SPECTRAL ANALYSIS OF HEART RATE VARIABILITY IN NEURALLY MEDIATED SYNCOPE COMPARED TO HEALTHY SUBJECTS

SUMMARY:
Heart rate variability (HRV) represents the widely used method for the assessment of the autonomic tone. Time domain parameters, like standard deviation of all RR intervals and spectral analysis, expressed as the spectral power density (PSD) in both low frequency (LF: 0.05 – 0.15Hz) and high frequency (HF: 0.15 – 0.50 Hz) are the most frequent parameters used in clinical practice. Low HRV parameters in heart failure and myocardial infarction are correlated with the risk of a high incidence for ventricular arrhythmias and sudden cardiac death. The prognostic impact of low HRV parameters is well studied in numerous studies. Neurally mediated syncope represents one of the most frequent conditions for admission and hospitalization. The aim of our study was to assess the autonomic imbalance during head-up tilt test in patients that had syncope and to compare it with healthy subjects. Spectral analysis of the ECG signals was performed using the autoregressive analysis.

Keywords: Syncope, autonomic imbalance, healthy subjects, tilt test.

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BACKGROUND

Syncope is a symptom characterized by a period of transient loss of consciousness (T-LOC) that is brief in duration, self-limited, and due to a spontaneously reversible inadequacy of cerebral nutrient flow. The most common responsible factor is cerebral hypoperfusion due to transient hypotension. Syncope has many possible precipitating causes. However, the principal etiologies may be classified into three categories: (1) reflex (neurally mediated) faints, (2) orthostatic faints, and (3) cardiac (cardiovascular) faints [1].

Neurally mediated syncope is a disorder of the autonomic regulation of postural tone, which results in hypotension, bradycardia, and loss of consciousness. A wide variety of stimuli can trigger this reflex, the most common stimulus being orthostatic stress. Typically, a patient with neurally mediated syncope experiences nausea, lightheadedness, a feeling of warmth, and pallor before abruptly losing consciousness [2]. Syncope is a sudden loss of postural tone followed by rapid, spontaneous recovery. It affects all ages, from the pediatric to the elderly [2]. The human body has the capacity to maintain a stable blood pressure and to react at various conditions that change this steady state. Main factors are postural changes, and the main mechanisms are reflex mediated. Prolonged stand-up is followed by a shifting of blood from the thorax to the abdomen and lower extremities. This shift in blood volume can markedly decrease the cardiac output, followed by loss of postural tone and faint.

The pathogenetic mechanisms of syncope are still poorly understood. It is emphasized that the stimulation of ventricular vagal receptors would be produced by an enhancement of heart contractility due to an exaggerated cardiac sympathetic activation. The possibility that an initial cardiac sympathetic overactivity might promote vasovagal reactions is supported by the clinical observation of a transient rise in heart rate before syncope [6]. This increase of the resting heart rate, leads to the hypothesis of an autonomic imbalance in syncope.

Spectral analysis of heart rate variability offers the opportunity to assess the contribution of both sympathetic and parasympathetic components in the modulation of the regulation mechanisms during neurally mediated syncope.

Numerous previous studies have observed different types of modulation by the sympathetic tone during syncope. It was noticed a heterogeneity of changes from increased sympathetic activity to unchanged contribution compared to basal conditions.

Heart rate variability, quantifies the contribution of the spectral components in the modulation of the regulation mechanisms involved in the pathogenesis of syncope. Very low frequency (VLF: 0.01 -0.05 Hz), low frequency (LF: 0.05 -0.15 Hz) and high frequency (HF: 0.15 - 0.50 Hz) are the main components of the spectral analysis. But two major oscillatory components can be identified in the power spectrum of RR variability: a high-frequency (HF) component at ‘0.25 Hz, considered a marker of vagal modulation of the sinoatrial node, and a low-frequency (LF) component at ‘0.10 Hz, considered, when normalized, a marker of sympathetic modulation [4].

Very low frequencies are modulated by thermoregulation and other complex mechanisms described in other studies (fig. 1). The guidelines for heart rate variability have been established in the mid 90’s, as emphasized by the Task Force of The European Society of Cardiology and The North American Society of Pacing and Electrophysiology [7].

Various spectral methods have been used for the analysis of the HRV, and they may be classified as nonparametric (fast Fourier transform) and parametric.

The main advantage of parametric methods such as autoregressive (AR) method is that the smoother spectral components can be distinguished independently of the selected frequency bands. Consequently, they allow an accurate estimation of power spectral density with automatic calculation of the LF and HF power components [6].

METHOD

The aim of our study was to highlight the complex heart rate modulation in patients with syncope and to analyze the behavior of RR intervals dynamics compared to young healthy subjects.

The study was performed at the Cardiology Clinic of the Emergency County Hospital Timis, University of Medicine “Victor Babes” Timisoara, Romania. The patients group (12 men, 8 women) with mean age 57.4 years, described syncope or pre-syncope symptomatology. A control group consisted of 12 young health subjects (5 men and 7 women) with mean age of 30.3 years was used to compare data and to record data in a healthy group. All subjects have been in sinus rhythm.

Subjects were placed on an electrically driven tilt table, and the ECG was monitored by a Cardiax V 3.50.4 ECG system by IMED Co Ltd, Hungary.
During the procedure subjects were asked to breathe at a constant rate of 15 breath/min (0.25 Hz). After 15 minutes in the supine position, the table was rotated for 15 minutes to a 90° upright position that was maintained for 30 minutes. None of the healthy subjects experienced syncope or any symptoms.

