Original Article

Heart Rate Variability in Patients With Alcohol Withdrawal Syndrome

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ABSTRACT

Background: The purpose of this study was to clarify the dynamics of heart rate variability (HRV) in the dynamics of alcohol withdrawal syndrome relief.

Methods: We examined 31 patients at an average age of 43.9 ± 5.2 years with alcohol withdrawal syndrome (the middle stage, the period of maintenance therapy) and 15 volunteers of comparable age. The control points for assessing HRV were 1 to 2, 3 to 5, 6 to 9, and 10 to 15 days after stopping alcohol consumption. Electrocardiography was performed using the software and hardware complex Polyspectr-12 (Neurosoft, Russia). HRV was evaluated using a set of statistical and spectral analytical methods, including the coefficient of variation (%), and spectral analysis indicators (based on the fast Fourier transform algorithm using all points without smoothing). The geometric analysis of the cycles of nonlinear cardiac rhythm waves was performed using a chaos test via the method of Gavrilushkin (2007).

Results: In our patients with alcohol withdrawal syndrome in the rehabilitation period, there was a pronounced instability of the heart rhythm, which was manifested in the increasing role of its intracardiac regulation mechanisms and the stimulating effect of sympathicotonia. The most pronounced shifts in HRV were detected in the period from 3 to 9 days after the cessation of alcohol consumption. Additionally, the risk of arrhythmogenic complications in alcohol withdrawal syndrome was highest from the third to the ninth day of the rehabilitation period.

Conclusions: Our patients with alcohol withdrawal syndrome in the rehabilitation period exhibited a pronounced instability in their heart rhythm, manifesting itself in the increasing role of its intracardiac regulation mechanisms and the stimulating effect of sympathicotonia. *(Iranian Heart Journal 2020; 21(4): 100-106)*

KEYWORDS: Alcohol withdrawal syndrome, Heart rate variability, Cardiac rhythm, Spectral analysis

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The negative impact of systematic alcohol consumption on the cardiovascular system is well known. [1-5] At the same time, cardiovascular pathology may be present in the dynamics of the alcoholization of patients, [3, 5-7] burdening, in particular, the tolerance of the withdrawal period, [2, 3, 8-10], and develop as a result of ethanol-induced damage to the circulatory system and blood elements. [9-11] Thus, numerous manifestations of cardiomyopathy of alcoholic origin and alcohol-dependent pathology of the microcirculatory bed and cerebral vessels have been described. [1, 4, 8, 12] In individual studies, it has been shown that the most significant influence on the severity and generalization of the pathology of the cardiovascular system of this genesis is the age at which alcohol-containing products are consumed. [4, 7, 12, 13]

Despite the abundance of information about the nature of the damage to the cardiovascular system of patients, there are relatively few data concerning the features and completeness of the recovery of heart rate variability (HRV). This is also important from the point of view of the high rhythm of arrhythmias in this group of patients during abstinence. [2, 13] In addition, the assessment of HRV can act as the fastest and most sensitive parameter for relieving alcohol withdrawal syndrome in general. [5, 7]

In this regard, we sought to clarify the dynamics of HRV in the dynamics of alcohol withdrawal syndrome relief.

METHODS

We examined 31 patients with alcohol withdrawal syndrome (the main diagnosis: F10.222, dependence syndrome due to alcohol abuse, the middle stage, the period of maintenance therapy; the average age = 43.9 ± 5.2 y) and 15 volunteers of comparable age. The main group and the comparison group were mainly represented by men (83.9% and 80% of the subjects, respectively). The correction of withdrawal syndrome was performed according to the traditional scheme.

