Parasympathetic Nerve Function Status in Chronic Tobacco Users

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Abstract

Introduction: Tobacco use is one of the most widely spread bad habits. It is one of the leading preventable causes of premature death, disease and disability. The World Health Organization reported that tobacco smoking killed 100 million people worldwide in the 20th century and warned that it could kill one billion people around the world in 21st century. Bangladesh ranked among top tobacco consuming countries where 57,000 people over the age of 30 die each year from tobacco-related illness.

Objective: To assess the effects of tobacco use on parasympathetic nerve function status.

Methods: A total number of 150 male subjects were selected, among them 50 were apparently healthy non-tobacco chewer non-smoker subjects (group A) - control, 50 were apparently healthy tobacco smoker non-chewer (group B) - experimental, 50 were apparently healthy tobacco chewer non-smoker (group C)- experimental. For statistical analysis one way ANOVA (post-hoc) test were performed by computer based software SPSS- 23.0 version for windows. Significance for the statistical test would be predetermined at a probability value of less than 0.05 ($p<0.05$). Ethical consideration was achieving an informed consent after briefing objectives. Quality was assured through avoidance of missed data, filling of code, regular entry of data and careful data analysis.

Result: In this study smokers revealed significant decreased level of parasympathetic function status in tobacco smokers as compared to tobacco nonsmokers.

Conclusion: Decrease in heart rate occur in tobacco smokers than tobacco nonsmokers.

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Introduction

Tobacco use is a risk factor for many diseases, especially affecting the heart, liver, and lungs, as well as many cancers[1]. There are two kinds of commonly used tobacco products in Bangladesh i.e. smoking and smokeless tobacco products. Men smoke cigarettes and bidi, and chew tobacco leaf such as zarda, sadapata, gul, khoinee. However, women usually do not smoke but chew tobacco leaf. The Bangladesh Health and Demographic Survey 1997 revealed that among the respondents aged 10 years or more 41.1% of males and 4% of females smoked cigarettes or other forms of smoking tobacco such as bidi or hukkah.[2] Tobacco is a plant grown for its leaves, which are dried and fermented before being put in tobacco products. Tobacco contains nicotine, that can lead to addiction. For this reason, it is difficult to quit for so many people who use tobacco. Many potentially harmful chemicals found in tobacco or created by burning it.[3] A person uses nicotine in any tobacco product readily absorbs into the blood and immediately stimulates the adrenal glands to release the hormone epinephrine (adrenaline). Adrenalin stimulates the blood pressure, breathing, and heart rate by stimulating central nervous system. Severe health effects of tobacco use comes from other chemicals although nicotine is addictive. Lung cancer, chronic bronchitis, and emphysema occurs due to tobacco smoking. It increases the risk of heart disease, which can lead to stroke or heart attack. Smoking has also been linked to other cancers, leukemia, cataracts, and pneumonia. All of these risks apply to use of any smoked product, including hookah tobacco. Mouth cancer is the effect of using smokeless tobacco.[3] Bangladesh has been implementing surveys under GTSS (Global Tobacco Surveillance System) since 2004 regularly at periodical intervals which includes GATS(Global Adult Tobacco Survey). GATS was implemented initially in 14 countries. More than half of the world's smokers live and that bear the highest burden of tobacco use including Bangladesh. The purpose of GATS was to systematically monitor adult tobacco use (smoking and smokeless) and track key tobacco control interventions. GATS also provides key for monitoring MPOWER policy package developed by WHO which includes: **M**onitor tobacco use and prevention policies, **P**rotect people from tobacco smoke, **O**ffer help to quit tobacco use, **W**arn about the dangers of tobacco, **E**nforce bans on tobacco advertising, **R**aise taxes on tobacco.[1]

The autonomic nervous system is composed of afferent nerve fibers located throughout the body, including the lungs heart, and vasculature.[4] It is the part of the nervous system that is responsible for regulation and integration of internal organs' functioning. Together with the endocrine and immunological systems it determines the status of the internal environment of the organism and adjusts it to its current needs, thus enabling adaptation of the internal environment to changes in the external environment. Disorders of autonomic regulation, directly afflict the nervous system as well as those afflicting other organs, where they trigger pathological symptoms.[5] A strong association was observed between cigarette smoking and diabetic neuropathy among diabetic patients. Cigarette smoking may contribute to tissue hypoxia and subsequent injury to the neural microvasculature. Patients smoking $\geq$30 pack-year in a lifetime were more likely to have neuropathy than patients smoking less than this amount. Many affected patients developed their neuropathy before 30 pack- year of smoking.[6] There are several tests for assessment of autonomic nervous system function. Most of the tests are based on evaluation of the cardiovascular reflexes triggered by performing specific provocative maneuvers. Changes in heart rate during orthostatic testing and Valsalva maneuver, as well as during deep breathing, reflect parasympathetic modulation.[6] The valsalva ratio is a reliable indicator of the parasympathetic activity, which is responsible for the recovery of the heart rate after strenuous activities like the Valsalva maneuver.[7] Heart rate response to deep breathing and standing (30^{th}:15^{th} ratio) was significantly decreased in some study.[8,9]

Objective: **This study was done to** assess the effects of tobacco use on parasympathetic nerve function status.

