

Review Article

Type of Food and Risk of Oral Cancer

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Cancer is the eventual outcome of the interaction between genetic factors and environmental exposures. Nutrition and diet, as environmental factors and determinants of growth and body composition can contribute to the risk of some human cancers such as oral cancer. This article explains the ways of carcinogenesis and the effect of diet on this process, especially focusing on head, neck, and oral cancers.

To reduce the risk of oral and pharyngeal cancer, especially squamous cell carcinoma, the most common oral cancer, diet must be optimized, primarily to reduce calorie intake, mono-unsaturated fat, and red or processed meat. Consumption of fruits, vegetables, and cereals, which are the major source of vitamins and fiber, should be adequate in the daily diet.

Optimal levels of daily allowance of micronutrients like vitamin C, E, antioxidants, zinc, β -carotene, and folate are effective in prevention of oral cancer.

Consumption of fried or broiled foods and employment of microwave cooking, because of formation of heterocyclic amines, must be avoided because of increasing risks of oral cancer including the salivary gland tumors.

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Introduction

“Nutrition refers to the status of body cells in terms of necessary materials or nutrients required for physiologic growth and metabolism.”¹

Nutrition and health are closely connected and malnutrition can seriously endanger health. The consequences are a higher risk of developing disease. Of these, cancers are of special importance, because they are the second most important cause of premature adult death after cardiovascular disease, globally.² Cancer is the eventual outcome of the transformation of normal cells by DNA-reactive, genotoxic carcinogens and growth promotion of mutated cells by enhancing factors.³ Thus, cancer is the product of interaction of genetic factors and environmental exposures like ionizing radiation, smoking, specific infectious

agents, and dietary factors, which develops over a long time and goes through many stages.⁴⁻⁶

In this article, the relationship of head and neck cancer, especially oral squamous cell carcinoma (SCC) with dietary factors, nutritional deficiencies and their mechanisms of actions will be reviewed.

The diet and cancer link

According to World Health Organization (WHO) reports, 35 – 55% of human cancers and approximately 15% of oropharyngeal cancers can be attributed to dietary deficiencies or imbalances.^{7,8}

The relationship between nutrition and cancer has to be approached from two different points of views:

- The direct effect of carcinogens present in food and food additives (i.e., direct carcinogenesis).
- *In vivo* synthesis of carcinogens caused by changes in metabolism due to altered dietary habits (i.e., indirect carcinogenesis).

These add up to effects of diet on energy balance, risk of obesity, hormonal, and metabolic responses related to energy balance.⁹⁻¹¹

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Molecular targets for bioactive food components

Numerous food components may be important in activating one or more steps in carcinogenesis. Much evidence exists that both essential and non-essential dietary components can alter this process.¹²

Figure 1 illustrates the multiple steps where bioactive food components can interact with genes and their expression in altering phenotypes. Genes can influence absorption, metabolism, transport of bioactive food component, or its site of action and thus, influence the overall response to diet.¹² Bioactive food components can also alter the genetic expression of a host of cellular events that influence cancer outcomes.¹²

The magnitude of the problem of identifying which dietary component is the most important in increasing or decreasing the risk is evident considering that thousands of compounds are consumed each day.

Among the dietary factors influencing cancer growth, with regards to the head and neck and especially oral SCC, fiber, antioxidants (β -carotene, tea, fresh fruits, and vegetables), animal fat, frying or broiling protein foods, and micronutrients (vitamin C, E, and K, zinc, folate)

were studied (Table 1) and seemed to offer the best hopes for growth inhibition.¹²⁻¹⁶

Antioxidants and fiber

Oxidative damage is recognized as playing a role in the pathogenesis of cancer, which could arise from incorrect nutritional habits and lifestyle practices. This process can cause DNA damage, which is a basic mechanism of cancer induction. Assessment of oxidative DNA damage in 24 vegetarians, compared to 24 nonvegetarians, showed that DNA strand breaks oxidized purine were significantly lower in vegetarians.^{17,18}

