

Short-term acute effects of gutkha chewing on heart rate variability among young adults: A cross-sectional study

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ABSTRACT

Background and Objectives: An increase in the consumption of smokeless tobacco has been noticed among high school, college students, and adults. Despite the antiquity and popularity of chewing tobacco in India, its effects have not been investigated systematically in humans. The aim of this study was to investigate acute effects of gutkha chewing on heart rate variability (HRV) among healthy young adults. **Materials and Methods:** A total of 60 young adult males were included in the study. Each individual was asked to chew tobacco and subjected to HRV analysis. HRV analysis using short-term electrocardiogram recording was used to measure HRV parameters before gutkha chewing and at 5, 15, and 30 min after chewing tobacco. One-way analysis of variance and paired *t*-test was used to assess changes over time. **Results:** There was a significant increase in heart rate (HR) during tobacco chewing. Mean HR at baseline measured 73.0 ± 6.2 bpm. There was a rise in mean HR to 83.7 ± 9.1 bpm at 5 min during tobacco chewing and gradual reduction to baseline observed after 15 min followed by no significant change till 30 min. The normalized low-frequency power and LF/high-frequency (HF) power ratio were elevated after 5 min; however, normalized HF power was reduced after 5 min tobacco chewing. **Conclusion:** Gutkha is closely associated with traditional cardiovascular risk factors as detected by a transient enhancing sympathetic activity during tobacco chewing in the form of increased HRV parameters or an imbalance between sympathetic and parasympathetic neural activity among healthy young adults.

Key words: Electrocardiogram, gutkha, heart rate variability, smokeless tobacco, young adult

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INTRODUCTION

Oral use of smokeless tobacco (ST) has existed for thousands of years and has gained popularity in various areas of the world.^[1,2] ST is used in “dipping” and “chewing” form. Gutka

(or gutkha) is in use in India, Pakistan, South-East Asia, and in the UK.^[1-6] Gutkha is industrially prepared and has a longer shelf life. Its growth has been so rapid that it has overtaken the smoking of tobacco in India, being especially popular amongst younger generations and women.^[5-8]

ST products contain, among other constituents, nicotine and known carcinogenic chemicals such as tobacco-specific N-nitrosamines, benzopyrene, nitrate,

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cadmium, lead, arsenic, nickel, and chromium.^[9,10] A number of adverse human health outcomes such as periodontitis; oral leukoplakia and submucous fibrosis; gastrointestinal abnormalities; oropharyngeal, esophageal, and pancreatic cancers; as well as cancer of the stomach have been linked to ST use. Other potential adverse health effects of ST may include toxicity of the immune, reproductive and/or cardiovascular systems.^[6,10-13]

Cardiovascular disease (CVD) is the leading cause of death worldwide, responsible for over 17 million deaths globally and tobacco has been estimated to directly cause 10% of all CVD worldwide.^[14-16] The epidemiological evidence on cigarette smoking in relation to CVD is compelling, but the relationships between CVD and smokeless types of tobacco, is limited and remains uncertain. A systemic review with meta-analysis confirmed an association between the use of ST and risk of fatal myocardial infarction (MI) and stroke.^[15] Combining information from both developing and developed countries, it is observed that odds of having acute MI was more among users of ST compared to nontobacco users.^[17-20]

Due to the high background rates of CVD, even a small increase in risk clearly could represent a large public health impact in countries that have a high prevalence of ST use.^[1,2,7,21] Multiple studies have reported that all forms of tobacco use is highly prevalent in youth and adult and in both men and women in India. The prevalence of ST use is estimated at 33% for men and 18% for women in India.^[3,5,7,16,19,22] An increase in consumption of ST has been noticed among high school, college students, and adults and indeed represents a health concern of growing magnitude among these groups.

The cardiovascular system is influenced by the autonomic nervous system (ANS). Few researchers have thrown light on possible acute autonomic effects^[23,24] and hemodynamic changes of ST in the form of heart rate variability (HRV)^[25-29] and various studies as well document the consequence of addictive qualities of ST often changing into lifelong habit with cumulative and more deleterious effects on health.^[30,31]

Despite the antiquity and popularity of gutkha chewing in India, its effects have not been investigated systematically in young adults. Few population-based estimates exist on the prevalence and determinants of gutkha chewing in India. Previous reports have described long-term harmful effects of ST on various body parameters, but little is known about short-term effects of ST on HRV parameters particularly those involving healthy young adults. Given the growing prevalence and global use of culturally-specific tobacco products, including gutkha, the present study was undertaken to investigate short-term acute

effects of gutkha chewing on HRV among healthy young adults exposed to gutkha chewing.

