


Comparison of periodontal inflammatory parameters among habitual *gutka*-chewers and *naswar*-dippers: a split-mouth retrospective clinical study

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ABSTRACT

Objective: The aim of the present split-mouth retrospective study was to compare the clinical periodontal parameters among *gutka*-chewers and *naswar*-dippers.

Methods: A structured questionnaire was used to record demographic information. Jaw quadrant in which, *gutka* or *naswar* were placed were defined as “test-sites”. The remaining jaw quadrants were designated as “control-sites”. Clinical [plaque index (PI), bleeding on probing (BOP), probing pocket depth (PPD) and clinical attachment loss (CAL)] and radiographic [alveolar bone loss (ABL)] parameters were compared among *gutka*-chewers and *naswar*-dippers in the test- and control sites. Data were analysed using non-parametric Wilcoxon signed rank test followed by *post hoc* analyses with the Bonferroni correction. $p < .05$ were considered statistically significant.

Results: Seventy-five *gutka*-chewers and 72 *naswar*-dippers with mean ages of 45.2 ± 0.8 years and 47.3 ± 2.8 years, respectively were included. *Gutka*-chewers and *naswar*-dippers were consuming their respective smokeless tobacco product 10.2 times and 8.5 times daily for 15.1 ± 2.7 and 12.3 ± 3.4 years, respectively. Among *gutka*-chewers and *naswar*-dippers, scores of PI, BOP, $PPD \geq 4$ mm, CAL and ABL were significantly higher in the test-sites compared with their respective control-sites ($p < .01$).

Conclusions: Periodontal inflammatory parameters were poorer in the test-sites among *gutka*-chewers and *naswar*-dippers compared with the control-sites.

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Introduction

Gutka is one of the several smokeless tobacco (ST) formulations that is generally a mixture of powdered tobacco, areca-nut, slaked lime (aqueous calcium hydroxide paste) and fragrances such as menthol and saffron (Figure 1(A)) [1]. *Gutka* is commercially available in sachets (average weight 3.5 g) [1]; and is commonly consumed in South Asian countries including India, Pakistan, Bangladesh, and Sri Lanka [2,3]; however, due to its global export, *gutka* is also consumed by immigrants in countries such as United Kingdom and the United States [4–6]. *Gutka* is placed in the buccal vestibule and gently chewed and sucked. It is then held in the buccal vestibule for a prolonged duration and continued to be gently chewed and sucked intermittently. The contents may either be swallowed or spat out when desired. Likewise, *Naswar* (also known as *Nass* or *Niswar*) is a form of dipping ST product and is an amalgam of ground tobacco leaves (*Nicotina rustica*), slaked-lime, wood ash and flavourings such as cardamom and menthol [7]. *Naswar* also contains a small quantity of water and colouring agents such as indigo (average weight 9.2 g) [7,8]. *Naswar* is commonly sold in small polythene pouches (almost the size of a tea bag) (Figure 1(B)) [9].

Usually a small bolus of *naswar* is manually shaped into a ball and placed in the buccal vestibule between the mandibular premolars and first molar teeth. It is gently sucked intermittently for extended periods of time and spat out when desired.

Habitual use of ST products is a significant risk factor for periodontal inflammatory conditions, such as gingivitis and periodontitis [10–12]. Several studies [3,13] have reported that scores of clinical (plaque index [PI], bleeding on probing [BOP], probing pocket depth [PPD] and clinical attachment loss [CAL]) and radiographic (alveolar bone loss [ABL]) parameters of periodontal inflammation are significantly higher among habitual ST product users compared with individuals not using tobacco in any form. To our knowledge from indexed literature, there is a dearth of studies that have compared periodontal inflammatory parameters among individuals using different types of ST products using a split-mouth design. It is hypothesized that (i) among *gutka*-chewers and *naswar*-dippers, periodontal inflammatory parameters are worse in the test-sites (buccal vestibules in which, *gutka* or *naswar* are placed, respectively) compared with the control-sites (buccal vestibules in both arches in which, *gutka* or *naswar* are not placed, respectively); (ii) since *gutka* has more dry



Figure 1. (A) Gutka sachet; (B) Naswar pouch.

weight of tobacco than *naswar*, clinical periodontal parameters are worse among *gutka*-chewers than *naswar*-dippers.

The aim of the present split-mouth retrospective study was to compare the clinical periodontal parameters among *gutka*-chewers and *naswar*-dippers.

Materials and methods

Ethical guidelines

The present study was performed in accordance with the Declaration of Helsinki. The study was approved by the research ethics committee of the College of Dentistry, Ziauddin Medical University, Karachi, Pakistan. Volunteering individuals were requested to read and sign a consent form, which was printed in simple English and Urdu (national language of Pakistan). All participants were informed that participation in the present study is completely voluntary and that they reserved the right to terminate their participation at any stage of the investigation without penalty.