Methods

This cross sectional analytical study were conducted in Department of Physiology, Rangpur Medical College, Rangpur. After obtaining permission a total 150 male subjects who fulfilled the inclusion and exclusion criteria were enrolled in the study after briefing them objectives of the study. Subjects with established obstructive coronary artery disease, unstable coronary syndromes, currently alcoholics or on athletic training were excluded. The subjects were apparently healthy young adult male aged 20–40 years with habit of smoking and chewing tobaccofor >3 years. 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. Among them 50 were apparently healthy non-smoker non-chewer subjects (group A) - control, 50 were apparently healthy tobacco smoker non chewer(group B) – experimental and 50 were apparently healthy tobacco chewer non-smoker (group C)– experimental. For statistical analysis one way ANOVA (post-hoc) test were performed by computer based software SPSS- 23.0 version for windows. Significance for the statistical test would be predetermined at a probability value of less than 0.05 ($p<0.05$). Ethical consideration was achieving an informed consent after briefing objectives. Quality was assured through avoidance of missed data, filling of code, regular entry of data and careful data analysis.

Test procedure for parasympathetic function

1. Heart rate response to valsalva maneuver:[10]

The subjects were asked to lie down comfortably. Then they were asked to blow into rubber tube connected to manometer to raise the mercury up to a height of 40 mm Hg by continuous blowing. The level were maintained at that mark for 15 seconds and ECG were continuously recorded. ECG was recorded for 30 seconds more after this maneuver with patient sitting.

The maneuver were performed three times with one minute intervals between. The result were expressed as the Valsalva ratio, which is the ratio of the longest R-R interval within 20 beats of ending the maneuver to the shortest R-R interval during the maneuver, measured with a ruler from the electrocardiogram trace. The mean of the three Valsalva ratios is taken as the final value.

Normal ≥1˙21, Borderline 1˙11-1˙20,
Abnormal ≤1˙10.[10]

2. Heart rate response to deep breathing:[10]

The subjects were asked to lie down comfortably and then asked to take deep inspirations for 5 seconds followed by deep expiration for 5 seconds, thus completing one breathing cycle (06 breaths/ min) and repeat this for 3 times. An electrocardiogram were recorded throughout the period of deep breathing and repeat for such 3 cycles with an indicator use to indicate the onset of inspiration and expiration. The maximum and minimum heart rate during each 10 seconds breathing cycle measured. The mean of the differences during 3 successive 10 seconds breathing cycle taken for calculating the heart rate variation.

Heart rate variation= maximum heart rate-minimum heart rate.

Normal ≥ 15 beats/ min, Borderline 11- 14 beats/ min, Abnormal ≤10 beats/ min[10].

3.Heart rate response to standing (30th :15th ratio):[10]

The test were performed with the patient lying quietly on a bed and the heart rate were recorded continuously on an electrocardiograph. Then patient were asked to stand up as quickly as possible without any support, and the point at starting to stand is marked on the electrocardiogram. The characteristic heart rate response were expressed by 30th:15th ratio.

The longest R-R interval around 30th beat after standing up to the shortest R-R interval around 15th beat will be calculated.

Normal ≥1˙04, Borderline 1˙01-1˙03, Abnormal ≤ 1˙00.[10]

Result

Heart rate response to valsalva maneuver: The mean ± SD of valsalva ratios were 1.5443 ± 0.2196, 1.3650± 0.2370 and 1.4760± 0.2485in group A, B and C respectively. (Table I& figure I).In this study mean values of valsalva ratios were compared between group A and group B, group A and group C.The mean values were significantly ($p < 0.001$) lower in group B than group A, no significant difference ($p > 0.05$) among group C and group A
(Table - II).

Table I: Showing mean ± SD of valsalva ratio in the study subjects of different groups

Groups	Valsalva Ratio
A (n=50)	1.5443 ± 0.2196
B (n=50)	1.3650 ± 0.2370
C (n=50)	1.4760 ± 0.2485

A = non-tobacco chewer non-smoker (Control) healthy subjects.
B = tobacco smoker non chewer (Experimental) healthy subjects.
C= tobacco chewer non-smoker (Experimental) healthy subjects.

