

EFFECT OF BETEL NUT CHEWING IN CONJUNCTION WITH TOBACCO ADDICTION ON DISTRIBUTION OF UPPER AERO DIGESTIVE TRACT TUMORS**ANIL AGRAWAL^a, ASHOK KUMAR^{b1}, BABITA AHLAWAT^c,
SHYAMAKANT PRASAD^d, NAVDHA CHAUDHARY^e AND PAWAN GOEL^f**^aDepartment of ENT, Shyam Shah Medical College, Rewa, Madhya Pradesh, India^{bd}Department of ENT, SHKM GMC, Nalhar, Mewat, Haryana, India^cDepartment of Dentistry, SHKM GMC, Nalhar, Mewat, Haryana, India^dDepartment of Pedodontics and Preventive Dentistry, Eklavya Dental College, Kotputli, Jaipur, Rajasthan, India^fDepartment of Community Medicine, SHKM GMC, Nalhar, Mewat, Haryana, India**ABSTRACT**

A number of risk factors such as tobacco, human papilloma virus, areca nut, alcohol have been termed in the literature as causative agents for head and neck squamous cell carcinoma (HNSCC). Areca nut, when mixed with tobacco products or wrapped in the leaf of the piper betel plant, named as betel nut. Areca nut chewing is associated with acute as well as chronic effects. The acute effects are worsening of asthma, low blood pressure, and rapid heart rate while chronic effects comprise dependency, oral submucosal fibrosis (OSF), precancerous oral lesions and HNSCC. Betel-quin chewing is quite widespread and has achieved an amount of social acceptance in India, Sri Lanka, Pakistan, Bangladesh, Thailand, Cambodia, Malaysia, Singapore, Indonesia, Philippines, New Guinea, Taiwan and China. This has been amalgamated into several of the religious and cultural rituals of ethnic groups within the Indian sub-continent. Though many studies concluded that the regular chewing of betel-quin containing tobacco was carcinogenic in humans, there was inadequate evidence to demonstrate that this was also true of chewing betel-quin without tobacco. The present study shows that cases that use betel nut in addition to other tobacco products develop carcinoma of buccal mucosa as comparison to those who use tobacco products without betel nut at higher probability.

KEYWORDS : Callus, Femur, Paediatric, TENS

A number of risk factors such as tobacco, human papilloma virus, areca nut, alcohol have been termed in the literature as causative agents for head and neck squamous cell carcinoma (HNSCC). Areca nut consumption has been related to oral cancer in studies from South East Asian countries. (Gupta & Warnakulasuriya, 2002 and Muttagi et al, 2012)

Areca nut is the seed of the fruit of the oriental palm, Areca catechu. It is used by an estimated 200-400 million people, mainly Indo Asians and Chinese. (Warnakulasuriya et al., 2002) Areca nut has a long history and is widespread in India, Sri Lanka, Pakistan, Bangladesh, Thailand, Cambodia, Malaysia, Singapore, Indonesia, Philippines, New Guinea, Taiwan and China. It has been deeply ingrained in many sociocultural and religious activities of many ethnic groups within the Indian subcontinent. (Williams, 1995). These are thin slices of the nut with or without tobacco products and are wrapped in the leaf of the piper betel plant. Therefore the more common name is betel nut. Ordinarily chewed but the stem or the inflorescence of Piper betel may also be consumed. The leaf is folded into a funnel shape and all other ingredients are added into it, ensuing in a quid. The fibrous pericarp of the

fruit is removed and the seed or the endosperm used for chewing. The constituents in the betel-quin (pan) vary not only between nations but also communities and individuals. However, the major components are the leaf of Piper betel, the nut of Areca catechu, lime, and katha, an extract of the wood of Areca catechu. (International Agency for Research on Cancer, 1985) In health point of view, the key factor is whether tobacco is added to the above ingredients or not. Tobacco is shredded, sun dried tobacco from Nicotinatobaccum or Nicotinarustica. There are at least 40 million regular tobacco chewers in the Indian sub-continent.

Arecoline has been isolated from the basic nut and has major effects on cholinergic neurones in addition to range of other alkaloids namely, arecaidine, guracine, guacine, and arecolidine. (Warnakulasuriya et al., 2002) The recent development of capillary electrophoresis techniques should facilitate the identification of further bioactive molecules including carcinogens as well as providing diagnostic and treatment monitoring aids. Though areca nut chewing is associated acute effects such as worsening of asthma, low blood pressure, and rapid heart rate but most important consideration is the relation

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between areca nut use and the development of HNSCC and its precursor's leukoplakia and OSF. (International Agency for Research on Cancer, 1985 and Zain, 1999 and Thomas & Kearsley, 1993) It has long term ill effects with some individuals develop a dependency syndrome. An IARC working party concluded that while there was sufficient evidence to show that the regular chewing of betel-quist containing tobacco was carcinogenic in humans, there was inadequate evidence to demonstrate that this was also true of chewing betel-quist without tobacco. (International Agency for Research on Cancer, 1985)

The present study was conducted on a group of 102 proven cases of HNSCC visiting the OPD in the Department of ENT of a tertiary care centre over a period of three years; the information regarding tobacco addiction in a formulated questionnaire with respect to parameters like duration, and frequency of areca nut chewing alone or in addition to other tobacco products or using tobacco without areca nut chewing was collected. The data was recorded and analysed to establish a comparison of various classified diagnosis with respect to addiction to tobacco with and without betel nut.