Inclusion and exclusion criteria

The following inclusion criteria were entailed: (a) self-reported *gutka*-chewers (subjects who reported to be consuming one *gutka*-sachet daily since ≥ 12 -months); and (b) self-reported *naswar*-dippers (subjects who reported to be dipping *naswar* once daily since ≥ 12 -months). Subjects with the following characteristics were excluded: (a) refusal to sign the consent form (b) habitual tobacco-smokers and alcohol-users; (c) patients with self-reported systemic diseases such as acquired immune deficiency syndrome, diabetes mellitus, hepatitis B and/or hepatitis C and cardiovascular diseases; (d) patient that reported to have used antibiotics within the past three months; and (e) patients that reported to have undergone periodontal therapy (surgical or non-surgical) within the past three months. In addition, third molars were also excluded.

Study participants and grouping

A cohort study was performed between October 2015 and July 2016 at the College of Dentistry, Ziauddin Medical

University, Karachi, Pakistan. Individuals who reported to be consuming one *gutka* sachet daily since ≥ 12 -months were *Gutka*-chewers. Individuals who reported to be dipping *naswar* at least once daily since ≥ 12 -months were *Naswar*-dippers. Among *gutka*-chewers and *naswar*-dippers the jaw quadrant in which, *gutka* and *naswar*, respectively were placed were defined as "test-sites". The remaining jaw quadrants in which, the participants were not placing their respective ST product were designated as "control-sites".

Interview questionnaire

A trained interviewer (TA) presented a structured written questionnaire to all participants. Information regarding age, gender, education status (undergraduate level education – primary school and college education for a combined period of 12 years; graduate level education – post-4-year college degree) were recorded in a questionnaire sheet. The questionnaire sheet also recorded duration and daily frequency of *gutka* or *naswar* usage, location of *gutka* or *naswar* placement in the mouth, family history of tobacco use, reason for *gutka* or *naswar* usage, and daily tooth brushing (once, twice or more).

Assessment of periodontal parameters

Periodontal parameters (PI [14], BOP [15], PPD (4–6 and >6 in mm) [16] and CAL [17]) were assessed at six sites per tooth (mesio-facial, mid-facial, disto-facial, mesio-lingual, mid-lingual and disto-lingual). BOP and PI were recorded at 6 sites per tooth for absence or presence of bleeding, based on dichotomous scoring system. The scores ranged as follows; 0 – no visible bleeding/plaque, 1 – visible bleeding/plaque. PPD was measured to the nearest mm using a graded periodontal probe (Hu-Friedy, Chicago, IL, USA). Number of missing teeth were also recorded. All periodontal examinations were carried out by a trained examiner (ZA) who was blinded to the study groups (*gutka*-chewers or *naswar*-dippers) and sites (test- or control-sites). The kappa value for intra-assessor reliability with respect to CAL was 0.91.

Assessment of alveolar bone loss

Digital full-mouth radiographs were taken using a dental radiography machine (CareStream Dental LLC, Atlanta, GA, USA). The radiographs were viewed on a calibrated computer screen (Samsung SyncMaster digital TV monitor, Seoul, Korea) using a software program (Image Tool 3.0 Program; Department of Dental Diagnostic Science, University of Texas Health Science Centre, San Antonio, TX, USA). ABL was defined as the vertical distance from 2 mm below the cemento-enamel junction (CEJ) to the most crestal part of marginal bone. ABL was presented as the average of the sum of the mean mesial and distal ABL [13]. All radiographic examinations were performed by a trained and calibrated investigator (ZA) ($kappa = 0.89$). Third molars and teeth surfaces on which, the CEJ and/or the crestal bone were not clearly visible due to of technical reasons (such as dental restorations, interproximal caries, overlapping of teeth, and/or poor radiographic quality) were not assessed.

Statistical analyses

Statistical analyses were carried out using a statistical software (SPSS, v.20.0 for Windows, IBM, Chicago, IL, USA). The alpha level was set at 0.05. Normality of distribution of the variables was tested with Kolmogorov–Smirnov and Shapiro–Wilk tests and confirmed with Q–Q plots. The significance of differences in periodontal parameters between *gutka*-chewers and *naswar*-dippers and the test- and control-sites within each group were determined using the non-parametric Wilcoxon signed rank test. Bonferroni *post hoc* adjustment test was used for multiple comparisons. Stepwise logistic regression analysis was employed to identify explanatory variables for periodontal outcomes, controlling for the effect of possible covariate such as age, education status, daily frequency, duration of habit, and duration of placement of ST products. The direction and strength of association between periodontal outcomes and covariates were assessed by generating odds ratios, the precision of which could be measured by 95% confidence intervals. Power analysis was performed with a computer software (nQuery Advisor 5.0; Statistical Solutions, Saugus, MA, USA). Power analysis was based on the supposition that a mean difference of 0.5 mm and 1 mm in ABL and PPD, respectively should be detected at a significance level of 0.05 and a desired study power of at least 80%. It was estimated that a sample size of 68 individuals per group will achieve 95% power with a 0.05 two-sided significance level.