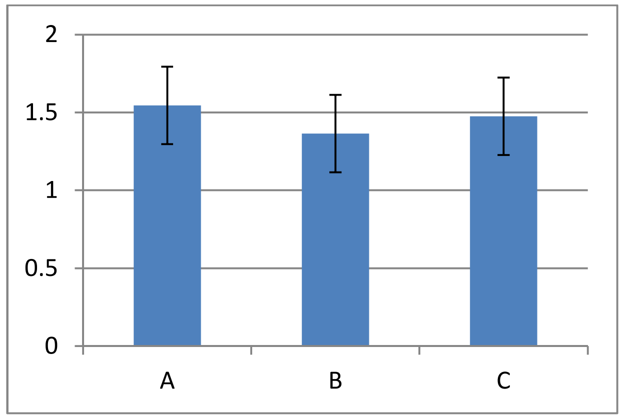

Figure 1. Bar diagram showing mean (± SD) of valsalva ratio in group A (Control), B (Experimental).and group C (Experimental).

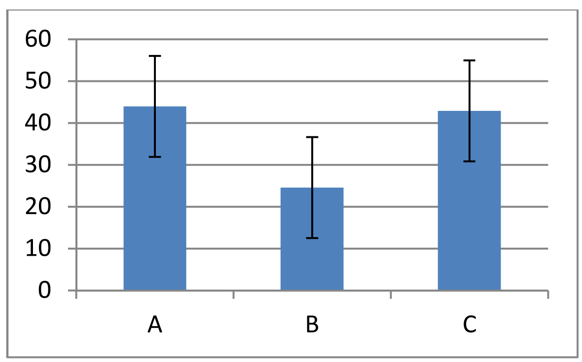

Figure 2. Bar diagram showing mean (± SD) of heart rate response to deep breathing in group A (Control), B (Experimental).and group C (Experimental).

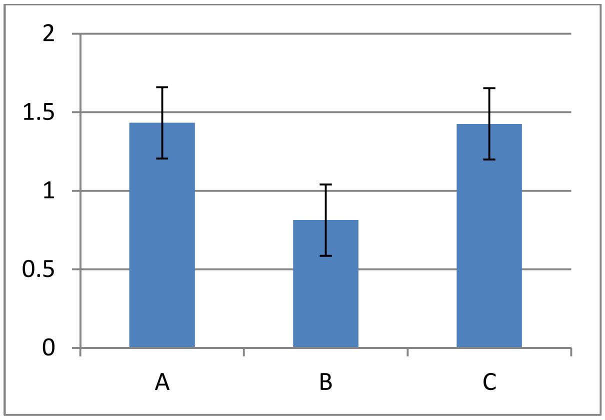

Figure 3. Bar diagram showing mean (± SD) of heart rate response to standing in group A (Control), B (Experimental).and group C (Experimental).

Table II :Showing statistical analysis of mean ± SD of valsalva ratio in the study subjects of different groups**.**

Analysis between the groups done by One – way ANOVA (Post Hoc Test)

Groups	mean ± SD	P value
A/B	1.5443 ± 0.2196/1.3650 ± 0.2370	0.000 ***
A/C	1.5443 ± 0.2196/ 1.4760 ± 0.2485	0.953 NS

A = 3 non-tobacco chewer non-smoker (Control) healthy subjects.
B = tobacco smoker non chewer (Experimental) healthy subjects.
C= tobacco chewer non-smoker (Experimental) healthy subjects.

Normal value of heart rate response to valsalva maneuver: ≥1˙21.[10]

Heart Rate Response to Deep Breathing

The mean ± SD of heart rate response to deep breathingwere 43.9333 ± 19.9048, 24.5637 ± 12.0594 and42.8543 ± 23.85601 in group A, B and C respectively. (Table III and Figure - 2). In this study mean values of heart rate response to deep breathingwere compared between group A and group B, group A and group C.The mean values were significantly ($p < 0.001$) lower in group B than group A, no significant difference ($p > 0.05$) among group C and group A (Table IV).

Table III: Showing mean ± SD of heart rate response to deep breathing in the study subjects of different groups

Groups	Heart rate response to deep breathing
A (n=50)	43.9333 ± 19.9048
B (n=50)	24.5637 ± 12.0594
C (n=50)	42.8543 ± 23.85601

A = Apparently healthy subjects of non-tobacco chewer non-smoker (Control).
B = Apparently healthy subjects of tobacco smoker non chewer (Experimental).
C= Apparently healthy tobacco chewer non-smoker(Experimental).
Normal value of heart rate response to deep breathing :≥ 15 beats/ min[10].

