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Original Research Article

Comparing the efficacy of lycopene & lycopene with hyaluronidase in management of oral sub mucous fibrosis-A clinical study

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ABSTRACT

Introduction: Oral submucous fibrosis (OSMF) is a scarring disease of the oral cavity that develops over time. Lycopene is a potent antioxidant found in tomatoes that has the best singlet oxygen quenching capability and a strong capacity to quench other free radicals in vitro of all the dietary carotenoids. A protein called hyaluronidase, which is found in mammalian sperm and testes, hydrolyzes hyaluronic acid to alter the permeability of connective tissue.

Objective: To determine the effectiveness of lycopene and lycopenehyaluronidase in treating OSMF, as well as a comparison of their effectiveness.

Materials and Methods: 45 people with OSMF were enrolled in the study and divided into three groups. Patients in Group A received two evenly divided doses of Lycored 16 mg twice daily for three months. Patients in Group B received LycoRed and a 1500 IU intralesional injection of hyaluronidase twice a week for three months. Patients in Group C received placebo pills. The patients were evaluated at the end of three months. We observed the opening of the mouth, visual examination, palpatory findings, and burning sensation.

Results: For lycopene and lycopene–hyaluronidase combination, there was a statistically significant difference in mouth opening and burning sensation compared to placebo.

1. Introduction

Oral submucous fibrosis (OSMF) is a persistent, scarring oral condition.OSMF was once assumed to be a disorder exclusive to the Indian subcontinent, China, and other Asian regions, but it is now recognised to be a global issue due to rise in the number of migrant populations suffering from it. Several therapy options have emerged over time, but no single cure has been discovered to date.[1]

A potent antioxidant found in tomatoes, lycopene is produced via the Lyc-O-Mato technique, preserving its natural proportions with other substances in commercially available pharmaceutical forms.[2] Lycopene has the greatest ability to inactivate singlet oxygen and other free radicals in vitro out of all the dietary carotenoids.[3] The adverse relationship between lycopene intake and cancer risk has been demonstrated, particularly for cancers of the prostate, pancreas, bladder, cervix, and oral leukoplakias because of its capacity to alter dysplastic modifications.[3,4] In addition to its antioxidant effect, lycopene's anticancer activity is also attributed to the overexpression of connexin

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and the activation of gap junctional communication.[5,6] By hydrolyzing hyaluronic acid, a polysaccharide found in the intercellular ground substance of connective tissue, hyaluronidase, an enzyme produced from mammalian testes and sperm, alters the permeability of connective tissue. Hyaluronidase produces longer-lasting advantages when combined with steroid preparations than either drug does when used alone. When employing hyaluronidase injections, improvements in mucous membrane health, burning sensation, and trismus were seen.[7] In this study, the efficacy of lycopene and lycopene–hyaluronidase combination was evaluated and compared in the treatment of OSMF.

2. Materials and Methods

Total 48 patients were included in our study after undergoing clinical evaluation, investigation, and biopsy and who had stage 2 OSMF (as defined by More et al.).[8] There were three groups, each with 16 patients. For three months, patients in Group A given capsule Lycostar, a 100 percent natural lycopene supplement, twice daily in equal quantities from Mankind Pharmaceuticals in India. Additionally, Lycostar includes phytonutrients, zinc, and selenium. Patients in Group B who were taking Lycostar were given an intralesional injection of 1500 IU of hyaluronidase (Hynidase; Rallis India Ltd, Mumbai, India) twice a week for three months. Patients in Group C received placebo pills. Patients were evaluated after three and six months. We consider the mouth opening characteristics, palpatory results, and burning feeling. A vernier calliper was used to measure the interincisal distance, which was used to evaluate how wide open the mouth was, and a visual analogue scale was used to evaluate the burning sensation. Complete, partial, stable, illness progression, and complications were used to categorise the responses [Table 1]. Muscle exercise and cessation of the habit were common to all groups.

3. Result

Nine patients out of 48 were lost to follow-up, three from each of the three groups. To assess the efficiency of the treatment, an unpaired t test was employed. The mouth opening and burning sensation were statistically different between the lycopene and lycopene-hyaluronidase groups and the placebo group. [Tables 2 and 3]. Lycopene-hyaluronidase combination group did not substantially differ from lycopene alone in terms of burning sensation, visual findings, or palpatory results despite a change in mouth opening. [Table 4].

In contrast to the control group's increased mouth opening of 46.2%, the lycopene and lycopene-hyaluronidase groups displayed a 100% response after treatment. While the lycopene group as a whole responded only partially to the burning sensation, the lycopene-hyaluronidase combination demonstrated a full response.

In the createria of burning sensation, 100% of the lycopene group showed a partial response, whereas lycopene-hyaluronidase combination showed a complete response in 7.2 percent of cases and a partial response in the remaining cases. Control patients had a 38.5 percent partial response rate, a 30.8 percent stable response rate, and a 30.8 percent progression rate.

