Indian Journal of Psychiatry 54(3), Jul-Sep 2012

Alcohol-dependence syndrome: Postural challenge on heart rate variability

S. Sucharita1,2, Johnson Pradeep3, Anoop Vincent3, M. Vaz1,2, K. Srinivasan1,3
1Human Physiological Laboratory, St. John’s Research Institute, St. John’s National Academy of Health Sciences, 2Department of Physiology, St. John’s Medical College, 3Department of Psychiatry, St. John’s Medical College and Hospital, Bangalore, Karnataka, India

ABSTRACT

Background: Cardiac autonomic involvement in Alcohol-Dependence Syndrome (ADS) patients has been demonstrated using conventional autonomic tests. Resting heart rate variability (HRV) without normalization has also been reported.

Aims: To evaluate cardiac autonomic changes with postural challenge using HRV in ADS and controls while controlling for confounding factors.

Settings and Design: Cross-sectional study involving 27 male subjects with ADS and age-matched healthy controls.

Materials and Methods: Clinical assessments included Schedules for Clinical Assessment in Neuropsychiatry and Severity of Alcohol Dependence Questionnaire. Spectral measures of HRV while lying and with active standing were assessed.

Results: There was an attenuated response in delta high-frequency (P=0.06) and delta low-frequency (P=0.04) power to standing in ADS subjects compared with controls.

Conclusion: Patients with ADS appear to have attenuated cardiac vagal and sympathetic responses to standing. HRV with postural challenge may help earlier recognition of autonomic dysfunction in ADS.

Key words: Alcohol-dependence syndrome, cardiac sympathetic and parasympathetic dysfunctions, heart rate variability, postural challenge

INTRODUCTION

It has been estimated that about 62.5 million in India consume alcohol and that there has been a significant increase in the per capita consumption of alcohol in recent times.[1] The lifetime risk of developing alcohol dependence in men is around 10%, and this constitutes a significant public health problem.[2] Autonomic nervous system dysfunction affecting sudomotor, vasomotor and cardiac function has been described in alcohol dependence, but has been less clearly evaluated than in other conditions such as diabetes.[3] Recent studies using conventional autonomic tests have indicated that cardiac autonomic neuropathy in patients with Alcohol-Dependence Syndrome (ADS) may show reversal with strict abstinence.[4]

Many factors associated with ADS are known to impact measures of autonomic function. These include co-morbid psychiatric conditions such as depression and anxiety, liver disease, duration of ADS, concurrent psychotropic medications including medications used to treat alcohol withdrawal states, patient’s nutritional status and presence of peripheral neuropathy. In most of the studies of cardiac autonomic function in alcohol-dependent subjects, investigators have failed to take into account many of these
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In addition, some of the earlier studies carried out prior to the Task Force recommendations have used different frequency ranges for the power spectra without normalization for total power, while others have used only the time domain method for heart rate variability (HRV) analysis. The current study attempts to control for some of these confounders within the limits of the study design to evaluate the true autonomic changes in ADS. The current study also uses postural challenge as a stimulus to evaluate the autonomic changes as previous studies have shown that various physiological maneuvers such as active standing, passive head-up tilt or active standing that impose a perturbation on the steady functioning of the autonomic nervous system may help uncover subtle deficits in autonomic function.

MATERIALS AND METHODS

Twenty-seven male subjects with ADS who were admitted to an inpatient deaddiction program following detoxification were recruited in the study. They were screened for the severity of withdrawal symptoms using Clinical Institute Withdrawal Assessment of Alcohol scale, revised (CIWA-Ar).[7] and were included in the study only if their score was less than eight. Exclusion criteria included medical disorders (hypertension, cardiac disorders, liver disease including cirrhosis and hepatitis, pancreatitis, chronic lung disease, diabetes mellitus, thyroid dysfunction), major psychiatric disorders such as psychotic, depressive and anxiety disorders, alcohol-related delirium and clinical nutritional deficiencies. Healthy, age-matched controls were also recruited. None of the control subjects drank alcohol currently or in the past. Before recruitment, details of the procedure were discussed, an explanatory statement was provided to the subjects and written, informed consent was taken. The study was approved by the Institutional Ethics Committee.

