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## **Understanding the Factors Involved with Oral Cancer**

### **Introduction**

Oral cancer is the growth of cells that negatively affects the tissue of the oral cavity (6). The oral cavity includes the floor of the mouth, tongue, palate, oropharynx and lips, and accounts for about forty percent of cancers that occurs in the head and neck (8). Often the first indication of oral cancer is evidenced by a growth or sore that is always present and not self healing. It has been proposed that 43 percent of cancer related deaths are caused by tobacco use, alcohol consumption, unhealthy diet, inactive life style and/or infections (4). Tobacco use and heavy alcohol consumption are the two major risk factors for oral cancer and are present in about 75 percent of total oral cancers incidents (1). About 25 percent of cases with an oral cancer diagnosis are caused by genetic and nutritional factors (8). Overall, in the United States, oral cancer accounts for about 2 percent of the total cancer-related deaths (8).

### **Formation of Oral Cancer**

Oral cancer is a progressive disease, similar to the formation of any other type of cancer, in which normal epithelium tissue goes through a series of mutations leading to the formation of cancer (1). While all types of cancers can be seen in the oral cavity, the most common occurrence of oral cancer is squamous cell carcinoma, cancer of the epithelial tissue (4). Oral lesions found in the oral cavity and the oropharynx are early indications of possible areas where cancer may develop over time. Leukoplakia and erythroplakia are precancerous lesions found in

the oral cavity that commonly develop over time into squamous cell carcinoma. (4) Leukoplakia is one of the most common precancerous lesions found on the oral cavity (8). When present, Leukoplakia appears as a white plaque-like lesion commonly found on the lining of the cheeks, back of the lips, floor of the mouth, and/ or on either side of the tongue of the oral cavity. (15) These lesions are not able to be removed by brushing off, and if still present after two weeks, a biopsy is necessary. (15)

Erythroplakia lesions are less commonly found than leukoplakia lesions but are more commonly linked with squamous cell carcinoma or abnormal development of the epithelial (6). Erythroplakia is the red equivalent of leukoplakia, which appears as a pearly lesion, red in color and at times can also have white spots on the perimeter of the lesion, an indication of leukoplakia (15). This lesion is not always easily defined by its boundaries, as it has an irregular shape, merging areas of inflammation, and includes the rest of the mucous membrane epithelium of the mouth (15). The lesion's presence is highly correlated with the development of carcinoma. As a result, it is normally found in individuals that are at high risk of oral cancer. This has been seen in people who are heavy smokers, drinkers, and are over the age of 40 (15/6). These lesions, when seen in high risk individuals, are normally present before bleeding or discomfort.

## **Oral Cancer Risk Factors**

### **Genetics Impact on Oral Cancer**

The use of genetics in the studying of protein structure / function has led to a greater understanding of the molecular process of oral cancer. Generally speaking, there is a 10 percent

link between the genetic component and cancer. (1). Several research studies are working to link the role of genetics to the development of oral cancer by exploring findings that indicated similar clustering formations (4/7). These clustering formations have been seen in different ethnic groups however, current studies are limited and further research is needed to obtain a better outcome (1). The further examination of the genetic changes and gene expression may possibly be the best resource in better understanding the molecular pathogenesis of oral cancers (4). Understanding the patterns of gene mutations in oral cancer may lead to the development of stronger hypothesis on the causes of the formation of specific tumors.

A recent study by Brennan examined the nature of a p53 mutation in individuals with head and neck squamous cell carcinomas (1). Research from this study suggested that there was evidence of greater p53 mutations in individuals who were exposed to high concentrations of tobacco and alcohol than those individuals that did not have any exposure (1/4). It is hypothesized that alcohol increases the impact that smoking has by allowing for an increase in the absorbance of carcinogens from the cigarette smoke (1).

### **Tobacco's Impact on Oral Cancer**

The use of tobacco is the world's most common cause of cancer of the oral cavity, pharynx, larynx, esophagus, stomach, pancreas, liver, kidneys, urinary bladder, uterine cervix, and bone marrow (4). Second hand smoke and exposure to environmental tobacco smoke increases lung cancer risk (2). Tobacco composed of nicotine rich leaves which are cured by drying and fermentation for the purposes of smoking or chewing (3). The nicotine in the tobacco leaves is only a small part of the composition of the tobacco leaf and accounts for only 5 percent

of the total dried weight of the leaf. Nicotine is primarily absorbed when tobacco smoke is inhaled into the lungs, and absorbed through the lining of the oral cavity when chewed. Tobacco, typically consumed by cigarette smoking is connected to 25 percent of all oral cancer cases (9). Cigarette smoke has been found to have more than 60 potential cancer causing chemicals in it with at least 16 found in tobacco that does not get burnt (9/2). The most cancer causing aspect of cigarettes is tobacco specific nitrosamines which are known to be carcinogenics including nicotine derived nitrosamine ketone, N-nitrosornicotine, and polycyclic aromatic hydrocarbons (9). These three carcinogens ( NNN, NNK, and PAH) have been connected to causing oral cancer. (2)

