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Does areca nut use lead to dependence?

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Abstract

Background: The areca nut is consumed by approximately 10% of the world's population, and its consumption is associated with long-term health risks, with or without tobacco additives. However, it is not known whether its use is associated with a dependence syndrome, as is seen with other psychoactive substances.

Objective: To examine whether areca nut usage (with or without tobacco additives) could lead to the development of a dependence syndrome.

Methods: Three groups: [a] persons using areca nut preparations without tobacco additives [$n = 98$]; [b] persons using areca nut preparations with tobacco additives [$n = 44$]; and [c] 'Non-users' were systematically assessed using a checklist for the use of areca or areca + tobacco products, patterns of use, presence of a dependence syndrome in users, features of stimulant withdrawal and desired/beneficial effects.

Results: 38.8% and 40.8% of the 'areca' group satisfied definitions of current substance-dependence according to DSM-IV and ICD-10 criteria respectively. 79.5% of the areca + tobacco group satisfied criteria for current dependent use according to both DSM-IV and ICD-10 criteria. Both the groups reported a well-delineated withdrawal syndrome and similar attributions for desirable effects of use.

Conclusion: Areca nut use by itself and more so with tobacco additives, is associated with the development of a dependence syndrome in a substantial numbers of users.

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1. Introduction

The areca nut is the fourth most commonly used drug worldwide after tobacco, alcohol, and caffeine. Its use is an endemic habit throughout the Indian subcontinent, large parts of South Asia, and Melanesia and is commonly used among migrated communities in Europe, Africa and North America (Gupta and Ray, 2004; Nelson and Heischouer, 1999). It has been estimated that over 600 million people worldwide chew areca nut in some form (Gupta and Warnakulasuriya, 2002). Recent data suggests that the prevalence of areca nut use is rising in countries like India, Taiwan whereas it is in decline in some countries such as Thailand (Gupta and Ray, 2004; Gupta and Warnakulasuriya, 2002; Warnakulasuriya, 2002). Various epidemiological surveys have estimated areca nut use at 29.7% and 37.8% respectively among women and men over 35 years in Mumbai, India; 72% of

males and 80% of females between 5 and 75 years in the Pacific island of Palau (80% use tobacco mixtures), and 20–40% of the population, above the age of 15 years in India, Nepal and Pakistan (Gupta and Ray, 2004). Areca nut use is also becoming increasingly frequent among youth, where it may serve as a gateway to tobacco use (Rajan et al., 2007; Chandra and Mulla, 2007).

The areca nut, is the dried seed of *Areca catechu* L., belonging to the family *Palmaceae*. It is often mistakenly referred to as the betel nut as it is commonly chewed along with the *Piper betel* leaf (Burnell and Yule, 1996). Areca nut use is a part of many Asian and Pacific cultures and often takes place at ceremonies and gatherings, and preparation techniques vary from region to region. In ancient Indian texts, the areca nut has been described as a therapeutic agent for its stimulant and relaxant properties. The areca and areca juice play an important ceremonial and cultural role in many countries including Myanmar (where it is called *kunya*), the Solomon Islands and Vietnam. Due to this cultural tradition, the use of the areca nut has been widespread and is considered a part of daily life, even in women and young

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children in whom the use of other stimulants, such as tobacco, is considered unacceptable (Strickland, 2002; Changrani and Gany, 2005).

In India (the largest consumer of areca nut), the nut is traditionally cut into small pieces and chewed as it is or wrapped in a “betel vine leaf” along with slaked lime (calcium hydroxide) and condiments which include clove, cardamom, catechu (*kattha*), and other spices for extra flavouring. Experienced chewers might mix the areca nut with tobacco (the drug effect of the nicotine in tobacco is thought to resemble that of areca nut). The betel leaf is a different species of plant than the areca nut, and not in the areca family, but the Piper family (same as pepper and Kava). This preparation of betel leaf with or without areca nut is commonly referred to as *paan* in India and Pakistan, and is available widely. Areca nut is also sold in processed, ready-to-eat pouches called *paan masala*, which is a mixture of many spices whose primary base is areca nut crushed into very small pieces. Sometimes the areca mixture also includes tobacco; in this case, the product is called *gutkha* or *mawa* (a preparation containing thin shavings of areca nut, tobacco and slaked lime) (Gupta and Ray, 2004).

