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Review article about nutrition and primary prevention of oral cancer

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ABSTRACT

Cancer is a worldwide problem that is caused by a variety of different factors increasing over a number of years. Oral cancer is a very prevalent disease and one of the most 10 common causes of death. It is important that the risk factors can be controlled. Selecting the correct health behaviors and preventing exposure to convinced environmental risk factors can help to prevent the expansion of cancer. Scientists guess that as many as 30-40 percent of all cancer-related deaths are caused by human behaviors such as smoking, consumption of alcohol, poor diet quality and physical inactivity. This result explains the tendency in the following behaviors that can influence the possibility of getting cancer, especially oral cancer in addition to providing information and classes about healthy eating habits and a subsequent healthy lifestyle at home. In fact, a diet rich in fresh fruits, whole grains and vegetables can decrease the risk of the oral cancer because of certain compounds such as vitamin C, E, carotenoids and lycopene. Moreover, limit consumption of meat, particularly processed meat, and replace it with vegetable proteins and fish (rich of omega 3) are helpful and effective.

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Introduction

Oral cancer is one of the most prevalent and the 10th familiar cause of death. The prevalence of oral cancer is less than 3% of all cancers in the United States but it is the eight most common cancer in males and the fifteenth most common in females (1). There is more than 400,000 oral and pharyngeal cancers diagnosed in the world and about 36,500 new cases and oral cancer still causes more than 7,800 deaths each year in the United States (2). In Iran, oral cancer is estimated to affect more than 3,923 cases in 2009 (3). Approximately 94% of all oral malignancies are cancer of squamous cell (4). The cause of oral squamous cell carcinoma is multifactoral. No single causative agent (carcinogen) has been obviously accepted. It is likely that more than a single factor is needed to produce such a malignancy. Researched showed that 1/3 of all cancer-related deaths were caused by incorrect human behaviors such as smoking, consumption of alcohol, poor diet quality and physical inactivity (5,6). Therefore, we hope to increase lifetime and life quality with the better recognition of effective risk factors and applying them in life meanwhile preventing mental illness in the patient suffering from cancer and reducing the high cost.

Cancer mechanism

Cancer is the general name for a group of diseases in which normal homeostatic cellular

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control is lost and cells grow constantly, invading and overwhelming the surrounding normal tissues. Among the main steps toward malignancy are alterations in the DNA. In this research, a great part is attributed to review the DNA changes that can be responsible for transforming the cells of the oral cavity and oropharynx to cancerous cells (1). A mutation of the p53 gene is often found in DNA of oral cancer cells. This gene produces protein that normally works to prevent cells from growing too much and helps to destroy cells with too wide DNA damage for the cells to repair. Damage to p53 DNA can increase the growth of abnormal cells and the creation of cancers. Many researches have been reported that the tests detecting these p53 gene changes may let very early detection of oral and oropharyngeal tumors and surgical margins. DNA from a papillomavirus (HPV) was mixed with the patient's own DNA that was an extra DNA change finding in some oral cancers (7). Some parts of the HPV DNA made the cells to produce proteins that inactivated the p53 protein (8). Studies on HPV DNA tests may help in diagnosing these cancers (9).

Literature review

Alcohol and smoking

Consumption of alcohol is well recognized as a cause of growth of cancer. Alcohol consumption increases the risk and the development of cancer in oral cavity, pharynx, nasopharynx, laryngeal and liver (10). Prevalence and the risk of cancer in upper aerodigestive tract such as esophagus, oral cavity, pharynx and larynx increase along with the amount of alcohol consumed (above 25 g/day). Individuals drinking 100 g/day have a 4- to 6-fold increased risk of these cancers compared to light or non-drinkers (11). Case-control studies have concluded that the risk was time-dependent and the combination of alcohol and tobacco abuse may increase a risk of oral cancer by a factor of 15 up to 80 folds over long periods (12,13). Studies in developed countries showed that combination of smoking and alcohol consumption have been reported for 75% of all upper aerodigestive cancers (14,15). Several mechanisms have been explained for the carcinogenic effect of alcohol consumption at these areas. One of the metabolite of alcohol is acetaldehyde, which changes the DNA leaning to cell proliferation (16). Alcohol may perform as a solvent for other carcinogens (tobacco smokers), may generate reactive oxygen and nitrogen species and may interfere with metabolism of other micronutrients (17). Risk of cancer will increase by approximately 7-12% for every additional 10 gr /day of alcohol. This association is probably mediated by an increase in estrogen levels (18). There is a weaker evidence for a reduced risk of non-Hodgkin lymphoma in alcohol drinkers (3,19). Cirrhosis of the liver, similarly, is found in at least 20% of males with oral cancer. Nutritional deficiencies are associated with heavy alcohol consumption that may increase the risk of oral cancer development (1). A study showed that around 12500 cancer cases were related to alcohol consumption and this range was around 30% for oral cavity and pharynx with the highest range in the UK each year (20).