The control points for assessing HRV were 1 to 2, 3 to 5, 6 to 9, and 10 to 15 days after stopping alcohol consumption. Electrocardiography was performed using the software and hardware complex Polyspectr-12 (Neurosoft, Russia). The study of HRV indicators was performed in the supine position in compliance with the standard conditions for registering a cardiointervalogram. HRV was evaluated using a set of statistical and spectral analytical methods, including the coefficient of variation (%), and spectral analysis indicators (based on the fast Fourier transform algorithm using all points without smoothing): the total power of the spectrum (TR, ms^2), the absolute and relative powers of the low-frequency (PLF, ms^2) and high-frequency (PHF, ms^2) bands, and the power ratio (LF/HF, in normalized units). [5, 7]

The geometric analysis of the cycles of nonlinear cardiac rhythm waves was performed using a chaos test via the method of Gavrilushkin (2007) with the selection of cycles or shapes with different contents of points in them (Nn). [14] The main evaluation parameters of the chaos test were the predictor of the heart rate (the indicator of isolation of the myocardium from external regulatory influences), the levels of imbalance in regulation and autonomic system balance, and the stress level in regulatory systems. [7, 14]

Statistical data processing was performed using Microsoft Excel 2007 and the SPSS software, version 11.0.

RESULTS and DISCUSSION

Considering the formed main group of subjects, it could be noted that its representatives were characterized by a fairly early start of systematic alcohol

consumption (the average value for the group = 24.6 ± 4.2 y) and a long period of alcoholism (18.6 ± 5.4 y). In addition, the majority of the patients (89.3%) had a burdened heredity for alcoholism. All this suggests that by the time of the examination, examined subjects might have a detected pathology of the cardiovascular system, which can put an imprint on HRV.

The analysis of the primary statistical indicators of heart activity (the average duration of cardiac RR-interval [RRNN] and the standard deviation from the average cardiac cycle [SDNN]) allowed us to establish significant differences from the level of the comparison group only at the early stage of rehabilitation (the first-second day after stopping alcohol consumption). They appeared in moderate tachycardia, accompanied by an increase in SDNN values ($P < 0.05$ compared with the level typical for healthy volunteers).

In our opinion, the data obtained for the parameters pNN50 (the proportion of cardiac RR-cycles whose duration differs by 50 ms from the previous one) and the coefficient of variation (the maximum deviation of the duration of the cardiac cycle) are of particular diagnostic interest. These indicators, statistically reflecting the stability of heart rate regulation, can act as indicators of the risk of arrhythmias. [1, 4, 8]

We found that the level of the pNN50 instability of the cardiac rhythm in our patients with alcohol withdrawal syndrome was present for up to between 6 and 9 days. Concerning the coefficient of variation in the main group, as a whole, we observed significant differences only within 3 to 5 days after the cessation of alcohol intake (Fig. 1). At the same time, the proportion of patients with a high risk of arrhythmias was 36.4% on days 1 to 2 of rehabilitation, 41.2% on days 3 to 5, 38.9% on days 6 to 9, and only 18.1% thereafter. Therefore, it is advisable to control the development of this

complication for up to 9 days of the withdrawal period.

The trends associated with heart rate dysregulation revealed by statistical indicators were also observed in relation to cardiorespiratory coupling (Fig. 2). Thus, the initial period of rehabilitation (1–5 days of treatment) was characterized by a significant decrease in the level of this parameter ($P < 0.01$), followed by its normalization by 6 to 9 days. This further indicates the instability of heart activity during this period.

The revealed changes in the structure and pattern of the heart rate total reflect the imbalance of regulatory influences that result from the action on the myocardium, primarily of the components of the autonomic nervous system. The analysis of HRV data by Baevsky allowed us to establish a pronounced activation of the sympathetic regulation circuit (according to the level of the stress index [$P < 0.05$] relative to the subjects of the comparison group), which also persisted until the ninth day after the cessation of alcohol intake (Fig. 3A). These changes were naturally accompanied by a decrease in the amplitude of the mode, which significantly differed from the norm from day 3 to day 9 of the rehabilitation period ($P < 0.05$). The instability of the total vegetative effect on the cardiac rhythm was also reflected in the dynamics of spectral analysis parameters, in particular, the integral ratio of spectrum power in the low- and high-frequency ranges (Fig. 3B). We found that changes in this indicator in patients with alcohol withdrawal syndrome were multidirectional. Accordingly, a significant shift toward moderate sympathicotonia was detected only on days 1 to 2 of the rehabilitation period ($P < 0.05$), while afterward, it increased non-linearly, returning to the normal range and significantly exceeding the initial level ($P < 0.05$ compared with the beginning of

treatment). Consequently, adequate systemic correction of patients' condition contributes to the normalization of regulatory effects on the heart rate, reducing the risk of the occurrence and/or cardiac complications of chronic alcoholism.