1.1. Pharmacology

The areca nut contains several psychoactive compounds. Arecoline, the principal alkaloid in areca nut, acts as an agonist primarily at muscarinic acetylcholine receptors, acts as a stimulant of the central and autonomic nervous system, and causes increases in the levels of monoamines such as noradrenaline, as well as acetylcholine at higher doses. This leads to subjective effects of increased well-being, alertness and stamina. Arecaine, another active ingredient, may have anxiolytic properties through inhibition of gamma-amino butyric acid (GABA) reuptake. These properties are likely to confer upon the areca nut a strong potential for abuse and dependence. The preferred route of administration, chewing, leads to rapid absorption of these alkaloids through the buccal mucosa, leading to an onset of these effects within 5 min, lasting for about 2–3 h (Winstock, 2002).

1.2. Adverse health consequences of areca nut use

Prolonged use of the areca nut has significant adverse effects on health. There is enough evidence to suggest that areca nut products, even those without tobacco, are associated with an increased risk for the development of oral malignancy (oral squamous cell carcinoma) and its precursors leukoplakia and oral submucous fibrosis (OSF), with the risk being greatest for *paan masala* (Trivedy et al., 2002).

1.3. Abuse and dependence potential

Areca-quinid 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 (Winstock, 2002). An earlier study (Chandra et al., 2002) examined areca nut use in non-substance abusing, psychiatrically ill patients. Using a modified version of the

Fagerström test, they found that 7% of their patients met criteria for “severe” use, which the authors considered present if any one of the following were present: daily chewing, chewing within 1 h of awakening, difficulty in avoiding chewing, and increasing the quantity chewed.

Small-scale studies (Pickwell et al., 1994; Winstock et al., 2000) suggest that areca use may result in a dependence syndrome, though large-scale studies testing this hypothesis are lacking. Winstock et al. (2000) reported that 10 out of 11 current and former heavy betel nut users, reported cessation withdrawal effects with the mean severity of Dependence Score of 7.3 consistent with the existence of a dependence syndrome among those who use areca nut products. However 55% of their sample used tobacco–areca combinations and the report recommended further research to delineate the relative contributions of areca nut and tobacco to this clinical picture. The current study was undertaken to investigate whether use of areca nut (with and without tobacco additives) leads to the development of a recognizable dependence syndrome.

2. Method

2.1. Study population

250 Subjects were approached to purposively construct three groups: [a] persons using areca nut preparations without tobacco additives, designated here as ‘areca’ [$n=100$]; [b] persons using areca nut preparations with tobacco additives, designated here as ‘areca + tobacco’ [$n=50$]; and [c] ‘Non-users’ who had not used areca or tobacco products [$n=100$]. Use was defined as having consumed areca or areca + tobacco containing products at least once in the last 12 months.

Subjects were chosen from among patients admitted for non-substance related psychiatric disorders and psychiatrically unaffected relatives of patients with neurosurgical or neurological emergencies at the National Institute of Mental Health and Neurosciences, Bangalore, India. The latter were not formally screened for absence of psychiatric illness, but were included if they had no prior history of seeking treatment for a psychiatric illness.

The Institute Ethics Committee approved the study. After complete description of the study to the subjects, written informed consent was obtained from all participants and parents of subjects under 18 years of age. Subjects admitted for a psychiatric illness continued to receive treatment as usual, and confidentiality of the information was guaranteed to all participants.

2.2. Instrument

Information regarding areca nut usage and their correlates was collected using a checklist, specifically designed for the study. This checklist included:

- [A] Socio-demographic details such as age, gender, educational level, socioeconomic status and psychiatric illness status (affected/unaffected).
- [B] Information on pattern of use: frequency of use (daily or less than daily); quantity used on typical using day (since the preparations of the substance were highly variable, especially in case of the unprocessed preparations, subjects were asked to denote the number of usual units of the preparation on a typical using day); preparation of areca nut used; co-morbid use of other substances and the age at initiation of use.
- [C] Questions to determine the presence of dependent use of areca products derived from the Structured Clinical Interview for DSM-IV, Module E: Substance Use Disorders, modified for areca nut use (SCID-IV; First et al., 1995). These pertain to the domains of (1) tolerance; (2) withdrawal; (3) loss of control—substance taken in larger amounts or for longer than intended; (4) persistent desire or unsuccessful efforts to cut down or control substance use; (5) salience—great deal of time spent in activities necessary to obtain

the substance, use the substance, or recover from its effects; (6) important social, occupational, or recreational activities are given up or reduced because of substance use; (7) the substance use is continued despite knowledge of having a persistent physical or psychological problem that is likely to have been caused or exacerbated by the substance; (8) an additional item from the Schedules for Clinical Assessment in Neuropsychiatry (SCAN; World Health Organization, 1994) was also included, to tap the domain of Craving—defined as a strong desire or sense of compulsion to take the substance.

