



Effect of Lycopene on Signs in Patients with Different Stages of Oral Cancer

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Abstract

Background: Oral cancer is a major problem in the Indian subcontinent where it ranks among the top three types of cancer in the country and is eighth most common cancer worldwide. It is often preceded by precancerous or premalignant lesions, and conditions such as- Leukoplakia, Erythroplakia and Oral sub mucosal fibrosis.

Materials and Methods: A total of 142 patients who presented with clinical signs and symptoms of premalignant and malignant Stages of Oral Cancer were enrolled in the study. However, of which, 39 patients were excluded due to- patients expired (n=5); not reported for the next follow up (n=23); posted for radiation (n=2) and for surgery (n=9); during the study period. After exclusion of above 39 patients, 103 patients were eligible to include in the study, of them which, 88 were males and 15 were females.

Results: Socio demographic data of the patients:

In the present study, amongst 103 eligible patients, 88 (85.43%) were males and 15 (14.56%) were females. Majority of the patients were uneducated that constituted 70.87% (n=73) while educated patients was 29.12% (n=30). And also, 67.96% (n=70) of patients were identified from rural area and rest of 32.04% (n=33) from urban area.

Conclusion: In the present study, substantial improvement and decrease in disease severity was observed with selected (Lycopene) antioxidant therapy in different stages of oral cancer patients. Thus, antioxidants are overall favorable for early cases of oral premalignant lesions and conditions to cease and delay the disease progression.

Keywords: Anti oxidant, Lycopene, Oral cancer.

Introduction

Oral Cancer in different regions of the world, with the age-adjusted rates varying from over 20 per

100,000 populations in India, to 10 per 100,000 in the U.S.A, and less than 2 per 100,000 in the Middle East^[1]. Oral Cancer encompasses

neoplastic lesions involving the Lip, Oral cavity and Oropharynx thereby, the vast majority of these lesions are Squamous Cell Carcinomas. "Oral Cancer" can be divided into three categories: a) Carcinomas of the Oral cavity proper b) Carcinomas of the lip vermilion c) Carcinomas arising in the Oropharynx. Oral Cancer is often preceded by precancerous or premalignant lesions and conditions such as Leukoplakia, Erythroplakia and Oral Sub Mucosal Fibrosis (OSMF)^[2]. WHO defined Leukoplakia as a white patch or plaque that cannot be characterized clinically or pathologically as any other disease^[3]. WHO defined Erythroplakia as a fiery red patch that cannot be characterized clinically or pathologically as any other definable disease. It is much less common than Leukoplakia but it has the greatest potential for malignant transformation. Erythroplakia is often flat with a smooth or granular surface^[4]. OSMF is a chronic disorder characterized by fibrosis of the mucosal lining of the upper digestive tract involving the Oral cavity, Oropharynx and frequently the upper third of the Oesophagus^[5]. The major risk factors are Tobacco (both smoked and smokeless forms), betel quid chewing and Alcohol. More than 4000 different chemicals are found in Tobacco and Tobacco smoke. More than 60 of these chemicals are known to cause cancer. Antioxidants may be regarded as those substances which will significantly delay or inhibit the oxidation of a substance and protect the body against oxidative damage. Insufficient levels of antioxidants or inhibition of antioxidant enzymes causes oxidative stress and damage or kills the cells. The antioxidants act by breakage of chain reaction, reducing concentration of reactive oxygen species, scavenging initiating radicals, chelation of transition metal catalyst^[6]. Lycopene is a major carotenoid found in tomato which has potent anticancer activity in many types of cancer. The antioxidant property of Lycopene has potent benefits in Oral potentially malignant lesions. Because of its high number of conjugated di-enes,

Lycopene is one of the most potent antioxidants, with a single oxygen quenching ability twice as high as that of β -Carotene and 10 times higher than that of α -Tocopherol. Lycopene has been ranked as highly potent antioxidant followed by α -Tocopherol, α -Carotene, β -Cryptoxanthin, Zeaxanthin, β -Carotene and Lutein^[7].

Materials and Methods

Study centre: Subjects for the present study were enrolled from a private clinic of Cancer department located in the southern part of the India.

Subjects: A total of 142 patients who presented with clinical signs and symptoms of premalignant and malignant stages of Oral Cancer were enrolled in the study. Among them 39 patients were excluded due to reasons: patients expired (n=5); not reported for the next follow up (n=23); posted for radiation (n=2) and surgery (n=9); during the study period. After exclusion of above 39 patients, 103 eligible patients were included in the study, of them which, 88 were males and 15 were females. Institutional Human Ethics Committee reviewed and authorized the study protocol (MGM/VCOP/PHARM.D/V/2015/15/07/3). After explanation of the study details and intention to patients, Patient Informed Consent (PIC) was obtained from all participated patients.