It is evident from the present study that maximum cases of carcinomas arising from oral cavity that use betel nut in addition to other tobacco products were of carcinoma buccal mucosa as comparison to those who use tobacco products without betel nut with a higher probability.

MATERIALS AND METHODS

The study was carried out on one hundred and two patients who presented with biopsy proven HNSCC in the Department of ENT of a tertiary care centre over a period of three years. The patient was made comfortable and a detailed clinical, personal and past history with special reference to the information on tobacco addiction with respect to parameters like duration, and frequency of areca nut chewing alone or in addition to other tobacco products or using tobacco without areca nut chewing was collected. All the patients were subjected to the complete clinical examination; indirect laryngoscopy; direct laryngoscopy, nasopharyngoscopy and oesophagoscopy under local or general anaesthesia was done to localise the site of the tumour. Routine laboratory investigations along with radiological examination were done. TNM staging was done according to UICC classification (International Union against Cancer, 1997) and the classified diagnosis was made according to the ICD-9 coding. Statistical analysis was done by Chi-Square test on comparison of various classified diagnosis with respect to addiction to tobacco with and without betel nut.

OBSERVATION AND RESULTS

The study shows correlation of chewing tobacco with and without betel nut with classified diagnosis of upper aerodigestive tract (UADT) tumors. The present study shows out of 102 proven cases 90 cases gives the long

Table 1 : Distribution of Cases on the Basis of Classified Diagnosis

Classified Diagnosis	Cases using tobacco products without betel nut	Cases using betel nut in addition to other tobacco products	P Value	Sig.
Carcinoma buccal mucosa	7	18	.032	S
Carcinoma tongue	9	10	.66	NS
Carcinoma lower alveolus	4	2	.21	NS
Carcinoma floor of mouth	3	0	N.A.	NS
Total carcinomas arising from Oral Cavity	23	30	Correlation r=±758	

Classified Diagnosis	Cases using tobacco products without betel nut	Cases using betel nut in addition to other tobacco products	P Value	Sig.
Carcinoma hypopharynx	17	2	.024	S
Carcinoma oropharynx	8	5	.22	NS
Carcinoma larynx	2	3	.11	NS
Total carcinomas arising in UADT; beyond Oral Cavity	27	10	Correlation r=±434	

standing history of addiction for the chewing of tobacco products with and without betel nut. Among these 90 cases of cancers 50 cases were having history of using tobacco products without betel nut whereas rest 40 cases using betel nut in addition to other tobacco products. The distribution of these cases on the basis of classified diagnosis into seven groups was as depicted in the table 1. Out of total 90 cases 53 cases develop carcinomas arising from Oral Cavity whereas rest 37 cases develop carcinomas arising in UADT; beyond Oral Cavity.

Among the 50 cases those who use tobacco products without betel nut, 23 developed carcinomas arising from oral cavity whereas 27 developed carcinomas arising in UADT; beyond oral cavity. Among the 40 cases those who use betel nut in addition to other tobacco products, 30 developed carcinomas arising from oral cavity whereas only 10 developed carcinomas arising in UADT; beyond oral cavity. (Correlation factor = ± 0.758)

Those who use tobacco products without betel nut out of 27 cases who developed carcinomas arising in UADT; beyond Oral Cavity 17 were of carcinoma hypopharynx whereas among cases those who use betel nut in addition to other tobacco products, out of 30 cases who developed carcinomas arising from Oral Cavity 18 were of carcinoma buccal mucosa. (Correlation factor = ± 0.434)

Thus it is evident from this study that maximum cases that use betel nut in addition to other tobacco products were of carcinoma buccal mucosa as comparison to those who use tobacco products without betel nut were of carcinoma hypopharynx at higher probability.

DISCUSSION

For years, there has been a belief that the inclusion of tobacco into the betel-quid is primarily found among the Bangladeshi community and the observation has been confirmed by Health Education Report of Black and Minority Ethnic Groups in England (International Agency for Research on Cancer, 1985). Areca nut chewing is a unique problem in India and other Southeast Asian countries. (Muttagi et al., 2012) Areca nut is a highly addictive substance with the score for mean severity of dependence as 7.3 (in a range of 112) similar to the

problematic use of amphetamines. Habituation and addiction to daily chewing of the quid has also been reported amongst the people hailing from the Gujarat state in India. (Malaovall et al., 1976 and Canniff et al., 1976) There have been reports of usage of these products in Asian migrants to the United States, the United Kingdom, Singapore, Australia, Germany, South Africa etc (Changrani, 2006 and Farrand and Rowe, 2006 and Nunez-de la Mora et al., 2007). In contrast to the western literature wherein smoking, alcohol and human papilloma virus have been described as major risk factors for head and neck SCC, There were reported studies of increased risk for the development of oral malignancy in Areca nut only users. (Nunez-de la Mora et al., 2007 and VanWyk et al., 1993) Adding tobacco to the quid is indeed a confounder in many studies, but there are some populations such as Taiwanese who do not add tobacco to the betel and areca quid. The reported relative risk for oral cancer among those who chew areca only in the Taiwanese population is 58.4 (95% confidence interval 7.6 to 447.6). (Lu et al., 1996) The admixture of tobacco products further increases the likelihood of developing oral malignancy. Both duration and daily frequency of areca use increase the risk of developing cancer, suggesting a dose response relation. (Lu et al., 1996)

