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The effects of chewing areca/betel quid with and without cigarette smoking on oral submucous fibrosis and oral mucosal lesions

Y-H Yang[1], Y-C Lien[1], P-S Ho[2], C-H Chen[3], JSF Chang[4], T-C Cheng[5], T-Y Shieh[6]

[1]*Graduate Institute of Oral Health Sciences, College of Dental Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan;* [2]*School of Dental Hygiene, College of Dental Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan;* [3]*School of Dentistry, College of Dental Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan;* [4]*Buddhist Dalin Tzu Chi General Hospital, Chiayi, Taiwan;* [5]*Mutan Health Station, Ping-Tong County, Taiwan;* [6]*Oral Health Research Center, Kaohsiung Medical University, Kaohsiung, Taiwan*

OBJECTIVES: The purpose of this study was to investigate the risk of areca/betel quid chewing with or without cigarette smoking on oral submucous fibrosis (OSF) and other oral mucosal lesions.

METHODS: A stratified case–control study was designed. There were in total 102 patients with oral mucosal lesions or OSF (confirmed pathologically) in the case group. OSF ($n = 62$) and oral mucosal lesions ($n = 62$) in 102 subjects were separately analyzed for men and women investigating their risks.

RESULTS: For OSF, people with both smoking and chewing habits had a statistically significant odds ratio (OR) 8.68 (95% CI = 1.87, 40.23). For the group of people with chewing habit only and without any lifetime cigarette smoking habit, the OR was 4.51 (95% CI = 1.20, 16.94). For other oral mucosal lesions, people with mixed habits and chewing only had also significant risks (OR = 8.37 and 3.95, respectively). For both OSF and other oral lesions, the ORs of mixed habits and chewing only were both higher in women than in men.

CONCLUSIONS: The areca/betel quid used in Taiwan does not contain any tobacco product. The only way of areca/betel quid could synergize with any tobacco product is through cigarette smoking. A statistically significant association with oral mucosal lesions and OSF was still found in the group of areca/betel quid chewing only.
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Keywords: areca/betel quid, oral submucous fibrosis, oral lesions, case–control study

Correspondence: Tien-Yu Shieh, Oral Health Research Center, No. 100 Shih-Chuan 1st Rd, Kaohsiung Medical University, Kaohsiung 807, Taiwan. Tel.: +886 7 312 1101 ext 2338, Fax: +886 7 313 5340, E-mail: tiyush@kmu.edu.tw
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Introduction

The areca or betel quids consumed in India and many other Southeast Asia countries mostly contain tobacco. Hence, it has been difficult to establish the individual risk effect from the areca nut only. The areca/betel quid chewing is also a popular habit in Taiwan. The areca/betel quid consumed in Taiwan has never contained any tobacco. However, majority (87%) of areca/betel quid chewers in Taiwan were, in fact, reported to be cigarette smokers (Yang *et al*, 2002). Therefore, many oral lesions related research in Taiwan still did not have significant statistical power to clarify the effect of areca/betel quid from tobacco product. In aboriginal communities of Taiwan, the proportion of people with areca/betel quid chewing but without any cigarette smoking habit is relatively higher (37% of areca/betel quid chewers). Anecdotally, it is still common to see oral mucosal lesions in those patients with areca/betel chewing habit only. The purpose of this study was to investigate the risk of betel quid chewing with or without cigarette smoking on oral submucous fibrosis (OSF) and other oral mucosal lesions.

Methods

Study subjects

Since 1997, a total of 1321 residents of all ages in the Mutan community were screened for oral mucosal lesions, and 300 of these residents were invited for further pathological diagnosis. Of these 131 persons completed further clinical examination in addition to providing a biopsy. The detailed interview of their areca/betel quid chewing and smoking histories were successfully obtained from 102 patients.