Sufficient antioxidative status (overthreshold values of natural essential antioxidants) is crucial in free radical defense. Intakes of protective food commodities (e.g., fruits, vegetables, dark grain products, grain sprouts, and oil seeds) were significantly higher in vegetarians. On the other hand, their diet was significantly more rich as a source of antioxidants and fiber.¹⁹

The relationship between the frequency of consumption of a selected number of foods and oral cancer risk was analyzed in a case-control study in Italy on 105 cases. Besides significant and strong direct correlation with kinds of tobacco such as cigar, opium, smokeless tobacco,²⁰ and alcohol,

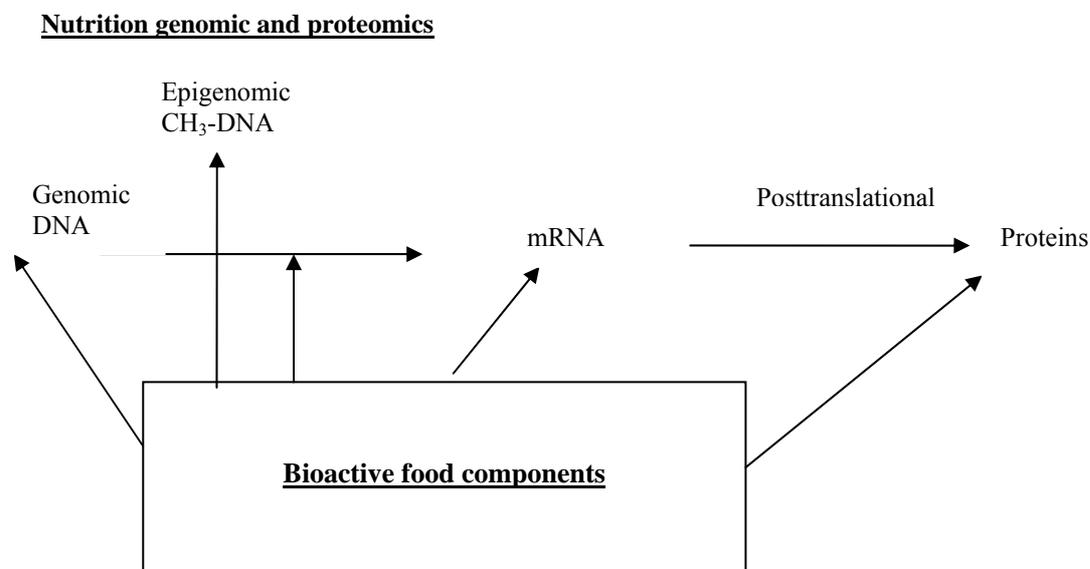


Figure 1. Influence of bioactive food components on genetic, epigenetic, and proteomic events.

Table 1. Correlation between the risk of oral cancer, especially squamous cell carcinoma with environmental factors (food and habits) in the USA, Asia, and Europe.

Risk factors	USA	Asia	Europe
Habits			
Tobacco smoking	Very strong	Very strong	Very strong
Alcohol consumption	Moderate	Possible	Moderate
Opium smoking	No data	Moderate	No data
Dietary factors			
Low intake of antioxidants and fiber (fruits, vegetables, oil seed, tea, soy, ...)	Strong	Strong	Strong
High intake of monounsaturated fat (fried foods, pork, pasta, red meat, cheese, ...)	Strong	Possible	Strong
Low intake of micronutrients (vitamin C, E, zinc, folate, ...)	Strong	Possible	Strong
Cooking method			
Frying/broiling	Strong	No data	Strong
Microwave	Strong	No data	Strong
High calorie intake/obesity	Strong	Possible	Strong

Very strong and strong: present evidence show high relative risk; moderate = present evidence show moderate relative risk; possible = no data on relative risk but data suggest the possibility of relation; no data = there is no data in this field.