MATERIALS AND METHODS

This descriptive cross-sectional study was conducted in Davangere, a South Indian district. The subjects were apparently healthy male young adults aged 17–24 years with habit of chewing gutkha for <3 months. A thorough history regarding regular athletic training exercises, medical conditions, and the medications taken in the past 6 months was obtained followed by clinical and systemic examinations. Subjects with established obstructive coronary artery disease, unstable coronary syndromes, currently smokers, and alcoholics or on athletic training were excluded. The sample size was estimated using the formula $N = (Z_{\alpha/2})^2 s^2/d^2$. A pilot study conducted on 5 young adults resulted in a standard deviation (SD) of 5 and with a probability of 95%, and at an error rate of 5%, the minimum sample size required was estimated to be 24 subjects, after the allowance of 20% for nonrespondents is assumed, the corrected sample required was 30 subjects, however, a total of 60 subjects participated in the study. The study was approved by Institute's Ethics Committee. Skin preparation, electrode placement, and related protocols were similar to the established guidelines.

After obtaining consent, all the 60 subjects were asked to abstain from gutkha chewing and caffeine beverages 2 h prior to the electrocardiogram (ECG) recording. Skin preparation, electrode placement, and related protocols were similar to the established guidelines. ECG was acquired using digital ECG system, an instantaneous heart rate (HR) at RR intervals were continuously plotted at rest, 5, 15, and 30 min after tobacco chewing using Niviqure software analysis V:52 [Niviqure Meditech Pvt Ltd, Bengaluru, India] on a Microsoft window based computer. ECG was performed at rest and followed by recordings. HRV analysis was assessed by Spectral analysis of series of successive RR interval (frequency domain analysis). Parameters analyzed included the time domain parameter mean HR, low-frequency (LF) (0.04–0.15 Hz), power in normalized unit (n.u), high-frequency (HF) power in n.u (0.15–0.4 Hz), and LF/HF ratio.

Statistical analysis

The results are expressed as mean \pm SD or percentages. SPSS Software version 17.0 (SPSS Inc., IBM Corporation, Chicago, IL, USA) was used for analysis. The analysis for significant differences at different time intervals was performed using one-way analysis of variance. $P < 0.05$ was considered significant.

RESULTS

Demographic descriptions of the research population are shown in Table I. Among 32 male boilermaker construction

workers, the age ranged from 17 to 24 years. All the participants were relatively healthy. The mean levels of the HRV parameters at baseline, postgutkha chewing, and at different intervals are summarized in Table 2.

Analysis of HRV by frequency domain analysis after gutkha chewing showed an increase in parasympathetic and sympathetic nervous system (SNS) activity compared to baseline as reflected in an increase in HR, LF, and HF values.

The comparison between the relative percentage of LF and HF, during different time intervals after gutkha chewing shows there was a significant increase in HR, LF, and HF variables at 5 min and 15 min, however, the difference in any of the variables of frequency domain showed no statistically significant change after 30 min of gutkha chewing [Table 2]. The comparison of the LF/HF ratio obtained after gutkha chewing showed a significant difference at 5 min and 15 min and relatively no difference at 30 min as compared to baseline [Table 2 and Figure 1].

DISCUSSION

The ST (gutkha) users in this study are very young at age and were in the productive part of their life. The effect of exposure to various forms of ST on HR and HRV has been mentioned in the literature. For this reason, by no means short-term gutkha exposure deserves a lack of scientific interest. An exhaustive search of literature did not yield many studies related to short-term exposure to gutkha and HRV. Since there are no studies till date assessing the acute effects of gutkha chewing

on HRV among young Indians, our study has been the first in this untrodden path.

