Evaluation of Sympathovagal Balance in Oncological Patients by Spectral Methods

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Abstract. The anthracyclines are antineoplastic drugs with cardio- and neurotoxicity. The aim of study was to determine the effect of anthracycline therapy on spontaneous fluctuation of circulatory variables. Systolic and diastolic blood pressures (SBP, DBP) and inter-beat intervals (IBI) were recorded for 5 minutes (Finapres, breathing at frequency of 0.33 Hz). Power spectra of SBP, DBP and IBI, low/high frequency ratio (LF/HF) and baroreflex sensitivity (BRS, BRSf) were calculated. We found a statistically significant decrease of SBP, DBP, BRS and BRSf in patients in comparison with controls, the changes of the power spectra of SBP, DBP, IBI and LF/HF were not different. We can conclude that anthracycline therapy has an effect on the function of the autonomic nervous system (ANS), but the spectral analysis is not sensitive enough to reveal the anthracycline-induced ANS impairment.

1 Introduction

The autonomous nervous system (ANS) is an essential regulator of the cardiovascular system. Heart rate variability (HRV) with a fast Fourier transform analysis of the inter-beat intervals (IBI) has been used to evaluate ANS activity in different situations (e.g. hypertension, measurement of psychological stress, development of the ANS in newborns) [1, 2, 3, 4]. The low-frequency (LF) component is influenced by both sympathetic and parasympathetic activity and high frequency component (HF) by parasympathetic activity. The LF/HF ratio has been proposed as an index of the sympatho-vagal balance [4].

Anthracycline chemotherapeutic agents have a broad effect on a variety of childhood malignancies. The cardiotoxicity of these drugs limits their aggressive use. The chronic administration of anthracyclines may be associated with subclinical abnormalities of cardiac function [5, 6]. The mechanisms by which anthracyclines exert their cytotoxic activity are complex. It may include free-radical-mediated myocyte damage, adrenergic dysfunction, intracellular calcium overload, and the release of cardiotoxic cytokines [7]. Anthracyclines also interact with the autonomous nervous system [8, 9].

The aim of the present study was to determine the effect of anthracycline therapy on spontaneous fluctuation of circulatory variables.

2 Methods

One hundred subjects (13 – 21 years of age) were divided into 2 groups (group Co – healthy children, adolescents, and young adults, number of subjects: n=60; group Op – oncological patients after anthracycline therapy for acute lymphoblastic leukaemia, n=40). They were examined in sitting and resting positions. Systolic and diastolic blood pressures (SBP, DBP) and inter-beat intervals (IBI) were recorded beat-to-beat for 5 min (Finapres, Ohmeda, USA; controlled breathing at a frequency of 0.33 Hz). Power spectra of SBP, DBP and IBI, cross-spectra of IBI and SBP, and low frequency/high frequency ratio (LF/HF) were calculated. The gain factor, e.g. modulus H(f) of the transfer function between variations in

SBP and IBI, was calculated at a frequency of 0.1 Hz according to the formula: H(f) = Gxy(f)/Gxx(f), where Gxy(f) corresponded to the cross-spectral density between SBP and IBI, and Gxx(f) corresponded to the spectral density of SBP. The value of the modulus at a frequency of 0.1 Hz was taken as a measure of BRS [10]. Using the same formula, the modulus at a frequency of 0.1 Hz was also calculated for the instantaneous values of the heart rate and systolic blood pressure as the second index of baroreflex sensitivity (BRSf, expressed in Hz/mmHg [11]. LF/HF ratio was calculated from normalized spectra of IBI (LF at frequency 0.0417-0.15 Hz; HF at 0.1583-0.4 Hz) in each subject. The Wilcoxon test was used for statistical evaluation.

