



2017

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DOI: <http://dx.doi.org/10.18590/mjm.2017.vol3.iss3.3>

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## Recommended Citation

Nabrinsky, Edward; Hasan, Badar; Asif, Talal; and Pauly, Rebecca R. (2017) "Betel nut use and hyperglycemia," *Marshall Journal of Medicine*: Vol. 3: Iss. 3, Article 3.

DOI: <http://dx.doi.org/10.18590/mjm.2017.vol3.iss3.3>

Available at: <http://mds.marshall.edu/mjm/vol3/iss3/3>

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## **Betel nut use and hyperglycemia**

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The authors have no financial disclosures to declare and no conflicts of interest to report.

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## Abstract

Betel nut chewing previously has not been common in North America, yet it is the fourth major source of addiction and abuse worldwide. Approximately 700 million individuals, or 10 % of the global population, chew betel nut on a regular basis. It is important for patient safety and improved quality to recognize its use in uncontrolled diabetes. Our case is of a 49 year-old Burmese female with PMH of DM2, HTN, and benign paroxysmal positional vertigo (BPPV) who presented with a complaint of dizziness. Patient denied alcohol or tobacco use, but reported a 20-year history of betel nut chewing (4-5 times/day). Physical exam showed oral mucosa was dry with poor dentition along with eroded enamel and gums. Point-of-care glucose was extremely elevated at 522 mg/dL with HbA1c of 10.8%. Dix-Hallpike maneuver was negative and CTA of the head and neck was unremarkable. Neurology was also consulted regarding her dizziness, and MRI head demonstrated no acute infarct or hemorrhage. Throughout admission, patient's point of care glucose fluctuated between 91 and 316 (mg/dL), with several daily spikes. Her dizziness improved by day 2 of hospitalization. At the time of discharge, her glucose was controlled on 50 units of glargine at night-time along with 8 units of insulin at meals. After a negative initial workup for occult causes of dizziness, it was concluded that her 20-year history of betel nut chewing contributed to dizziness and hyperglycemia. Multiple studies show high risk of diabetes, increased likelihood of coronary artery disease and all-cause mortality in betel nut users. Specifically, one study in Taiwan demonstrated increasing incidence ratios of type II diabetes with increasing age.

1.4 million Americans are diagnosed with diabetes every year. It is the seventh leading cause of death in US, and costs \$69 billion in reduced productivity. Prevention and tight glycemic control remain the core of diabetes management. With an increasing Indian and South Asian immigrant population, physicians need to be aware of potential harmful effects of betel nut to improve quality of care. Screening for betel nut use should be a routine part of social history in susceptible populations. Counseling should be provided to educate patients about its harmful effects, and cessation should be encouraged.

## Keywords

betel nut, hyperglycemia

## Introduction

Betel nut chewing previously has not been common in North America, yet it is the fourth major source of addiction and abuse worldwide and with increased globalization becomes an entity with which we need to be familiar.<sup>1</sup> With approximately 700 million individuals or 10 % of the global population<sup>2</sup> chewing betel nut on regular basis, it is important to recognize its associated health hazards.

## Case Report

49 year-old Burmese female with PMH of DM2, HTN, and benign paroxysmal positional vertigo (BPPV) presented to the Emergency Department (ED) with complaints of dizziness and subjective fevers for the past 10 days. She described the room as spinning around her, denied

loss of consciousness, chest pain, or shortness of breath. She had questionable adherence to her daily medication regimen, which included meclizine 25 mg BID and insulin glargine 45 units at nighttime. Patient denied alcohol or tobacco use. Family history was negative for diabetes or hypertension but patient reported a 20-year history of betel nut chewing; specifically, she would chew betel nuts with lime paste and betel leafs 4-5 times per day, both socially and in isolation.

In the ED, patient was afebrile with vitals remarkable for an elevated heart rate of 103/min. She weighed 58kg and had BMI of 23.5 kg/m<sup>2</sup>. Physical exam showed patient in no acute distress. Oral mucosa was dry with no pharyngeal exudate, and poor dentition was noted along with eroded enamel and gums. Dix-Hallpike maneuver was negative. CTA of the head and neck were unremarkable. Patient was given 1L normal saline bolus along with 25 mg of meclizine, and was admitted to the hospital for uncontrolled diabetes.

