

NUTRITIONAL SUPPLEMENTS IN ORAL CANCER

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ABSTRACT

Cancer is still one of the most leading causes of death worldwide, with new cases rapidly emerging every day in developed and developing countries alike. Oral cancer and head and neck cancer remains the sixth most commonly occurring malignant tumor. The main causes are tobacco and alcohol, although the diet is currently considered an important determinant of its development. In this scenario along with other modalities, supplements in diet like vegetables and fruits which are rich in phytochemicals and antioxidants (vitamins A, C, E etc.) can play an important role in suppressing the growth of cancer. Some of these chemopreventive and chemotherapeutic agents known to us are selenium, tomatoes (lycopene), spirulina, neem, green tea, turmeric and other few medicinal mushrooms. Various nutrients in the diet have specific mechanisms of action, which help prevent cancer and increase the risk of occurrence, growth and spread. Fried food and diet rich in red meat with pro-inflammatory effects increase the risk of developing oral cancer whereas food like vegetables, fruits, green tea and curcumin are known to reduce its risk. This abstract emphasizes the importance and need of these natural treatments against oral cancer.

KEYWORDS: Oral cancer, Nutrition, fruits, vegetables.

INTRODUCTION

One of the most common and life-threatening disease worldwide is oral cancer with only 50% survival rate. Approximately, 400,000 people worldwide are diagnosed with new cases of oral carcinoma annually. Even though it affects both gender groups, it has shown more prevalence in men more with the incidence rate varying from 1 to 10 cases per population of 100,000 according to 2005 World Health Report. The spread of carcinoma is 12.6 per a population 100,000 in India. Females (20.5%) are less affected than males (48.2%). 30 to 35% of the Indian population is diagnosed with oral carcinoma every year.

A variety of phytochemicals and antioxidants found in diet supplements such as spirulina, selenium, EGCG (green tea), neem, lycopene (tomatoes), curcumin (turmeric), and few known medicinal mushrooms, are gaining recognition as effective chemo-preventive and chemotherapeutic agents. Function of antioxidants is inhibition of oxidation of free radicals. Antioxidant properties are present in vitamins A, E, C and Beta

Carotene. Free radicals are oxidants that are unpaired electrons and are thought to interact with DNA causing cell damage and cancer. Maintaining a healthy lifestyle (yoga, meditation) along with the diet provide a holistic approach to the long-term remission and prevention from cancer.^[1]

More often than not, role of diet in oral malignant growth is overlooked. Pathological analysis of 300,000 new cases worldwide each year, its incidence is significantly high in individuals with habit of smoking, tobacco chewing, and alcohol intake.

The National Cancer Institute and the American Cancer Society gave recommendations regarding the diet with choice of food and certain advisories that is.

- Maintaining a desirable body weight,
- eating a varied diet,
- including new variety of fruits and vegetables in the daily diet,
- consuming food highly rich in fibre,
- decreasing the total intake of fats (30% less than the total calories),

- limiting the consumption of alcohol,
- limiting the consumption of salted food or food preserved with nitrates

A few studies show a little impact of dietary supplementation on malignancy occurrence; while others show that supplementation with antioxidants may adversely affect the frequency of malignant growth and cardiovascular sicknesses or no impact. In a new examination, El-Rouby showed that lycopene can apply defensive impacts against 4-nitroquinoline-1-oxide actuated tongue carcinogenesis through a decrease in cell expansion and improved cell attachment, proposing another approach for the anti-invasive effect of lycopene. Edefonti et al. reported that diets of animal origin and consisting of animal fats are directly whereas the ones rich in plant based diet such as vegetables, fruits and vegetable fats are inversely proportional to risk of developing oral and pharyngeal cancer.^[2]

Cancer patients need a diet high in calories and protein because cancer increases the metabolic rate, needs to rebuild damaged tissues and supplement nutrients lost by cancer. It has been observed that people on high-protein diet and high-calorie diet are able to cope with high doses of drugs and side effects of the therapy much more than those unable to maintain normal diet. Maintaining normal weight or controlling weight loss have shown significant positive response to treatment implied for carcinomas, which allows better recovery.^[4]

Cancer treatments, which include surgery, chemotherapy, and radiation therapy, are also associated with malnutrition. Removal of cancerous tissues is the main reason for adverse reactions in response to surgeries. The most common adverse events in oral cancer patients include dysphagia; a previous study reported that about 50% of oral cancer patients had dysphagia after surgery. Dysphagia, dumping syndrome, and increased defecation are often induced by esophageal resection. 80%–90% and 50%–60% of surgical patients exhibit early satiety and reflux, respectively, after food intake.^[7]

