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RESEARCH ARTICLE

Assessment of cardiovascular autonomic functions in substance abusers - A cross-sectional study

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ABSTRACT

Background: Drug abusing is a worldwide major cause of preventable morbidity and mortality. Substance abusing affects the cardiovascular system by several mechanisms. **Aims and Objectives:** The objective of the present study was to study the effect of drugs on the cardiovascular autonomic functions among different drug abusers and also to identify early neurological damage in autonomic system so that proper counseling and timely intervention can be undertaken. **Materials and Methods:** This cross-sectional study was done at GGS Medical College, Faridkot, Punjab, during the period from August 2012 to July 2013 in 50 drug abusers within the age group of 15-45 years, as well as in age matched 50 healthy controls. The subjects were recruited from Faridkot region of Punjab which included subjects from general population and the patients admitted in Drug De-addiction Centre of GGS Medical College and Hospital, Faridkot, Punjab. Prior informed written consents were obtained from them after explaining to them, the procedure and the purpose of the study tests. Lying to standing test was carried out for assessing parasympathetic reactivity and hand grip test for sympathetic reactivity. **Results:** After applying the '*t*' test for the difference between the two sample means, it was observed that there was a highly significant difference between the mean values of the parasympathetic function tests among the drug abusers and the controls (i.e., $P < 0.001$). The 30:15 ratio (response to standing) had significantly decreased in the drug abusers as compared to those in the controls. Also a highly significant difference was observed between the mean values of the sustained handgrip test in the drug abusers and controls (i.e., $P < 0.001$). **Conclusion:** This study provides good evidence for autonomic dysfunction following chronic abuse of different drugs. By using these simple tests, we can detect the early involvement of the autonomic nervous system before the clinically related symptoms appear and they are thus useful in taking steps to prevent the further progress of the disease.

KEY WORDS: Autonomic Function Tests; Hand Grip Test; Lying to Standing Test; Substance Abuse

INTRODUCTION

Drug addiction is a chronic, often relapsing brain disease because the abuse of drugs leads to changes in all systems of the body. It causes immediate and long-term problems. The most common types of drugs that people abuse fall into four categories: Stimulants, depressants, hallucinogens, and opioids. While the effect of each group of drugs is different, all of them are harmful to our body.

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Opium abuse is a major health problem in developing countries including our country. Despite of legal restriction and administrative control, the use of illicit drugs (like opium, heroin etc.) has increased considerably in many parts of North India. More than 180 million people around the world have tried illegal drugs at least once, of whom 13.5 million are

opium dependent. The effects of opium are essentially those of morphine. The major effects of opium are on the central and autonomic nervous system (ANS).[1] Morphine tends to manipulate the tone of ANS in the body interacting at various levels. Thus, it is an autonomically active drug.[2]

Tobacco smoking is an intentionally invited health hazard affecting both active as well as passive smokers. The overall death rate for male smokers is 70% greater than for male nonsmokers.[3] Smoking affects the cardiovascular system by several mechanisms. The hemodynamic effects of smoking appear to be mediated by nicotine.[4]

Alcoholism, another one of the greatest epidemics of modern times, is a chronic progressive often fatal disease, which is more common in males of our population. Alcohol, specifically ethanol, is a potent central nervous system (CNS) depressant with a range of effects on all systems particularly on ANS. Chronic ingestion of ethanol is known to cause cardiac dysfunction, most notably as congestive cardiomyopathy leading to sudden death due to arrhythmias.[5] Autonomic neuropathy has been found to be a relatively common and life threatening complication of alcohol abuse.[6]

It is estimated that 20% of Americans have used prescription drugs for non-medical reasons, which is prescription-drug abuse. Sedatives, tranquilizers, and stimulants are used recreationally, a practice that has increased in recent years. Like prescription drugs, there are too many illegal drugs such as marijuana, lysergic acid diethylamide, or heroin which are unhealthy for the user's body, mind, and social life.[7]

It is a well-known fact that ANS control many aspects of bodily systems. Autonomic literally means "self-governed." Interaction of sympathetic and parasympathetic nervous system is important in maintaining homeostasis in the body. If antagonistic control of both branches of the ANS gets disturbed, then it results in autonomic dysfunctions. Dysfunction at any level of ANS (central, preganglionic or postganglionic or at effector organ), results in generalized dysautonomia. Since, the prime function of ANS is to maintain cardiovascular system homeostasis, therefore derangement of ANS function at any level is manifested by cardiovascular reflexes integrity evaluation test.[8]

Quantitative cardiovascular autonomic function tests are widely used to detect, verify, and quantify the cardiovascular autonomic dysfunction. They have been tested for their validity and reliability. These tests are performed since their procedures are straightforward, reproducible, and non-invasive. Hence, in the present study, non-invasive autonomic function tests were used to demonstrate the effect of chronic abuse of different drugs on autonomic functions in order to evaluate the presence of any impairment of the autonomic activity in such individuals.

