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Original Research

Effectiveness of oral colchicine with intralesional hyaluronidase and triamcinolone acetonide in patients with OSMF

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ABSTRACT:
Background: Oral Submucous Fibrosis (OSF) is a chronic condition almost exclusively occurring among Indians and to a lesser extent in the other Asiatic people. The present study was conducted to compare effectiveness of oral colchicine with intralesional injection of hyaluronidase or injection triamcinolone acetonide in patients with OSMF. **Materials & Methods:** 36 clinically and histologically confirmed cases of OSMF were divided into 2 groups of 18 each. Group I were treated with tablet colchicine 0.5 mg twice daily with an intralesional injection of hyaluronidase 1500 IU with 0.5 ml of lignocaine hydrochloride at weekly interval for 12 weeks. Group II patients were treated by administering tablet colchicine 0.5 mg twice daily with an intralesional injection of triamcinolone acetonide 10 mg/ml at weekly interval for 12 weeks. Outcome assessment was done pre- operatively and post- operatively. **Results:** Group I had 12 males and 6 females and group II had 11 males and 7 females. Pre- op and post- op blanching was seen in 18 and 12 and 18 and 14 in group I and group II respectively. Burning sensation was seen in 17 and 10 in group I and 16 and 12 group II pre- op and post- op respectively. Ulceration was present in 15 and 8 in group I and 17 and 10 in group II pre- op and post- op respectively. Limited mouth opening was seen in 17 and 9 and 18 and 11 in group I and II pre- op and post- op respectively. The difference was significant (P< 0.05). **Conclusion:** Both combination of drugs was effective in management of OSMF cases. Colchicine in addition with hyaluronidase resulted in superior results.
Key words: Colchicine, Hyaluronidase, OSMF.

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INTRODUCTION

Oral Submucous Fibrosis (OSF) is a chronic condition almost exclusively occurring among Indians and to a lesser extent in the other Asiatic people. However, with the increase in immigration of people from the Indian subcontinent, dental professionals in many developed countries will encounter this disease in the near future.[1]

Oral submucous fibrosis (OSF) is a chronic disease that produces scars, tissue fibrosis, and precancerous lesions. It frequently occurs in the buccal mucosa.[2] Pathological characteristics include chronic inflammation, excessive collagen deposition in the connective tissues below the oral mucosal epithelium, local inflammation in the lamina propria or deep connective tissues, and degenerative changes in the muscles. OSF patients experience a severe burning sensation in the mouth after ingesting spicy foods. Other symptoms of OSF include dry mouth, pain, taste disorders, restricted tongue mobility, trismus, dysphagia, and altered tone. This disease contributes significantly to mortality because of its high malignant transformation rate (1.5–15%).[3]

A wide range of treatment including drug management, surgical therapy, and physiotherapy have been attempted till date, with varying degrees of benefit, but none have been able to cure this disease. Colchicine is an alkaloid chemically known as colchicinum-N- (5,5,79-Tetrahydro-1,2,310-tetramethoxy-9- oxobenzo [alpha] heptalen-7-yl) acetamide.[4] Various studies have established the role of colchicine as an antifibrotic agent by inhibiting collagen synthesis and increasing collagenolytic activity. It has been used in reducing fibrosis in liver and kidney diseases. Besides, it also has some anti-inflammatory properties. This anti-inflammatory

property is related to drug's effect on polymorphonuclear leukocytes and monocyte chemotaxis, leukocyte adhesiveness, and also its effect on prostaglandin E, which suppresses the leukocyte function.[5] The present study was conducted to compare effectiveness of oral colchicine with intralesional injection of hyaluronidase or injection triamcinolone acetonide in patients with OSMF.

MATERIALS & METHODS

The present study was conducted among 36 clinically and histologically confirmed cases of OSMF of both genders. All were informed regarding the study and their consent was obtained.