ROLE OF ANTIOXIDANTS IN ORAL CANCER

A vitamin A precursor Beta-carotene found in fruits and vegetables of colour such as dark green, orange or yellow like sweet potato, spinach, carrots, oranges, mango and papaya. These beta carotenes are basically free radical scavenging antioxidants. They are immunomodulators that increased the activity of tumor necrosis factor-alpha, inhibits mutagenesis and inhibits cancer cell growth (Shetti et al. 2011; E Siva Prasad Reddy 2011). Serum beta carotene levels seem to dip in some oral premalignant conditions. Therefore its supplementation (30 mg/day) has shown promising results in the regression of these lesions.^[1] Beta-carotene is antioxidants, protecting from DNA damage.^[10]

RETINOIC ACID (VITAMIN A)

Animal products such as milk, meat and eggs are main source of carotene and retinoic acid. The main actions of retinoic acid are to inhibit keratinization and Enhances cellular immunity. They suppress and mildly reverse the progression of leukoplakia and provide cytotoxic and cytostatic effects on cancer cells. They are known to impact RNA, DNA, and gene expression and interfere with carcinogenic binding and stimulation. (Shetti et al. 2011; Reddy 2011; Thriveni et al. 2011).^[11]

L-ASCORBIC ACID (VITAMIN C)

Vitamin C is obtained from citrus fruits such as kiwi, papaya, strawberries, and mango. The daily intake (recommended in USA) of ascorbic acid is roughly between 100-120 mg/per day. In the case of smokers, daily intake of nearly 140 mg/day can reduce L-AA concentration in serum leukocytes. L-AA has an antioxidantizing property and responds with the superoxide made because of the cells' ordinary metabolic cycles; these inactivations of superoxide repress the formation of nitrosamines during protein digestion and help avoid damage to the DNA and cell proteins.

Although, there has been no clear indication of secondary cancers, Vitamin C intake has reported reduced risk of development of primary cancers. There is no established recommended dose as of now, however, there is significant risk control observed. Vitamin C and vitamin E together have shown to have a synergistic effect (elimination of free radicals in the cell membrane) in such conditions. Vitamin C protects against the production of nitrosamine and the association between DNA and certain carcinogens which causes chromosomal damage consequently lowering the risk of developing cancer via different mechanisms.

No evidence in the prevention of oral, pharyngeal, or esophageal cancer has been observed on the consumption of dark yellow fruits such as orange, apricots and lemons. A study from Brazil gave evidence in support of intake of banana in reducing the risk of carcinoma in head and neck by approximately 77%. This could be due attributed to the fact that it contains carotenoids, vitamins, phenolic acids and biogenic amines with antioxidant effects.^[10]

A-TOCOPHEROL (VITAMIN E)

A-tocopherol (AT) is the most widely recognized and most dynamic type of nutrient E. It is abundantly present in plant oil, margarine, and green leaves. The suggested everyday limit rates for adults are 10 mg/day for men and 8 mg/day for females. Known for its antioxidant properties, Vitamin E maintains and protect cellular membranes from lipidic peroxidation. AT functionally are free radical scavenging, immune function maintaining, membrane integrity supporting, and cancer cell differentiation inhibiting and cytotoxic.

Hence known to repress mutagenicity and nitrosamine formation.^[1]

30% reduction in risk was proved in one the studies wherein one or more supplements for vitamins A, C, E, or B-complex were recommended for minimum of 6 months. However, that study revealed that only vitamin E has provided with risk reduction of significance. This can also be due to the fact that no one used just one vitamin supplement and could be a contributed synergistic effect. 50% drop in risk with vitamin E was quite consistent even in certain amount of tobacco and alcohol use, fruit and vegetable intake, consumption of other supplements, and dietary vitamin E.^[3]

SPIRULINA

The blue-green microalgae *Spirulina*, is utilized in everyday diets of locals in Africa and America. *Spirulina* is the best food containing cancer prevention agents, phytonutrients, fundamental unsaturated fats, probiotics, and nutraceuticals. *Spirulina* abundantly contain protein, B-vitamins, beta-carotene, chlorophyll, gamma-linolenic acid, minerals, sulfolipids, superoxide dismutase, glycolipids, phycocyanin, and enzymes. The supplements present in *Spirulina* help the invulnerable framework and improve the body's capacity to produce new blood cells to forestall infection and malignancy (Mathew et al. 1995).^[1]