ST affects the cardiovascular system and causes diseases such as MI stroke, and high blood pressure.^[1,3,4,10,14-19] The cardiovascular system is influenced by the ANS. Among the different available noninvasive techniques for assessing the autonomic status, HRV has emerged as a simple, noninvasive method to evaluate the sympathovagal balance at the sinoatrial level and most widely performed measure of autonomic function.^[32-36] This test produces a sensitive, specific, and reproducible indirect measure of autonomic activity on cardiac function. Under frequency domain analysis (HRV frequency spectra), it is now known HF component is attributed to parasympathetic influences on the heart and LF component is due to both parasympathetic nervous system (PNS) and SNS activity. Impact of the nicotine on cardiovascular autonomic functions can be best diagnosed using the HRV assessment. Short-term HRV analysis from a 5 min record of ECG is a better way for understanding the autonomic status. Smoking tobacco has been proved to alter the ANS by many studies published,^[11,12] however, the effect of ST on the cardiovascular autonomic functions was studied through this HRV assessment.

In the present study, we observed an immediate cardiovascular autonomic response, as measured by significant increase in the 5-min resting HRV parameters to short-term gutkha exposure among young adults. We did not find much difference in the 30 min HRV parameters compared with baseline; but there was a trend toward an increase of PNS activity as measured by increased HR, HF, and LF.^[20,22]

Our observations are consistent with the findings of study by Wolk et al.^[24] which revealed, an acute increase in HR with the use of ST (snuff). However, in a study by Pakkala et al.^[29] Assessing the HRV among gutkha users, observed that the HRV parameters—time and frequency domain, showed significantly

Table 1: Participants demographics

Characteristics	Mean±SD or n (%)
Age (years)	19.8±2.02
Male	60 (100)

SD: Standard deviation

Table 2: Comparison of the HRV frequency domain parameters of the participants at different time intervals (after gutkha chewing)

Parameter	Baseline	5 min	15 min	30 min	P
HR	73.0±6.2	83.7±9.0	78.4±7.5	73.0±5.1	0.000** A 0.0001 B 0.0301# C
LF	45.1±7.4	73.1±8.5	64.6±8.8	45.4±7.2	0.000** A 0.0001 B 0.140# C
HF	34.1±5.4	31.5±4.6	20.0±3.5	34.0±5.4	0.000** A 0.0001 B 0.106# C
LF: HF	0.88±0.3	3.2±0.5	1.68±0.3	0.92±0.3	0.000** A 0.014 B 0.442# C

**Highly significant; #Not significant. A: Baseline versus 5 min; B: Baseline versus 15 min; C: Baseline versus 30 min; HRV: Heart rate variability; HR: Heart rate; LF: Low-frequency; HF: High-frequency

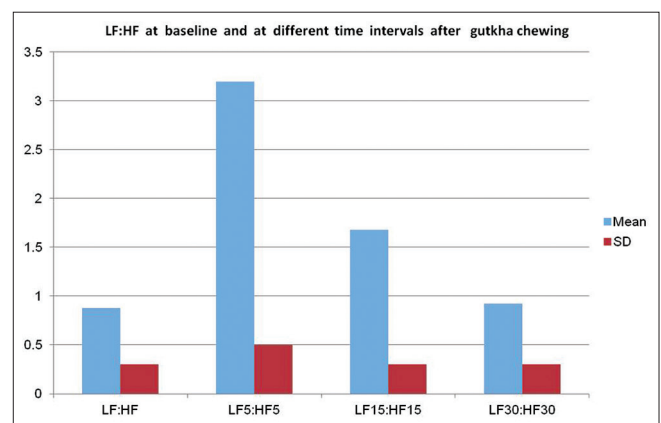


Figure 1: Low-/high-frequency ratio variation among the participants at different time intervals after gutkha chewing

decreased values during the third month and sixth month recording after the exposure.

The results of the study by Mohesh, *et al.* are in not concurrence with our study, where use of dipping tobacco (ST) showed no difference in mean HR and significant decrease in frequency domain measures (very LF and LF) representing the impaired sympathetic activity of the heart.

The results of this study suggest gutkha chewers experience an immediate rise in HR and rapid HRV response to acute tobacco exposure that do not persist 60 min following the end of exposure.^[7,18] However, in agreement with some^[29] but not all investigators, we were unable to show that the use of gutkha is associated with permanently raised HR and HRV variables. As is evident from this study, the hazards of gutkha are only partially known. The issue that further needs to be resolved is: Does the immediate changes in HR and HRV parameters on intake of gutkha have any long-term deleterious effects on the heart and the vascular system?