MATERIALS AND METHODS

The present cross-sectional study was carried out in the Department of Physiology, GGS Medical College, Faridkot, Punjab, India, during August 2012 to July 2013 in a sample of 50 drug abusers within the age group of 15-45 years, as well as in age matched 50 healthy controls. The control subjects were recruited randomly from nearby residential areas of the institution and the cases were taken from the patients admitted in Drug De-addiction Centre of this tertiary health care institute of Punjab by convenient sampling. The study was approved by the Institutional Research and Ethics Committee. Written informed consent was obtained from each individual as per the guidelines of Helsinki.

A self-designed, pre-tested substance use questionnaire (proforma) was administered to all subjects prior to the test where the type of substance abuse, family history of substance abuse, its frequency, quantity, and density of substance consumption, age at first substance abuse, total duration of substance use, time of last use was determined.

The substance abusers which were recruited for this study were alcoholics, opiate addicts (heroin, morphine), tobacco chewers/smokers, pharmaceutical drugs addicts (using cough syrups, pain killers, anti-emetics, etc.).

Those subjects with a history of any major illness such as hypertension, diabetes mellitus, and peripheral neuropathy in the past or present were excluded from the present study. The subjects were instructed not to consume coffee, tea, or cola, 12 h before the tests and were asked to have a light breakfast 2 h before the tests. The subjects were asked to relax in the supine position for 30 min. The resting heart rate was recorded on a standard electrocardiograph (ECG) from lead II. The blood pressure (BP) was measured by using a sphygmomanometer. The following cardiovascular autonomic function tests were performed.

Parasympathetic Function Test

Heart rate response to standing (postural tachycardia index)

The subjects were asked to lie on the examination table quietly and the resting heart rate was being recorded on the ECG. They were then asked to stand-up unaided, while the ECG was continuously recorded for another 1 min. The shortest R-R interval at or around the 15th beat and the longest R-R interval at or around the 30th beat were measured.[9] The result was expressed as 30:15 R-R ratio, i.e., longest R-R interval at the 30th beat/shortest R-R interval at the 15th beat. It is more than 1.04 in normal subjects and <1.0 when there is autonomic disturbance. This test is considered as a measure of cardiac vagal function.

Sympathetic Function Test

The sustained handgrip test

The subjects performed maximum voluntary contraction (MVC) by gripping the hand grip dynamometer, as hard as possible for few seconds and maximum force exerted was noted down. After giving rest for few minutes, the subjects performed isometric exercise at 30% of MVC by gripping the hand grip dynamometer for 3-5 min or till the subject could sustain the effort comfortably. Systolic BP (SBP) and diastolic BP (DBP) were recorded at an interval of 1 min during the period of exercise and change in SBP and DBP were noted. The response was considered as the difference between maximum BP obtained during the exercise and the resting BP.[10] The value of more than 15 mm of Hg rise in DBP was taken as normal sympathetic response, 11-15 mm of Hg as borderline, and 10 mm of Hg or less as abnormal. This test is an indicator of the sympathetic insufficiency.

Statistical Analysis

The collected data were analyzed by applying student unpaired *t*-test using the SPSS system (version 16.0 SPSS Inc., Chicago, IL, USA). A $P < 0.05$ was considered to be statistically significant.

RESULTS

After applying the Student's *t*-test for the difference between the two sample means, a highly significant difference was observed between the mean values of the Parasympathetic function test (30:15 ratio) in the drug abusers and controls (i.e., $P < 0.0001$). It was seen that the 30:15 ratio (response to standing) had significantly decreased in the drug abusers as compared to those in the controls (Table 1).