The risk factors involved with individuals that partake in smoking are higher than those who have stopped smoking, and as the time from stopping progresses, the person's risk then decreases. Other forms of tobacco use have been evaluated to observe the impact its use has on oral cancer (9). Chewing tobacco has been observed in studies that evaluated the amount of tobacco chewed over a period of time demonstrated a correlation with the outcome with oral cancer. This has been observed in area of India and other country where social use of chewing tobacco is high (3). These societies are also ones where diet, oral health and education levels are low leading to these and other risk factors to contribute to the negative outcome of oral cancer (9). The amount of oral cancer is high and increasing in areas that are not as industrial because education programs informing individuals not to smoke and informing them of the negative impaction are not currently being done (13). Counties like the United States that have active programs in inform individuals of the negative side effects or smoking have seen a significant decrease in oral cancer concentrations.

When tobacco consumption is paired with the that of alcohol , in the risk of oral cancer is significantly increased. The use of tobacco and the intake of alcohol consumption are commonly linked together for the causes of cancer of the oral cavity, pharynx, larynx, esophagus because the common relationship of the user to partake in both (3). This relationship between the impact the use of alcohol and tobacco have on the risk factors for oral cancer were the focus of a study that in India (9). This case controlled study quantified moderate drinking to 8 to 25 drinks a week, and 20 - 45 packs of cigarettes smoked a year (9/13). From this study it was concluded that when both substances are joined the risk factor of oral cancer is 11 times greater(9).

The connection between tobacco smoke and oral cancer has been understood to impact the outcome of oral cancer in a more drastic way when individuals partake in both. This can be seen when evaluating the frequency and duration of daily cigarette smoking and the development of oral cancer. Individuals who are occasional smokers are seen to have a decrease in the risk of oral cancer similar to those of non smokers (9). Additionally, heavy smokers are at the highest risk for oral cancer. Individuals that have smoked for over 20 years with a daily intake of higher than 20 cigarettes, have been observed to have a remarkably higher risk for oral and neck cancer (3).

### **Alcohol Consumption Impact on Oral Cancer**

Alcohol consumption is similar to tobacco intake in that the actual amount consumed has a direct effect on the risk factors for possible oral cancer. Individuals that consume 4 to 5 or

more drinks daily increase their risk factor for oral cancer by 2 to 3 times higher risk than that of a non drinker (7). Heavy alcohol drinking accounts for 7 to 19 percent of oral cancer cases which increases even more when these individuals also take part in tobacco smoking/chewing (7).

The main active ingredient in alcohol is ethanol which is produced by the fermentation of carbohydrates from grains and fruits by yeasts. Ethanol is not the only carcinogen in alcoholic drinks but other components including nitrosamines, acrylamide, oxidized polyphenols also play a role and contribute to it but are not as significant as ethanol (7). When alcohol comes in contact with the body it is metabolized by alcohol metabolizing enzymes called alcohol dehydrogenase. This process oxidizes ethanol to acetaldehyde, and aldehyde dehydrogenase, that detoxifies acetaldehyde to acetate (10). The acetaldehyde is an important factor in the impact of the oral cancer effect of ethanol allowing it to have several mutagenic impacts on DNA (10).

### **Oral cancer Prevention and Treatment**

Cancer in general is one of the most common causes of death, with more than 6 million deaths and more than 10 million new cases each year. The major risk factors include tobacco and high alcohol consumption and are often seen as the key link in the cause of oral cancer.

Understanding how tobacco and alcohol separately affect the development of cancers is difficult because individuals that use tobacco often tend to use of alcohol additionally. Dietary factors fall second to tobacco use as a usually preventable cause of cancer (5). The impact that diet has on cancer is a public health factor which needs to be addressed widely to create a better understanding of the importance of diet in people's every day lives (5). Global studies have concluded that higher intakes of fruits and vegetables aid in reducing the probability of oral

cancer, and the consumption of very hot drinks and foods are seen to typically increase the risk of cancer in the oral cavity and pharynx (5/6). These findings are preliminary and further research must be done before a conclusion can be made.

Several treatments have been developed for individuals with oral cancer which include surgery, radiotherapy, chemotherapy, immunotherapy, and gene therapy (12). Surgery has been the most common and established starting treatment for oral cancer. As treatments have developed, ionizing radiation has been used, allowing for a possible non- surgical treatment method but is most commonly used in conjunction with post surgical procedures (12/14). Chemotherapy was used for treatment method in the example of Cis-platinum which is an anti tumor drug, but this treatment was found out not to work in the long term (14). Further research in more effective and innovative treatment is still currently in development. Methods that combine these treatment are being used to fight oral cancer.

## **Conclusion**

Oral cancer's ability to affect varying risk factors mainly including the correlation between high concentrations of tobacco, and alcohol use. Other factors include genetic variability, oral lesions and diet are also include in the risk factors of developing oral cancer (5/6). Affecting the frequency of this risk factors have been observed to reduce the chance of oral cancer. The importance on screening and active awareness of an individuals oral health is imperative in controlling and treating oral cancer. Further research in secondary risk factors including diet, viruses and other controllable situations are being evaluated to aid in better treatment and preventive methods (11).

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