Although chewing areca nut has been found to be associated with oral cancer and recently with development of primary hepato cellular and esophageal carcinoma. (Tsai et al., 2001 and Wu et al., 2001) In a study on series of female patients with head and neck cancer who had the habit of chewing only areca nut without any history of tobacco usage in any form, majority of cases were of tongue and buccal mucosa among oral cancers, but was the first time to highlight the association of hypopharynx carcinoma with areca nut chewing habit, which has not been studied in the literature so far (Muttagi et al., 2012).

A retrospective study (1983-1989) of oral squamous carcinomas and concomitant oral habits on South African Indians from Natal, analyses confirmed an association between nut chewing and cheek cancer. The data showed that the areca nut habit with or without tobacco use is important in the development of oral squamous carcinoma. Elimination of this habit can reduce the risk in

these women substantially (89-91%) if all other factors remain the same. The study shows SSC of the cheek (buccal mucosa, alveolar sulcus and gingiva) occurred most frequently, especially in women (57/89 i.e. 64%), while in men tongue cancer predominated (22/54 i.e. 41%). Ninety-three per cent of women (83/87) and 17% of men (9/54) habitually chewed the areca nut. Thirty-nine of 57 women (68%) with cheek cancer and 21/25 (84%) with tongue cancer only chewed the nut (no tobacco, snuff or smoking) (VanWyk et al., 1993).

In a multicentre matched case-control study on 91 cases of oesophageal squamous-cell carcinoma and 364 matched controls from three tertiary-care hospitals in Karachi, Pakistan examined through structured questionnaire about the chewing areca nut alone, betel quid with tobacco, oral snuff (Snuff Dipping) and cigarette smoking. Multivariable conditional logistic regression model showed that after adjusting for the effect of ethnicity, ever chewed areca nut alone (adjusted matched odds ratio (mOR (adj))=3.7; 95% confidence interval (CI): 1.6-8.5), ever chewed betel quid with tobacco (mOR(adj)=12.8; 95% CI: 6.3-26.2), ever practiced snuff dipping (mOR (adj)=4.3; 95% CI: 1.6-11.7) and ever smoked cigarettes (mOR (adj)=2.9; 95% CI: 1.4-5.9) were significantly and independently associated with oesophageal SSC. (Akhtar et al., 2012)

In a study on 1522 pathology-proven patients with upper aerodigestive tract squamous cell carcinoma (UADT-SCC) to investigate the independent and synergistic effects of alcohol, tobacco-free betel-quid (TF-BQ), and cigarette use. It was proved that alcohol and tobacco bestowed increased risks of earlier tumor occurrence only for oral/pharyngeal and oral cancers, respectively, TF-BQ was consistently observed to confer elevated age-associated risks for each UADT-SCC (adjusted hazard ratio (aHR)=1.6-2.3). Alcohol and TF-BQ joint consumers experienced a stepwise increased cumulative risk (CR) of contracting carcinomas of the larynx (46.2%), esophagus (47.5%), pharynx (53.5%), and oral cavity (60.5-71.0%), with >68% of CRs found among drinkers who started chewing before age 20.

Both groups of betel nut (Alcohol+Betel+Cigarette and Alcohol+TF-BQ) users exhibited earlier diagnosis ages than non-users: 10 years ahead for oral cancer, 7, 17, and 12 years earlier for pharyngeal, esophageal, and laryngeal cancers (Lee et al., 2011).

CONCLUSION

Areca nut chewing is a significant risk factor in the genesis of oral potentially malignant and malignant lesions. The role of areca products in causing oral fibrosis, malignancy and perhaps contributing to other diseases has raised important public health concerns, but still the products are inadequately labelled with no health warning labels and no restrictions on its sale to children or consumption in public places on contrary its usage is culturally bound and is an integral aspect of several customs.

Though there is a need to establish the carcinogenic effects of areca nut at a genetic or molecular level in these cases, in the mean time to control this condition to develop wide spread health education programs are necessary to reach both urban and rural populations in education and motivation against the habit of chewing areca nuts. Its deleterious effect needs to be highlighted in all cancer prevention campaign. The sale and production of areca nut should be discouraged. In addition to this administrative decisions may be expected on the part of governments regarding accurate labelling of the products, especially with respect to admixture with tobacco is an important requirement whereas outright bans or restriction may probably be counterproductive. Being a health person identification of dependence to areca nut and facilities for treatment and programmes to reduce harm in addition to further research, both clinical and experimental on the biomedical and psychosocial consequences of areca usage are needed.

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