Data such as name, age, gender etc. was recorded. Patients were divided into 2 groups of 18 each. Group I were treated with tablet colchicine 0.5 mg twice daily with an intralesional injection of hyaluronidase 1500 IU with 0.5 ml of lignocaine hydrochloride at weekly interval for 12 weeks. Group II patients were treated by administering tablet colchicine 0.5 mg twice daily with an intralesional injection of triamcinolone acetonide 10 mg/ml at weekly interval for 12 weeks. Clinical diagnosis was based on burning sensation in mouth, blanching of mucosa, presence of vesicles or ulceration in oral cavity, and reduced mouth opening. Outcome assessment was done pre-operatively and post- operatively. Results thus obtained were subjected to statistical analysis. P value less than 0.05 was considered significant.

RESULTS

Table I Distribution of subjects

Groups	Group I	Group II
Method	Colchicine 0.5 mg+ Inj hyaluronidase	Colchicine 0.5 mg+ inj triamcinolone acetonide
M:F	12:6	11:7

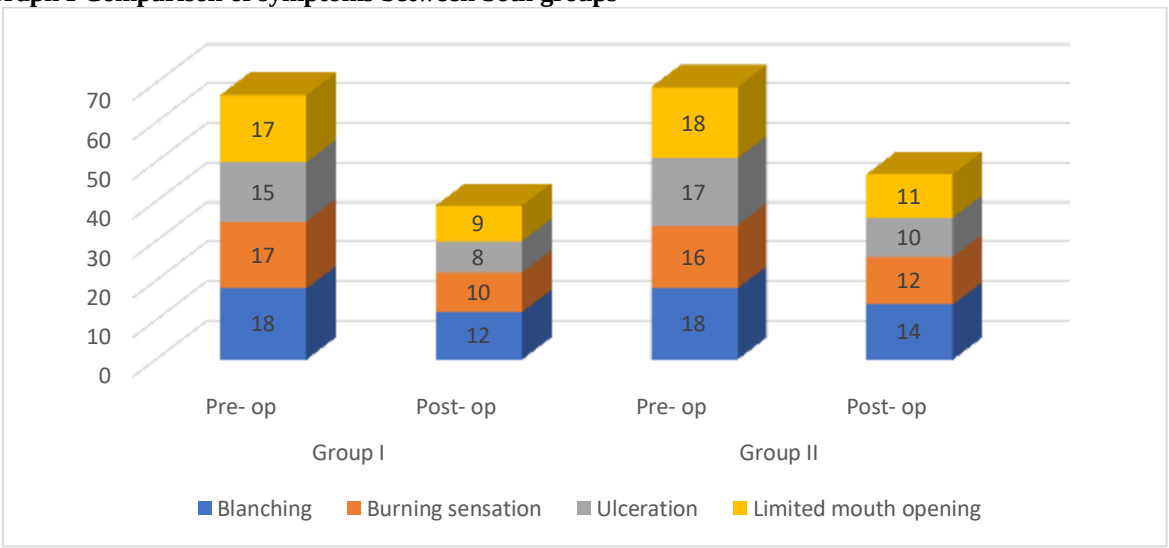
Table I shows that group I had 12 males and 6 females and group II had 11 males and 7 females.

Table II Comparison of symptoms between both groups

Symptoms	Group I		Group II		P value
	Pre- op	Post- op	Pre- op	Post- op	
Blanching	18	12	18	14	0.01
Burning sensation	17	10	16	12	0.02
Ulceration	15	8	17	10	0.04
Limited mouth opening	17	9	18	11	0.05

Table II, graph I shows that pre- op and post- op blanching was seen in 18 and 12 and 18 and 14 in group I and group II respectively. Burning sensation was seen in 17 and 10 in group I and 16 and 12 group II pre- op and post- op respectively. Ulceration was present in 15 and 8 in group I and 17 and 10 in group II pre- op and post- op respectively. Limited mouth opening was seen in 17 and 9 and 18 and 11 in group I and II pre- op and post- op respectively. The difference was significant (P< 0.05).

