

COMMENTARY

Khaini Chewing Damages Chromosomes 2q, 3p and 21q: Occurrence in a South Asian Population

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Abstract

Chewing Khaini, damages chromosomes, in the form of loss of heterozygosity (LOH), identified on the long arm of chromosome 2 (2q), the short arm of chromosome 3 (3p) and the long arm of chromosome 21 (21q) of oral cancer cases who had quid chewing habit of more than 10 years duration, and chewed 10-15 times a day.

Key Words: Quid (smokeless tobacco) chewing - chromosomal damage - oral cancer - Indians and South Asia

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Introduction

It has been estimated that, each year 390,000 cases of oral and oro-pharyngeal cancers are being diagnosed world wide, and this number is only includes those who have reported to a doctor or a dentist. There are many unreported oral cancer cases living in remote rural areas of developing countries, who do not have access to health care providers. Oral cancer is identified as fifth most common cancer in the world (Parkin et al., 2005) and is a particularly big problem in south Asian countries, where over 250 million people (17% of the total population) use smokeless tobacco (SLT), of which 95% living in India, 82% in Bangladesh and 13% in Sri Lanka. The habit of SLT in South Asia could be considered as one of the major contributors for the higher mortality and morbidity rate. Surveys among young populations have revealed that 10-20% of those aged 13-15 years have an SLT habit. In India where many chewing tobacco products are advertised in mass media, this is more prevalent in underserved youth. Alarming, 45-71% are exposed to SLT (Cochrane Systemic Review on Oral Cancer 2007).

Oral Cancer in India

India is known as a store house of oral cancer. Although a significant proportion of the world population is affected by oral cancer, the incidence rates are highest in India. In some parts of the country oral cancer accounts for 30-35% of all cancers, compared to 1-5% in Japan and other industrialised countries (La Vecchia et al., 1997). In India, annually 75,000-80,000 new cases of oral cancer are reported. The age-standardized incidence rate per 100,000 population was calculated as 12.8 in males and 7.5 in females (Moles et al., 2008). Rates increased among the

population less than 50 years old, between the years 1983-1987 and 1995 (Gupta, 2006). In India, the number of newly diagnosed tobacco-related cancers has been estimated at approximately 250,000 out of 700,000-900,000, each year (Gupta, 2006).

Khaini Chewing in India

Areca nut may be considered as an independent risk factor for occurrence of oral cancer (Warnakulasuriya, 2006) and chewing tobacco and/or betel-nut are also strongly associated with oral submucosal fibrosis (OSMF), an oral pre-cancerous lesion (Mehta et al., 1981). There are various brands of chewing tobacco available in India, including Gutkha, Pan masala, Khaini, Pan -parag and other branded sachets are commonly available. Notably, Khaini is a popular brand, especially used by the people living in the North and North-Eastern part of the country, where incidence rates of oral cancer is alarmingly high.

Home made preparations are usually composed of sun dried boiled tobacco leaf mixed with wet slaked lime. The users chew the product; ingest saliva containing extracted Khaini, sometimes spit out the excess saliva (usually red tinted), and hold the chewed bolus of Khaini in the lower vestibule of the buccal cavity. The users usually become addicted due to the nicotinic effect of the product and many chew Khaini 10-15 times every day for 15 -20 years. Khaini sachets (for example-KUBER Scented) are now being exported to Europe and America.

Studies on Khaini associated oral cancer and its adverse effects on health, in terms of carcinogenesis, were investigated at cellular level. The tumour suppressor genes (TSGs) are playing a preventive role to protect a person from onset of oral cancer. But the people, who have developed Khaini chewing associated oral cancer, are at

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a high risk of deletions of TSGs. Mutagenicity screening with the Ames test detected high mutagenicity of Khani product, suggestive of carcinogenic effects (Stich et al., 2009). Studies on Khaini associated oral cancer and its adverse effects on health, in terms of carcinogenesis, have been investigated at the cellular level. The tumour suppressor genes (TSGs) are playing a preventive role to protect a person from onset of oral cancer. But the people, who have developed Khaini chewing associated oral cancer, are at a high risk of deletions of TSGs.

Khaini Chewing and Chromosomal Damage

It has been identified that Khaini, as one of the most dangerous products causing damage to the chromosomes having important tumour suppressor genes (Yamamoto et al., 2007). Chewing Khaini, damages chromosomes, in the form of loss of heterozygosity (LOH), which has been identified on the long arm of chromosome 2 (2q), the short arm of chromosome 3 (3p) and the long arm of chromosome 21 (21q). Noticeably, all of these damages were observed in chewing Khaini associated oral cancer cases. An investigation was conducted with the tissue samples, obtained from biopsy proven oral squamous cell carcinoma cases who had a Khaini chewing habit for more than 10 years, and 10-15 times a day. The study was carried out to investigate the LOH at 2q, 3p and 21q by using 9 microsatellite markers. LOH was detected in 25 (96.2%) out of 26 informative samples at one and more of the loci examined. On the basis of the results, two commonly deleted regions were identified and a detailed deletion map was constructed. In the first region, a high frequency of LOH was observed at the D3S1007 locus (53.8%) on 3p25, which is located in the region neighbouring the VHL (von Hippel-Lindau) gene. In the second region, LOH was concentrated at the D3S966 locus (50.0%) on 3p21.3, suggesting the presence of a putative tumour suppressor gene (TSG) associated with OSCC. These results strongly suggest that there are at least two candidate TSGs located on chromosome 3p, and which was found altered in chewing Khaini associated OSCC. Another study in India had already identified fourteen novel differentially expressed genes (12 up-regulated and 2 down-regulated) from Khaini associated oral neoplastic lesions (dysplasia) (Rohatgi et al., 2006). Therefore, it is obvious that Khaini chewing associated oral cancer cases are experiencing chromosomal damages which is a serious public health concern for the community at risk.

Awareness on Ill-effects of Chewing Tobacco

Oral cancer awareness initiatives are inadequate or non-existing in South Asian countries. Evidence based information on causation of oral cancer is not disseminated to the people at risk and educational initiatives for prevention are not available. Although several studies have elucidated mutagenic effects of tobacco products, the information is not imparted to the community at risk.

The government and authorities will therefore firstly have to disseminate the information on chromosomal damage and its consequences and then develop a

community awareness programme based on the information, targeting the high risk population groups thus potentially protecting them from pre-mature death.

FCTC, India and Chewing tobacco

There exists a WHO Framework Convention on Tobacco Control (FCTC), but an Indian tobacco control initiative is not mentioned in it specifically. India is a signatory of the FCTC but it is yet to implement the FCTC suggestions and inputs thoroughly and successfully (Choudhury, 2006; WHO Framework Convention on Tobacco Control, 2009,). It is by no accounts an easy job controlling the chewing of tobacco in public places. It is easy to identify smokers and stop them, due to the negative effect of smoking has on surrounding others i.e. passive smoking. However, it is a whole another issue identifying someone chewing and then asking them to stop what is after all perfectly legal and harmless, at least to everyone else other than the individual.

Nevertheless, it is imperative for himself or herself to find ways to tackle this situation, and thus help reduce the rate of chewing-tobacco induced mortality and morbidity of oral cancer in the SE Asian communities.

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