Study design

A stratified case–control study was designed to investigate the risk of areca/betel quid chewing alone and

areca/betel quid chewing with cigarette smoking habit on oral mucosal lesions. A total of 102 patients with oral mucosal lesions (confirmed pathologically) consisted the case group. The case group was then classified into several sex/age-group (5 year age interval) categories, and each category had different numbers of patients. Hence, for each age category, the same number of participants without any mucosal lesions following screening was obtained from a community based survey study. The reason for conducting the stratification instead of the ordinal 1–1 matched study was that many patients had the same sex and almost the same ages; for example, in the study data, 11 OSF patients were women and with ages ranging 70–74 years. Therefore, a 1–1 match may lead to slightly different results with different arrangement of 11 controls in the same sex/age-group category.

Statistical analysis

Given the stratification design, the Mantel–Haenszel chi-square tests were adapted to assess differences between case and control groups while stratified by sex/age-group categories for various factors. Apparently, in the case group, only one patient had no prior history of areca/betel quid chewing. As for the OSF patients, all of the patients had areca/betel quid chewing history. Hence, it was impossible to compute the odds ratios for the effects of areca/betel quid on OSF patients by the ordinary Mantel–Haenszel estimates of the odds ratios. Instead, the adjusted logit estimates of the odds ratio and 95% confidence intervals (Haldane, 1955; Woolf, 1955) was computed. The main computational difference was that if any cell frequency in a sex/age-group category was zero, then we added 0.5 to each cell of the sex/age-group category. The statistical computation was carried out by using the SAS V8.02 software.

Areca/betel quid

There are three major types of betel/areca quid in Taiwan (Yang *et al*, 2001). In the aboriginal community, majority of the people chewed betel quid or stem quids. None contained chewing tobacco.

Results

Since 1997, among a total of 1321 residents of all ages screened for oral mucosal lesions, 131 persons with at least one oral lesion were confirmed positive by biopsies. The detailed interview for their areca/betel quid chewing and smoking history were successfully obtained from 102 patients.

The diagnoses from pathological reports are shown in Table 1. Among these 102 patients, 76 (74.5%) are women, and 26 are men (25.5%). Only 51.0% of these patients had one type of lesion, and the others had multiple oral lesions in their first screening results. OSF was the most prevalent disease (60.8%), followed by keratosis (39.2%) and epithelial hyperplasia (39.2%). Nine cases of squamous cell carcinoma and two cases of verrucous carcinoma were also identified by screening. Comparisons of lesions between men and women were not significantly different with all *P*-values being higher than 0.05.

For men and women with lesions, their ages, habits of areca/betel quid chewing and type of quid chewed were not significantly different. Smoking habits however, were significantly different ($P < 0.0001$) (Table 2). Only one woman was without any lifetime areca/betel quid chewing habit. There were 73 of 102 patients (71.6%; 26.9% in men and 86.8% in women) with only areca/betel quid chewing habit and without any cigarette smoking habit in their lifetime. The average age ($\pm$s.d.) was 64.9 ($\pm$13.2) years old, and 88.3% were older than 50 years of age. The cigarette smoking habit was mostly seen in men (73.1%), while only women (11.8%) was reported with a smoking habit. For the types of quid, 50.0% of subjects chewed betel quid only, 25.5% chewing stem quid only and 15.7% chewed both betel quid and stem quid. Men and women were not different in terms of the types of quid.

Considering the ranking of prevalence of lesions in different combinations of areca/betel quid chewing and smoking habits as well as types of quid (Table 3), OSF was the most prevalent lesion in every combination of areca/betel quid chewing and smoking habits. The hyperparakeratosis was more prevalent in chewing

Table 1 Pathological results for the case group

	Total		*Men*		*Women*		
	n	%	n	%	n	%	P-*value*
Total	102		26		76		
With lesions, one or more							
1	52	51.0	14	53.8	38	50.0	0.9198
2	42	41.2	10	38.5	32	42.1	
3	7	6.8	2	7.7	5	6.6	
4	1	1.0	0	0.0	1	1.3	
Lesions							
Oral submucous fibrosis (OSF)	62	60.8	18	69.2	44	57.9	0.3068
Keratosis	40	39.2	12	46.2	28	36.8	0.4012
Epithelial hyperplasia/acanthosis	40	39.2	7	26.9	33	43.4	0.1369
Squamous cell carcinoma	9	8.8	1	3.8	8	10.5	0.2999
Epithelial dysplasia	8	7.8	1	3.8	7	9.2	0.3798
Verrucous carcinoma	2	2.0	1	3.8	1	1.3	0.4218

