



Effectiveness of Triamcinolone and Hyaluronidase in Alleviation of Clinical Spectrum in Patients with Oral Sub Mucous Fibrosis

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Abstract

Introduction: The following study has discussed the efficacy of triamcinolone and hyaluronidase as well as its improvement in clinical features. Fibrosis of the tissue, precancerous lesions, and scarring of the tissue is caused by a persistent condition known as oral submucous fibrosis (OSMF) where buccal mucosa is the most prominent site to be affected.

Methods: The department of Otorhinolaryngology in our institution carried out a study in which sixty individuals were given injections of triamcinolone and hyaluronidase to determine the effectiveness of the drugs in treating OSMF. The study was carried out on patients who had already been diagnosed with OSMF.

Results: The bulk of the patients were ranging between 20 to 30 years with the majority falling into the former category. In comparison to the number of females, there was a preponderance of males. 48.3% of patients had symptoms for a period of less than a year. 45 percent of patients showed an increase in interincisal distance of between 1 and 5 millimeters, whereas 31 percent of patients showed no change in the distance. By the end of the 12-week follow-up period, 95% of patients showed significant improvement in mouth opening, 96.7% showed a reduction in the burning sensation, 93.3% showed a reduction in the blanching of the mucosa, and 81.7% showed a reduction in the amount of ulceration.

Conclusion: The study concludes that there is reduction in all the presenting symptoms of OSMF on treatment with triamcinolone and hyaluronidase. Moreover, statistical analysis has obtained more effective outcomes.

Keywords: Submucous Fibrosis; Triamcinolone; Hyaluronidase; Pre Cancerous; OSMF

Introduction

Oral sub mucosal fibrosis (OSMF) is a premalignant disorder affecting the oral cavity that results in tissue fibrosis and scar bands. One of the most frequently targeted sites for this condition is the buccal mucosa. Prominent pathogenic signs include localized muscle degeneration, increased collagen deposition, chronic inflammation, and inflammation of the deeper tendons and ligaments [1,2]. Patients with OSMF frequently experience an intense burning sensation on their lips after ingesting spicy food. Other potential indicators of OSMF include trismus, dry mouth, discomfort, altered taste, minimal tongue movement, and difficulty swallowing.

Its greater probability of malignant transformation (1.9-15.4%) raises the mortality rate [3,4].

The causes of OSMF include autoimmune disorders, deficiency of Vitamin C, B, and iron, consuming spicy foods, chewing betel nuts, human papillomavirus (HPV) infection, and genetic abnormalities [5]. According to epidemiological research, chewing betel nuts is one of the most significant risk factors, and the risk multiplies when betel nut and tobacco consumption are combined [6].

It is widely accepted that OSMF is a risk factor for oral cancer. A prior study found that patients with OSMF had a 1.21% likelihood

of developing oral cancer. This research was conducted in China. In contrast, it has been noted that 7.9% of OSMF patients in India develop oral cancer [7]. Previous research has identified a clear link between the onset of oral cancer and the duration of OSMF, as well as the degree of severity of its symptoms. Following an early OSMF diagnosis, oral cancer can show up three to sixteen years later [8].

Ingestion of betel nuts is the main cause of OSMF. Thick bands of collagen fibrils deposited beneath the epithelium, rete-peg formations, and other epithelial changes are all part of the histology of OSMF. At various OSMF phases, epithelial changes could vary from atrophy with hypoplasia to hyperplasia and/or dysplasia. Increased connective tissue fibrosis causes a change in epithelial compliance, which in turn encourages the onset of carcinomatous processes such as the epithelial-mesenchymal transition [5]. Oral ulceration, burning sensation, and restricted mouth opening are the most common initial symptoms of OSMF. The patient may experience difficulties as a result of these side effects, which interfere with daily activities. Following tissue damage, myofibroblasts differentiate into contractile and secretory cells in order to produce an extracellular matrix, and releases cytokines [9].

Molecular pathology techniques for diagnosing OSMF emphasize biomarkers that result in abnormal collagen deposition and include both noninvasive and invasive testing. The invasive detection method finds biomarkers in solid tissue and serum. The noninvasive method looks at the mucosa using optical instruments to find biomarkers in saliva [10].

Surgery and conservative procedures involving molecular technologies, are the main modality of treatment for OSMF.