Results

Characteristics of the included study sample

In total, 147 male subjects (75 *gutka*-chewers and 72 *naswar*-dippers) were included. The mean ages of *gutka*-chewers and *naswar*-dippers were 45.2 ± 0.8 years and 47.3 ± 2.8 years, respectively. *Gutka*-chewers and *naswar*-dippers were consuming their respective ST product 10.2 times and 8.5 times daily for 15.1 ± 2.7 and 12.3 ± 3.4 years, respectively. A family history of tobacco use was reported by 80% *gutka*-chewers

Table 1. General characteristics of the study population.

Characteristics	<i>Gutka</i> -chewers	<i>Naswar</i> -dippers
Number of individuals	75	72
Mean age (years)	45.2 ± 0.8	47.3 ± 2.8
Daily frequency (no. of times/day)	10.2/day (8.1, 12.4)	8.5/day (6.0, 13.2)
Duration of habit (years)	15.1 ± 2.7 (12.2, 17.3)	12.3 ± 3.4 (9.9, 15.7)
Duration of placement of ST product in the mouth (in minutes)	40.4 ± 3.5 (36.4, 43.7)	33.5 ± 2.2 (31.1, 35.8)
Family history of tobacco-use (%)	80%	81.9%
Education status		
Undergraduate level	68%	50%
Graduate level	16%	12.5%
Uneducated	16%	37.5%
Reason for using the ST product		
Manage psychological stress (%)	68.1%	75%
Fresh breath (%)	16%	None
No reason (%)	15.9%	25%

Minimum and maximum values represented in round brackets.

and 81.9% *naswar*-dippers. Sixteen percent *gutka*-chewers and 37.5% *naswar*-dippers were illiterate. Management of psychological stress was the most common reason for ST consumption, which was reported by 68.1% *gutka*-chewers and 75% *naswar*-dippers (Table 1). Tooth brushing once daily was reported by 92% *gutka*-chewers ($n = 69$) and 86.1% *naswar*-dippers ($n = 62$). *Gutka*-chewers were placing *gutka* in the right buccal vestibule and *naswar*-dippers were dipping the ST product in the in the left buccal sulcus between the mandibular premolars and first molar teeth.

Clinical periodontal and radiographic parameters

Among *gutka*-chewers, scores of PI ($p < .001$), BOP ($p < .001$), PPD ≥ 4 mm ($p < .001$) and CAL ($p < .001$) were significantly higher in the test-sites compared with the control-sites. Among *naswar*-dippers, scores of PI ($p < .001$), BOP ($p < .001$), PPD ≥ 4 mm ($p < .001$) and CAL ($p < .001$) were significantly higher in the test-sites compared with the control-sites. Scores of PI, BOP, PPD ≥ 4 mm and CAL were comparable among test-sites in *gutka*-chewers and *naswar*-dippers. There was no statistically significant difference in the scores of PI, BOP, PPD ≥ 4 mm and CAL in the control-sites among *gutka*-chewers and *naswar*-dippers (Table 2).

Alveolar bone loss

Among *gutka*-chewers and *naswar*-dippers, scores of ABL were significantly higher in the test-sites compared with their respective control-sites ($p < .001$). There was no statistical difference in scores of total ABL in the test-sites among *gutka*-chewers and *naswar*-dippers. In the control-sites, scores of ABL were 1.8 mm and 2 mm among *gutka*-chewers and *naswar*-dippers, respectively (Figure 2).

Stratification of periodontal parameters for *gutka*-chewers and *naswar*-dippers according to the daily frequency, duration of placement and habit of smokeless-tobacco

There was no statistically significant difference in the scores of PI, BOP, PPD ≥ 4 mm, CAL and ABL among *gutka*-chewers

Table 2. Clinical periodontal parameters at the test and control-sites among *gutka*-chewers and *naswar*-dippers.

Parameters	<i>Gutka</i> -chewers (n = 75)		<i>Naswar</i> -dippers (n = 72)	
	Test-site	Control-site	Test-site	Control-site
Plaque index	57.6 ± 5.2 ^a	20.5 ± 4.1	52.2 ± 10.3 ^b	25.6 ± 3.9
Bleeding on probing	63.4 ± 6.8 ^a	30.3 ± 7.1	56.6 ± 9.3 ^b	28.5 ± 5.7
Probing pocket depth ≥4 mm	22.4 ± 5.1 ^a	4.2 ± 1.1	25.6 ± 4.7 ^b	3.6 ± 0.9
Clinical attachment loss (in millimetres)	5.5 ± 1.2 ^a	0.5 ± 0.2	4.8 ± 1.3 ^b	0.6 ± 0.2

^aCompared with the control-sites among *gutka*-chewers ($p < .001$).