Fruits and vegetables

In modern nutrition research, it is advised to consume a diet rich in fruits and vegetables. Many studies showed that around 5% of cancers and 56% of oral and pharyngeal cancers have linked to fewer than five portions a day (400 g/day) consumption of fruits and vegetables in the UK (20). Many mechanisms were associated to their protective effects. Thus, a diet rich in fresh fruits, vegetables and whole grains can decrease the risk of the cancer because of certain compounds such as vitamin C, E, carotenoid and lycopene that support the immune system. Our immune system will fight off useless invaders in our body as well as cancer cells. There are many things that we can eat to increase the potency of our immune system as well as many cancer-fighting foods. Nevertheless, remember that there is no single phenomenon food or ingredient that be able to protect against cancer. However, eating a colorful diversity gives the best protection. Phytochemicals are the substances in the structure of these colorful fruits and vegetables that have a potent disease fighting ability and increase the immune system defense in the body, kill cancer cells and act as an inhibitor of vascular growth of cancer cells and spreading the malignant tumor (20). Antioxidants are important in the body because of their defense against cancer and helping the cells to maintain their function. Fruits and vegetables are the best sources of antioxidants such as beta-carotene, vitamin C, vitamin E and selenium (21). Studies showed that consumption of greater vegetables and fruits had a protective effect against cancers of the oral cavity, lung, pharnynx, stomach, esophagus, endometrium, colon and pancreas. Consumption of vegetables especially raw vegetables was found to be protective. Eithy-five percent of studies have been shown that raw vegetable consumption had a protective effect. Alliums vegetables, carrots, green vegetables, cruciferous vegetable and tomatoes had a practically reliable protective effect (22). Other vegetables for example allium vegetables (garlic, onion, leeks and scallions)

are essentially effective and they have protective effects on stomach and colorectal cancers (23). Moreover, the light-collecting molecule chlorophyll and its derivatives in all green plants are effective at binding polycyclic aromatic hydrocarbons (carcinogens largely derived from incomplete combustion of fuels), heterocyclic amines (generated when grilling foods), aflatoxin (a toxin from molds in foods, which causes liver cancer) and other hydrophobic molecules. After this process, the chlorophyll-carcinogen complex is much difficult for body to absorb (24,25). Another benefit of eating plant-based foods is that it will also increase fiber intake. One of the most effective factors for health is dietary fibers. Several studies have been indicated that dietary fiber intake has protective effect against cancer. The average intake of fiber from nutritional source per person is 14 gr per day. The amount of fiber is higher in natural and unprocessed food. There is no fiber in meat, dairy, sugar or white foods like white bread, white rice and pastries.

The other name of fiber is roughage or bulk that is the part of plants (grains, fruits and vegetables) and body cannot digest them. Fibers play a key role in keeping the digestive system clean and healthy. The fibers move foods through digestive tract and decrease the harm effect of cancer-causing compounds before they can harm the digestive tract.

Studies indicated that each daily portion of 80-100 grams of fruits or vegetables reduced the risk of oral cancers up to 80% and squamous cell carcinomas of the esophagus by approximately 20% and stomach cancer by about 30% (26,27).

Antioxidants

Reactive oxygen species (ROS) is categorized to chemically reactive molecules containing oxygen in forms such as superoxide anions (O_2^-), hydroxyl radicals, hydrogen peroxide (H_2O_2), produced as a result of normal aerobic metabolism. Highly reactive radical species can oxidize lipids, proteins and DNA, potentially leading to various diseases including cancer, arteriosclerosis and cardiovascular and inflammatory diseases. Indeed, oral administration of vitamins C (L-ascorbic acid) and E attenuated exercise induced oxygen stress (28). Vitamin C and E are the antioxidants that protect the body against oxidative stress damages (29). Vitamin C is an aqueous material that is in the cytosol and extracellular fluid, which interacts directly with free radicals.

