บทความปริทัศน์
Review Article

Diet, Consumption Related Behaviors and Primary Prevention of Oral Cancer

Patchanee Chuveera
Department of General Dentistry, Faculty of Dentistry, Chiang Mai University

ชม.ทันตสาร 2545; 23(1-2) : 35-40
CM Dent J 2002; 23(1-2) : 35-40

Abstract

This review article investigates the role of diet and related consumption behaviors in relation to risk of oral cancer. Preventable aspects of oral cancer are also discussed in order to provide primary prevention strategies. It has been suggested that tobacco use, alcohol consumption, and diet are associated with oral cancer. Evidence regarding tobacco and alcohol consumption as risk factors is extensive and consistent. Tobacco smoking has been widely recognized as a risk factor in developed countries while smokeless tobacco such as tobacco chewing, snuffing, and betel quid chewing are more reported as important factors in the developing world. Alcoholic drink appears to increase oral cancer risk regardless of the forms. Moreover, combination of tobacco and alcohol use has been found to increase the risk far greater than either substance used alone. Several studies on food and oral cancer found that meat and meat products, particularly salt-preserved meat and fish, are associated with increased risk of oral and pharyngeal cancer. Findings for other food groups such as staple diet and diary products are inconsistency. However, fruit and vegetable are consistently reported to provide a significant protective effect against oral cancer. Based on the accumulated evidence, the feasible policy, particularly for resource scarce countries in order to reduce oral cancer burden, is to encourage people to avoid tobacco use and alcohol consumption together with promoting of healthy diet consumption, mainly fruit and vegetable.

Key Words: oral cancer, diet, tobacco, alcohol, primary prevention

Introduction

Oral cancer is the fifth most common cancer ranked by the World Health Organization in 1996. Global cancer incidence and mortality rates vary across the world and the highest rates are generally registered in a few developing countries including India, Pakistan, Bangladesh and parts of South East Asia.[1] Recent reports have also noted increasing incidence and decreasing of age of presentation in developed countries particularly in many European countries.[2,3,4] As oral cancer is a gastrointestinal site, and as the mouth is exposed to every food consumed, it is suspected that diet and consumption related behaviors would greatly effect on the risk of oral cancer. In this paper, while aspect of diet and related behaviors such as etiologic factors are investigated, the protective role of diet in prevention of oral cancer is also emphasized. Strategies for primary prevention based on scientific evidence are also recommended in order to reduce the global cancer burden.

Diet and related consumption behaviors as risk factors

Most studies agree that tobacco use, alcohol consumption, and nutrition factors account for almost all oral cancer cases. Tobacco and alcohol, even though not normally classified as nutrients, are orally administered and thus are often considered along with diet factors. Evidence related to each factor will be discussed as following.

Tobacco

Tobacco has been identified consistently as the major risk factor for oral and pharyngeal cancers. While tobacco smoking has been widely recognised as a risk factor in developed countries,[2] smokeless tobacco (i.e., tobacco chewing and snuffing) and other chewing habit such as betel quid chewing are more reported as important factors in the eastern world.[5] The majority of patients in most surveys are or have been regular tobacco users. Considering cigarette smoking independently, the risk (demonstrated by odd ratio) increases significantly with number of cigarettes smoked per day and the duration of smoking.[6,7] For pipe or cigar smokers, the risk is greater than for cigarette smokers.[6,7] Bidi smoking (hand rolled, tobacco wrapped in tendu or temburni leaf) has been shown to be significantly associated with oral cancer in a Bombay study[8]. Surprisingly, bidi smoking is not limited only in subpopulation of developing countries. A report in the U.S. has raised a concern of the increasing trend in the use of bidi among U.S. teenagers. It showed that up to 40% of students have tried bidi and up to 16% are current users.[9] A recent hospital- based case-control study in Southern India demonstrated the significant association between increased risk and chewing habit[10]. It shows that 49% of oral cancer among men is attributed to pan-tobacco (a mixture of betel leaf, areca nut, lime, and tobacco) chewing and the risk is more elevated among women (odd ratio= 6.1 in men and 46 in women). Tobacco chewing has also shown a significant association with oral cancer and this increases with increasing length of exposure. Risks are greatest at anatomic sites where the product has been held in contact the longest time and also increase risk of cancer of other organs such as oesophagus, larynx and stomach.[11] On average, those who smoke at all have three to five times the risk of oral cancer compared to those who do not.[6] Fortunately, cessation of smoking has been found associated with a reduced risk to normal level after 10 years after cessation.[6,7]