^bCompared with the control-sites among *naswar*-dippers ($p < .001$).

and *naswar*-dippers after stratification of data for daily frequency of ST consumption (Figure 3(a–d)).

Scores of PI, BOP, PPD ≥4 mm and CAL were statistically significantly higher among individuals carrying *gutka* in the buccal vestibule for 21–30 min ($p < .05$) and more than 30 min ($p < .05$) compared with those carrying *gutka* in the buccal vestibule for up to 10 min. ABL was significantly higher among *gutka*-chewers carrying *gutka* in the buccal vestibule for more than 21–30 min ($p < .05$) and more than 30 min ($p < .05$) compared with individuals placing *gutka* in the buccal vestibule for up to 10 min. Among *naswar*-dippers, scores of PI, BOP, PPD ≥4 mm and clinical AL were statistically higher among individuals dipping *naswar* for more than 30 min compared with individuals dipping *naswar* for up to 10 min ($p < .05$). ABL was significantly higher among individuals dipping *naswar* in the buccal vestibule for more than 30 min ($p < .05$) compared with individuals dipping *naswar* for up to 10 min. There was no statistically significant influence of the duration of *gutka* or *naswar* usage on the severity of PI, BOP, PPD ≥4 mm, CAL and ABL among *gutka*-chewers and *naswar*-dippers, respectively (data not shown).

Regression analysis to control confounders

The logistic regression analysis revealed that periodontal outcomes showed statistically significant difference even after adjusting for age, education status, daily frequency, duration of habit, and duration of placement of ST products ($p > .05$) (Table 3).

Discussion

It is well-known that clinical periodontal parameters is worse in ST product users compared with individuals not using tobacco in any form [13,18]. However, to our knowledge, this is the first study that compared periodontal inflammatory parameters among individuals consuming different types of ST products (*gutka* and *naswar*) in relation to the site of ST placement (test-site) and control-sites (buccal vestibules in which, ST was not placed). The present retrospective clinical split-mouth study was based on two hypotheses. According to the first hypothesis, scores of PI, BOP, PPD, CAL and ABL are significantly higher in the test-sites among *gutka*-chewers and *naswar*-dippers compared with their respective control-sites. The second hypothesis was that the above-mentioned clinical periodontal parameters are worse among *gutka*-chewers than *naswar*-dippers since *gutka* has more dry weight of tobacco than *naswar*. The results reported in the present investigation are in accordance with the first hypothesis.

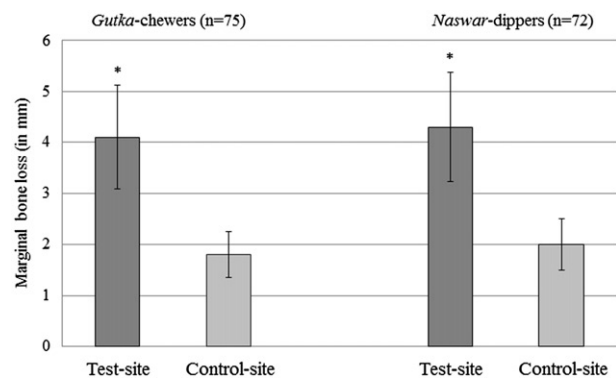


Figure 2. Mean ± SD of total alveolar bone loss (in mm) in the test- and control sites among *gutka*-chewers and *naswar*-dippers.

This could be explained by the essential constituents of *gutka* and *naswar* such as slaked lime and powdered tobacco that increase the expression of reactive oxygen species in the periodontal tissues and proinflammatory cytokines (such as tumour necrosis factor- α , interleukin (IL)-6, IL-1 β and matrix metalloproteinase-8 and 9) in whole saliva of tobacco users compared to subjects not using any form of tobacco [19]. Moreover, nicotine in tobacco induces hyperaemia in the gingival blood vessels possibly by stimulation of sensory nerves and the consequent release of vasodilatory peptides from their peripheral endings [20]. Furthermore, in-vitro studies have indicated that nicotine impairs the function and proliferation of gingival fibroblasts [21], increases integrin beta-1 expression [22], reduces collagen production [23] increases the fibroblast collagenase activity [24] and enhances alveolar bone loss [25]. These are possible factors that contributed towards significantly higher scores of PI, BOP, PPD ≥4 mm, CAL and ABL in the test-sites compared with the control-sites among *gutka*-chewers and *naswar*-dippers. Since *gutka* has additional dry weight of tobacco compared with *naswar*, it is postulated that clinical periodontal parameters are worse in *gutka*-chewers than *naswar*-dippers (second hypothesis of the present findings). Interestingly, the results indicated no statistical difference in PI, BOP, PPD ≥4 mm, CAL and total ABL upon comparison of the test-sites among *gutka*-chewers and *naswar*-dippers. One explanation for these results is that irrespective of whether a ST product is in moist form or dry, the detrimental effects of nicotine (such as those described above) on periodontal tissues remain persistent. This suggests that *gutka* and *naswar* are hazardous to oral health and neither form of ST product can be considered less hazardous than the other. Therefore, public health awareness programs should regularly be performed to discourage the consumption of nicotine containing products and educate the public about the