Three (or more) of the domains 1–7, occurring any time in the same 12-month period were required for a diagnosis of areca/areca and tobacco dependence according to DSM-IV criteria. Similarly, 3 or more of domains 1–3, 5, 7–8 needed to have been experienced or exhibited at some time during the previous year for a diagnosis areca/areca and tobacco dependence according to ICD-10 criteria.

[D] Items relating to symptoms of stimulant withdrawal—constructed from common withdrawal symptoms experienced by persons using stimulants and nicotine (items taken from Amphetamine Withdrawal Questionnaire (AWQ; Srisurapanont et al., 1999): domains of craving, dysphoria, anhedonia, increased appetite, fatigue, agitation/anger/irritability, anxiety/feeling tense, increased sleep, vivid, unpleasant dreams and slowing of movement over the previous 24 h and the Hughes–Hatsukami Scale for Nicotine Withdrawal (Hughes and Hatsukami, 1986): angry/irritable/frustrated, anxious/tense, depressed, restless/impatient.

Instead of having to mark a Likert-type scale, respondents were asked to endorse whether the symptom was present or absent during withdrawal. Additionally, subjects were allowed to free-list up to four additional symptoms.

[E] Desired effects of areca product use: Subjects were asked to free-list their reasons for taking areca/areca + tobacco products.

2.3. Data analysis

Information collected was analysed using the Statistical Package for Social Sciences [SPSS10]. The subjects were divided into users and non-users, and the group of users was further subdivided into an 'areca' group, and an 'areca + tobacco' group. Further analyses looked at differences between psychiatrically ill and unaffected subjects. The primary focus in this paper is on the frequencies computed for patterns of use (quantity and frequency), the criteria for dependent use, withdrawal symptoms and desired effects as endorsed by the areca and areca + tobacco groups. Independent sample *t*-tests were used to compare continuous variables, and χ^2 tests were used to compare categorical variables between the groups. Multiple linear regressions were also computed among areca and areca + tobacco users, using selected predictor variables in order to predict the likelihood of developing dependence (with DSM-IV criterion count as the criterion/dependent variable).

3. Results

Of the 250 subjects interviewed, 162 (64.8%) reported areca/areca + tobacco use (users), and 88 did not. However, due to incomplete information in some of the records, the analyses included 98 subjects in the 'areca' group, 44 subjects in the 'areca + tobacco' group and 88 subjects in the non-user group.

Users were significantly older than non-users, were more likely to be women and from a rural background and to belong to lower socio-economic strata. There was a trend towards lower educational achievement among users compared to non-users, though this did not reach statistical significance. Non-users had a significantly lower family history of tobacco and alcohol use as well as betel use. The use of substances other than areca/areca + tobacco products across all three groups was low and did not differ significantly between them [Table 1].

The areca group was significantly younger and more educated than the areca + tobacco group, but did not differ in terms of gender, marital status, urban/rural background, socio-economic status or psychiatric status, family history of tobacco, alcohol or betel use, concurrent use of substances other than areca/areca + tobacco products [Table 1].

There was no significant difference between the areca and areca + tobacco group with respect to age at onset of use of all areca products. The former, though, had significantly lower frequency of daily use and quantity of substance used on typical using days. Their use of betel quid as the preferred vehicle of areca ingestion was significantly higher than in the areca + tobacco users. The latter had a higher preference for direct ingestion of plain or flavoured preparations in sachets than the areca users [Table 2]. Psychiatrically ill areca + tobacco users used higher quantities of the substance and had marginally higher frequencies of daily use, than unaffected users, but this did not reach statistical significance. Conversely, psychiatrically ill areca users used lower quantities of the substance and had lower frequencies of daily use, than unaffected areca users, but this difference too, did not reach statistical significance [Table 2].

