Print ISSN: 2321-6379
Online ISSN: 2321-595X

Original Article

Cardiac Autonomic Function Tests in Tobacco Chewers

Kavita Goyal[1], Anupama Gupta[2], Rajesh Gupta[3]

[1]Assistant Professor, Department of Physiology at School of Medical Sciences and Research, Sharda University, Greater Noida, Uttar Pradesh, India, [2]Professor, Department of Physiology, Pt. BDS PGIMS, Rohtak, Haryana, India, [3]Professor, Department of TB and Respiratory Medicine, Pt. BDS PGIMS, Rohtak, Haryana, India

Abstract

Introduction: Tobacco use is a public health concern worldwide as well as in India. It can be used in both smoked and smokeless forms. Smokeless tobacco is used either in chewed, sniffed, or sucked form. It affects the cardiovascular system and causes diseases such as high blood pressure, myocardial infarction, and stroke. Nicotine in tobacco is found to alter the cardiovascular autonomic functions. Impact of the nicotine on cardiovascular autonomic functions can be best diagnosed using the heart rate variability (HRV) assessment.

Materials and Methods: A total of 60 male subjects in the age group of 25–50 years – 30 tobacco chewers and 30 tobacco non-users of minimum 10 pouch years, were included in the study. Subjects with history of hypertension, cardiopulmonary, or endocrine disorder were excluded from the study. Overnight abstinence from tobacco use in any form was recommended. Basal electrocardiograph was recorded in lead II for 5 min using Digitalized Polyrite D. Frequency domain parameters – very low frequency (VLF), LF, high frequency (HF), and LF/HF ratio were recorded. Data obtained were analyzed statistically by unpaired *t*-test and statistical significance was set at $P < 0.05$.

Results: All the anthropometric parameters including age, height, weight, and body mass index were comparable among the two groups. There was no significant change in heart rate and RR interval in both groups. A highly significant ($P < 0.001$) decrease in VLF and HF was seen in chewers. A significant ($P < 0.05$) decrease in LF was seen in chewers. LF denotes both sympathetic and parasympathetic activity and HF reflects parasympathetic (vagal) influence. A significant ($P < 0.05$) increase in LF/HF ratio was seen in chewers. Increase in LF/HF ratio signifies increase in sympathetic activity.

Conclusion: HRV analysis in tobacco chewers has revealed the disturbances in cardiac autonomic regulation by increasing sympathetic activity predisposing the subjects to various cardiovascular diseases. Hence, active intervention to quit tobacco even in the smokeless form is required.

Key words: Autonomic, Chewers, Heart rate variability, Smokeless tobacco, Smoking

INTRODUCTION

Tobacco is one of the biggest public health threats the world is facing. Its use is the leading preventable agent of death in the world. According to the WHO, 5.4 million deaths are reported annually due to tobacco and the number is expected to rise to 8 million in the next 25 years. Nearly 80% of tobacco smoking population resides in developing countries.[1] Prevalence of smokeless tobacco (SLT) use is 26% which is far greater than smoking (14%) among adults as reported by Global Adult Tobacco Survey report of India.[2]

Tobacco is being used for about 1000 years by humans. Its consumption is mainly done in two forms: Smoked tobacco and SLT. Smoking is done in the form of bidis, cigarettes, hookahs, pipes, and cigars. Nicotine is the principal constituent of tobacco responsible for its addictive character, but other smoke constituents also contribute to the strength of the addiction. The use of tobacco without burning is referred to as SLT.

In India, SLT is consumed in several forms, for example, snuff/naswar (finely ground tobacco leaves), chewing

Access this article online

www.ijss-sn.com

Month of Submission : 07-2021
Month of Peer Review : 08-2021
Month of Acceptance : 08-2021
Month of Publishing : 09-2021

Corresponding Author: Dr. Kavita Goyal, House no 352, Sector 14, Hisar, Haryana - 125 001, India.

tobacco (loose and sweetened tobacco leaves), zarda/kiwan (paste), paan (betel/quid), and khaini/mawa (tobacco with lime). Tobacco chewing is the most common form of SLT practiced in India. It is presumed to be harmless and a less "social evil" than smoking. Furthermore, due to various anti-smoking campaigns and law policies, it is considered as a safe alternative to smoking.[3]