Study Design: After the patients allowed to their regular clinical diagnosis, screening of subjects for the study was done. Then participants underwent set of pre programmed steps, firstly by obtaining PIC to access their data and their partaking in the study, secondly if patients were identified with potential risk factors counseling was made to trigger off to halt the habits then, followed by an observation of a set of signs (like blanching of Oral mucosa, presence of Fibrous bands, Trismus, restriction of Tongue movements, Depapillation of Tongue, Deviated/ Bud like Uvula) in an individual patient, prior and after antioxidant therapy with Lycopene.

Results

Figure 1: Socio demographic data of the patients

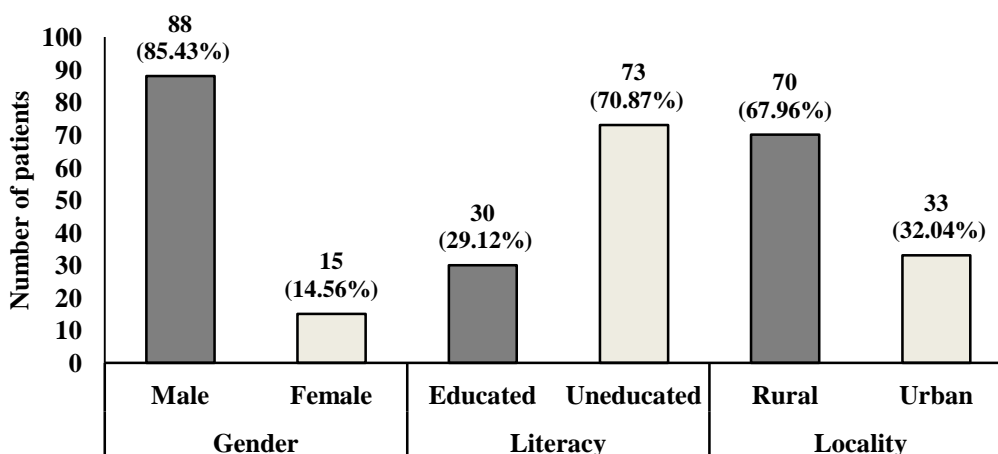


Figure 2: Type of predisposing factors

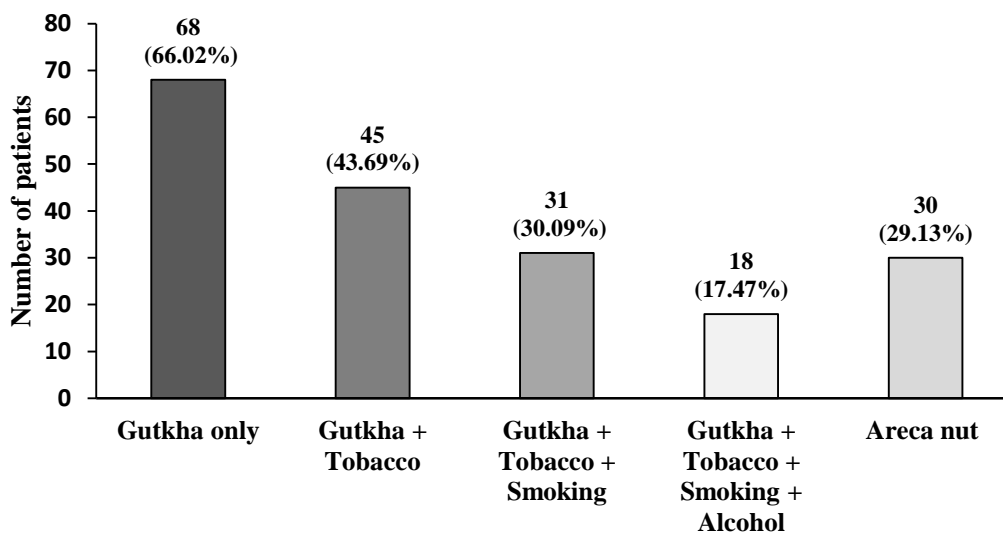


Table 1: Patients distribution based on age incidence

| S. No | Age group (years) | Total (n=103) | |
|-------|-------------------|---------------|------------|
| | | No. | Percentage |
| 1 | 20-29 | 36 | 34.95% |
| 2 | 30-39 | 30 | 29.13% |
| 3 | 40-49 | 21 | 20.39% |
| 4 | 50-59 | 8 | 7.76% |
| 5 | 60-69 | 6 | 5.82% |
| 6 | 70-79 | 1 | 0.97% |
| 7 | 80-89 | 1 | 0.97% |