Of the 'areca' group 38.8% satisfied DSM-IV criteria and 40.8% satisfied ICD-10 criteria for dependent use. 79.5% of the areca + tobacco group satisfied criteria for dependent use according to both DSM-IV and ICD-10 criteria [Table 3]. When the individual criteria for dependence were considered, the commonest criteria endorsed by the areca group was multiple attempts at abstinence (77.6%) followed by withdrawal symptoms (51%), craving (39.8%) and tolerance (37.8%). The only criterion which was not endorsed by any of the areca group was 'giving up activities to use the substance'. In contrast, the commonest criteria endorsed by the areca + tobacco group were withdrawal symptoms (84.1%), followed by tolerance, loss of control, craving and salience (77.3% each). 12% of this group reported giving up activities to use substances.

A significantly greater proportion of women users satisfied DSM-IV criteria for dependent use compared to male users among both areca (50% vs. 22.5%; $\chi^2 = 7.6$, d.f. 1, $p = 0.006$) as well as areca + tobacco groups (92.6% vs. 58.8%; $\chi^2 = 7.3$, d.f. 1, $p = 0.007$).

The frequency of the items endorsed pertaining to the desirable or beneficial effects of use and symptoms of withdrawal for both the groups are illustrated in Table 2. Both the areca and areca + tobacco group attributed reasons in similar order of frequency. These were, in descending order, improvement of mood, improvement of performance, aid to digestion, aid in social situations and reduction of body-aches. 51% of the subjects in the areca group reported withdrawal symptoms compared to 84.1% in the areca + tobacco group. Subjects in the areca group reported almost the same ranking of symptoms as in the areca + tobacco group, though at a lower frequency [Table 2].

Amongst areca + tobacco users, a greater proportion of subjects with psychiatric illness than those without, tended to satisfy criteria for dependent use, though this difference did not attain statistical significance. The reverse was observed for areca users, in whom a greater proportion of subjects (not reaching

Table 1

Socio-demographic factors, psychiatric status, concomitant substance use and family history of substance use in non-users, areca users and areca–tobacco mixture users

	Non-users (N=88)	Areca (N=98)	Areca + tobacco (N=44)	Differences between users and non-users		Differences between areca and areca + tobacco users	
				t; d.f.	p	t; d.f.	p
Age	35.4 (12.1) years	38.7 (10.7) years	44.5 (11.4) years	$F=9.3$; d.f. 2	<0.0001	2.9; 140	0.004
Sex—female	42%	59.2%	61.4%	$\chi^2=6.9$; 1	0.006	$\chi^2=0.1$; 1	0.5
Education	6.5 (5.4) years	5.5 (4.9) years	2.9 (4.4) years	$t=-1.94$	0.054	2.8; 140	0.005
Marital status				$\chi^2=8.9$; 2	0.012	$\chi^2=0.4$; 2	0.8
Married	82%	93%	91%				
Unmarried	18%	6%	7%				
Separated/widowed	–	1%	2%				
Residence				$\chi^2=0.4$; 1	0.054	$\chi^2=1.4$; 1	0.8
Urban	50%	40%	30%				
Rural	50%	60%	70%				
Socio-economic status				$\chi^2=3.4$; 2	0.19	$\chi^2=1.2$; 2	0.6
Upper	8%	9%	7%				
Middle	21%	35%	27%				
Lower	71%	56%	66%				
Psychiatric illness	67%	60%	59%	$\chi^2=1.2$; 1	0.27	$\chi^2=0.6$; 1	0.8
Schizophrenia	18.2%	12.2%	9.4%				
Mood disorders	37.5%	37.8%	45.5%				
Common mental disorders	11.4%	11.2%	4.5%				
Use of other substances	11.5%	16.3%	25.7%	$\chi^2=3.6$; 3	0.4	$\chi^2=3.6$; 6	0.7
Alcohol	2%	4%	5%				
Tobacco (smoking)	9%	12%	16%				
Both	1%	–	–				
Family history—substance use				$\chi^2=11.8$; 3	0.008	$\chi^2=3.9$; 2	0.14
Alcohol	3	7%	7%				
Tobacco	5%	7%	18%				
Both	5%	–	–				
Family history of areca use	26%	42%	55%	$\chi^2=8.9$; 1	0.003	$\chi^2=2$; 1	0.203

statistical significance) without psychiatric illness than those affected satisfied criteria for dependent use [Table 3].