**Table 1.** Laboratory results at the time of admission

Lab Measurement	Patient's lab value	Reference range
Hemoglobin	11.3	12.0-16.0(g/dL)
Hemoglobin A <sub>1c</sub>	10.8	4.6-6.2%
Glucose (serum)	248	70-99(mg/dL)
Potassium	3.0	3.6-5.1(mEq/L)
TSH	3.83	0.3-5.6 (U/ml)

The patient's previous hemoglobin A<sub>1c</sub> levels were unknown. Repeat point-of-care glucose was elevated at 522, and patient was started on her home dose of 45 units of insulin glargine at nighttime, along with sliding scale insulin. She initially required 20 units. Neurology was consulted regarding her dizziness, and MRI head demonstrated no acute infarct or hemorrhage.

Blood sugars remain uncontrolled, ranging in the 300s after initiation of her home regimen and sliding scale insulin; insulin lispro 8 units with mealtime was started on hospital day 2. Throughout admission, patient's point of care glucose fluctuated between 91 and 316 (mg/dL), with several spikes throughout the course of each day. Her dizziness improved by day 2 of hospitalization. At the time of discharge, her glucose was controlled at 91 mg/dL on 50 units of glargine at nighttime along with 8 units of insulin at meals.

After a negative initial workup for occult causes of dizziness, it is likely that her 20-year history of betel nut chewing contributed to patient's initial presentation of dizziness and hyperglycemia. She stated that the betel nuts were readily available at the local Burmese supermarket, and either she or her friends would purchase them. Regarding her use of betel nut, patient stated that if she had not consumed a nut for several hours, she would start to feel anxious and upset. She was not aware of any stigma attached to chewing betel nuts, and had not heard of any potential side effects or link to oropharyngeal malignancies. She was encouraged to cut back and attempt to discontinue her use, despite her longstanding history and cultural background.



**Figure 1.** Photo showing oral hygiene of patient. Enamel is eroded from history of betel nut chewing. Grinded enamel turns black, and also blackens the dentine. Pieces can become wedged between the teeth causing gaps where food can lodge promoting tooth decay.<sup>1</sup>



**Figure 2.** Friends of patient brought this to her room. From top left: “chuunam” (lime paste), betel leaf, and areca nut; these ingredients together make up betel nut’s chewable form.

## Discussion

Betel chewing is more prevalent in tropical Pacific, Southeast Asia and parts of East Africa, with an origin of at least 2000 years.<sup>3</sup> Betel nut can be wrapped with betel leaves (paan) or with tobacco (pedal quid); additional ingredients vary with geographic location. Its use generates euphoria<sup>3</sup> among users that contributes to widespread use; however, it has an array of negative effects including but not limited to oral, esophageal, and hepatocellular carcinoma, metabolic syndrome, hyperlipidemia, and type II diabetes.<sup>1</sup>

The main alkaloid in the betel nut, arecoline, is toxic. It increases appetite, causes coronary artery spasm, interferes with insulin induced glucose uptake, and inhibits adipogenic differentiation. Other substances used in betel nut increase release of inflammatory mediators including reactive oxygen species, C-reactive protein and tumor necrosis factor alpha, which are not only independent risk factors for cardiac outcomes but also induce insulin resistance.<sup>2</sup> Multiple studies show high risk of diabetes, increased likelihood of coronary artery disease and all-cause mortality in betel nut users.<sup>(4,1)</sup> Specifically, Tseng's study demonstrated how, in Taiwan, increasing incidence ratios of type II diabetes with increasing age could be viewed as a dose-response relationship with betel nut chewing.<sup>4</sup> Reports are also available for acute toxic symptoms if betel nut is consumed in increased quantity; manifestations include palpitations, chest tightness, dyspnea, tachycardia and even MI and coma.<sup>(5,6)</sup>

In addition to commonly known risk factors of obesity, ethnicity, positive family history for diabetes mellitus type 2, smoking and sedentary life style, betel nut use should be considered an associated modifiable risk factor for diabetes mellitus type 2 diagnosis and treatment.

## Conclusion

1.4 million Americans are diagnosed with diabetes every year. It is seventh leading cause of death in US and costs \$69 billion in reduced productivity.<sup>7</sup> The United States is undergoing a demographic shift with Asian migration, especially from Southeastern and Eastern Asia, growing exponentially in past three decades.<sup>8</sup> As prevention and tight glycemic control remain the core of diabetes management, screening for betel nut use must be part of regular office visits in susceptible populations, and counseling should be provided to educate patients about its harmful effects and encourage cessation.

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