Nicotine present in all tobacco products is well absorbed from mucosal surfaces, respiratory tract, and skin. In addition to nicotine, SLT contains nitrosamines, sodium, glucose, glycyrrhizinic acid, and grit.[4] It is one of the most important risk factors for the development of oral mucosal lesions including various oral pre-cancerous lesions such as lichen planus, lichenoid lesions, leukoplakia, and erythroplakia. Several cancers such as that of mouth, throat, cheek, gums, and lips are also attributed to tobacco chewing.[5] It also leads to teeth discoloration, dental cavities, and gum diseases due to the presence of glucose and flavoring agents present in SLT preparations.[4]

Cigarette smoking is major risk factor for the development of atherosclerosis, coronary heart disease, acute myocardial infarction (MI), and sudden cardiac death.[6] The risk of a non-fatal heart attack increases by 5.6% for every cigarette smoked.[7] However, tobacco chewing increases the risk of MI more than 2 folds.[8] Hypertension is significantly prevalent in both tobacco smokers and chewers. Use of tobacco either by smoking or chewing changes the lipid profile significantly.[9]

SLT also contains substantial amounts of nicotine, which is a cardioactive substance.[10] Impact of the nicotine on cardiovascular autonomic functions can be best diagnosed using the heart rate variability (HRV). Although local effects of SLT are widely known, systemic effects need exploration. Keeping this in mind, the present study has been undertaken to study the effect of SLT on HRV.

MATERIALS AND METHODS

The present study was conducted in the Department of Physiology, Pt. B.D. Sharma PGIMS, Rohtak, after getting approval from the Institutional Ethical Committee. A total of 60 male subjects of age group 25–50 years were included in the study. The subjects were divided into following two groups:

- Chewers – 30 male volunteers who were chronic tobacco chewers (non-smokers) for minimum 10 pouch years in continuation with the duration of 7 years or more
- Control – 30 male volunteers who had never used tobacco in any form (control group).

Chewers were further subdivided on the basis of number of pouch years of tobacco chewing as Group A and Group B. Group A consisted of chewers of <15 pouch years while Group B consisted of chewers of more than 15 pouch years.

Exclusion Criteria

- History or symptoms of any chronic cardiopulmonary, endocrine or metabolic, psychiatric disorder
- History or symptoms of any oral lesion
- History of any drug intake

Pouch Years

Tobacco chewing was quantified in pouch years. This was calculated as:

Pouch years = No. of pouches per day × years of chewing

Example: 1 pouch per day for 10 years = 10 pouch years (1 × 10 = 10).[4]

Preliminary preparation: Informed consent was taken from every subject to undergo the whole procedure. All the tests were conducted from 10 am to 1 pm to avoid diurnal variation. Overnight abstinence from tobacco use in any form was recommended. Subjects were asked to avoid tea, coffee, carbonated drinks, or heavy meals at least 2 h before the test procedure. The whole procedure was explained in detail to each subject in his own language to allay any apprehension or fear. The basic parameters such as age, weight, and height of subjects were recorded. Heart rate, respiratory rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial blood pressure (MAP) were taken and noted down.

For recording HRV, Digitalized Powerlab26T Polyrite D was used. Sampling rate was 256 Hz. High and low filters were set at 99 and 0.1 Hz, respectively. The screen sweep speed was kept at 30 mm/s. For R wave detector, channel 3, that is, electrocardiograph (ECG) channel 3 was used. The whole channel was selected for HRV analysis. Position of event is taken as maximum after threshold. Retrigger delay is taken as 0. Ectopics were excluded from the analysis. A number of ectopics and artifacts are shown by the machine. Maximum frequency is 0.5 Hz. Window used is welch type. Frequency band used is 0.04 <low frequency (LF) <high frequency (HF) <0.4 Hz. HRV report comprises various things: HRV spectrum, HRV tachogram, HRV delta NN histogram, etc.

After preliminary history taking and examination, the subjects were asked to lie down on the couch and made to relax in front of the Polyrite D system. The three disposable adhesive electrodes were attached to the left arm, right leg,

and left leg, respectively. The basal recording of ECG (Lead II) was taken for 5 min. Utmost care was taken to minimize the movements from subjects by instructing them not to move or speak while the recording is in progress. From the ECG, the analysis of HRV was done automatically in the machine and the printed report of HRV provided the data of required variables. The HRV is based on the duration of time interval between two R waves, graphically represented in the form of a RR interval tachogram. The functional value of tachogram is the duration of a RR interval (in millisecond) at a certain point of time. For analysis of HRV, there are two domains mainly "Time domain" and "Frequency domain" as described earlier. Spectral analysis of ECG was done by fast Fourier transformation method. Following HRV parameters were selected for study.

