

Betel quid and carcinogenicity: A holistic survey

Hina Mehrotra* and Puneet Ahuja

I.T.S. Dental College Hospital and Research Centre, Greater Noida, Gautam Budh Nagar
District, Uttar Pradesh – 201308

*Corresponding author's e-mail: drhinamehrotra@gmail.com

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ABSTRACT

Betel quid chewing has been a primeval practice in the Indian subcontinent and many parts of Asia, and is still widespread today. The term 'betel quid' is synonymous with 'paan', a more commonly used terminology used in India and neighbouring countries. A holistic survey of about 100 patients was taken into consideration to know the effects of betel quid. The adverse effects of consuming betel quid and the oral premalignant lesions associated with the habit are discussed in the present contribution. This may help the people in creating the awareness of this habit.

Key - words: Betel, cancer, Indian subcontinent, Piperaceae.

INTRODUCTION

Betel quid chewing is an age old practice in the Indian subcontinent and different Asian countries. The word 'quid' denotes a substance or a mixture of substances that is placed and retained in the mouth, and often swallowed. Apart from areca nut i.e., *Areca catechu* L. (Arecaceae family), it may contain a variety of ingredients, including betel leaf (*Piper betle* of family Piperaceae) and tobacco (*Nicotiana tabacum* of family Solanaceae) (IARC 2012). Areca nut, a major constituent of the betel quid, is the cotyledon of *Areca catechu*, a palm tree that grows in South and Southeast Asia and the Pacific islands (IARC 2012). Arecaidine, arecoline, guvacine and guvacoline are the four alkaloids conclusively present in areca nut (IARC 2004). Arecoline is the most abundant among them. Secondary and tertiary amines present in areca nut undergo nitrosation and give rise to N- nitrosamines. The nitrosation of arecoline may produce a variety of betel quid specific nitrosamines (BQSN) which interact with DNA, proteins or other targets forming adducts to exert their carcinogenic activity (Adhikari & De 2013).

There are many types of chewing habits in India

viz., betel quid (fresh betel leaf, fresh areca nut, slaked lime, catechu and tobacco), 'paan masala' (areca nut, slaked lime, catechu, condiments and tobacco), 'mainpuri' (tobacco, slaked lime, areca nut, camphor and cloves), 'mawa' (areca nut, tobacco and slaked lime), 'khaini' (tobacco and slaked lime), 'gutka' (an industrially manufactured tobacco rich item) and other smokeless tobaccos (e.g., 'mishri', 'gudhaku', and 'bajjar') (Chiba 2001).

The objective of this contribution is to create public awareness about the adverse effects of consuming betel quid and the oral premalignant lesions associated with the habit.

MATERIAL AND METHODS

A detailed survey of 100 patients reported to ITS Dental Hospital, Greater Noida, with the habit of consuming betel quid with or without tobacco was taken into consideration to rule out any other etiology. They were observed for any suspected lesions and biopsy was advised for those having the risk factors. The photographs of these patients were taken in order to keep their records. Long term follow up for these patients was recommended.

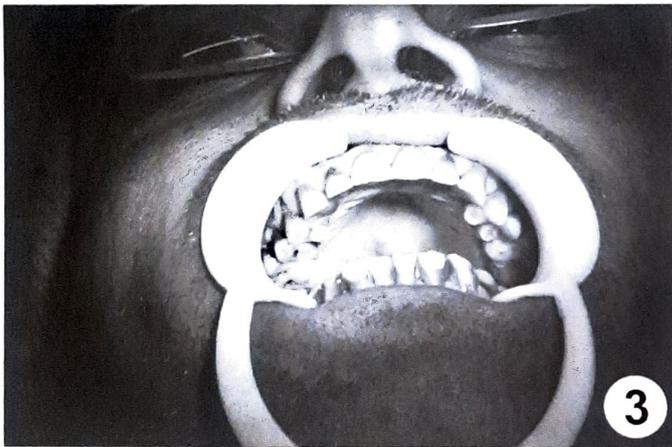
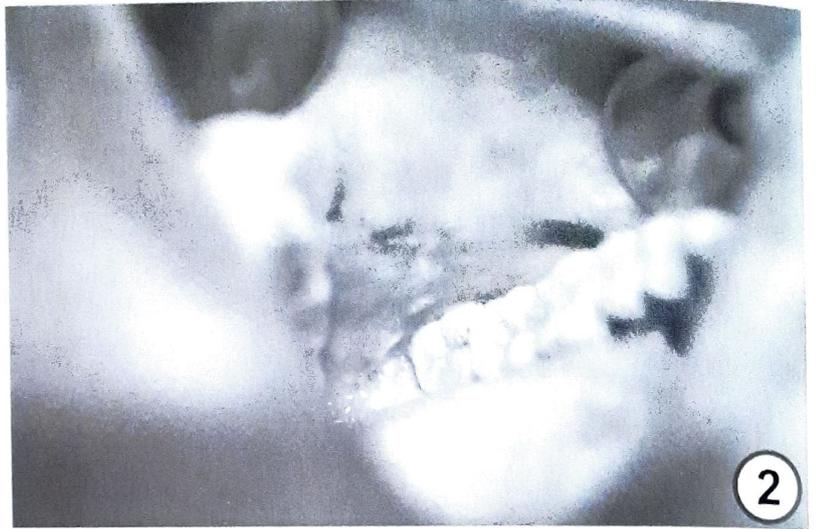