The trends discussed above were fully confirmed and clarified by the results of the chaos analysis of the cardiac rhythm (Fig. 4). In particular, the dynamics of the heart rate predictor, indicating the prevalence of intracardiac regulation mechanisms over extracardiac ones, indicated a significant isolation of the myocardium of patients with

withdrawal syndrome during the period at all the control points ($P < 0.05$ compared with the level typical for healthy people). The instability of autonomic influences on the rhythm shown above was manifested in an increase in the regulation imbalance and a combined decrease in the value of the parameter "autonomic misbalance", calculated from the indicators of the chaos test ($P < 0.05$). The demonstrated features of cardiac activity also predetermined a high level of stress in the regulatory systems.
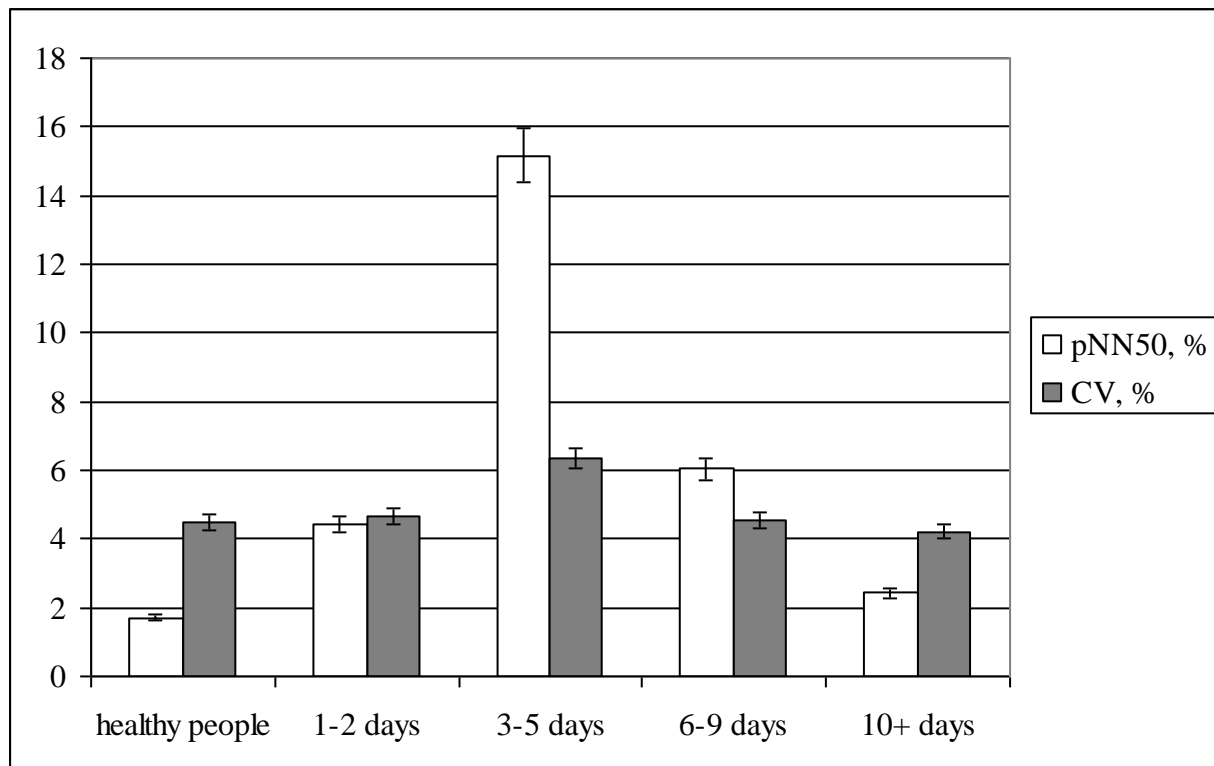

