WHAT OPTIONS DOES THE SUPINE-STANDING-SUPINE TEST OFFER TO PATIENTS WITH HYPERTENSION? DEMONSTRATIONS OF EXAMPLES.

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Aims: The purpose of the study was to demonstrate autonomic nervous system (ANS) changes associated with treatment in hypertensive patients and utilization of these measurements in practice.

Methods: Hypertensive patients were examined before the start of treatment and after blood pressure compensation. The telemetric system VarCor PF 5 was used for non-invasive heart rate registration and automatic evaluation of heart rate variability (HRV) parameters. The supine-standing-supine test with ortho-clinostatic loading in standard conditions was used for HRV evaluation.

Results: The influence of antihypertensive therapy on ANS was demonstrated in two cases. The first was a case of a responder to therapy and the second case was example of a non-responder to monotherapy regarding more therapeutic steps for blood pressure control. Different modes of results presentation are demonstrated: 3D graph, numeric form of standard parameters of HRV, computer interpretation of results by means of complex parameters and indices in numeric, graphic and verbal form with functional age calculation, cross graph of vagal activity index versus sympatho-vagal balance index was used for repeated measurements and follow-up. The increased spectral performance with augmented vagal activity and slope down of sympatho-vagal ratio are evident after blood pressure control achievement. Improvement of functional age parameter associated with blood pressure compensation is visible using a complex age-dependent parameters interpretation.

Conclusions: HRV evaluation in hypertensive patients provides new parameters for patient's examination. These parameters are influenced by both the illness itself and by pharmacotherapy. Such an approach offers more complex information about patient.

INTRODUCTION

Blood pressure (BP) is the result of peripheral vascular resistance, central venous pressure and cardiac output interactions. It is self-evident that heart rate is an important parameter of actual circulatory compensation as cardiac output is dependent on heart beat frequency. Blood pressure regulation in hypertensive patients is still inadequate despite increasing knowledge of the aetiopathogenesis of this condition and the wide range of pharmacotherapeutic modalities available. Blood pressure is continuously under the control of multiple regulatory processes including the ANS as a major regulatory and integrative system¹. Heart rate variability (HRV) measurement is a well-defined non-invasive method of evaluating the ANS (ref.²). Spectral analysis (SA) of HRV enables us to distinguish three main spectral components from short-term recordings: a high frequency (HF) component (0.15–0.40 Hz), a low frequency (LF) component (0.05–0.15 Hz) and a very low frequency (VLF) component (≤ 0.04 Hz) (ref.^{2,3}). The supine-standing-supine test is a mode of evaluating the short-term HRV records using standardised orthostatic loading for facilitation of sympatho-vagal balance. Detailed analysis of large number of HRV parameters can be simplified using age-standardised parameters in the

spectral analysis of HRV and by the method of complex indices assessment⁴.

METHODS AND CLINICAL APPLICATION

The activity of the ANS is dynamic variable representing the reaction of ANS to currently operating external and internal stimuli in interaction with responses to stimuli acted in past⁵. Therefore the supine-standing-supine test was used for HRV evaluation. This test consists in assessment of autonomic reactions based on short-term record of heart rate in defined conditions. Examined patient stayed 5 minutes in every position for 300 RR intervals recording, value of "window" parameter was 256 (ref.^{6–8}). Record of RR intervals and HRV analysis were provided by using of VarCor PF5 microcomputer system for telemetric assessment of short term heart rate variability in time and frequency domain with application of fast Fourier transformation and partially modified algorithm CGSA (coarse-graining spectral analysis)⁹. Measured parameters with similar course and age dependency were processed by method of complex indicators with calculation so called functional age by method of Stejskal and Šlachta^{5, 10, 11}.

Four types of results were assessed:

- 1) Three dimensional (3D) graph of HRV.
- 2) Results in numerical form. Parameters: RR (ms), Power VLF (ms^2), Power LF (ms^2), Power HF (ms^2), Power spectral density – PSD VLF (ms^2/Hz), PSD LF (ms^2/Hz), PSD HF (ms^2/Hz), Frequency VLF (Hz), Frequency LF (Hz), Frequency HF (Hz), Coefficient of variance – CCV VLF, CCV LF, CCV HF, Relative VLF (%), Relative LF (%), Relative HF (%), VLF/HF, LF/HF, VLF/LF, MSSD (ms^2), Total power (ms^2).
- 3) Results processed by mean of age-standardised parameters with calculation of functional age with computer interpretation of ANS outcomes in numeric, graphic and verbal forms.
- 4) Points of intersection of complex indices: vagal activity index versus sympatho-vagal balance index in cross graph for longitudinal follow-up.