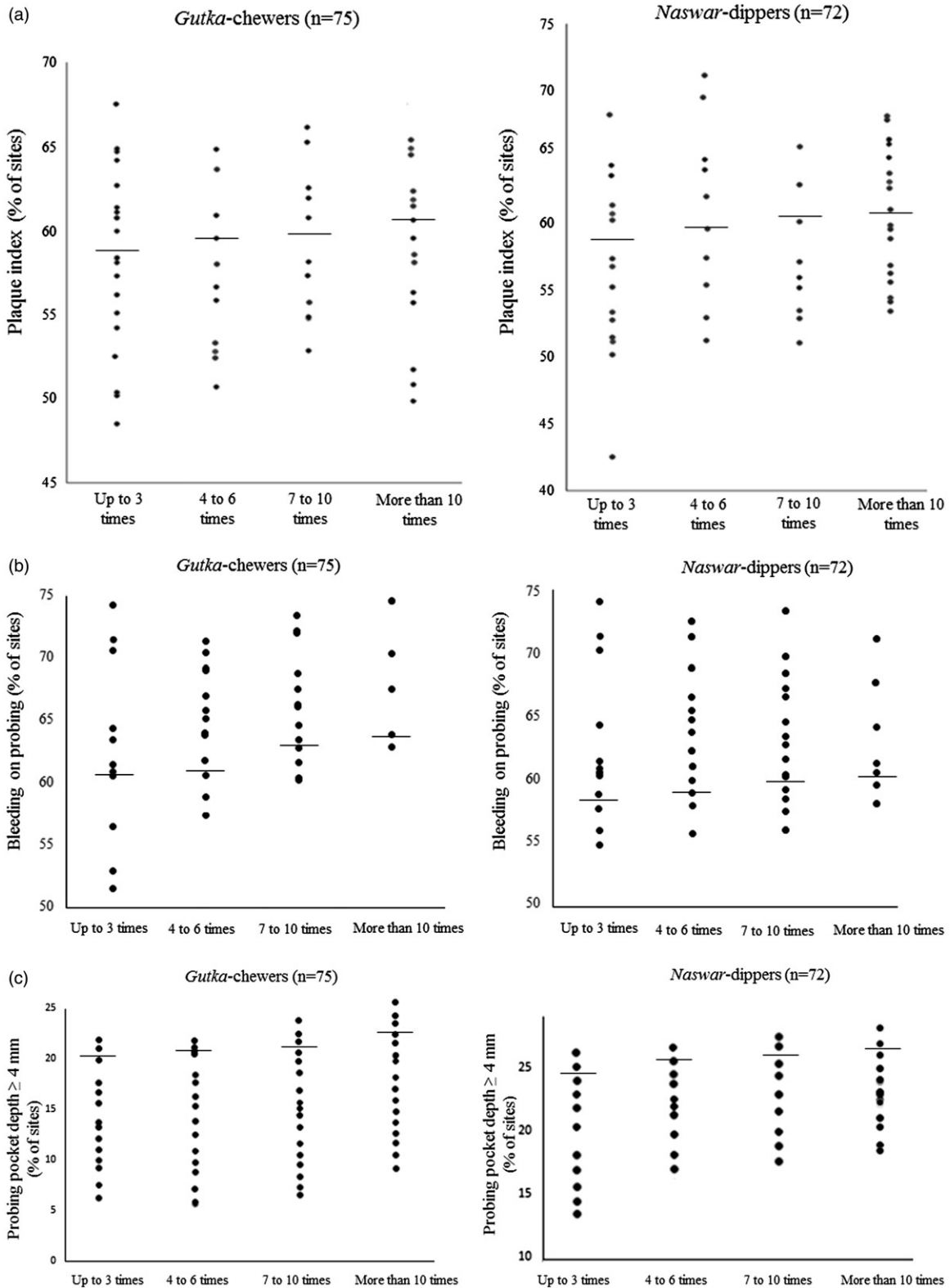


Figure 3. (a) Dot plots and median values of plaque index (PI) (Y-axis) with reference to the daily frequency of smokeless tobacco consumption (X-axis) among *gutka*-chewers and *naswar*-dippers. Plaque index was presented as the percentage of sites that displayed dental plaque upon clinical examination. (b) Dot plots and median values of bleeding on probing (BOP) (Y-axis) with reference to the daily frequency of smokeless tobacco consumption (X-axis) among *gutka*-chewers and *naswar*-dippers. BOP was presented as the percentage of sites that displayed BOP upon clinical examination. (c) Dot plots and median values of probing pocket depth (PPD) of ≥ 4 mm (Y-axis) with reference to the percentage of sites that displayed a PPD ≥ 4 mm. (d) Dot plots and median values of clinical attachment loss (AL) (Y-axis) with reference to the daily frequency of smokeless tobacco consumption (X-axis) among *gutka*-chewers and *naswar*-dippers. Clinical AL was presented in millimeters. (e) Dot plots and median values of alveolar bone loss (ABL) (Y-axis) with reference to the daily frequency of smokeless tobacco consumption (X-axis) among *gutka*-chewers and *naswar*-dippers. ABL was presented in millimeters.

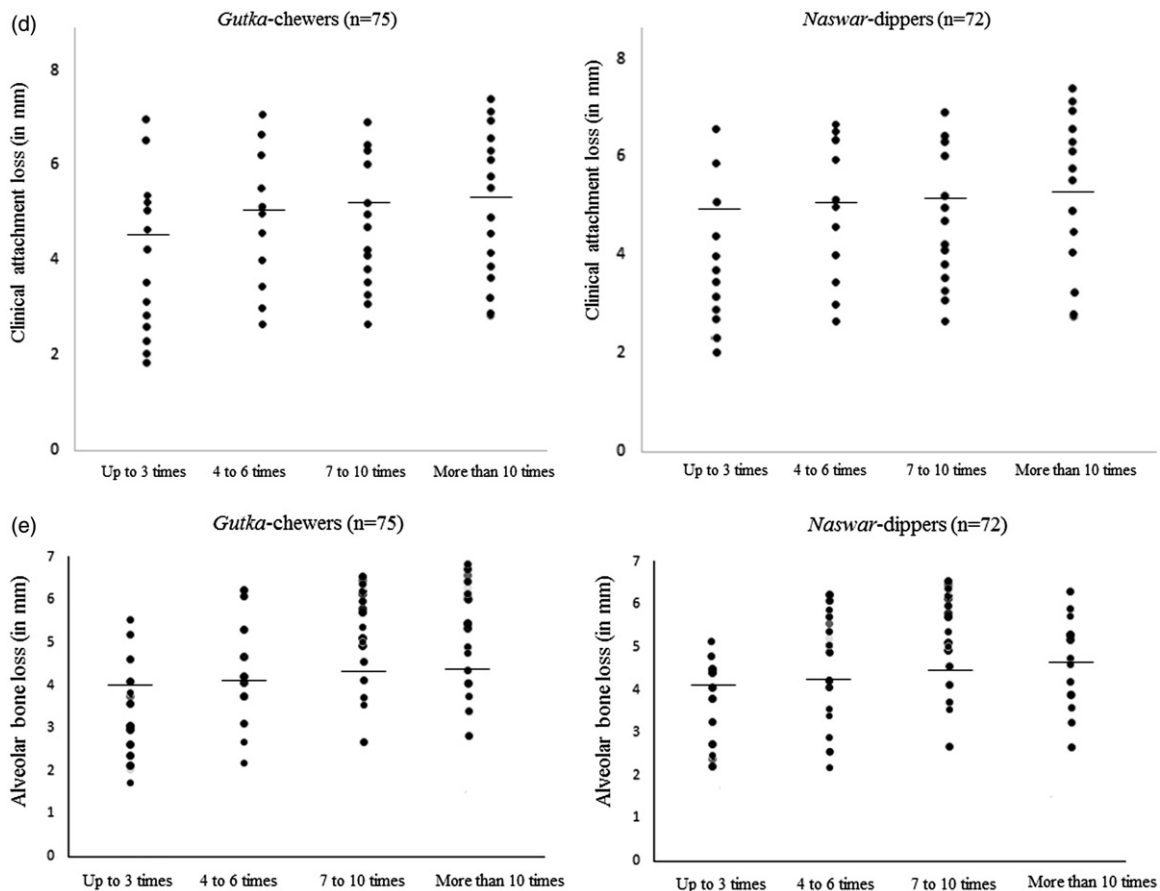


Figure 3. Continued.

Table 3. Logistic regression model for age, education status, daily frequency, duration of habit, and duration of placement of ST products influencing periodontal outcomes with odds ratios, 95% confidence intervals (CI) and *p*-values.