- Mean heart rate (beats/min)
- Mean RR interval (seconds)
- Very low frequency (VLF) (ms^2)
- LF (nu)
- High frequency (HF) (nu)
- LF/HF ratio.

Statistics

All the data obtained by above two procedures were analyzed by a commercially available software package SPSS software. Statistical significance between chewers and controls was determined using Student's unpaired t-test. $P < 0.05$ was considered statistically significant and $P < 0.001$ was considered highly statistically significant.

RESULTS

There was no significant difference in the anthropometric parameters including age, height, weight, and body mass index of chewers. Furthermore, there was no statistical significance between heart rate, RR interval, SBP, DBP, and MAP in the two groups.

There was no significant change in heart rate and RR interval in both groups. A highly significant ($P < 0.001$) decrease in VLF and HF was seen in chewers. LF was seen to be decreased significantly ($P < 0.05$) in chewers. LF denotes both sympathetic and parasympathetic activities and HF reflects parasympathetic (vagal) influence. A significant ($P < 0.05$) increase in LF/HF ratio was seen in chewers. Increase in LF/HF ratio signifies increase in sympathetic activity. Significant decline in VLF and LF is suggestive of an increased sympathetic activity in chewers.

Group A consists of chewers with <15 pouch years of chewing and Group B consists of chewers with more than 15 pouch years of chewing tobacco [Table 2]. There was highly significant increase in the mean heart rate in Group B. The mean RR interval was decreased in Group B but the decrease was statistically insignificant. In Group B, the mean values of VLF and LF were increased. However, the change was highly significant ($P < 0.001$) for LF only. There was highly significant ($P < 0.001$) increase in LF/HF ratio in Group B. These suggest deterioration of cardiac functions with increase in pouch years of tobacco chewing.

DISCUSSION

Tobacco in any form trebles the risk of cardiac disease. About 30% of all deaths from heart disease are due to smoking. Cardiovascular effects of smoking occur within minutes with rise in HR up to 30% in the first 10 min.[11,12] Tobacco contains nicotine which increases heart rate and blood pressure.[9] SLT use results in considerable systemic exposure to nicotine.[13] The predominant cardiovascular effects of nicotine result from activation of the sympathetic nervous system. The state of sympathovagal balance is used for the prediction of many cardiovascular dysfunctions.[14] Studies in both SLT users and smokers have shown cardiac sympathovagal imbalance.[7,15-19] Nicotine increases the cardiac output by increasing both the heart rate and the myocardial contractility.[20] Furthermore, it may contribute to atherosclerosis by affecting lipid metabolism, coagulation, hemodynamic status, or causing endothelial injury. These effects lead to diseases such as MI, stroke, and high blood pressure.[15,21-23]

We found highly significant decline in VLF and LF in chewers [Table 1]. The LF power spectrum is evaluated in the range from 0.04 to 0.15 Hz. LF is thought to represent both sympathetic and parasympathetic activities. This indicates higher sympathetic activity in chewers.[15] Similar findings were reported by Glad *et al.* in their study of short-term HRV in dipping tobacco users. Pakkala *et al.*, while studying HRV among khaini users, reported a statistically significant decrease in VLF and LF after 3 months.[16] However, Itagi *et al.*, in their study on acute effects of

Table 1: Comparison of heart rate variability parameters in controls and chewers

Parameters	Control (Mean±SD#)	Chewers (Mean±SD)	*P* value
HR (beats/minute)	73.94±15.0	80.21±9.56	0.059
RR interval (seconds)	760.09±93.38	744.19±150.66	0.628
VLF (ms^2)	1977.13±1104.22	501.58±416.83	0.0001
LF (nu)	59.91±12.87	53.72±10.95	0.048
HF (nu)	47.07±63.16	22.94±6.39	0.0001
LF/HF	2.02±0.92	2.52±0.91	0.035

*P<0.05=Significant, **P<0.001=Highly significant, #SD=Standard deviation, VLF: Very low frequency, LF: Low frequency, HF: High frequency,

Table 2: Comparison of HRV in Group A (<15 pouch years) and B (>15 pouch years) of chewers