Graph I Comparison of symptoms between both groups



DISCUSSION

Oral submucous fibrosis (OSMF) is a chronic, complex, irreversible precancerous condition characterised by juxta-epithelial inflammatory reaction and progressive fibrosis of the submucosal tissue i.e. lamina propria and deeper connective tissue.[6] Oral submucous fibrosis is a chronic disease affecting the oral mucosa, as well as the pharynx and the upper two-thirds of the esophagus. There is substantial evidence that lends support to a critical role of areca nuts in the etiology behind oral submucous fibrosis. Causative factors of OSF include autoimmunity, vitamin B, C, and iron deficiencies, chewing betel nut, consumption of spicy foods, human papilloma virus (HPV) infection, and genetic mutations.[7] Epidemiological studies have shown that chewing betel nut is one of the most significant risk factors for OSMF. Among OSF patients in China, 62.3% have the habit of chewing betel nuts. Certain studies also reported that habits such as chewing and smoking tobacco and drinking alcohol increase the risk of OSMF.[8] The present study was conducted to compare effectiveness of oral colchicine with intralesional injection of hyaluronidase or injection triamcinolone acetonide in patients with OSMF.

In present study, group I had 12 males and 6 females and group II had 11 males and 7 females.

Daga et al[9] included 30 patients of clinically diagnosed Grade II OSMF. Patients were divided randomly into two groups: Group A patients were treated by administrating tablet colchicine and intralesional injection of hyaluronidase and group B patients were treated by administering tablet colchicine and intralesional injection of triamcinolone acetonide. Results showed improvement in mouth opening and reduction in burning sensation was seen more in Group A patients. Improvement in blanching of mucosa was seen in both the groups.

We observed that pre- op and post- op blanching was seen in 18 and 12 and 18 and 14 in group I and group II respectively. Burning sensation was seen in 17 and 10 in group I and 16 and 12 group II pre- op and post- op respectively. Ulceration was present in 15 and 8 in group I and 17 and 10 in group II pre- op and post- op respectively. Limited mouth opening was seen in 17 and 9 and 18 and 11 in group I and II pre- op and post- op respectively.

Colchicine has been shown to inhibit collagen synthesis. It has been reported that colchicine inhibited procollagen secretion and its conversion to collagen and thus specifically inhibited collagen synthesis.[10] It disrupts the microtubule formation and inhibits microtubule polymerization by binding to tubulin. Colchicine also exerts an anti-inflammatory effect by its destabilizing action on microtubules.[11] It blunts the tumor necrosis factor alpha (TNF-α)-induced activation of macrophages and diminishes the number of TNF-α receptors on the surface of macrophages and endothelial cells. It also interrupts the mast cell degranulation process, thus preventing the release of inflammatory mediators. The correlation of TNF-α levels with the severity of OSMF has been recognized.[12]

Krishnamoorthy et al[13] in their study fifty OSF patients were divided randomly into two groups and treated for 12 weeks. Group 1-Patients were administered tablet colchicine orally, 0.5 mg twice daily and 0.5 ml intralesional injection Hyaluronidase 1,500 IU into each buccal mucosa once a week. Group 2-Patients were administered 0.5 ml intralesional injection Hyaluronidase 1,500 IU and 0.5 ml intralesional injection Hydrocortisone acetate 25 mg/ml in each buccal mucosa once a week alternatively. Thirty-three percent in group 1 got relief from burning sensation in the second week. Inter group comparisons of increase in mouth opening and reduction in histological parameters indicated that group 1 patients responded better than group 2.

Colchicine, with its anti-inflammatory and antifibrotic action, has been used in reducing fibrosis in liver and renal diseases. The use of colchicine in OSMF has been reported by very few studies till date. At a minimal dose of colchicine of 0.5 mg orally, no side effects were noticed.[14] The combination of colchicine with hyaluronidase is beneficial due to the different mechanisms of action of both drugs which leads to additive effect. Besides, addition of colchicine with other drug gives the advantage of low dose of colchicine used and thus decreased toxicity.[15]

CONCLUSION

Authors found that both combination of drugs were effective in management of OSMF cases. Colchicine in addition with hyaluronidase resulted in superior results.

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