Covariate	Odds ratio	95% CI	<i>p</i> Value
Age	2.03	0.97, 5.48	.046
Education status	2.95	1.26, 4.83	.028
Daily frequency	2.22	1.09, 5.34	.031
Duration of habit	2.88	1.2, 6.12	.016
Duration of placement	1.76	1.3, 4.1	.025

Covariates were simultaneously adjusted for all variables. Bold denotes statistically significant result at $p < .05$ in direction of increased risk.

harmful effects of tobacco-based products on oral and general health. It is worth mentioning that in the present study, 16% of *gutka*-chewers and nearly 37% of *naswar*-dippers were illiterate.

The frequency and duration of ST usage has been reported to influence the severity of oral inflammation including periodontal disease and malignant transformations [26,27]. Singh et al. [26] reported that periodontal inflammation was worse in individuals using ST products for over five years compared with individuals with a shorter history of T usage (<5 years). The present findings corroborates with the study by Singh et al. [26] since the average duration of ST usage among *gutka*-chewers and *naswar*-dippers was approximately 15 and 12 years, respectively. Moreover, when the present data was stratified with relation to the duration of ST usage, it was observed that there was no statistical difference in the severity of periodontal conditions among

gutka-chewers and *naswar*-dippers who had been consuming ST for up to five years and those who had a longer history of *gutka* and *naswar* use (≥ 10 years). This suggests that individuals with a shorter duration of ST consumption (up to five years) of ST usage are as susceptible to periodontal disease as are individuals with a significantly longer history of ST use (>10 years). Data stratification also showed that either chewing *gutka* or dipping *naswar* at least three times daily for at least 10 min exposed the consumers to periodontal inflammation. This suggests that a time duration as short as 10 min is sufficient to induce an inflammatory effect of ST products in the mouth. Nevertheless, placement of ST products in the mouth for durations less than 10 min and less frequently (<3 times daily) should not be considered as safe.

Few limitations that may be taken into regard is that tobacco smokers and patients with systemic diseases were excluded. It is well-recognized that cigarette smoking and systemic diseases such as diabetes mellitus are known risk factors of periodontal disease [28,29]. It is postulated that (a) clinical periodontal parameters are poorer in cigarette smokers with *gutka*-chewing and/or *naswar*-dipping habits compared to individuals smoking solely cigarettes; (b) clinical periodontal parameters are worse in immunosuppressed *gutka*-chewers and *naswar*-dippers as compared to systemically healthy *gutka*-chewers and *naswar*-dippers. Further studies are warranted to test these hypotheses. All included subjects were approximately 45-years-old. It is well-recognized that advancing age is a risk-factor for periodontitis [29].

It is therefore assumed that old-aged subjects (e.g. over 70 years old) who utilise ST products experience worse periodontal inflammation as compared to relatively younger individuals (such as those reported in this study, 45 years old). Further investigations are needed in this regard. Another important limitation is the carry-over effect. There is certainly a possibility that the ST products (*gutka* and *naswar*) can induce an inflammatory response in the control-sites (buccal vestibule opposite to the vestibule in which such products are placed). It seems difficult for ST users to prevent the tobacco products from reaching the control-sites. In order to determine the inflammatory response of ST products in the control-sites, a separate research study based on the following groups would be needed: Group 1: Individuals using ST products (Group 1a: test sites and Group 1b: control sites) and Group 2: individuals not using tobacco in any form (both buccal vestibules may serve as control-sites). It is hypothesized that periodontal inflammatory parameters (such as PI, BOP, PPD \geq 4 mm and CAL) are poorer in the control-sites in ST product users compared with individuals not using tobacco in any form. However, further studies are warranted to test this hypothesis. It is imperative for clinicians and health care providers to be aware of the deleterious effects of ST products and educate the community about the detrimental effects of tobacco products on health and simultaneously emphasize on the importance of regular oral hygiene maintenance, dental visits towards a better quality of life.

This study concludes that clinical periodontal parameters were poorer in the test-sites among *gutka*-chewers and *naswar*-dippers compared with the control-sites.

Disclosure statement

No potential conflict of interest was reported by the authors.