In order to predict the likelihood of developing dependence due to areca use, a multiple regression analysis was performed with the DSM-IV criterion count in areca users as the dependent variable and the following predictors (independent variables): quantity used per typical using day, frequency of use, age at onset of use, gender, education, socio-economic status, presence of psychiatric illness, family history of betel and other substance use, and co-morbid use of other substances. Using the enter method, a significant model emerged ($F_{10,73}=18.42$, $p<0.0005$. Adjusted R square=0.716). The significant variables were: frequency ($\beta=5.4$; $p<0.0005$), quantity ($\beta=3.3$; $p=0.002$) and education ($\beta=-2.8$; $p=0.007$).

Similarly, in order to predict the development of dependence with areca + tobacco products, multiple regression analysis was performed with the DSM-IV criterion count in areca + tobacco users as the dependent variable and the same variables as above as predictor variables. Using the enter method, a significant model emerged ($F_{10,32}=12.95$, $p<0.0005$. Adjusted R square=0.802). The significant variables were: frequency ($\beta=8.1$; $p<0.0005$) and age at onset of use ($\beta=-2.1$; $p=0.04$).

4. Discussion

4.1. Dependence syndrome with areca use

About two out of five persons using areca-nut preparations (*without tobacco additives*) had developed a recognizable pattern of dependent use, satisfying both DSM-IV (38.8% of areca users) as well as ICD-10 (40.8% of areca users) criteria for current dependence. Expectedly, given the addiction potential of nicotine, the prevalence of dependence among those using areca preparations with tobacco additives was much higher than among persons using areca alone. Nevertheless, this study highlights the potential risk for developing dependence in people using areca alone and extends the findings from a few previous small-scale studies which have hinted that areca use may result in a dependence syndrome (Pickwell et al., 1994; Winstock et al., 2000). There are also a couple of case reports that have documented neonatal withdrawal syndromes in newborns pre-natally exposed to this drug (Garcia-Algar et al., 2005; López-Vilchez et al., 2006).

Expectedly, the areca + tobacco users reported a withdrawal syndrome on abstaining or decreasing consumption. Areca users

Table 2
Patterns of use; desired/beneficial effects and withdrawal symptoms associated with areca use

Patterns of use	Areca (N=98)	Areca + tobacco (N=44)	t; d.f.	p
Age at onset of use (all users)	25.8 (10.1) years	24.8 (9.7) years	−0.5; 140	0.2
Psychiatrically unaffected	25.2 (11) years	25.6 (10.7) years	−0.1; 47	0.9
Psychiatrically ill	26.1 (9.6) years	24.3 (9.2) years	0.8; 76	0.4
Units per typical using day (all users)	2.6 (2.3)	6 (4.5)	−4.7; 53.5	<0.0005
Psychiatrically unaffected	3 (2.7)	4.8 (3.5)	−2.2; 55	0.03
Psychiatrically ill	2.3 (2)	6.8 (5)	−5.8; 83	<0.0005
Frequency—daily use (all users)	48%	79.5%	$\chi^2 = 12.5; 2$	<0.0005
Psychiatrically unaffected	53.8%	77.8%	$\chi^2 = 13.3; 2$	<0.0005
Psychiatrically ill	44.1%	80.8%	$\chi^2 = 24.7; 2$	<0.0005
Preparation			$\chi^2 = 235.4; 6$	<0.0005
Plain or flavoured (sachets)	57.7%	75%		
Betel quid	37.1%	22.7%		
Other	5.2%	2.3%		
Desired/beneficial effects	Psychiatrically ill users		Psychiatrically unaffected users	
	Areca (N=59) (%)	Areca + tobacco (N=26) (%)	Areca (N=39) (%)	Areca + tobacco (N=18) (%)
Improves mood	44.1	84.6	59	72.2
Improves performance/alertness	25.4	76.9	35.9	44.4
Helps digestion	25.4	38.5	23.1	33.3
Aids social interactions	22	38.5	20.5	16.7
Reduces aches	52.9	47.1	10.3	5.6
Withdrawal syndrome				
Craving	33.9	80.8	48.7	72.2
Sadness/dysphoria	16.9	53.8	43.6	44.4
Dryness of mouth	20.3	57.7	35.9	38.9
Agitation/anger/irritability	13.6	57.7	28.2	33.3
Anxiety/feeling tense	23.7	46.2	28.2	48.4
Decreased performance	16.9	50	25.6	38.9
Fatigue/lethargy	15.3	53.8	23.1	22.2
Altered taste	11.9	46.2	23.1	33.3
Impaired concentration	10.2	50	17.9	16.7
Increased sensitivity to pain	15.3	38.5	15.4	27.8
Increased daytime drowsiness	12.1	36.7	12.4	27.2
Slowing of movement	7	25	2.1	6.8
Vivid/unpleasant dreams	–	6.4	–	4.3

