Analysis of the autonomic nervous system through barorreflex sensitivity processing during hemodialysis

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Abstract

Acute hypotensive episodes are common during dialysis sessions, and represent a serious problem. Spectral analysis of heart rate variability (HRV) and systolic blood pressure variability is performed to obtain barorreflex sensitivity (BRS) and to study the behaviour of the autonomic nervous system (ANS) during the hemodialysis. The BRS index in the HF band is significantly different in patients being prone and resistant to hypotension ($p<0.05$).

Keywords: Baroreflex Sensitivity, Dialysis, Heart Rate Variability, Hypotension, Systolic Blood Pressure Variability.

1 Introduction

One of the main problems during dialysis treatments are the hypotension events, which affect to nearly 3 out of every 10 patients, causing cardiocirculatory collapse, and the abrupt end of the dialysis. The origin is still unknown, and some studies have demonstrated that this hypotension events lead to an increase of mortality (Shoji et al., 2004). Due to this, it is highly desirable to develop methods to prevent these events.

The hypothesis of this study is that the origin of these hypotension events may be a malfunction of the autonomic nervous system (ANS). Baroreflex sensitivity (BRS) measures reflex changes in interbeat interval induced by changes in arterial pressure, and may not work properly in patients suffering these events (Rovere, Pinna and Raczak, 2008). There exist different methods to assess BRS, among which joint spectral analysis of heart rate variability (HRV) and systolic blood pressure variability (SBPV) is one of the most common. Three bands are established in the power spectrum of HRV and SBPV: very low frequency (VLF: < 0.04 Hz), low frequency (LF: 0.04 to 0.15 Hz) and high frequency (HF: 0.15 to 0.4 Hz).

We studied HRV and SBPV in a database of patients undergoing hemodialysis to determine whether hypotensions and/or patients prone to suffer hypotension events during hemodialysis can be predicted from BRS measurements.

The parameters used in this study are α_{LF}^{i} and α_{HF}^{i}, which represent BRS assessed by the ratio between HRV power and SBPV power in the LF and HF bands, respectively, computed only when spectral coherence between HRV and SBPV in the LF and HF bands exceed a statistically determined threshold.

2 Material and Methods

2.1 Database

The study population consists of 16 patients with end-stage renal failure who underwent regular hemodialysis threetimes a week. A total of 30 sessions were acquired during the entire clinical treatment at Park Dialys, Lund, Sweden, and Helsingborg Hospital, Helsingborg, Sweden, lasting from 3 to 5 hours, in order to obtain the electrocardiogram signal (ECG) and the blood pressure (BP) signal.

Each patient has been classified as being hypotension-resistant (R) or hypotension-prone (P) based on their previous clinical history. Besides, they have also been classified as being diabetic (D) or non-diabetic patients (ND), making four groups: RD, RND, PD and PND. See Table 1 for study population characteristics.

Symptomatic hypotension occurred in 5 of the 30 sessions (one in the resistant group and the others in the prone group), of which 2 were acute (systolic blood pressure fall larger than 30 mmHg per 10 minutes prior to hypotension).

The ECG signal was recorded using a standard 12-lead configuration, and digitalized at a sampling rate of 1000 Hz and amplitude resolution of 0.06 μV (Siemens-Elema AB, Sweden); the blood pressure signal was measured in the finger using a Finapres (Ohmeda, Netherlands) and sampled at a rate of 200 Hz with a MP100 data acquisition system (Biopac, USA).

The subsequent analysis was performed in 5-minute segments where stationarity of the cardiovascular signals was assumed.

Characteristic	R	P
# Patients	7	9
# Measurements	11	19
Male/Female	6/1	6/3
D / ND	3/4	5/4
Age (year)	58.6 ± 13.5	65.6 ± 10.6
Weight (kg)	86.9 ± 19.5	83.1 ± 19.9

Table 1. Study population characteristics

2.2 Heart rate variability

First, QRS detection marks are obtained from the ECG signal by ARISTOTLE, using a rule based on the QRS complex center of gravity. The heart rate (HR) signal is derived from the QRS detection marks, following a method based on the integral pulse frequency modulation (IPFM) model, which also accounts for the presence of ectopic beats (Mateo and Laguna, 2003), and sampled at 4 Hz obtaining $d_{HR}(n)$. The VLF component is obtained by low-pass filtering $d_{HR}(n)$ using a cut-off frequency of 0.03 Hz and denoted $d_{HRM}(n)$. Finally, the HRV signal is obtained as $d_{HRV}(n) = d_{HR}(n) - d_{HRM}(n)$.