GREEN TEA

Green tea is derived from the *Camellia sinensis* plant, with black and green being the most popular varieties. Green tea polyphenols having anticarcinogenic properties along with EGCG (epigallocatechin-3-gallate) are the most biologically active catechin known to inhibit tumor initiation and its promotion, induction of apoptosis, and inhibition of cell replication rates, thus suppressing the tumor development.^[1]

High concentrations of catechins and flavins can be detected in saliva after an hour of green tea intake, inducing a slow release of these compounds in the oral cavity. Thus, it can be effective in preventing periodontal diseases and dental caries.

Green tea was shown to potency against multiple cancers for its chemo preventive potential including oral cancer (Ramshankar & Krishnamurthy, 2014). Green tea is non-toxic, inexpensive, and can be consumed orally. A study completed by the Academy of General Dentistry reported positive results that swishing green tea in the mouth effectively suppresses the growth of oral cancer cells (Tsao et al., 2009). A similar study provides evidence that green tea eliminates cancer existing cells. These findings are being associated with the antioxidant polyphenols present in the tea. They remove free radicals and hence prevent gene mutation. In another study done at The University of Texas M.D. Anderson Cancer

Center, green tea extracts were used in tablet form to test the efficacy of green tea. The Utilization of green tea extract proved a tremendous effect on patients suffering from oral leukoplakia (Tsao et al., 2009). Oral leukoplakia is characterized by the increased formation of precancerous cells that may lead to oral cancer development.^[9]

NEEM

Gallic acid, catechin, and epicatechin are phytochemicals identified with oral cancer, which have a carcinogenic agent detoxifying chemical, glutathione. Catechin is known to suppress the production of metalloproteases, reduction in migration, invasion and induction in the apoptosis of neoplastic cells. It suppresses nuclear factor κ -b (NF κ -b) given its anti-inflammatory properties, thus inducing the apoptosis of malignant cancer cells (Dutta et al. 2012).^[1]

LYCOPENE

It is quite possibly the strongest antioxidant. Lycopene is a bright red carotene, a phytochemical and a carotenoid pigment, found in red food such as tomatoes, red carrots, watermelons, grapefruits and papayas. It is hypothesized that it prevents atherogenesis and carcinogenesis by protecting organic molecules, including, proteins, lipids, lipoproteins, and DNA. Tissue levels and serum in lycopene in certain literature was found to be inversely linked with the risk of prostate cancer, coronary heart disease, breast cancer and oral premalignant lesions/conditions. Different investigations showed that lycopene when prescribed in a dose of 4-8 mg/day orally for 90 days prompts an inversion of dysplastic changes in the oral leukoplakia and 16 mg/day in oral submucous fibrosis.^[1]

The chronic diseases for example cardiovascular diseases, degenerative diseases and bone disorders, lycopene showed up a significant role in prevention and treatment. Thus it is marked as worthy in the treatment of potentially malignant oral conditions and as a protective factor because it regulates lipid peroxidation and reduced glutathione.^[10]

CURCUMIN

Curcumin is a phenolic pigment which is yellow in colour and extracted from turmeric. It is popular for its anti-carcinogenic and several other therapeutic benefits. Curcumin induce apoptosis and inhibit cell growth in oral cancer cells and also shows antitumor activity. A calculated day to day dose of up to 10 g can repress initiation, promotion, and metastasis of the neoplasm (Dutta et al. 2012; Devasagayam et al. 2004).^[1]

Curcumin is widely popular for its benefits such as healing properties since it is an antioxidant, antiangiogenic, anti inflammatory and anticancer.