Parameters	Group A (<15 pouch years) (*n*=15) (Mean±SD#)	Group B (>15 pouch years) (*n*=15) (Mean±SD)	*P* value (Group A vs. Group B)
HR (beats/minute)	72.81±7.83	87.61±3.86	<0.001**
RR interval (seconds)	0.788±0.12	0.700±0.16	0.116
VLF (ms^2)	439.72±531.56	563.44±281.54	0.432
LF (nu)	45.01±6.13	62.43±6.44	<0.001**
HF (nu)	24.51±5.95	21.55±6.93	0.227
LF/HF	1.92±0.45	3.13±0.84	<0.001**

*P<0.05=Significant, **P<0.001=Highly significant, #SD: Standard deviation. LF: Low frequency, HF: High frequency, VLF: Very low frequency

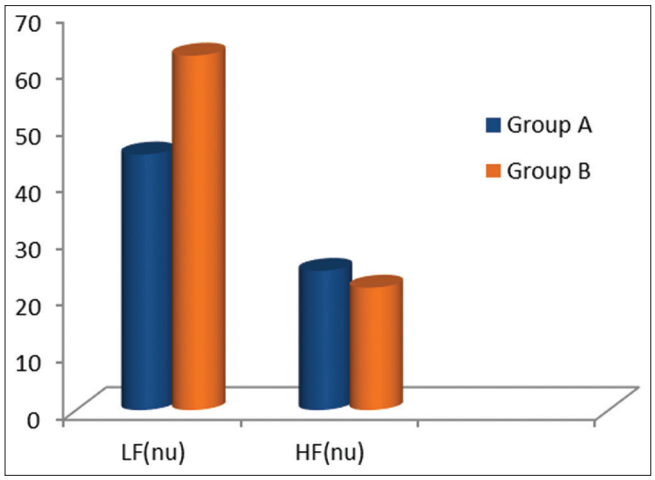

Figure 1: Low frequency and high frequency in Groups A (<15 pouch years) and B (>15 pouch years)

gutkha consumption on HRV, reported significant increase in LF after 5 min and 15 min of gutkha chewing.[17]

The HF power spectrum is evaluated in the range from 0.15 to 0.4 Hz.[18] There is highly significant decline in HF in our study in chewers reflecting a decrease in the parasympathetic activity [Figure 1].[24] Pakala *et al.*, on studying HRV in khaini users, reported that the mean value of the HF power was of lower magnitude after 3 and 6 months, but the decrease was not statistically significant.[16] However, contrary to our findings, few studies reported an increase in HF power.[17,25]

The LF/HF ratio is used to indicate balance between sympathetic and parasympathetic tones. A decrease in this score might indicate either increase in parasympathetic or decrease in sympathetic tone. It is considered together with absolute values of both LF and HF to determine what factor contributes in autonomic imbalance.[18] We observed a significant increase in LF/HF in chewers, indicating an increase in the sympathetic activity.[14] These values were in agreement with Pakkala *et al.*[16]

In our study, we observed, decrease in the mean RR interval and increase in the mean HR and BP in chewers or chewers, though insignificant. Nicotine causes vasoconstriction possibly through alteration of a cyclic GMP-dependent vasoactive mechanism.[25] Significant rise in the DBP is of great concern as any increase in the diastolic BP is an indicator of hypertension. This can lead to all possible cardiovascular diseases in near future.

CONCLUSION

HRV is an index of vagal tone and reflects the balance between parasympathetic and sympathetic maneuvers. HRV analysis in tobacco chewers has revealed the disturbances in cardiac autonomic regulation due to increased sympathetic activity predisposing the subjects to various cardiovascular diseases. HRV can be used as a non-invasive tool for screening in preclinical derangement of cardiac functions.

Thus, tobacco chewing is detrimental for cardiac functions. Hence, active intervention to quit tobacco even in the smokeless form is required.

ACKNOWLEDGMENT

We would like to express our sincere thanks to all the staffs of the Department of Physiology, Pt. BD Sharma, PGIMS, Rohtak, and the subjects of the study who have helped us in making this work a reality.