PLATE I

1. Trismus (reduced mouth opening due to rigidity of cheeks); 2. Blanching of cheeks; 3. Blanching of palate; 4. Homogenous leukoplakia (note the uniform thin white area); 5. Thin white radiating lines present on the cheek (Wickham's striae).

DISCUSSION

It has been observed that 88 out of 100 patients had changes in their oral mucosa irrespective of the duration of consumption of betel quid. Some of these changes are already available in published literature, however, based on present study these are discussed below in detail:

Betel quid and carcinogenicity

The chewing of tobacco with betel quid results in high exposure to carcinogenic tobacco-specific nitrosamines (TSNAs) i.e., up to ~1000 mg/day. The carcinogenic TSNAs such as N-nitrosornicotine (NNN), 4-(N-methyl-N-nitrosamino)-1-(3-pyridyl)-1-butanone (NNK) and N-nitrosoanabasine (NAB), along with volatile nitrosamines N-nitrosodimethylamine and N-nitrosodiethylamine, have been detected in the saliva of chewers of betel quid with tobacco (Adhikari & De 2013).

The carcinogenic effects of betel quid have been demonstrated experimentally on several animals. Muir and Kirk (1960) in their study painted an aqueous extract of betel quid containing tobacco on the ears of mice that resulted in Squamous Cell Carcinomas (SCC) in two of 12 mice. In another experiment carried out by Suri et al. (1971) Dimethyl sulphoxide (DMSO) extracts of areca nut only, tobacco only, and areca nut plus tobacco were painted on hamster cheek pouches. They observed that eight out of 21 animals developed local SCC and 19 out of 21 formed leukoplakia when treated with areca nut extract. Ranadive et al. (1976) and Thomas & Kearsley (1993) opined that tobacco enhanced the carcinogenicity.

Oral potentially malignant disorders associated with betel quid

Reichart and Nguyen (2008) in their study showed that the prevalence of oral mucosal lesions was significantly higher in the betel quid chewer group than non-chewers. Betel chewer's mucosa was seen in 66%, oral submucous fibrosis (OSF) in 13% and leukoplakia in 3.9%. Lichen planus was observed in 5.2% of this group as compared to 1.5% in the group of non-chewers.

Oral Submucous Fibrosis (OSF)—Oral submucous fibrosis is now globally accepted as a disease of the Indian and South East Asian countries due to a high rate of malignant transformation amongst oral potentially malignant disorders (Gupta et al. 2008). Earlier it was described in detail by Pindborg and Sirsat (1966). The chewing of betel quid (containing areca nut, tobacco, slaked lime or other species) has been recognized as one of the most important risk factors for OSF as supported by the epidemiological evidence (Rajalalitha & Vali 2015). The disease is characterized by dysphagia and trismus due to rigidity of the cheeks (Plate 1, fig. 1). There has been a rapid increase in the prevalence of the disease in India due to an upsurge in the consumption of areca nut which is found in the betel quid.

The disease has been diagnosed on the basis of some specific clinical criteria. However, according to Auluck et al. (2008) the most common initial symptoms are burning sensation especially during consumption of spicy food, fibrous bands, dry mouth, blanching and ulceration on the oral mucosa (Plate 1, figs. 2, 3).

Oral leukoplakia—It has been reported that oral squamous cell carcinoma is associated with potentially malignant disorders in 15-48% cases, while oral leukoplakia (OL) has been identified as the most frequent potentially malignant disorder of oral mucosa (Parlatescu et al. 2014). Oral leukoplakia is a potentially malignant lesion. A study from Taiwan has reported that betel quid without tobacco might increase the risk of oral pre-cancers such as oral leukoplakia (Jacoba et al. 2004). In India, most betel quid contains tobacco which aggravates the risk of developing oral precancerous lesion. Clinically there are two main types of leukoplakia: homogeneous and non-homogeneous. The homogeneous leukoplakia is a uniform, thin white area often altering with normal mucosa (Plate 1, fig. 4). The non homogeneous type is a red and white lesion, with a predominantly white surface. The malignant transformation of oral leukoplakia in annual average is 1% in different populations and geographic areas with the higher risk reported by 43% (Parlatescu et al. 2014). It is recommended that the patients diagnosed with such features should be followed up for long term.