Physical therapy

Carbon monoxide poisoning, gas gangrene, and decompression sickness are all treated with hyperbaric oxygen therapy (HBOT). By lowering the production of IL-1 β and TNF- α , HBOT promotes fibroblast death and reduces fibroblast activity. It also dampens the generation of several cytokines that promote inflammation, including IL-1, IL-6, and IL-10 which also reduces production of reactive oxygen substances. HBOT has a therapeutic impact because it exhibits anti-inflammatory & antioxidant properties, which possess fibroblast activity characteristics [11].

Drug therapy

The main objectives of pharmacological therapy for OSMF are extracellular matrix breakdown and anti-inflammation. The effects of methylprednisolone, betamethasone, and dexamethasone are comparable to those of glucocorticoids. When given intralesionally, synthetic corticosteroids significantly enhance mouth opening and decrease burning in OSMF patients. Extracellular matrices like collagen and hyaluronan are broken down by the proteolytic enzymes chymotrypsin and hyaluronidase. When treating OSMF, they are usually administered alongside corticosteroids [12].

A xanthine derivative called pentoxifylline is utilized primarily to lessen muscle discomfort. It limits leukotriene production, inhibits phosphodiesterase and TNF- production in mononuclear cells induced by lipopolysaccharide (LPS), and reduces the inflammatory process. Pentoxifylline increases mouth opening and decreases burning sensation, thereby alleviating clinical symptoms encountered in OSMF [13].

Every buccal mucosal lesion received a 1500 IU hyaluronidase infusion, and patients with OSMF received an additional weekly dose of 0.5 mg of oral allopurinol administered twice daily. The burning sensation subsided, the mouth opening improved, and the histology markers decreased after the second week. Patients with grade II OSMF who had weekly injections of 0.5 mL of lignocaine hydrochloride in addition to the indicated dosages reported less burning and boosted mouth opening after 12 weeks [14].

Materials and Methods

Study design

Total count of 60 individuals were enrolled in a hospital-based prospective study to assess if triamcinolone and hyaluronidase injections improved the signs and symptoms of OSMF patients. The study was conducted on OPD/IPD patients and was carried out in the otorhinolaryngology department at our tertiary care center. All patients underwent routine evaluations for HIV, HBs Ag, hemoglobin, total and differential counts, and red blood cells. To measure mouth opening the Vernier caliper inter incisor distance was first employed. Triamcinolone 40 mg/ml submucous injection and injection of hyaluronidase 1500 IU were delivered subcutaneously to the buccal mucosa and white fibrotic bands. A follow-up was conducted during this procedure on a weekly basis for eight weeks, in

addition to the tenth and twelfth weeks following the final injection.

Inclusion and exclusion criteria

Individuals with a clinical diagnosis of oral sub mucous fibrosis who chew areca nut or any of its derivatives were included in the study, participants who were between the ages of 20 and 50 years and who gave informed consent for the study were included in the research study.

The study excludes patients who were younger than 20 years or older than 50 years, patients diagnosed with OSMF that has advanced into malignancy, patients diagnosed with any other malignancies such as head and neck cancer or oral cancer, patients who additionally presented with decreased mouth opening because of other conditions such as TMJ perichondritis, and subjects who are currently undergoing any other treatments or drug therapies for OSMF.

Statistical analysis

Mean and Standard deviation are used to present quantitative data. Using the findings of the normality test, an unpaired t test is used to compare the research groups. A percentage and frequency table is used to convey qualitative data. The Fisher test, student t test, and Chi-Square test are used to determine whether there is any relationship between the research groups. P value of 0.05 or less is considered significant in this study.

Results

In this research study, the following statistical analysis was conducted among 60 participants. According to Table 1, 60% of the participants were in the age group of 20-30-year-olds, 31.7% were in the age group of 31 to 40, and 8.3% were in the age group of 50. A significant number of the patients were in the age group of 20 to 30 years, followed by 31 to 40 years, and finally 41 to 50 years. There are a total of sixty people included in the sample. The average age of the participants was 29.87 years, with a standard deviation of 7.02 years.

On the other hand, a discussion about the sex distribution of the participants is included in table 2. The study sample had a total of 68.3% males and 31.7% females, with 41 males and 19 females re-

Age (years)	N	%
20-30 years	36	60%
31-40 years	19	31.7%
41-50 years	5	8.3%
Total	60	100%
Mean ± SD	29.87 ± 7.02	

Table 1: Distribution of patients according to Age.

spectively. The M:F ratio is given as 2.16:1, which means that for every 2.16 males, there is 1 female in the sample. The results suggest that the sample has more males, as they constitute a significantly larger proportion of the sample than females.