A serious concern about the use of gutkha among children and young adults is that it may introduce them to cigarette smoking.^[2,7,37,38] Oral tobacco gives a prolonged absorption of nicotine, and the overall nicotine exposure is as high or higher than that achieved by cigarette smoking.^[24,25] It is, however, still controversial whether gutkha causes the same (or greater) degree of dependency as cigarettes.

CONCLUSION

Within the limits of the present study, it can be concluded that gutkha is closely associated with traditional cardiovascular risk factors as detected by increased HRV parameters, and therefore, it should be accepted as harmful as cigarette smoking for cardiovascular system. However, limitations of the present study warrant consideration, we did not assess the quantity or duration of gutkha use, which prevented examination of dose response. This study is just the tip of an iceberg and we recommend that further longitudinal studies with larger sample size should be conducted to detect whether gutkha is an independent risk factor for cardiovascular events and also it should be included to fight program against tobacco use.

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. WHO SEARO. Report on Oral Tobacco Use and Its Implications in

- South-East Asia. 2004. Available from: http://www.searo.who.int/tobacco/topics/oral_tobacco_use.pdf. [Last accessed on 2013 Dec 09].
- World Health Organization. Sentinel Tobacco Use Prevalence Survey in India. New Delhi: WHO, SEARO; 2001.
 - Akhtar S, Sheikh AA, Qureshi HU. Chewing areca nut, betel quid, oral snuff, cigarette smoking and the risk of oesophageal squamous-cell carcinoma in South Asians: A multicentre case-control study. *Eur J Cancer* 2012;48:655-61.
 - Saleheen D, Zaidi M, Rasheed A, Ahmad U, Hakeem A, Murtaza M, *et al.* The Pakistan Risk of Myocardial Infarction Study: A resource for the study of genetic, lifestyle and other determinants of myocardial infarction in South Asia. *Eur J Epidemiol* 2009;24:329-38.
 - Ray CS, Gupta P, de Beyer J. Tobacco use surveys and reports. In: *Research on Tobacco in India: An annotated Bibliography of Research on Use, Health Effects, Economics and Control Efforts*. Washington: World Bank; 2003. p. 1-32.
 - Gupta PC, Ray CS. Smokeless tobacco and health in India and South Asia. *Respirology* 2003;8:419-31.
 - Soni P, Raut DK. Prevalence and pattern of tobacco consumption in India. *Int Res J Soc Sci* 2012;1:36-43.
 - Warren CW, Riley L, Asma S, Eriksen MP, Green L, Blanton C, *et al.* Tobacco use by youth: A surveillance report from the Global Youth Tobacco Survey project. *Bull World Health Organ* 2000;78:868-76.
 - Al-Rmalli SW, Jenkins RO, Haris PI. Betel quid chewing elevates human exposure to arsenic, cadmium and lead. *J Hazard Mater* 2011;190:69-74.
 - Willis D, Popovch M, Gany F, Zelikoff J. Toxicology of smokeless tobacco: Implications for immune, reproductive, and cardiovascular systems. *J Toxicol Environ Health B Crit Rev* 2012;15:317-31.
 - Johnson GK, Slach NA. Impact of tobacco use on periodontal status. *J Dent Educ* 2001;65:313-21.
 - Aro P, Ronkainen J, Storskrubb T, Vieth M, Engstrand L, Johansson SE, *et al.* Use of tobacco products and gastrointestinal morbidity: An endoscopic population-based study (the Kalixanda study). *Eur J Epidemiol* 2010;25:741-50.
 - Shankaran K, Kandarkar SV, Contractor QQ, Kalro RH, Desai HG. Electron microscopic observations in gastric mucosa of habitual tobacco chewers. *Indian J Med Res* 1994;99:267-71.
 - Piano MR, Benowitz NL, Fitzgerald GA, Corbridge S, Heath J, Hahn E, *et al.* Impact of smokeless tobacco products on cardiovascular disease: Implications for policy, prevention, and treatment: A policy statement from the American Heart Association. *Circulation* 2010;122:1520-44.
 - Critchley JA, Unal B. Health effects associated with smokeless tobacco: A systematic review. *Thorax* 2003;58:435-43.
 - Gupta BK, Kaushik A, Panwar RB, Chaddha VS, Nayak KC, Singh VB, *et al.* Cardiovascular risk factors in tobacco-chewers: A controlled study. *J Assoc Physicians India* 2007;55:27-31.
 - Yatsuya H, Folsom AR; ARIC Investigators. Risk of incident cardiovascular disease among users of smokeless tobacco in the Atherosclerosis Risk in Communities (ARIC) study. *Am J Epidemiol* 2010;172:600-5.
 - Gupta R, Gurm H, Bartholomew JR. Smokeless tobacco and cardiovascular risk. *Arch Intern Med* 2004;164:1845-9.
 - Gupta R, Gupta N, Khedar RS. Smokeless tobacco and cardiovascular disease in low and middle income countries. *Indian Heart J* 2013;65:369-77.
 - Alexander M. Tobacco Use and the Risk of Cardiovascular Diseases in Developed and Developing Countries. 2013. Available from: <https://www.repository.cam.ac.uk>. [Last accessed on 2013 Nov 20].
 - Heck JE, Marcotte EL, Argos M, Parvez F, Ahmed A, Islam T, *et al.* Betel quid chewing in rural Bangladesh: Prevalence, predictors and relationship to blood pressure. *Int J Epidemiol* 2012;41:462-71.
 - Krishnamurthy S, Ramaswamy R, Trivedi U, Zachariah V. Tobacco use in rural Indian children. *Indian Pediatr* 1997;34:923-7.
 - Raghavendra T, Pakkala A, Ganashree CP. Acute effect of Gutkha chewing on cardiopulmonary efficiency in short term users. *J Alcohol Drug Depend* 2013;1:115.