Vitamin E is a lipid-soluble and flows into cellular membranes to interrupt lipid peroxidation by transferring its own hydrogen. Vitamin E is converted to a vitamin E radical, which is reduced by vitamin C to regenerate vitamin E. This reaction in turn produces vitamin C radicals, which are regenerated by glutathione (29). There are many more foods containing antioxidant that have some benefit effects on the cancer prevention and reducing the damaging effects of oxidative stress.

Vitamin C

Vitamin C, or ascorbic acid, has been studied as an antioxidant agent against cancer (30). Ascorbic acid is toxic to cancer cells at high concentrations (31). Vitamin C contains effective substances. Its therapeutic effects are clearly depending on dietary intakes (32,33). The benefits of antioxidant administration to reduce the oxidative stress and DNA damage remain controversial. Another property of vitamin C, intravenous ascorbate, may be a helpful adjuvant therapy for cancer with no negative side effects when administered properly (34-36).

Alpha and Beta-carotenes

Carotenoids, colorful compounds of plants, have been shown that they can dynamically decrease the cancer risk. Fruits and vegetables contain beta-carotene. Beta (β)-carotene does not have an influential protective effect in pharmacological doses. There is several studies indicating that dietary carotenoids are cancer preventative. Many studies have been shown that alpha (α)-carotene was a stronger protective agent than its famous isomer β–carotene and overall intake of carotenoids was more protective than a high intake of a single carotenoid. The best source of α-carotene is carrots and carrot juice, although pumpkins and winter squash are regarded as second most-dense sources. The carrots have approximately one microgram of α-carotene for every two microgram of β-carotene, thus they are the most common sources of this compound (37,38).

Lycopene

Lycopene are one of the different carotenoids that have been found to be very protective, principally for prostate cancer. Tomatoes are the major dietary source of lycopene, with the lycopene in cooked tomatoes being more bioavailability than that in raw tomatoes. Several prospective cohort studies have shown that there was an association between high consumption of lycopene and reduced incidence of prostate cancer (39). In addition, lycopene was even more protective for advanced stages of prostate cancer, with a 53% decrease in risk. One cohort study of men has been shown that lycopene or frequent tomato intake was associated with about a 30- 40% decrease in risk of prostate

cancer, particularly advanced prostate cancer. Moreover, the people who took the lycopene for 3 weeks had smaller tumors, less involvement of the surgical margins and less diffuse involvement of the prostate. They also showed that higher consumption of lycopene is associated with lower angiogenic possible in tumors (40).

Other Antioxidants

Consumption of many more substances will have some advantages for cancer therapy. These substances are found and detected in foods, but their effective doses for therapy are much higher than the normal concentration in food. For example, grape seed extract contains proanthocyanidin, which shows anticarcinogenic properties (41). Lemon (citrus) is a phenomenal product to kill cancer cells. It is 10000 times stronger than chemotherapy drugs. The compound of this tree has been shown to be 10000 times more effective than the product adrinamycin, a drug normally used a chemotherapeutic agent in the world. Lemon causes slowing the growth of cancer cells. More astonishing about lemons effect is that it only destroys malignant cancer cells and it does not affect healthy cells (42). Moreover, one substance named flavonoid epigallocatechin-3-gallate (EGCG), which is in green tea. It can inhibit metalloproteinases, among several possible other mechanisms (42). Several studies introduced various other herbal substances and extracts that might be benefit for cancer therapy (42).

Vitamin D

The active form of vitamin D is produced primarily from the exposure of the skin to sunshine. The concentration of the active hormonal from of vitamin D or calcytriol is strongly regulated by the kidneys. This active hormonal from of vitamin D has the potent anticancer properties. It has been discovered that various types of normal and cancerous tissues including prostate cells, colon tissue, breast, ovarian and lung cancer cells have the ability to convert this from of vitamin D in the body (43). A recent study found that the people with a higher consumption of milk showed a 16% risk reduction of bowel cancer (44,45).

Vitamin A

Vitamin A is one of the soluble vitamins in lipid. Vitamin A deficiency produces excessive keratinization of the skin and mucous membranes. Researchers have suggested that the vitamin may play a protective or preventive role in oral precancer lesions and in cancer as well. Some believed that the blood levels of retinol and the amount of dietary beta-carotene ingestion are inversely proportional to the risk of oral squamous cell carcinoma and leukoplakia. Furthermore, long-term therapy with retinoic acids and beta-carotene has been related with a regression of at least some leukoplakic lesions and a concomitant reduction in the severity of dysplasia within such lesions (1).