The above mentioned testing applied in ten previously healthy persons (without any pharmacotherapy) with new diagnosis of hypertension indicated for pharmacotherapy. Thus the only variable was new medicament therapy. All patients were in sinus rhythm. All patients were examined

in the morning time fasting, with omission of tabaco, coffee and alcohol. The first examinations were provided before start of pharmacotherapy and control examinations were performed from one to three weeks later when blood pressure control was provided.

RESULTS

There is possible to find two different situations in the group of hypertensive patients. On the one hand we can find good response to started therapy and BP value in control examination in normal range. On the other hand control BP measurement reveals persistent hypertension despite of therapy and next therapeutic step is necessary. Both cases are demonstrated with their findings in supine-standing-supine test. The first case presents woman with good response to betablocker administration: Figures 1–3. The opposite situation demonstrates man without BP improvement after betablocking agent administration and there were three therapeutic steps necessary to achieve target BP level: Figures 4–6, Table 1.

Fig. 1. 3-D graph of SA HRV during supine-standing-supine test in woman 27 years. Legend: x axis frequency (Hz), y axis power spectral density (ms^2/Hz), z axis time course of test T1 supine, T2 standing, T3 supine (each 300 seconds). Enhanced total spectral power and especially HF component are markedly visible.
A. Before treatment BP 140/90 mmHg (therapy indication according to BP Holter monitoring).
B. Control examination with blood pressure compensation on Bisoprolol 5mg daily BP 120/70 mmHg.

Fig. 2. Numerical form of SA HRV. Hypertensive woman 27 years. Markable rising of all spectral component especially in supine position where are approximately twofold values.

A1. Before treatment – standing position.

A2. Before treatment – final supine position.

B1. Control examination with blood pressure compensation on Bisoprolol 5 mg daily – standing position.

B2. Control examination with blood pressure compensation on Bisoprolol 5 mg daily final – supine position.

A1

Record: 0001 filtered (8.11.2005 8:17:32)					Hardware: VarCor PF6				
Analysis type: VLF, window: 256					Analysis date: 30.4.2007 13:46:34				
Frequency bands borders [Hz]: VLF: 0,020, LF: 0,050, HF: 0,150					Frequency axis [Hz]: 0,500				
Interval: 2									
	Average	St. dev.	St. dev. %						
Power VLF	165,33	10,55	6,38	CCV VLF	1,7428				
Power LF	235,48	21,91	9,30	CCV LF	2,0799				
Power HF	261,61	3,51	1,34	CCV HF	2,1923				
PSD VLF	10505,81	1305,19	12,42	Rel. VLF	24,96				
PSD LF	6016,27	371,00	6,17	Rel. LF	35,55				
PSD HF	4632,47	144,48	3,12	Rel. HF	39,49				
Freq. VLF	36,09	1,98	5,49						
Freq. LF	78,65	6,59	8,38	NN50	4				
Freq. HF	258,81	1,33	0,51	pNN50	1,33				
VLF/MF	0,6317	0,0352	5,57	MSSD	411,52				
LF/MF	0,9004	0,0864	9,59	Total power	662,42				
VLF/LF	0,7101	0,0946	13,32						
RR	0,7378	0,0358	4,85	Breath freq.	???				

Units: Power [ms2], PSD [ms2/Hz], Freq [mHz], R-R [s], Breath freq. [breaths/min]

A2

Record: 0001 filtered (8.11.2005 8:17:32)					Hardware: VarCor PF6				
Analysis type: VLF, window: 256					Analysis date: 30.4.2007 13:46:34				
Frequency bands borders [Hz]: VLF: 0,020, LF: 0,050, HF: 0,150					Frequency axis [Hz]: 0,500				
Interval: 5									
	Average	St. dev.	St. dev. %						
Power VLF	68,67	14,08	20,50	CCV VLF	0,9904				
Power LF	159,04	15,58	9,80	CCV LF	1,5073				
Power HF	432,69	10,91	2,52	CCV HF	2,4861				
PSD VLF	4002,70	1094,25	27,34	Rel. VLF	10,40				
PSD LF	4907,56	259,82	5,29	Rel. LF	24,08				
PSD HF	14739,46	1297,96	8,81	Rel. HF	65,52				
Freq. VLF	40,35	2,16	5,36						
Freq. LF	85,89	3,56	4,15	NN50	25				
Freq. HF	237,46	1,11	0,47	pNN50	8,33				
VLF/MF	0,1596	0,0370	23,21	MSSD	904,37				
LF/MF	0,3684	0,0442	12,01	Total power	660,40				
VLF/LF	0,4290	0,0555	12,93						
RR	0,8367	0,0388	4,64	Breath freq.	???				