Various studies claim Different carcinogenesis substances induced by 4NQO (4-nitroquinoline 1-oxide) are significantly reduced on administration of curcumin (100 mg/kg for 3 months).^[10]

MUSHROOMS

Mushroom species such as shiitake, maitake, reishi, and ceratinagaricus inhibit malignant growth and develop resistance to carcinogens giving in to the constitution of specific glucans and proteoglycans (polysaccharide peptides) (Kidd 2000). Medicinal mushrooms containing purified bioactive compounds are a potentially important and new source of anticancer agents. Extraordinary mutagenic and anticancer activity were established in these four mushrooms.^[1]

RED FRUITS

Grapes, blackberries and red berries consist bulk quantities of polyphenols for example resveratrol. Resveratrol functions as a regulator for cell division, cell growth, cell migration, cell adhesion, and cell invasion. It is also known to control apoptosis and angiogenesis properties because of its antioxidant, anti-inflammatory and anti-cancerous potential.^[10]

GARLIC

Garlic belongs to the family liliaceae. In addition to its use as a flavor, it is popular for its therapeutic effects as an antioxidant, anti-inflammatory, anti-carcinogenic, and antimicrobial compound. Although only one valid study support the evidence of garlic consumption as preventive factor against cancer, alot of literature claim that phytochemical found in garlic could increase the enzyme activity by detoxifying carcinogens.^[10]

FOLATE

Vegetables, beans, cereals, and pasta contain folic acid or folate also named as vitamin B9. Folate functions in DNA synthesis, methylation and in cell cycle repair, thereby controlling the risk of oral carcinoma development. This is achieved because of the epithelium's capacity to continuous proliferate and regenerate. An inversely proportional relationship was proved in one of the studies, between presence of large amount of folate and the risk of developing oropharyngeal cancer. This inverse association corresponds higher relativity in oral cancer. This increased risk was found to be far more in heavy drinkers who had low levels of folate in their system.^[10]

SELENIUM

Found in beef, chicken, walnuts and game (bush meat) Selenium is popular mineral with antioxidant and pro-apoptotic properties. Thus, it aids in DNA repair. Serum selenium is a preventive factor in oral cancer in addition with large amount of fish and fruits consumption. This is especially effective with cessation of tobacco and alcohol consumption.^[10]

ZINC AND COPPER

Zinc is one of the most popular mineral obtained from proteins of animal origin (pork, sheep and beef). Dietary sources like legumes, cereals, nuts and yeast are also good sources of zinc. With copper, zinc can form a compound that aids in many biological functions like free radicals elimination by enzymatic activity. Moreover, zinc also plays a vital role in DNA synthesis, immune response and regulation of gene transcription.^[10]

STARCHY FOOD

Starchy food, especially the ones with refined cereals in the RDS, is being linked with risk escalation in carcinoma affecting head and neck region. Certain studies claim that cereals, whole grain and dietary fiber intake significantly lower the risk of oral cancer.^[10]

MEATS

Although some studies have reported increased risks associated consumption of meat in high to moderate consumption, few other studies have reported protective or inconsistent pattern in developing cancer. In a Brazilian investigation, charcoal grilled meat was found to have increased risk of oral cancer, but other studies in the United States have found negligible evidence of such claims. Similarly, studies have also suggested that salted fish and meat or processed meat or nitrite-containing meat could be linked to elevated risks of oral cancer in certain population or subgroup. However, all these claims hold no significant ground to be sufficiently corroborated and thus require further study. Fish consumption has also been identified as potentially risk reducing in relation to Oral cancer risk in a lot of studies. Several other investigations do not claim such associations.^[3]

DAIRY FOODS

Consumption of milk has been associated to prevention of risk of developing cancer in some studies while in other investigations it didn't prove to be true. On the other hand, cheese intake has been linked with an elevated risk in some of the studies.^[3]

VARIOUS HERBAL SUPPLEMENTS AS COMPLEMENTARY TREATMENTS FOR ORAL CANCER

ANTHOCYANINS

Recent studies have shown that black raspberries frozen and dried (FBR, *Rubus leucodermis*, Rosaceae) exhibit cancer preventing properties both in vivo and in vitro because of high content of anthocyanins (Mallery et al., 2007). Anthocyanins are antioxidants found in fruits such as black raspberries and other plants with bright-colored leaves and flowers. Various studies also claim that application of anthocyanin gel to the mouth suppress genes that promote the growth of cancer cells.

ASPARAGUS

Asparagus or shatavari (wild asparagus, *Asparagus officinalis*, Liliaceae) is a vegetable known for

containing high amount of glutathione and enzyme L-asparaginase. Glutathione is an endogenous antioxidant with a potent anticarcinogenic property (Mitra, Prakash, & Sundaram 2012). Asparagus (Asparaginase enzyme) can be potentially utilized as a complementary treatment for cancer as an adjunct (Shrivastava et al., 2015). It has proved benefits in the treatment of bacterial infections and with remarkable efficacy in chemotherapy. Shoots/edible portions of the asparagus plant have shown antitumor activity with the potential to inhibit growth of human leukemia cells (Shao et al., 1996). Cancer patients prone to infections given their decreased immune function can be provided such complementary treatment.^[9]

RECOMMENDATIONS FOR PREVENTION OF CANCER

BODY FAT

Stay as possibly lean within the normal range of body weight as one can.