Probiotics

Bacteria exist in the intestinal generally have symbiotic relationships with their host. The helpful bacteria which can be utilized in the small intestine produce natural antibiotics, keep pathogenic bugs healthy (preventing diarrhea and infections) and produce some vitamin B. These bacteria help with food digestion by preparing more enzymes in the small intestine such as lactase and also support the immune system for helping to prevent food allergies. They prevent cancer at various stages of growth, improve mineral absorption and also maximizing food utilization (46). However, the balance of beneficial and potentially pathogenic bacteria in the gut is dependent on the diet. Vegetable fiber increases the growth of beneficial bacteria. A group of Adventist vegetarians was found to have a lot of helpful bacteria in addition to a lower rate of pathogenic bacteria in vegetarian's diet compared to non-vegetarians on a conventional American diet. Probiotics also produce short chain fatty acids in the colon, which acidify the location of colon. If lower PH of colon is correlated with the lower prevalence of colon cancer, moreover, probiotics decrease the level of procarcinogenic enzymes such as beta-glucuronidase, nitroreductase and azoreductase (47). Researches on probiotics and disease are still in their initial steps because the effective results of probiotics on health benefits are different and there is a variation in strains of bacteria.

Meat and Fat

Several researches showed that vegetarians had about fifty percent less probability to develop cancer compared to those who eat meat. It is recommended to take the meat in diet but no more than fifteen percent of total calories (ten percent is even better) per day. However, it will be necessary to avoid high amount of red meat consumption because it is high in saturated fat. Thus, meat should be eaten sparingly. Studies showed that the high-fat diets have been linked to higher rate of cancer and saturated fat was particularly dangerous. Finally, depending on how it is prepared, meat can develop carcinogenic compounds. It does not need to cut out meat completely and become a vegetarian. Most

people consume far more meat than usual. We can cut down cancer risk gradually by reducing the amount of animal-based products and by choosing the healthier meats such as beans and other plant-based protein sources and select leaner meats such as fish, chicken or turkey.

A high intake of salt and salt-preserved foods increases the risk of stomach cancer. People eating more than 16 g/day of salt have 2 to 3 times higher risk compared to people eating 10 g/ day or less (48). High consumption of salt may increase cancer risk by increasing sensitivity of the lining of stomach to material carcinogens such as nitrates or by directly causing mucosal damage and inflammation. Meats are nutrient foods that provide amino acids especially essential amino acids. Several studies have been advised to take a low red meat. A major benefit of cutting down the amount of consuming meat is that it is automatically cut out a lot of unhealthy fat. Eating a diet high in fat increases the risk for many types of cancer. However, cutting out the fat entirely is not the answer, either. In fact, some types of fat may actually protect against cancer. The trick is to choose fats wisely and eat them in moderation.

Fats that increase cancer risk

The two most damaging fats are saturated fats and trans fats that increase the cancer risk. Saturated fats are found mainly in animal products such as red meat, whole milk dairy products and eggs. Trans fats, that are named hydrogenated oils, are created by adding hydrogen to liquid vegetable oils to make them more solid and less likely to spoil, which is very good for food manufacturers and very bad.

Fats that decrease cancer risk

The best fats are unsaturated fats, which come from plant sources, are liquid at room temperature, and decrease the cancer risk. Primary sources include olive oil, canola oil, nuts and avocados. Furthermore, we should focus on omega-3 fatty acids, which fight inflammation and support brain and heart health. Good sources include salmon, tuna and flaxseeds (48).

Conclusion

Cancer is a worldwide problem and oral cancer is one of the most prevalent cancers and one of the 10th familiar causes of death with a complex etiology. Tobacco use and alcohol consumption is widely considered to be its major risk factors. Low beta-carotene, fruits and vegetables intakes have been associated with an increased risk of oral cancers. A low intake of vitamin C has been associated with an increased risk of cancers of the stomach, esophagus and oral cavity. However, balanced intake of omega 3 and 6 fats, vitamin D and probiotics and reduced sugar intake have been advised. Many studies showed that the use of vitamin E supplements was correlated with a diminished risk of oral and pharyngeal cancers. As reviewed above, reduction of cancer rate have been reported in studies of human diets. These reductions are depending on the factors mentioned in this review.

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Conflict of Interest

The authors declare no conflict of interest.

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