Oral lichen planus—Oral lichen planus is a common autoimmune mucocutaneous disease which is characterized by the presence of radiating white, gray, velvety, thread-like papules in a linear, annular and retiform arrangement forming typical lacy, reticular patches, rings and streaks. A tiny white elevated dot is present at the intersection of white lines known as striae of Wickham (Plate 1, fig. 5). The lesions are present bilaterally anywhere in the oral cavity but commonly occur on buccal mucosa, tongue, lips, gingiva, floor of mouth and palate and may appear weeks or months before the appearance of cutaneous lesions (Gupta et al. 2015). Stoopler et al. (2003) reported a case of lichen planus induced by the use of betel quid. A quid-induced lichenoid oral lesion has also been reported among the betel quid users (Anand et al. 2014). It resembles oral lichen planus but there are specific differences. It is now termed as 'betel-quid lichenoid lesion'. This lesion may revert to normal with the quitting of the habit.

CONCLUSIONS

As evident from the above discussion it is clear that consumption of betel quid has a significant effect on the oral mucosa. An urgent measure should be taken up to curb this ongoing epidemic of betel nut habit. The manufacturer sale and consumption of such products should be banned by the government and strict actions should be taken on the defaulters. Awareness programs for educating the public about the harmful effects of betel nuts, alarming signs and symptoms of this disease may encourage the people to quit this betel quid habit.

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REFERENCES

- Adhikari A. & De M. 2013. Toxic effects of betel quid. *International Journal of Human Genetics* 13(1): 7-14.
- Anand R., Dhingra C., Prasad S. & Menon I. 2014. Betel nut chewing and its deleterious effects on oral cavity. *Journal of Cancer Research and Therapeutics* 10: 499-505.
- Auluck A., Rosin M.P., Zhang L. & Sumanth K.N. 2008. Oral submucous fibrosis, a clinically benign but potentially malignant disease: Report of 3 cases and review of the Literature. *Journal of the Canadian Dental Association* 74(8): 735-740.
- Chiba I. 2001. Prevention of betel quid chewers' oral cancer in the Asian-Pacific area. *Asian Pacific Journal of Cancer Prevention* 2: 263-269.
- Gupta M.K., Mhaske S., Ragavendra R. & Imtiyaz. 2008. Oral submucous fibrosis – Current concepts in Etiopathogenesis. *People's Journal of Scientific Research* 1: 39-44.
- Gupta S. & Jawanda M.K. 2015. Oral lichen planus: an update on etiology, pathogenesis, clinical presentation, diagnosis and management. *Indian Journal of Dermatology* 60(3): 222-229.
- IARC. 2004. Monographs on the evaluation of carcinogenic risks to humans, Volume 85, Betel quid and areca-nut chewing and some areca-nut-derived nitrosamines, 1st Ed. International Agency for Research on Cancer, Lyon.
- IARC. 2012. Working Group on the evaluation of carcinogenic risks to humans, International Agency for Research on Cancer, World Health Organization. A review of human carcinogens, 1st Ed. International Agency for Research on Cancer, Lyon.
- Jacob B.J., Straif K., Thomas G., Ramadas K., Mathew B., Zhang Z.-F., Sankaranarayanan R. & Hashibe M. 2004. Betel quid without tobacco as a risk factor for oral precancers. *Oral Oncology* 40: 697-704.
- Muir C.S. & Kirk R. 1960. Betel, tobacco and cancer of the mouth. *British Journal of Cancer* 14: 597-608.
- Parlatescu I., Gheorghe C., Coculescu E. & Tovar S. 2014. Oral leukoplakia – an Update. *Mædica* 9(1): 88-93.
- Pindborg J.J. & Sirsat S.M. 1966. Oral submucous fibrosis. *Oral Surgery Oral Medicine Oral Pathology* 22: 764-779.
- Rajalalitha P. & Vali S. 2005. Molecular pathogenesis of oral submucous fibrosis – a collagen metabolic disorder. *Journal of Oral Pathology & Medicine* 34(6): 321-328.
- Ranadive K.J., Gothoskar S.V., Rao A.R., Tezabwalla B.U. & Ambaye R.Y. 1976. Experimental studies on betel nut and tobacco carcinogenicity. *International Journal of Cancer* 17: 469-476.
- Reichart P.A. & Nguyen X.H. 2008. Betel quid chewing, oral cancer and other oral mucosal diseases in Vietnam: a review. *Journal of Oral Pathology & Medicine* 37: 511-514.
- Stoopler E.T., Ernesta P. & Thomas P.S. 2003. Betel quid-induced oral lichen planus: a case report. *Cutis* 71: 307-311.
- Suri K., Goldman H.M. & Wells H. 1971. Carcinogenic effect of a dimethyl sulphoxide extract of betel nut on the mucosa of the hamster buccal pouch. *Nature* 230: 383-384.
- Thomas, S. & Kearsley J. 1993. Betel quid and oral cancer: A review. *European Journal of Cancer Part B: Oral Oncology* 29(4): 251-255.