PHYSICAL ACTIVITY

Stay physically active as a part of everyday life.

FOOD AND DRINKS THAT INDUCE WEIGHT GAIN

Limit intake of energy-rich food and sugar-laden drinks.

PLANT FOODS

Improve diet in plant origin food.

ANIMAL FOOD

Avoid consuming red meat and processed meat.

ALCOHOLIC DRINKS

Limit consumption of alcoholic drinks.

PRESERVATION, PROCESSING AND PREPARATION

Reduce intake of salt, moldy cereals (grains) and pulses (legumes)

DIETARY SUPPLEMENTS

Target nutritional needs through only diet; dietary supplements are usually not advised for cancer prevention.

BREASTFEEDING

Breastfeeding is encouraged instead of artificial formulas.

CANCER SURVIVORS

Follow guidelines for cancer prevention.^[6]

GUIDELINES PREVENTION

- Encourage smoking discontinuance.
- Discourage more than moderate alcohol consumption.

- Promote the National Cancer Institute's Five a Day of fruit and vegetable servings and the American Cancer Society (ACS) Diet for Cancer Prevention.
- ACS diet guidelines.
- Eat a variety of healthful foods, with an emphasis on plant sources.
- Try to eat at least five to seven servings a day of fruits and vegetables, including citrus fruits and dark-green and deep-yellow vegetables.
- Choose whole grains in preference to processed (refined) grains and sugars.
- Limit consumption of red meats, especially those high in fat and processed.
- Choose food that maintains a healthy weight.
- Adopt a physically active lifestyle.
- Adults: engage in at least moderate activity for 30 min or more on 5 or more days of the week.
- Children and adolescents: engage in at least 60 min per day of moderate to vigorous physical activity at least 5 d per week.
- Maintain a healthy weight throughout life.
- Balance calorie intake with physical activity.

INTERVENTION

- Provide Medical Nutrition therapy (MNT) consistent with treatment and post treatment needs.
- Recommendations of the ACS.
- Plan diet based on nutrient needs and individual side-effects experiences.
- Recommendations for after treatment ends.
- Ask your registered dietitian (RD) to work with you to develop a balanced eating plan.
- Choose a variety of foods from all the food groups. Use the ACS Guidelines for Nutrition for Cancer Prevention.
- Eat plenty of high-fiber foods, such as whole-grain breads and cereals.
- Decrease the amount of fat in your meals by baking or broiling foods.
- Choose low-fat milk and dairy products.
- Avoid salt-cured, smoked, and pickled foods.
- Drink alcohol only occasionally if you choose to drink^[3]

CONCLUSION

Undoubtedly malignant growths of the mouth and pharynx, and additionally the more extensive scope of threatening neoplasms that influence the aerodigestive tract, can be forestalled by burning-through an eating regimen wealthy in cell reinforcements, known new vegetables, and various other organic products. Preparation of smoked groceries, simmered and barbecued food sources are found to have certain degree of reduction in malignant growth. Balancing of liquor utilization to given suggested rules (restricting units of cocktails to two for men and one for ladies daily) will reduce the danger of malignant growths in

the oral cavity as well as pharynx. The message at the core of the '5 A DAY' program – to eat essentially five segments (400 g/day) of an assortment of foods grown from the ground every day. Just as eating '5 A DAY', ensure against different problems, the eating regimen ought to incorporate entirety grains (for example earthy colored rice, wholemeal bread and pasta) and additionally beats with each dinner. (2009).^[12]

Diet rich in vegetables and fruits is beneficial attributing to different micronutrients, such as lycopene, polyphenols, flavins, catechins and curcuminoid, slow digesting starches, carotenes, minerals (zinc, selenium and copper), vitamins (A, B, C, and E), folate and omega 3 acids. Fish and animal products are also rich sources of these minerals. All these compounds have different mechanisms of action, and in combination, may have synergistic antioxidant, anti-angiogenic, anti-inflammatory and anti-proliferative effect.^[10]

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