Alcohol

Alcohol is another major factor linked to the development of oral cancer. The evidence is extensive and consistent even when other risk factors are taken into account. In never smokers, Fioretti et al[12] have found three-fold higher in risk among drinkers than non drinkers. The direct relation with the duration of habit has also been found. Blot et al[6] have demonstrated increased risk in heavy drinkers compared to light drinkers. Various forms of alcoholic beverage have also been studied. Studies in the U.S. tend to suggest higher risk from consuming hard liquor or beer rather than wine. In contrast, a study conducted in Northern Italy points to wine as the main alcoholic risk factor among non smokers in this region[12]. It appears, therefore, that most frequently used types of alcoholic drink in each population accounts for the most determinant in that geographic area. This also indicates that alcohol appears to increase oral cancer risk regardless of the forms it takes. The effect of alcohol-containing mouthwash has also been the subject of several studies of oral cancer. A large population-based case control study in the United States found excess risks of mouthwash use to be 40% among males and 60% among females after adjusted for the effects of tobacco and alcohol.[13] In this study, elevated risks were confined to users of mouthwash containing high concentrations of alcohol (25%). In other studies, evidence of the association of mouthwash use and oral cancer has been inconsistent.[14-20] A more recent study in Puerto Rico yields no evidence of an increased risk of oral cancer associated with mouthwash use. The adjusted odd ratio associated with using mouthwash with an alcohol content of 25% or greater in this study was equal to 1.0.[21] However, an elevated, but not statistically significant, risk among the small number of

subjects who neither smoked cigarettes or drank alcohol (among whom the researcher assumed an effect of alcohol containing mouthwash to be most likely evident) was also emphasized. These inconsistent findings indicate the need for further research to clarify the effects of alcohol-containing mouthwash in the etiology of oral cancer.

Synergistic effect of tobacco and alcohol

The joint effect of tobacco and alcohol has been examined and found to have a synergetic effect. Most studies suggest that the combination of tobacco and alcohol use increases the risk in multiplicative way rather than just additive way. For instance, Franceschi et al reports an 80- fold increase in males practising both heavy smoking and heavy drinking compared to the baseline group who were non-smokers and also abstainers or light drinkers.[7] Blot et al[6] shows more than 35- fold increased risk for those who consume two or more packs of cigarettes and more than four alcoholic drinks per day compared to those who consume lower amount of both products. The mechanism of interaction is still unclear. One suggestion is that alcohol may simply act as a solvent and thus facilitating the passage of carcinogens through cellular membranes[2] However, consistent finding from most epidemiologic studies indicates that the combined use of alcohol and tobacco increases the risk of oral cancer far greater than either independently. Unfortunately, most of those who smoke also consume alcohol. Synergistic effect of cigarette smoking, alcohol drinking and betel chewing is also a subject of interest. According to a study from Taiwan where the habit of betel quid chewing is widespread, betel quid chewers who also smoked cigarettes and consumed alcohol run the highest risk of oral cancer[22]. The risk is as high as 100- fold greater than the risk among those who combined the habits of cigarettes smoking and alcohol drinking without betel quid chewing, or 123- fold higher than in abstainers.

Diet as an etiologic factor

Although tobacco use and alcohol abuse are most often referred to as the chief contributors, it is also claimed that diet is responsible for some of the remaining of cancer cases and may influence the effects of tobacco and alcohol.

Meat and meat products appear to be associated with increased risk in several studies.[23-26] De Stefani et al have found a strong association of cancer of upper aerodigestive tract with red meat intake[25] Salted meat is specifically reported in this study to be associated with an increase risk of 60% for esophageal cancer.[25] Besides salted meat, ingestion of salted fish, particularly Cantonese-style salted fish, is consistently reported to be an important risk factor for nasopharyngeal cancer.[27-29] High consumption of salted meat and salted fish is responsible for an excess risk of oral and pharyngeal cancer in a Shanghai study with the association to be stronger for mouth than for pharynx.[26]. It is suspected that N-Nitroso compound, which are particularly high in preserved meat and fish, may contribute to the association of salted foods with certain tumors.[26] A study in Brazil found that eating charcoal-grilled meat at least four times per week is associated with a five ñfold increase in risk.[30] Butter or animal fat intake have been suggested as a risk factor in European studies.[12,31] A study in India has also implied the effect of meat consumption by showing the significance of non-vegetarian diet as a high risk factor compared to vegetarian diet.[8] Some indigenous staple diet ,such as cassava[30] and maize[32], has been claimed to increase the risk. It has been explained that a high intake of particular dietary staples may be an indication of a poor diet in general and that inadequate nutrition enhances cancer risks. Moreover, high content of leucine in maize may influence carcinogenesis and alcohol may aggravate the nutritional deficiency introduced by maize-rich diet.[2] However, a recent study in Greece reports significant evidence that consumption of cereals and starchy roots is associated inversely with the risk[23]. The relationship between cereal products and the risk of cancer of the mouth and pharynx may depend on the degree to which these product are refine.[29] A recent major review of oral cancer risk in association with milk and dairy products, coffee, and tea have also been investigated. However, a recent major review has found limited evidence and/or inconsistent