Table 2 Comparison of men and women with oral lesions in their quid chewing and cigarette smoking habits

	Total		*Men*		*Women*		
	n	%	n	%	n	%	P-*value*
Total	102		26		76		
Age group (years)							
20–49	12	11.8	6	23.1	6	7.9	0.0949
50–64	28	27.5	5	19.2	23	30.3	
65+	62	60.8	15	57.7	47	61.8	
Areca/betel quid							
Yes	101	99.0	26	100.0	75	98.7	0.5567
No	1	1.0	0	0.0	1	1.3	
Cigarette smoking							
Yes	28	27.5	19	73.1	9	11.8	<0.0001
No	74	72.5	7	26.9	67	88.2	
Chewing/smoking							
Both chewing and smoking	28	27.5	19	73.1	9	11.8	<0.0001
Chewing only	73	71.6	7	26.9	66	86.8	
None of both habit	1	1.0	0	0.0	1	1.3	
Type of quid							
Both betel and stem quid	16	15.7	3	11.5	13	17.1	0.8510
Betel quid only	51	50.0	13	50.0	38	50.0	
Stem quid only	26	25.5	7	26.9	19	25.0	
Other types	8	7.8	3	11.5	5	6.6	
No chewing habit	1	1.0	0	0.0	1	1.3	
Age							
Mean and s.d. in years	64.88	13.18	59.59	17.70	66.68	10.79	0.0171

areca/betel quid without cigarette smoking group, and the betel quid type group. There were more cases of squamous cell carcinoma in the quid only group. Those patients who chewed both betel quid and stem quid had higher prevalence of acanthosis.

There were 62 patients with OSF (Table 4). All of the case subjects had areca/betel quid chewing habit, while in the control group 22.6% were without chewing habit. Looking at the chewing or smoking habits, amount of quids per day and types of quids, the Mantel–Haenszel chi-square tests had shown that the sex/age-group stratified chi-square tests were all significant, except for 'amount of quids per day' and 'type of quid' in men, at 0.05 level. People with both cigarette smoking and areca/betel quid chewing habit had statistically significant odds ratio (OR) 8.68 (95% CI = 1.87, 40.23). For the group of people with chewing habit and without any lifetime cigarette smoking habit, the OR was 4.51 (95% CI = 1.20, 16.94). Considering men and women separately, only both smoking and chewing group had shown significant effect (OR = 7.66, 95% CI = 1.40, 41.92). For women, the chewing only group had shown significant effect (OR = 5.6, 95% CI = 1.12, 28.03). The amount of more than '10–29' and '30 and more' counts of quids per day had significant ORs (4.55, 10.34, respectively). Among the different type of quids, the betel quid with an OR of 6.45 (95% CI = 1.60, 26.07), had the highest risk.

There were 62 patients with hyperparakeratosis, epithelial hyperplasia or hyperorthokeratosis (Table 5). Almost all of the case subjects had areca/betel quid chewing habit, while in the control group 24.2% were without any chewing habit. Looking at the chewing or smoking habits, amount of quids per day and types of quids, the Mantel–Haenszel chi-square tests showed that the sex/age-group stratified chi-square tests were all significant, except for 'amount of quids per day' and 'type of quid' in men. People with both cigarette smoking and areca/betel quid chewing habit had statistically significant OR of 8.37 (95% CI = 1.71, 40.98). For the group of people with chewing habit and without any lifetime cigarette smoking habit, the OR was 3.95 (95% CI = 1.23, 12.68). Considering men and women separately, both smoking and chewing groups had shown significant effect (OR = 7.99, 95% CI = 1.19, 53.68). For women, the chewing only group had shown significant effect (OR = 4.19, 95% CI = 1.09, 16.10). The frequencies of more than '10–29' and '30 and more' quids per day had significant ORs (3.77, 6.31, respectively). Betel quid with an OR of 5.92 (95% CI = 1.73, 20.23), was the quid of highest risk.