Figure 1: Statistical parameters of heart rate variability in the patients with alcohol withdrawal syndrome are illustrated herein.
pNN50: Proportion of the cardiac cycles whose duration differs by 50 ms from the previous one; CV, Coefficient of variation (maximum deviation of the duration of the cardiac cycle)
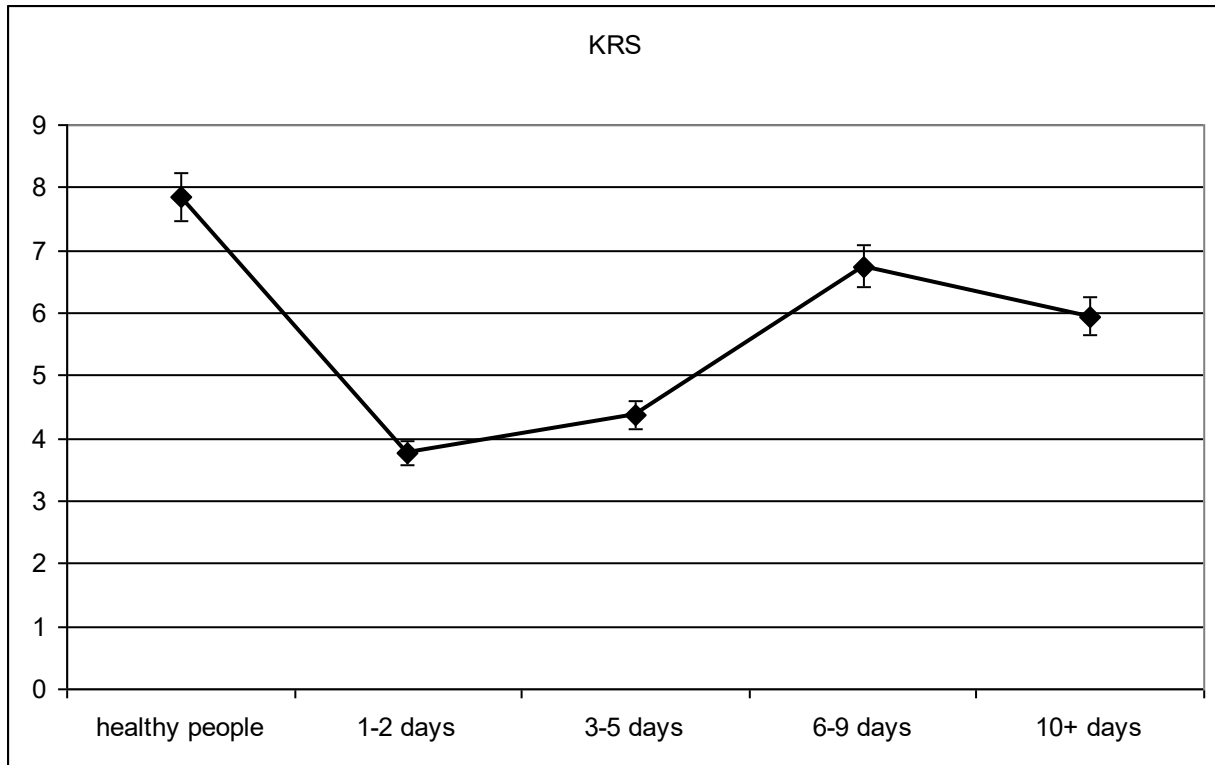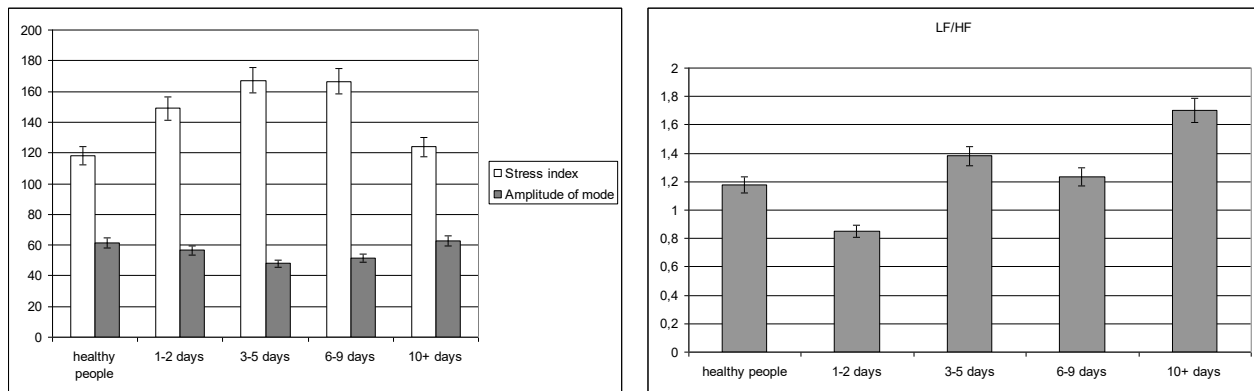
Figure 2: Cardiorespiratory coupling in the patients with alcohol withdrawal syndrome is depicted herein (in rel. un.).