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References

- [1] Gupta PC, Ray CS. Smokeless tobacco and health in India and South Asia. *Respirology*. 2003;8:419–431.
- [2] Nair S, Schensul JJ, Bilgi S. Local responses to the maharashtra gutka and pan masala ban: a report from mumbai. *Indian J Cancer*. 2012;49:443–447.
- [3] Javed F, Vohra F, Al-Kheraif AA, et al. Comparison of periodontal inflammatory conditions among habitual gutka chewers and betel quid chewers. *Oral Dis*. 2015;21:437–442.
- [4] Changrani J, Gany FM, Cruz G, et al. Paan and gutka use in the united states: a pilot study in Bangladeshi and Indian-Gujarati immigrants in New York city. *J Immigr Refug Stud*. 2006;4:99–110.
- [5] Banerjee SC, Ostroff JS, Bari S, et al. Gutka and tambaku paan use among south Asian immigrants: a focus group study. *J Immigr Minor Health*. 2014;16:531–539.
- [6] Khaja AH, Ali Zwiad A, Tarakji B, et al. The dependence on smokeless tobacco in the South Asian communities in East London. *Glob J Health Sci*. 2015;8:194–198.
- [7] Sajid F, Bano S. Effects of smokeless dipping tobacco (naswar) consumption on antioxidant enzymes and lipid profile in its users. *Pak J Pharm Sci*. 2015;28:1829–1833.
- [8] Hecht SS, Hoffmann D. Tobacco-specific nitrosamines, an important group of carcinogens in tobacco and tobacco smoke. *Carcinog*. 1988;9:875–884.
- [9] Cogliano V, Straif K, Baan R, et al. Smokeless tobacco and tobacco-related nitrosamines. *Lancet Oncol*. 2004;5:708
- [10] Fisher MA, Taylor GW, Tilashalski KR. Smokeless tobacco and severe active periodontal disease, nhanes iii. *J Dent Res*. 2005;84:705–710.
- [11] Kamath KP, Mishra S, Anand PS. Smokeless tobacco use as a risk factor for periodontal disease. *Front Public Health*. 2014;2:195–198.
- [12] Kulkarni V, Uttamani JR, Bhatavadekar NB. Comparison of clinical periodontal status among habitual smokeless-tobacco users and cigarette smokers. *Int Dent J*. 2016;66:29–35.
- [13] Al-Askar M, Abduljabbar T, Vohra F, et al. Comparison of self-perceived oral symptoms and periodontal parameters among habitual shamma-chewers, gutka-chewers, and non-chewers. *Quintessence Int*. 2017;48:251–260.
- [14] O'Leary TJ, Drake RB, Naylor JE. The plaque control record. *J Periodontol*. 1972;43:38.
- [15] Newbrun E. Indices to measure gingival bleeding. *J Periodontol*. 1996;67:555–561.
- [16] Armitage GC, Svanberg GK, Loe H. Microscopic evaluation of clinical measurements of connective tissue attachment levels. *J Clin Periodontol*. 1977;4:173–190.
- [17] Pihlstrom BL. Measurement of attachment level in clinical trials: probing methods. *J Periodontol*. 1992;63:1072–1077.
- [18] Javed F, Tenenbaum HC, Nogueira-Filho G, et al. Severity of periodontal disease in individuals chewing betel quid with and without tobacco. *Am J Med Sci*. 2013;346:273–278.
- [19] Seyedroudbari SA, Khan MM. In vitro effects of smokeless tobacco extract on tumor necrosis factor-alpha (TNF-alpha) and interleukin-1beta (IL-1beta) production, and on lymphocyte proliferation. *Toxicol*. 1998;36:631–637.
- [20] Mavropoulos A, Aars H, Brodin P. The acute effects of smokeless tobacco (snuff) on gingival blood flow in man. *J Periodont Res*. 2001;36:221–226.
- [21] Esfahrood ZR, Zamanian A, Torshabi M, et al. The effect of nicotine and cotinine on human gingival fibroblasts attachment to root surfaces. *J Basic Clin Physiol Pharmacol*. 2015;26:517–522.
- [22] Snyder HB, Caughman G, Lewis J, et al. Nicotine modulation of in vitro human gingival fibroblast beta1 integrin expression. *J Periodontol*. 2002;73:505–510.
- [23] Ramp WK, Lenz LG, Galvin RJ. Nicotine inhibits collagen synthesis and alkaline phosphatase activity, but stimulates DNA synthesis in osteoblast-like cells. *Proc Soc Exp Biol Med*. 1991;197:36–43.
- [24] Wendell KJ, Stein SH. Regulation of cytokine production in human gingival fibroblasts following treatment with nicotine and lipopolysaccharide. *J Periodontol*. 2001;72:1038–1044.
- [25] Bosco AF, Bonfante S, de Almeida JM, et al. A histologic and histometric assessment of the influence of nicotine on alveolar bone loss in rats. *J Periodontol*. 2007;78:527–532.
- [26] Singh GP, Rizvi I, Gupta V, et al. Influence of smokeless tobacco on periodontal health status in local population of north India: a cross-sectional study. *Dent Res J*. 2011;8:211–220.
- [27] Garg KN, Raj V, Chandra S. Trends in frequency and duration of tobacco habit in relation to potentially malignant lesion: a 3 years retrospective study. *J Oral Maxillofac Pathol*. 2013;17:201–206.
- [28] Albandar JM, Streckfus CF, Adesanya MR, et al. Cigar, pipe, and cigarette smoking as risk factors for periodontal disease and tooth loss. *J Periodontol*. 2000;71:1874–1881.
- [29] Genco RJ, Borgnakke WS. Risk factors for periodontal disease. *Periodontol* 2000. 2013;62:59–94.