Socio demographic data of the patients: In the present study amongst 103 eligible patients, 88 (85.43%) were males and 15 (14.56%) were females. Majority of the patients were uneducated that constitute of 70.87% (n=73) while educated

patients was 29.12% (n=30). 67.96% (n=70) of patients were identified from rural area and rest of 32.04% (n=33) from urban area (Fig 1). The age incidence of patients was shown in Table 1. It is perceptible that highest incidence was found

between the age groups 20 to 29 (n= 36; 34.95%) followed by 30 to 39 (n=30; 29.13%) and 40 to 49 (n=21; 20.39%). Among the various predisposing factors, chewing of smokeless forms of Tobacco was identified as common etiological factor.

Consuming of Gutkha was found to be high i.e., 66.02% (n=68), next Gutkha along with Tobacco, Smoking, and Alcohol was found to be low 17.47% (n=18) (Fig 2).

Fig 3: A bar graph showing the improvement in clinical signs in patients with different stages of Oral cancer after treating with Lycopene

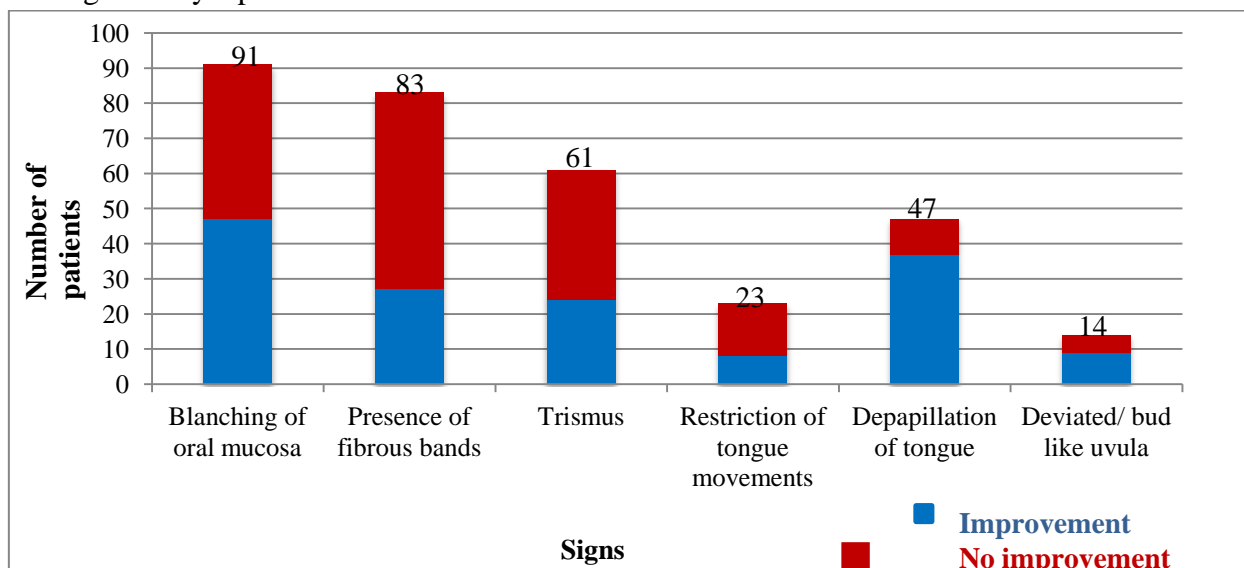


Table 3: Showing the effect of antioxidants on symptoms in patients with different stages of Oral cancer

| S.No | Symptoms | No. of cases | percentage | Antioxidant therapy | | | |
|------|-----------------------------|--------------|------------|---------------------|------------|----------------|------------|
| | | | | Improvement | | No improvement | |
| | | | | No. | percentage | No. | percentage |
| 1 | Burning sensation | 98 | 95.14% | 69 | 70.48% | 29 | 29.59% |
| 2 | Difficulty in mouth opening | 67 | 65.05% | 50 | 74.62% | 17 | 25.37% |
| 3 | Difficulty in swallowing | 76 | 73.79% | 33 | 43.42% | 43 | 56.58% |
| 4 | Taste change | 22 | 21.36% | 15 | 68.18% | 7 | 31.81% |
| 5 | Dryness of mouth | 3 | 2.91% | 2 | 66.67% | 1 | 33.33% |
| 6 | Excessive salivation | 21 | 20.39% | 5 | 23.80% | 16 | 76.19% |
| 7 | Difficulty in speaking | 17 | 16.50% | 10 | 58.82% | 7 | 41.17% |
| 8 | Vesicles and ulcers | 32 | 31.07% | 22 | 68.75% | 10 | 31.25% |