For each 5-min segment the power spectrum of $d_{HRV}(n)$ is computed using the Welch periodogram with a rectangular window of 360 s overlapped 120 s. The power in the LF and HF bands is computed integrating the power spectrum in the corresponding bands, and denoted $P_{HR_{LF}}$ and $P_{HR_{HF}}$, respectively.

2.3 Systolic blood pressure variability

Systolic blood pressure measures are obtained detecting the maximum value of each pulse wave, using a method based on the derivative of the BP signal and a time-varying threshold. From the value and location of each maximum the systolic blood pressure signal, $d_{BP}(n)$, is computed using spline interpolation at 4 Hz. Using the same procedure as in the previous section, the following signals and parameters are computed: $d_{BPM}(n)$, $d_{BPV}(n)$, $P_{BP_{LF}}$ and $P_{BP_{HF}}$.

2.4 Barorreflex sensitivity

Then, BRS parameters are computed in the LF and HF bands as (Laude et al., 2004): $\alpha_{LF}^{\hat{}} = \frac{P_{HR_{LF}}}{P_{BP_{LF}}}$ and $\alpha_{HF}^{\hat{}} = \frac{P_{HR_{HF}}}{P_{BP_{HF}}}$, respectively. BRS parameters are considered only if the spectral coherence between $d_{HRV}(n)$ and $d_{BPV}(n)$ is above a statistically determined threshold of 0.7. The threshold is determined as the 97th percentile of the statistical distribution of the maximum value of the spectral coherence between two white noises. Spectral coherence is estimated using the minimum variance distorsionless response (MVDR) method (Benesty, Chen and Huang, 2006), which presents higher spectral resolution than Welch periodogram.

2.4 Statistical analysis

Each subject is characterized by the median value of $\alpha_{LF}^{\hat{}}$ and $\alpha_{HF}^{\hat{}}$ during the whole treatment. A Kolmogorov-Smirnov test is applied to the data to find out whether the data follows a normal distribution or not. The result of this test is negative, so the Kruskal–Wallis analysis is used to test equality of population medians among groups. Whenever the p-value is below 0.05, the two groups are considered significantly distinct.

3 Results

The median and median absolute deviation (MAD) of BRS parameters is computed among all subjects in the prone and resistant groups, and displayed in Table 2 with the associated p-value.

Parameter	P	R	p-value
$\alpha_{LF}^{\hat{}}$	0.26 ± 1.0e-04	1.83 ± 1.8e-04	NS
$\alpha_{HF}^{\hat{}}$	0.24 ± 1.2e-05	4.64 ± 9.2e-05	< 0.05

Table 2. Median±MAD of BRS parameters in prone (P) and resistant (R) groups. NS: non-significant, p > 0.05.

Prone and resistant patients present differences only in the HF band. In order to study the parameters of prone and resistant subjects independently from diabetes, which is known to alter ANS regulation, new groups are suggested to study: prone-diabetic (PD) vs. resistant-diabetic (RD), and pronenon diabetic (PND) vs. resistant-non diabetic (RND). It can be observed that the only discriminant parameter is α^2_{HF} in the diabetic subgroup.

4 Discussion

Despite the fact that different approaches to reducing the incidence of intradialytic hypotension have been proposed and extensively evaluated in recent years, the problem has not yet found a satisfactory solution. Many patients suffer from a large number of ectopic beats, sometimes implying that the HRV analysis may not be reliable, so that alternate measurements of ANS activity can be helpful (Solem, Nilsson and Sörnmo, 2004).

The BRS parameter α^2_{HF} can discriminate between prone and resistant patients when considering either our whole database or the diabetic subgroup, but not in the non diabetic subgroup. In (Sapoznikov, Backenroth and Rubinger, 2010) BRS is stated to be unaltered in intradialytic hypotension.

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