EDITORIAL:

Tobacco Consumption And The Menace Of Oral Cancer In Karachi

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Oral cancer is among the leading cancer type in South Central Asian men. In India, oral cancer is the leading cancer type among men and third most common cancer among women[1] Oral precancerous lesions (PCLs) such as leukoplakia and submucous fibrosis have a variably reported incidence from 0.4% to 24% from different parts of the world with a transformation rate of 2–12% to frank malignancies.[2] In Pakistan, cancer of the oral cavity and pharynx are amongst the commonest type of cancer. According to the reports published by Pakistan Medical Research Council (PMRC), it was the commonest cancer among males and second highest to breast in females.[3,4,5] More recent data shows that oral cavity cancer in Karachi South ranks second in both genders with similar rates in both.[6]

An increase in the prevalence of oral cancer among young adults is a cause of special concern. There has been a 60% increase in the number of cases under 40 years of age with tongue cancer over the past 30 years. During the last 5-6 years it has been observed in one of the major hospitals in Karachi that the disease is appearing more in younger individuals, youngest being 12 years old. Major contributors in this increased incidence include various forms of chewable tobacco along with different additives that are used. These combinations are mostly in the form of Gutka, in particular Manpuri. In addition betal quid containing areca nuts with fungus Aspergillus, HPV infection, familial predisposition and mutations of tumor suppressor genes have also been implicated.[7] A survey in Karachi indicated that 36% of the males and 44% females chew pan or pan with tobacco. The age specific rates show a gradual rise to a maximum in the 7th decade in both sexes.[8]

Tobacco is a conventional agricultural product. As soon as the crop of tobacco is ready, leaves are separated to be dried in sunlight. Special protective measures are taken to protect these tobacco leaves from rain, humidity, and water. When the leaves are dried out, they are heated in a particular furnace and are then used for making various consumable products, such as, cigarettes, niswar, gutka, and betel quid etc. Certain products are also made by dipping these in tobacco juice. China, Cuba, America and Pakistan are top producers of tobacco. Pakistan is also included in the list of high quality tobacco producers.

Use of tobacco is as old as human civilization. The mode of its usage has been changing from one era to another. Until the 18th century, in this part of the world the use of tobacco had been restricted to chewable niswar form. During 19th century, tobacco in the form of cigar and in 20th century as cigarette became common. Today the use of tobacco is in the form of cigar, cigarette,

niswar and in so many other forms also. In modern times, there are two basic modes of tobacco consumption that is smoked and chewable tobacco. Smoking is through cigarette, cigar, shisha, chillum, huqqa and birri. Similarly, tobacco is consumed through mouth or nose without burning it. Chewable tobacco is used by chewing, by sucking, by applying its paste on teeth, stuffing tobacco between teeth and cheek, and finally by snuffing via nose. In recent times, there is a remarkable increase of consumption of these tobacco products in our population.

Dried niswar, humid niswar, common niswar, sutwali niswar, green niswar, black niswar, bannu niswar, swabi niswar, chaman niswar and also niswar and gutka from hawalian, kheni, narampatta, chemon, mishri, maras, plag, shama, tobacco tikkya, and tambak are included in the category of sucking tobacco addictions. Chewable tobacco is usually consumed by mixing additives like betel leave, betel nut, ikk-muk, qiwam , mawa, yung, narumpatta, tobacco chewing gum and zarda. Grounded tobacco with the addition of fragrance and flavor is used for sniffing. This includes dried and liquid niswar. Special tobacco tooth pastes are prepared for cleansing of teeth and treating toothache, e.g., red toothpaste, cream-wali niswar and gharhako. In Pakistan more than 50 types of niswar are prepared from tobacco leaves. Amongst these, F- 16 prepared at Mansehra and Lajawab, prepared at Haripur are very popular. The one prepared at Hawalian is also exported outside Pakistan. In addition to these, the niswar prepared at Bannu, Swabi and Chaman are also liked by niswar users. For preparing Kali niswar: Chai-2.5kg, tobacco-4 kg, water 2.5 kg, and gum powder 250gms are mixed together. Then all these ingredients are grinded for 20 to 25 minutes followed by one hour more mixing, until they are homogenized. To prevent niswar from drying, Noushadar is added. This procedure requires two machines and three persons to complete this whole process of niswar making. Approximately 300 tablets of niswar are made per hour by this method. Black niswar is famous because of its place of origin and flavor, like, Bannu niswar, Saddi niswar, Satt-wali niswar and cardamom-containing niswar. During the past two decades several studies have contributed to a growing awareness of the importance of relatively common genetic and acquired susceptibility factors in modulating risks associated with exposure to various carcinogens. These studies provide substantial evidence that inherited differences exist which is related to the individual capacity of enhancing or detoxifying carcinogens by existing enzyme systems.

Polycyclic aromatic hydrocarbons (PAHs), nitrosamines, aldehydes and ketones form the major carcinogens present in tobacco. Tobacco smoke contains pyrolysis products, which are generated due to high temperatures at the burning tip, whereas smokeless tobacco is rich in nitrosamines.[9] The concomitant use of betel quid leads to a 50-fold increase in reactive oxygen species generated.[2] Most of the carcinogenic moieties in tobacco are metabolically processed by xenobiotic-metabolizing enzymes in two broad steps: phase I mediated by cytochrome p450s (CYPs) and phase II catalyzed by glutathione **S**-transferases (GSTs), **N**-acetyltransferases, etc. Phase I reactions expose functional groups of the substrates and therefore yield highly reactive intermediates. These intermediates form the substrates for phase II reactions that involve their conjugation with endogenous molecules such as glutathione (GSH) and thus facilitate their elimination.[1]

The coordinated expression and regulation of these xenobiotic-metabolizing enzymes (XMEs) determines the outcome of carcinogen exposure. Understanding this phenomenon in the Pakistani context where oral cancers are most predominant not only becomes significant but also particularly difficult as the consumption of tobacco occurs in several forms (use of smokeless tobacco with or without additives and smoking of cigarettes and/or bidis) and most often, as mixed habits. Sequence variation in genes coding for tobacco metabolizing/detoxifying enzymes,

such as members of the cytochrome P450 (CYP) and glutathione S-transferase (GST) families may potentially alter individual susceptibility to oral cancer. However, isolated sequence variants in carcinogen-metabolizing genes may be modest to moderate risk factors, explaining the inconsistent results. On the other hand, combinations of genotypes each conferring a small relative risk may add up to a relative risk large enough to be observed in epidemiological studies.[10]

The three xenobiotic-metabolizing enzymes reported in studies, i.e. CYP1A1, GSTM1 and GSTT1, significantly alter oral cancer risk singly and in combination. Further, specific tobacco exposures appear to modulate this risk. Thus there is a complexity of the interplay between genetic and environmental factors as determinants of oral cancer risk.

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