3 Results

We found a statistically significant decrease of systolic and diastolic blood pressures in group Op in comparison with Co (SBP: 102±14 vs. 112±12; 58±5 vs. 64±11 mmHg; $p<0.01$). Also, BRS was significantly lower in the patients (8.4±4.4 vs. 10.6±5.5 ms/mmHg; $p<0.05$). On the other hand, the changes of the power spectra of SBP, DBP, IBI (see Fig.1A) and modulus – at 0.1 Hz corresponds to baroreflex sensitivity (Fig.1B) and the LF/HF ratio were not different.

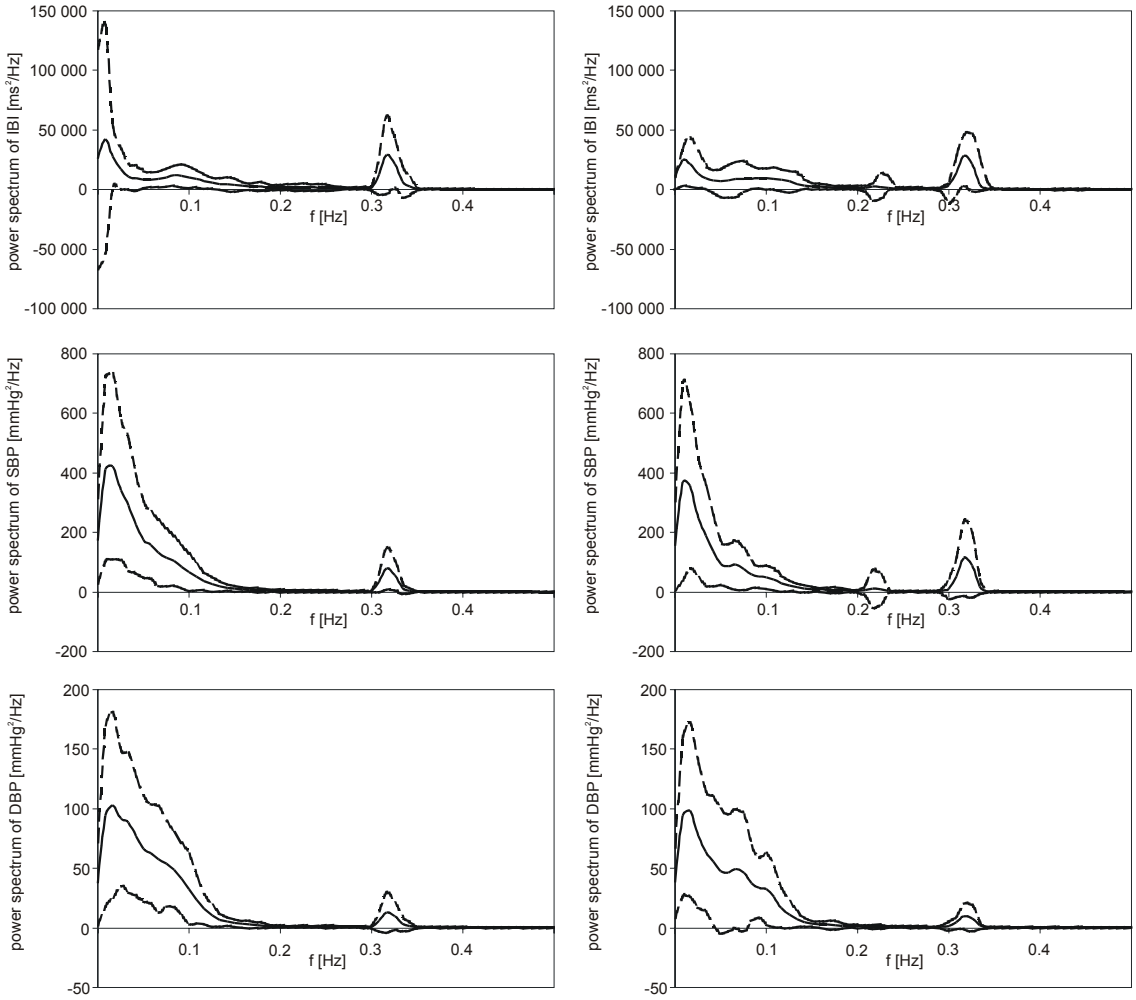

Fig. 1A: Spectral analysis of spontaneous fluctuation of circulatory variables. The left column shows the power spectra of IBI, SBP, and DBP in patients after anthracycline therapy, the right column shows the power spectra of IBI, SBP, and DBP in healthy controls. No difference between patients and controls was found. The full line (in the middle) presents the mean value of the power spectrum and the dotted lines represent ± standard deviation.