Clinical staging and treatment out comes with antioxidants drug (Lycopene): Study patients were distributed according to their clinical stage. Patients presenting with premalignant lesions were found to be more and the percentage is 49.51% (n=51). On the whole, Leukoplakia cases were found to be in top (n=43; 41.74%). Next to Leukoplakia, Oral submucosal fibrosis (OSMF) was found to be high i.e., 24.27% (n=25) followed by Buccal mucosal cancer with 16.5% (n=17). The most common sign observed was blanching of Oral mucosa, which was reported in 91

patients. Fibrous bands were reported in 83 patients. 61 patients showed Trismus and 23 patients showed restricted tongue movements. Deviated Uvula was observed in 14 patients and Depapillation of Tongue was observed in 47 patients (Table 3). After the treatment with antioxidants drugs for a period of 2-3 months, blanching of Oral mucosa was improved in 51.65% patients. The sign presence of Fibrous bands was improved in 32.53% patients. Restriction of tongue movements improved in 34.78% patients whereas Trismus improved in

39.34% patients. Depapillation of tongue is cured in 78.72% patients while Deviated or Bud like Uvula cured in 64.28% patients. (Fig 3)

Discussion

In our study we found highest incidence of premalignant stages in 3rd and 4th decade of life i.e, 66 out of 103 cases (64.07%) aged between of 20 to 40 years. This corresponds with Rohit Mehrotra et al., who recorded 44 out of 64 cases i.e, 68.75% to be in 3rd and 4th decades^[8]. Wahi et al^[9]., Zachariah et al^[10]., and Mehta et al^[11]., have also reported highest between 3rd and 4th decade of life.

Although premalignant stages affect both sexes, male predominance for this condition has been noted in many studies. In our present study, males n=88 (85.43%) were dominating. The male to female ratio found to be 5.9:1, which was similar to Rohit Mehrotra et al^[8]., who recorded 6.5:3.4. It is likely to correspond with studies conducted by V. K. Hazarey et al^[12]., and S.U. Burungale et al^[13]., which shown male to female ratio of 4.9:1 and 7:1 respectively. In addition, it also corresponds with Ahmad et al^[14]., in their studies at Patna dental college, Patna, Bihar, reported a male to female ratio of 2.7:1. Even studies from China showed higher prevalence among males^[15]. The reason for male predominance is because of easy availability of Gutkha and other related products among youngsters. Moreover males are the working gender and money earner among Indian subcontinent. Areca nut/betel quid, Gutkha is chewed for variety of reasons such as stress reliever, mouth freshener, improving concentration and digestion after food. Whereas females are more conscious about their aesthetic values and it is considered socially unacceptable for a female to get Gutkha from Gutkha vendors. Majority of females in our study were addicted to areca nut or betel quid. In females with poor socio economic status and elder age reverse Smoking is one of the cause noted in few patients.

Almost all the patients have at least habit of taking either of forms of Tobacco. In our study we found

that most common etiological factor is Gutkha chewing seen in 68 out of 103 patients i.e, 66.02%. These findings are in agreement with the reports given by Vanaja Reddy et al^[16]., and Supadminidevi et al^[17]., they concluded that the occurrence of premalignant condition is more faster and more severe in Gutkha chewers as compared to other forms of areca nut products chewers. Alcohol with Gutkha showed increased progression of the disease.^{[14][15]} Findings of our study, however, not consistent with the findings of Wahi et al^[9]., Santhosh Patil et al^[18]., in whose reports, areca nut was the common etiological factor.

In our study the antioxidant used is Lycopene. The specificity of using Lycopene is significant from the findings of Niranzena panneer et al., they concluded that Lycopene is efficacious in improving the mouth opening and reducing other symptoms in patients with Oral sub mucosal fibrosis and no side effects were reported with its usage^[19].

However, in other studies only a few symptoms were examined with antioxidant therapy to assess the role of antioxidants. But, in our study we concentrated on set of clinical signs and symptoms to assess the clinical outcomes of antioxidants more effectively. The discussion aims at use of drugs such as Lycopene which is available everywhere at low cost.

Conclusion

In the present study substantial improvement and decrease in disease severity was observed with selected (Lycopene) antioxidant therapy in different stages of Oral cancer patients. Thus, antioxidants are overall favorable for early cases of Oral premalignant lesions and conditions to cease and delay the disease progress.

Hence, it offers non invasive option that yields significant improvement. In conclusion, antioxidant therapy should be coupled with cessation of predisposing factor to improve patient disease condition.

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Conflict of interests

All authors report no conflict of interest

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