Table 3
Dependence syndrome in areca users

Item	Areca only (N=98) (%)	Areca + tobacco (N=44) (%)		
1 Tolerance	37.8	77.3		
2 Withdrawal	51	84.1		
3 Loss of control	35.7	77.3		
4 Multiple attempts at abstinence	77.6	54.5		
5 Salience	35.7	77.3		
6 Giving up activities to use the substance(s)	0	12		
7 Use despite knowledge of harm	34.7	63.6		
8 Craving	39.8	77.3		
Dependence				
DSM-IV criteria	38.8	79.5		
ICD-10 criteria	40.8	79.5		
Item	Psychiatric illness		Psychiatric illness	
	Affected	Unaffected	Affected	Unaffected
Dependent (ICD 10)	33.9%	51.3%	84.6%	72.2%
		$\chi^2 = 2.9; 1 p = 0.1$	$\chi^2 = 1; 1 p = 0.5$	
Dependent (DSM-IV)	32.2%	48.7%	84.6%	72.2%
		$\chi^2 = 2.7; 1 p = 0.1$	$\chi^2 = 1; 1 p = 0.5$	

too, reported a relatively muted, yet well characterized withdrawal syndrome in keeping with the general pattern expected in stimulant withdrawal. This phenomenon, when coupled with the observation that the majority of areca users had made multiple unsuccessful attempts at abstinence in the absence of any socio-occupational dysfunction, and that a large proportion of them reported significant craving, underlines the addictive potential of areca use on its own. Combined use of areca and tobacco significantly increases the rate of dependence.

The relative rankings of withdrawal symptoms in subjects using areca alone were strikingly similar to those obtained from persons who used both areca and tobacco, though their individual frequencies were lower. This indicates that the symptoms of areca nut withdrawal are similar to those in subjects also using tobacco, and that combined use was associated with a more severe withdrawal syndrome. Some of the symptoms found in both groups, such as dry mouth, are not commonly associated with nicotine withdrawal. It is unclear whether these symptoms are specifically related to areca nut pharmacology. Arecoline, the major alkaloid of areca nut, has been extensively studied and betel chewing has been documented to produce a sense of well-being, euphoria, heightened alertness, sweating, salivation, a hot sensation in the body and increased capacity to work (Chu, 2001). Withdrawal would be expected to produce effects in the reverse direction.

4.2. Predictors of dependence

Increased frequency of use, larger quantities used on typical using occasions and lower education, appear to predict 72% of the likelihood of developing more severe dependence (DSM-IV criterion count) due to areca use. In the case of persons using areca + tobacco products, increased frequency of use and earlier age at onset of use predicted 80% of the likelihood of increased severity of dependence. Gender, educational level, socio-economic status, presence of psychiatric illness, family history of betel and other substance use, and co-morbid use of other substances, did not appear to have significant influence.

4.3. Public health implications

It is now well accepted that all areca nut products, even those without tobacco, are associated with OSF which has been established as a highly precancerous condition. The relative risk of malignant transformation in the oral mucosa of OSF patients compared to tobacco users without any precancerous lesion or condition has been estimated at around 400. So, areca users are potentially more liable to develop OSF and cancer over a relatively shorter duration and die earlier compared to smokers. Tobacco in areca nut mixtures, although not a causative factor for OSF, is believed to be responsible for a higher occurrence of OSF due to its effect of increasing addiction and thereby causing higher exposure to areca nut chewing (Nair and Mathew, 2005). The popularity of areca nut mixtures, like *mawa*, *paan masala* and especially *gutka*, has spawned an epidemic of OSF among young individuals in India (Gupta and Ray, 2004). A variety of other harmful consequences, such as hepatocellular

carcinoma, cholinergic toxicity, toxic psychosis, and neurologic complications have also been described with areca preparations (Chu, 2001; Chung et al., 2006; Deng et al., 2001; Mack, 2001; Winstock, 2002). In view of these concerns, the Ministry of Health and Family Welfare of the Government of India ruled, in 1993, that all products containing *supari* (areca nut), such as *paan masala* and *gutka* should carry a statutory warning about its injurious effects (Mangla, 1993).