results.[29] The possible role of poor nutritional status has also been suggested by the finding of inverse association of body mass index (BMI) with oral cancer risk.[33] It has been explained that increased body weight may be an index for better nutritional status, but it is also not clear that weight loss may resulted from the effect of cancer.

The role of diet as a protective factor

The growing epidemiologic literature from diverse geographic areas is supportive of the protective effects of fruit and vegetable based diet. Of fifteen case-control studies reviewed by World Cancer Research Fund and American Institute for Cancer Research in 1997, thirteen studies reported statistically significant protective association, for at least one vegetable and/or fruit category, with odd ratio range from 0.2 to 0.6.[29] Later studies also confirm the result[12,23,25,34,35]. The evidence is most consistent for carrots, citrus fruits and green vegetable. Of other fruits and vegetable reported, a population–based case-control study in Shanghai particularly suggests oranges, tangerines and Chinese white radish,[26] while fresh tomatoes and green peppers are recommended in a large Italian study.[36] A case-control study in India shows that those who do not eat vegetables daily have twice the risk as those with daily consumption.[37] Francheschi et al.[24] reports that frequent consumption of vegetables, citrus fruit, fish and vegetable oils, especially olive oil, are the major features of a low-risk diet for cancer of the oral cavity and pharynx. The recent evidence from Greece[23] is also consistent with others. It attributes the low incidence of oral carcinoma in this region, even though having high prevalence of smoking and regular habit of alcohol consumption, to the traditional high consumption of fruit, cereals and olive oil in this population.

It is believed that some specific micronutrients in fruit and vegetable could protect against cancers through their antioxidant activities.[38,39] In addition, fibre, irrespective of its source (vegetable, fruit, or grain) have also been found to exert a strong protective effect.[34,40] Among studies investigating the role of vitamin and other micronutrients on oral carcinogenesis ,vitamin C, carotinoids, vitamin E, folate, riboflavin, retinol, iron, zinc, and selenium are of particular interest. Inverse associations are generally observed with some inconsistent findings. Consistent results are, however, reported specifically for dietary vitamin C intake.[29,34,35] There are increasing intervention studies using micronutrients as chemopreventive supplements. Many of these studies have shown associations with reduced risks of oral cancers and precancer. For example, intervention trials in tobacco smokers and chewers with and without precancerous lesions have included selenium and zinc in combination with other nutrients.[41-43] A cocktail of vitamin A, selenium, riboflavin, and zinc has led to a significant regression of precancerous lesions[41-43] and lower risk of developing new lesion in non-lesion group.[43] Even though a significant amount of data regarding antioxidants in prevention and treatment of cancer have accumulated, the risk of over consumption of nutrient supplements should also be considered. In general, it is more sensible to obtain antioxidants from food rather than in supplement form.

Conclusion

Oral cancer, even though it has been considered as a cancer of traditional societies and has more prominence in developing countries, is rapidly increasing in developed countries particularly most European countries.[3] Alcohol and tobacco are the two most widely recognised risk factors and increasing use has been noted to be the most obvious reason for the increase rates observed. The rather modern (for developing countries) consumption patterns of smoking and various types of alcohol consumption and the transition into diets high in saturated fat, refined food, and low in fibre could also multiply the risks already attributed by indigenous factors in the developing world, as these countries are becoming more industrialized and urbanized. An explicit example has been shown in the group of subjects studied in a southern Thailand province[5], where the highest incidence in the nation has been found; alcohol drinking, tobacco smoking, together with betel quid chewing and smokeless tobacco habits are also commonly practised in that region. Moreover, a tendency to deficient nutritional status in low socioeconomic

groups could intensify the risk. In most developing countries, the medical and economical resources may not exist to cover the rising burden of cancer. Primary prevention by encouraging people to change their risk behaviours and consume a healthier diet could be the only feasible policy option. Balanced nutritional status and maintenance of appropriate body weight should be included in national health programs. Public awareness of the etiologic factors and preventable aspect of oral cancer should be raised together with enforcement of legislations regarding tobacco and alcohol products. In short, much of the world's burden of oral cancer, in agreement with cancer over all, could be prevented by cessation of tobacco use, avoidance of alcohol consumption and eating healthy food, mainly high consumption of fruit and vegetable.