24. Wolk R, Shamsuzzaman AS, Svatikova A, Huyber CM, Huck C, Narkiewicz K, *et al.* Hemodynamic and autonomic effects of smokeless tobacco in healthy young men. *J Am Coll Cardiol* 2005;45:910-4.
25. Mohesh MI, Ratchagan K, Sundaramurthy A. A study of short term heart rate variability in dipping tobacco users. *Asian J Med Sci* 2014;5:91-4.
26. Puri A, Chaudhary G, Srivastava R, Tiwari S. Electrical disturbance in heart by smokeless tobacco. *J Assoc Physicians India* 2013;61:332-4.
27. Siddiqui SS, Hasan SN, Aggarwal T, Singh D. A comparison of 12 lead ECG status of tobacco smokers, tobacco chewers and nontobacco users. *Natl J Med Res* 2013;3:203-5.
28. Pakkala A, Ganashree CP, Raghavendra T. A study of heart rate variability among khaini users: A form of smokeless tobacco in India. *Muller J Med Sci Res* 2013;4:64-7.
29. Pakkala A, Ganashree CP, Raghavendra T. A study of heart rate variability among Gutkha chewers from a rural farming background in India. *J Alcohol Drug Depend* 2013;1:118.
30. Dikshit RP, Kanhere S. Tobacco habits and risk of lung, oropharyngeal and oral cavity cancer: A population-based case-control study in Bhopal, India. *Int J Epidemiol* 2000;29:609-14.
31. Asplund K. Smokeless tobacco and cardiovascular disease. *Prog Cardiovasc Dis* 2003;45:383-94.
32. Heart rate variability: Standards of measurement, physiological interpretation and clinical use. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. *Circulation* 1996;93:1043-65.
33. Shields RW Jr. Heart rate variability with deep breathing as a clinical test of cardiovagal function. *Cleve Clin J Med* 2009;76 Suppl 2:S37-40.
34. Kamath MV, Fallen EL. Power spectral analysis of heart rate variability: A noninvasive signature of cardiac autonomic function. *Crit Rev Biomed Eng* 1993;21:245-311.
35. Malliani A. Association of heart rate variability components with physiological regulatory mechanisms. In: Malik M, Camm AJ, editors. *Heart Rate Variability*. Armonk, New York: Futura Publ. Comp., Inc.; 1995. p. 173-88.
36. Litvack DA, Oberlander TF, Carney LH, Saul JP. Time and frequency domain methods for heart rate variability analysis: A methodological comparison. *Psychophysiology* 1995;32:492-504.
37. Chandra PS, Mulla U. Areca nut: The hidden Indian 'gateway' to future tobacco use and oral cancers among youth. *Indian J Med Sci* 2007;61:319-21.
38. World Health Organization. Tobacco: Deadly in Any form or Disguise. Geneva: World Health Organization; 2006. Available from: http://www.who.int/tobacco/communications/events/wntd/2006/Report_v8_4May06.pdf. [Last accessed on 2015 Jan 23].