Table 3 demonstrates the average length of symptoms which

Sex	N	%
Male	41	68.3%
Female	19	31.7%
Total	60	100%
M:F Ratio	2.16:1	

Table 2: The distribution of patients by sex.

shows less than one year in 29 (48.3%) individuals, 1-3 years and more than three years in 27 (45%) and 4 (6.7%) patients, respectively. 48.3% of patients experienced symptoms for less than a year and the least duration of symptoms seen for less than 3 years.

Duration of Symptoms	N	%
<1 year	29	48.3%
1-3 years	27	45%
>3 years	4	6.7%
Total	60	100%

Table 3: Patient distribution based on the length of symptoms.

On another side table 4 showed the comparison with the increase in interincisal distance. By the end of the 12-week follow-up phase, 19 patients, or 31.7% of the total, did not show any signs of an increase in the space between their interincisal teeth. 27 patients, or 45%, had an increase in interincisal distance of between 1 and 5 millimetres, whereas 12 patients, or 20%, and 2 patients, or 3.3%, had increases of 6 to 10 millimetres or more, respective-

ly. The Chi-Square test revealed that there was a statistically significant increase (p 0.05) in the inter-incisal distance during the course of the follow-up period.

Furthermore, table 5 showed comparison with improvement in mouth opening. On completion of treatment and the 12-week follow-up phase, 57 patients or 95% of study participants were able to open their mouth and only three patients were still unable

Inter- incisal distance	Time of presentation	1 week	2 weeks	3 weeks	4 weeks	5 weeks	6 weeks	7 weeks	8 weeks	10 weeks	12 weeks	P Value
1-5 mm	5	5	8	9	13	16	22	24	25	28	27	<0.05
6-10 mm	0	1	1	3	4	5	5	7	10	10	12	
>10 mm	0	0	0	0	0	0	1	1	1	2	2	
No increase	55	54	51	48	43	39	32	28	24	20	19	
Total	60	60	60	60	60	60	60	60	60	60	60	

Table 4: Comparison of Increase in inter-incisal distance during follow-up period.

Improvement in mouth opening	Time of presentation	1 week	2 weeks	3 weeks	4 weeks	5 weeks	6 weeks	7 weeks	8 weeks	10 weeks	12 weeks	P Value
Yes	9	10	12	16	21	27	30	35	42	49	57	<0.05
No	51	50	48	44	39	33	30	25	18	11	3	
Total	60	60	60	60	60	60	60	60	60	60	60	

Table 5: Comparison of Improvement in mouth opening during follow-up period.

to open their mouth completely. The Chi-Square test revealed that there was a statistically significant increase in mouth opening during the subsequent follow-up period (p less than 0.05).

At the end of the 12-week follow-up period, burning sensation was lowered in 58 (96.7%) patients, which was decreased in just 3 patients before beginning of the treatment; however, the symptom remained in 2 (3.3%) persons after the therapy. According to the findings of the Chi-Square test, which were statistically significant at the 0.05 level, the sensation of burning diminished noticeably over the follow-up phase as shown in table 6.

On the other hand, approximately 59 patients presented with mucosal blanching prior to the beginning of therapy. By the end of the 12-week follow-up phase, only 4 patients had persistent mucosal blanching, which demonstrates a decline in mucosal blanching post treatment. The Chi-Square test showed that throughout the follow-up period, there was a significant reduction in mucosal blanching. This reduction was statistically significant (p 0.05) (Table 7).

Table 8 showed the comparison of decrease rate of Ulceration during the follow up period. By the time 12-week follow-up phase was over ulceration had improved in 49 patients. This supports that the treatment was successful in lowering the severity of ulceration in a greater number of patients. The Chi-Square test showed that there was a significant lower incidence of ulceration throughout the length of the follow-up period. This reduction was statistically significant p less than 0.05 as shown in Table 8.

Discussion

A potentially malignant disorder of the oral mucosa known as oral submucous fibrosis (OSMF) mostly affects individuals in South and Southeast Asia. It has been demonstrated that the combination of oral colchicine and injection hyaluronidase improved mouth opening and burning sensation while having no discernible adverse effects [15].

Oral submucous fibrosis is a common premalignant condition caused by ingesting areca nuts and other irritants in various forms. Considering the fact that hyaluronidase and hydrocortisone

Blanching of mucosa	Time of presentation	1 week	2 weeks	3 weeks	4 weeks	5 weeks	6 weeks	7 weeks	8 weeks	10 weeks	12 weeks	P Value
Absent	1	3	8	13	20	27	34	41	46	50	56	<0.05
Present	59	57	52	47	40	33	26	19	14	10	4	
Total	60	60	60	60	60	60	60	60	60	60	60	

Table 7: Comparison of Blanching of oral mucosa during follow-up period.