consumption of six food items (i.e., milk, meat, cheese, carrots, green vegetables, and fruits) were inversely and significantly correlated with development of oral cancer.²¹ The strongest protection was apparently attributed to the frequent consumption of fruits (antioxidants and fiber), which appears to be a particularly important protective factor against development of oral cancer.²¹⁻²²

Another case-control study on 227 women in North Carolina, USA, with oral cavity or pharyngeal cancer and 405 matched controls showed the protective effect of diets rich in fruits and vegetables.²³

Antioxidants can inhibit or decrease the production of components, which can induce cancer caused from frying or broiling protein and foods that generate heterocyclic amines.³

The tobacco-specific nitrosamine, which is one of the most important etiologic factors in oral SCC, and polycyclic aromatic hydrocarbons undergo specific activation and detoxification process, and may be important carcinogens. Their reactions are controlled by antioxidants such as quercetin in vegetables, genistein in soy, sulforaphane in broccoli, and 3-methylindole and isothiocyanates in similar protective foods.³

Besides antioxidants, the beverage tea can act as an antioxidant and inhibit the carcinogenic effect of cigarette and tobacco, esophagus, or lung.²⁴⁻²⁶

Studies indicate that the risk of oropharyngeal cancer is lower with higher bread and cereal intake. These dietary fibers should be increased to 25 – 35 g per day for adults. One approach to achieve this goal is the “fiber first diet,” a diet designed based on adequate intake of grains

especially cereals, vegetables, and fruits, which reduces both the calorie and fat intake.²⁷

Energy balance and fat food diet

Energy balance results from the exact equilibrium between caloric intake and caloric expenditure. A caloric intake larger than caloric expenditure results in overweight or even obesity, which have been recognized as risk factors for the development of cancer.²⁸

Epidemiologic studies, intended to establish a relationship between the energy balance, physical activity, and cancer, discussed the influence of various factors on the obesity and risk of cancer.²⁹ Among these factors, macronutrients, especially fats responsible for calorie intake were discussed.²⁷⁻³⁰

Investigations concerning the role of dietary lipids have demonstrated correlation between fat intake and carcinogenesis.³² On the other hand, it was shown that lipid consumption including its amount and composition is closely related to the development or prevention of tumors.³³

Essential fatty acids such as fish oil and vegetables rich in n-3 polyunsaturated fatty acids must be incorporated into diet and have a protective effect against cancer. This effect would be related to an increasing production of anti-proliferative metabolites. On the contrary, monounsaturated fatty acids like n-9 oleic acid, as the main source of fat, behave as a tumor promoter in breast, colon, oral, and salivary gland cancers.³⁴⁻³⁷

Possible mechanisms through which fatty acids may influence carcinogenesis include effects on membrane integrity, increase in lipid peroxidase, and impairment of nutrient metabolism.³⁸

There are evidence that qualitative and quantitative differences in dietary lipids can alter the membrane fatty acid composition of both normal and neoplastic cells, hence, modifying physical and chemical environment of human receptors and enzymes of tumor cells.³⁸

A case-control study in Brazil evaluated fat food habitual intake as a risk factor for the development of oral cancer. Results showed that foods rich in fat content, such as pork, bacon, pasta, cheese, red meat, fried foods, meat fried, or cooked at high temperature or in microwave were significantly associated with the risk of oral cancer (Table 2).³⁹ Fried foods, meat fried or cooked at high temperature or in microwave can be carcinogen because of the production of heterocyclic amines.³⁹⁻⁴¹

Dietary factors associated with reduced risk of oral cancer include herbal tea, apple, margarine, milk, and citrus fruit or juice.³⁹

Micronutrients

Although a great deal of attention has been given to protein and malnutrition in patients with head and neck cancer, micronutrients like vitamin C, E, β -carotene, lycopene, folate, and zinc have important roles in carcinogenesis.⁴²⁻⁴⁶ It seems that apart from the antioxidant properties of these substances, polymorphism in the detoxifying enzyme GST activity and other metabolic genes can also modulate the risk of cancer. These processes are also modulated by the plasma level of micronutrients.⁴⁷