Discussion

In our study population, the prevalence of areca/betel quid chewing was high among both men (85.6%) and women (93.4%) (Yang *et al*, 2001). However, there were more cigarette smokers in men (63.9%) then in women (13.1%). Our case group primarily bared the same scenario that almost all of the case groups are areca/betel quid chewers, but male cases had 73.1% cigarette smokers while these were only 11.8% cigarette smokers among female cases. Nevertheless, men and women were not very different in their types of chewing quid. The prevalence rates of various oral lesions by pathological diagnosis had shown no statistical differences between men and women; however, the rates of hyperorthokeratosis were higher in men (15.4%) then in women (5.5%) with borderline significance ($P = 0.0975$).

Table 3 Comparing the prevalence rates of lesions among different combination of chewing and smoking habits

Quid chewing and cigarette smoking combination				*Types of chewing quids*			
Both chewing and smoking (n = 28)		*Chewing only* (*n* = 73)		*Betel and stem quid* (n = 16)		*Betel quid only* (n = 51)		*Stem quid* (n = 26)	
OSF	67.9	OSF	58.9	OSF	62.5	OSF	60.8	OSF	61.5
Epithelial hyperplasia	25.0	Hyperparakeratosis	37.0	Epithelial hyperplasia	31.3	Hyperparakeratosis	37.3	Epithelial hyperplasia	38.5
Hyperparakeratosis	25.0	Epithelial hyperplasia	35.6	Hyperparakeratosis	25.0	Epithelial hyperplasia	33.3	Hyperparakeratosis	26.9
Hyperorthokeratosis	21.4	Squamous cell carcinoma	9.6	Acanthosis	18.8	Squamous cell carcinoma	9.8	Squamous cell carcinoma	11.5
Squamous cell carcinoma	7.1	Dysplasia	8.2	Dysplasia	6.3	Dysplasia	9.8	Dysplasia	7.7
Dysplasia	7.1	Acanthosis	6.8	Verrucous carcinoma	6.3	Hyperorthokeratosis	7.8	Hyperorthokeratosis	3.8
Acanthosis	3.6	Hyperorthokeratosis	2.7	Squamous cell carcinoma	0.0	Acanthosis	3.9	Acanthosis	3.8
Verrucous carcinoma	3.6	Verrucous carcinoma	1.4	Hyperorthokeratosis	0.0	Verrucous carcinoma	2.0	Verrucous carcinoma	0.0

Different types of areca/betel quid were also related to different pathological results. The betel quid group had higher percentage of hyperparakeratosis, while the stem group had more epithelial hyperplasia. The prevalence rate of acanthosis was high (18.8%) in the group of people chewing both betel and stem quid.

From previous studies, OSF was hardly found in non-areca quid chewers. Hence, in many studies, the occasional areca nut chewers or ex-chewers were used as the reference group when computing the odds ratios. In India (Sinor *et al*, 1990), a case–control study with men as the majority of OSF cases (58 men and two women) used occasional areca nut chewers as the reference group. Their case–control study showed ORs of 29.9–780.0 for areca nut chewers with various level of use of tobacco product. Also in the same study, an OR of 78.0 (four in the OSF case group and two in the control group) for chewers of betel quid without tobacco was also identified. Another case–control study from India (Shah and Sharma, 1998) also had all OSF cases with chewing and/or smoking habits. Although the ORs were not computed, the risks were evident from their findings: 21.6% of quid chewers, 20.8% of quid chewers with tobacco, 13.1% of pan masala users and 25.4% of pan masala users with tobacco in the OSF cases, while only 5.9, 1.8, 1.4 and 2.7%, respectively, in the control group. In Pakistan (Maher *et al*, 1994), a case–control study with ex-chewers as the reference group had found an OR of 64 (95% CI = 15, 274) for quid chewers with tobacco, and an OR of 32 (95% CI = 6, 177; seven in the OSF case group and nine in the control group) for quid chewers without tobacco. In this study, women comprised most of the OSF cases (48 men and 109 women). An earlier hospital-based case–control study (93 men and one woman) (Lee *et al*, 2003) had shown an OR of 57.9 (95% CI = 16.0, 209.6) for people with both chewing and smoking habit, and an OR of 39.3 (95% CI = 7.5, 206.9) for people with chewing habit only.

