

POSITION STATEMENT

Uttar Pradesh Association of Physicians of India Position Statement: Betel Quid (Paan) and Diabetes

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Abstract

Betel quid (paan) chewing is common in India, especially in Uttar Pradesh. Betel quid has multifaceted relationship with health, including metabolic and psychosocial health. The current recommendations have been released keeping in view the public health and clinical importance of this addictive behavior. The objective of this document is to offer clinical guidance for screening, diagnosis and management of co-occurring betel quid chewing among persons with Diabetes Mellitus (DM). The document aims to provide education and guidance to clinicians engaged in care and management of persons with DM, and improve access to treatment for co-occurring betel quid chewing among persons with DM. The current recommendation grades are based on published evidence, and categorized as strong, intermediate, weak and no evidence. The strength of these recommendations is based on the level of evidence.

Scope and Purpose

Betel quid (paan) chewing is common in India, especially in Uttar Pradesh. Betel quid (paan) has multifaceted relationship with health, including metabolic and psychosocial health. The Indian College of Physicians Position Statement on Addictive disorders among persons with diabetes (2017)¹ have addressed this important aspect of health and clearly advise against betel quid (paan)-chewing. A grade 3B evidence/ recommendation is given to this statement.

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public health and clinical importance of this addictive behavior. The objective of this document is to offer clinical guidance for screening, diagnosis and management of co-occurring betel quid (paan) chewing among persons with Diabetes Mellitus (DM). The document aims to provide education and guidance to clinicians engaged in care and management of persons with DM, and improve access to treatment for co-occurring betel quid chewing among persons with DM.

Grading of Evidence

The current recommendation grades

are based on published evidence, and categorized as strong, intermediate, weak and no evidence. The strength of these recommendations is based on the level of evidence. The categories of the level of evidence and strength of recommendation are listed in Tables 1 and 2, respectively.³ The American

Table 1: Evidence level used for rating various recommendations³

Evidence level	Evidence rating	Methodology
1	Strong	Meta-analysis of randomized controlled trials Randomized controlled trials
2	Intermediate	Meta-analysis of non randomized prospective or case-controlled trials, systemic literature review Non randomized controlled trials Prospective cohort study Retrospective case-control study
3	Weak evidence	Cross-sectional study Surveillance study Consecutive case series Single case reports, observational study, pilot study
4	No evidence	Theory, opinion, consensus, review or pre-clinical study

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Table 2: Grading of strength of recommendations³

Grade	Strength of recommendations
A	Strong
B	Intermediate
C	Weak
D	Not evidence based

Association of Clinical Endocrinologists has used such an approach previously. Most recommendations are extrapolated from literature on substance use disorder, as limited literature exists about DM comorbid with addictive (substance use) disorders. It must be noted that different evidence levels can be mapped to the same recommendation grade by 'adjusting up' or 'adjusting down' depending on the importance and relevance based on expert opinion.

Epidemiology

Betel quid is perhaps the fourth most popular psychoactive substance in the world, after caffeine, nicotine and alcohol.⁴ At least 600 million people worldwide chew betel quid.⁵ Uttar Pradesh reports a high consumption rate of betel quid chewing, especially in studies on persons with oral malignancy.^{6,7}

Betel quid has a few core constituents (areca nut (*supari*), betel leaf (*paan ka patta*), slaked lime (*chuna*) and tobacco), though other ingredients may be added as per preference. These include aniseed, cardamom, rose petal preserve and catechu (*katha*) (Table 1). The term 'sweet paan' or 'meetha paan' is used to describe a tobacco-less variant of betel quid, in which the sweet flavor is derived from these spices. However, it does contain other ingredients including areca nut (commonly called *geele supari*).

Betel Quid Dependence

Betel quid use can be associated with a level of addiction or dependence that is similar to that of other psychoactive substances. Tobacco (smokeless form) present in betel quid is a psychoactive substance with well-accepted addictive properties. Apart from and independent of presence of tobacco, betel quid does have psychoactive properties owing to the presence of areca nut. It has clearly been shown that addictive potential of areca nut is not based upon simultaneous use of tobacco in the mixture.^{8,9} Additionally, areca nut has been established as a proven

Table 3: Proposed Mechanism of Action

Release of pro-inflammatory mediation
• Prostanoids, interleukin-6, tumor necrosis factor α
• Reactive oxygen species
Arecoline-induced adipocyte dysfunction
• Inhibition of adipogenic differentiation
• Induction of adenylyl cyclase-dependent lipolysis
• Inhibition of insulin-induced glucose uptake
Arecoline-induced competitive inhibition of γ -aminobutyric receptors
• In brain, leading to increased appetite
• In pancreas, altering insulin secretion
Autonomic effect
Central sympathetic effect
• Tachycardia
Parasympathetic effect
• Coronary artery spasm
• Vitamin D deficiency

carcinogen.

Areca contains 4 main alkaloids: arecoline, arecaidine, guvacine, and guvacoline. These alkaloids create a sense of alertness and wellbeing, by binding to GABA receptors.