After applying the Student's *t*-test for the difference between the two sample means, an extremely significant difference was observed between the mean values of the sustained handgrip test in the drug abusers and controls (i.e., $P < 0.0001$). It was seen that the response in drug abusers was blunted and came in the range of borderline response and also the difference was statistically highly significant (Table 2).

Table 1: Comparison of mean values of autonomic function tests in drug abusers and controls (parasympathetic function test)

Parasympathetic function test	Mean±SD		*P* value	Significance
	Drug abusers (*n*=50)	Controls (*n*=50)		
30:15 ratio (response to standing)	0.99±0.07	1.09±0.1	0.0001	HS

HS: Highly significant, SD: Standard deviation

Table 2: Comparison of mean values of autonomic function tests in drug abusers and controls (sympathetic function test)

Sympathetic function test	Mean±SD		*P* value	Significance
	Drug abusers (*n*=50)	Controls (*n*=50)		
Sustained handgrip test (rise in diastolic pressure) mm hg	11.92±5.08	15.68±5.15	0.0004	HS

HS: Highly significant, SD: Standard deviation

DISCUSSION

In this study, heart rate response to standing was measured (30:15 ratio) to assess the parasympathetic activity and BP responses to sustained hand grip was measured to assess sympathetic activity. The 30:15 ratio or the response to standing is a parameter which is useful for assessing the reactivity of the parasympathetic system. In this study, a decrease in the 30:15 ratio was found to be statistically highly significant in the drug abusers (0.99 ± 0.07) as compared to that in the controls (1.09 ± 0.1), thereby indicating a reduced parasympathetic activity. In the sustained handgrip test, we measured the rise in the DBP at the point, just before the release of the handgrip and it was seen that the rise in the diastolic pressure was significantly less in the drug addicts (11.92 ± 5.08) as compared to that in the controls (15.68 ± 5.15), thus suggesting a decrease in the sympathetic reactivity. It could be due to the damage to the vagus nerve because of chronic use of drugs leading to decrease in vagal tone and hence increase in sympathetic reactivity.

In previous studies, researchers found the similar results. Gould et al. (1986) and Tayade and Kulkarni (2013) found statistically highly significant changes in the 30:15 ratio in smokers as compared to those in the non-smokers.[11,12] Similarly, Tayade and Kulkarni (2013) and Mervi et al. (1994) also found that the rise in the diastolic pressure was significantly less in the smokers as compared to that in the non-smokers, thus suggesting a decrease in the sympathetic reactivity.[12,13] The reason could be that smoking impairs the barore flex sensitivity in humans, which leads to increase in the BP and the heart rate due to increase in the levels of plasma catecholamines.[14,15]

Similarly, Choudhary et al. also showed a marked difference in all parasympathetic and sympathetic nerve function tests

in the opium addict and control group. The values of 30:15 ratio were highly significantly lower ($P < 0.001$) in opium addict group compared to those of control. While in hand grip test, there was significant difference in SBP difference ($P > 0.05$) and statistically highly significant decrease in DBP ($P < 0.001$).[16] The results of significantly lower DBP in drug addicts as compared to controls were also reported by other studies.[17,18] Moreover, Johnson et al. (1988) have studied extensively on parasympathetic dysfunction affecting the vague nerve in heavy drinkers who shows depressed reflex heart rate responses. Hence, in alcoholics, there is a strong evidence of parasympathetic neuropathy.[19]

Malpas et al. (1991) studied cardiac autonomic function in 23 alcohol dependent men by standard tests of autonomic function. They found, in all there was peripheral or CNS damage or both and some showed vagal neuropathy.[20] Chronic effects of alcohol are due to thiamine deficiency. Chronic deficiency leads to degeneration of nerve cells, reactive gliosis, and atrophy of cerebellum and peripheral nerves including autonomic nerves.[5]

Different investigators suggested that the vagal tone is reduced or loss of vagal tone occur in opium abusers. As a consequence barore flex activity may be decreased. The reason for decrease in parasympathetic tone in opium addicts could be due its interference to release of neurotransmitter at preganglionic parasympathetic efferent neurons and its peripheral anticholinergic effect.[21] The decrease sympathetic autonomic tone in opium addicts could be that the morphine decrease the central sympathetic outflow and its inhibitory effect on release of neurotransmitter in preganglionic neurons and also its direct antagonize action of sympathetic effect on end organ.[21]

Limitation of Study

The limitations of the study is small sample size and also the effect of duration of exposure to different drugs on cardiovascular autonomic functions can be studied between different drug abusers and be the area of future research.

