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Areca-Nut Abuse and Neonatal Withdrawal Syndrome

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ABSTRACT

Areca-nut chewing occurs widely in South Asia and the Indian subcontinent. Here we present a case of neonatal withdrawal syndrome in an infant born to a woman who was a chronic areca-nut user. Arecoline, the principal neuroactive alkaloid in areca nuts, was found in the mother's placenta.

BETEL-QUID CHEWING IS common in some areas of Asia and among immigrant populations living in Europe and North America.¹ It is the fourth most commonly used drug worldwide after tobacco, alcohol, and caffeine.² Betel is composed of the sliced nut (areca nut or betel nut) of the areca palm (*Areca catechu*), the leaf of the betel pepper (*Piper betle*), and lime.² Because of the "positive" effects attributed to betel use, some women continue to consume this preparation during pregnancy, especially to prevent morning sickness.³ Because of the migration flux of Asian people to industrialized countries, European hospitals are being faced with pregnant Asian women who consume betel nut during pregnancy and possibly with newborns prenatally exposed to this drug.⁴ Here we report a case of neonatal withdrawal syndrome in an infant born to a woman who was a chronic areca-nut user.

CASE REPORT

A female newborn presented with irritability and hypertonia 48 hours after a eutocic delivery at 38 weeks of gestation (Apgar scores at 1, 5, and 10 minutes: 9, 10, and 10, respectively). The infant was born to a healthy 38-year-old mother who was an immigrant from Bangladesh and came to the obstetrics emergency department for childbirth. The mother reported no toxic habits and no visits to any obstetrician during gestation. The infant's weight was 3090 g, her length was 49 cm, and her head circumference was 34 cm. She was admitted to the section of neonatology because of the risk for neonatal infection of vertical transmission related to the mother's uncontrolled pregnancy. Results of routine laboratory

testing including serum chemistry and electrolytes, serologies (HIV, hepatitis C virus, hepatitis B surface antigen, toxoplasma, rubella, and syphilis), hematology, and urinalysis were within normal limits or negative. Urine testing of the mother and the infant for drugs of abuse including opiates, cocaine, cannabis, amphetamines, benzodiazepines, barbiturates, and ethanol produced negative results. Neonatal abstinence syndrome was assessed every 3 hours by using the scoring system of Kaltenbach and Finnegan.⁵ An ultrasonographic study of the brain through the anterior fontanelle was unrevealing. On the third day of life, treatment with phenobarbital (intramuscular bolus of 15 mg/kg followed by 8 mg/kg per day orally) was started because Finnegan scores were >8. The mother showed a brownish-red discoloration of the oral mucosa and tongue (see Figs 1 and 2), and it became known that she was a chronic areca chewer even during pregnancy. After 5 days of treatment with phenobarbital, withdrawal symptoms in the infant improved. Suspected fetal exposure was confirmed by detection of arecoline in the placenta (0.012 μ g/g of placental tissue), the only biological matrix available at the time of the analysis, by high-performance

Key Words: areca nut, arecoline, neonatal withdrawal syndrome, addiction, pregnancy, newborn

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liquid chromatography/electrospray quadrupole mass spectrometry.⁴ The diagnosis of neonatal abstinence syndrome resulting from maternal consumption of areca nut was established.

DISCUSSION

It is estimated that 600 million people worldwide chew areca nut in some form. The betel-nut quid or pan, a piece of areca nut chewed alone or mixed with tobacco and slaked lime (calcium hydroxide) wrapped in betelvine leaf, is widely used as a stimulant (because of the cholinergic agent, arecoline) or a relaxant (because of the arecaidine and guvacine) as an endemic habit throughout the Indian subcontinent, large parts of South Asia, and Melanesia.^{1,2} This habit is also apparent in migrant communities from these areas. Studies on Asian communities living in the United Kingdom (almost 3% of the total United Kingdom population) show that betel-quid chewing habits are highly diffused among the United Kingdom Bangladeshi population (79–96%), moderate among mixed Asian groups (27–47%), and prevalent among Asian adolescents (from 22% to 77% depending on ethnic group).⁶

Betel-quid chewing has been claimed to produce a sense of well-being, euphoria, warm sensation of the body, sweating, salivation, palpitations, heightened alertness, and increased capacity to work.⁷ These effects seem to be habit related and dose dependent. Addiction and withdrawal syndrome were also observed together with cholinergic toxicity, toxic psychosis, and neurologic complications.^{7,8} Arecoline, the areca-nut principal alkaloid, acts as an agonist at the muscarinic and nicotinic acetylcholine receptors and seems to be responsible for the central cholinergic stimulation.^{7,8} Both arecoline and arecaidine increased the release of catecholamines from chromaffin cells. Betel-quid chewing was found to produce an elevation in the plasma concentrations of nor-



FIGURE 1
View of the mother's brownish-red tongue.



FIGURE 2
View of the mother's brownish-red gums.

epinephrine and epinephrine, causing sympathetic activation.⁷

Acute significant toxicity after betel-nut chewing has been reported as a rare event. From a total of 42 000 calls received at the Taiwan Poison Control Center, there were 17 cases that were possibly related to betel consumption. The majority of patients (11 of 17) developed symptoms of mild to moderate severity (nausea, vomiting, dizziness, tachycardia/palpitations); however, severe symptoms such as coma, respiratory failure, and acute myocardial infarction and related manifestations were also reported (6 cases).⁹ Treatment of betel-nut overdose is symptomatic with supportive measures. Routine use of atropine is not recommended but could be administered in cases of severe acute cholinergic crisis.³

Chewing areca nut on an habitual basis is known to be deleterious to human health, especially in relation to the increased risk for developing oral cancer.¹⁰ Areca-nut withdrawal has been identified only in heavy users,¹¹ but as far as we are aware, neonatal withdrawal syndrome has not been reported previously. This case adds evidence to adverse pregnancy outcome associated with chronic areca-nut exposure.¹²

In pregnant women who are immigrants from Asian countries, the possibility of areca-nut use must be investigated by asking about toxic habits and by checking for red stains on the teeth, gingiva, and oral mucosa.

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