showed the baseline symptom scores in both groups before treatment. Burning sensation had a mean score of 4.34 in the ALA group and 4.20 in the non-ALA group, with an overall mean of 4.27. Dryness scores were nearly similar in both groups (ALA: 4.02, non-ALA: 3.98). Trismus was comparatively higher in the ALA group (3.80) than the non-ALA group (3.14), with an overall mean of 3.47. Blanching and fibrous bands were also reported with high baseline scores in both groups (overall means: 4.22 and 4.47, respectively). Restriction of tongue movement had lower baseline scores (overall mean: 2.98). Stomatitis scores were 3.94 in the ALA group and 4.08 in the non-ALA group, while soft palate involvement had an overall mean of 4.35. The mean inter-incisal distance was 1.564 cm in the ALA group and 1.776 cm in the non-ALA group, with an overall mean of 1.67 cm.

Table No.4: Comparison of Pre- and Post-Treatment Symptom Scores between ALA and Non-ALA Groups.

Symptom / Parameter		ALA Group (Mean ± SD)	Non-ALA Group (Mean ± SD)	p-value
Burning	Pre	4.34 ± 0.895	4.20 ± 0.904	0.438
	Post	1.54 ± 0.579	3.22 ± 0.790	0.001
Dryness	Pre	4.02 ± 0.892	3.98 ± 0.742	0.808
	Post	1.54 ± 0.579	3.22 ± 0.790	0.001

Trismus	Pre	3.80 ± 0.639	3.14 ± 1.010	0
	Post	1.76 ± 0.625	3.72 ± 0.497	0.001
Blanching	Pre	4.06 ± 1.038	4.38 ± 0.753	0.081
	Post	1.54 ± 0.579	3.22 ± 0.790	0.001
Fibrous Bands	Pre	4.50 ± 0.647	4.44 ± 0.541	0.616
	Post	1.76 ± 0.625	3.72 ± 0.497	0.001
Tongue Movement Restriction	Pre	3.04 ± 1.702	2.92 ± 1.602	0.717
Tongue Movement Restriction	Post	0.74 ± 0.899	2.72 ± 1.356	0.001
Stomatitis	Pre	3.94 ± 1.096	4.08 ± 0.900	0.487
	Post	0.76 ± 0.771	3.38 ± 0.697	0.001
Soft Palate	Pre	4.46 ± 0.579	4.24 ± 0.657	0.079
	Post	1.54 ± 0.579	3.22 ± 0.790	0.001
Inter-incisal Distance (cm)	Pre	1.564 ± 0.654	1.776 ± 0.587	0.091
	Post	3.24 ± 0.637	2.518 ± 0.610	0.001

Table 4 showed that baseline symptom scores were largely comparable between the ALA and non-ALA groups ($p > 0.05$). After treatment, however, the ALA group demonstrated significantly greater improvement across most parameters. Burning sensation, dryness, trismus, blanching, fibrous bands, tongue movement restriction, stomatitis, and soft palate involvement all showed highly significant reductions in the ALA group compared to the non-ALA group ($p = 0.001$). Inter-incisal distance also improved more in the ALA group (3.24 ± 0.637 cm) than in the non-ALA group (2.518 ± 0.610 cm, $p = 0.001$). These findings indicated that alpha lipoic acid provided superior symptomatic relief and improvement in mouth opening compared to standard therapy alone.

Table No.5: ***Distribution of Disease Grades Before and After Treatment in ALA and Non-ALA Groups***

Stage	**ALA Group (n=50)**	**Non-ALA Group (n=50)**	**Total**	**p-value**
Pre-treatment				
Grade 2	16	22	38	0.151
Grade 3	34	28	62	
Post-treatment				
Grade 1	36	7	43	0.0001
Grade 2	13	36	49	
Grade 3	1	7	8	

Table 5 showed the distribution of disease grades before and after treatment. At baseline, 38% of patients were Grade 2 and 62% were Grade 3, with no significant difference between the ALA and non-ALA groups (p = 0.151). After treatment, a majority of patients in the ALA group improved to Grade 1 (36/50, 72%), whereas only 7/50 (14%) in the non-ALA group achieved Grade 1. Higher grades persisted mainly in the non-ALA group. The post-treatment difference between groups was highly significant (p = 0.0001), indicating superior efficacy of alpha lipoic acid in disease regression.

DISCUSSION

OSMF continues to be a major oral health issue in India, primarily due to its strong association with areca nut and tobacco consumption and its potential for malignant transformation. Due to its high morbidity and significant risk of malignant transformation, continuous efforts have been directed toward developing more effective management strategies [4, 8]. In this study, ALA was evaluated as an adjunct to intralesional triamcinolone acetonide and hyaluronidase.