Units: Power [ms2], PSD [ms2/Hz], Freq [mHz], R-R [s], Breath freq. [breaths/min]

B1

Record: 0001 filtered (28.11.2005 8:15:32)					Hardware: VarCor PF6				
Analysis type: VLF, window: 256					Analysis date: 30.4.2007 13:48:40				
Frequency bands borders [Hz]: VLF: 0,020, LF: 0,050, HF: 0,150					Frequency axis [Hz]: 0,500				
Interval: 2									
	Average	St. dev.	St. dev. %						
Power VLF	463,62	28,20	6,08	CCV VLF	2,4134				
Power LF	647,53	20,34	3,14	CCV LF	2,8521				
Power HF	247,23	5,51	2,23	CCV HF	1,7624				
PSD VLF	36111,85	5682,17	15,73	Rel. VLF	34,13				
PSD LF	23889,49	1063,06	4,45	Rel. LF	47,67				
PSD HF	3696,38	548,15	14,83	Rel. HF	18,20				
Freq. VLF	28,71	3,41	11,89						
Freq. LF	73,01	8,64	11,84	NN50	11				
Freq. HF	240,64	8,25	3,43	pNN50	3,67				
VLF/MF	1,8766	0,1278	6,81	MSSD	670,53				
LF/MF	2,6214	0,1239	4,73	Total power	1358,39				
VLF/LF	0,7155	0,0264	3,69						
RR	0,8922	0,0549	6,15	Breath freq.	???				

Units: Power [ms2], PSD [ms2/Hz], Freq [mHz], R-R [s], Breath freq. [breaths/min]

B2

Record: 0001 filtered (28.11.2005 8:15:32)					Hardware: VarCor PF6				
Analysis type: VLF, window: 256					Analysis date: 30.4.2007 13:48:40				
Frequency bands borders [Hz]: VLF: 0,020, LF: 0,050, HF: 0,150					Frequency axis [Hz]: 0,500				
Interval: 5									
	Average	St. dev.	St. dev. %						
Power VLF	168,49	15,75	9,35	CCV VLF	1,3223				
Power LF	439,67	44,69	10,16	CCV LF	2,1361				
Power HF	1138,57	71,49	6,28	CCV HF	3,4374				
PSD VLF	16895,18	415,12	2,46	Rel. VLF	9,65				
PSD LF	29068,70	1796,43	6,18	Rel. LF	25,17				
PSD HF	13443,01	417,42	3,11	Rel. HF	65,18				
Freq. VLF	24,03	0,94	3,89						
Freq. LF	107,14	0,00	0,00	NN50	78				
Freq. HF	230,16	16,67	7,24	pNN50	26,00				
VLF/MF	0,1478	0,0060	4,08	MSSD	3295,70				
LF/MF	0,3881	0,0516	13,30	Total power	1746,73				
VLF/LF	0,3886	0,0633	16,28						
RR	0,9816	0,0557	5,68	Breath freq.	???				

Units: Power [ms2], PSD [ms2/Hz], Freq [mHz], R-R [s], Breath freq. [breaths/min]

Fig. 3. Computer interpretation of ANS evaluation by method of complex parameters and indices in numeric, graphic and verbal form with so called functional age calculation. Woman 27 years. After BP compensation so called functional age is appropriate to calendar age.
A. Before treatment.
B. Woman 27 years BP compensation on Bisoprolol 5 mg daily.

Fig. 4. Graphic form of SA HRV during supine-standing-supine test. Man 39 years “non responder” to monotherapy. Therapeutic success is associated with increased spectral activity at final examination – D.
A. Examination before treatment BP 180/110 mmHg.
B. Betaxolol 20 mg with BP 160/110 mmHg.
C. Betaxolol 20 mg and Ramipril 5 mg BP 150/100 mmHg.
D. Final result with BP 140/83 mmHg under control on combination of Betaxolol 20 mg and Ramipril 10mg daily.

Table 1. Numerical form of SA HRV. Man 39 years “non responder” to monotherapy. The results demonstrate high LF/HF ratio (sympathovagal balance) and weak total spectral performance before treatment and gradual improvement of spectral performance and especially HF component (CCV HF) during therapy.