Studies have shown that DNA adducts, which are a reliable indicators of genotoxic damage, are significantly and inversely correlated with the intake of β -carotene and vegetables.⁴⁷

Stratification by GST genotype showed a strong inverse correlation of DNA adducts levels with increasing consumption of vegetables, fish, β -carotene, vitamin C, niacin, potassium, and folate.⁴⁷

Vitamin E and β -carotene can also cause regression of oral leukoplakia.⁴⁸

Assessment of serum zinc in patients with head and neck cancer indicates that the baseline zinc status is correlated with tumor size and the stage of malignancies.⁴⁶

Alcohol-nutrient interaction in oral cancer etiology

There is compelling epidemiologic evidence of an association between diet and alcohol for oral, pharyngeal, and laryngeal cancer.⁴⁹ It is unlikely that a quantitative relationship and a biologic mechanism of interaction be the same for all cancers but descriptive studies suggest that as the percentage of caloric intake from alcohol is increased, the daily consumption of protein, carbohydrate, fiber as well as many micronutrients is steadily and significantly decreased.⁵⁰⁻⁵²

Conclusion

The complex process of carcinogenesis is mainly due to environmental factors and diet is one of these factors, which epidemiologic evidence has implicated its vital role in the etiology of several forms of human cancer such as those involving the oral and head and neck.

There is convincing evidence that we can reduce the risk of cancer, including that of oral cancer through changing diet by

- avoiding the formation of carcinogens,
- reducing their metabolic activation, and
- increasing their detoxification.

Diet high in vegetables, fruits, antioxidants, tea, and fiber decrease the risk of oral and pharyngeal cancer. Because these nutrients can prevent the activation of carcinogens and increase their detoxification, especially the effects of tobacco, which is one of the most important factors in oral SSC.

Consumption of alcohol and diets high in monounsaturated fat, red or processed meat, frying or broiling foods, and employment of microwave cooking increase the risk of oral cancer including salivary gland tumors. The same is true for regular physical activity and energy balance because fat,

Table 2. List of numbers of food items and their intake frequency related to oral cancer.³⁹

Dietary factors associated with increased risk of oral cancer		Dietary factors associated with reduced risk of oral cancer	
Terms	Frequency	Terms	Frequency
Pork meat	≥ Once per week	Herbal teas	≥ Twice per week
Pasta	≥ Twice per week	Apple	≥ Once per week
Fried food	≥ Four per week	Margarine	≥ Seven per week
Cheese	≥ Once per week	Milk	≥ Seven per week
Eggs	≥ Thrice per week	Citric fruits or juices	≥ Thrice per week
Alcoholic beverages	≥ Seven per week		
Red meat	≥ Five per week		

especially animal's fat, is the reason of calorie intake.

Micronutrients like vitamin C, E, β -carotene, folate, and zinc have an important role in prevention of oral cancer. These factors can cause polymorphism in detoxifying enzyme GST₁ and other metabolic genes, which modulate the risk of cancer and decrease the genotoxic damage.

In accordance with these studies, it can be concluded that nutritional intervention is one of the most valuable means of cancer prevention.

To address the decreased prevalence of oral cancer, the following must be considered. avoiding tobacco, limiting alcohol intake, choosing a predominantly plant-based diet, reducing fat intake (monounsaturated type), red or processed meat, avoiding exposure of meat to open flames, usage of aluminum foil to wrap meat before roasting, and using microwave ovens in order to reduce formation of heterocyclic amines. Intake of optimal levels of micronutrients such as vitamin C, E, β -carotene, folate, and antioxidants are recommended.

Such dietary improvements not only reduce the risk of oral cancer but also contribute to a healthy life to an advanced age.

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