4.4. Special populations at risk

Statutory warnings unfortunately do little to limit sales. Our data point to the fact that women and younger people especially from rural and/or lower socio-economic backgrounds with poorer educational attainment were more likely to be using areca products alone or in combination with tobacco. Women users were also significantly more likely than male users to have dependent use. Areca users are significantly younger than the areca + tobacco users, though both groups report similar ages at initiation of the chewing habit. The absence of sequential data does not allow us to determine whether there is a chronological stepwise progression from areca to areca + tobacco products, yet information from the literature fuels speculation that it may be so (Chandra and Mulla, 2007).

The respondents' free listing of desired/beneficial effects when arranged post-hoc provided common categories such as: improving mood and performance, enhancing alertness and performance, promoting digestion, aiding social interactions and reducing aches and pains. The predominant themes obtained fit into the picture of users attempting to reverse a negative affect state. Previous studies in this population have documented that women substance users attribute tension relief as the prime motive for their substance use, unlike men who are more likely to attribute enhancement of positive expectancies (Benegal et al., 2005). Areca use, with its documented abilities of producing a sense of well-being, euphoria, heightened alertness, and an increased capacity to work (Chu, 2001), may well be sought to self-medicate negative affect states. The widespread cultural tradition which views consumption of the areca nut as a part of daily life provides sanction for its use by women and young children, in whom the use of other stimulants, such as smoking tobacco, would be considered unacceptable (Changrani and Gany, 2005). Also, while the ill effects of smoking are fairly well known, awareness regarding the effects of chewing areca nut is minimal (Gunaseelan et al., 2007).

Since, 60% of both user groups suffered from psychiatric illness, it is but natural to enquire whether psychiatric illness increases the risk of using areca and developing dependent patterns of use. Psychiatrically ill subjects using areca + tobacco preparations, consumed relatively larger quantities and had greater prevalence of daily use of than the unaffected subjects. Likewise, dependent use was more common in areca + tobacco users with psychiatric illness, than in the unaffected subjects using the same preparation. Conversely, unaffected subjects using areca alone, used marginally higher quantities of the drug and had more prominent daily use, than affected subjects. They also had a greater proportion of dependent users

than affected areca users. None of these differences were a statistically significant; however, it is interesting to speculate that the psychiatrically ill subjects were more likely to choose or settle on areca preparations with tobacco admixture for the relatively higher reward and reinforcement signals from the contained nicotine and consequently more likely to develop dependent use with these substances. Persons with severe mental disorders, for example, have been observed to have higher rates of smoking and other substance use (Schuckit, 2006). This view is indirectly supported by the higher values given by the affected group to expectancies of desired/beneficial effects of areca + tobacco preparations compared to the ratings of unaffected users [Table 2].

4.5. Limitations

Certain limitations of the study need to be mentioned. First, our sample included a large number of psychiatrically ill patients, which poses an independent risk factor for substance abuse and dependence. Second, the 'unaffected' subjects were not systematically screened or assessed for psychiatric disorder. Finally, given the nature of the study sample one cannot draw population-based estimates from this study. Using a randomly ascertained sample from the general population would have provided greater generalizability to the findings.

4.6. Conclusion

The study does suggest that a substantial proportion of areca users develop dependence. It addresses a little-studied aspect of the consequences of use of a socially sanctioned substance with significant health implications. These findings, though preliminary, provide support for the concept of an identifiable areca nut dependence syndrome, which can be diagnosed using criteria very similar to the ones currently used for other substances of abuse. Further research is needed to replicate this finding in larger, community-based samples. Given the high rates and health risks associated with long-term usage, screening for areca nut dependence should be more widely applied in populations where areca use is prevalent.

We hope that delineating a dependence syndrome may convey attention upon a public health problem hitherto relatively ignored. However, this raises further concerns regarding intervention, namely early detection and treatment of persons with areca-nut dependence, areas which have been little studied in the past.

Conflict of interest

The authors declare that there is no conflict of interest.

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