In our study, all of the case subjects had areca/betel quid chewing habit, and again the majority of patients were women (44 women and 18 men). Both the habits of quid chewing without cigarette smoking and quid chewing with cigarette smoking had shown significant effects (OR = 4.51 and 8.68, respectively) in OSF. Since the people with cigarette smoking habit were primary men, the effect of chewing with smoking was significant in men, but not in women. In contrast, most women had only chewing habit, and the effect for women was only significant in chewing only habit. While most of research (except Pakistan) had shown important risks from areca/betel quid chewing with or without tobacco product primarily in men, our study result had importantly shown significant risks from chewing areca quid for women to develop OSF.

As for the previous studies (Sinor *et al*, 1990; Maher *et al*, 1994; Shah and Sharma, 1998), the dose–response effect by computing the frequency of chewing a day also had significant effects. Consuming more than 10 a day had significant risks (OR = 4.55 for 10–29 counts, OR = 10.34 for 30 or more). The average age of patients was much higher in our study

Table 4 Comparison of areca/betel quid chewing status in OSF patients and controls

		Case		*Control*				*95% Confidence intervals*	
Variable	*Items*	n	*%*	n	*%*	P-*value*	*OR*	*Lower*	*Upper*
Total		62		62					
Chewing/smoking	Chewing and smoking	19	30.6	9	14.5	0.0004	8.68*	1.87	40.23
	Chewing only	43	69.4	39	62.9		4.51*	1.20	16.94
	None of both habit	0	0.0	14	22.6		1.00		
Areca/betel quid	Yes	62	100.0	48	77.4	0.0002	5.99*	1.98	18.11
	No	0	0.0	14	22.6		1.00		
Number of quids per day	30+	26	41.9	5	8.1	<0.0001	10.34*	2.39	44.73
	10–29	26	41.9	27	43.6		4.55*	1.16	17.84
	1–9	10	16.2	16	25.8		3.66	0.71	18.91
	No chewing	0	0.0	14	22.6		1.00		
Type of quid	Betel and stem quid	10	16.1	9	14.5	0.0022	4.94*	1.03	23.82
	Betel quid only	31	50.0	17	27.4		6.45*	1.60	26.07
	Stem quid only	16	25.8	15	24.2		3.96	0.79	19.69
	Other types	5	8.1	7	11.3		5.43	0.48	61.39
	No chewing habit	0	0.0	14	22.6		1.00		
Men		18		18					
Chewing/smoking	Chewing and smoking	14	77.8	6	33.3	0.0138	7.66*	1.40	41.92
	Chewing only	4	22.2	5	27.8		2.88	0.28	29.34
	None of both habit	0	0.0	7	38.9		1.00		
Areca/betel quid	Yes	18	100.0	11	61.1	0.0087	5.92*	1.29	27.24
	No	0	0.0	7	38.9		1.00		
Number of quids per day	30+	5	27.8	2	11.1	0.0571	4.88	0.47	50.32
	10–29	9	50.0	5	27.8		5.89	0.92	37.57
	1–9	4	22.2	4	22.2		9.00	0.66	122.79
	No chewing	0	0.0	7	38.9		1.00		
Type of quid	Betel and stem quid	2	11.1	2	11.1	0.1064	4.80	0.25	93.00
	Betel quid only	8	44.4	6	33.3		4.71	0.61	36.61
	Stem quid only	5	27.8	2	11.1		4.80	0.59	39.05
	Other types	3	16.7	1	5.6		11.70	0.50	275.47
	No chewing habit	0	0.0	7	38.9		1.00		
Women		44		44					
Chewing/smoking	Chewing and smoking	5	11.4	3	6.8	0.0209	15.00	0.43	524.53
	Chewing only	39	88.6	34	77.3		5.60*	1.12	28.03
	None of both habit	0	0.0	7	15.9		1.00		
Areca/betel quid	Yes	44	100.0	37	84.1	0.0064	6.07*	1.22	30.23
	No	0	0.0	7	15.9		1.00		
Number of quids per day	30+	21	47.7	3	6.8	<0.0001	16.85*	2.57	110.59
	10–29	17	38.6	22	50.0		3.34	0.44	25.29
	1–9	6	13.6	12	27.3		2.04	0.25	16.80
	No chewing	0	0.0	7	15.9		1.00		
Type of quid	Betel and stem quid	8	18.2	7	15.9	0.0152	5.00	0.78	31.97
	Betel quid only	23	52.3	11	25.0		8.47*	1.26	56.97
	Stem quid only	11	25.0	13	29.5		3.00	0.25	36.47
	Other types	2	4.5	6	13.6		1.80	0.04	79.42
	No chewing habit	0	0.0	7	15.9		1.00		