References:

1. Marshall JR, Boyle P. Nutrition and oral cancer. *Cancer Causes and Control* 1996;7:101-111.
2. La Vecchia C, Tavani A, Franceschi S, Levi F, Corrao G, and Negri E. Epidemiology and prevention of oral cancer. *Oral Oncology* 1997 ;33(5):302-312.
3. Mackenzie J, Ah-See K, Thakker N, et al. Increasing incidence of oral cancer amongst young persons: what is the aetiology? *Oral Oncology* 2000; 36: 387-389.
4. Moynihan P. The British Nutrition Foundation oral task force report- issues relevant to dental health professionals. *British Dental Journal* 2000; 188(6): 308-12.
5. Kerdpon D, Sriplung H, Kietthubthew S. Expression of p53 in oral carcinoma and its association with risk habits in southern Thailand. *Oral Onchology* 2001; 37:553-557.
6. Blot WJ, McLaughlin JK, Winn DM, et al. Smoking and drinking in relation to oral and pharyngeal cancer. *Cancer Research* 1988;48:3282-7.
7. Franceschi S, Talamini R, Barra S, et al. Smoking and drinking in relation to cancers of the oral cavity, pharynx, larynx and esophagus in Northern Italy. *Cancer Research* 1990; 50: 6502-6507.
8. Rao DN, Ganesh B,Ra ors, Desai PB. Risk assessment of tobacco, alcohol and diet in oral cancer- a case-control study. *Inter J Cancer* 1994; 58(4): 469-73.
9. Fisher L. Bidis- The latest trend in U.S. teen tobacco use. *Cancer Causes and Control* 2000;11:577-578.
10. Balaram P, Sridhar H, Rajkumar T, et al. Oral cancer in southern India: the influence of smoking, drinking, pann-chewing and oral hygiene. *Int J Cancer* 2002; 98(3): 440-5.
11. Mattson ME, Winn DM. Smokeless tobacco: association with increased cancer risk. *NCI Monogr* 1989; 8: 13-6.
12. Fioretti F, Bosetti C, Tavani A, Franceschi S, and La Vecchia. Risk factors for oral and pharyngeal cancer in never smokers. *Oral Oncology* 1999;35:375-8.
13. Winn DM, Blot WJ, McLaughlin JK,et al. Mouthwash use and oral conditions in the risk of oral and pharyngeal cancer. *Cancer Research* 1991; 51: 3044-7.
14. Weaver A, Fleming SM, Smith DB. Mouthwash use and oral cancer: carcinogen or coincidence? *J Oral Surg* 1979; 37: 250-3.
15. Wynder EL, Kabat G, Rosenberg S, Levenstein M. Oral cancer and mouthwash use. *J Natl Cancer Inst* 1983;70:255-60.
16. Blot WJ, Winn DM.Oral cancer and mouthwash. *J Natl Cancer Inst* 1983;70:251-3.
17. Young TB, Ford CN, Brandenberg JH. An epidemiologic study of oral cancer in a statewide network. *Am J Otolaryngol* 1986; 7: 200-8.
18. Mashberg A, Barsa P, Grossman ML. A study of the relationship between mouthwash use and oral cancer. *J Am Dent Assoc* 1985;110: 731-4.
19. Kebat GC, Herbert JR, Wynder EL. Risk factors for oral cancer in women. *Cancer Res* 1989; 49: 2803-6.
20. Elmore JG, Horwitz RI. Oral cancer and mouthwash use: evaluation of the epidemiologic evidence. *Otolaryngol Head Neck Surg* 1995; 113: 253-61.
21. Winn DM, Diehl SR, Brown LM, et al. Mouthwash in the etiology of oral cancer in Puerto Rico. *Cancer Causes and Control* 2001; 12: 419-29.