The demographic profile revealed that the majority of patients were within the 31–40-year age group (39%), followed by 41–50 years (27%), consistent with findings by Srivastava et al., [9] who also reported a peak prevalence in the 30–40-year range. Males accounted for a greater proportion of cases (83%) compared to females (17%), Similarly, Goel et al., [10] also noted male predominance (84%). This gender disparity may be attributed to higher rates of areca nut and tobacco consumption among men in Indian populations.

Habitual analysis demonstrated a strikingly high prevalence of tobacco use (95%) and betel nut chewing (73%), supporting observations made by Nilesh K et al. [11] and Ali H et al., [12] where nearly all patients reported some form of areca nut habit. The widespread availability and social acceptance of these products continue to be key contributors to the persistence of OSMF. A similar observation was reported by Daga et al., [13] in which all patients had a habit of gutka chewing, emphasizing the lack of awareness and easy availability of these products.

The distribution of haemoglobin levels among the study participants, showing that 85% had normal levels, while 15% exhibited mild anaemia. This indicates that a subset of patients with oral submucous fibrosis (OSMF) may experience reduced haemoglobin, likely linked to nutritional deficiencies or chronic tobacco use. In comparison, Karthik et al. [13] observed significantly lower mean Hb (10.85 mg/dL) and serum iron (55.53 µg/dL) levels in OSMF patients compared to controls. Contrary to this, Goyal et al. [8] reported that 96% of OSMF patients had normal routine investigations, with only 4% showing iron deficiency, suggesting that anaemia is generally uncommon in this condition. Moreover, Meena V [14] study suggested that decreased serum iron may serve as a predictor for disease progression and could have a potential link with oral carcinogenesis. While most OSMF patients maintain near-normal haematologic values, advancing

disease may predispose to iron deficiency and anaemia, emphasizing the need for early nutritional intervention.

Before treatment, both the ALA and non-ALA groups had similar severity of symptoms. After treatment, however, the ALA group demonstrated significantly greater improvement across most parameters. Burning sensation, dryness, trismus, blanching, fibrous bands, tongue movement restriction, stomatitis, and soft palate involvement all showed highly significant reductions in the ALA group compared to the non-ALA group.

This aligns with the research by Rao et al., [15] where all clinical parameters were significant in Group I (ALA group); however, in Group II (non-ALA group), only mouth opening and burning sensation showed a significant difference. The research conducted by Borle and Borle [16] hypothesized that, the administration of different drugs through intralesional injections may contribute to intensified fibrosis and significant trismus.

Regarding disease grades after treatment, a majority of patients in the ALA group improved to Grade 1 (72%), whereas only 14% in the non-ALA group achieved Grade 1. Higher grades persisted mainly in the non-ALA group. This post-treatment difference between groups was highly significant, indicating the superior efficacy of ALA in disease regression. Ak SK et al. [7] reported that the most significant change was observed by the 6th month visit, where only 2 cases reported a burning sensation compared to 8 in the control group. This suggests that ALA treatment had a substantial impact on reducing burning sensation over time, whereas the control group did not experience a similar reduction.

Rao et al. observed changes in disease stage from pre-treatment to post-treatment in the ALA group. Group I showed improvements in Stage I and Stage II with a statistically significant difference. They concluded that the antioxidant, ALA has a definitive protective role and can be recommended for clinical use. Shrinivas et al., [17] observed that Group I initially had limited mouth opening, which improved following treatment. Similarly, Groups II, III, and IV showed varying degrees of improvement in mouth opening post-treatment.

Overall, the results of this study reinforce the role of ALA as a valuable adjunct in OSMF treatment. Integrating ALA into therapy protocols may enhance patient outcomes, improve functional recovery, and potentially reduce disease progression. To the best of our knowledge, there is a lack of published literature on a universally accepted protocol and recommending an optimal pharmacological regimen for the treatment of OSMF, underlining a critical gap in current research.

CONCLUSION

The study concluded that alpha lipoic acid significantly improves clinical outcomes in patients with OSMF. Patients receiving ALA showed marked reductions in symptoms, along with a significant increase in inter-incisal distance, reflecting improved mouth opening. ALA is a safe and effective adjunctive therapy that,

when combined with standard intralesional treatment, can significantly improve patient outcomes and may play a key role in slowing disease progression. Further studies with larger sample sizes are required to validate these findings.

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