(64.88 ± 13.18 years) reflecting the age structure of the aboriginal community, than in previous studies (e.g. 30.42 ± 10.86, Shah and Sharma, 1998), In other reported studies 71 of 157 OSF cases were 21–40 years old (Maher *et al*, 1994) and 57% of OSF cases were 25–34 years old (Sinor *et al*, 1990). Our study population therefore had more elderly people and possibly longer exposure to risk habits. Also, it is generally difficult to invite younger people to attend clinics for further investigation. Being busy and not finding anything wrong were the two most common excuses given for non-attendance.

There are various types of chewing quids in Taiwan. Lee *et al* (2003) had found that in the general population of Taiwan, the areca quid had higher risk for OSF than the betel quid. In our study population where the areca quid with inflorescence of *Piper Betle Linn*. is not common, the betel quid appeared to have higher risk than the stem quid to develop OSF.

Leukoplakia is associated with both areca/betel quid chewing and tobacco smoking. Hence, leukoplakia can be considered to be prevalent in Southeast Asia countries. In terms of the relationship between oral mucosal lesions (primarily leukoplakia) and tobacco smoking, a study from Japan showed an odds ratio of 3.34 (95% CI = 1.95, 5.71) (Ikeda *et al*, 1991) for smokers having leukoplakia. In USA, the school children 12–17 years of age had a relative risk of 3.21(Kleinman *et al*, 1994). A case–control study from Kenya (Macigo *et al*, 1995) showed an odds ratio of 8.4 for smokers of having leukoplakia.

Table 5 Comparison of areca/betel quid chewing status in other oral mucosal lesion patients and controls