22. Ko YC, Huang YL, Lee CH, et al. Betel quid chewing, cigarette smoking and alcohol consumption related to oral cancer in Taiwan. *J Oral Pathol Med* 1995; 24:450-3.
23. Petridou E, Zavras AI, Lefatzis D, et al. The role of diet and specific micronutrients in the etiology of oral carcinoma. *Cancer*2002;94(11):2981-2988.
24. Franceschi S, Favero A, Conti E, et al. Food groups, oils, and butter, and cancer of the oral cavity and pharynx. *Br J Cancer* 1999;80:614-20.
25. De Stefani E, Deneo-Pellegrini H, Mendilaharsu M, Ronco A. Diet and risk of cancer of the upper aerodigestive tract-1. Foods. *Oral Oncology* 1999; 35:17-21.
26. Zheng W, Blot WJ, Shu XO, et al. Risk factors for oral and pharyngeal cancer in Shanghai, with emphasis on diet. *Cancer Epidemiology, Biomarkers& Prevention.* 1992; 1: 441-8.
27. Yuan JM, Wang XL, Xiang YB, et al. Preserved foods in relation to risk of nasopharyngeal carcinoma in Shanghai, China. Int. *J. Cancer* 2000; 85: 358-63.
28. Ward MH, Pan WH, Cheng YJ, et al. Dietary exposure to nitrite and nitrosamines and risk of nasopharyngeal carcinoma in Taiwan. Int. *J. Cancer* 2000; 86:603-9.
29. World Cancer Research Fund & American Institute for Cancer Research. Food, nutrition, and the prevention of cancer: a global perspective. Washington DC,1997
30. Franco EL, Kowalski LP, Oliveira BV, et al. Risk factors for oral cancer in Brazil: A case-control study. Int. *J Cancer* 1989; 43:992-1000.
31. Levi F, Pasche C, La Vecchia C, et al. Food group and risk of oral and pharyngeal cancer. Int. *J Cancer* 1998;77: 705-9.
32. Franceschi, Bidoli E, Baron AE, La Vecchia C. Maize and risk of cancer of the oral cavity, pharynx and esophagus in northeastern Italy. *JNCI* 1990; 82:1407-11.
33. Kebat GC, Chang CJ, and Wynder EL. The role of tobacco, alcohol use, and body mass index in oral and pharyngeal cancer. Int. J. *Epidemiol* 1994;23:1137-1144.
34. Macfarlane GJ, Zheng T, Marshall P, et al. Alcohol, tobacco, diet and the risk of oral cancer: a pooled analysis of three case-control studies. *Oral Oncol. Eur J Cancer* 1995; 3B(3): 181-7.
35. Negri E, Franceschi S, Bosetti C, et al. Selected micronutrients and oral and pharyngeal cancer. Int. *J Cancer* 2000; 86: 122-7.
36. Franceschi S, Bidoli E, Baron AE, et al. Nutrition and cancer of the oral cavity and pharynx in North-East Italy. *Int J Cancer* 1991; 47:20-5.
37. Notani PN, Jayant K, Role of diet in upper aerodigestive tract cancer. *Nutr Cancer* 1987;10;103-13.
38. Steinmetz KA, Potter JD. Vegetable, fruit and cancer.1- Epidemiology. *Cancer Causes and Control* 1991;2:325-57.
39. Steinmetz KA, Potter JD. Vegetable, fruit and cancer.2- Mechanisms. *Cancer Causes and Control* 1991;2:427-42.
40. Soler M, Bosetti C, Franceschi S, et al. Fiber intake and the risk of oral, pharyngeal and esophageal cancer. *Int J Cancer* 2001; 91: 283-287.
41. Krishnaswamy K, Prasad MPR, Krishna TP and Pasricha S. Selenium in cacer- a case control study. *Indian J Med Res* 1993; 44:87-92.
42. Prasad MPR, Mukunda MA, Krishanaswamy K. Micronuclei and carcinogen DNA adduct as intermediate end point in nutrient intervention study on oral precancerous lesions. *Eur J Cancer Part B Oral Oncol* 1995; 31B:155-9.
43. Krishnasawamy K, Prasad MP, Krishna TP, et al, A case study of nutrient intervention of oral precancerous lesion in India. *Eur J Cancer Part B Oral Oncol* 1995; 31B:41-8.

Reprint requests:

Dr. Patchanee Chuveera, Department of General Dentistry, Faculty of Dentistry, Chiang Mai University, Chiang Mai 50200 E-mail: dnoplrtt@chiangmai.ac.th