CONCLUSION

This study provides good evidence for autonomic dysfunction following chronic abuse of different drugs. The aim of the current study was to create awareness among different drug addicts and in society about harmful effects of drug addiction and drug dependence on nervous system mainly autonomic functions. By using these simple and non-invasive tests, we can detect the early involvement of the ANS before the clinically-related symptoms appear and they are thus useful in taking steps to prevent the further progress of the disease.

REFERENCES

1. Kalant H. Opium revisited: A brief review of its nature, composition, non-medical use and relative risks. Addiction. 1997;92(3):267-77.
2. Holaday JW. Cardiovascular effects of endogenous opiate systems. Annu Rev Pharmacol Toxicol. 1983;23:541-94.
3. Szczensy LB, Holbrook JR. Cigarette Smoking. In: William RN, editor. Environmental and Occupational Medicine. 2nd ed. Boston: Little Brown and Company; 1992. p. 1211-22.
4. Sharma S. New approaches in smoking cessation. Indian Heart J. 2008;60 2 Suppl B: B34-7.
5. Thirumaran M, Balasubramanian K, Rao BV, Muralikrishnan. Heart rate variability analysis in alcohol dependant individuals using time domain measures. Sch J Appl Med Sci. 2013;1(5):419-22.
6. Duncan G, Johnson RH, Lambie DG, Whiteside EA. Evidence of vagal neuropathy in chronic alcoholics. Lancet. 1980;2(8203):1053-7.
7. Grover S. The effect of drug abuse on society. Available from: http://www.ehow.com/087932_effect-drug-abuse-society.html. [Last cited on 2014 Jul 07].
8. Kaijser L. Autonomic nerve function tests – Need for standardization? Clin Physiol. 1986;6:475-9.
9. Piha SJ. Cardiovascular autonomic function tests. Responses in healthy subjects and determination of age related reference value. Rehabil Res Cent. 1988:1-148.
10. Kapoor N, Sharma R, Ashat M, Huria A, Mishra G. Assessment of cardiovascular autonomic functions to predict development of pregnancy used hypertension. Nepal J Obstet Gynaecol. 2011;6(1):41-5.
11. Gould GA, Ashworth M, Lewis GT. Are cardiovascular reflexes more commonly impaired in patients with bronchial carcinoma? Thorax. 1986;41(5):372-5.
12. Tayade MC, Kulkarni NB. The effect of smoking on the cardiovascular autonomic functions: A cross sectional study. J Clin Diagn Res. 2013;7(7):1307-10.
13. Kotamäki M. Smoking induced differences in autonomic responses in military pilot candidates. Clin Auton Res. 1995;5(1):31-6.
14. Manecia G, Groppelli A, Di Rienzo M, Castiglioni P, Parati G. Smoking impairs baroreflex sensitivity in humans. Circulation. 1997;273(3):H1555-60.
15. Grassi G, Seravalle G, Calhoun DA, Bolla GB, Giannattasio C, Marabini M, et al. Mechanisms responsible for sympathetic activation by cigarette smoking in humans. Circulation. 1994;90(1):248-53.
16. Choudhary K, Chawla VK, Choudhary S, Chawdhary V, Choudhary R. A study on autonomic functions in chronic opium abusers. Sch J Appl Med Sci. 2014;2(6C):3000-4.
17. Kapoor R, Singh SH, Gandhi A. Autonomic functions and audiovisual reaction time in heroin addicts. Indian J Physiol Pharmacol. 1993;37(3):209-12.
18. Prystav GH. Autonomic responsivity to sensory stimulation in drug addicts. Psychophysiology. 1975;12(2):170-8.
19. Johnson RH, Robinson BJ. Mortality in alcoholics with autonomic neuropathy. J Neurol Neurosurg Psychiatry.

1988;51(4):476-80.
20. Malpas SC, Whiteside EA, Maling TJ. Heart rate variability and cardiac autonomic function in men with chronic alcohol dependence. Br Heart J. 1991;65(2):84-8.
21. Opioid agonists and antagonists. Available from: http://www.icuadelaide.com.au/files/primary/pharmacology/opioids.pdf 2014. [Last cited on 2015 Apr 10].

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