REFERENCES

1. World Health Organization. WHO Report on the Global Tobacco Epidemic: The MPOWER Package. Geneva: World Health Organization; 2008. p. 8.
2. Global Adult Tobacco Survey India Report. New Delhi: Ministry of Health and Family Welfare, Government of India; 2010. p. 72.
3. Council on Scientific Affairs. Health effects of smokeless tobacco. JAMA 1986;255:1038-44.
4. Al-Ibrahim MS, Gross JY. Tobacco use. In: Walker HK, Hall WD, Hurst JW, editors. Clinical Methods: The History, Physical and Laboratory Examinations. 3rd ed. Boston: Butterworths; 1990. p. 214-6.
5. Williams NS, Bulstrode CJ, O'connell PR. Bailey's and Love's Short Practice of Surgery. 26th ed. Boca Raton: Taylor and Francis Group; 2013.
6. Burns DM. Nicotine addiction. In: Longo DL, Kasper DL, Jameson JL,

Fauci AS, Hauser SL, Loscalzo J, editors. Harrison's Principles of Internal Medicine. 18th ed. New York: McGraw Hill; 2012. p. 3560-4.
7. Vollset SE, Tverdal A, Gjessing HK. Smoking and deaths between 40 and 70 years of age in women and men. Ann Intern Med 2006;144:381-9.
8. Centers for Disease Control and Prevention. Smoking and Tobacco Use Health Effects of Cigarette Smoking; 2010. Available from: http://www.cdc.gov/tobacco/data_statistics/fact_sheets/health_effects/effects_cig_smoking/index.html. [Last accessed on 2020 Oct 12].
9. Shrivastava R, Jha R, Kumar R. Comparative study of tobacco chewers and smokers as a risk factor for cardiovascular disease. Indian J Appl Res 2014;4:26-7.
10. Squires WG Jr., Brandon TA, Zinkgraf S, Bonds D, Hartung GH, Murray T, *et al*. Hemodynamic effects of oral smokeless tobacco in dogs and young adults. Prey Med 1984;13:195-206.
11. Saha U. Tobacco interventions and anaesthesia a review. Indian J Anaesth 2009;53:618-27.
12. Barry J, Mead K, Nabel EG, Rocco MB, Campbell S, Fenton T, *et al*. Effect of smoking on the activity of ischemic heart disease. J Am Med Assoc 1989;261:398-402.
13. Benowitz NL, Porchet H, Sheiner L, Jacob P. Nicotine absorption and cardiovascular effects with smokeless tobacco use: Comparision with cigarettes and nicotine gum. Clin Pharmacol Ther 1988;44:23-8.
14. Pal GK, Pal P, Nanda N. Comprehensive Textbook of Medical Physiology. New Delhi: Jaypee The Health Sciences Publisher; 2017.
15. Glad M, Ratchagan K, Sundaramurthy A. A study of short term heart rate variability in dipping tobacco users. Asian J Med Sci 2013;5:91-4.
16. 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 and Res 2013;4:64-7.
17. Itagi AH, Arora D, Patil NA, Bailwad SA Yunus GY, Goel A, *et al*. Short-term acute effects of gutkha chewing on heart rate variability among young adults: A cross-sectional study. Int J Appl Basic Med Res 2016;6:45-9.
18. Vollset SE, Tverdal A, Gjessing HK. Smoking and deaths between 40 and 70 years of age in women and men. Ann Intern Med 2006;144:381-9.
19. Behera J, Sood S, Gupta R, Kumar N, Singh M, Gupta A, *et al*. Assessing autonomic function in smokers. Am J Physiol 2010;3:712-5.
20. Lucini D, Bertocchi F, Malliani A, Pagani M. A controlled study of the autonomic changes produced by habitual cigarette smoking in healthy subjects. Cardiovasc Res 1996;3:633-9.
21. Gilman SL, Zhou X, editors. Smoke: A Global History of Smoking. London: Reaktion Books; 2004.
22. Sharma S. New approaches in smoking Cessation. Indian Heart J 2008;60:34-7.
23. Benowitz NL. Nicotine and cardiovascular disease. In: Adlkofer F, Thurau K, editors. Effects of Nicotine on Biological Systems. Basel, Switzerland: Birkhauser Verlag; 1991. p. 579-96.
24. Pittilo RM. Cigarette smoking and endothelial injury: A review. Adv Exp Med Biol 1990;273:61-78.
25. Tayade MC, Kulkarni NB. The effect of smoking on the cardiovascular autonomic functions: A cross sectional study. J Clin Diag Res 2013;7:1307-10.

How to cite this article: Goyal K, Gupta A, Gupta R. Cardiac Autonomic Function Tests in Tobacco Chewers. Int J Sci Stud 2021;9(6):96-100.

Source of Support: Nil, **Conflicts of Interest:** None declared.