

CARDIOVASCULAR AUTONOMIC DISTURBANCES IN EARLY PARKINSON'S DISEASE

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ABSTRACT

Aim of this study was to assess the cardiovascular autonomic function in early Parkinson's disease.

SUBJECTS AND METHODS

Forty patients with Parkinson's disease (PD) were included, 23 males and 17 females, aged $57,38 \pm 6,18$ years, all in I Hoehn- Yahr stage of severity, with duration of disease $2,1 \pm 0,78$ years, without any subjective dysautonomic complaints. Twenty healthy persons, 10 males and 10 females, aged $57 \pm 6,6$ years, were included as control group.

We performed orthostatic test with assessment of the systolic blood pressure and the heart rate in active standing and the variability of heart rate in deep breathing.

RESULTS

We found borderline results respective Ewing criteria in 25% of patients in the three tests. The rest of the patients showed normal results.

There is statistically significant difference between the patients and the control group only for the variability of heart rate in deep breathing.

The patients with borderline results had statistically higher average age and disease severity than the patients with normal results. We found also significant differences regarding the systolic blood pressure decrease, the 30: 15 ratio and the variability of heart rate in deep breathing. The duration of the disease was the factor not influencing our results.

DISCUSSION

We established disturbances of the cardiovascular autonomic control in 25% of our patients, despite the statistical difference only for the variability of heart rate in deep breathing.

The presence of borderline results for the blood pressure and the heart rate indicates both sympathetic and parasympathetic dysfunction even in the early stages of PD.

CONCLUSION

There is a tendency to appearance of cardiovascular autonomic disturbances even in drug naive, early stage PD patients. Despite their asymptomatic course in the early stages, also established in other studies, the presence of patients with borderline results of the routine tests is of definite interest for the clinical practice.

INTRODUCTION

Parkinson's disease (PD) is a multisystem disease with neurodegenerative involvement of the autonomic nervous system (ANS), as well as the extrapyramidal system. Dysautonomic symptoms appear of all the somatic systems with the disease progression. The cardiovascular autonomic disturbances are next to the gastrointestinal in frequency, but they have higher impact on the disease and on the quality of life of PD patients (10).

Disorders of the control of blood pressure (BP), heart rate (HR) and regional circulation are described in 20%- 58% of patients, but they are symptomatic in small part of them. These disturbances are typical for the late stages of the disease, but their clinical manifestation is possible even in initial stages (3, 4, 7, 12, 13). In the early stages the dysautonomias are mainly asymptomatic and could be detected by means of laboratory tests (8, 10).

Aim of this study was to assess the cardiovascular autonomic function in early Parkinson's disease.

SUBJECTS

Forty patients with Parkinson's disease (PD) were included, 23 males and 17 females, aged $57,38 \pm 6,18$ years, all in I Hoehn- Yahr stage of severity, with duration of disease $2,1 \pm 0,78$ years, without any subjective dysautonomic complaints. The patients were diagnosed respective the UK Parkinson's Disease Society Brain Bank Criteria. None of the patients had dysautonomic symptoms, or concomitant cardiovascular disease. The intake of food, drinks or drugs, affecting ANS, was discontinued 12 hours before the study.

Twenty healthy persons, 10 males and 10 females, aged $57 \pm 6,6$ years, were included as control group.

METHODS

In standard conditions the following routine cardiovascular autonomic tests were performed:

1. Orthostatic test: assessment of decrease of the systolic blood pressure after active standing on the first and fifth minutes. It is accepted that the orthostatic decrease is higher on the first minute and over the fifth restores completely in a case of normal autonomic regulation (14).

2. Orthostatic test: assessment of the changes of heart rate after active standing. The fifteenth and thirtieth RR interval were measured and the ratio 30: 15 was calculated (the longest RR interval over the 30th beat divided on the shortest RR interval over the 15th beat).

3. Test with deep breathing: assessment of the variability of the heart rate in deep breathing (HRDB). The difference between the maximal and the minimal heart rate is calculated for 6 respiratory cycles per minute. The average value was calculated of 3 successive respiratory cycles.

In the analysis of the results are respected widely accepted referent values (1, 8, 9, 11).

Independent Samples T test was used for statistical analysis.

RESULTS AND DISCUSSION

All the control subjects showed normal results. There is statistically significant difference ($p < 0,01$) between the patients and the control group only for the variability of heart rate in deep breathing. Regarding the other indices: initial systolic BP, orthostatic decrease of the systolic BP on the 1st and 5th minutes, initial HR and 30:15 ratio, there is not statistically significant differences (Table 1.).

Borderline results of the three tests showed 25% of our patients. Our results are similar to the lower limit of the range of cardiovascular autonomic disturbances most probably due to the lower disease severity of our patients (1, 7, 8, 9).

Our results showed in 15% of the examined patients both sympathetic and parasympathetic cardiovascular dysregulation and isolated cardiovagal dysfunction in 10% of cases.