The study subjects were diagnosed as ADS using ICD-10 diagnostic criteria,[8] the age of onset of starting was assessed using the definition of Grant et al.[9] age of onset of problem drinking, dependence and total duration of drinking were assessed using alcohol section of Schedules for Clinical Assessment in Neuropsychiatry (SCAN).[10] and the severity of alcohol dependence was assessed using Severity of Alcohol Dependence Questionnaire (SADQ).[11] Subjects were questioned for symptoms suggestive of autonomic nervous dysfunction and underwent a detailed physical examination that included a comprehensive clinical neurological examination and anthropometric measures (height, weight, waist and hip circumference). Routine laboratory tests included resting ECG, chest X-ray, liver function tests and pancreatic enzymes, blood glucose, hemoglobin and coagulation parameters. Patients were detoxified, medication-free and were between 14 and 21 days after the last drink at the time of autonomic evaluation. Autonomic evaluation was performed early in the morning after an overnight fast. Subjects rested for 30 min so that sympathoadrenal activation would return to baseline values as suggested by Copeland et al.[12] Beat-to-beat heart rate evaluation was performed for a total duration of 10 min (5 min supine and 5 min standing). Data were subjected to power spectral analysis and details regarding signal acquisition and power spectral analysis of heart rate variability have been described earlier.[13,14]

RESULTS

The mean age of the alcohol dependence group and control participants was 35.6±7.3 years vs. 35.4±7.9 years, respectively. The mean age of starting alcohol use, problem drinking and dependence was 17.7±9.1 years, 21.3±10.1 years and 25.2±12.6 years, respectively. The mean severity scores was 27.7±17.9 and the duration of alcohol use was 7.56±5.59 years. Anthropometric measurements were similar between ADS subjects and controls.

The resting heart rate and systolic and diastolic blood pressures were also similar in both the groups. Peripheral neural examination was normal and none of the subjects had clinically significant autonomic symptoms. In both groups, evaluated separately, high frequency (HF) in absolute units fell significantly with standing while low frequency (LF) (normalized) and the LF/HF ratio rose significantly [Table 1]. Delta changes in HRV measures (standing-supine) were also calculated. These data indicated that the alcohol-dependence group had a lower delta HF (P=0.06) and a significantly lower delta LF (P=0.04) response when expressed in absolute units compared with the controls [Table 1]. These delta differences were not statistically significant when the data were represented in normalized units.

None of the clinical variables such as age of starting alcohol use, age of onset of problem drinking, age of onset of dependence and duration of alcohol use within the subjects with ADS correlated with the heart rate variability parameters.

DISCUSSION

The present study examined cardiac autonomic modulation with postural stress in a carefully selected group of male patients with ADS and healthy controls using spectral measures of heart rate variability. The data indicate that both groups had vagal withdrawal with standing; the change (delta HF) was, however, smaller in patients with ADS as compared with that in the healthy controls. Cardiac vagal involvement in chronic alcoholic dependence syndrome has been reported using conventional tests.[15] However, an attenuated response in LF power to active standing
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suggestive of cardiac sympathetic involvement, to the best of our knowledge, has not been reported by others. this may be related to the measurement of HRV that we adopted in this study, namely change in HRV measures over resting values during the first few minutes in response to active standing. previous research has suggested that perturbation in autonomic nervous system may help uncover subtle deficits in cardiac autonomic system that may be missed if one relies only on baseline measures of HRV. further, the role of LF component as a marker of sympathetic activity has been contested when interpreted during postural challenge. this could be overcome when change of posture is used as a stimulus, which leads to release of baroreceptor restraint of sympathetic activity together with vagal withdrawal. Therefore, LF is considered to be a marker of sympathetic activity when interpreted during postural challenge.

Although cardiac sympathetic involvement is considered to be rare among patients with ADS, a few instances of orthostatic hypotension have been reported in chronic alcohol-dependent individuals. None of the subjects from the present study had ever suffered from syncope. while the etiopathogenesis of alcohol-induced autonomic neuropathy is not known, the dose-dependent relationship between alcohol consumption and the degree of the lesions of the autonomic nervous activity suggests a direct toxic effect of alcohol or its metabolites on axons or neuron body cells through alterations in ionic channels, membrane fluidity and formation of oxygen free radicals are plausible mechanisms.

 Within the group of subjects with alcohol dependence, we did not find any associations between various clinical variables such as age of onset of drinking, age of onset of problem drinking, severity of ADS and measures of heart rate variability. This could be due to many factors. First, the sample size was relatively small and was calculated to allow detection of differences of HRV between the groups as a primary outcome. Second, subjects with ADS who had co-morbid medical/psychiatric conditions were not included in the study; these patients would likely be those with the most severe dependence. Thus, majority of the subjects included in the study were moderately dependent on alcohol according to SADQ. Finally, none of the participating subjects had any clinically significant autonomic symptoms.

In conclusion, in the present study, there were alterations in cardiac sympathetic and parasympathetic modulation using spectral measures of HRV in response to postural change in a group of well-characterized male subjects with ADS compared with healthy controls.

Clinical implications

This study has found that postural challenge combined with spectral measures of HRV uncovered cardiac sympathetic and parasympathetic alterations in cardiac autonomic function in patients with ADS even though they did not report any symptoms of autonomic dysfunction. This procedure can help clinicians in recognizing cardiac autonomic dysfunction early and can help implement therapeutic/preventive measures. Interventions aimed at arresting further declines in autonomic function could be the focus of future studies.

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Source of Support: Nil, Conflict of Interest: None declared