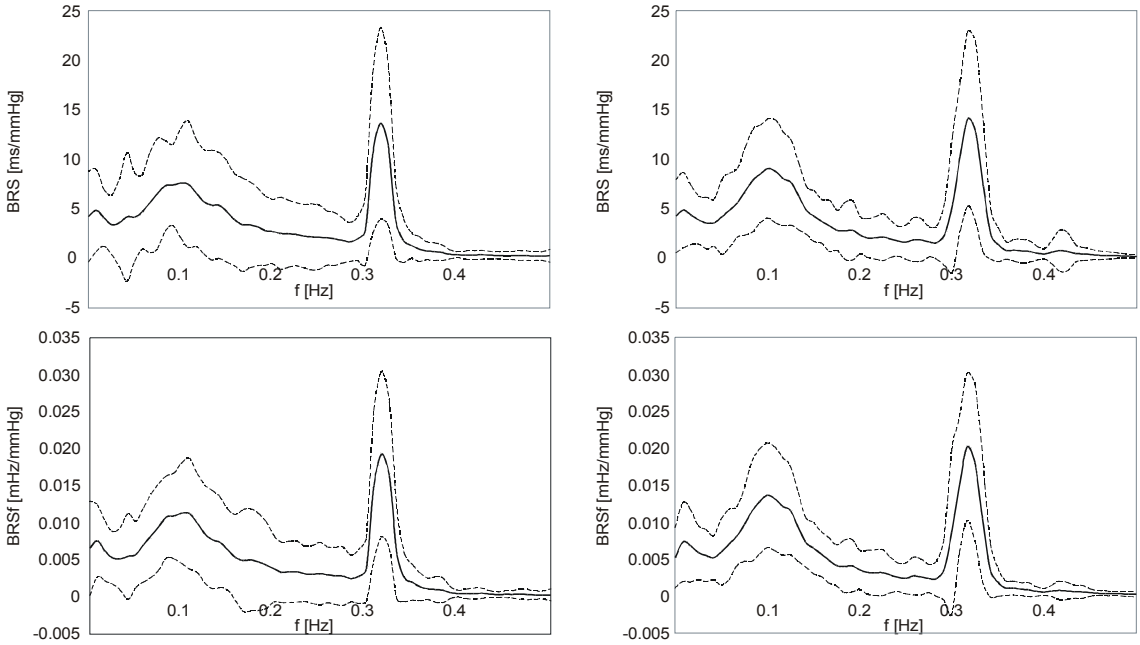

Fig. 1B: Spectral analysis of spontaneous fluctuation of circulatory variables. The left column shows the power spectra of modulus (at 0.1 Hz corresponds to baroreflex sensitivity) in patients after anthracycline therapy; the right column shows the power spectra of modulus in healthy controls. No difference between patients and controls was found. The full line (in the middle) presents the mean value of the power spectrum and the dotted lines represent ± standard deviation.

4 Discussion

The changes of the blood pressures generally show a negative effect of anthracycline therapy on the function of the sympathetic branch of the ANS, as confirmed by our former results [12]; the decrease of BRS indicates the diminished parasympathetic activity. The spectral analysis of circulatory variables did not reveal any significant changes. It seems that the method is not sensitive enough to reveal subtle changes of the ANS.

5 Conclusion

We can conclude that anthracycline therapy has an effect on the function of the autonomic nervous system, but the spectral analysis of spontaneous fluctuation of circulatory variables is not sensitive enough to reveal the anthracycline-induced autonomic nervous system impairment.

Acknowledgements

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