The Betel Quid Dependence Scale, developed and tested in Taiwan and Guam, has been validated to measure betel quid dependence.^{10,11} It assesses three domains: 'physical and psychological urgent need' (7 item) 'increasing dose' (5 items), and 'maladaptive use' (4 items). Persons who practiced addition of tobacco to the betel quid mixture, and who reported a greater frequency of chewing, or a longer period of chewing, were found to have greater dependence on betel quid.

Adverse Effects

Cancer

Betel quid has been classified as a Group I carcinogen by the International Agency for Research on Cancer.¹² It is linked to cancer of oral cavity, pharynx, esophagus, liver, biliary tract and uterus.^{13,14}

Metabolic Syndrome

Betel quid has adverse effects on metabolic health. Betel nut contains nitrosated derivatives of arecal alkaloids. Apart from their psychoactive and tumorigenic effects, they are shown to have diabetogenic and obesogenic effects in animal¹⁵ as well as clinical studies.

The Taiwan Longitudinal Survey on Aging has shown that past betel

quid chewing is positively associated with new onset diabetes in Taiwanese adults aged 53 years or more.¹⁶ In a community-based study of 993 'healthy' Bangladeshis living in east London, betel nut consumption was associated with increased waist size in both men and women; and increased glucose levels in women.¹⁷ A met analysis of 17 Asian studies (5 cohort studies, 12 case control studies), including 388134 participants has shown an increased risk of obesity (adjusted relative risk [aRR] 1.047; $p < 0.001$); metabolic syndrome (aRR 1.051, $p = 0.01$), diabetes (aRR 1.47, $p < 0.001$), hypertension (aRR 1.45, $p = 0.06$), cardiovascular disease (aRR 1.2, $p = 0.02$), and all-cause mortality (aRR 1.21, $p = 0.02$), with betel quid chewing.¹⁸ Various mechanisms of action have been proposed to explain the metabolic effects of betel quid. These are listed in Table 3.¹⁹

Renal Disorders

A small study of eight patients proposed that betel quid chewing may predispose to urinary stone disease, perhaps because of the high intake of slaked lime.²⁰ A retrospective review of charts of Taiwanese 3264 men has shown a higher prevalence of chronic kidney disease in betel nut users (adjusted odds ratio 2.572, 95% CI 1.917-3.451). This association is independent of other factors including smoking, alcohol use, and diabetes.²¹

Vitamin D Levels

Betel nut chewing may contribute to hypovitaminosis D. In a pilot study conducted among 33 healthy British Bangladeshis, serum 1, 25 dihydroxy vitamin D showed an inverse correlation with betel quid chewing. Betel chewing, therefore, could aggravate the metabolic effects of vitamin D deficiency.²²

Infectious Disease

In Cambodia, Betel quid use is associated with an increase in risk of infectious disease, including HIV/AIDS, dengue fever, tuberculosis and typhoid, especially in women. It is postulated that betel quid chewing may increase propensity to infection by immunosuppression, injury to the oral mucosa (facilitating oral entry pathogens) or faeco-oral contamination of its ingredients.²³

Mortality

A Bangladeshi cohort study-carried

out among 20033 adults living in Araihasar, over 10 years, has shown a greater risk of all-cause mortality and cancer-related mortality (HR 1.55, 95% CI hazard ratio (HR) 1.26; 95% confidence interval (CI) 1.09-1.44) (1.09-2.22), with betel quid chewing. There was no correlation of betel quid chewing with cardiovascular disease (HR 1.16; 95% CI 0.93-1.43). The duration and intensity of betel quid use demonstrated a dose-response relationship with all-cause mortality. The population attributable fraction for betel use was 14.1% for all-cause mortality, and 24.2% for cancer.²⁴

Transgenerational Impact

There is evidence that betel nut consumption during pregnancy may have adverse effects on birth weight, newborn neurological status and pregnancy outcome.²⁵ A community-based screening programme from Taiwan reports that longer duration and earlier onset of paternal betel chewing and smoking may increase the risk of metabolic syndrome in offspring, independent of each other.²⁶

Uttar Pradesh (UP) Association of Physicians of India (API) Recommendations

Based upon the data presented above, the UP API suggests the following:

1. All persons with diabetes should be screened for betel quid use and dependence (Grade A, EL 2).
2. All persons using betel quid should be counselled to stop (Grade A, EL 2)
3. All persons not using betel quid should be counselled not to begin (Grade A, EL 2)
4. All persons dependent upon betel quid should be offered appropriate non-pharmacological therapy (Grade A, EL 4)
5. All persons dependent upon betel quid, especially with evidence of

metabolic or health impairment due to this, should be referred to a qualified mental health specialist for further management (Grade A, EL 4)

6. All persons using betel quid, with comorbid conditions or complications, should be referred to appropriate health care providers (Grade A, EL 4)
7. Public health campaigns to limit the use of betel quid must be promoted and encouraged (Grade A, EL 4)
8. Research must be promoted to create validated betel quid dependence scales in Hindi and Urdu, and to assess various deaddiction strategies (Grade A, EL 4)

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