		Case		*Control*				*95% Confidence intervals*	
Variable	*Items*	n	*%*	n	*%*	P-*value*	*OR*	*Lower*	*Upper*
Total		62		62					
Chewing/smoking	Chewing and smoking	17	27.4	8	12.9	0.0010	8.37*	1.71	40.98
	Chewing only	44	71.0	39	62.9		3.95*	1.23	12.68
	None of both habit	1	1.6	15	24.2		1.00		
Areca/betel quid	Yes	61	98.4	47	75.8	0.0005	4.92*	1.73	14.00
	No	1	1.6	15	24.2		1.00		
Number of quids per day	30+	22	35.5	6	9.7	<0.0001	6.31*	1.49	26.72
	10–29	30	48.4	27	43.5		3.77*	1.15	12.37
	1–9	9	14.5	14	22.6		2.12	0.44	10.34
	No chewing	1	1.6	15	24.2		1.00		
Type of quid	Betel and stem quid	7	11.3	10	16.1	0.0020	2.19	0.34	13.89
	Betel quid only	32	51.6	14	22.6		5.92*	1.73	20.23
	Stem quid only	17	27.4	16	25.8		3.70	0.87	15.83
	Other types	5	8.1	7	11.3		2.78	0.29	26.68
	No chewing habit	1	1.6	15	24.2		1.00		
Men		15		15					
Chewing/smoking	Chewing and smoking	11	73.3	5	33.3	0.0342	7.99*	1.19	53.68
	Chewing only	4	26.7	4	26.7		3.31	0.32	34.14
	None of both habit	0	0.0	6	40.0		1.00		
Areca/betel quid	Yes	15	100.0	9	60.0	0.0152	6.26*	1.17	33.56
	No	0	0.0	6	40.0		1.00		
Number of quids per day	30+	4	26.7	2	13.3	0.0650	3.91	0.26	59.53
	10–29	9	60.0	4	26.7		5.89	0.92	37.57
	1–9	2	13.3	3	20.0		9.00	0.10	831.78
	No chewing	0	0.0	6	40.0		1.00		
Type of quid	Betel and stem quid	0	0.0	2	13.3	0.0703			
	Betel quid only	9	60.0	4	26.7		6.14	0.78	48.42
	Stem quid only	4	26.7	2	13.3		5.80	0.49	69.20
	Other types	2	13.3	1	6.7		15.00	0.18	1236.18
	No chewing habit	0	0.0	6	40.0		1.00		
Women		47		47					
Chewing/smoking	Chewing and smoking	6	12.8	3	6.4	0.0287	9.30	0.52	165.53
	Chewing only	40	85.1	35	74.5		4.19*	1.09	16.10
	None of both habit	1	2.1	9	19.1		1.00		
Areca/betel quid	Yes	46	97.9	38	80.9	0.0114	4.23*	1.11	16.08
	No	1	2.1	9	19.1		1.00		
Number of quids per day	30+	18	38.3	4	8.5	0.0012	7.61*	1.39	41.71
	10–29	21	44.7	23	48.9		2.77	0.59	12.99
	1–9	7	14.9	11	23.4		1.74	0.32	9.40
	No chewing	1	2.1	9	19.2		1.00		
Type of quid	Betel and stem quid	7	14.9	8	17.0	0.0330	2.19	0.34	13.89
	Betel quid only	23	48.9	10	21.3		5.80*	1.26	26.77
	Stem quid only	13	27.7	14	29.8		2.93	0.49	17.60
	Other types	3	6.4	6	12.8		1.52	0.11	21.23
	No chewing habit	1	2.1	9	19.1		1.00		

The effects of areca quid and tobacco chewing on oral mucosa were primarily demonstrated from India (IARC, 1985). The range of oral lesions that are associated with these risk habits were reviewed by Trivedy *et al* (2002). In Mehta's data, when combining cases from all study areas of India, one can find that people with the habit of chewing betel quid and smoking had the highest risk, and the habit of chewing tobacco quid was next. In India, the group of people with only betel quid–chewing habit without tobacco use was hardly identified (three of 430 subjects with leukoplakia).

In Taiwan, the oral mucosal lesions (or leukoplakia) were commonly seen in people with quid chewing and/or smoking habits. Lee *et al* (2003) found ORs of 40.2 (95% CI = 16.3, 99.2), 10.0 (95% CI = 3.1, 32.7) and 2.4 (95% CI = 1.0, 5.5) for both chewing and smoking, chewing only and smoking only, respectively. Our study had found not only the risk of having oral lesions from both chewing and smoking habits, but also the risk of developing leukoplakia from chewing only (without any tobacco use).

Since our study data were from a community screening, the characteristics of chewing and smoking habits had also been revealed in our study results. In Taiwan, a male areca/betel quid chewer had a very high chance that he was also a cigarette smoker. However, a female chewer was generally not a cigarette smoker. Hence, in general the cigarette smoking effect in addition to the areca/betel quid chewing can be misinterpreted as a gender effect. Therefore, it was important for our study

to look at the risks of chewing and smoking for men and women separately. For both OSF and oral mucosal lesions, the ORs of mixed habits and chewing only were all higher in women than in men. Like in many Southeast Asia countries in which men consisted most of the areca/betel quid chewers, the importance of prevention on quid related lesions or conditions in women in Taiwan would need to be emphasized, too.

Conclusion

The areca/betel quid in Taiwan does not contain any tobacco product. The only way of areca/betel quid effect could synergize with tobacco is through cigarette smoking. In many Southeast Asia countries, the effect from tobacco is not easy to be separated. In Taiwan, we were able to identify a group of people with only betel quid chewing habit, and without any cigarette smoking habit. A statistically significant association with oral mucosal lesions and OSF was still found in the group of areca/betel quid chewing only.

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