A. Statistical parameters of heart rate variability   B. Spectral analysis of heart rate variability

Figure 3: Dynamics of the statistical and spectral parameters of heart rate variability in the patients with alcohol withdrawal syndrome are illustrated herein.
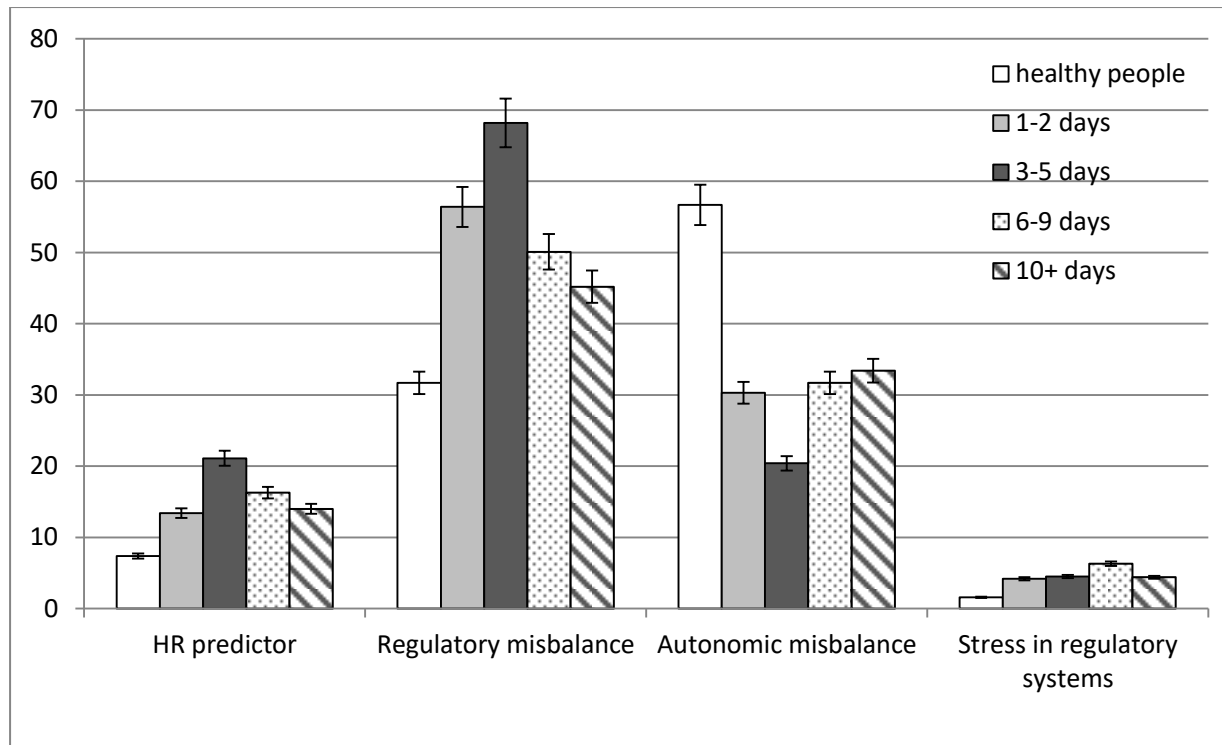
Figure 4: Results of the chaos analysis of the cardiac rhythm in the patients with alcohol withdrawal syndrome are illustrated herein (in rel. un.).