Table IV: Statistical analysis of mean ± SD of heart rate response to deep breathing in the study subjects of different groups**.**

Groups	mean ± SD	P value
A/B	43.9333 ± 19.9048/24.5637 ± 12.0594	0.000 ***
A/C	43.9333 ± 19.9048/ 42.8543 ± 23.85601	0.953 NS

Analysis between the groups done by One – way ANOVA (Post Hoc Test):
A = Apparently healthy subjects of non-tobacco chewer non-smoker (Control).
B = Apparently healthy subjects of tobacco smoker non chewer (Experimental).
C= Apparently healthy tobacco chewer non-smoker(Experimental).
Normal value of heart rate response to deep breathing :≥ 15 beats/ min.[10]

Heart rate response to standing(30th: 15thratio): The mean ± SD of heart rate response to standing were 1.4320 ± .22709, 0.8137 ± .30202 and1.4250 ± .24278 in group A, B and C respectively. (Table –Vand Figure - 3).

In this study mean values of heart rate response to deep breathingwere compared between group A and group B, group A and group C.

The mean values were significantly ($p < 0.001$) lower in group B than group A, no significant difference ($p > 0.05$) among group C and group A (Table VI).

Table V: Showing mean ± SD of heart rate response to standingin the study subjects of different groups

Groups	Heart rate response to standing
A (n=50)	1.4320 ± .22709
B (n=50)	0.8137 ± .30202
C (n=50)	1.4250 ± .24278

A = 3 non-tobacco chewer non-smoker (Control) healthy subjects.
B = tobacco smoker non chewer (Experimental) healthy subjects.
C= tobacco chewer non-smoker (Experimental) healthy subjects.

Table VI :Showingstatistical analysis of mean ± SD of heart rate response to standing in the study subjects of different groups.

Groups	mean ± SD	P value
A / B	1.4320 ± .22709/ 0.8137 ± .30202	0.000 ***
A / C	1.4320 ± .22709/ 1.4250 ± .24278	0.953 NS

Analysis between the groups done by One –way ANOVA (Post Hoc Test)

Discussion

Throughout the world Coronary Artery Disease (CAD) is a major cause of premature death and disability. Tobacco use is an important and an avoidable cause of CAD. The use of tobacco is increasing worldwide, especially among the young people. The present study was carried out to assess parasympathetic nerve function parameter in the chronic tobacco users. In the present study, the findings of the parameters in apparently healthy control group were within normal ranges and also similar to those reported by the various investigators from different countries.

Heart rate response to valsalva maneuver

In this study, the valsalva ratio was measured in healthy individual, tobacco smoker non chewer and chewer non smokersubjects.

In smokers non tobacco chewerssubjects, the mean of heart rate response to valsalva maneuver were lower but significant ($p < 0.001$) than those of control subjects. These findings are in agreement with those reported byMotilal CT and Kulkarni NB[7] and Motilal C and Nandkumar B[9] and Singh K and Sood S[11].

In tobacco chewers non smokers subjects, the mean of heart rate response to valsalva maneuver were lower but not significant ($p > 0.05$) than those of control subjects. These findings are in agreement with those reported by Begum N et al[8] and Shivaji J, Joshi A and Vasantrao A[12].

Heart rate response to deep breathing

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In smokers non tobacco chewerssubjects, the mean of heart rate response to deep breathing were significantly lower ($p<0.001$) than those of control subjects. These findings are in agreement with those reported byMotilal C and Nandkumar B,[9] Tayade MC and Kulkarni NB[13]Birajdar G, Prasad NB and PurandareVR[14]and Singh K and Sood S.[11]

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Heart rate response to standing

In this study, the heart rate response to deep breathingwas measured in healthy individual, tobacco smoker non chewer and chewer non smokersubjects.

In smokers non tobacco chewerssubjects, the mean of heart rate response to deep breathing were significantly lower ($p<0.01$) than those of control subjects. These findings are in agreement with those reported byMotilal C and Nandkumar B,[9] Tayade MC and Kulkarni NB[13] and Birajdar G, Prasad NB, PurandareVR.[14]

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Findings of this study is similar to other studies of various investigators. They suggested that impairment of parasympathetic nerve functions occurred in tobacco users. This could be due to vagal tone is reduced or loss of vagal tone due to cigarette smoking. Again, vagal damage causes reduction of heart rate to various stimuli. As a consequence, baroreflex activity may be decreased in smokers.

Conclusion

Parasympathetic function tests are feasible, nonsurgical and easy to carry out. By these tests, we can detect early involvement of autonomic nervous system before clinically related symptoms appear and thus are useful to take protection to prevent further progress of the disease.

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