4. Discussion

Lycopene acts by lowering reactive oxygen species, it reduces the inflammatory response found in OSMF and changes the expression of specific genes that are important for both collagen synthesis and collagen breakdown.[9] Additionally, it boosts lymphocyte stress resistance and reduces the inflammatory response. The enzyme hyaluronidase is crucial in altering tissue permeability. In our study. Hyaluronidase with lycopene produced improved results when compared to lycopene, but this difference was not statistically significant.

There are numerous studies that have evaluated mouth opening in OSMF after lycopene use. The maximal mouth opening improved in 69.56 percent of the individuals, which was evidence that lycopene was successful in lowering the objective indications of OSMF, according to a 2007 study by Kumar et al.[10] and a subsequent investigation by Karemore and Karemore.[11]

A statistically significant difference between the lycopene and lycopene-hyaluronidase combinations and the control was also found in our research. When compared to lycopene, lycopene-hyaluronidase did not show a statistically significant change in mouth opening. The primary cause of the burning sensation in OSMF is epithelial atrophy, which results from juxtaepithelial inflammation, increased fibrosis, and weakened vasculature. Lycopene is essential for reducing fibrosis and inflammation, which promotes the regeneration of the epithelium and lessens burning pain. The combination of lycopene and hyaluronidase reduced the burning feeling on average more than lycopene alone, but the difference was not statistically significant. Similar neither lycopene nor lycopene-hyaluronidase combo changed the visual and palpatory findings and most of these changes appeared irreversible.

Sunderraj et al. study[12] indicated that 20% constant response rate and an 80% full response rate based on comparable criteria. According to our research, treating OSMF with lycopene alone resulted in a considerable increase in mouth opening and a reduction in burning sensation, however treating OSMF with lycopene plus hyaluronidase only produced somewhat better effects that, overall, were not statistically significant. Nine study participants were lost to follow-up, which was one of the

Table 1: Posttreatment assesment criteria

Posttreatment response	Visual and palpatory findings	Burning sensation	Mouth opening
Partial	Reduction in stage but not to stage 1	Reduction in grade without complete resolution (VAS)	Increase in the mouth opening that ranging from 0.4 to 1 mm
Complete	Shift to stage 1	Burning sensation is completely absent that is shift to grade 0 (visual analog scale [VAS])	Increase in the mouth opening that ranging from 2 to 3 mm
Disease progression	There is increase in stage	There is increase in grading (VAS)	Decrease in the mouth opening

Table 2: Variation (mean) of burningsesation,mouth opening, and visual and palpatory finding between lycopene & Control group.

	Group	N	Mean	Standard deviation	P value
Burning sensation	Lycopene only	13	2.7689	0.84314	P < 0.0001
	Control	13	0.7592	0.86341	
Change in mouth opening	Lycopene only	13	2.6243	0.85863	0.002
	Control	13	1.1989	1.08184	
Visual and palpatory findings	Lycopene only	13	0.069	0.2695	0.316
	Control	13	0.000	0.000	

Table 3: Variation (mean) of burningsesation,mouth opening, and visual and palpatory finding between lycopene & Control group.

	Group	N	Mean	Standard deviation	P value
Burning sensation	lycopene–hyaluronidase	13	3.2986	0.95076	P < 0.0001
	Control	13	0.0775	0.87241	
Change in mouth opening	lycopene–hyaluronidase	13	3.3921	1.03481	P < 0.0001
	Control	13	1.2407	1.08184	
Visual and palpatory findings	lycopene–hyaluronidase	13	0.149	0.3824	0.149
	Control	13	0.000	0.000	

Table 4: Variation (mean) of burningsesation,mouth opening, and visual and palpatory finding between lycopene & lycopene–hyaluronidase combination

	Group	N	Mean	Standard deviation	P value
Burning sensation	Lycopene only	13	2.8121	0.82905	0.094
	lycopene–hyaluronidase	13	3.2732	0.97068	
Change in mouth opening	Lycopene only	13	2.5284	0.86863	0.053
	lycopene–hyaluronidase	13	3.2935	1.13283	
Visual and palpatory findings	Lycopene only	13	0.086	0.2885	0.6558
	lycopene–hyaluronidase	13	0.149	0.4123	

study's minor flaws. The long-term effects of hyaluronidase have been shown in prior studies, but they could not be assessed in the current study also.

5. Conclusion

Thus we reach on the conclusion that Lycopene appears to be a very promising antioxidant for treating OSMF. Given the paucity of studies on the use of lycopene to treat oral premalignant lesions, diseases, and cancer, additional study with larger sample sizes and longer follow-up is required to both confirm its efficacy and determine the maximum amount of lycopene that may be used safely. Even though hyaluronidase did not have a statistically significant impact, more analysis and research are still required.

6. Conflict of Interest

The authors declare no relevant conflicts of interest.

7. Source of Funding

None.

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