CONCLUSIONS

The results of the present study showed that in patients with alcohol withdrawal syndrome in the rehabilitation period, there was a pronounced instability of the heart rhythm, which was manifested in the increasing role of its intracardiac regulation mechanisms and the stimulating effect of sympathicotonia. The most pronounced shifts in HRV were detected in the period from 3 to 9 days after the cessation of alcohol consumption. Further, the risk of arrhythmogenic complications in alcohol withdrawal syndrome was highest from the third to the ninth day of the rehabilitation period.

Conflict of Interest
The authors hereby declare no conflicts of interest.

Ethical Approval

All the procedures performed in the current study were in accordance with the standards of the Local Ethics Committee of Privolzhsky Research Medical University and the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

REFERENCES

1. Carr G. Alcoholism: a modern look at an ancient illness. Prim. Care. 2011;38(1):9-21.

2. George A, Figueredo VM. Alcohol and arrhythmias: A comprehensive review. J. Cardiov. Med. (Hagerstown). 2010;11:221-228.

3. Husain K, Mejia J, Lalla J, Kazim S. Dose response of alcohol-induced changes in BP, nitric oxide and antioxidants in rat plasma. Pharmacol Res 2005;51(4):337–343.

4. Ohkubo T, Metoki H, Imai Y. Alcohol intake, circadian blood pressure variation, and stroke. Hypertension. 2009;53:4-5.

5. Romanowicz M, et al. Changes in heart rate variability associated with acute alcohol consumption: current knowledge and implications for practice and research. Alcohol Clin. Exp. Res. 2011;35(6):1092-1105.

6. Guo R, Ren J. Alcohol and acetaldehyde in public health: From marvel to menace. Int. J. Environ. Res. Public Health. 2010;7:1285-1301.

7. Martusevich AK, Peretyagin SP, Zhukova NE. Adaptive possibilities of the heart under intoxication of different intensity. Functional diagnostics. 2011;(2):20-23.

8. Albano E. Alcohol, oxidative stress and free radical damage. Proc. Nutr. Soc. 2006;65:278-290.

9. Bailey SM. A review of the role of reactive oxygen and nitrogen species in alcohol-induced mitochondrial energy metabolism. Free Radic. Res. 2003;37:585-596.

10. Bardag-Gorce F, et al. The cyclic pattern of blood alcohol levels during continuous ethanol feeding in rats: the effect of feeding S-adenosylmethionine. Exp. Mol. Pathol. 2010;88:380-387.

11. Cederbaum AI, Lu Y, Wu D. Role of oxidative stress in alcohol-induced liver injury. Arch. Toxicol. 2009;83:519-548.

12. Chen Y, et al. Effects of alcohol on bone metabolism and biomechanical property of mice. Sheng Wu Yi Xue Gong Cheng Xue Za Zhi. 2009;26:780-782.

13. Schuchardt V. Alcohol and the peripheral nervous system. Umsch 2000;57(4):196–9.

14. Kiselev SV, Gavrilushkin AP, Medvedev AP, Shelepnev AV. Geometrical analysis of non-linear chaotic heart rate fluctuations as a novel method of functional diagnostics of the cardiovascular system. Russian Journal of Cardiology. 2000;(6):76-79. (In Russ.)