ECG signals and RR intervals were recorded and the spectral analysis was performed using fast Fourier transform (FFT) and autoregressive analysis (AR).

The R-R interval series corresponding to supine and standing position were selected, respectively, just before and just after the change of position. The FFT and AR spectra were then calculated from this interpolated and detrended 512 seconds window width R-R interval with HRV Analysis Software 1.1 for Windows (The Biomedical Signal Analysis Group, Department of Applied Physics University of Kuopio, Finland).

Two frequency bands were considered: (1) LF band from 0.045 to 0.15 Hz and (2) HF band from 0.15 to 0.4 Hz (fig. 1).

The AR spectrum was calculated by fitting a 32th-order AR model, into the R-R data [6]. Autoregressive analysis furnished both the power and the central frequency of the oscillatory components. The LF and HF components were defined as those with central frequencies within band limits. Central frequencies were around 0.1 Hz and 0.25 Hz for the LF and HF components, respectively [4, 6]. Low-frequency and HF oscillatory components are represented in absolute (square milliseconds) units.

### Statistical analysis

For the statistical analysis we have used Graph Pad Prism. All numeric variables were expressed as mean and the statistical analysis was performed using Student’s t-test and correlation analysis by Pearson method. A p value < 0.05 was considered statistically significant.

### RESULTS

The resting mean heart rate in the syncope patients group was 67 b/min compared to the healthy subjects, 76 beats/min (p: 0.01). During the 900 upright position the mean heart rate in the syncope patients group was 82b/min vs. 92 b/min in the young healthy group (p: 0.05). Statistically significant differences of the mean heart rate have been measured also between resting conditions and the 900 up-right position in both groups (table 1). The mean RR interval (ms.) didn’t show significant differences at 900 up-right position. The main resting parameters in resting conditions are summarized in table 1.

### Table 1. Clinical data in both study groups during resting conditions.

<table>
<thead>
<tr>
<th></th>
<th>Syncope</th>
<th>Healthy</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>57.4</td>
<td>30.3</td>
<td>0.0003</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>62.8</td>
<td>86.2</td>
<td>0.0003</td>
</tr>
<tr>
<td>Mean heart rate (b/min)</td>
<td>67.6</td>
<td>76.2</td>
<td>0.01</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>150</td>
<td>120</td>
<td>0.05</td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td>90</td>
<td>70</td>
<td>0.05</td>
</tr>
</tbody>
</table>
The head up tilt test and the 90° up-right position has induced changes in both clinical data and in the spectral analysis parameters of heart variability in the syncope patients group but also in the healthy subjects. In the syncope group the 90° up-right position is followed by an important increase of the mean heart rate, 67.6 b/min vs 82.3 b/min (p: 0.0002). This sympathetic over activity is also noticed in the healthy group even if not with the same magnitude, 76.2 b/min vs 92.8 b/min.

The spectral analysis of heart rate variability in both study groups, reflects the intensity of the sympathetic activity during the 90° up-right position, and the reduced vagal modulation of the heart rate. All this aspects are observed when the measurements are made in absolute (square milliseconds) units or reflected by the LF/HF ratio as a measure of the autonomic imbalance during head-up tilt test (Fig. 2).

The changes induced by 90° up-right position on the heart rate variability parameters, in time domain and in frequency domain are summarized in table 2. The spectral pattern of the heart rate variability are reflected in fig. 2.

The main spectral power is in the 0.01 – 0.15 Hz, reflecting a high sympathetic tone.

The AR analysis in some cases can be performed using higher model order to obtain a better representation of the spectral components of heart rate variability. In the case above, we have used an AR model of 30.

**DISCUSSIONS**

High resting heart rate and an increase of the sympathetic tone at 900 up-right position characterize the pattern of healthy subjects during the head-up tilt test, even in free of symptomatology subjects. This behavior reflects the autonomic modulation during postural changes.

In syncope patients, a lower mean heart rate in resting conditions will prove a significant increase of the values during head-up tilt test. In both situations we deal with a reduced vagal activity and a higher sympathetic tone activity. These changes are reflected independently of the method that is used to assess the spectral components of heart rate variability. Fast Fourier transform or autoregressive analysis reflects these aspects.

The specificity and sensitivity of the HUTT test are hard to determine because of methodologic differences in the test’s performance. The absence of a “gold standard” also makes it difficult to determine normal versus abnormal results. Nevertheless, with “normal” volunteers and with patients who have a history typical of NMS, the reported specificity is about 90%, and the reported sensitivity ranges from 32% to 85% [6]. Other studies [5] highlight the fact that the main effect of tilt test seems to be the reduction of the vagal activity rather the high sympathetic activity.

Our study is a focus in the mechanisms that are involved in the neutrally mediated syncope and highlight the contribution of the autonomic tone in both syncope patients and healthy subjects. Further studies will be focused on the correlation between heart rate and blood pressure during neutrally mediated syncope.

**Table 2.** Heart rate variability parameters during the 90° up-right position

<table>
<thead>
<tr>
<th></th>
<th>Syncope</th>
<th>Healthy</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean RR (ms)</td>
<td>829</td>
<td>765</td>
<td>ns</td>
</tr>
<tr>
<td>SDNN (ms)</td>
<td>69</td>
<td>68</td>
<td>ns</td>
</tr>
<tr>
<td>LF/HF</td>
<td>3.4</td>
<td>3.94</td>
<td>ns</td>
</tr>
</tbody>
</table>

SDNN – standard deviation of all RR intervals, LF/HF – autonomic index

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References:
2. Michele Brignole ·David G. Benditt SyncopeAn Evidence-Based Approach – Springer Verlag 2011