Changes of average values of SA HRV results in standing position during supine-standing-supine test in “non-responder” to therapy. Units: Power (ms ²), PSD (ms ² /Hz), Frequency (Hz), MSSD (ms ²).				
	Before treatment	Betaxolol 20 mg	Betaxolol 20 mg Ramipril 5 mg	Betaxolol 20 mg Ramipril 10 mg
Power VLF	94.68	184.71	97.62	211.02
Power LF	441.39	125.41	285.71	280.05
Power HF	78.55	43.03	57.10	125.81
PSD VLF	7132.61	12109.15	5781.95	18066.58
PSD LF	14630.74	5148.76	13780.51	6387.71
PSD HF	1927.80	722.98	1385.24	6982.08
Freq. VLF	24.21	38.48	39.94	24.41
Freq. LF	103.49	53.43	97.75	109.24
Freq. HF	163.68	178.88	172.0	154.18
VLF/HF	1.2071	4.37	1.7955	1.6891
LF/HF	5.6109	2.9329	5.1252	2.2485
VLF/LF	0.2160	1.4901	0.3380	0.7540
CCV VLF	1.1472	1.4785	0.9815	1.4256
CCV LF	2.4771	1.2183	1.679	1.6423
CCV HF	1.0450	0.7136	0.7506	1.1008
Rel. VLF	15.40	52.3	22.17	34.21
Rel. LF	71.62	35.51	64.87	45.40
Rel. HF	12.78	12.19	12.96	30.39
Total power	614.62	353.14	440.43	616.88
MSSD	352.5	359.33	346.84	549.05

Changes of average values of SA HRV results in final supine position during supine-standing-supine test in “non-responder” to therapy. Units: Power (ms ²), PSD (ms ² /Hz), Frequency (Hz), MSSD (ms ²).				
	Before treatment	Betaxolol 20 mg	Betaxolol 20 mg Ramipril 5 mg	Betaxolol 20 mg Ramipril 10 mg
Power VLF	242.51	85.1	154.96	173.18
Power LF	703.40	404.58	503.92	432.33
Power HF	215.59	312.25	283.47	397.43
PSD VLF	13730.89	5742.66	14201.2	15484.24
PSD LF	15966.1	8429.26	16507.8	13575.32
PSD HF	7556.72	9632.7	7898.5	6803.03
Freq. VLF	38.81	45.65	21.58	26.54
Freq. LF	108.11	107.8	133.22	136.74
Freq. HF	151.25	154.5	176.2	163.24
VLF/HF	1.135	0.2744	0.5457	0.4379
LF/HF	3.2886	1.3024	1.7803	1.0912
VLF/LF	0.3457	0.2105	0.3098	0.4006
CCV VLF	1.6716	0.9031	1.1511	1.1248
CCV LF	2.8468	1.9692	2.0759	1.771
CCV HF	1.5761	1.73	1.5570	1.7039
Rel. VLF	20.88	10.61	16.44	17.27
Rel. LF	60.56	50.45	53.47	43.11
Rel. HF	18.56	38.94	30.08	39.63
Total power	1161.50	801.93	942.35	1002.94
MSSD	776.81	797.54	851.19	1472.57

Fig. 5. Computer interpretation of ANS evaluation by method of complex parameters and indices in numeric, graphic and verbal form with so called functional age calculation. Man 39 years “non responder” to monotherapy. Changes in complex parameters during therapy with final improvement of functional age parameter are demonstrated.

A. Examination before treatment BP 180/110 mmHg.

B. Betaxolol 20 mg with BP 160/110mmHg.

C. Betaxolol 20 mg and Ramipril 5 mg with BP 150/100 mmHg.

D. Final result with BP 140/83 mmHg under control on combination of Betaxolol 20 mg and Ramipril 10 mg daily.

A

B

C

D

Fig. 6. Longitudinal follow-up of patient with hypertension by assessment of complex HRV indices expressed in cross graph. Man 39 years “non responder” to monotherapy. Legend: axis x vagal activity index, axis y sympatho-vagal balance index.

1. Before treatment BP 180/110 mmHg.
2. Betaxolol 20 mg BP 160/110 mmHg.
3. Betaxolol 20mg + Ramipril 5 mg BP 150/100 mmHg.
4. Betaxolol 20mg + Ramipril 10mg BP 140/83 mmHg.

The first result (1) is in the left lower quadrant (low vagal activity, sympathetic predominance – usually visible in ill persons with inadequate regeneration). Next control result (2) shifts to the left upper quadrant (low vagal activity, low sympathetic activity – usually visible in persons with bad physical and mental condition). Third examination (3) with fall of vagal activity and attenuation of sympatho-vagal balance. The final examination result (4) in the left upper quadrant with shift to right (trend to enhance vagal activity) is in the border of normal range.

CONCLUSIONS

HRV is one of reputable prognostic factors of cardiovascular mortality. SA HRV during supine-standing-supine test offers evaluation of sympatho-vagal balance⁴. ANS on the one side participate on etiopathogenesis of hypertension and on the other side is under influence of antihypertensive medicaments. Therefore examination of HRV in hypertensive patients offers next evaluative

parameter beside proper blood pressure measurement. This approach allows view of patients and his therapy in more details. Proper examination taking about 30 minutes regards standard conditions, sinus rhythm of patient and high quality recording of RR intervals.

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