Decrease in Ulceration	Time of presentation	1 week	2 weeks	3 weeks	4 weeks	5 weeks	6 weeks	7 weeks	8 weeks	10 weeks	12 weeks	P-Value
Yes	2	4	7	9	13	19	24	30	37	42	49	<0.05
No	58	56	53	51	47	41	36	30	23	18	11	
Total	60	60	60	60	60	60	60	60	60	60	60	

Table 8: Comparison of Decrease in Ulceration during follow-up period.

acetate are the ideal formulations for its medical management, its standardization is yet to be achieved. The weekly intervals between injections were a drawback with this current treatment strategy. We compared the efficacy of weekly hydrocortisone acetate and hyaluronidase with 15-day intervals of triamcinolone acetonide and hyaluronidase in a research investigation. There was no statistically significant difference in the two groups’ symptom scores or histological improvement in terms of sign score. Due to the more affordable price and reduced scheduled visits, patients regarded triamcinolone acetonide/hyaluronidase therapy to be more comfortable. There were no adverse effects noted as well [16].

Chewing areca nut and other irritants can cause oral submucous fibrosis (OSMF), a chronic, complex, and possibly premalignant condition. Juxta-epithelial development of fibrous tissue in the buccal mucosa and pharynx marks this stealthy process. At the moment, OSF is spreading throughout Southeast Asia, North America, and Europe. The objective of the study is to compare the efficacy of intralesional injections of triamcinolone and hyaluronidase with one another, as well as intralesional injections of triamcinolone with injectable hyaluronidase and oral colchicine. Two study groups. Group A and B, were established. Patients in group A received intralesional injections of hyaluronidase, 2% lidocaine, and triamcinolone acetonide. For three months, Group B received intralesional administration of trimethoprim-acetonide, hyaluronidase 1500 IU in 2 ml, 2% lidocaine, and oral colchicine 0.5 mg twice a day. Patients in Group B improved significantly more, with improvements in mouth widening and a reduction in burning discom-

fort. The Group B therapy regimen produces greater improvements in mouth opening and burning within the oral cavity. No adverse consequences were reported by the members of either group [17].

In a previous study, the effectiveness of topical curcumin mucoadhesive semisolid gel, external triamcinolone acetonide/hyaluronidase muco adhesive semisolid gel, and a combination of both was evaluated in the treatment of oral submucous fibrosis (OSMF). Each participant in groups I, II, and III received a single mucoadhesive semisolid gel containing curcumin, triamcinolone acetonide, hyaluronidase, or a combination of all three. The group that received the three medication combinations was shown to have the most wide mouth opening when compared to the other two groups. It was noted that the triamcinolone & hyaluronidase group experienced less burning on the VAS than the other two groups. It must have been discovered that, in comparison to groups I and II, group III pharmaceutical therapy showed a larger change in mucosa coloration. Therefore, we can determine whether curcumin can benefit those with OSMF. Two more potent medications, trimetidine and hyaluronidase, were incorporated together to maximize consumption and to improve drug delivery [18].

Oral sub mucous fibrosis (OSMF) affects the mouth and teeth; it is a chronically uncomfortable condition that may be malignant. The entire oral cavity is impacted, and the illness can often be persistent, leading to a reduction in mouth opening that can eventually reach the pharynx. Placental extract or locally administered corticosteroid injections at appropriate concentrations can be some-

what helpful, even in the absence of complete systematization in medical care. Nevertheless, a topical hyaluronidase and steroid combination shows better results than any single treatment. On further examination post treatment, oral mucosal blanching, excruciating ulcers, and burning sensations have all significantly decreased. Henceforth, dexamethasone with hyaluronidase injection is an efficient way to treat Grade III OSMF, and it may even be able to completely reduce the morbidity related to surgical care [19].

Conclusion

Oral sub mucous fibrosis is a precancerous condition of the oral mucous membrane. It is solely related to lifestyle habits, which can be avoided through implementing new lifestyle choices. Symptoms improve after receiving injections of hyaluronidase and triamcinolone. There is an improvement in the interracial distance, a decrease in ulceration, a reduction in the burning sensation of the oral mucosa, an increase in mouth opening, and a decrease in tissue blanching. According to this study, there are no negative effects from using these medications and the symptoms of oral sub mucous fibrosis were significantly alleviated.

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