The comparative analysis showed borderline results for the orthostatic test in 15% of the patients (Ta-

ble 2).

We established borderline values in 17,5% of our patients for the 30:15 ratio (Table 3).

Assessing the variations of HRDB we found borderline results in 22,5% of our patients (Table 4).

The patients with borderline results had significantly higher UPDRS part III and UPDRS total scores. Our results support the opinion of worst cardiovascular autonomic function in patients with more severe PD (8).

The only index not influencing the results is the disease duration.

The Ewing's five tests are the most applied cardiovascular autonomic function tests (1, 8, 9). Most of the authors indicate the variations of HRDB as most sensitive and sufficient to detect autonomic dysfunction (8, 10). This is the test demonstrating borderline results in largest range of our patients– 22,5%. These data gave us the reason to accept cardiovascular autonomic dysfunction in the patients despite the lack of symptoms.

Disturbed variations of HRDB are reported in about 54% of patients, especially with rigidity and bradikinesia as initial symptoms. Such changes are found even in parkinsonians in the early stages of the disease and are due to the involvement of the dorsal vagal nucleus and locus coeruleus (3, 10, 12).

SPECT and PET studies found generalized denervation with loss of sympathetic terminals in the heart, thyroid gland, kidney cortex in PD patients with symptomatic orthostatic hypotension (2, 4, 5, 6, 13). This symptom is believed the most dangerous for the patient's life and it is observed in 20% of cases, most often in advanced disease severity stages respective UPDRS (3, 6, 8).

CONCLUSION

Cardiovascular autonomic disturbances could be found even in the early stages of PD. Despite their predominantly asymptomatic course, also established in other studies, the dysautonomias are of definite interest for the clinical practice. It is well known the increase of their severity and frequency with the advance of the disease and it is accepted that the dysautonomic symptoms are an important comorbidity factor. The detection of autonomic disturbances in the early stages of PD could contribute to adequate follow up and treatment of the patients.

Table 1. Results of the patients and the control subjects

Index	Patients	Control subjects
Initial systolic BP (mm Hg)	128,83 ± 8,65 116- 151	127,75 ± 7,6 116- 143
Decrease of the systolic BP on 1 st minute (mm Hg)	-5,05 ± 2,04 -9 – +2	-5,45 ± 4,78 -2 - -9
Decrease of the systolic BP on 5th minute (mm Hg)	2,25 ± 1,55 0- 6	1,85 ± 1,31 0- 4
Initial HR (beat/min.)	73,8 ± 7,83 59- 92	72,65 ± 8,08 57- 84
Variations of HRDB (beat/min.)	16,133 ± 2,07* 11,33- 20	17,499 ± 1,66* 15,33- 20,33
30:15 ratio	1,095 ± 0,049 1,01- 1,2	1,114 ± 0,047 1,05- 1,2

*p<0,01

Table 2. Comparative data for the patients with borderline and normal results

Index	Patients with borderline results	Patients with normal results
Age (years)	62,17 ± 5,88* 53- 67	56,36 ± 6,17* 49- 69
Disease duration (years)	2,17 ± 0,75 1- 3	2,14 ± 0,85 1- 3
Decrease of the systolic BP on 1 st min. (mm Hg)	-13,83 ± 2,79* -11- -19	-4,96 ± 2,69* -1- -10
UPDRS- total	12,67 ± 0,75* 8- 16	7,75 ± 3,001* 3- 15
UPDRS- part III	8 ± 2,79* 4- 10	4,93 ± 1,72* 3- 9

*p<0,01

Table 3. Values of the initial HR and the 30: 15 ratio for the patients with borderline and with normal results

Index	Patients with borderline results	Patients with normal results
Age (years)	62 ± 5,39* 53- 67	56,39 ± 5,95* 49- 69
Disease duration (years)	2,29 ± 0,76 1- 3	2,06 ± 0,79 1- 3
30:15 ratio	1,026 ± 0,01* 1,01- 1,04	1,109 ± 0,04* 1,05- 1,2
UPDRS- total	13 ± 3,21* 8- 16	7,24 ± 2,55* 3- 13
UPDRS- part III	7,86 ± 1,77* 5- 10	4,64 ± 1,64* 3- 9

*p<0,01

Table 4. Comparative data for the variations of HRDB of the patients with borderline and normal results

Index	Patients with borderline results	Patients with normal results
Age (years)	61,89 ± 5,73* 53- 69	56,06 ± 5,74* 49- 68
Disease duration (years)	2,11 ± 0,78 1-3	2,10 ± 0,79 1- 3
Variations of HRDB (beat/min.)	13,15 ± 1,17* 11,33- 14,67	16,997 ± 1,33* 15- 20
UPDRS- total	12 ± 0,78* 8- 16	7,16 ± 2,71* 3- 15
UPDRS- part III	7,78 ± 2,11* 4- 10	4,45 ± 2,11* 3- 7

*p<0,01

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